9th National Thalassemia Conference

"Care & Cure"

Saturday - Sunday 24th & 25th November, 2018

Organized by :

National Thalassemia Welfare Society

in association with

Department of Pediatrics

Kalawati Saran Children's Hospital, New Delhi,

Lady Hardinge Medical College and Associated Hospitals, New Delhi

at Swarn Jayanti Auditorium, LHMC & Hospitals, New Delhi

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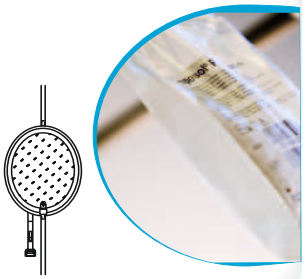

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Souvenir

9th National Thalassemia Conference

"Care & Cure"

Saturday - Sunday 24th & 25th November, 2018

at

Swarn Jayanti Auditorium

Lady Hardinge Medical College and Associated Hospitals,
New Delhi

Organizers

National Thalassemia Welfare Society

KG-1/97, Vikas Puri, New Delhi-110018
Mob. 9311166710, 711, 712
e-mail : ntws2015@gmail.com, www.thalassemiaindia.org

in association with

Department of Pediatrics

Kalawati Saran Children's Hospital, New Delhi
&
Lady Hardinge Medical College and Associated Hospitals, New Delhi

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भारत सरकार
MINISTER OF
SOCIAL JUSTICE AND EMPOWERMENT
GOVERNMENT OF INDIA

सत्यमेव जयते

कार्यालयः 202, सी विंग, शास्त्री भवन,
नई दिल्ली–110115
Office : 202, 'C' Wing, Shastri Bhawan,
New Delhi-110115
Tel. : 011-23381001, 23381390, Fax : 011-23381902
E-mail : min-sje@nic.in
दूरभाषः 011-23381001, 23381390, फैक्सः 011-23381902
ई-मेलः min-sje@nic.in

MESSAGE

I am happy to know that National Thalassemia Welfare Society is holding 9th National Thalassemia Conference on 24-25th November, 2018 on the theme "Care & Cure Made Easy" at Swaran Jayanti Auditorium LHMC, New Delhi.

I have been informed that National Thalassemia Welfare Society, a NGO was formed by parents, patients and doctors with commitment and dedication to provide better care for thalassemics and to initiate control of thalassemia. I have also been informed that around 1200 patients/parents & 200 doctors are expected to participate in the Conference.

A Souvenir is proposed to be published by the National Thalassemia Welfare Society on this occasion.

I send my good wishes to National Thalassemia Welfare Society for all success of the event.

26.10.18

(Dr. Thaawarchand Gehlot)

हंसराज गंगाराम अहिर
HANSRAJ GANGARAM AHIR

सत्यमेव जयते

गृह राज्य मंत्री
भारत सरकार
नार्थ ब्लाक, नई दिल्ली – 110001

MINISTER OF STATE FOR
HOME AFFAIRS
GOVERNMENT OF INDIA
NORTH BLOCK,
NEW DELHI - 110001

MESSAGE

I am delighted to know that National Thalassemia Welfare Society is organizing 9th Thalassemia Welfare Conference on 24th & 25th November 2018 in association with department of paediatrics Kalawati Saran Children's Hospital at Swaran Jayanti Auditorium LHMC, New Delhi. I have been informed that Ministry of Health and Family Welfare Government of India is also collaborating in this Conference.

Thalassemia and Sickle Cell are most common blood disorders in India. Their treatment is complex, traumatic and costly. Although the Government of India has initiated programs for management and prevention of Thalassemia and Sickle Cell Anaemia, but the NGOs have to play an equally important role in its management and control.

Inclusion of Thalassemia and Sickle Cell Disease in the Disabilities list in Rights of Persons with Disabilities (RPWD) 2016 will give them a chance to live their life with pride and dignity.

I extend my heartiest greetings and best wishes to organizers and delegates of conference.

(**Hansraj Gangaram Ahir**)

New Delhi
29.10.2018

Office Tel. : 011-23092870, Fax No. : 011-23094890
Residence : 2, Safdurjung Lane, New Delhi - 110011 Tel. : 011-23016855, 23016865

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प्रोफेसर (डा.) बलराम भार्गव, पदम श्री
एमडी, डीएम, एफआरसीपी (जी.), एफआरसीपी (ई.), एफएसीसी,
एफएएचए, एफएएमएस, एफएनएएस, एफएएससी
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महानिदेशक, आई सी एम आर

Prof. (Dr.) Balram Bhargava, Padma Shri
MD, DM, FRCP (Glasg.), FRCP (Edin.),
FACC, FAHA, FAMS, FNASc, FASc
Secretary to the Government of India
Department of Health Research
Ministry of Health & Family Welfare &
Director-General, ICMR

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वी. रामलिंगस्वामी भवन, अंसारी नगर
नई दिल्ली - 110 029 (भारत)
Indian Council of Medical Research
Department of Health Research
Ministry of Health & Family Welfare
V. Ramalingaswami Bhawan, Ansari Nagar
New Delhi - 110 029 (INDIA)

MESSAGE

Thalassemia is a serious genetic blood disorder requiring multi-specialty approach for its management. Over 200 mutations have been identified to cause thalassemia. According to ICMR 5.51% Delhites are thalassemia carriers and overall 3.9% population of Indian are thalassemia carriers. Public awareness and thalassemia screening followed by antenatal diagnosis is the only way to prevention. Better treatment strategies are also required.

ICMR is in the process of initiating a registry on hemoglobinopathies. It will be helpful in ascertaining the burden of hemoglobinopathies in India and quantum of measures required for management and prevention of these serious genetic disorders.

I believe that deliberations of this conference will give an impetus to better management and control of thalassemia. I extend my heartiest wishes for the success of 9th National Thalassemia Conference.

Balram Bhargava

(Balram Bhargava)

Tele.: 26588204, 26589620, Fax (Off.) : 91-11-26588662, E-mail: secy-dg@icmr.gov.in

World Health Organization
REGIONAL OFFICE FOR South-East Asia
Metropolitan Hotel, Bangla Sahib Road, Connaught Place, New Delhi-110001, Tel: 91-11-23370804, Fax: 91-11-23370197, Website: www.searo.who.int

National Thalassemia Conference, 24–25 November

Message from Dr Poonam Khetrapal Singh, Regional Director, WHO South-East Asia Region

Thalassemia is an inherited hematologic disorder that is one of the most common single gene disorders globally. Around 300 000 to 400 000 babies are born every year with a severe case of the disorder, many of which are in the WHO South-East Asia Region, including India.

Region-wide, up to 40% of the population carries significant hemoglobin mutations, resulting in increased rates of infants born with thalassemia. Among other conditions, the disorder results in chronic anemia, skeletal deformities, slowed growth rate, jaundice, organ dysfunctions and increased risk of infections. People suffering thalassemia often require lifelong blood transfusion and medical care. Multiple blood transfusions increase the risk of acquiring blood-borne infections, including hepatitis C and HIV among others.

Though the treatment of thalassemia has improved (as reflected in the increased life expectancy of people diagnosed with the disorder), it is still without a cure. This has brought its own challenges, including an increase in complications such as bone disease, infertility, the need for repeated blood transfusions and chelation therapy, as well as iron overload. These conditions affect patients' health and well-being throughout the life-course.

Thalassemia and associated conditions can nevertheless be controlled. Critical to doing so is promoting education and awareness, intensifying screening to assess thalassemia's burden, and making necessary facilities available for genetic counselling, prenatal diagnosis and appropriate treatment.

The safety and adequacy of blood is an important component of the management and treatment of thalassemia. Considerable efforts have been made by countries across the Region to increase voluntary, nonremunerated blood donations to enhance the availability of and access to safe blood.

Against the Region's annual estimated requirement of 18 million units of blood, for example, around 15.9 million units are collected every year. Around 82% of that blood is provided by voluntary, nonremunerated donors. This is especially important for people who suffer from thalassemia and are at greater risk of contracting transfusion transmissible infections (TTIs) due to repeated blood transfusions. In the South-East Asia Region, 100% of the blood collected is screened for TTIs, with all countries now focusing on enhancing the quality of blood donated to avoid harm to recipients.

Region-wide, countries are also working to provide the necessary support to affected populations, especially in rural areas. That includes, where possible, developing cost-effective facilities for stem cell transplantation. As part of this, encouraging awareness at all levels – from the general public to policymakers – is crucial to achieving a number of outcomes, including strengthening thalassemia programmes, collecting data to better understand the extent of the problem, and providing quality-controlled screening, diagnosis and genetic counselling among other services. Civil society should be an integral part of this process, as it has been in the past.

As we mark International Thalassemia Day, we must never forget the effort patients, parents, civil society and the medical community have made to ensure thalassemics across the world live a long and dignified life. Their continued drive will result in further advances. WHO is committed to supporting these efforts, to ensuring all people everywhere have access to safe blood and strong blood product systems, and to enhancing health and well-being across the South-East Asia Region.

Dr Poonam Khetrapal Singh
Regional Director
WHO South-East Asia Region

डॉ. कमलेश कुमार पाण्डेय
मुख्य आयुक्त
Dr. Kamlesh Kumar Pandey
Chief Commissioner

R-11845

सत्यमेव जयते

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दिव्यांगजन सशक्तिकरण विभाग
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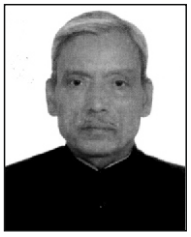
भारत सरकार
Office of the Chief Commissioner for Persons
with Disabilities (Divyangjan)
Department of Empowerment of Persons
with Disabilities (Divyangjan)
Ministry of Social Justice and Empowerment
Govt. of India



Dated: 18th October, 2018

MESSAGE

It gives me immense pleasure to know that the National Thalassemia Welfare Society, New Delhi, is organizing 9th National Thalassemia Conference on 24th & 25th November, 2018 at Delhi.

Thalassemia is an inherited blood disorder in which the body makes an abnormal form of hemoglobin. The disorder results in excessive destruction of red blood cells, which leads to anemia. Anemia is a condition in which body doesn't have enough normal, healthy red blood cells and depends upon lifelong repeated blood transfusion & iron chelating drugs.

I am confident that the said ensuing "National Thalassemia Conference", will provide a very effective forum for creating awareness, promoting shared understanding on relevant issues and also for interchange of ideas. I am sure that the set of suggestions which is likely to emerge from the deliberations of the said Conference would serve as useful guidelines for early detection and early intervention.

I convey my best wishes to this Conference and also wish its grand success.

(Dr. Kamlesh Kumar Pandey)

Dr. J.S. Arora,
General Secretary,
National Thalassemia Welfare Society,
KG-1/97, Vikas Puri,
New Delhi - 110018

सरोजनी हाउस, 6, भगवान दास मार्ग, नई दिल्ली - 110 001. दूरभाष : 23386054, 23386154, Fax : 011-23386006
Sarojini House, 6, Bhagwan Dass Road, New Delhi-110001, Tel. : 23386054, 23386154, Fax : 011-23386006
Email : ccpd@nic.in • Website : www.ccdisabilities.nic.in

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स्वास्थ्य सेवा महानिदेशालय
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MINISTRY OF HEALTH AND FAMILY WELFARE
DIRECTORATE GENERAL OF HEALTH SERVICES

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दूरभाष : २३३४३६८४ फैक्स : ६१-११-२३३४०५६६
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& ASSOCIATED HOSPITALS
NEW DELHI-110001 (INDIA)
Phone : 23343984 Fax : 91-11-23340566
E-mail : director-lhmc@gov.in

MESSAGE

LHMC is proud to host 9th National Thalassemia Conference on 24th & 25th November 2018 with theme "Care and Cure Made Easy". It is being organized by National thalassemia Welfare Society in association with Department of Pediatrics, Kalawati Saran Children's Hospital, New Delhi. I am happy to note that Ministry of Health Govt. of India is also collaborating in this conference. I understand that eminent faculty from India and abroad will provide state of the art knowledge and updates.

Thalassemia is one of the commonest genetic disorders and it requires a multispecialty approach for management. Thalassemia patients have different problems in adulthood from those of in childhood. LHMC is the only centre in India where we have separate adult thalassemia unit in medicine department.

I wish the organizers a grand success.

Dr. Rajiv Garg
Director
डॉ. राजीव गर्ग / Dr. Rajiv Garg
निदेशक / Director
लेडी हार्डिंग मेडिकल कॉलेज एवं सह-अस्पताल
Lady Hardinge Medical College & Assoc. Hospitals
नई दिल्ली-110001 / New Delhi-110001

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राज्य आयुक्त (दिव्यांगजन)

T. D. Dhariyal
State Commissioner for Persons with Disabilities

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राष्ट्रीय राजधानी क्षेत्र, दिल्ली सरकार
25 डी, माता सुंदरी मार्ग, नई दिल्ली- 110002.

C/o the State Commissioner for Persons with Disabilities
Govt. of N.C.T. of Delhi, 25-D, Mata Sundari Road
New Delhi-110002.
Phone : 011-23216001/02 Fax : 011-23216005
E-mail : comdis.delhi@nic.in
Website : www.discomm.delhi.gov.in

PS/SCPD/Thal/2018/ 1253

Dated the 30th October, 2018

MESSAGE

It is a pleasure that National Thalassemia Welfare Society is organising its 9th National Thalassemia Conference on 24th and 25th November 2018 at Lady Harding Medical College, New Delhi. The conference will provide an opportunity to the stakeholders to share information and knowledge about thalassemia and persons living with it.

2. It is perhaps the most opportune time for such a conference when thalassemia has been included among the 21 disabilities in the Rights of Persons with Disabilities Act, 2016. Governments are now mandated to make schemes and programmes to prevent the occurrence of disabilities, provide free health care in the vicinity specially in rural areas, subject of course to family income and also sponsor awareness campaigns and disseminate information. Awareness among all the stakeholders about prevention, care and treatment of thalassemia is critical

3. I am confident that this conference will contribute to more closer partnerships among the primary stakeholders, the NGOs and the Government which is important for leveraging the efforts of the organisations like National Thalassemia Welfare Society.

4. I sincerely hope that this conference will generate valuable ideas and strategies for prevention, treatment and care in the Indian context and help the concerned authorities in the Government to frame schemes and programmes for creation of awareness, setting up of more treatment and care centres especially in the remote and far-flung areas, development of human resources and for research.

5. My best wishes for a very successful organisation of the conference and desired outcome.

Dhariyal
(T.D. Dhariyal) 30.10.18

Dr. J.S. Arora,
General Secretary,
National Thalassemia Welfare Society,
India.

THALASSAEMIA INTERNATIONAL FEDERATION
In official relations with the World Health Organization

HEADQUARTERS
31 Ifigenias, 2007 Nicosia, Cyprus • P.O.Box 28807, 2083 Nicosia, Cyprus
Tel.: +357 22 319 129, Fax: +357 22 314 552, E-mail: thalassaemia@cytanet.com.cy

9th National Thalassaemia Conference
24 – 25 November 2018
New Delhi

MESSAGE BY

MR PANOS ENGLEZOS

PRESIDENT OF THE THALASSAEMIA INTERNATIONAL FEDERATION

Dear friends,

On behalf of the Board of Directors of the Thalassaemia International Federation (TIF), I feel extremely privileged to welcome you all to yet another extremely interesting National Thalassaemia Conference, the 9th in its series, organized by the National Thalassaemia Welfare Society (NTWS), on 24 – 25 November 2018, in New Delhi, India.

Undeniably, this Conference is being held at a time when there is genuine promise, optimism and hope for a brighter future for patients with haemoglobin disorders based on the dramatic scientific advances currently in the pipeline for completion and placement on the market or on the horizon for very near future achievements. Thus, under the theme of 'Care and Cure Made Easy', this Conference, with its high level and diverse programme, promises to provide an outstanding opportunity for all involved stakeholders to share knowledge and discuss the challenges of improving the health and quality of life of those affected by haemoglobinopathies in India, but also globally. Furthermore, as a congregation of a huge number of participants from across India, this Conference is a unique forum facilitating the discussion concerning the scientific advances in the field, as well as a platform to exchange experiences, and build new friendships, collaborations, partnerships and networks.

Haemoglobin disorders have indisputably progressed over the past 30 years from virtually unknown diseases with little knowledge on their management, into a radically different phase. These diseases are now both effectively preventable and appropriately treatable, and our children, now more than ever have the prospect for a brighter future, more so with the scientific advances of recent years which promise to revolutionize even further the curative options and treatment as well as the quality of life of patients worldwide, including those living in India.

At the core of TIF's activities remains our undivided commitment of providing all patients with thalassaemia across the world equal access to quality health and other care. Together with our patients, their parents and families and the healthcare community, TIF continues its common journey with all involved stakeholders, with a united voice taking forward the prioritization of haemoglobinopathies in every country's health agenda. It is imperative now more than ever to secure and maintain the strongest political commitment globally, at the international level with official health-related authorities such as the World Health Organization and the United Nations, as well as nationally, at the level of the national health authorities, in order to ensure a brighter future for our patients wherever they may live and irrespective of culture, religion, and social status.

TIF remains committed to supporting all the efforts undertaken in India, a country particularly close to our hearts, to ensure that every patient has access to quality healthcare. The achievements throughout time, but in particular in more recent years in India, as a result of the actions of the Central and State Governments of India have been immense and commendable. This momentum must be sustained and even strengthened with relentless hard work, devotion and dedication to realize the ultimate goal – a better future for every patient.

We are fully aware, and very proud, of the significant progress promoted by the Central and State Governments of India for improving access to quality care for more patients than ever before, and of the inclusion of thalassaemia in the Disability Bill of 2016, which has opened the door for more opportunities of our patients in education, employment and social integration in general.

The Thalassaemia Associations from across India, and particularly our host, the NTWS, are to be congratulated for uniting their voice and efforts, and for their persistence to reach such achievements which have truly benefited the patients on numerous levels. Furthermore, we particularly welcome the maturation of the patient community in the creation of the Patient Advocacy Group (PAG), which has added a new dimension to the profile of thalassaemia in this great country.

Last but not least, allow me to congratulate Dr JS Arora for his commitment, passion and devotion through the years in promoting policies for thalassaemia, and Mrs Shobha Tuli, a distinguished member of TIF's Board of Directors, serving for over two decades as Vice-President, for her admirable contribution at the national, regional and international level.

I hope that the proceedings, deliberations and outcomes of this Conference meet your needs and expectations and I wish you great success.

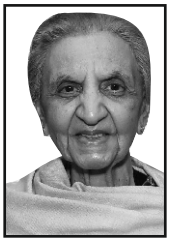
Cordially,

Mr Panos Englezos
President
Thalassaemia International Federation

NATIONAL THALASSEMIA WELFARE SOCIETY

ORGANISATION FOR AWARENESS OF THALASSEMIA AND TO HELP THALASSEMICS

KG-1/97, VIKAS PURI, NEW DELHI-110018 Tel.: 9311166710-711-712 Fax.: 91-11-28543576
Website : thalassaemiaindia.org
(Estd. 1991, R. No. S/26823. Registered under Societies Registration Act XXXI of 1860)



MESSAGE

It's a matter of pride for us that we are holding our 9th National Thalassemia Conference, in association with Dept. of Pediatrics, Kalawati Saran Children's Hospital at LHMC on Saturday, Sunday 24th & 25th November 2018, which will be followed by Workshops at Kalawati Saran Children's Hospital & Rajiv Gandhi Cancer Research Institute on 26th November 2018.

National Thalassemia Welfare Society has always been in the forefront in disseminating the latest development in the field, among Doctors, Thalassemics & Parents. This conference is another effort in this direction.

I am delighted and proud to say that Thalassemia has been finally included in the RPWD Act 2016. We have fought a strong battle for over 20 years to get inclusion of Thalassemia & other blood disorders in the list of disabilities in this act.

I have been told that Dy. Chief Commissioner for Persons with Disabilities MOSJE Govt. of India and commissioner disability Government of Delhi will be enlightening us on benefits and provisions in the RPWD act 2016 for thalassemics and other blood disorders in the capacity building workshop.

I appreciate the efforts of my colleagues, sponsors, delegates and distinguished International & National guest faculty for their help in organizing the 9th National Thalassemia Conference and also making it a success.

Surendar Saini

(Km. Surrendar Saini)

9th National Thalassemia Conference

"Care & Cure"

Saturday - Sunday 24th & 25th November, 2018

PROGRAMME

Registration & Breakfast : 8AM to 9AM

Day 1, Saturday 24th November 2018

S. No.	Topic	Speaker	Minutes	Timings	Chairpersons
	Session I Transfusion Therapy		**09:00 am to 10:00 am**		
1.	Low Hb level causes & solutions	Dr. V.P. Choudhry	20	9:00 to 9:20am	Dr. Kavita Juneja
2.	Shocks & Shockers in Transition of care from adolescence to adults	Dr. Jagdish Chandra	20	9:20 to 9:40am	Dr. Bhavna Dhingra
3.	Splenectomy -3Ps (Prevention planning & post care)	Dr. Alok Hemal	20	9:40 to 10:00am	Dr. Sunita Sharma
	Session II Chelation		**10:00 am to 11:50 am**		
1.	Monitoring Why & How	Dr. AP Dubey	20	10:00 to 10:20am	
2.	Iron overload assessment MRI T2* is a necessity not a Luxury	Dr. Praveen C. Sobti	20	10:20 to 10:40am	Dr. Nikhil Sheth
3.	Initiation of iron chelation	Dr. Rajiv Bansal	20	10:40 to 11:00am	Dr. Kirti Nanal
4.	Combining chelators When & How	Dr. Sunil Gomber	20	11:00 to 11:20am	Dr. Rekha Harish
5.	Panel Discussion	Moderator Dr VPC + All above 7 speakers	30	11:20 to 11:50am	
	Inauguration			**11:50 am to 01:00 pm**	
	Lunch			**01:00 pm to 02:00 pm**	

	Session III Vital Organ Care			**02:00 pm to 03:20 pm**	
1.	National policy on Heamoglobinopathy	Mrs. Vinita Srivastava	20	02:00 to 02:20pm	Dr. D.D. Golani Dr. Rakhi Maiwal
2.	Save your Liver	Dr. Yogesh Chawla	20	02:20 to 02:40pm	
3.	Care of Heart in TM & NTDT	Dr. Vikas Kohli	20	02:40 to 03:00pm	
4.	Risk of TTI in Thalassemics	Dr. Veena Doda	20	03:00 to 03:20pm	
	Session IV Prevention & Transfusion reducing agents			**03:20 pm to 05:00 pm**	
1.	Practical Prevention	Dr. Sangeeta Gupta	20	03:20 to 03:40pm	Dr. Seema Kapoor Dr. CBS Dangi Dr. Manas Kalra
2.	Hemoglobin Enhancers	Dr. Antonio Piga	30	03:40 to 04:10pm	
3.	Comprehensive Care of Thalassemia	Dr. Jagdish Chandra	30	04:10 to 04:40pm	
4.	Panel Discussion	Moderator Dr. Jagdish Chandra + Post Lunch speakers	20	04:40 to 05:00pm	
	There will be no Tea Break - Tea & Biscuits will served continuously 10.00am to 12.00 noon & 3.00pm to end of the last session				
	FIT meeting			**05:30 pm to 07:30 pm**	
	Cultural			**05:30 pm to 08:00 pm**	
	Dinner			**08:00 pm**	

Registration & Breakfast **08:15 am to 08:45 am**

Day 2, Sunday, 25th November, 2018 Patients & Parents Session

S. No.	Topic	Speaker	Minutes	Timings	Chairpersons
	Session V Intermedia need extra care			**09:00 am to 09:50 am**	
1.	Care of NTDT	Dr. Prantar Chakrabarty	30	09:00 to 09:30am	Dr. Alka Mathur Dr. J.M. Khunger Dr. Anil Samaria
2.	Thrombosis in thalassemia	Dr. V.K. Khanna	20	09:30 to 09:50am	
	Session VI Cure			**09:50 am to 11:40 am**	
1.	Stem Cells transplant	Dr. Alok Srivastva	25	09:50 to 10:15am	Dr. CB Das Gupta Dr. Dharama Choudhry Dr. Gaurav Kharya
2.	Life after BMT	Brig. Dr. Ajay Sharma	25	10:15 to 10:40am	
3.	Gene Therapy a reality	Dr. Sandeep Soni	30	10:40 to 11:10am	
4.	Panel Discussion	Dr. Dinesh Bhurani Moderator	30	11:10 to 11:40am	
	Session VII Patients Perspective			**11:40 am to 01:00 pm**	
1.	Treatment adherence and Quality of life	Dr. Michael Angstiniotis	20	11:40 to 12:00noon	Mrs. Shobha Tuli Dr. J. Sardana Dr. Vinky Rughwani
2.	Patient Role in Decision Making	Mrs. Anubha Taneja Mukherjee	10	12:00 to 12:10pm	
3.	Adolescence Psychosocial issues	Ms Sangeeta Wadhwa	10	12:10 to 12:20pm	
4.	Patient engagement & empowerment	Dr. J.S. Arora	20	12:20 to 12:40pm	
5.	Patients Experience, Achievement	Dr. Ravi Dhanani	10	12:40 to 12:50pm	
6.	Social Networking and CSR Funding	Mr. Prabhat Sinha	10	12:50 to 01:00pm	
	Lunch			**01:00 pm to 02:00 pm**	

	Session VIII A2P (Adolescence to Parenthood)			**02:00 pm to 03:30 pm**	
1.	Wonderful adolescence (Growth & Puberty) including Diabeties & Thyriod	Dr. Anju Seth	35	02:00 to 02:35pm	Dr. Suman Mendiratta Dr. A.G Radhika Dr. Richa Arora
2.	Bone Disease in Thalassemia	Dr. Rashid Merchant	20	02:35 to :2:55pm	
3.	Motherhood Thalassemia Major, Minor, Intermedia (Fertility & Pregnancy care)	Dr. Manju Puri	25	02:55 to 03:20pm	
4.	Question & Answer		10	03:20 to 03:30pm	
	Workshop on Capacity Building - Govt Initiatives & Ground Reality			**03:30 pm to 05:00 pm**	
1.	RPWD Act 2016 What it means to Thalassemics	Dr. S.K. Prasad	15	03:30 to 03:45pm	Mr. Panos Englezos Dr. Ratna Devi Mr. Prabhat Sinha Dr. J.S. Arora
2.	Disability certification, Grievances & Redressal	Dr. T.D. Dhariyal	15	03:45 to 04:00pm	
3.	National Policy on Haemoglobinopathies and Govt. Initiative	Mrs. Vinita Srivastava	15	04:00 to 04:15pm	
4.	Health Facilities and Disability Certification ground reality	Dr. J. Sardana Mr. NN Vidhyarthi Gagandeep Singh Chandok	5 5 5	04:15 to 04:30pm	
5.	State Initiatives on Thalassemia Care	Dr. S.K. Arora	15	04:30 to 04:45pm	
6.	Panel Discussion	Dr. Androulla, Dr. Michael Mrs. Shobha Tuli + All Speakers	15	04:45 to 05:00pm	

There will be no Tea Break - Tea & Biscuits will served continuously 10.00am to 12.00 noon & 3.00pm to end of the last session

Day 2, Sunday, 25th November, 2018 Doctor Session Seminar Hall, 1st Floor					
Registration & Breakfast				10:00 am to 10:30 am	
S. No.	**Topic**	**Speaker**	**Minutes**	**Timings**	**Chairpersons**
	Doctor Session I			**10:30 am to 11:30 am**	
1.	Challenges in Diagnosis of Thalassemia Syndrome	Dr. H. Pati	20	10:30 to 10:50am	Dr. K.K. Koul Dr. Neelam Sood
2.	Transfusion Hepato-splenomegaly & Allo - Immunisation	Dr. V.P. Choudhry	20	10:50 to 11:10am	
3.	Clinical & Laboratory Monitoring of Thalassemia	Dr. Maitreyee Bhatacharya	20	11:10 to 11:30am	
	Doctor Session II			**11:30 am to 12:40 pm**	
1.	Iron Overload and Monitoring	Dr. Praveen C. Sobti	20	11:30 to 11:50am	Dr. Ritika Sud
2.	Chelation which, why and how much	Dr. Amita Mahajan	30	11:50 to 12:20pm	Dr. Sanjay Choudhry
3.	Transfer to adult care	Dr. Jagdish Chandra	20	12:20 to 12:40pm	Dr. Shubha Laxmi Margekar
	Doctor Session III			**12:40 pm to 01:40 pm**	
1.	Growth & Puberty	Dr. Anju Seth	20	12:40 to 01:00pm	Dr. Sanjeev Digra
2.	Endocrine Problems	Dr. Rajni Sharma	20	01:00 to 01:20pm	Dr. Shishir Seth
3.	Fertility & Pregnancy in Thalassemia Major & NTDT	Dr. Vatsla Dadhwal	20	01:20 to 01:40pm	Dr. Ashwani Sood
	Lunch			**01:40 pm to 02:20 pm**	
	Doctor Session IV			**02:20 pm to 03:00 pm**	
1.	NTDT diagnosis transfusion & chelation	Dr. Sarmila Chandra	20	02:20 to 02:40pm	Dr. Nupur Parakh Dr. Nitu Nigam Dr. Piali Mandal
2.	NTDT complications	Dr. V.K. Khanna	20	02:40 to 03:00pm	

	Doctor Session V			03:00 pm to 04:10 pm	
1.	BMT 4Ps - Preparing, Planning, Post care & Procurement (of stem cells)	Dr. Dinesh Bhurani	30	03:00 to 03:30pm	Dr. N.K. Mehra Dr. M. Mahapatra Dr. CBS Dangi
2.	Gene Therapy/ Gene Editing	Dr. Sandeep Soni	20	03:30 to 03:50pm	
3.	Hb Enhancers	Dr. Antonio Piga	20	03:50 to 04:10pm	
3.	Panel Discussion	All Speakers Moderator Dr. Dinesh Bhurani	20	04:10 to 04:30pm	

There will be no Tea Break - Tea & Biscuits will served continuously 10.00am to 12.00noon at end of the last session

WORKSHOP

on

Practical Management of Thalassemia
On Monday 26th November, 2018
at
Kalawati Saran Children's Hospital, Bangla Sahib Rd,
Connaught Place, New Delhi, – 110001

PROGRAMME

SESSION I		09:00am to 12:30pm		
S. No.	**Topic**	**Speaker**	**Minutes**	**Timings**
1.	Welcome, introduction & objectives of the workshop	Dr. Jagdish Chandra	15	09:00 – 9:15am
2.	Diagnosis of Thalassemia Syndrome – Clinicaltion	Dr. Jasdeep	10	09:15 - 9:25am
3.	Diagnosis of Thalassemia Syndrome – Laboratory	Dr. Sunita Sharma	10	09:25 – 9:35am
4.	Blood Transfusion Therapy	Dr. Nupur Parakh	20	09:35 - 9:55am
5.	Iron Chelation	Dr. V.P. Choudhry	20	09:55-10:15am
	Tea Break		**15**	**10:15-10:30am**
6.	Group A- Visit to Blood Bank		60	10:30-11:30am
	Group B – Visit to TDCC			
7.	Group A- Visit to TDCC		60	11:30-12:30pm
	Group B –Visit to Blood Bank			
8.	Discussion			12:30pm

Followed by Lunch

Organisers
National Thalassemia Welfare Society &
Department of Pediatrics Kalawati Saran Children's Hospital, Delhi

WORKSHOP

on
Stem Cells Transplantation
On Monday 26th November, 2018
at
Rajiv Gandhi Cancer Institute and Research Centre,
Sector-7, Rohini, Delhi 110085

PROGRAMME

Breakfast : 10.00 am to 10.30 am

SESSION I			09:00am to 12:30pm	
S. No.	**Topic**	**Speaker**	**Minutes**	**Timings**
1.	Introduction	Dr. Dinesh Bhurani	10	10:30- 10:40am
2.	Pre-Transplant Identification & Preparation of Patient & Donors : Post-Transplant Domicile Care	Dr. Gauri Kapoor	10	10:40 - 11:10am
3.	Transplant Harvesting & Conditioning	Dr. Rahul Bhargawa	30	11:10 - 11:40am
4.	Cord Blood/MUD and Haplo - Identical Transplant	Dr. Rayaz Ahmed	30	11:40 - 12:10pm
5.	Visit to Transplant unit in groups	Dr. Narendra Agarwal	50	12:10 - 1:00pm
6.	Panel Discussion	Moderator Dr. Dinesh Bhurani	30	1:00 – 1:30pm

Followed by Lunch

Organisers
National Thalassemia Welfare Society &
Department of Hemato-Oncology & Bone Marrow Transplant
Rajiv Gandhi Cancer Institute and Research Centre

BIO-DATA SPEAKERS

Dr. (Brig.) Ajay Sharma (Retd.)

- Senior Consultant Deptt. of Clinical Haematology and Stem Cell Transplantation SGRH.
- Formerly Head, Deptt. of Clinical Haematology and Stem Cell Transplantation, R & R Hospital, Delhi Cantt. He has special interest in Haematology & Oncology

Dr. Alok Hemal

- Professor, Department of Pediatrics, Dr. RML Hospital, New Delhi
- Special Interest In Hemato-oncology & Pediatric HIV.
- National Convener Pediatric HIV Indian Academy Of Pediatrics.
- Specialist Training from Royal College Of Pediatric & Child Health London UK
- 50 Research Publications In National & International Journals.
- Many Presentation In National & International Conferences.

Dr. Alok Srivastava

- Professor of Medicine, Department of Haematology
- Head, Centre for Stem Cell Research. Christian Medical College, Vellore

Dr. Amita Mahajan

- ❖ Sr Consultant Pediatric Hematology & Oncology Indraprastha Apollo Hospital, Delhi
- ❖ Trained at AIIMS and UK
- ❖ Medical Advisor :- Thalassemics India, Foundation Against Thalassemia, Can Kids Leukemia Crusaders

Dr. Androulla Eleftheriou, TIF Executive Director

- Postgraduate in Biochemistry, Microbiology and Virology, and Business Administration from London universities.
- Awarded scholarships by the Cyprus government, the WHO and the Fulbright Commission.
- Member of European Haematology Association (EHA).
- Chair of the Higher Scientific Committee of SITA (Sultan Bin Khalifa International Thalassemia Award).
- Published extensively in peer reviewed journals and is the Chief Editor of TIF Magazine.

Dr. Antonio Piga

- ❖ Professor of Pediatrics and Dean of the school of medicine at S. Luigi University Hospital of Torino University, Italy
- ❖ He is involved in research on Luspatercept, drug to increase haemoglobin level in thalassemia

Dr. Anju Seth

- Director Professor Department of Pediatrics & In-charge Div. of Pediatric Endocrinology, Lady Hardinge Medical College, New Delhi
- > 90 papers in peer reviewed journals
- President, Indian Society of Pediatrics & Adolescent Endocrinology
- Program Director, Pediatric Centre of excellence in HIV, LHMC
- Chairperson, Causality assessment subdivision of National AEFI Committee
- Areas of interest: Disorders of vitamin D & calcium metabolism, growth & thyroid disorders, Pediatric HIV, have been providing comprehensive endocrine care to children with thalassemia for more than 15 years

Dr. A.P. Dubey

- Professor of Paediatrics ESI Medical College & Hospital
- Former Director Professor & Head Department of Paediatrics MAMC & LN Hospital
- Chief investigator for Delhi Govt. project on "Antenatal screening of mothers for thalassemia"
- Established Paediatric Research & Genetics Lab at LN Hosp.
- MCI inspector for recognition of UG & PG curriculum and also for DNB course.
- Delhi State Doctor's Award in 2011.

Dr. Dinesh Bhurani

- Director, Department of Haemato-oncology & Bone Marrow Transplant unit, Rajiv Gandhi Cancer Institute & Research Centre, Rohini, New Delhi
- He is the first DM of Hematology in India
- DM Clinical Haematology from CMC, Vellore & FRCPA from Australia.
- He has done more than 500 transplants at RGCI & Research Centre, Rohini, New Delhi

Dr. H. Pati

- ❖ Professor of Haematology, AIIMS, New Delhi
- ❖ Editor, Indian J Hematology & Blood Transfusion
- ❖ Co-editor of 5 Hematology books including deGruchy's Clinical Hematology.
- ❖ Fellow of International Medial Sciences Academy Indian College of Pathologists

Dr. Jalbala Sardana

- MBBS from LHMC (1975) and M.S. Ophthalmology (1980)
- Proud mother of Late Dr. Anjali Sardana, an inspiration for her to work for Thalassemia
- Founder secretary of Thalassemia Children Welfare Society in Bareilly
- Joint Secretary of Federation of Indian Thalassemic
- State coordinator of Thalassemic International Federation
- Women of the Year 2016 award by Golden Era Society for her services in the field of Thalassemia
- Honored by IMA on Doctors Day in 2016 for services to Thalassemic children
- Instrumental in getting Free Leucodepleted, NAT tested blood for all Thalassemia children without replacement from IMA Blood Bank Breilly
- Free chelation medicine from district hospital Bareilly & free investigations

Dr. Jagdish Chandra

- ❖ Director Prof Deptt of Pediatrics, LHMC & KSCH Hospital Delhi
- ❖ Director LHMC: March 2016-Oct 2017
- ❖ Member expert group of MoHFW Govt of India for guidelines for prevention and management of hemoglobinopathies
- ❖ Chairperson, Hodgkin Lymphoma study group of InPOG from 2014-2017
- ❖ Received Shri V R Lokeshwar Oration of PHO 2014

- ❖ Received Fellowship of Indian Academy of Pediatrics 2003
- ❖ Member PHO expert group for drafting guidelines for managing: ITP, Aplastic anemia, Blood component therapy
- ❖ Received WHO extra-regional Fellowship in Pediatric Hematoloy-Oncology 1998
- ❖ Published over 180 articles , chapters in international and national journals and book

Dr. J.S. Arora

Thalassemialogist, Msc in Haemoglobinopathy, University College London

General Secretary : National Thalassemia Welfare Society since
Federation of Indian Thalassemics

Member: Ethics Committee
IIT Delhi
Lady Hardinge Medical College and Associated Hospitals, New Delhi
ITS Dental College Hospital & Research Centre, Greater Noida

Founder Member: Indian Alliance of Patient Groups

Founding Trustee: Genomics And Public Health Foundation

Formerly: Coordinator Thalassemia Cell Govt. of Delhi
Member Advisory Committee - D D U Hospital Govt. of Delhi

"Life Time Service Award" from PHO Chambers of IAP

Patients for Patient Safety (PFPS) Champion India

Member: Patients for Patient Safety Advisory Group

Dr. Maitreyee Bhattacharyya

- M.D.(Medicine) D.M (Clinical Haematology), AIIMS, New Delhi.
- Professor & Director, Institute of Haematology & Transfusion Medicine, Kolkata.
- In charge , nodal center for State Thalassaemia Control Programme
- Publications : 48 International & 24 National Journals
- Area of interest Thalassemia & Coagulation disorders

Dr. Manju Puri

- Director Professor Department of Obstetrics & Gynaecology LHMC, New Delhi

Dr. Michael Angastiniotis

- Studied Thalassaemia (Biochemistry-Prenatal diagnosis), Genetics, and Haematology/Oncology from UK through scholarships of the Cyprus government, WHO and the British Council.
- Member of the Thalassaemia Control Programme, Cyprus and WHO ad-Hoc advisory committee on the control of haemoglobin disorders in the 1980s
- Served as consultant to the East Mediterranean region of WHO and director WHO Collaborating Centre for thalassaemia.
- Director, Pediatric Department, Makarios Hospital, Nicosia (1989 – 2001)
- TIF, Medical Advisor since 2004.

Mr. Prabhat Sinha

- Head- Patient Advocacy, Policy and Communications
  Novartis Oncology
- Prabhat leads the Communications, Policy and Patient advocacy function at Novartis Oncology.
- Prabhat has overall responsibility of managing partnership with patient groups and ensuring integration of patient's perspectives internally.
- He has also worked with State government of Uttar Pradesh where he managed a World Bank supported women health project and agencies like Sightsavers International and CARE USA.

Dr. Prantar Chakrabarti

- Assistant Professor in Haematology at IHTM, Kolkatta
- Postdoctoral training in clinical haematology at the AIIMS, New Delhi
- He was instrumental in setting up the State Thalassemia Control Programme of Government of West Bengal in 2008 and is a nodal officer of the programme till date.
- He has designed and implemented an innovative software THALAMON for monitoring thalassemia patients and carriers.

Dr. Praveen C. Sobti

- MD, DCH, Fellow of the International Medical Sciences Academy, Director, Guru Teg Bahadur Sahib Charitable Hospital
- Former Professor of Pediatrics Incharge Hemato-oncology, Dayanand Medical College & Hospital and Christian Medical College Ludhiana

Author of 25 chapters

- **Awards**
  - Parman Patra by the Govt. of Punjab for outstanding work done for thalassemia
  - Honorary Mayor President of Baton Rouge, Louisiana State, USA
- **Membership**
  - Founder of Punjab Thalassemia Welfare Society
  - Member National Advisory Board of Thalassemia
  - Member Global Advisory Board of Thalassemia

Dr. Rajiv Bansal

- **Senior Consultant & HoD Pediatrics at Santokba Durlabhji Hospital, Jaipur**
- In-charge of Thalassemia unit, at SDMH
- Past President of IAP Jaipur branch,
- Recently elected President of Rajasthan state branch of NNF.
- Keen interest in Neonatology, pediatric hematology and pediatric respiratory diseases.

Dr. Rajni Sharma, MD

- Division of Pediatric Endocrinology Department of Pediatrics AIIMS, New Delhi
- Former faculty in Pediatrics LHMC, New Delhi (2009-2014)
- Former Senior Research Associate CSIR (Pediatric Endocrinology, AIIMS
- Joint Secretary of Indian Society for Pediatric and Adolescent Endocrinology
- 40 indexed publications and 12 book chapters

Dr. Rashid Merchant

- ❖ Senior Paediatrician in Mumbai, passionately involved in the care of children by HIV/AIDS, Thalassemia and Primary Immune Deficiency.
- ❖ Former Dean and Professor of Paediatrics (Mumbai University).
- ❖ Former Honorary Consultant Paediatrician, Nanavati Super Specialty Hospital, Mumbai

Dr. Ravi Bipinbhai Dhanani

- ❖ Masters in Social Work and PhD in the Thalassemia from Rajkot, Gujarat.
- ❖ Assistant Professor at Shree Matrumandir College, Saurashtra University, Rajkot
- ❖ Member of Board of studies of social work, Saurashtra University, Rajkot.
- ❖ Trustee, Shree Balmukund Seva Sanstha Charitable Trust, Rajkot.
- ❖ Trustee, Thalassemic Jan Jagruti Trust, Ahmedabad.
- ❖ Organized 50 Blood Donation and screened more than 7000 students in Saurasthra Region.
- ❖ He has received various awards, from national and international organizations

Dr. Sandeep Soni

MBBS, MAMC, and MD (Pediatrics) LHMC & KSCH, New Delhi
Fellowships:
BMT, Hadassah University, Jerusalem, Israel
Pediatrics Hemato-oncology, Children's Hospital Montefiore, NY
Stem Cell Transplant, MD Anderson Cancer Ctr,
Currently: Assoc. Professor of Pediatrics, Stanford University
Division of Stem Cell Transplant and Regenerative Medicine
Lucile Packard Children's Hospital, Palo Alto, CA
Clinical Research is –
SCT for Thalassemia and Sickle Cell Disease
Gene therapy for Thalassemia and Sickle Cell

Dr. Sangeeta Gupta

- ❖ Director Professor, Obs & Gynec. MAMC & LN Hospital, New Delhi
- ❖ In-charge, Fetal medicine Clinic at MAMC & LNH , New Delhi
- ❖ Vast experience in invasive procedures
- ❖ Awarded Commonwealth Scholarship in 2007
- ❖ Trained in Fetal Medicine at St.George's Hospital, London
- ❖ Faculty of FNB training programme - High Risk Pregnancy & Perinatology
- ❖ Has many publications & contributions in various text-books
- ❖ Editor AOGD bulletin 2016-17

Dr. Sarmila Chandra

- ❖ Haemato-oncologist, trained in AIIMS Delhi and University of Ulm West Germany.
- ❖ She has been working as Consultant Haematologist in Kothari Medical Centre, Bhoruka Blood Bank and recently in Narayana Health RTIICS, Kolkata as head of haematology.
- ❖ Consultant haematologist in IHTM Medical College at its inception.
- ❖ Advisor to Thalassaemia Society and Haematology Foundation

Dr. S.K. Arora

Chest Physician by qualification

Addl Director Health, Govt of Delhi

Presently looking after

National Haemoglobinopathies Control Programme

National Program for Health Care of Elderly &

National Tobacco Control Programme in Delhi State.

He has done lot of scientific research on health care, written number of Scientific papers.

Awards

Prestigious Delhi State Award

He is gold medallist & recipient of highest International award in Tobacco control - WHO World No Tobacco Day Award for his extraordinary contribution in South East Asia Region

Dr. Sunil Gomber

- Director, Professor and Head Department of Pediatrics UCMS & Guru Teg Bahadur Hospital, Delhi.
- In-charge Paediatric Hemato-oncology division of the department of Pediatrics.
- Fellow Indian Academy of Pediatrics (FIAP).
- WHO temporary adviser & National faculty for integrated management of child hood & neonatal illness (IMNCI).

Dr. Vatsla Dadhwal

- Professor Division of maternal fetal medicine department of Obs. & Gynaec., AIIMS New Delhi
- Fetal medicine : Diagnostic and therapeutic interventions including intrauterine transfusions, interventions in complicated twins
- High risk pregnancy
- Nodal officer for PPTCT programme
- Chairperson AOGD Fetal Medicine subcommittee 2017-19

Dr. Vikas Kohli

- Fellow American Academy of Pediatrics
- Fellow American College of Cardiology
- Diplomat American Board of Pediatrics American Board of Pediatric Cardiology
- Trained in Pediatric Cardiology at the University of Miami.
- Former Director of Pediatric Cardiology at RTIICS, Kolkata;
- Former Incharge of Non-Invasive Lab, Sir Ganga Ram Hospital.
- Awarded the American Heart Association/Genentech Award 1996
- Area of interest is Fetal Cardiology (Fetal Echocardiography)
- He has written more than 5 chapters.
- On Board of Editors for 3 Journal and reviewer for 5 Journals.

Mrs. Vinita Srivastava

- Senior National Consultant in Ministry of Health with eighteen years of experience in Health and Social Sector.
- She has been awarded by many prestigious institutions her for excellent work.
- Currently she is taking care of Blood cell in the MOHF under the dynamic leadership of Sri Manoj Jhalani, Additional Secretary and Mission Director NHM, GOI.
- Blood cell was given responsibility of blood disorders related disease. The blood cell has recently released the guidelines of hemoglobinopathies and developing hemophilia guidelines.

Dr. Veena Doda

- Former HOD Deptt. of Transfusion Medicine, Dr. RML Hospital, New Delhi

Dr. V.K. Khanna

- Co-Chairman, Department of Pediatrics, Institute of Child Health, SGRH, New Delhi.
- In-charge of the Preeti Tuli Thalassemia Unit at SGRH.
- Vice President of Thalassemics India
- Regional scientific coordinator from India to the TIF, Cyprus.
- Involved in the care of thalassemia patients and research work on thalassemia for the last 34 years.
- Organized many national and international conferences, workshops, seminars and check-up camps for thalassemia.

Dr. V.P. Choudhry
Senior Consultant
Fortis Escorts Hospital, Faridabad
Batra Hospital & Medical Research Center, New Delhi
Former Professor & Head Professor of Hematology, AIIMS New Delhi
Former Director, IGICH, KABUL

Expert Committee Member :

- National Policy on Thalassemia-Ministry of Health

Editor :

- Recent Advances in Hematology
- Thalassemia Care & Control 2000

Medical Advisor :

- Honorary Medical Advisor to Armed Forces Medical Services
- Federation of Indian Thalassemics
- National Thalassemia Welfare Society

Awards :

- Dr S.K. Sood Life Time Achievemnt Award by DSH- 2018
- Dr K.C. Chaudhuri Life Time Achievement Award by Ind J Pediatr - 2018
- Lifetime achievement award by IAP - 2008
- Dr. B.N. Dara Award by National Thalassemia Welfare Society- 2001

Dr. Yogesh Chawla

- Padma Shri award recipient
- Ex Director PGIMER
- Former Prof. & Head, Department of Hepatology PGIMER, Chandigarh
- Presently: Chairman Academics and Professor Emeritus Kalinga Institute of Medical Sciences, Bhubaneshwar
- Research Council Member of CSIR-Institute of Genomics and Integrative Biology (IGIB)
- Member Board of Management SRM University, Chennai
- Member Board of Management Pushpawati Singhania Institute, New Delhi

Dr. Sanjay Kant Prasad

A Post Graduate and Doctorate in Psychology with specialization in Clinical and Rehabilitation Psychology having more than 28 years of experience in the field of Disability and Rehabilitation programme, policies, education and research.

Work Experience

- **Deputy Chief Commissioner, D/o EPwD, MoSJE, Govt. of India**
- Director, NCDS, IGNOU
- Programme Officer - DEP-SSA, MHRD-IGNOU project
- Sr. Programme Officer- Rehabilitation Council of India (RCI)
- Addl. Prof. cum Jt. Director- JMISH, Patna
- Lecturer in Psychology cum Jt. Director, JMISH, Patna

Mr. TD Dhariyal

❖ Disability commissioner Delhi

Mr. N.N. Vidhyarthi

Previous Experiences:

Script-writer producer and director for commercial ads films

Active participant and contributor in social movement

Current Working as:

Founder and secretary of Thalassemia Welfare Association, Bihar

Founder and Secretary of "Aap aur Hum" (Donate blood - save life)

Ms. Sangeeta Wadhwa

- Qualified Counseling Psychologist
- MBA in Healthcare & Hospital Administration
- P.R.O & Counselor
- At Shri Hashu Advani Memorial Foundation - Healthcare & Thalassaemia Centre, Chembur, Mumbai.
- Advisor to Thalassaemia Patients and Parents for last 15 years
- Founder of YTA (YOUTH THALASSEMIA ALLIANCE)
- Member of National & International Thalassemia Societies
- Participated in Marathon race for Thalassaemia awareness
- Articles published on her Life in Hindustan Times
- Interview on National TV IBN (Zindagi live) Channel

Main AIM: Face - Fight - Finish Thalassaemia

Mrs. Anubha Taneja Mukherjee

- Public Policy Lawyer, Member Secretary, Patients Advocacy Group, Thalassemics India
- A lawyer by training and works as a Director in the Public Affairs & Advocacy Division in a communications firm.
- Has been closely involved in the establishment of the Thalassemia Day Care Centre at a central government hospital in Delhi
- Now driving Thalassemics India's patients advocacy programme through the Patients Advocacy Group as its Member Secretary.

Mr. Gagandeep Singh Chandok

- The President of the Thalassaemia and Sickle Cell Society of Bangalore
- Profession :- Transaction Analyst for Risk and Compliance in a BPO MNC
- Ran the TCS Marathon
- Started a Petition for Gene Therapy : National policy for prevention, care and cure strategies.
- Part of the organising committee for the 'Update on Thalassaemia Conference' October 2017 at Mumbai.
- Invited as Motivational Speaker by Lets Help Some1 for Thalassaemia Educational Seminar at Mumbai
- Part of the organising committee for the Thal Night Event, May 2018

BIO-DATA CHAIRPERSONS

Dr. A.G Radhika

- Consultant, Obs & Gyn. UCMS & GTB Hospital, Delhi
- FOGSI National Coordinator for Clinical Research 2017-19
- Cochrane Author & Expert Reviewer Gynec. Oncology Group & Wounds Group
- Member South Asian Cochrane Network
- Expert Reviewer, National Institute for Health Research, UK
- WHO Fellow: Advanced Course on Monitoring and Evaluation: Innovations in a Dynamic Health Systems Environment
- More than 70 publications

Invited expert

- Member Regional National Mentoring Committee on STIs
- Invited expert -Joint US-ICMR for meeting on PRE-EMPT study for the prevention of Pre-eclampsia in low resource countries

Dr. Alka Mathur

- ❖ Graduated from LHMC and received short term training in Hematology at AIIMS
- ❖ Established Thalassemia Day Care Centre at Hindu Rao Hospital May 2004, in charge since then.

Dr. Anil Samaria

- ❖ MD Medicine, Diploma in Diabetology, fellowship in Endocrinology
- ❖ Professor in department of Medicine
- ❖ Nodal officer of Multi disciplinary research unit
  J. L. N. Medical college Ajmer

Dr. Ashwani Sood

- Prof & Head, Deptt of Pediatrics and Adolescent Medicine IG Medical College Shimla (HP)
- Chief Co-ordinator, Medical Education Unit.
- Convenor-IAP -ICMR Consultative Group on AMR.
- Member Secretary State AEFI Committee.
- Member MCI (2007-11)

Dr. Bhavna Dhingra, (MD, DNB)

- Faculty in Pediatrics at AIIMS Bhopal
- US Certified Pediatric Bioethicist
- Hematology Training at AIIMS, Delhi
- Former faculty at KSCH, LHMC Delhi
- 35 indexed publications
- Presented 45 papers
- Contributed 25 book chapters

Dr. CBS Dangi

(M.Sc. & Ph.D. in Genetics)

- Prof. & Dean. Paramedical Sciences & Faculty of Science, RKDF University, Bhopal (M.P.)
- Clinical Geneticist

Field of Specialization:

- Genetics, Biotechnology, Hemoglobinopathies, Molecular, Cyto Genetics

Fellowships

- Research fellowship from Thalassaemia International Federation (TIF), Nicosia,

Cyprus in 2005.

- Research fellowship from Christian Medical College (CMC),Vellore Oct. 3rd to Oct. 28th 2005.
- Chairman of Examination committee of Science Division of **RKDF University** Bhopal (M.P.).
- Chairman, Institutional Ethical Committee (IEC) of **RKDF Medical College &**
- Publications Research National & International Citations: 28
  Research Center, Bhopal
- State Coordinator of **Thalassemia International Federation** ,Cyprus in M.P. from 26th May 2014.
  - Establish **Thalassaemia Surveillance Cell & Research Centre** 2009 at People's Hospital, Bhopal.

Dr. CB Das Gupta (MD,FIAP)

- Pioneer in Rajasthan for Care of Thalassemics since 1991
- State Coordinator of BPNI 1992-2007
- Awarded by Govt. of Rajasthan in 2005,2009 for Extraordinary Work in Child Health related issues.
- Faculty in National & State Pediatric Conferences since last 15 yrs
- Editorial Advisory Board Member of Ped. Journals
- FIAP 2014'

Dr. D. D. Golani

- MD (Internal medicine)-1985 from Delhi University
- Fellow of Indian Academy of Echocardiography
- Senior consultant at DDU Hospital-Delhi Govt. Hospital
- Keen interest in echo-cardiac study of thalassemic patients

Dr. Dharma Choudhary

- Director Bone Marrow Transplant, BLK Super Speciality Hospital, New Delhi.
- Area of Interest: Transplant for Hemoglobinopathies (Thalassemia Major & Sickle Cell disease), Bone Marrow failure syndrome (Aplastic anemia / Fanconi anemia), Haplo Identical transplant, Graft versus Host disease.
- Conducted > 250 transplant for thalassemia major.
- > 50 publications in international journals
- Member of American Society of Bone Marrow Transplant

Dr. Gaurav Kharya

- Senior Consultant & Head Pediatric Hematology Oncology Immunology & Bone Marrow Transplant Artemis Hospital, Gurgaon
- Worked as fellow in pediatric hemato-oncology, immunology & BMT The Great north Children's hospital, Newcastle UK and St Mary's hospital, Imperial College NHS trust, London, UK
- Dr Kharya has a vast experience in transplanting children with various blood disorders benign or malignant, immunological diseases etc nationally and internationally.
- Dr Kharya is credited for doing the first haploidentical bone marrow transplant for sickle cell disease in India haploidentical BMT in a 5 month old baby suffering from severe combined immunodeficiency
- Dr Kharya has done close to 700 transplants for various diseases along with his team members.

Dr. J.M. Khunger
MBBS, MD, DM (Haemat) AIIMS
Senior Consultant Haematologist
V. M. Medical College & SafdarJang Hospital, New Delhi

- ❖ Vice President, Indian Society of Haematology & Blood Transfusion (2016-17)
- ❖ Secretary, Delhi Society of Haematology (2007-2009) & (2012-2015)

Dr. Kirti Nanal

- M.D.(Paediatrics).
- HOD Paeditrics & I/C Thalasaemia unit NDMC, Charak Palika Hospital, N.D.

Dr. K.K. Koul

- ❖ Professor & Head of P.G.Deptt. of pathology, Govt. Medical College, Jammu.
- ❖ Sr. Consultant Haematology, G.M.C associated Hospitals Jammu.
- ❖ Medical Advisor J&K State Thalassemia Welfare Society, Jammu.

Dr. Kavita Juneja

- ❖ Medical doctor with 38 ears of experience in the public health.
- ❖ Working extensively for Thalassemia major patients, counseling, management and screening for carriers of their families and also facilitating effective screening of children at school level at all the government schools

Dr. M. Mahapatra

- ❖ Professor, Department of Haematology, AIIMS, New Delhi

Dr. Manas Kalra

- FNB in Pediatric Hematology Oncology
- 3 year Fellowship in Pediatric Oncology and BMT from CHW, Sydney
- Currently, Consultant at Indraprastha Apollo Hospital, Delhi

Dr. Neelam Sood

- Head of Department, Pathology and Lab Medicine, DDU Hospital, Govt. of NCT, New Delhi.
- DNB teacher and guide of their thesis works besides other hospital works.
- Received WHO fellowship and recipient of State Award in 2018.
- She has numerous publications in national and international journals to her credit and is also a reviewer for many journals.
- Nodal officer of Thalassemia project at DDUH.
- Her area of interests Hemoglobinopathy and histopathology.

Dr. Nikhil Sheth

- Senior Paediatrician
- He Has Worked Under Dr A. Piga (Italy) and Dr Paul Telfer (U K)
- Exclusively working for Thalassemics All over Gujarat since 2000.

Dr. Nitu Nigam

Present Designation:

Assistant Professor, Cytogenetics Unit , Dept. Of Centre For Advance Research, KGMU, Lucknow, UP, India

- Phd-worked At Department Of Medical Genetics ,sgpgims Lucknow. 2003
- Postdoctoral Fellowship At James Cancer Institute, The Ohio State University,
- Columbus, Ohio, USA –Nov 2003-April 2006
- Publications: Journal articles: 22

Dr. N.K. Mehra

- Former Dean of AIIMS New Delhi
- Currently holds the prestigious position of 'Dr C.G. Pandit National chair'.
- Developed of the new specialty of Transplant Immunology and Clinical Immunogenetics Department at AIIMS
- Fellow of the Indian National Science Academy (FNA), and World Academy of Sciences (FTWAS).
- Former chief Editor of international journal 'Frontiers in Immunology''.
- Received title of 'Chevalier of the National Order of Merit' from French President in 2003.
- Received highest International Award from the Iranian Research Organization for Science and Technology.
- Received Dr BR Ambedkar award for excellence in Medical Research, highest award of ICMR.
- His book 'The HLA System in Medicine and Biology' received high international acclaim.

Dr. Nupur Parakh

- Senior Medical Officer
- Kalawati Saran Children's Hospital

Dr. Piali Mandal

- ❖ MD, Paediatrics
- ❖ Associate Professor, Department of Paediatrics

AFFILIATIONS:

- ❖ Lady Hardinge Medical College And Kalawati Saran Children's Hospital
- ❖ Keen Interest In Hemato-oncology. Working At Ksch In The Division Of Hematology For Last 4.5 Years

Mr. Panos Englezos

President: Thalassaemia International Federation (TIF)

Dr. Rakhi Maiwal

- ❖ Associate Professor of Hepatology at Institute of Liver and Biliary Sciences.
- ❖ Special interest in renal dysfunction in patients with cirrhosis and liver failure and critical care hepatology
- ❖ Incharge of the Liver Intensive Care at ILBS.
- ❖ Published original articles in indexed journals and has 52 publications.

Dr. Rekha Harish

- Professor & Head Department of Paediatrics .
- Examiner to various Medical Universities in North India.
- Reviewer for Indian-Paediatrics, IJP, JIMMS Journal of Paediatric Surgery;
- Chief-coordinator Thalassemia-Day-Care Centre at GMC Jammu
- National Convener IAP Task Force for Prevention of Childhood Obesity and Life Style Disorders 2012 -2015.
- Chairperson FSSAI Expert Group for laying guidelines for National School Canteen.

Dr. Richa Arora Agarwal

- M.D.Pediatrics
- Diploma Endocrinology - University of South Wales, MRCP (UK)
- **Present Occupation : Consultant Pediatric Endocrinology** -
  - Fortis Hospital, Shalimar Bagh
  - Jaipur Golden Hospital
  - Rajiv Gandhi Cancer Institute, Rohini
  - Rainbow Hospital, Panipat

Dr. Ritika Sud

- Associate Professor
- Presently working as: Associate Professor of Medicine at Lady Hardinge Medical College and associated Hospitals, New Delhi.
- Has over 50 publications in National and International journals.
- Chaired sessions and delivered Lectures in several national level conferences viz.

DIABCON, API-DSC and APICON Annual Conferences

- ❖ Coordinator of the Adult Thalassemia transition care program.
- ❖ Has started Preventive Cardiology Clinic and Hematology Clinics and presently part of Hematology and Endocrinology Clinics at LHMC
- ❖ Areas of special interest are Hematology and Endocrine disorders

Dr. Sanjay Choudhry

- ❖ Fellow In Neonatalogy (AIIMS)
- ❖ Advanced Training In Pediatric Intensive Care (P.G.I.M.E.R)
- ❖ HoD Paediatrics & In-charge Thalassemia Unit, B.S. Ambedkar Hospital Rohini.

Dr. Sanjeev Kumar Digra, DCH, MD

- ❖ Professor Pediatrics, Govt. Medical College Jammu
- ❖ Coordinator Thalassemia Day Care Centre
- ❖ Consultant I/C Pediatric Hematology-Oncology ward
- ❖ Coordinator Pediatric HIV-AIDS
- ❖ Publications in national & international journals

Dr. Suman Mendiratta

- MD OB Gyn (AIIMS), FMAS(WALS)
- Medical superintendent, North DMC Medical College & Hindu Rao Hospital.
- HOD (Obstetrics & Gynecology)
- DNB teaching faculty, Guide & Examiner.
- Incharge Premarital counseling clinic.

- Project coordinator Thalassemia control program (MCD).
- Member of AOGD, FOGSI, NARCHI, IFS, SFM & NTWS.
- Awards – C L Jhaveri & Chief of Army staff award.
- Publication – Numerous National and International Publications
- Written a booklet on thalassemia prevention “An Insight into Thalassemia”.

Dr. Sunita Sharma

- ❖ MD (Pathology)
- ❖ Currently working as Director Professor and Chairperson Department of Pathology LHMC N. Delhi.
- ❖ Working in field of hematology for last 23 years
- ❖ About 90 publications in various national and international journals
- ❖ Published a book, ‘Concise Haematology’ for undergraduates in 2018.
- ❖ Several projects on coagulation abnormalities in thalassemic children

Dr. Shubha Laxmi Margekar

- MD (Medicine) from Gandhi Medical College, Bhopal(2007)
- Associate Professor of Medicine at LHMC, New Delhi.
- Recognised examiner for MBBS,BDS.
- Several publications in journals and books.
- Participated in Several multi-centric international clinical trials.
- Recipient of Dr J.C. Patel and Dr. B.C. Mehta Award in APICON 2014.
- Fellowship of Indian Association of Clinical Medicine in 2016.
- Conducted Several patient education programme.

Ms. Shobha Tuli

- Shobha Tuli Secretary, Thalassemics India since1993
- Supported the establishment of a thalassemia unit at Sir Ganga Ram Hospital, in New Delhi, known as the 'Preeti Tuli Thalassemia Unit'.
- Vice President on TIF's Board.
- President of “Federation of Indian Thalassemics” since 2000 .
- Advisor to the Indian Red Cross Society, Govt of India from 2003-2006.
- Advisor & Coordinator to the BMT Centre at BL Kapur Memorial Hospital, New Delhi.
- State Award received from Dept. of Social Welfare Govt. Of NCT Delhi in 1998.
- George Englezos Award' bestowed by TIF, Cyprus in 1999.
- Life Time Service award given by the Indian Academy of Paediatrics in 2011.

Dr. Seema Kapoor

- Professor Paediatrics, in-charge Genetic Unit, Maulana Azad Medical College, Delhi.
- In charge Delhi State Lab For Prenatal Diagnosis In Thalassemia.
- Member of ICMR task force on inborn metabolic errors.
- Member of national new born screening committee.
- Awarded 25 GOLD medals .

Dr. Shishir Seth

- Dr Shishir Seth MD, DM (Clinical Hematology),
- Fellow Leukemia/ Bone Marrow Transplant (Vancouver-Canada)
- Consultant- Hemato-Oncology & Bone Marrow Transplant

Dr. Vinky Rughwani

- **Chairman :-** Ethical Committee Maharashtra Medical Council , Mumbai**.**
- **Member :-** Maharashtra State Pharmacy Council, Mumbai.
- **Member :-** Maharashtra State Blood Transfusion Council, Mumbai.
- **Director** :- Thalassemia and Sickle Cell Centre, Nagpur.

DR B.N DARA AWARD

Dr. Androulla Eleftheriou

TIF Executive Director

Dr Androulla Eleftheriou obtained her graduate and postgraduate degrees in Biochemistry, Microbiology and Virology, and Business Administration from London universities.

She has been awarded a number of scholarships by the Cyprus government, the World Health Organization and the Fullbright Commission.

Through her work with TIF, Dr Eleftheriou has carried out numerous projects of local, national, regional and international scope, working closely with international experts, local health professionals and thalassaemia associations worldwide.

She is involved in the development and coordination of many joint activities and projects with official health-related organizations and agencies, national and regional health authorities and with numerous disease and non-disease specific patient/parents organizations.

She is member of European Haematology Association (EHA) and the Chair of the Higher Scientific Committee of SITA (Sultan Bin Khalifa International Thalassemia Award).

Dr Eleftheriou has also published extensively in peer reviewed journals and is the Chief Editor of TIF Magazine. The author of numerous position papers, she has received a certification for Capacity Building from Harvard University and been awarded the Panos Englezos Award by TIF in 2003 for her contribution to the promotion of TIF's mission and activities.

BEST SOCIAL WORKER AWARD

Mr. Thadaram Tolani

Thadharam K. Tolani, aged 78 years is founder Chairman of Tolani Sewa Sankalp. Tolani Sewa Sankalp conducts Thalassemia Minor Checkup camps all over India and it is the only organisation in India that undertakes such camps at large scale.

He organized his first camp on 20/01/1989 in Thane and initially restricted to Thane, Ulhasnagar, Mumbai etc. till 2009.Then from August 2010 onwards he started conducting camps all over India.

His organisation Tolani Sewa Sankalp has till now conducted 265 camps in 188 cities of 8 states Maharashtra, Gujarat, Rajasthan, Madhya Pradesh, Uttar Pradesh, Chhatisgarh, Haryana and Karnataka. They have screened 59146 persons with Hb HPLC, of which 8294 were found Thalassemia carriers i.e 14%. Higher carrier rate may be due to most of the camps were organised in Sindhi community, which has the highest prevalence.

CONTENTS

From Secretary's Desk

-Dr. J. S. Arora

National Thalassemia Welfare Society was formed on **23rd November, 1991** by patients, Parents, Doctors & well-wishers at AIIMS. At that time the word Thalassemia was hardly known, even amongst medical fraternity. At that time there were only 3 transfusion centers in Delhi with little amenities even at AIIMS. The transfusions were given in casualty along with seriously ill patients. Blood was in acute shortage and most of the thalassemics were dependent upon single Blood Bank Indian Red Cross Blood Bank. Packed Red blood cells were not easily available and Leuco depletion was unheard. Though Desferal was available but cost and unavailability of infusion pump was a great barrier besides painful administration. Transmission of transfusion transmitted infections was very high. Though pre-natal diagnostic facility was available at AIIMS but thalassemia carrier screening was hardly advised to pregnant women resulting into many Thalassemia Major Births. Outside Delhi things were worst except Mumbai & Vellore.

From 3 Transfusion Centres in1991 now we have 21 (13 Govt.) Thalassemia units in Delhi & NCR. The most remarkable achievement of NTWS has been in getting cooperation from all the concerned doctors (Hematologists, Pediatricians, Blood Banks & Head of the Institutes) and the blessings of the Government.

To achieve our objective of creating optimum facilities at minimum cost we liaison with the Government of Delhi. Under Bhagidari scheme **Directorate of Health Services** in consultation **with National Thalassemia Welfare Society formed a "Thalassemia Cell"** to monitor the various initiatives taken by the Government. I have been privileged coordinator of the Thalassemia Cell since its inception. **I am proud to say that our major achievements have been FREE all three chelating agents for every patient registered in Delhi Government Hospitals. Earlier VAT (Sales tax) was exempted on blood filters and all chelating agent but it pains to inform that with introduction of GST once again we have to pay trading tax. We are trying our best to get waiver on drugs and equipment used in thalassemia and Sickle Cell Anaemia.**

One of our biggest achievements have been FREE pre-natal diagnostic facility at Lok Nayak Hospital. It's free for everyone who needs it

Following other major steps have been undertaken under Thalassemia Cell Department of Directorate of Health Services of Govt. of Delhi venture:

- Massive Thalassemia campaign. Advertisements were put in various newspapers. Publishing of brochures & poster on Thalassemia awareness. Hoardings have been put at prominent places in the Capital.
- Thalassemia screening of pregnant women in antenatal clinics of all major Hospitals.
- DHS Govt. of Delhi in association with NTWS produced two 27 minutes film "Chetna" and "Jagriti" on Thalassemia awareness.
- A five-day mega event "Thalassemia Chetna Yath Yatra" from 22nd Nov to 26th 2001, flagged off by the then Hon'ble Chief Minister of Delhi.
- A health parade with a Tableau on Thalassemia marked the World Health Day observed by Directorate of Health Services, Govt. of Delhi in 2003
- A protocol on thalassemia was published in both English and Hindi languages. It was launched by the then Hon'ble Health Minister in 2005.
- Directorate of Health Services assigned NTWS to prepare registry of thalassemia patients taking transfusions in Delhi, which NTWS completed proficiently in 2013.

In February 1994, we organized our 1st National Thalassemia Conference which was also 1st of its kind in India. At that time there were only 11 Thalassemia Societies in India. We Invited and offered free registration & accommodation to all of them so that everybody should attend. Over 300 persons attended the 2 day conference. A meeting of all the associations was called during the conference, 6 of them joined to form the **Federation of India Thalassemics**.

To fulfill our objective to enrich power of knowledge amongst thalassemia families and doctors, we in association with Department of Haematology A.I.I.M.S. organized

- 1st National Thalassemia Conference, Feb. 1994, inaugurated by DGHS.
- 2nd National Thalassemia Conference, Dec.1997 inaugurated by Director AIIMS.
- 3rd National Thalassemia Conference, Apr. 2001, inaugurated by the then Hon'ble Chief Minister of Delhi.
- 4th National Thalassemia Conference, May. 2003 inaugurated by the then Hon'ble Minister of Health, Govt. of NCT, Delhi.
- 6th National Thalassemia Conference, Nov 2010 inaugurated by Director General ICMR and Secretary Ministry of Health, Govt. of India.
- 7th National Thalassemia Conference, April 2014 inaugurated by Dean AIIMS

- 8th National Thalassemia Conference, December'2016 inaugurated by Sh. Hansraj Ahir Hon'ble MoS, Home Affairs Govt. of India and Guest of Honour Sh. Satyendar Jain, Hon'ble Minister of Health Govt. of Delhi.
- Symposium on Thalassemia & Deferiprone in March 1995 to launch the world's first Oral iron chelator, inaugurated by the Dean AIIMS
- Workshop on Prenatal Diagnosis of Thalassemia in Pregnancy Nov' 2010.
- Workshop on Challenges in Diagnosis of Thalassemia Nov 2010.
- Workshop for patients Capacity Building, April 2014
- Workshop on Challenges in Diagnosis of Thalassemia Dec' 2016.

NTWS in association with Department of Paediatrics, LHMC and Kalawati Saran Children's Hospital organized

- Training Program on Thalassemia Care, Apr. 2004 inaugurated by MS & Principal of LHMC & KSC Hospital
- 5th National Thalassemia Conference, Nov. 2006 inaugurated by the then Hon'ble Minister of Finance, Govt. of NCT, Delhi.
- "Thalassemia Symposium III", Aug'08

NTWS in association with Directorate of Health Services Govt. of Delhi and MAMC & LN Hospital organized

- Symposium on Thalassemia. May 2005, the then Hon'ble Minister of Health was chief guest & Hon'ble Minister of Finance was guest of Honour

NTWS in association with Department of Paediatrics, UCMS & GTB Hospital organized

- Workshop on Thalassemia in Nov 2006 inaugurated by the secretary health Govt. of NCT Delhi.
- Workshop on Thalassemia, April 2014.

NTWS in association with Department of Haematology Army Research & Referral Hospital, New Delhi organized

- Workshop on Stem Cell Transplantation in Thalassemia, December 2016.

Patient Capacity Building workshops were held in April 2014 and December 2016 parallel to 7th & 8th National Thalassemia conferences. During these workshops unique initiatives were

taken to motivate the patients/parents and activists for a better treatment, to live a near normal healthy life. This time again we are organizing capacity building workshop alongwith 9th National Thalassemia Conference.

NTWS is organizing **"9th National Thalassemia Conference"** in association with Department of Paediatrics Kalawati Saran Children's Hospital (KSCH) on 24th & 25th November, 2018 at Swarn Jayanti Auditorium, AIIMS, New Delhi, followed by **Workshop on Practical Management of Thalassemia at KSCH** and **Workshop on Stem Cells Transplantation at Rajiv Gandhi Cancer Research Institute, Rohini, New Delhi** On Monday 26th November, 2018.

In these academic meetings International & National faculty of repute have been invited and over 400-600 patients, parents and doctors benefited every time. In our last two conference (7th & 8th NTC), representation crossed over 1000 patients/parents/Doctors with high number of adult patients.

Since inception our aim has been to strengthen existing societies and encourage the formation of new Thalassemia societies in other districts. Wherever there were more than 25 patients, we encouraged them to join & form new Thalassemia association. Where Thalassemia associations already existed but were inactive we infused enthusiasm and made them vibrant.

In this regard within two months of formation of NTWS we started visiting other parts of India and started organizing CMEs and checkup camps. First such camp was organized at Kota in February 1992. During last 27 years we have visited and organized lectures and check-up camps several times in most of cities like Faridabad, Gurgaon, Karnal, Rohtak, Hisar, Sirsa, Agra, Meerut, Bareilly, Varanasi, Aligarh, Lucknow, Dehradun, Kota, Jodhpur, Shri Ganganagar, Udaipur, Chittoregarh, Gwalior, Jabalpur, Bhopal, Shahdol, Indore, Raipur, Amritsar, Jalandhar, Patiala, Karnal, Jammu, Srinagar, Patna, Dhanbad, Bhillai, Dibrugarh and many more.

Voluntary blood donation drive has been another area where we focused since beginning and gave an impetus in last 12 years. In last 12 years we have organized about 600 blood donation camps and collected around 32,000 units of blood.

I associated with disability moment since Jan 1996 when first "People with Disability" act was passed, which did not have any mention of Thalassemia. Our President Km Surrendar Saini Ji

played a key role in bringing thalassemia in the first amendment list. We had written countless letters, had innumerable meetings with the authorities & activists of other disabilities and participated in various meetings, workshops and protests to strongly put our demand for inclusion of Thalassemia in the list of disabilities for the purpose of disability act. We are delighted to say that at last we have got Thalassemia, Sickle cell anemia and Hemophilia included in the "Disability Act 2016". The act was passed by the parliament on eve of our last conference 9th NTC, 16th December 2016. Persons affected with blood disorders have not been given reservation in the act. We are continuing our fight to achieve this necessary amendment.

Central Government notified the guidelines for the purpose of assessing the extent of specified disabilities in a person on 4th January 2018. The criteria of scoring the disability in Blood disorders like thalassemia and sickle cell was confusing so representation was made by various thalassemics, thalassemia associations and haematologists to make easy and feasible. New guidelines will be notified shortly.

Government of India has taken many initiatives for the care and control of Haemoglobinopathies in last 3 years. Formation of guidelines for Prevention and Management of Haemoglobinopathies, draft National policy on Haemoglobinopathies is ready, Rights of Persons With Disabilities 2016 passed, rules notified etc. are some of them. Thalassemics can now envisage normal healthy life with esteem and dignity. The great soul behind all these developments is Mrs. Vinita Srivastva, Senior National Consultant in Ministry of Health and Family Welfare Govt. of India, under the guidance and able leadership of Mr. Manoj Jhalani Additional Secretary and Mission Director National Health Mission. I have no hesitation in saying that all Thalassemics are indebted to Mrs Vinita and Mr Manoj Jhalani for their yeoman's work for the cause of Thalassemia

As human needs and wishes never end we would like to request the duo great angel officials to accomplish our following demands also.

- NAT tested blood without replacement
- Free all three chelating agents for every thalassemic
- Thalassemia screening of all pregnant women
- Anti Natal diagnostic facilities in all state capitals

I am confident that if we all (Thalassemia associations, medical fraternity, central & state governments) work together these goals are feasible within a decade.

Challenges in Diagnosis of Thalassemia Syndromes

- Dr. H. Pati

The haemoglobinopathies are a group of autosomal recessive disorders characterised by either a reduced synthesis of one or more normal globin chains (the thalassaemia), the synthesis of a structurally abnormal globin chain (the hemoglobin variants) or in a few cases by both phenotypes (the reduced synthesis of a Hb variant, e.g. Hb E). As a group they are the most common single gene disorder in the world and are found at high frequencies in many geographic areas where falciparum malaria has been or still is prevalent, due to carriers being protected against dying from malaria. The Thalassemia are diseases caused by decreased expression of one of the two globin chains of the hemoglobin molecule. Decreased expression can result from deletion of the structural genes, mutations that result in decreased RNA synthesis, processing, or stability; or mutations resulting in decreased protein synthesis or stability

α-Thalassemia is the most common single-gene disorders with more than twenty percent of the world population being affected α-Thal is also commonest Hemoglobinopathy in India, but it is not a cause of serious genetic risk, as milder form (- α/α α) seen in India. In India Incidence of Beta Thalassemia among Sindhis, Punjabi Hindus, Lohanas, Jat Sikhs varies from 1.5 - 3.6 % in different states across the country.

The diagnostic challenges occur in the following scenarios.

- B-thal Trait with normal / Borderline HbA2
- α- thal trait hidden along with other Hemoglobinopathy
- mimics another Hemoglobinopathy (Misdiagnosis)
- difficulty in identifying rare Hemoglobinopathy
- post- transfusion suppression of Hb F/ dilution: Diagnostic problem as diagnostic criteria not fulfilled. Also small peaks of Hb E/ D from donor create problem
- Diagnostic difficulty in complicated states : hypersplenism, IDA, megaloblastic crisis, Aplastic crisis

For detection of beta Thalassemia trait conventionally Hb A2 levels are used. CBC parameters are only suggestive, but are not diagnostic. The conventionally used CBC counts with a high RBC count, low MCV, MCH and normal RDW can be seen in other conditions along with BTT , like the following conditions:

- In B-thal trait (BTT)
- αα/-- thal trait
- δβ-thal trait
- Hb E trait
- Hb EE homozy state
- Hb DD homozy state
- BTT with Hb Q India
- Hb H dis (some cases)

BTT may occur with normal or borderline HbA2 in conditions such as Silent BTT mutations, βTT + αTT, and when in association with Hb H.

Molecular defects in α- Thalassemia :

The Deletional (α0-thal) is common in south east Asian countries such as in Philippines, China, Thailand, with gene frequency is approximately 3-15% . Also, α+ -thal [either deletional (-α) or non-deletional (αT) also occur in these countries.
Indian Hb H pts Genotypes commonly are
––SEA/– α3.7, ––SA/– α3.7, ––SEA/– α3.7 Sallanches, ––α3.7/–α3.7Sallanches .
[SEA/THAI / MEDTERANEAN are α0 types.. α3.7 & α4.2 are α+ types.

Hb H Disease

In Hb H disease, Hb H variable ranging from 1- 20%, levels are more in α0 cases. HbH being a fast moving Hb has mobility higher than HbA at alkaline pH and has a tendency to form multiple small inclusions on being incubated with a redox dye such as brilliant cresyl blue (Golf ball inclusions) If the presence of HbH is suspected in these cases it is reasonable to reduce the length of time that the gel is run.
They present with Leg ulcer, Gallstones, Jaundice, hypersplenism is common. Acute haemolytic episodes are frequent, triggered by fever, infection, pregnancy, oxidant drugs. Hb H data from AIIMS data included 9 pts with the age ranging from 1-50 yr and the clinical features were jaundice (3/9 patients) ,hepatosplenomegaly (4/9 patients),intermittent Transfusion required in 6/9 pts HbA2 low 0.8%–1.7%, Hb H (by CZE) mean 5.6% (range: 1.4%–30.3%) Hb H inclusion test positive in all 9/9 cases.

Thalassemia l Intermedia: diagnostic issues
-The commonly encountered molecular defect in Thalassemia Intermedia are as follows:

Homozygous B-thal with mild [β+] or silent β-globin mutation
Hb S-B thal/ Hb E-B thal
Co-inheritance of determinants of ? λ-chain [Gγ Xmn1 polymorphism ? High Hb F]
Hb H disease
Dominant B-thal
Unstable haemoglobins
Co-inheritance of α-thal [triple- α] in Homozygous B-thal
BTT with Hb Lepore

Major Clinical differences in Thaassemia versus Major versus Thalassemia Intermedia:

Gallstones are seen in 10-20% versus 55-65% patients in Thalassemia Intermedia, this problem is accentuated by about 6% of Indian population having Gilbert's heterozygygote genotype. Extramedullary haematopoiesis is seen in nil to 20-25% pts whereas venous thrombosis is seen in nil to 22-28% pts. Leg Ulcer in nil to 20-30% patients. Many BTT present with jaundice are due to this.

Hereditary Unstable Haemoglobin

Hb HPLC Hb CZE in these cases may be normal or misleading with falsely high Hb A2 and or

increased Hb F. The PBS findings may be normal or highly abnormal and in some cases there may be gross mismatch with HPLC/HBCZE report. Heinz body test in these cases is positive. β-globin gene sequencing gives definitive diagnosis.

Dominant β-thalassaemia and related diagnostic difficulties

In cases of Dominant β-thalassaemia on HPLC only Hb A2 increased. On doing parental studies BTT is seen in only 1 parent. However these are clinically severe (like Thal Intermedia): and present with, splenomegaly, jaundice, gallstones, iron overload, extramedullary hematopiesis, and increased reticulocyte count. Heinz body test is positive .Molecular study a must for diagnosis. There are More than 30 dominantly inherited alleles producing unstable β-globin chain.

IDA complicates Diagnosis in cases:

Increased Severity of anemia these cases is wrongly diagnosed as Thalassemia Intermedia as anemia is disproportionate to Hb variant. In Thal trait, Hb A2 is lower, in Hb E trait quantity of Hb E is lower, in Q India trait quantity of Hb Q lower.

Dilemma of whether a patient is a Carriers of δ thal or HPFH :

In Both these cases there would be increased Hb F [5-30%] however in δ thal Thal trait there is anemia , Microcytosis, and heterocellular Hb F distribution. Though HPFH mostly are asymptomatic, but non-deletion types can show Microcytosis and heterocellular Hb F distribution also.

Investigating Post-transfused pts

HPLC/ CZE may show small variant of peaks of asymptomatic donor with HbS, HbD Punjab , HbE trait (upto 14.0%) .

Multi-transfused β-Thal major pt showing Hb F of 6%; due to suppressed Hb F , may not be suspected of it & unnecessary bone marrow may be done to diagnose other conditions such as DBA/ CDA

To conclude

- Diagnosis of hemoglobinopathies requires an integrated comprehensive approach using relevant clinical details, RBC indices, peripheral blood morphology, Hemoglobins detection & quantification must be done along with parents / family studies. sometimes molecular methods must be used .

Thalassemia Minor and Major: Current Management

-Dr. V.P. Choudhry

Key Words:
Thalassemia Minor, Thalassemia Major, Chelation Therapy, Long term Survivals

Abstract

Thalassemia is common genetic disorder. It has been estimated thta nearly 5 crores persons have thalassemia carrier in our country. They are asymptomatic and are deducted on blood tests. These persons are at same risk of developing iron deficiency anemia and need iron therapy in presence of iron deficiency anemia has been reviewed.

Nearly twelve thousands children with thalassmeia major (Homozygous state) are born every year. These children often present with significant anemia along with hepatosplenomegaly during infancy. These children require early diagnosis & institution of therapy with repeated blood transfusion & chelation therapy. Adequate dose of chelation therapy is essential to maintain serum ferritin around 1000 ng/ml. With present protocol of management thalassemic children have near normal life. Bone Marrow Transplantation offers cure for these children. Results of bone marrow transplantation are best when performed below 7 years of age.

Thalassemia Minor

India has ethnically diverse population of 1.25 billion. Prevalence of Thalassemia carrier / trait / minor varies between 1 to 17 % of population with an average of 3.5%. In a large multi-centric study undertaken in six states of India by Indian Council of Medical Research involving over 56000 school children the prevalence of thalassemia minor was 2.78%.[1] It is heterozygous state and individual has mutation in one chain of β globin for hemoglobin. Individuals with Thalassemia minor are usually asymptomatic. They often have mild anemia varying between 9-11 gm/dl. Some individuals have normal hemoglobin levels. Anemia worsens in presence of nutritional deficiency such as iron, folic acid or vitamin B_{12}. Red cell indices reveal MCV below 80fl and MCH below 27 **picograms**/cell. Red cell counts may be normal or slightly increased. Peripheral smear show microcytic hypochromic picture with occasional target cells. Diagnosis of Thalassemia minor / carrier / trait / is confirmed by estimation of Hb A_2 which is more than 3.5% on hemoglobin electrophoresis by HPLC. It is essential to differentiate it from iron deficiency anemia[2] (Table 1). Rarely Hb A_2 may be low in presence of severe iron deficiency anemia due to suppression of hematopoiesis. In such a situation hemoglobin electrophoresis by HPLC should be repeated after correcting iron deficiency anemia. Thalassemia carriers have same risk of developing iron deficiency anemia

as general population. They should be given iron therapy whenever they have evidence of iron deficiency anemia.

Now silent thalassemia carrier state has been identified in which person are asymptomatic and their all RBC indices such as hemoglobin level MCV, MCH are within normal limits. In some cases HbA_2 levels even may be normal. Silent carriers are suspected when children are diagnosed as Thalassemia major. Following mutations have been identified in persons with silent thalassemia carrier state. At times some individuals with homozygous state with these mutations are asymptomatic.

1. Cap + 1 (A-C) (4% of carriers in Punjab have this mutation
2. IVS-II – 844
3. 92 C (C-T)
4. 101 ?(C-T)

It is essential to exclude silent carrier while counseling a individual with thalassemia minor for marriage.

Management

Persons with thalassemia minor are usually asymptomic. There hemoglobin levels may be normal or mildly sub-normal. Hemoglobin levels are usually vary between 10-12 gm/dl. Various hematological parameters are normal including serum iron studies and serum ferritin levels.

Except the MCV and MCH are low while RBC is higher. These individuals are at the same risk of developing anemia as in general population. The causes of anemia in these individuals are similar to the community. Iron deficiency anemia is the most frequent and thalassemics minor are at the same risk of developing IDA. Thalassemics minor should be given iron therapy as and when indicated. IDA cannot be diagnosed on peripheral blood picture alone as microcytic and hypochromic picture is observed in IDA as well as in thalassemia minor. The diagnosis of IDA can be established by serum iron studies or by serum ferritin levels. Iron therapy in these individuals should be administered for period of six months after establishing its diagnosis. It is essential to determine the underlying cause of IDA which also needs appropriate management. Iron therapy if given imperically does not lead to iron overload. All these individuals should receive folic acid routinely. Generally it is belived that persons with thalassemia minor should not be given iron therapy because they will develop iron overload which is totally wrong belief among doctors of various systems of medicine.

Anemia in these individuals may develop from other causes such as megaloblastic anemia,

anemia secondary to blood loss to various factors, PNH, refractory anemia,celiac disease, aplastic anemia, mylodysplastic anemias etc. These patients will need appropriate treatment after establishing the diagnosis.

Thalassemia Major

WHO has estimated that 4.5% of the World's populations are affected by Thalassemia & allied disorders. Thalassemia belt that spans across counteries such as Italy, Greece, Cyprus, Sardinia, Turkey, Saudi Arabia,[3] Iran, Afganisthan, Pakistan, India & South East Asian countries Indonesia, Burma & Thailand. (Fig. - 1). National wide survey by ICMR under Jai Vigyan Mission project has revealed that nearly 4% of people in India have Thalassemia Minor (5 crore), while nearly twelve thousands children with Thalassemia major are born in India every year. There are nearly 1.25 lakh Thalassemic children in India. Thalassemia is very common in certain communities like Punjabies, Sindhis, Gujaratis, Bengalies, Parsis etc. It is more common among Punjabies who have migrated from West Pakistan with prevalence of over 15%. Prevalence of Thalassemia in Northern Western & North East Part of India is higher while it is less common in South. Hemoglobin E. Disease either alone or in combination with Thalassemia is much more common in North Eastern states.

CLINICAL PRESENTATION :-

It is serious inherited blood disorder in which red cell survival in greatly reduced due to imbalance between α & β chains. The clinical picture is dependent on four major factors viz (i) reduced hemoglobinisation of red cells (ii) incresed hemolysis (iii) ineffective erythropoiesis & (iv) extramedullary hematopoiesis.[4]

Infants are normal at birth & develop anemia between 3-18 months of age. Anemia is progressive, persistant and does not respond to any hematanic therapy. Infants become irritable and have poor development if left untreated. They develop prominence of frontal, facial bones and hepatosplenomegaly as a result of ineffective erythropoiesis. Facial changes are termed as thalassemic facies. (Fig II) They are at higher risk of developing recurrent infectious due to decreased immunity. Iron absorbtion increases as a result of (a) hypoxia and (b) ineffective erythropoiesis which gets deposited in skin, liver, heart & endocrine glands. However, the main source of iron overload in these children is from blood transfusion. Poor growth, abnormal facies and hepatosplenomegaly does not occur if these children are managed early with current protocols.

DIAGNOSIS

It is based upon the presence of (a) moderate to severe anemia (b) reduced red cell indicies such as MCH, MCV, MCHC (c) microcytic & hypochromic picture with anisocytosis and poikilocytosis on peripheral smear (d) increased foetal hemoglobin level for age (20-90%) and normal or reduced Hb A_2 levels. Bilirubin levels may be raised which will be predominently unconjugated. S. Iron levels, transferrin saturation & ferritin level may be normal or raised depending upon the age of the child. Radiological changes are often present in older children, which are secondary to marrow expansion which include sun-ray appearance of skull, cortical thinning of long bones with osteoporosis of vertebrae and (b) small bones of hands & feet.

MANAGEMENT

With current protocols of management (Table II) it has been observed that children born after 1995 have normal life. (Fig. III)

BLOOD TRANSFUSION THERAPY

Current recomendations state blood transfusion therapy should be initiated as soon as diagnosis is established & if hemoglobin levels are below 7 gm /dl at least on two occasions.[5]

Investigations such as :- a) Complete blood grouping (ABD, Rh, + along with Kell, Kidd, M,N, lewis etc systems b) Family studies for genetic counselling c) HLA typing of sibling & parents for future possibility of bone marrow transplantation. Should be carried before starting transfusion therapy & d) Hepatitis B vaccination should be given if it has not been given earlier.

Among various transfusion regimens now it is recomended to treat these children with high transfusion therapy in which pre transfusion hemoglobin should be maintained at 10 gm because of its multiple advantages (Table III)

It is preferable to transfuse fresh blood which is leucodepleted as transfusion of lymphocytes results in (a) suppression of the immune system and (b) reduces the risk of non hemolytic febrile reaction, (c) prevents the development of alloimmunisation of human leucocyte antigen (HLA) class I antigens and (d) prevents CMV infection. Packed cell transfusion should be given at 3-4 weekly interval and each time 10-15 ml/kg of blood can be transfused over 3-4 hours.

Approximately 180 ml/kg of packed cell are required per year in non splenectomised children. Children with cardiac disease or in presence of congestive cardiac failure should receive only 5 ml / kg of blood under close monitoring.

CHELATION THERAPY

Each unit of packed cell contains 200-250 mg of elemental iron which is released in the body with breaking of red cells. It is the major source of iron which gets deposited in liver, heart & various endocrine glands. Increasing iron deposition in various organs results in their dysfunction. Body iron levels can be measured by (a) serum ferritin (b) liver & cardiac biopsies, (c) SQUID & MRI T_2. Ferri scan etc. Among these serum ferritin in most practical & can be monitored every three monthly. Among various other tests MRI T^*_2 is now practical and provides liver & cardiac iron overload more precisely. Now, it is of great help in chelation therapy. Other tests are carried to assess the function of various organs, such as ECHO, TSH, T3 T4, growth hormone levels, serum Testesterone, FSH, LH, bone mineral density etc.

Presently three iron chelators have been approved & are being widely used either ringly or in combination to ensure effective chelation therapy. Chelation therapy should be initiated when S. ferritin is > 1000 ng/ml or child has received 15-20 units of transfusion.

Desferrioxamine (DFO) is an hexadentate where one molecule of DFO binds with one molecule of iron. It has very short life & needs to be administered continuously with the help of infusion pump subcutaneously (SC) over 12-14 hours daily. It should be started by 2 years of age & ferritin level should be maintained between 1000-1500 ng/ml. Its dose is 30-50 mg / kg/day. Addition of vitamin C (100 mg / day) increases the iron excretion. It is fairly safe & has minimal toxicity. Its parentral administration may results in bradycardia, hypotension, rigors, headache, photophobia. Subcutaneou administration causes local pain, induration, irritability & redness. Prolonged administration may results peripheral field defects, sensori-neural hearing loss.

Deferiprone[6] was the first oral drug developed in Hider's laboratory. It has been shown to the effective in dose of (70-100 mg / kg /day). It is more effective than DFO in mobilizing intracellular iron from the heart. It needs to be given in 2-3 daily doses. Its side effect include nausea, abdominal pain, diarrhea. Nearly 20% of children wiht high serum ferritin level develop arthropathy and less 1% develop severe neutropenia.

ICL 670 is new class of tridentate two molecules of chalator binds with one iron molecule to

form ferric molecule complex. It is twice as effective as DFO. It chelates iron from reticulo-endothelial cells and parenchymal cells of various organs. It also prevents myocardial cell iron uptake & removes iron directly from myocardial cells. This drug has half life of 11-16 hours & needs to be given in single dose of 30-40 mg / kg daily. Its side effects include abdominal pain, diarrhoea, vomiting skin rash etc. These symptoms are usually mild. There is no arthralgia, cardiac, occular or vestibular side effects. Now, it is considered as gold standard chelating agent.

COMBINATION THERAPY.

Children who have high levels of serum ferritin or have cardiac liver & endocrine dysfunctions should be treated with combination therapy such as. a) DFO & deferiprone b) DFO & ICL – 670. or c) Deferiprone & ICL – 670.[7] The advantage of combination therapy includes a) Access to different iron pools, b) prevents non transferrin bound iron accumulation, c) better compliance and above all improves quality of life. DFO may be given twice or thrice a week while other agents are given daily. It is preferable that combination therapy should be administered under supervision of an expert care.

SPLENECTOMY

It has been proved that if we maintain hemoglobin above 10 gm /dl, hypersplenism doesn't occur. With standard treatment, splenomegaly and hypersplenism have become a rarity in the developed countries. However, in our country many children develop splenomegaly and hypersplenism because of poverty and poor facilities. If the child has already developed splenomegaly and signs of hypersplenism, then splenectomy is indicated. It should be undertaken only after 6 years of age because of higher chances of sepsis. Splenectomy is also indicated if the yearly requirement of packed cells is 200 cc/kg or more. Decrease in WBC and platelet count is a late manifestation of hypersplenism. All children needing splenectomy should receive pneumococcal, H influenza and meningococcal vaccine at least 3 to 4 weeks prior to surgery. The family should be counseled regarding the risks & benefits of splenectomy. Prophylactic penicillin therapy must be continued life-long after splenectomy. Episode of infection should be treated promptly with broad spectrum antibiotics and children should be hospitalized. All efforts should be made to isolate the micro organism for appropriate antibiotic therapy.

BONE MARROW TRANSPLATATION

It offers permanent cure and better future for children. The credit for the first bone marrow transplantation in thalassemia major goes to E. Donald Thomas who performed this procedure

in an 18 month old thalassemia child in 1982 using a HLA matched elder sister as donor. This child was cured of thalassemia. Since then many centers in the world and twenty five in India have initiated BMT facilities. The principles of bone marrow transplatation include (a) to destroy and prevent regeneration of defective stem cells, (b) sufficient immune suppression for good engraftment, (c) to infuse stem cells with the normal gene, (d) to prevent GVHD with proper combination of immuno suppression and infection management.[8]

Three most important adverse prognostic factors for survival and event-free survival have been observed in large studies which include. a) Presence of hepatomegaly (2 cm below costal margin), b) Portal fibrosis & c) Iron overload (S. Ferritin > 1000 ng/ml).

Based upon these factors children have been divided into three classes. Class I when all these factors are absent. Class II when one or two factors are present and children with presence of all factors are termed as class III. Event free survival in more than 97 percent of cases in class I & 66 percent in class III cases. All children should be treated with current protocols to maintain them in class I & perform BMT at the earliest possible.

LONG TERM SURVIVALS

Over the years long term survivals with current management protocols have increased significantly. Multi centric studies has revealed that children born after 1995 have near normal life (Fig III).[9] In our country survivals have improved and majority of children have seen in second and third decade of life who are on adequate transfusion and chelation therapy form early childhood.

KEY MESSAGES :-

1. Thalassemia is very common in country.
2. Diagnosis should be established during infancy.
3. Current protocols of therapy have improved the survival & quality of life. Now, child can live near normal life.
4. Bone marrow transplant offers, complete cure & should be undertaken as soon as possible

Table – I Differences Between IDA & Thalassemia Minor

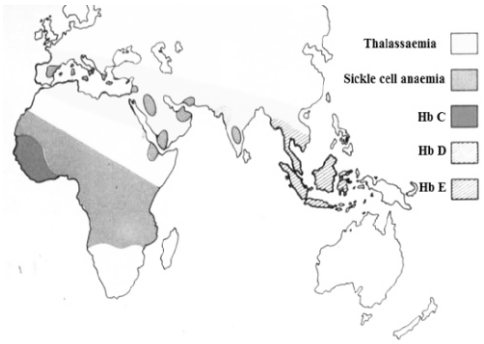
TABLE II. Principles of management.

i) Regular blood transfusion to maintain pre transfusion Hb above 10 gm/dl
ii) To maintain S. Ferritin level below 1000 ng/ml by use of irons chelators either singly or in combination.
iii) Early detection & management of complications of blood transfusion & chelation therapy
iv) Regular monitoring of growth & development, hematological & biochemical parameters.
v) Spleenectomy if required
vi) Early detection & management of endocrine problems
vii) Pyschosocial support.

Table : III Advantages of high transfusion

i) Ensures normal growth & devleopment
ii) Decreases ineffective erythropoiesis & prevents osteoporosis & facial deformities.
iii) Prevents splenomegaly
iv) Decreases iron absorption from intestines
v) Normal development of immune system
vi) Normal physical & psychological well being
vii) Better quality of life

Figure1: World Map of Thalassemia



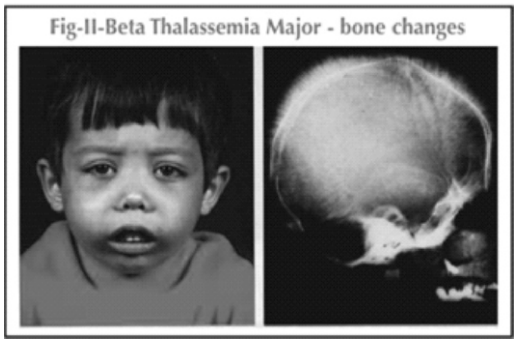
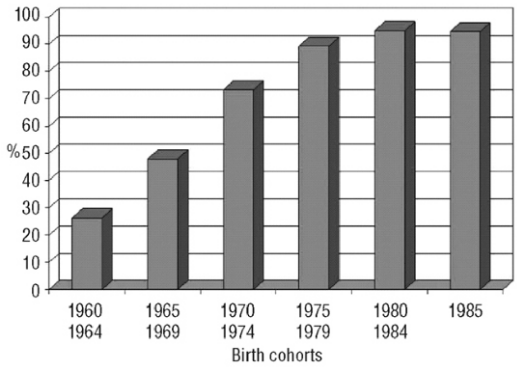


Figure 3: Survival in 2009 of Italian patients included in the Seven Centers Study, according to birth cohort.



(Ref of Fig 3: Caterina Borgna-Pignatti. Haematologica March 2010 95: 345-348)

Splenectomy -3Ps (Prevantion Planning & Post Care)

-Dr. Alok Hemal

INTRODUCTION

Thalassemia belongs to a heterogeneous group of disorders where there is a defective synthesis of haemoglobin chains. Depending on the type of chain affected they are classified into alpha and beta thalassemia. The major pathophysiology is an increased susceptibility of red blood cells to destruction in the reticuloendothelial system, mainly in the spleen, resulting in its enlargement (splenomegaly). Although the requirement of splenectomy has been reduced in the recent years many patients still require splenectomy. The major therapeutic rationale for the procedure is to decrease blood consumption in transfusion dependent patients with the ultimate goal of reducing the iron overload.But as spleen plays important role to remove micro-organisms and produce antibodies to enhance the immune response,the role of splenectomy in non transfusion dependent patients is controversial and also due to increased complications of the procedure like thromboembolism. This emphasizes the need for the examination of spleen through physical examination and/ or by ultrasonography throughout the followup care of these patients.

INDICATIONS OF SPLENECTOMY

- Splenectomy is the main therapy in reducing hemolysis,leading to a significant rise in red cell span .
- Splenectomy is reserved only for certain situations due to risk of thromboembolism, pulmonary hypertension and infections. Splenectomy should generally be avoided in NTDT patients younger than 5 years

The common indications for the procedure are:

- Worsening anemia leading to poor growth and development
- When transfusion therapy is not possible or iron chelation therapy is unavailable
- Hypersplenism leading to worsening anemia, leucopenia, or thrombocytopenia and causing clinical problems such as recurrent bacterial infections or bleeding
- Splenomegaly accompanied by symptoms such as left upper quadrant pain or early satiety
- Massive splenomegaly (largest dimension >20 cm) with concern about possible splenic rupture

INDICATION	COMMENT
Increased blood requirement that prevents adequate control with iron chelation therapy	Annual transfusion volume (75% haematocrit) used to flag an increased blood requirement (200–220 ml/kg/year) Alloimmunization, concurrent infections, suboptimal transfusion therapy should be ruled out
Hypersplenesim	Alloimmunization, concurrent infections, suboptimal transfusion therapy should be ruled out
Symptomatic splenomegaly	Cytopenias
	Accompanied by symptoms such as left upper quadrant pain or early satiety
	Massive splenomegaly causes concern about possible splenic rupture

PREVENTION

The need for splenectomy is reduced through the early diagnosis and initiation of transfusion.

- Timely diagnosis
- Initiation of regular transfusion protocols
- Sometimes splenomegaly due to periods of under-transfusion with blood of inappropriately low haemoglobin may be reversible. In this situation, the patient should be placed on an adequate transfusion program for several months and then re-evaluated before considering splenectomy
- Chelation therapies
- Regular follow up and monitoring through physical examination and investigations

PLANNING

There are many approaches for the splenectomy procedure including laparoscopic techniques. Regardless of the procedure of choice, every splenectomy patient must undergo a thorough preoperative assessment which includes a physical exam, adequate size measurements of the spleen obtained using ultrasonography, blood counts and workup for coagulopathy as well as

obtaining informed consent.Intraopreative antibiotics like broadspectrum antibiotics(ceftriaxone/cefotaxime) with vancomycin should be given depending upon the severity and susceptibility of infection.Proper care to be taken for perioperative complications like bleeding,atelectasis and subphrenic abscess. Subcutaneous heparin injections and compression stockings should be used as deep vein thrombosis prophylaxis. The most important being the immunisation against the capsulated bacteria to prevent OPSI (Overwhelming Post Splenectomy Infection). The most important being *Streptococcus pneumonia* followed by *Hemophilus influenza* and others.For urgent or emergency splenectomy vaccines are given on at least 7days postoperatively or on day of discharge whichever comes first.It is safe to give all vaccinations at same time using different sites.

Streptococcus pneumoniae	At least 2 weeks in advance of a splenectomy and then in 3-5 years	• Rate of protection is 70-85% • The immune response is poor in children less than two years of age
Haemophilus influenzae type B	At least 2 weeks in advance of a splenectomy and single dose	
Neisseria meningitides	At least 2 weeks in advance of a splenectomy and then in 3-5 years	
Influenza virus vaccination	Annual	• To prevent this febrile illness that might otherwise require intensive evaluation and management of a febrile episode in the splenectomised host

POST OPERATIVE CARE

The immediate post operative period requires appropriate fluid management. The prophylaxis for DVT (Deep Vein Thrombosis) should be given due to increased risk in these patients. Portal vein thrombosis is documented in 0 to 50% patients after the procedure and is managed with anti coagulant therapies. Hematologic derangements such as granulocytosis and thrombocytosis are common. Anti platelet is reserved for platelet levels above $1000x10^9/L$ The most important care in post splenectomy patients is important as the risk for infection remains life-long. The patients who underwent emergency splenectomy should receive immunisation within 7 days post-op. They should be prescribed with anti microbial prophylaxis for the prevention of same and to treat the infections.

Minimum recommendations for duration of antibiotic prophylaxis:

- Prophylaxis for at least three years following splenectomy
- At least 6 months following an episode of severe sepsis

Consider lifelong prophylaxis for:

- Patients who have had an episode of severe sepsis, particularly after a second episode
- Patients on immunosuppressive therapies

Child Antibiotic Prophylaxis

First line Under 1 year Penicillin V 62.5mg bd

1 – 5years Penicillin V 125mg bd

5-18 years Penicillin V 250mg bd

If cover also needed for H.*influenzae* in child give amoxicillin instead

If penicillin allergic, macrolides like Roxithromycin or Erythromycin are used. Amoxicillin is used as a standby antibiotic.

The patient education is very important after the procedure.Patient should be given charting regarding dos and don'ts and immunisation cards and antibiotics prophylactic checklist. Early consultation should be advised if any symptoms develop. They should be advised for the minimal animal handling. Patients travelling to endemic areas should receive appropriate chemoprophylaxis for malaria as they are severe in asplenic patients.

CONCLUSION

In certain group of thalassemic patients who are transfusion dependent with complications such as hypersplenism, splenectomy is still indicated.Evenafter total splenectomy, the relief offered to thalassemia patients is temporary. The complications of the procedure which were a major concerns before has been reduced after the introduction of improved operative techniques and prevention of infections through the immunisation and prophylactic antibiotics. OPSI which is a dreaded complication has been reduced through the same. However the role of splenectomy in non transfusion dependent patients is still a debate and further studies are warranted.

Monitoring of Transfusion Therapy

-Dr A.P. Dubey

Transfusion Therapy:
Red blood cell (RBC) transfusions are the principal supportive intervention for patients with thalassemia major (TM), and are used intermittently in thalassemia intermedia. In patients with TM, transfusion therapy is often initiated before one year of age. All thalassemia patients need to maintain a pre-transfusion hemoglobin level between 9.5 to 10.5 gm% for their optimum growth and development. Complications directly related to transfusions include blood-borne infections, development of anti-RBC antibodies (both auto- and alloimmunization), and allergic, febrile or delayed hemolytic transfusion reactions.

Transfusion requirements
For chronically transfused patients, a complete blood count (CBC) should be obtained prior to each transfusion, with the goal to maintain a pre-transfusion hemoglobin level of 9.5-10.5 g/dL. For this, they require transfusion of 15 ml/kg body weight of packed red blood cells at an interval of 3-4 weeks for the whole life. Therefore a close monitoring of the Hb level (both pre and post transfusion), annual blood requirement, any transfusion reactions and other side effects is mandatory. It is recommended to obtain a RBC antigen profile prior to initiating transfusions, which aids in clinical evaluation should new RBC antibodies develop. Extended RBC antigen matching beyond ABO and RhD to include C, E and Kell is recommended in thalassemia because allo-antibodies are most commonly directed towards these antigens.

Transfusion reactions

All patients with thalassemia should be monitored for allergic and febrile transfusion reactions, which typically occur during or immediately after transfusion. Premedication with acetaminophen and diphenhydramine should be considered in patients with a history of febrile or urticarial reactions, respectively. Immune-mediated hemolytic transfusion reactions can be acute or delayed up to 14 days. During a reaction, laboratory evaluation may reveal a new RBC allo- or autoantibody, anemia, indirect hyperbilirubinemia, and/or hemoglobinuria. When present, anti-RBC antibodies can complicate cross-matching, reduce survival of transfused cells and delay safe provision of blood. There is limited published support for immunomodulation to treat allosensitization. The alloimmunization rate among transfused patients enrolled in TCRN studies was 16.6%]. The most common RBC antigens identified in alloimmunized patients were anti-E, -Kell, -C and -Kidd. When pre-transfusion hemoglobin levels are significantly lower than predicted based on transfusion volume and interval in an asymptomatic patient, laboratory investigation for a transfusion reaction should be considered.

Transfusion-associated infections

Transfused patients with thalassemia should receive all routine age-appropriate immunizations and should have annual surveillance serologic testing for Hepatitis A, Hepatitis B, Hepatitis C, and HIV. As testing for Hepatitis C has become widely available, fewer young

patients seroconvert. Once a patient has seroconverted for any of these pathogens, annual surveillance practices should follow disease-specific guidelines, such as annual liver ultrasound and alpha-fetoprotein monitoring for risk of hepatocellular carcinoma secondary to Hepatitis B or C.

Ideally transfusion facility for these patients should be available in a dedicated Day care center with facilities of Hb estimation, blood transfusion, emergency drugs, data recording and some recreation activities. Table I summarizes the various monitoring activities.

Growth & Bone Disease

Growth failure occurs in 25-28% of patients, regardless of the thalassemia syndrome. Contributing factors include chronic anemia or inadequate transfusion support, chelation toxicity, nutritional deficiencies, growth hormone deficiency, and other iron-associated endocrinopathies as outlined above. Children and adolescents with thalassemia should have linear growth and weight measured regularly. Patients receiving chronic transfusion therapy should be assessed at least quarterly. Growth velocity should be calculated annually from birth until the end of the growing period (females: 18 years, males: 21 years). Sitting height should be measured every 6 months to assess for truncal shortening associated with chelator toxicity. Head circumference should also be measured every 6 months to assess for skull changes due to anemia and ineffective erythropoiesis

Endocrine Effects:

Hypogonadism

Hypogonadism occurs in 50-60% of patients with thalassemia major. Iron deposition in the pituitary results in deficient gonadotropin secretion (secondary hypogonadism), and is partially reversible by intense chelation therapy. Clinicians should be familiar with pubertal manifestations, their onset, and examination by Tanner staging to evaluate for hypogonadism. Lack of sexual development by age 13 years in girls or 14 in boys, primary amenorrhea by age 16, or secondary amenorrhea should all prompt further evaluation. Adolescents should undergo complete physical examination with Tanner staging every 6 months throughout puberty. Failure to complete puberty within 4 years after its onset may also indicate development of hypogonadism. Annual monitoring of serum gonadotropins (LH and FSH), early morning testosterone (for males), and estradiol (for females) are biochemical markers that can be helpful in the evaluation of hypogonadism. Menstrual history and reproductive health should be reviewed annually.

Diabetes

Diabetes mellitus has been reported among 14% of transfused patients with thalassemia major in North America. Limited data suggest that both low serum insulin, due to iron-induced beta cell toxicity, and insulin resistance are involved in its pathogenesis. In the TCRN, patients

were screened with a fasting glucose annually beginning at age 10 years. Hemoglobin A1C, which is used as an index of diabetes control in the general population, is unreliable in thalassemia because it is affected by hemolysis and regular transfusions.

Hypothyroidism, Hypoparathyroidism and Calcium Metabolism

The prevalence of hypothyroidism in thalassemia is approximately 8-10%, thus annual screening with free thyroxine (T4) and TSH concentration is recommended. Hypoparathyroidism occurs in 2% of North American patients with thalassemia and is associated with severe iron overload. Independent of hypoparathyroidism, patients with TM also have high rates of hypercalciuria, (up to 50%) and nephrolithiasis (approximately 10%). Therefore monitoring of serum and urine calcium along with annual PTH and vitamin D is also recommended.

Liver and Spleen:

Most of the thalassemics have liver and spleen enlargement. Major causes of hepatomegaly include iron deposition, extramedullary hematopoiesis and liver fibrosis. Therefore liver size should be measured regularly at 3 monthly intervals. Spleen plays a major role in removing defective RBCs from the circulation and hence enlargement of spleen is a usual feature in these patients specially in those who have not been able to maintain their Hb in the recommended range (between 9.5 -10.5g/dL). Splenomegaly creates problems in maintaining proper transfusion regimes and the blood requirement increases significantly. Hence splenic size monitoring is very important is these patients and should be done regularly at 3 monthly interval. If the annual PRBC requirement increases to more than 200ml, splenectomy may be advised. Post splenectomy, the transfusion requirement falls down significantly and becomes more stable.

Table I: Monitoring of Thalassemia Patients

Monitoring quarterly		Monitoring yearly	
Test	**Date**	**Test**	**Date**
Serum ferritin		HBsAg	
Billirubin total		Anti-HBs Ab	
Direct/indirect		HCV	
SGOT		HCV RNA	
SGPT		HIV	
SAP		Audiogram (if on Desferal)	
GGTP		Ophthalmology check up (if on Desferal)	
Proteins total		Blood sugar F	
Albumin		PP	
Globulin		$FT_{3\ (pg/ml)}$	
Urea		$FT_{4\ (ng/ml)}$	
Creatinine		TSH (I.u./ml)	
Uric acid		ECG	
Calcium		PTH	
Phosphorous		LH	
Height		FSH	
Weight		Oestradiol	
		Cortisol	
		Bone mineral density	
		Vitamin D levels	

Iron chelation assessment: MRI T2* is a necessity and not a luxury

-Dr. Praveen C. Sobti

Thalassemia syndromes are the commonest single gene disorders worldwide. There are approximately 1,00,000 patients with thalassemia syndromes in the country with nearly 10,000 new thalassemic children born every year. Optimal management of these patients involves safe blood transfusion, adequate iron chelation and multidisciplinary care for monitoring and treatment of complications.

Availability of oral iron chelators has improved dramatically the outcomes and the quality of life in these patients. Accurate and reliable assessment of iron overload forms the premise of appropriate iron chelation therapy. Various invasive and non-invasive techniques are available for assessment of iron overload. MRI has emerged as the standard of care for the same and plays an indispensable role in diagnosing and monitoring iron overload status in thalassemia.

Principles of MRI

Each tissue in the body has different magnetic properties due to variations in the number of hydrogen atoms and their interactions. When placed inside a magnet, the hydrogen atoms which are present in a random alignment otherwise, get aligned. Application of external energy to these aligned hydrogen atoms disrupts their alignment transiently. The hydrogen atoms return to their original state once the energy source is removed and transmit signal that can be acquired by the coils placed around the tissue. The time at which these signals are captured is called echo time {TE}. A normal tissue becomes darker with increasing TE.

Iron is stored in body tissue as ferritin and hemosiderin. Both of these are paramagnetic, i.e, they show magnetic properties when placed inside a magnet. The presence of these magnetic forces alters the alignment of hydrogen atoms in the tissue and the image on MRI becomes darker as compared to a normal tissue when measured at same TE. The darkening effect is similar to half-life of radioactive decay. The half-life of spin echo image is termed as T2 and that of a gradient echo image is termed T2*. R2 and R2* are the rates of signal decay and are reciprocals of T2 and T2*.

T2 (ms) = 1/R2 (Hz)

T2* (ms) = 1/R2* (Hz)

Iron overload in Liver: The liver iron concentration (LIC) measured by MRI shows significant correlation with serum ferritin as well as the LIC measured on a liver biopsy specimen. LIC gives a good estimate of total body iron as 70% of the total body iron is found in the liver. The iron uptake in the liver is transferrin mediated whereas in other organs like heart and endocrine glands iron toxicity is mediated by the non-transferrin bound iron. Hence, there

is no correlation between LIC and siderosis in the pituitary gland. There is correlation between LIC and cardiac iron overload only at high LIC.

Cardiac iron overload*: MRI T2 imaging is the primary method used to assess the cardiac iron overload. A stop-light schema (Table 1) has been derived based on the risk of development of cardiac arrhythmias and congestive heart failure.

	Red	*T2*<10 ms*
	Yellow	*T2* 10-20 ms*
	Green	*T2*>20ms*

There is no correlation with MRI T2* and left ventricular ejection fraction.

Iron overload in pancreas: Pancreas is the third most common organ studied in patients with iron overload. It has the advantage of being studied in the same T2* as liver. Pancreas iron precedes the iron accumulation in the myocardium. Absence of iron overload in pancreas has a 100% negative predictive value for cardiac iron overload. Pancreatic R2* has also been correlated with the risk of impaired glucose tolerance and diabetes.

Iron overload in pituitary gland*:* Preclinical iron deposition in the pituitary can be detected by the MRI, providing an opportunity to intensify chelation before gland shrinkage and permanent hypogonadism occur.

Benefits of MRI over other techniques

Serum ferritin is the most widely used parameter for the assessment of cardiac iron overload as it is easily available, inexpensive and can be repeated frequently. The trend of serum ferritin gives useful information regarding the body iron stores. A single ferritin value does not correlate well with LIC or myocardial iron overload. Serum ferritin is affected by factors like inflammation, hepatitis and ascorbate deficiency. Serum ferritin also underestimates the liver iron overload in patients with non-transfusion dependent thalassemia.

Merits and demerits of different techniques of iron assessment are discussed in table 2.

Technique	Serum ferritin	Liver iron content by liver biopsy	Hepatic and cardiac MRI T2*
Merits	Easily available Inexpensive Long term control linked to prognosis	Most reliable estimate of body iron status Gives information regarding liver inflammation	Non-invasive Not affected by inflammation Can detect preclinical iron overload.
Demerits	Indirect estimate Affected by other co-morbid conditions Does not reflect the individual organ status.	Invasive May yield false results due to patchy involvement Not easily acceptable to patients Difficult to obtain repeated values.	Technically demanding Requires a validated centre Cannot be repeated as frequently as serum ferritin

Clinical implications

1. Detection of preclinical iron overload: The ability of MRI T2* to detect the iron accumulation in heart and endocrine organs even before the development of the clinical symptoms has a profound effect on management of patients with chronic iron overload. A decline in left ventricular ejection fraction is more likely to occur in patients with cardiac MRI T2* < 10 ms and more than 50% patients with cardiac T2*<6 ms developing symptomatic heart failure in one year. This provides a window period in which the iron chelation can be intensified, thus preventing development of complications.

   The development of MRI has also helped in diagnosing and monitoring patients with de novo cardiac iron overload without severe hepatic iron overload. Long term data suggests that although severe iron overload in liver predisposes to cardiac iron overload but there is no LIC threshold that can rule out cardiac iron overload. A follow up MRI also helps in assessing response to chelation therapy.
2. Optimization of iron chelation therapy: Detection of iron overload in different organs helps in tailoring chelation therapy in patients with iron overload. Chelation therapy could be modified in up to 37% patients after MRI T2* in thalassemia patients.
3. Assessment of efficacy of different iron chelation regimen: MRI T2* is currently being used as an end point in all clinical trials on efficacy of different chelation regimen. A study in thalassemia patients from North India on long term deferiprone monotherapy found that these patients had a high probability of moderate to severe hepatic iron overload and low probability of severe cardiac iron overload. Patients

with hepatic iron overload can thus be started on alternate chelation regimen.

4. Improvement in survival: The cardiac MRI T2* helps in detection of iron overload and thus the likelihood of developing cardiac failure. The iron chelation therapy, thus, can be tailored as per the individual need and reducing the mortality in patients with iron overload. In a large cohort of patients from seven centres across Italy, absence of cardiac MRT T2* was found to be a strong predictive factor for death.

Guidelines for clinical practice

- All patients on chronic transfusion therapy should undergo an annual MRI scan to detect the cardiac and hepatic iron overload after the age of 10 years.
- Patients a cardiac T2* < 10 milliseconds should be evaluated at 6-month intervals given their risk of cardiac decompensation and patients in heart failure should be scanned at 3-month intervals.

Iron Overload Assessment with Magnetic Resonance Imaging Using T2* Methods

-Dr. Juliano Lara Fernandes

Introduction

Magnetic resonance imaging (MRI) is considered the gold standard for noninvasive assessment of iron overload in many different diseases. After its introduction in 2001 in a seminal paper by Anderson et al the mortality form cardiac diseases fell significantly in patients with thalassemia major (TM) in places of the world where the method gained widespread acceptance along with regular access to modern chelation therapies.

The role of MRI is now central to management decisions in iron overload and the most current recommendations statements and guidelines use liver and heart iron concentrations determined by MRI as the main guide to choosing chelation regimens and dosing. Because of the importance of this diagnostic tool in the care of patients with iron overload, this article will try to elucidate the main technical challenges in implementing, performing and interpreting MRI studies with T2* methods for clinicians taking care of such population

What is needed to perform liver and cardiac iron overload assessment with MRI?

To perform regular and accurate MRI studies for iron overload assessment there are three components to be addressed: (1) the MRI unit itself; (2) the necessary software to acquire the images; (3) the software to interpret and quantify the studies.

The MRI scanner used in these exams are standard 1.5T scanners whose manufactures usually are Siemens, GE and Philips. While it is possible to perform the exams at 3.0T, the technical challenges are higher and the upper limits of iron assessment in the liver are limited by the hardware. Therefore, in general, it is recommended that 1.5T scanners be chosen for this task.

These scanners are usually used for many different purposes and do not have to have any special hardware add-ons.

Once the hardware is resolved, the next step in performing the exams is to make sure that the scanner has the supplied software to acquire the images used for iron assessment. These programming codes are called sequences and already come with the scanners. While there are different sequences and ways to acquire liver images for iron overload assessment, this article will basically cover the T2* method as this is also the only one routinely used for the heart as well. Thankfully, in the last years most of the vendors mentioned have already included as a regular option the T2* sequences necessary to perform iron studies in the liver and heart. These sequences have now been standardized across different platforms and little changes are necessary to implement them out-of-the-box.

Once the images have been acquired, they should be interpreted for the quantification of the iron content in the different organs imaged. This can be done with dedicated commercial

software or be accomplished with other options using a spreadsheet or other non-commercial software. The basic principles are the same for every option as are the mistakes that can be made during this process. We have recently shown that the process is software independent and will result in the same numbers as long the general principles of the interpretation methods are followed.

T2* imaging

Both the liver and heart can be imaged with T2* MRI sequences. T2* is a measurement of time and represents the transverse relaxation of the signal after a radiofrequency pulse is applied to the tissue by the scanner. Without going into the more deep physics aspects of MRI, this relaxation time is one of the components generated by each tissue and depends on how coherent all the molecules sampled are aligned with the scanner's magnet field. Because iron disrupts the homogeneity of the field, the more iron there is in a determined tissue, the faster the signal intensity generated by that organ will drop. An explanation of this differences can be found in Figure 1. R2* is just the ratio of T2* calculated as 1000/T2*. It does not represent a different technique, just a different form of presenting the same number.

In order to construct the decay curves used to calculate the T2* values, during scanning the organ in focus (whether the heart, liver, pancreas, etc) is imaged with different echo times. These echo times represent the different time between the radiofrequency impulse generated by the scanner and the reception of the signal back to the coils which function as antennas that capture the signals echoed in the organs. With modern T2* sequences, all echoes (usually in the number of 8 to 12) are generated in only one single 10-12 second breath-hold. Therefore, to generate the T2* decay curves for each organ, only one single breath-hold is needed. This is why more than one organ can be analyzed in the same exam, the differences being only in changing the imaging plane and adjusting for ECG gating in the case of the heart. The technical details for each sequence are beyond the scope of this manuscript and can be found in the reference papers. For the liver only one type of T2* sequence is normally used with the pancreas being imaged in the same way. For the heart, there are scanners in which a so-called bright blood image is acquired in which the blood has bright signal. The coefficient of variation of most bright blood images are around 7-8% in comparison to the lower values of 4% found in black blood sequences. Nevertheless, any of these two types of images can be clinically used for iron overload assessment of the heart.

The whole MRI exam for iron overload assessment is fairly quick, being completed in 15 to 30 minutes depending on patient compliance and the need to acquire extra information of the organs imaged such as cardiac volumes and function for example. It does not require any contrast or sedation and a child over the age of seven can routinely undergo the study without any hassle.

Typical images of the liver and heart using the T2* techniques can be seen in figure 2 and 3 respectively.

Interpreting the images

The images generated by the scanner have to be analyzed in order for us to obtain the T2* values that will allow the estimation of the iron concentrations in each organ of interest. In order to do so, we have to transfer these images to one dedicated software such as CMRTools, CVI42, MedisQMass, etc or use the workstations already available in the scanner for the analysis along with non-commercial software. Using the heart as an example (with the liver using exactly the same methods), one has to first draw in the image a region of interest (ROI) in order to read the mean signal intensity of that region. By reading the ROI in each image with different echo times (TEs) a table can be generated that will have a set of 8 to 12 groups of TEs and respective ROIs as exampled in Figure 4.

From these sets of TEs and ROIs a fitting curve is then drawn using the decay equation

$SI = SI0.\exp(TE/T2^*)$

where SI represents the signal intensity, SI0 a fixed value dependent on the scanner and TE the different echo times. By fitting these datasets using the equation above, the T2* values can then be defined for each organ.

The major source of error when doing the interpretation happens when very high levels of iron, especially in the liver, are analyzed. This happens because with very high levels of iron, the T2* curve decays very fast. This means that the first echo time acquired by the MRI scanner has to be very low, close to 1.0ms or less. This is not as sensitive as the heart because this organ does not accumulate iron in such high concentrations as the liver and the first echo times can be higher close to 2.0ms. Despite starting very low, the rapid drop in signal with further echo times will result in a plateau of these values usually after three or four datasets. While there is some debate in the literature to what exactly this plateau signal means (whether they are just noise or truly represent a third variable in the decay equation) one has to acknowledge this problem and correct the fitting curve in order to avoid significantly overestimating the true T2* values. While one can use a different fitting equation that accounts for this offset, it is generally easier and as accurate to truncate the values once the plateau phase has been reached in order to ignore the higher TE values. This will result in a better fit of the data, usually with a correlation coefficient above 0.98. An example of a wrong fitting and the corrected truncated analysis are shown in Figure 5.

Clinically interpreting T2* images: LIC and MIC

While the MRI will allow us to calculate the T2* values for any organ in the body, these values are not directly and linearly correlated to the true concentration of iron the liver or the heart. Therefore, it is recommended that we transform the original T2* numbers into the final liver iron concentration (LIC) and myocardial iron concentration (MIC). In order to do so,

calibration curves have been obtained by simultaneously performing MRI of the liver and the heart while directly measuring iron from these two tissues through biopsies. This allowed the establishment of correlation curves that transform the original T2* numbers generated by the scanner to be transformed to more representative LIC and MIC values. While LIC has been used since the beginning of the method, it was not until 2011 that the correlation curves for MIC were published. Nevertheless, we now have standardized classification tables for both organs which allows the clinician to interpret and follow these values linearly along the patients appointments. No such correlations have been done for other organs. The classification tables for iron overload of the liver and heart are found below along with the reference papers used:

	LIVER (LIC)				HEART (MIC)		
	Normal	Mild	Moderate	Severe	Normal	Mild-Moderate	Severe
T2* (ms)	>14.1	14.1 – 3.7	3.7 – 1.7	< 1.7	>20	10-20	<10
R2* (Hz)	< 71	71 - 583	267 - 583	>583	<50	50-100	>100
Iron concentration (mg/g)	< 2.0	2 – 7	7 – 15	> 15	<1.16	1.16 – 2.71	>2.71

Myocardial Iron Concentration(MIC) calculation according to: Carpenter JP, et al. Circulation. 2011;123:1519-28

Liver Iron Concentration (LIC) calculation according to: Wood et al. Blood 2005;106:1460-1465

By using these tables, the clinician can then monitor the results of the chelation strategies over time. In general, a repeat MRI study is recommended every year for both the liver and heart starting at the age of seven if regular chelation is not granted or ten if the patient has good compliance to treatment.

Future perspectives

MRI for iron overload assessment has become more simple, standardized and faster since its introduction in 2001. The next steps in this technology is to make it even more efficient by allowing the whole exam to be acquired in under 10 minutes, significantly reducing the time inside the magnet with consequent reductions in cost and patient discomfort. Not only that, the interpretation and generation of accurate T2* values are now possible to be accomplished automatically without any human interference which should also simplify the post-processing of those images significantly.

More important, we have to make sure that access to MRI scanners is available to every patient that needs iron overload assessment as this will definitely have an impact in clinical outcomes. The new developments in the method will help increase the productivity of the exam and allow it to be even more cost-effective by allowing high throughputs of patients while maintaining the same rates of accuracy.

Figure 1: On a non-iron-loaded tissue, the T2* decay is relatively slow and despite longer echo times, will generate most of the original signal back. In a tissue with significant iron overload, the decay curve will drop very fast and the image will have little signal after a short time, generating black images. The interpretation, therefore, is that high T2* numbers represent less iron and lower T2* numbers represent more iron.

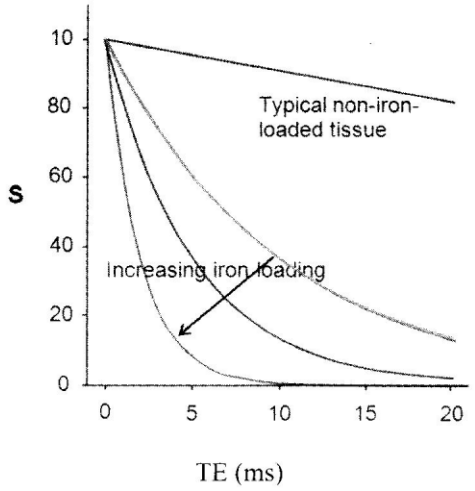
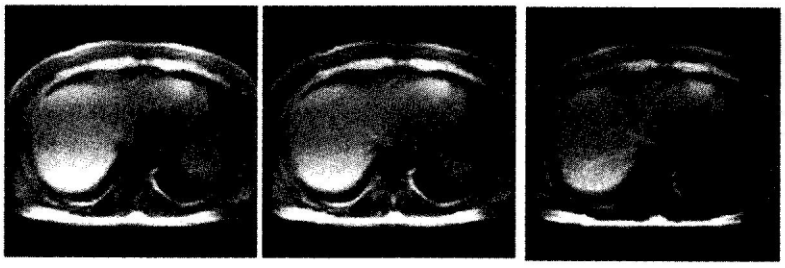


Figure 2: an example of a T2* image of the liver of a patient with normal iron overload (a) and severe iron overload (b) with three different echoes being shown.

(a)



(b)

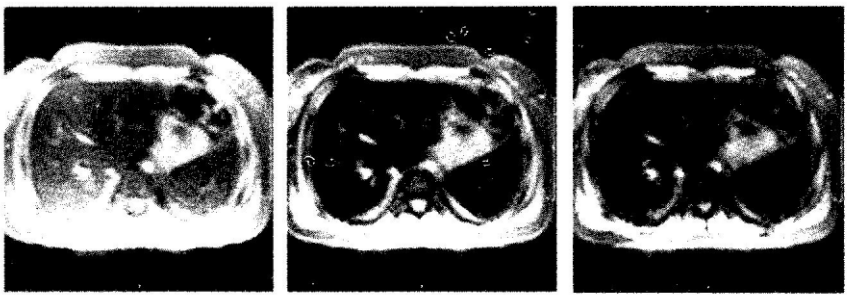
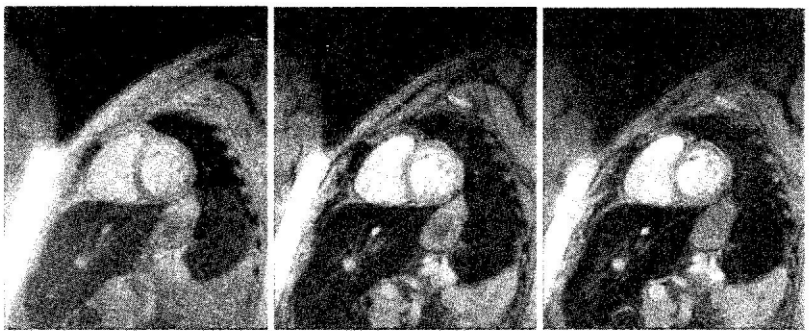


Figure 3: example of a T2* image of the heart of a patient with normal iron overload (a) and severe iron overload (b) with three different echoes being shown.

(a)



(b)

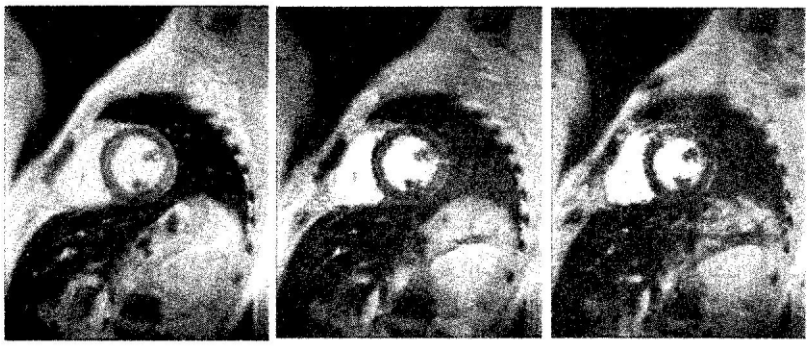


Figure 4: region of interest drawing in the heart and the respective table created from the values with the fitting curve of those points: the TE represent the echo times, ROI the signal intensity. In this case 9 images were acquired.

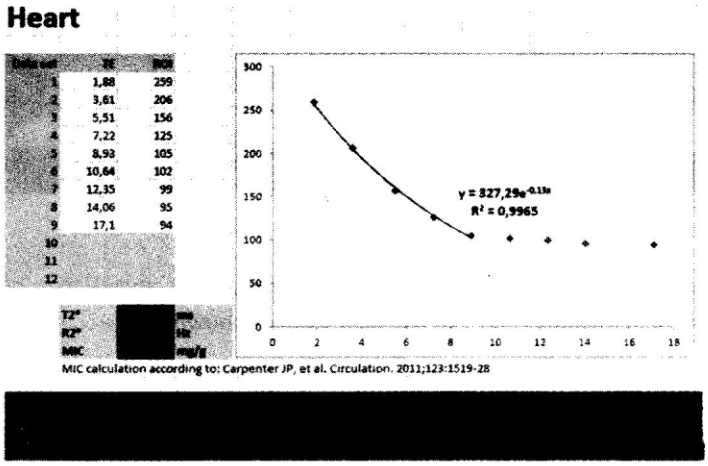
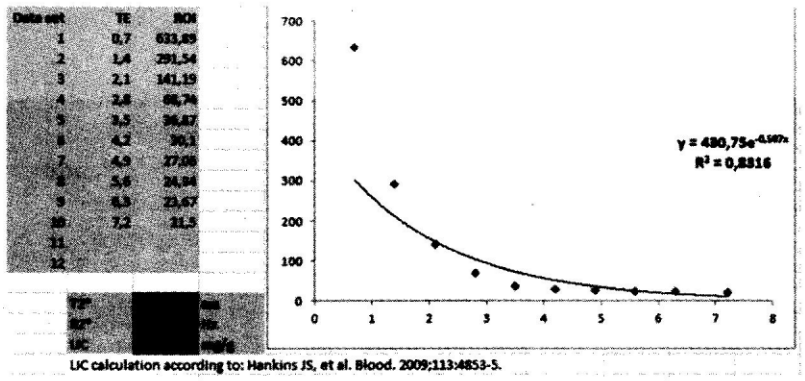


Figure 5: an example of the analysis of a liver with severe iron overload where all datasets were used to fit the data, overestimating the true T2* (a). Truncation was then used to correct for that problem resulting in a significantly better fitting resulting in the correct T2* value (b).

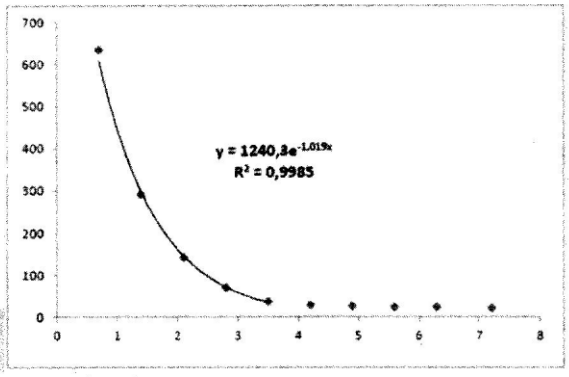
(a)



(b)

Data set	TE	ROI
1	0,7	633,89
2	1,4	291,54
3	2,1	141,19
4	2,8	68,74
5	3,5	36,87
6	4,2	30,1
7	4,9	27,06
8	5,6	24,34
9	6,3	23,67
10	7,2	21,5
11		
12		

T2*	[redacted]	ms
R2*		Hz
LIC		mg/g



LIC calculation according to: Hankins JS, et al. Blood. 2009;113:4853-5.

MRI T2* Iron Studies

-Dr. Sameer Sood

Iron Assessment in Liver and Heart by MRI

Introduction

The use of magnetic resonance imaging (MRI) to estimate tissue iron was conceived in the 1980s, but has only become a practical reality in the last decade. The technique is most often used to estimate hepatic and cardiac iron in patients with transfusional siderosis and has largely replaced liver biopsy for liver iron quantification. However, the ability of MRI to quantify extrahepatic iron has had a greater impact on patient care and on our understanding of iron overload pathophysiology. Motivation for MRI measurements
Iron overload is a surprisingly common clinical problem, arising from disorders of increased absorption such as hereditary hemochromatosis or thalassemia intermedia syndromes or through frequent blood transfusion therapy. Before the routine availability of chelation therapy, chronically transfused patients died from cardiac iron overload in their teens and twenties. Since the introduction of deferoxamine in the early 1970s, life expectancy has improved dramatically. However, despite improvements, mortality in middle age continued to be problematic. There are several reasons that mortality continued to be high. Recently, cardiac and liver iron estimates by MRI have become the primary outcome measures for clinical studies of iron chelation therapy.

Theoretical Basis of MRI Tissue Measurements

The use of MRI to estimate tissue iron was conceived in the early 1980s, but did not become practical until MRI technology matured 20 years later. The general concept is simple. MRI machines can generate images at various observation or "echo" times to vary the contrast among different organs. All organs darken with increasing echo time, but those containing iron darken more rapidly (Figure 1). T2* represents the echo time necessary for a tissue to become twice as dark. It may be thought of as a half-life, with small values representing rapid signal loss. Alternatively, image darkening can be expressed by R2*, its rate of darkening. Some investigators prefer to report R2* values rather than T2* values, because R2* is directly proportional to iron concentration. However, R2* values are simply 1000/T2* and vice versa, making it easily to convert one representation to another.

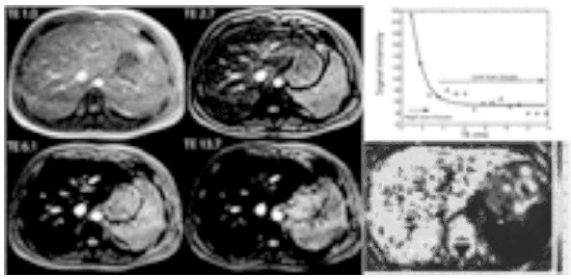


Figure 1.

(Left) Open circles represent liver signal intensity and solid line reflects the R2* fit at different echo times (TE). (Right) A map generated by calculating R2* values for every voxel in the image, with the reported liver iron concentration (LIC) represent the average liver R2* value scaled by a linear equation.

MRI scanners can also collect images suitable for T2 (and R2) analysis instead of T2* analysis, using radio waves rather than magnetic gradients to generate images at different echo times. Image analysis and iron quantification is similar whether using R2 or R2* images. R2 images take longer to collect and are used more frequently to evaluate liver iron concentration (LIC). Whereas cardiac T2 imaging is also possible, it is more challenging because of respiratory motion, limiting its widespread acceptance.

What Goes MRI Actually Measure?

Iron itself is invisible on an MRI. Instead, MRI detects iron's influence on the magnetic milieu of water protons diffusing in tissues. Typically, the magnetic fields in a clinical scanner are extremely homogenous, but iron within the tissues creates local magnetic field disturbances that cause the images to darken faster. Not all forms of iron are equally magnetically potent. Labile iron species, although toxic to the body, are magnetically silent at physiologic concentrations. Ferritin, the body's initial line of defense against circulating free iron, is weakly detectable by MRI when it is dispersed freely in the cytosol. However, ferritin aggregates and their breakdown product, hemosiderin, overwhelming determine tissue R2 and R2* (or T2 and T2*). The size and distribution of these iron stores powerfully modulate the relationship between iron concentration and the MRI signal intensity.

Impact of MRI Iron Imaging on Patient Management

The introduction of MRI to quantitate liver and cardiac iron had a profound impact on our understanding and management of cardiac iron overload. Anderson et al in 2001 demostrated all patients with cardiac T2* in the normal range (> 20 milliseconds) showed normal ventricular performance. As cardiac T2* decreased below 20 milliseconds (reflecting increasing cardiac iron), the likelihood of left ventricular dysfunction increased; this decline coincided with an increase in the estimated heart iron concentration. However, most patients with MRI-detectable cardiac iron still exhibited normal cardiac function and therefore MRI was able to detect cardiac problems before toxicity was manifested.

MRI Assessment of Liver Iron

Either liver R2 or liver R2* can be used to estimate LIC, depending on local expertise. Liver R2* images are the easiest and quickest to collect, but require specialized software to generate R2* and iron estimates. The upper limit of liver iron that can be reliably estimated by R2* depends on scanner specifications, but is generally 30-40 mg/g dry weight at 1.5 Tesla.

MRI Assessment of Cardiac Iron

Cardiac R2* (or T2*) is generally measured using the same scanner and software tools as those used for the measurement of liver R2* with associated ECG gating.

Future Impact of MRI

With routine cardiac screening, patients are now living long enough to encounter increasing iron-mediated endocrine morbidities. Diabetes, hypothyroidism, and hypogonadism remain common among thalassemia patients and are probably underdiagnosed. The pituitary gland is perhaps the most important initial target for further study because it is easily injured and damage can be difficult to detect until puberty. Hypogonadism occurs in approximately half of thalassemia patients and has long-term consequences for fertility, bone density, and quality of life. Preclinical iron deposition can be detected using R2 techniques whereas severe iron deposition is associated with decreased response to gonatropin releasing hormone challenge. Shrinkage of the pituitary gland is associated with more significant, irreversible loss of gonadotrophic production. Further clinical validation and technical standardization is necessary before pituitary MRI can be incorporated into routine clinical monitoring, but this is an active area of research.

Initiation of chelation

-Dr. Rajiv Kumar Bansal

Iron overload occurs very rapidly in patients who are on chronic transfusion programs. Since humans have no mechanism other than sloughing of the mucosa of their gastrointestinal tracts or menstruation to excrete excess iron, patients who are being transfused every three or four weeks gain 0.5 mg/kg per day of iron in excess of natural losses. Patients who are not on a transfusion regimen are also prone to iron overload due to significantly increased intestinal absorption of iron secondary to ineffective erythropoiesis. Iron overload is the major cause of morbidity for thalassemia patients. Iron overload is a leading cause of mortality and organ injury.

Iron is very toxic to tissue. Under normal circumstances, in humans, iron is transported bound to a carrier protein called transferrin. Transferrin transports iron into certain tissues. Because the iron is bound to this protein, other tissues are protected from the toxic effects of free iron. Patients on chronic transfusion rapidly acquire much more iron than can be bound by transferrin, and free iron levels increase in the blood. This free iron, or so called non-transferrin bound iron, is directly toxic to the heart and other tissues.

There are two goals of iron chelation therapy: the binding of toxic non-transferrin bound iron in the plasma and the removal of iron from the body. Detoxification of excess iron is probably the most important function of chelation therapy. It is clear that certain symptoms of iron overload, such as cardiac arrhythmia and heart failure, can be improved well before local tissue levels of iron have decreased by the continual presence of a chelator in the plasma.
In general, chelation should be started as soon as the patient becomes significantly iron loaded. Since removal of iron from normal tissues can result in toxicity from over-chelation, it is important to delay the start of chelation until the patient is significantly iron loaded. Since iron loading occurs much faster than toxicity develops, this delay will not put the patient in danger. The decision points are based on total amount of blood transfused, ferritin levels, and degree of iron loading based on liver iron concentration (LIC). Liver iron is measured by biopsy, MRI.

Chelation therapy should be started after about one year of chronic transfusions. This correlates with a serum ferritin of approximately 1,000 ng/mL. LIC is the best measure of total iron loading. LIC should be at least 3,000 µg/g dry weight before starting chelation. The general guidelines for iron chelation are gradually changing. Many experts are increasing the therapy in order to maintain a lower steady-state body iron store. While long-term prospective data is limited on these aggressive protocols, it is felt that more aggressive therapy may be more effective in preventing iron-induced organ injury. This needs to be balanced with the drug toxicity. While the standard recommendations have been to maintain a ferritin between 1,000 and 2,500 ng/mL, several programs are aiming to maintain serum ferritin at 500 ng/mL in adult patients.

In general, significant iron loading of the liver can be detected after about six months of monthly transfusions, while cardiac loading takes about eight to ten years. The liver loads linearly with time, whereas the heart remains devoid of iron for years. However, once it starts,

iron loading of the heart is very rapid. Evidence of liver damage can occur after about four years of transfusions. The onset of cardiac dysfunction is more complex and less well understood.

Over the past four decades, there have been dramatic improvements in survival for patients with thalassemia major due in large measure to improved iron chelators. Three chelators are approved for use in the India, parenteral deferoxamine and oral deferiprone & deferasirox. Many trials and worldwide clinical experience demonstrate that each of the three drugs can chelate and remove iron, and thereby prevent or improve transfusional hemosiderosis in thalassemia patients. However, the chelators differ strikingly in side-effect profile, cost, tolerability and ease of adherence, and (to some degree) efficacy for any specific patient.

- New and improved MRI techniques allow more precise quantitation of body iron burden and differential tissue deposition.
- Therapy can be tailored based on regular assessments of tissue iron levels.
- New orally effective chelators have improved compliance with therapy.
- Combination therapy allows for intensification of chelation in those with higher iron burdens, as well as allowing for adequate chelation in those who have dose-limiting toxicity with a single agent.

There are two goals of iron chelation therapy; the primary goal of chelation therapy is to maintain safe levels of body iron and the secondary goal is to rescue patients who have developed toxic levels of iron resulting in organ damage.

Unfortunately once iron overload has occurred the removal of excess iron is slow and may need several years of excellent compliance to treatment to completely clear the iron.

There are three drugs used for iron overload :

- Desferrioxamine (Desferal)
- Deferiprone (Kelfer)
- Deferasirox (Asunra/Oleptis/Desirox)

Our oldest patients with thalassaemia major in the Jaipur are now in their mid-40's and it is important to recognise that there is nothing to prevent them becoming senior citizens in few more years. Life expectancy for younger thalassaemia patients is predicted to be even longer if current treatment guidelines are followed. Good compliance with treatment is critical to a long life expectancy.

Desferrioxamine (DFO):

This was first used in the 1960's but has been mainstream treatment for iron overload since the late 1970's.

It is a good liver and heart iron chelator, however due to issues with compliance and concerns around toxicity , it is used less often.

Desferrioxamine (DFO) has to be given either subcutaneously or intravenously via an indwelling device such as a Hickman Line or Port-o-cath. In general the recommendation is to

take Desferrioxamine on 5 nights a week as a 12-hour infusion. Patients with more severe iron loading either in the heart or liver often receive Desferrioxamine as 24-hour infusions. Desferrioxamine can push the ferritin down quite rapidly and it is important to monitor the liver iron regularly to make sure that toxicity related complications do not develop and that the Desferal dose is not reduced too quickly if the liver iron is still high. Desferrioxamine is excellent for stabilising and reducing free iron and therefore good in acute heart failure or if there are abnormal heart rhythms.

Under full chelation with deferoxamine, about 50 percent of liver iron can be removed in four to six months. It takes about 17 months to remove half of the heart iron.

1. DFO is a hexadentate chelator, binding iron at a 1:1 molar ratio.
2. Old RBC iron storage will be released by reticuloendothelial system macrophages and precipitated by DFO and rapidly excreted through urine.
3. Non-bonded DFO will be internalized by liver parenchymal cells and attached to excess hepatic iron and excreted via bile.
4. DFO can directly absorb iron accumulation in cardiac muscle cells.
5. Due to DFO short plasma half-life, continuous injection is required for patient with iron overload until iron level disposal reaches to 15 mg daily. As a result of nocturnal injection of Deferoxamine, 20 to 50 mg of iron (600 to 1,500 mg per month) should be excreted through urine and feces daily. Therefore, it can minimize iron re -accumulation and decrease its storage if the transfusion is less than 4 packed RBC per month (less than 800 mg of iron). Although the treatment with DFO is effective, its infusions are time-consuming, expensive and painful in children. Moreover, they frequently have a negative impact on patient's quality of life.
6. Dose-dependent side effects of Deferoxamine are visual and auditory neurotoxicity due to chronic treatment and acute effects including abdominal pain, diarrhea, nausea, vomiting and hypotension. Accordingly, annual testing by optometrists and audiometerists is recommended.

Fortunately, most toxicity is reversible when DFO treatment is withdrawn. Treatment with high doses of DFO is associated with blood pressure increase in lungs. Deferoxamine therapy increases the risk of infection of mucormycosis, vibrio and yersinia. It should be mentioned that it cannot be seen with other iron chelators such as Deferasirox and Deferiprone because they do not work as siderophores.

Important things for you to know:

1. Desferrioxamine is only effectively working for as long as the pump is attached. It is therefore important to ensure that the pump does finish before it is removed in the morning and not to leave any infusion in the balloon or syringe otherwise the full dose is not administered.
2. If there are reactions at the sites of the infusion let your doctor know, we can have a small dose of hydrocortisone added into the infusion to reduce the reactions or increase the

volume of water so it is less irritating.

Deferiprone (DFP):

This has been in clinical use since the 1990's. Several studies have shown it to be very effective for clearing heart iron especially in conjunction with Desferrioxamine infusions. It is taken three times a day in a tablet / capsule form. Deferiprone does reduce ferritin in the majority of patients but there may still be raised liver iron levels. In this case patients are often given combination therapy to control the liver iron.

Side effects can limit a person's ability to take Deferiprone in particular the gastrointestinal (nausea and vomiting) effects and joint pains. In some cases a severely low white blood cell count (agranulocytosis) a serious side effect and means that that patient should not take Deferiprone again.

Important things for you to remember:

1. Most of the nausea and vomiting side effects do settle down so persevere with it and discuss with your doctor if there is anything that can be done to help manage them.
2. Always take the tablets three times a day as the short half-life means the medicine is removed from your blood soon after taking it. If you miss doses or only do it twice a day you have less hours of chelation and the Deferiprone is less effective.
3. Always try to get your full blood count checked as advised (weekly). If you develop a fever and sore throat stop the Deferiprone and have a blood test to make sure your blood count is OK.
4. If you are planning to start a family you need to stop Deferiprone 3 months prior to a planned pregnancy. If you accidentally become pregnant on Deferiprone stop this straight away.

Deferasirox (DFX):

This has been available for clinical use since 2006 and has been shown to be effective for both liver and heart iron in stable patients. It is available in a dispersible tablet and is taken once daily as a drink. Deferasirox can be given at an iron-reducing dose where the dose is slightly higher than iron loading from the blood transfusions in order to bring down the body iron, or it can be given at a maintenance dose where the aim is to maintain a stable body iron. There is now good data from clinical trials showing improvement in heart iron so it can now be used in stable patients with iron loading in the heart. Careful monitoring is required of kidney function and nausea, vomiting, diarrhoea and taste can affect compliance.

Important things for you to remember:

1. Most of the nausea and vomiting and diarrhoea side effects do settle down so persevere with it. You can take Deferasirox with food and it often helps if you leave the tablets for half an hour (in lukewarm water) to allow them to disperse properly in water before drinking. This makes the drink less chalky and gritty.
2. Kidney tests should be monitored monthly and if the ferritin falls very quickly the

kidney tests are more likely to go up. In this situation reducing the dose or having a short break is advised and this does correct the tests back to normal.

3. If you are getting side effects you must let your doctors know, as most of the side effects can be managed.

4. If you are planning to start a family you need to stop Deferasirox 3 months prior to a planned pregnancy. If you accidentally become pregnant on Deferasirox stop this straight away.

All three chelation agents have distinct advantages and disadvantages. Treatment is adjusted according to you as an individual and to meet your health and lifestyle needs.

Morbidity and mortality in thalassemia are linked closely to the adequacy of chelation. Recent evidence from Europe has shown that by normalizing the iron stores, not only are new morbidities prevented but reversal of many complications such as cardiac failure, hypothyroidism, hypogonadism, impaired glucose tolerance, and type 2 diabetes can also occur, improving survival and patients' quality of life

Iron is removed from different organs at different rates: hepatic iron burden usually improves more rapidly than cardiac iron burden with intensification of chelation. Therefore, both hepatic and cardiac iron must be measured to optimize chelation therapy. Ferritin level changes paralleled with liver iron concentration variations.In particular, ferritin levels above 2,500 ng/mL are associated with an increased risk of morbidity and mortality and should be trigger intensification of chelation therapy.

Deferasirox - Old Wine in the New Bottle

-Dr. V.P. Choudhry

Regular blood transfusion is the life line for all children with thalassemia major. Repeated blood transfusion results in iron overload which forms the major cause of morbidity and mortality. All thalassemic children will succumb to the disease in second decade of life, primarily due to cardiac failure or cirrhosis of liver if the iron overload is left untreated. Institution of adequate chelation therapy with the current protocols therapy along with regular blood transfusions to maintain pre-transfusion hemoglobin level of 10 gm/dl has improved the survival. Presently thalassemic children lead a normal life as was evident from multi-centric studies of 7 centers where over 90% of children born after 1980 (Fig 1). Adherence to adequate chelation therapy plays a key role for long term survivals.

Deferasirox dispersible tablets (DT) were approved in 2005 after extensive clinical trials in over 100 countries worldwide. Over the last 12 years it has evolved as a gold standard therapy. It became an ideal iron chelator as it was

a) effective oral iron chelator
b) it has high affinity for iron
c) has prolonged half-life (12-16 hours) and thus it is effective as single daily dose
d) it is lipid soluble and able to enter cardiac and hepatic cells easily to chelate iron
e) palatable
f) acceptable side effects
g) cheap drug so that it is affordable by majority

Majority of thalassemic children even in developed countries shifted to deferasirox from desferrioxamine therapy which is injectable needing prolonged administration with help of infusion pump. It was expensive and had several side effects. Deferiprone was the first oral chelator but had significant side effects such as joint pains, low white cell count and platelets. It needed to be administrated orally in three doses and needs regular blood monitoring (CBC) every month.

Deferasirox has long half-life of 12-16 hours and lipid soluble with high affinity for iron. It excretes iron primarily through stools. It is available in tablet form which can be dispersed in water or apple juice using a non-metallic stirrer and can be consumed as a drink once daily. As the drug is lipid soluble it enters cells of liver, heart, etc easily and is able to mobilize iron form these tissues effectively. Deferasirox over the year has become gold standard therapy and a

drug of choice as oral iron chelator. This drug has acceptable side effects which included diarrhea, nausea, abdominal pain, vomiting, headache, constipation; in varying proportion in different studies. Deferasirox also causes transient rise in blood urea, serum creatinine, transaminase levels which are dose dependent however these changes are not alarming. Maximum dose recommended is 40 mg/kg/day. Higher dose are not recommended because of various side effects. Children with higher ferritin levels are given combination therapy as the dose of deferasirox cannot be increased significantly. Over the years Deferasirox dispersible tablet (DT) are being recommended as effective chelating agent with acceptable safety. This drug is generally well tolerated and has improved the quality of life to greater extent. However there are problems of long term adherence to deferasirox DT such as palatability, gastrointestinal side effects and many children do not tolerate this drug and have shifted to other chelating drug either singly or combination therapy. Combination therapy is also recommended when any single chelating agent is unable to induce negative iron balance. Sub optimal chelation therapy results in various complications and high risk of morbidity and mortality at younger age (Table 1).

A new deferasirox film-coated tablets (FCT) has been developed with the same active compound. This drug has high bioavailability and can be taken with meals. Since the deferasirox FCT has high bioavailability and therefore its dose is 30% less than DT. It was expected that the side effects deferasirox (FCT) will be less as compared with DT form because of its better bioavailability. In controlled study over 170 cases the efficacy, safety of DT & FCT were compared. This study was presented in American Society Hematology (ASH) in December 2016. It was observed deferasirox FCT is an effective drug with better acceptability with lesser side effects such as abdominal pain, nausea, loose motions, vomiting's, constipation and headache etc as compared with deferasirox DT. Similarly FCT preparation was found to safer for liver and kidney over prolonged duration of study.

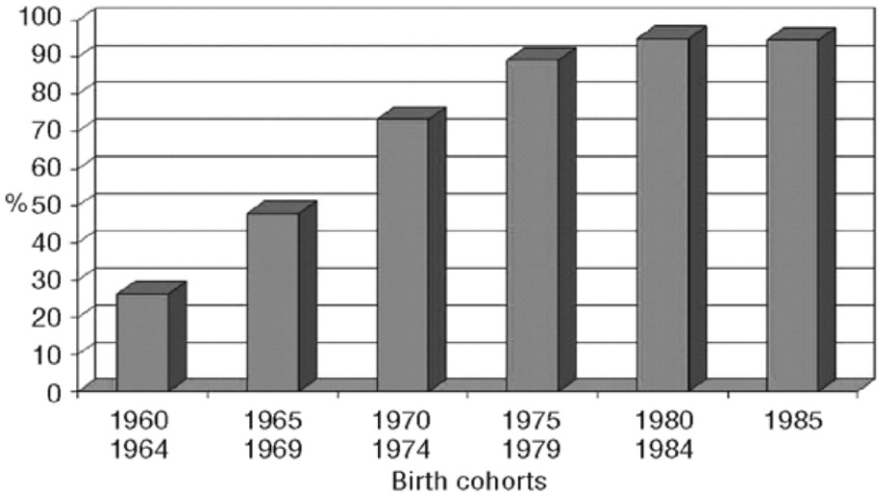
Deferasirox FCT is old drug with new carrier which is equally effective, better tolerable with lesser side effects. Hopefully the deferasirox FCT will be of great boon for those thalassemic patients who cannot tolerate deferasirox DT. Adequate chelation therapy is of paramount importance for long term survivals. The improvement in chelating agent will be of great help to thalassemic children to strict to adequate chelation therapy as per current protocols.

Table 1: Morbidity and mortality associated with non-adherence to iron chelation therapy

Outcome measures	Adequate or good chelation adherence	Poor or non-adherence
Survival upto 30 yrs. (%)	90	15
15-year survival (%)	100	52
Life expectancy (yrs)	46.2	22.2
Life time risk of cardiac disease (%)	60	96
Risk of diabetes (%)	9	54
Risk for hypogonadism (%)	47	81
Risk for hypothyroidism (%)	14	28

Huang Vicky et al. Blood 2015; 126:4748.

Figure 1: The life of patients with thalassemia major 2009 children over 7 centers



Borgna-Pignatti Caterina. Haematologica. 2010; 95:345-348.

Transition of Care of patients with Thalassemia from Pediatricians to Physicians

-Dr. Jagdish Chandra

A remarkable aspect of modern medicine is that many children with complex diseases-either congenital or acquired during childhood- are surviving to become adults. These diseases include transfusion dependent thalassemia (TDT), sickle cell disease and other hemoglobinopathies, congenital heart diseases, epilepsy and a host of neurodegenerative diseases, cystic fibrosis etc. The system or programs for transition of such patients from pediatrician to care by physicians are not in place in most of the developing countries. Even in developed countries such transition is beginning to happen.

It is important to differentiate transition from transfer. *Transition* is defined as "a movement, development, or evolution from one form, stage, or style to another." Medical *transition* is the process of moving from a pediatric medical system to an adult one. On the other hand, *Transfer* is the actual point in time at which responsibility for patient care is "handed off" to the adult provider.

Transition of care (TOC) is associated with its inherent challenges. The patients, parents as well as both teams of doctors-pediatricians and physicians face several challenges. In such situations, it is for the team of pediatricians to take on the responsibility of smooth and meaningful transition.

Over the years the number of patients with TDT entering adulthood has increased at least in larger cities. TOC facilities need to be in place for these patients to see the fruits of the efforts of years put in by families, pediatricians and patients themselves.

Challenges in transition of care:

Problems in TOC actually occur or are perceived to occur because of inherent nature of services provided by team of pediatricians and that of physicians. Pediatric care is family centered and focuses on growth and development of the patients. Growing independence of adolescents sometimes gets ignored and they are not part of decision making. Decisions, even complex ones are taken by the parents in consultation with the doctors. On the other hand physicians acknowledge autonomy and expect decisions mostly by patients themselves. They address issues related to sexuality and employment when the situation demands. However, family gets a back seat.

Following are the specific challenges faced by different stake holders in the process of TOC:

1. Challenges pediatricians face:
    a. Lack of faith in the competence of physician colleagues due to lack of knowledge of managing TDT and inadequate time they may devote for comprehensive care required
    b. Fear of adverse outcome on account of inexperience of adult care team in handling the complex management issues

c. Lack of communication with adult care team
d. Negative "research consequences" of a reduction in patient numbers and a loss in long term follow up
e. Negative financial consequences (in private set-up)

2. Challenges physicians face:
    a. Physicians may have little interest in "pediatric" disease. They also may be having very little time for a disease which was in the domain of pediatricians till now
    b. Physicians have very little or no experience in managing TDT as this is a new thing for them
    c. Clinics full of elderly sick patients are often alienating for young patients
    d. Extensive investigations and management reassessments required soon after the first meeting
    e. Some patients may already be having medical complications requiring specialized care
3. Challenges that patients may face:
    a. Fear of losing respected and loved care givers
    b. Being forced to trust new and unknown care givers
    c. Moving to adult services may be seen as a step closer to disease complications
    d. Infantilized and dependent self image among patients who are having growth retardation may be a hindrance
    e. Transition may require a change in self perception
    f. Individual rather than family approach of adult physicians requires adjustment
4. Challenges that parents/ families face:
    a. family centric vs individual centric approach of adult team
    b. Fear of losing most supportive environment
    c. May feel excluded from all decision making and marginalized

Overcoming the challenges/ barriers for smooth TOC:

The American Academy of Pediatrics states, "The goal of transition in health care for young adults with special health care needs is to maximize lifelong functioning and potential through the provision of high-quality, developmentally appropriate health care services that continue uninterrupted as the individual moves from adolescence to adulthood."
It is important that the TOC is regarded as an *opportunity rather than a burden*. The team of pediatricians should take the lead as they have better understanding of the disease and its management. In addition, they enjoy the trust of the patients and their families.

A "triple aim approach" is suggested which includes:

1. Development of self-management of the disease
2. Identifying and supporting the receiving team of physicians
3. Providing guidance to patients and families during transition

1. Development of programme of self-management:

While considering transition, adolescents and their families should be educated about its management. They may be aware of common management issues. What management issues need to reinforced should be identified. It should be identified whether patient himself/ herself is mature to handle the relevant issues. In some situations, parents' involvement will be required for some more time. The education of patients/ families should focus on:

a. Need for adherence to treatment being crucial for maintenance of health and quality of life
b. Adverse drug reactions and their management
c. Regular monitoring of the disease parameters as recommended including endocrine complications, cardiac and hepatic iron status, transfusion transmitted infections etc.
d. Issues related to physical, psychosocial development
e. Adolescent issues including development of secondary sex characters etc
f. Linking the patients / parents to support groups

Preparedness for TOC of all patients should be carefully assessed and decision for transition should be individualized.

2. Identifying and supporting the receiving team of physicians:

A team of physicians who will take care of adolescents and young adults with TDT should be identified.

This team should be empowered to manage the patients including the nuances by way of following:

a. Facilitating communication with the adult care team
b. Providing education regarding management of TDT
c. Establishing constant point of contact for ready solutions to intercurrent issues. The pediatric care team should never give an impression of "washing off" hands from the care of growing patients
d. Ensuring coordination of care for patients with special needs

3. Providing guidance to patients and families during transition:

Family and parents need support while their wards are being transferred to different set up. They will be helped by institutional and/or organizational policies and procedures for TOC. This should take into account the expectations of patients and families with regard to TOC. A point-of-contact for them should be designated throughout TOC.

TOC: Practical considerations:

1. Age of TOC: at what age transfer of care should actually take place has been debated. Opinions are expressed about taking into account the physical and mental developmental status of patients and their education status such has completion of school and entry into college. Most appropriate criteria will be that TOC of TDT should take place at the cutoff age for care of general patients by pediatric teams in the hospital. Attempt should be made to transfer the patients when they are well and not acutely ill.

2. Transfer of adequate records: Records of the patients should be transferred during TOC. A comprehensive list of data to be transferred to adult treatment team is given in Table 1.

3. Holding joint TOC clinic: a joint clinic should be organized for the patients being transferred (may be more than once). This clinic should be attended by pediatric and adult treating teams. Patients should be introduced to the new team they will be cared by. Special needs of the patients should be discussed by the teams and management plan should be drawn in advance.

Table 1: Records to transferred at the time of TOC

Introductory information of patients:
Name, age, sex
Physical growth / sexual growth:
Height, weight, BMI, SMR
Disease status:
Blood group
Annual transfusion requirement
Liver and spleen enlargement
Whether splenectomized
Iron overload status including serum
ferritin, cardiac and hepatic MRI
LFT, KFT
Chelation therapy
TTI if any:
Hep B, HCV, HIV
Complications:
Endocrinal, cardiac etc

Organization of Comprehensive Thalassemia Care

-Dr. Jagdish Chandra

Survival of patients with transfusion dependent thalassemia (TDT) has greatly improved over the last two to three decades. This has resulted from better understanding of the disease, better availability of blood, drugs and above all persons (doctors, nurses etc) looking after these patients with utmost care. In developing countries, the fruits of success are limited to patients in larger cities only. Improvements are required to reach the masses.

It can very well be realized that thalassemia which starts as a hemolytic anemia, attains the dimension of multisystem disease on account of complications mainly arising out of iron overload. A lifelong disease management is required for TDT. Like individuals with other severe diseases, patients with TDT will not survive childhood without appropriate treatment. Such outcome can be achieved only with comprehensive thalassemia care.

What is comprehensive care?

The only curative treatment for TDT is stem cell transplant which is not available to most patients because of limited availability of expertise, lack of donors with complete HLA match and lack of finances. As a result most patients receive regular transfusion and chelation therapy. Comprehensive care for TDT (CCTDT) should include availability of these and other treatment and care provided as conveniently as possible. Centres providing CCTDT should also focus on preventive aspects, quality of life (QOL) issues and transition of care to physicians caring for adults when the time arrives. Such services can best be provided by organizing the services at designated centres.

Functions of Comprehensive Care Centres:

A. Services to be provided:

1. **Day to day management:** day to day management including transfusion, chelation and monitoring of patients is the backbone of TDT management.

   The services should be organized taking into consideration the convenience of patients and families. Such small things as having a separate queue for registration to avoid mixing with long queue for general patients helps.

   The transfusion services should be in organized in a separate day care centre. The atmosphere in the day care centre should be friendly so that visit to the centre is enjoyable. This improves compliance.

2. **Continuing education of patients and families:** as TDT management is life long process, education of parents and care givers is important. The need for compliance to regular treatment should particularly be emphasized. Patients should be involved in self-management when they grow up and are ready to take up responsibility. Visits for transfusions should be utilized for this purpose.

3. **Monitoring:** A plan of regular monitoring of patients should be in place. Monitoring on some parameters may be required on every visit. Certain parameters are monitored quarterly and still other annually.

4. **Record maintenance**: record keeping is an essential component of CCTDT. Records should include data on transfusion-chelation requirements, special medical needs, complications etc. all parameters being monitored should be carefully recorded. These records help not only in day to day management, they also help identifying deviations, complications and special needs of patients.

B. <u>Developing Linkages:</u>

It is essential to have regular meaningful communication and develop linkages with the teams/ departments whose regular help is required in taking medical decisions. These include:

a. **Diagnostic services :** resource persons form Pathology department/laboratory should be identified. Their inputs are required for primary diagnosis, assessment of iron overload, monitoring for transfusion transmitted infections, hormonal assessment during adolescent years etc, the later may be carried out in different laboratory.

b. **Blood bank:** understandably, blood bank team plays an important role in CCTDT. They help in initial extended blood grouping, providing appropriate safe packed red cells, pre-storage filtration, assessment of alloimmunization etc.

c. **Referrals to specialists:** for appropriate management of TDT, referral to specialists in the field may be required. Such referrals are required for regular assessment such as that of pubertal growth by endocrinologist and echocardiography by cardiologists. If the specialists are identified before hand, they can be entrusted the care of patients in case complications arise. As far as possible, the routine referrals should take place on the day of transfusion to avoid additional visits.

d. **BMT services:** parents of all patients should be counselled for curative treatment that BMT offers. If the BMT services are not available within institution, separate centre may be identified who can take up the patients when they are ready for this treatment. Prospective candidates for transplant

e. **Prenatal diagnosis:** as parents of most of the patients are in reproductive age group and many may not have completed their families, antenatal diagnosis for thalassemia is required for prevention of birth of affected children. As the antenatal diagnosis is required to be completed in a short period during first trimester, it is essential to identify such families. They need to be referred to the teams undertaking prenatal diagnosis before the pregnancy is planned. This avoids unnecessary delay.

f. **Adult care providers:** for transition of care (TOC) of adolescents and adults with TDT, developing a program of TOC should be in place. (see a separate write up on TOC).

g. **Administration:** the hospital administration should always be kept informed the routine functioning of the centres. Administrative help is required for posting of resource, availability of services, drugs, filters etc. It is important that the administration realizes the need for uninterrupted supply of drugs and services for proper management of these patients.

h. **Support groups:** constant dialogue with support groups is helpful in improving the services for the patients in general. They help by advocacy of issues of importance and taking up matters with the government.

i. **National and other registries**: a communication with national and state level registries is an important aspect of CCTDT. This helps understanding the needs in the first place. It also helps generate the data for the purpose of advocacy.

C. **Constant Updating of Knowledge and Research:** medicine is a fast changing field. It must be realized that the patients receive best possible management. Hence it is important that the medical staff looking after the TDT patients keeps him/herself updated with the new development in the related field. For example, recent years have seen newer guidelines regarding for ferritin levels, double oral iron chelators, management of hepatitis C etc. Research should also be integral part of CTDT centres. The level of research may vary according to availability of resources and needs of the community. This may include operational research as well.

D. **Staff/ Resource at CCTDT centres:** the staff/ resource available at these centres should include dedicated pediatrician, medical officers, fellows and postgraduate students, nurses, medical social worker, data manager etc. CCTDT centre for children should be under overall charge of the pediatrician who provides the leadership. He should have adequate knowledge and expertise, motivation and leadership qualities. Number of different category of staff may be variable according to the number of patients enrolled at the centre.

It must be emphasized that commitment of the staff will determine the success of the centres. While staff may like to be rotated so that they do not lose skill in other areas, a certain length of working in CCTDT centre is necessary to understand the nuances of management and develop familiarity with the patients, families and their issues. To this end, rotation of staff should be undertaken in batches. When some of the new staff members have acquired the required skills, then only the older staff should be posted out.

Posting of fellows and postgraduate students is important for addressing the future needs.

E. **Correspondence and networking:** the centres should be having continuous correspondence with all stake holders. Having a dialogue with other same level centres will help knowing best practices at other centres which can be adopted. Correspondence with higher (state/ regional/ national level reference centres) is required for periodic reviews and referral of patients.

F. **Organization of thalassemia care in India:** as stated earlier, at the present time facilities for care of patients with TDT are existing in metropolitan and other larger cities in India. Recently, Govt of India has taken initiative for countrywide implementation of services for hemoglobinopathies. It is envisaged that apart from National Entre of Excellence (COE), state level COE will be established which will be playing a role of mentoring the district COEs. The CCTDT centres will be equipped for providing appropriate care for these patients. The government is putting up guidelines for diagnosis, management and prevention of hemoglobinopathies.

Impact of Comprehensive care centres: it is well recognized that having comprehensive care centres will have positive effect on thalassemia management. It will also improve quality of life of these patients.

At our hospital, thalassemia care services are provided through a Thalassemia day Care

Centre for pediatric patients established in the year 2000. The resources have been pooled up from within the hospital. The centre which has nearly 250 patients on rolls has only four nurses and two resident doctors. One senior pediatrician is overall in-charge of the centre and day to day working is supervised by one senior medical officer.

A look at our data shows that mean trough Hb levels of patients at present are 9.4 to 9.5 gm/dl which were ranging between 6.8 -7.5 gm/dl at the beginning. Mean serum ferritin levels currently range between 1128-2220 ng/ml which ranged between 3050-6382 ng/ ml in the beginning. The percentage of children with serum ferritin over 2500 ng/ ml has decreased from 81 % to 30.5 % among children over 15 yrs, from 91.1 % to 15 % in children between 10- 15 years, from 86.3 to 10.2 % between 5-10 years and from 57.1 % to 0% among children under 5 yrs age.

With constant dialogue with the hospital administration and physicians, an adult thalassemia day care centre has been started in 2008 where already over 80 patients are being managed. Twenty two more patients are under transition of care and will be shortly transferred to adult care team.

Treatment Adherence and Quality of Life

-Dr Michael Angastiniotis

Treatment Adherence and Quality of Life

Dr Michael Angastiniotis
Thalassaemia International Federation
New Delhi 24 -25 November 2018, 9th NTC

Adherence means sticking to treatment:
according to recommended schedule and dosage

If the patient takes less than that which can bring about the desired result,
then we say that the patient is non-compliant or non-adherent

Multi-transfused patients have a lot to adhere to!
Every day of their lives

Iron chelation is the most usual treatment skipped and the most dangerous!

Compliance
Implies passivity, following demands and direction.
Non compliant patients are seen as "rebels", incompetent, or nuisances.

Non compliant patients are seen as challenging the "status quo" of the doctor-patient relationship !!

Adherence
Implies an active role of the patient,
a collaboration with the physician.

It implies a self motivated decision to adhere to the advice of the doctor.
A tacit self regulation of illness and treatment.

Beyond adherence - concordance

Concordance is not synonymous with compliance or adherence!

- It is based on the notion that consultations between clinicians and patients are a negotiation between equals [1].
- It makes the distinction of how individual patients value the risks and benefits of a particular medicine which may differ from the value assigned by their clinicians [2]
- The doctor is the only buffer the patient has between science, providers and industry. This is the real privilege doctors have and their power and status derives from it. (C. Sotirelis – patient)

[1] Partnership in Medicine Taking: A Consultative Document. London: Royal Pharmaceutical Society of Great Britain and Merck Sharpe and Dohme; 1996
[2] Alaszewski A. A person-centred approach to communicating risk. PLoS Med. 2005;2:e41

Thalassaemia Patients are asked to comply many of the following treatments:

- Blood transfusion
- Iron chelation
- HCV / Liver Disease treatment
- Bone disease treatment
- Diabetes
- Cardiological monitoring
- Fertility treatment
- Endocrinological treatment
- Heart disease
- Additional specific complications (e.g. Infection protection
- Psychosocial issues

CAN YOU IMAGINE LIVING A LIFE THAT IS PRIMARIILY AIMED AT GETTING TREATMENT ?

The doctors' responsibility

- Doctor's motivation should always be clear in **seeking the optimum** for their patients.
- Doctor's application of scientific evidence should always be clear cut **in favour of the patient's interest.**
- Doctors should follow internationally accepted **guidelines** in making decisions for the patient NEVER "play safe" by unquestionably accepting guidance without forming an objective grounded personal opinion.
- The patient must know that the **motives**, the **experience** and the **judgement** of the doctor are certain
- Doctor must provide clear instructions on the drug, the need for its use, the dose, treatment times and warn about side effects

With these provisos the doctor/patient relationship is based on TRUST

Doctor's concerns: must be discussed with the patient and/or family

Without the constant presence of a chelating agent:

- LPI will damage cells and vital tissues
- Over time major organs are affected
- Increasing morbidity, reduced quality of life and reduced survival

Doctor wants the best for patients:

- Doctor knows what is coming if no adherence
- Non-adherence will cause worry, feeling of impotence, frustration
- Does not want to be blamed for the consequences

The patient's concerns

- I do not **believe** that this drug is doing me any good
- Sense of **futility** [So, why follow treatment if all is TRANSIENT ?]
- "My friend was on it but still got heart failure"
- "This drug is toxic"
- **I have side effects**
- "Doctor does not know what he is talking about"
- Treatment adds to social stigma

Why do patients have these thoughts? Causes are complex

- Psychosocial – depression, fatigue, helplessness
- Distance to travel so frequently
- Costs, especially where there is no universal coverage
- Therapy related – side effects
- Unfamiliar with the health system – e.g. new migrants, refugees
- Lack of counselling from the clinic

The most common cause globally is unavailability of the medications/cost = Involuntary non-adherence

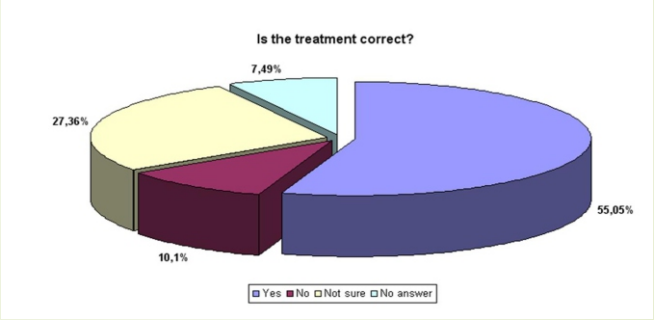
Please remember that:

- The benefits of iron chelation are not seen immediately
- The ill-effects of inadequate or interrupted treatment are not felt immediately - they come in time
- The illusion is that we are ok and will catch up with treatment later

A smoker smokes because cancer may never come

The dangers of non-adherence seem so far away!

Patient concerns – from a European survey



How does the patient cope?

- Blame the doctor – for not explaining/ not communicating
- By avoiding the issue – 'I am busy' 'denial'
- Distraction – forget thalassaemia
- Seeking support – from family, friends, the association, religion
- Seeking professional support

- 35% of adolescents with SCD pray once or more/day

Spirito A etal 1988, Milousheva J et al 1996, Cotton S et al 2009

Interrupting treatment:

- It is not an attitude of defiance or ignorance
- It is an expression of he need to normalise one's body and life
- Despite severe consequences and the risks to survival
- Adherence symbolises a threat to the normality of life
- Normalisation is a strategy of coping – enabling the individual to deal with anguish, uncertainty and suffering

Ganzella M, Zago MMF 2011

Measuring adherence

- There is no gold standard for measuring adherence
- Direct measurements, e.g. pill counts, blood levels of a drug, electronic 'medication event monitoring systems' (date and time when medication container is opened)
- Treatment outcomes – e.g changes in ferritin levels, or MRI measures
- Indirect measurements – interviews, questionnaires, self-reporting

Standard Questionnaires have been developed mostly using Likert scales so patients can grade their adherence: classic is the Morisky scale but also measures identifying patient beliefs about medication and quality of life questionnaires are used

It is hoped that 80% adherence can be reached although 'perfect' adherence can be as low as 40%

Health related quality of life (HRQOL)

WHO definition of Quality of Life

- **"An individual's perception of his/hers position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".**
- It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment
- Factors influencing quality of life include severity of anaemia, frequency of transfusions, adverse effects of chelation therapy, complications (heart, endocrines, liver), psychological disorders(such as depression and anxiety)

In thalassaemia non-adherence will result in complications which will considerably affect quality of life – heart failure, endocrinopathies (incl diabetes), growth, deformities, liver disease, bone disease

Measuring quality of life (is it constant?)

- Questionnaires have been developed and validated to measure QoL
- These may be generic (suited for all chronic diseases) SF36, EQ-5D & WHOQOL are commonly used and PedsQL for children
- They may be disease specific –

For thalassaemia TRANQOL (Klaassen RJ et al Br J Haematol 2014)

And STQOLI (Lyrakos GN et al Patient Prefer Adherence. 2012)

- They measure physical functioning and health, vitality, social functioning, emotional and mental health

These are useful tools to assess single patients or groups over time
Measures are affected by quality of treatment and adherence
Quality improvements can be monitored by HRQOL

In thalassaemia HRQOL

- **Different populations cannot be compared because quality of care can be very different, even within one country**
- **Well treated thalassaemia patients generally score well in surveys (Zani J Health Ps 2015)**
- **They score well because they have coping mechanisms aiming for positive adaptation and good quality of life:**

Avoidance/denial: passive coping, maladaptive - social withdrawal.

Distraction: forget the illness, reduce impact

Resignation - passive acceptance.

Seeking social support.

Problem solving, decision taking: playing an active role.

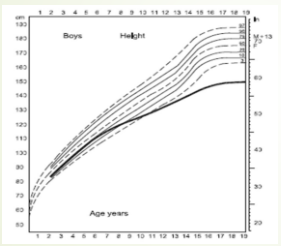
Blaming –Aggressive behaviour

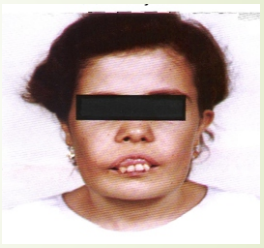
Spiritual support - role of religious belief (Meints SM et al Scand J Pain 2018)

The consequences of non-adherence

- **Patients sense of control over their illness decreases with increase in non-adherence**
- **Fears and uncertainties increase – poor social adjustment**
- **If Hb is kept low (below 9g/dl) – bone marrow expansion, deformities, poor growth, low vitality**
- **If iron chelation is not daily & at the correct dose: free iron radicals will damage cells and tissues – heart disease, hypogonadism, hypothyroidism, diabetes, liver damage**

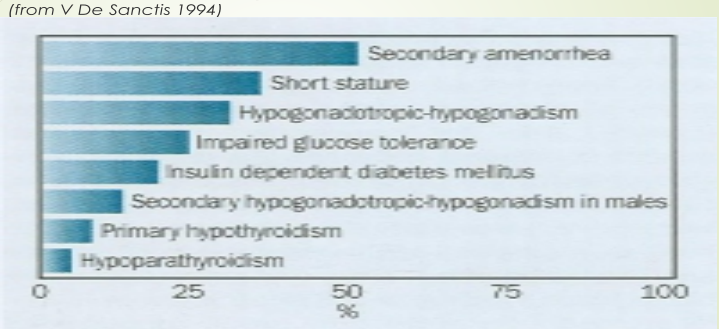
The consequences of non-adherence





Consequenses of non-adherence endocrine complications

(from V De Sanctis 1994)



Preventable causes of death in thalasaemia

- Cardiac deaths – coming down in well cared, adherent patients
- Endocrine deaths – also0 coming down
- Liver disease – not yet improved
- Thrombo-embolism – prominent cause in NTDT
- Pulmonary hypertension – still prominent cause of death in NTDT
- Infections – especially septicaemia - still prominent

Managing the non-adherence phenomenon

- Psychosocial support – especially encouraging patients to seek social contacts and talk freely about thalassaemia, also staff willing to listen
- Professional help for some patients – cognitive behaviour interventions to modify perceptions and improve adherence
- Increase patients trust and belief in the benefits of treatment – the clinics' job, doctors and nurses
- Use of technologies e.g. mobile apps as reminders and alarms
- Reducing financial burden to families – universal coverage
- The anticipation and adoption of innovations, which can reduce the burden of the condition and its treatment e.g. orally administered drugs, reducing transfusion requirements

The patient has a role in treatment adherence / concordance

Any patient can do this if given and accepts the right treatment

It is not just doctors

The patient has an active role and participation in his/her own care

Thank you for your attention

Growth & puberty in subjects with thalassemia

-Dr. Anju Seth

As children with thalassemia grow older, they become vulnerable to develop many endocrine complications. The underlying patho-physiological mechanism underlying these complications is excessive iron load, a consequence of repeated blood transfusions that these children receive from early childhood.

Endocrine glands have high levels of transferrin receptors that promote iron accumulation and hence increase vulnerability of these glands to iron toxicity. Iron stored in endocrine glands binds to intracellular transferrin. As the storage capacity of transferrin gets exceeded, pathological quantities of metabolically active iron catalyzes formation of free radicals, which in turn damage intra-membrane lipids and other macro-molecules, ultimately causing cell death and organ failure. In addition to magnitude of iron overload, the severity of clinical manifestations is also dependent upon presence of specific gene mutations.

Short stature and pubertal abnormalities are the commonest endocrinopathies observed in multi-transfused thalassemic subjects. At our Center, among the 89 thalassemic subjects above 10 years of age, 64% had short stature , while 54% had a pubertal abnormality.

Short stature:

Growth faltering can occur at all ages in these children. Many causes contribute toward growth galtering/short stature in these children (table 1). The relative contribution of various factors may vary at different ages. In children <5 years of age, hypoxia, nutritional factors and anemia are the major factors leading to short stature. These are all preventable in well managed children. In the age group of 5-10 yrs, the contributing factors include anemia and effect of iron over-load on GH-IGF1 axis. Beyond the age of 10 years, absent /reduced pubertal spurt due to involvement of hypothalamo-pituitary-gonadal axis makes a significant contribution. At all stages, co-morbidities can add further adverse influence. Children who are well transfused and adequately chelated have the best prognosis for reaching optimum height. At our Center we observed a negative correlation between height SDS and mean ferritin level and age at starting chelation.

Pubertal abnormalities:

A variety of pubertal disturbances can be seen in children with thalassemia (table 2). The underlying cause is usually damage to gonadotrophs situated in anterior pituitary leading to failure of adequate production of gonadotrophins LH & FSH. Direct gonadal damage by iron

overload is much less likely. In fact many subjects have normal ovarian function and can produce expected number of ova after stimulation and thus achieve fertility.

Presence of pubertal abnormalities has many implications apart from potential infertility. It contributes towards short stature due to absent/poor pubertal growth spurt. Associated poor sexual development contributes towards poor body image in the adolescent subject with thalassemia. Since sex steroids have an important role to play in pubertal bone mass accrual, these subjects fail to achieve optimum bone mass, a factor that contributes towards osteopathy observed thalassemia.

Clinical evaluation:

All children with thalassemia should have their growth monitored regularly since childhood. A record of height and weight should be maintained on a growth chart at 6 monthly interval to facilitate early detection of growth faltering. This would facilitate early evaluation and prompt management of underlying abnormality. In addition, evaluation for signs of onset of puberty and its progression should be assessed annually for all children above 10 years of age. All children with short stature and/or pubertal abnormalities should also be evaluated for presence of other endocrinopathies and co-morbidities (table 3).

Management:

Prevention is the best approach since efficacy of intensive chelation in reversing established endocrinopathies is unknown. Thus, preventing anemia through a regular transfusion schedule, optimum chelation, maintaining an adequate nutritional status and prompt recognition and treatment of co-morbidities form the cornerstones of endocrinopathy prevention.

Treatment of short stature involves addressing the underlying cause. These include:

- Treatment of anemia
- Correction of nutritional deficiencies if any
- Treatment of overt hypothyroidism
- GH treatment is indicated in established GH deficiency. These subjects often need higher doses due to co-existing partial GH insensitivity. In children with pubertal delay best results are observed with concomitant sex steroid replacement

Subjects with spontaneous pubertal onset are monitored carefully for progress of puberty. Those with failure to achieve spontaneous onset of puberty or with poor progression need replacement with sex steroids.

Key messages:

- Multiple endocrinopathies can develop in multi-transfused thalassemic children/adolescents
- Short stature & pubertal disturbances most common
- It is possible to have growth & sexual maturation without assistance, though many have stunted growth, sexual infantilism & poor fertility
- Regular clinical & lab screening after 10 years of age facilitates early detection & management

Table 1: Causes of short stature in children with thalassemia

Anemia causing chronic hypoxia
Calorie depletion
Delayed puberty
Thyroid dysfunction
Abnormalities of GH-IGF1 axis
Co-morbidities: HIV, hepatitis B
Bone dysplasia due to deferoxamine
Micro-nutrient deficiency specially Zn secondary to chelation
Hypersplenism

Table2: Spectrum of pubertal abnormalities in children with thalassemia

Delayed onset
Arrest at different stages
Common manifestations -Women
• Primary/secondary amenorrhoea
• Oligomenorrhoea
• Poor breast development
Common manifestations - Men
• Sparse facial & body hair
• Impotence
• Sperm abnormality-quality, morphology, motility

Table 3: Evaluation of a child with short stature/ pubertal abnormality

- Bone age assessment
- Co-morbidity screening: specially, hepatitis B,C, HIV
- T4,TSH
- LH, FSH, sex hormones (after 12-13 years if no clinical pubertal development, any time thereafter in case of pubertal arrest)
- IGF1 & IGFBP3: height SDS <-3: low levels indicate GH deficiency or defect in IGF1 generation
- GH provocation testing: ht SDS <-3 with delayed bone age

Endocrine Complications in Thalassemia Major

-Dr. Rajni Sharma

Endocrine complications can be seen in 50-60% adolescents with thalassemia major receiving regular iron chelation mostly attributable to iron overload of endocrine organs. Apart from disorders of growth and puberty which are the most common, other endocrine dysfunction may affect the quality of life and should be actively screened for on an annual basis (or earlier if symptoms appear) after the age of 10 years. These include

Hypothyroidism: Primary hypothyroidism has been reported of 6–16% in major series. Mostly cases have mild subclinical disease though overt primary hypothyroidism may occasionally occur. Tests include complete thyroid profile including T3, T4 and TSH.
Glucose intolerance and diabetes: Abnormalities in glucose metabolism generally develop in the second decade of life in thalassemia. It is attributed to the development of insulin resistance at the level of the liver owing to iron overload or pancreatic iron deposition leading to insulin deficiency. The prevalence of diabetes and impaired glucose tolerance is reported to be 8–11% in various studies. Tests include fasting and postprandial blood sugar.

Bone Problems

- Hypoparathyroidism: parathyroid gand hypofunction may result from iron deposition in the parathyroid glands leading to hypocalcemia and high serum phosphate. has been reported in approximately 10% of patients with thalassaemia.
- Osteomalacia and osteopenia: It is seen in upto 40-50% patients and can lead to fractures and spinal compression. It can result from multiple factors including hypogonadism (lack of sex steroids which are essential for bone mineralization), hypoparathyroidism, defecive GH-IGF-1 axis, marrow expansion, iron toxicity, vitamin D and calcium deficiency and toxic effects of iron chelators.
- Side-effects of chelation therapy.
    - Desferrioxamine: May cause spinal dysplasia with shortening of spine, short stature and osteopenia.
    - Deferiprone: side-effects include arthropathy of major joints and bony dysplasia of ulna and radius.
    - Deferasirox: may affect proximal renal tubular function leading to phosphate wasting and osteomalacia.

Patients should be screened for orthopedic deformities regularly. Tests for bone related health include serum calcium, phosphate, vitamin D and PTH. An annual bone mineral density with DEXA scan is also advisable after reaching adolescent age. Treatment for osteoporosis includes adequate hormone replacement therapy, calcium and vitamin D supplementation, and physical activity. Bisphosphonate therapy should be considered where indicated.

Thrombophilic Complications in Thalassemia

-Dr. V.K. Khanna

Life expectancy of thalassemics has increased with modern available treatment. However, some of the complications of the disease process which were under-recognised and under-reported earlier have recently sprung into prominence . One of these complications which needs due attention in clinical management is the hypercoagulable state. A hypercoagulable or thrombophilic state has been identified in children and adults with thalassemia. Thromboembolic events (TEE) occur more frequently in thalassemia intermedia (TI) than in thalassemia major (TM). In TI patients, thrombotic events are mostly venous and are seen primarily in splenectomized patients.

The hypercoagulable state in thalassemia has been attributed primarily to abnormalities in platelets and pathological red blood cells, although several other factors are believed to be involved. It is often a combination of these factors that leads to the hypercoagulable state. These factors (fig.1) are discussed briefly below.

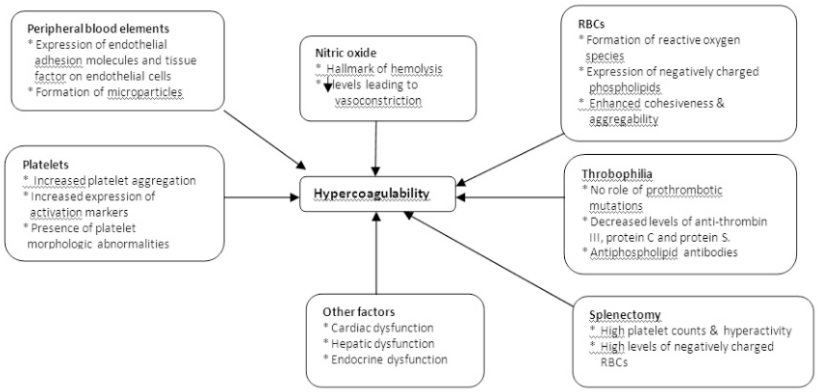


Fig. 1 Factors contributing to hypercoagulable state and thrombosis

Patients with thalassemia have activated platelets and increased platelet aggregation. Splenectomized β-thalassemia patients have high platelet counts and a shortened platelet survival due to enhanced platelet consumption.This shortened platelet life-span along with increased platelet aggregates may be associated with a chronic hypercoagulable state. The procoagulant effect of thalassemic RBCs might be the result of the presence of negatively charged phospholipids which increase thrombin generation. Splenectomized patients have a significantly higher number of these pathological negatively charged RBCs. It has also been shown that RBCs from thalassemia patients show increased cohesiveness and aggregability.

Presence of non-transferrin bound iron in patients with iron overload can cause oxidative

vessel injury. Iron overload with subsequent hepatic and endocrine dysfunction may also contribute to hypercoagulability. Thalassemia patients also have low levels of proteins C, protein S and antithrombin III and show monocyte, granulocyte and endothelial cell activation.

Splenectomy significantly increases susceptibility to thrombosis. Venous thrombosis is more prevalent in splenectomized β-TI who are not regularly transfused. Hypercoagulable state following splenectomy has been attributed to the presence of high platelet counts and to increased number of abnormal RBCs.

Clinical Experience

In a series of 83 patients followed for 10 years by Cappellini et al (2000), 29% developed either deep vein thrombosis, pulmonary embolism or portal vein thrombosis. All patients except one had undergone splenectomy. In a study of 8860 patients by Taher et al (2006) TEE were found to be 4.38 times more common in TI than in TM. More venous events were seen in TI while patients with TM had more arterial events. Most of the patients with TI who developed a TEE were splenectomized, non-transfused or had a Hb level below 9g/dl.

In one of the earlier studies, Logothetis and colleagues (1972) described a 'stroke syndrome' and neurological deficits consistent with transient ischemic attacks (TIAs) in 20% of 138 cases of TM. Borgna-Pignatti and colleagues (1998) described TIA along with other features like headache, seizures and hemiparesis in 2.2% of TM cases.

The incidence of overt stroke is higher in TM than in TI. Different studies have reported silent ischemic brain lesions in NTDT (fig.2). Older age, transfusion naivety and splenectomy were associated with a higher incidence.

Study	Patients (no.)	Mean age (yrs)	Result (silent ischemic brain lesions)
Manfree 1999	B-TI (16)	29	37.5%
Taher 2010	B-TI(30) Splenectomized	32	60%
Karimi 2010	B-TI(30) Splenectomized	24	26.7%
Metarugcheep 2008	HbE/β-Thal	31	24%

Guidelines for the management of NTDT. TIF Publication No. 19, 2013

Incidence of silent strokes in healthy individual of similar age group : 0-11%)

Manfree L et al. Am J Roentgenol 1999;173(6):1477-1480
Taher AT el al. .J Thromb Haemost 2010;8(1):54-59
Karimi M et al. Thromb Haemost 2010 ;103(5):989-993
Metarugcheep P et al.J med Assoc Thai 2008;91(6):889-894

Fig. 2 Presence of cerebrovascular disease in NTDT

Pulmonary hypertension in NTDT patients (primarily β-TI and HbE/β-thalassemia) is found to occur at a relatively high frequency compared to β-thalassemia major cases. A prevalence (based on echocardiographicfindings) of 10% to 78.8% has been reported in β-thalassemia with high prevalence in NTDT patients. The diagnosis was based on tricuspid valve regurgitant jet velocity (TRV) exceeding 2.5-2.8m/s which corresponds to a pulmonary artery systolic pressure exceeding 30-35mmHg. The use of echocardiography alone results in considerable number of false positive diagnosis. It is recommended that the diagnosis should be confirmed by right heart catheterization. However, it has been observed that when a threshold TRV of 3.2m/s is used, the positive predictive value of echocardiography was as high as 93.3%. PHT is the leading cause of right heart failure in NTDT.

The exact mechanism for the pathogenesis of PHT is not clear. Chronic anemia and hypoxia, iron overload, splenectomy, hypercoagulability and microthrombotic disease of the pulmonary circulation have been implicated in the pathophysiology of pulmonary hypertension in NTDT.

Preventive Strategies

Thelower rateof thromboticevents inregularly-transfused β-TM patients than TIpatients may be explained on the basis of transfusion therapy. Blood transfusion may reduce hypercoagulability by decreasing the number of abnormal RBCs with thrombotic potential. Since most thalassemia patients suffering from thrombotic events are splectomized and have large number of abnormal RBCs, one approach that has been suggested but needs confirmation is, to initiate regular blood transfusion in splenectomized patients.

Hydroxyurea has been shown to reduce phospholipids expression on the surface of RBCs thereby decreasing the production thrombin and coagulation activation in NTDT patients. The role of hydroxyurea in preventing thromboembolism in NTDT patients has not been established. However, lower rates of silent strokes in β-TI patients using hydroxyurea has been suggested in one study.

Although there is no data from clinical trials for effectiveness of anticoagulant and antiplatelet therapy for the prevention of thrombotic and cerebrovascular disease in thalassemia patients but few observations tend to support this form of therapy. One of these is the association betweenhighplateletcountandthrombosisand,theother ,istheobservedlowerrecurrence rate of thrombotic events in splenectomized β-TI patients who took aspirin after their first thrombotic event. It has also been suggested that aspirin and anticoagulants could be consideredin patientswith conditionsthat areknown independentpredictors ofthrombosis like pregnancy, sepsis and surgery.

The strong association between splenectomy and thrombotic events suggest that the procedure should be performed only when it is absolutely necessary, such as in cases of symptomatic massive splenomegaly or hypersplenism.

Recommendations of Thalassemia International Federation on NTDT and Thrombotic Disease

- NTDT patients with following factors should be considered at higher risk:
  - β-thalassemia intermedia.
  - splenectomy
  - never or minimally transfused
  - platelet count $\geq 500X10^{9}/L$
  - nucleated RBCs counts $\geq 300\ X10^{6}/L$
  - Hb< 9g/dl
  - history of pulmonary hypertension
  - iron overload (LIC $\geq$5mgFe/g dry weight or serum ferritin $\geq$800ng/ml)
  - pregnancy
  - personal or family history of thrombosis
  - conventional risk factors for thrombosis or cerebrovascular disease.
- Prophylactic intervention with anticoagulants or anti aggregants in high risk patients should follow standard guidelines.
- Aspirin therapy should be considered in splenectomized NTDT patients with platelet counts $\geq 500\ X10^{9/}L$.
- Transfusion therapy should be considered for primary or secondary prevention of thrombotic or cerebrovascular disease in high risk patients.
- Thereis notsuf ficient datato recommend ironchela tionor hydroxyureathe rapyfor the primary or secondary prevention of thrombotic or cerebrovascular disease, although when used for different indications, a beneficial effect may be observed.

The hypercoagulable state in thalassemia is due to multiple factors and a combination of these factors is responsible for a clinical thromoembolic events. The higher incidence of thrombotic events in TI as compared to TM is mainly related to transfusion naivety and splenectomy. For prevention of this complication an individualized approach after taking into consideration all associated risk factors is recommended.

No Bone Deserve a Break

-Dr. Rashid Merchant

Osteopathy in thalassemia major has emerged as a topic of interest since optimized transfusion regimenshave increasedlife expectancyand improvedquality oflife inthese children.It is clear that a large number of factors interact at the level of the osteoblast, osteoclasts and other cells to regulate the balance between net bone resorption and formation. Due to chronic anemia and expansion of bone marrow cavity there is loss of trabecular bone tissue resulting in osteopathy. The other factors are iron overload, iron chelators (especially deferioxamine) and genetic factors (polymorphism of VDR gene and COL1 gene). Endocrine factors like hypogonadism, aberrant vitamin D and PTH axis and low IGF-1 also contribute significantly forlow bonemass. Theimportant variablesfor evaluationof boneformation andresorption are 25 hydroxy vitamin D, parathyroid hormone (PTH), insulin like growth factor-1 (IGF-1), serum osteocalcin, urine or serum crosslaps and gold standard test for osteoporosis evaluation and risk for fracture is bone mineral densitometry (BMD).

in our experience in children with thalassemia major between 10-25 years of age 6had fractures, 9 avascular necrosis of hip, 2 tetany, 2 hypocalcemic seizures and 1 bowing of legs.Dual energy X-ray absorptiometry (DEXA) revealed osteopenia/ osteoporosis in 81% of children. All of them had high serum ferritin levels (Mean 5344 ng/ml). Serum calcium levels were low in 16% and high alkaline phosphatase was seen in 37% cases only. 25-OH vitamin D waslow in62%, hyperparathyroidismin38%, highurinary crosslapsin 55%,low IGF-1in 52% and elevated serum osteocalcin in 36% of these children. Endocrine evaluation in these series showed low levels of FSH, LH, estradiol and free testosterone in 14%, 3%, 44% and 90% respectively. As age advances the incidence of osteoporosis increased and was statistically significant. There was no statistical significant difference in any of the biochemical parameters studied between those with normal or abnormal DEXA. Pre-transfusion hemoglobin (Hb), transfusion requirement and chelation therapy used also did not show any significance in children with or without normal DEXA.

We recommend that for prevention and management of children for osteoporosis in thalassemia is to maintain adequate transfusion regimen to achieve Hb level above 9 g/dL and appropriate chelation therapy to target serum ferritin below 1000 ng/ml.BMD is the gold standard test for diagnosis of osteoporosis as it is non-invasive and easy to interpret. BMD by DEXA should be evaluated annually from 10 years onwards and earlier if symptomatic. Age matched Z scores in young children and T score in adults should be measured for diagnosis of osteopenia/osteoporosis.X-rays are indicated in symptomatic children for diagnosis of

fractures, avascular necrosis or compression of spinal vertebrae. MRI may be useful to diagnose degenerative changes, extramedullary hematopoiesis and disc prolapse.Biochemical evaluation (serum calcium, phosphorus, alkaline phosphatase) should be monitored after receiving 2 years of transfusion every 3-6 months.Hormonal investigations (25 OH vitamin D, PTH, endocrine hormones) and if needed serum osteocalcin, crosslaps should be monitored once a year if initial biochemical evaluation shows abnormality or if symptomatic or after 12 years of age.

All children should receive daily calcium intake from dietary source and supplements (0.5-1.0 g/day) upto 2.5 g/day. All children also should receive maintenance vitamin D (cholecalciferol)of1000IU/day .Incaseofdeficiency (25OHvitaminDlevels<30 ng/dL) should be treated with 60,000 IU/week for 2-6 months with monitoring for hypercalciuria and renal stone disease till vitamin D levels are within normal range. In children with hypogonadism and osteoporosis, hormone replacement therapy (HRT) is the first choice of treatment for 2 years with monitoring of correction of hypogonadism with trough sex steroid levels.Bisphosphonates should be used as second choice and in children without hypogonadism for duration of 3-5 years. Combination therapy with bisphosphonate and HRT can also be used in children with severe osteoporosis.Calcitonin nasal spray (200 IU/day) can be used to inhibit osteoclastic activity (elevated crosslaps or PTH levels) and especially in children with vertebral fractures.T eriparatide (iPTH) can be used in severe osteoporosis as anabolic agent for 2 years in children more than 18 years not responding to above therapies.

Motherhood Thalassemia Major, Minor, Intermedia (Fertility & Pregnancy Care)

-Dr. Manju Puri

Thalassemia is the commonest single gene disorder in the Indian population with 40 million carriers and 1,00,000 patients. Approximately 32,000 babies are born with a serious haemoglobin disorder each year in India; 10,000-12,000 being β thalassemia majors. Over the past few decades regular blood transfusion and iron chelation has dramatically improved the quality of life. A rapidly fatal disease in early childhood has been transformed into a chronic disease compatible with prolonged life hence the concerns about their fertility and motherhood.

Endocrine complications are the commonest in -TM & -TI and are attributed to iron overload and suboptimal chelation. Metabolically active iron catalyses the formation of free radicals, which damage membrane lipids leading to cell death and organ failure. Endocrine glands are particularly vulnerable requiring prompt recognition and treatment. Frequency of damage is lower in -TI than -TM and varies greatly according to severity of the anaemia and iron overload.

Women with TM, who are regularly transfused and well chelated, can become pregnant spontaneously or may suffer from infertility due to hypogonadotropic hypogonadism (HGHG) due to damaged pituitary and hypothalamus. In HGHG infertile women with undamaged ovaries pregnancy can be achieved with ovulation induction with gonadotropins however in those with damaged ovaries pregnancy can result from IVF with donor oocyte. The desire of the thalassaemic woman to become a mother should be viewed with special caution and sensitivity as it poses numerous medicolegal and ethical issues that need to be addressed prudently to optimize patients' quality of life and foetomaternal outcome. It is important to provide preconceptional counselling and evaluation of the patient prior to inducing ovulation induction or advising the patient to plan a pregnancy.

Pre-conceptional counselling includes apprising the patient of an increased risk to both mother and baby; cardiomyopathy in mother and FGR and or haemolytic disease in the foetus. The patient needs to stop iron chelation during pregnancy especially in 1st trimester due to its teratogenic effect predisposing her to an increased risk of new endocrinopathies during pregnancy. Partner screening and counselling is desirable if the partner is a carrier of a haemoglobinopathy. The preconceptional evaluation includes assessment for end organ damage that is pancreas, thyroid, heart and liver. Screening for viral infections and alloimmune antibodies. A bone density scan for osteoporosis and serum Vitamin D levels.
The woman's need for blood transfusions and compliance to iron chelation is reviewed. The

body iron burden is assessed through T2 cardiac MRI and Ferriscan or T2 liver MRI. The iron burden of body is optimized by aggressive chelation prior to conception. The woman is switched to safer chelating agents like desferrioxamine 3 months prior to ovulation induction. The immunization of the woman to Hepatitis B, influenza and pneumococcus vaccine is ensured. Antibiotic prophylaxis is splenectomised women is ensured and they are supplemented periconceptionally with folic acid 5 mg per day.

Early recognition of complications, institution of appropriate treatment including transfusion regimen and chelation therapy, and specific treatment of each complication are the keys to successful management. Meticulous follow-up by a multidisciplinary team in a comprehensive thalassemia centre as well as strict compliance with tailored treatment protocols are major prerequisites for achieving and maintaining an excellent prognosis of pregnancies in women with thalassemia.

Fertility and Pregnancy in Women with Thalassemia Major and Intermedia

-Dr. Vatsla Dadhwal

Beta Thalassemia is a hemoglobinopathy characterized by decreased production of beta globin chains causing alpha globin chains to accumulate and aggregate. This results in inadequate hemoglobin production. There is microcytic hypochromic anemia, ineffective erythropoiesis and hemolytic anemia. Diagnosis is made by detecting low HbA and increased HbA2 and HbF.

Types

thal minor/ trait: mild or no anemia thal major (BTM): severe form, only HbA2 and F detected. Severe anemia, transfusion dependent and develop complications of iron overload thal intermedia (BTI): present late in life, mild anemia, not transfusion dependent, may develop iron overload.

Fertility

BTM: infertility or subfertility is due to iron deposition in endocrine organs. Direct iron deposition occurs in hypothalamus and pituitary and ovaries. Iron deposition leads to organ damage through oxidative stress.
Majority of patients are infertile due to hypothalmic hypogonadism , associated with amenorrhoea, anovulation and infertility. Ovarian functions are usually preserved. These women require ovulation induction with gonadotropins to conceive.
Spontaneous pregnancy can occur in well chelated and transfused patient

Pregnancy management

BTI

Spontaneous conception and successful pregnancies occur but pregnancies are associated with complications.
Chronic anemia leads to abortions, preterm labour and intrauterine growth restriction. Endocrine complications due to hemosiderosis can occur, though less common compared to

BTM.

In a large study which included 83 pregnancies in 44 women, 20.5% ended in abortion, 77.1% had live biths and 2 had intrauterine death. Mean gestational age at delivery was 36.5 weeks and birth weight 2551gms. Cesarean section rate was 72.7%. 79.5% women required blood transfusions and 27.3% required transfusion for first time. There was increase in average ferritin levels before and after pregnancy.
Patients with BTI have increased incidence of thrombotic events.

BTM

Aggressive transfusion and iron chelation therapy has improved life expectancy and fertility with decrease in medical disability. Many cases of successful pregnancy have been reported. These pregnancies need to be monitored carefully for adverse outcome.

Preconception evaluation

- Transfusion needs
- Compliance with chelation
- Iron load status
- Indirect coomb's test
- Screen for infections-HIV, Hepatitis B and C
- Assess end organ damage from iron overload
- Genetic evaluation of partner and need for prenatal testing

Adverse effect on pregnancy depends on

- Presence of alloimmune antibodies
- Cardiac dysfunction
- Severe diabetes mellitus
- Liver dysfunction
- Active hepatitis/HIV
- Significant enlargement of spleen

Prenatal care

- Folic acid
- Interdisciplinary team
- Ferritin levels and blood counts
- Blood transfusions to maintain Hb 10g/dl
- Cardiac, endocrine, hepatic function at initial visit and repeat in each trimester
- Screen for diabetes and hypothyroidism
- Fetal growth and well being
- Iron chelating agents to be stopped in pregnancy .

In a recent large series of 58 pregnant women with BTM, intrauterine growth restriction and preterm delivery occurred in 40%, 15% developed IGT/abnormal GTT, there was increased need for transfusion , there was 60% increase in baseline ferritin. There were many twin pregnancies as most women conceived on ovulation induction using gonadotropins.
Cardiac involvement and arrhythmias are important cause of morbidity and death.

Delivery: route of delivery as per obstetric indications. Cesarean section rates are high because of cephalopelvic disproportion due to short stature or other pregnancy related complications.

Infection complications post allogenetics stem cell transplantation

-Dr. Dinesh Bhurani

Introduction

Allogeneic stem cell transplantation involves identification of a suitable stem cell donor who is matched at Human Leukocyte Antigens (HLA), and then preparation of the patient with a combination chemotherapy/ chemo-radiotherapy (conditioning regimen), stem cell infusion, graft versus host disease (GvHD) prophylaxis and infection prophylaxis/ monitoring. The patients remain immuno-suppressed during and after the transplantation for a prolonged period of time and at risk of variety of infections.

Reasons for heightened risk of infections in various phases of transplantation are:

1. Damage to mucosal barrier (usually recovers after 2-4 weeks, as soon as engraftment occurs)
2. Neutropenia (usually recovers after 2-4 weeks)
3. Humoral (B cell) immune-deficiency (usually recovers after 2-6 month or may be many years)
4. Cell mediated (T cell) immune-deficiency (usually recovers after 6 months to 1 year)
5. Thymic dysfunction due to effects of chemo-radiotherapy and GvHD also common in adults

Factors which may further prolong the immune recovery are

1. GvHD and its treatment specially steroids
2. HLA disparity/ mismatch
3. T cell depleted graft
4. CMV infection
5. Source of stem cells (more prolonged immune-suppression with cord blood and bone marrow stem cell transplantation as compared to peripheral blood stem cell transplants)

Infectious complications

Bacterial, fungal, protozoal and viral infections are a major cause of morbidity and mortality after allogeneic transplantation. The temporal pattern of infectious complications after allogeneic SCT is shown in Figure-1

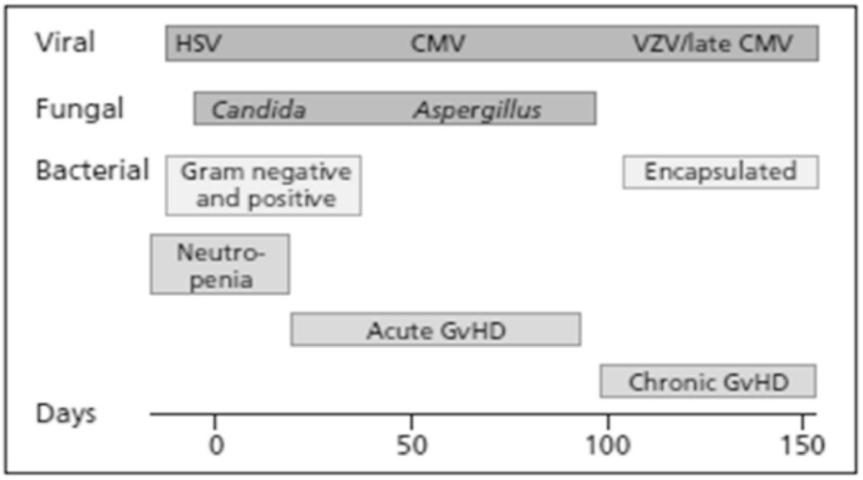


Fig-1. Temporal pattern of infectious complications after allogeneic stem cell transplantation

Bacterial Infections:

Bacteria are ubiquitous and even human body is colonized by many commensals. During transplantation, as soon as the mucosal barrier damages and neutrophil counts fall, these bacteria may invade the blood stream or may produce local site infections. Common bacterial infections in early post transplant phase are gram negative (E. Coli, Klebseilla, Pseudomonasspecies) andgram positive(staphylococcus species).Bacterial infections can produce septicaemia, hypotension and can rapidly be fatal.

Monitoring for bacterial infections include a close watch on body/ oral temperature as well as other vital signs like pulse rate, blood pressure respiratory rate and urine output. A temperature reading of 100.4F for 1 hour or a single reading of 101 F indicates a serious infectionandwarrant urgenttreatment. Thetreatmentconsists ofsendingblood culture and other appropriate culture (urine/sputum/ mucosal swabs) and starting broad spectrum antibiotics (specially covering gram negative bacilli) within 60 minutes of documentationof fever. Antibioticpolicy dependsupon institutionalculture sensitivity pattern. Usually a third generation cephalosporin is preferred with or without an aminoglycoside. With currently prevalent B-lactamase producing bacteria, the sulbactam/ tazobactam can be combined with an antibiotic. A carbapenem antibiotic can be used in first line or be reserved for 2nd line therapy. Antibiotics should be optimized as soon as the culture reports become available.

During later phases after transplantation (months to year), patient may remain immuno-deficient, especially for humoral immunity. This makes him vulnerable for infections with encapsulated bacteria (Pneumococcus and Haemophillus species). Long term prophylaxis with penicillin and immunization can help prevent these infections. These infections can be life threatening and should be treated aggressively with appropriate antibiotics.

Fungal infections

Fungal infections still remain a major complication and cause of death after SCT. A high index of clinical suspicion is therefore required in transplant patients, and most units administer systemic antifungal therapy early in the management of neutropenic fever. Risk factors for the development of fungal infection include prolonged neutropenia after SCT (early post transplant phase, 2-4 weeks), the use of high dose corticosteroids for treatment of GVHD (usually after 1 month of transplantation) and a history of prior fungal infection.

Candida infections typical manifest as oral thrush and less commonly as oesophageal candidiasis. Hepato-splenic candidiasis is seen occasionally, presenting with high spiking fevers at the time of engraftment in association with abnormal liver function tests. Ultrasound or computed tomography (CT) of the liver and spleen will confirm the diagnosis. Prophylactic use of fluconazole (400 mg daily) has proved effective in reducing the incidence of both superficial and invasive candidiasis. Patients who develop either hepato-splenic candidiasis or candidemia should be treated with systemic antifungals, usually liposomal amphotericin. All indwelling catheters must be removed. Culture and sensitivity must be sought as fluconazole - resistant Candida species such as Candida kruseii or Candida glabrata is of concern.

Aspergillus infections usually present prior to or shortly after engraftment. The most common manifestation is as invasive pulmonary aspergillosis (IPA), which typically presents with an antibiotic resistant fever, a significantly raised C reactive protein, and abnormal chest radiography or high resolution CT. Rarely invasive Aspergillus infections can present with cerebral or hepatic disease. Accurate diagnosis of Aspergillus infections remains problematic since spores are only rarely cultured from broncho-alveolar lavage fluid or infected tissues and the sensitivity and specificity of other currently available diagnostic techniques is low. Galactomannan in blood or broncho-alveolar lavage (BAL) and PCR technology are not enough sensitive and specific, though may be of help in establishing a probability of aspergillus infeciton. Operationally, the most helpful test in deciding whether IPA is a clinical possibility is high resolution CT of the chest, which should be obtained in all patients with a neutropenic fever that has persisted for more than 72hours. Whilethecharacteristicradiographicfeaturesofperipheralnodularshadows,

with or without evidence of cavitation or a 'halo' sign, may take weeks to develop, the presence of any significant pulmonary infiltrate substantially increases the likelihood of Aspergillus infection and is an indication for the consideration of treatment doses of liposomal amphotericin or voriconazole.

Viral Infections (Herpesvirus infection: CMV, HSV and Varicella zoster).

Though many viruses can cause illness during or after transplantation, the common and preventableviralinfectionsareherpesvirusesthatarecytomegalovirus(CMV),herpes simplex virus HSV, varicella zoster (VZ).

CMV: Human CMV is ubiquitous and present in 90-100% of the general population in India.CMV remainsdormant forlifelongand canbereactivated inimmunosuppressed states. CMV reactivation after allogeneic SCT can give rise to either asymptomatic infection or, less commonly, end organ damage (CMV disease) and death.

Patients at the highest risk of CMV reactivation are seropositive recipient, especially those who receiveT Cell depleted or unrelated donor grafts, and patients who develop GVHD requiring steroid therapy. CMV reactivation occurs in 40 80% of at risk patients and until recently a substantial number of such patients developed CMV disease (commonly pneumonia and rarely gastrointestinal ulceration, hepatitis and retinitis).

Primary infection of CMV seronegative patients may occur as a result of the infusion of stem cell or blood products from a CMV positive donor. For this reason seronegative transplant recipients should receive CMV negative or leucodepleted blood products to limit the possibility of primary infection.

Until recently CMV was the commonest cause of infectious death after allogeneic transplantation. It is now possible to detect low levels of CMV viremia after transplantation, using either polymerase chain reaction (PCR) based detection of CMV or detection of pp65 antigen in peripheral blood leucocytes (CMV antigenemia). The introduction of these sensitive diagnostic techniques coupled with the development of effective antiviral drugs has markedly reduced the incidence of CMV disease.

All patients at risk of CMV infection/ reactivation should undergo weekly/ biweekly PCR or CMV antigenemia testing from engraftment until 100 days after transplantation.

There are two strategies for prevention of CMV disease. One is primary prophylaxis and the other one is pre-emptive therapy. Giving anti CMV therapy to all patients or to specially high risk patients for prevention of viral reactivation is called primary prophylaxis. The drug of choice was injectable gancyclovir. The disadvantage of this strategy was that there was a high rate of neutropenia and secondary infections (neutropenic sepsis) in patients receiving gancyclovir. To avoid the risk of neutropenia to all patients, the primary prophylaxis strategy was dropped. Currently adapted strategy is

pre-emptive therapy, where the patient is regularly monitored for CMV viremia or antigenemia and as soon as the CMV reactivation is detected, the patient is subjected to gancyclovir therapy. The pre-emptive strategy is effective in preventing CMV disease while avoiding unwanted neutropenia/ toxicity to all patients.

Dosesof ganciclovir 5 10 mg/kgda ilya djusteda ccording torena lfunct ion. Them ajor side effect of ganciclovir is myelosuppression, which is especially problematic in patientstransplanted usingan unrelatedor cordblood donor.Randomized studieshave confirmed that this pre - emptive treatment strategy reduces the risk of CMV disease and death after sibling allogeneic transplantation. The use of prophylactic ganciclovir, which is administered regardless of whether there is evidence of CMV infection, does not improve outcome and is associated with significant bacterial and fungal infections consequent on high rates of my elotoxicity.

Foscarnet, a DNA polymerase inhibitor, has less myelotoxicity than ganciclovir and is effective as part of a pre - emptive approach, although it is associated with significant nephrotoxicity.

The incidence of CMV pneumonitis after allogeneic transplantation has substantially reduced since the advent of effective screening and pre - emptive treatment strategies. It occurs in patients with evidence of CMV reactivation within the first 100 days after transplantation and typically presents with dyspnoea, hypoxaemia and pulmonary infiltrates. Ganciclovir and foscarnet are often ineffective in patients with established CMV pneumonitis. However, recent studies have demonstrated significant activity of cidofovir, which is considered in some units as first line treatment in all patients with CMV pneumonitis. Cidofovir is nephrotoxic but can usually be safely administered if attention is paid to adequate hydration and other nephrotoxic drugs, particularly foscarnet, are discontinued. The role of high titre CMV immunoglobulin in the treatment of CMV pneumonitis remains unclear, although it is still widely used, if available.The effective treatment of CMV infection delays the development of an immune response to CMV and as a result late (beyond 100 days post - transplant) CMV reactivation and disease is increasingly observed. Risk factors for late CMV infection include previous CMV reactivation, lymphopenia and the presence of active GVHD.

HSV and VZ: Other members of the herpesvirus family have the potential to cause significant morbidity after allogeneic SCT. The incidence of HSV, which used to be very common in the first 30 days after SCT, has been sharply reduced by the use of prophylactic aciclovir. Reactivation of varicella zoster virus (VZV) occurs in up to 50% of at - risk patients after allogeneic SCT and typically presents as shingles with severe pain and a dermatomal vesicular eruption. Less commonly, VZV reactivation presents

with atypical pain (headache or undiagnosed abdominal pain) in the absence of a rash. PromptttreatmentofVZV infections withhigh -dose intravenousaciclovir is indicated after allogeneic SCT to prevent dissemination but also to reduce the severity of post - herpetic neuralgia.

Prevention/ Prophylaxis of infections:

Considerable progress has been made in the development of strategies to reduce the risk of infection after allogeneic SCT.

1. All patients should be nursed in single rooms, preferably with laminar airflow or high - efficiency particulate air (HEPA) filtration.
2. Antifungals for prophylaxis: fluconazole 400 mg daily, as an effective means of reducing Candida infection.
3. Anti viral prophylaxis: Aciclovir (200 400 mg four times daily) is usually administered to prevent herpes simplex virus (HSV) reactivation.
4. Antibiotics for prophylaxis:

a. Quinolone antibiotics (e.g. ciprofl oxacin 500 mg twice daily) are used by some units to reduce the risk of severe Gram -negative infections, although the evidence supporting this measure is inconclusive and practice should be guided by advice from local microbiologists concerning the prevalence and sensitivity of drug - resistant organisms.

b. Co -trimoxazole (480 mg twice daily three times per week) at the time of neutrophil engraftment (neutrophils >500 per uL) to prevent Pneumocystis jirovecii infection.

c. If allergic to co -trimoxazole, nebulized pentamidine (300 mg monthly) can be substituted, although it should be remembered that this provides incomplete protection from Pneumocystis pneumonia and for this reason some units prefer to use dapsone.

d. Allogeneic transplants, particularly recipients of TBI containing regimens, continue to be at long - term risk from infections caused by encapsulated bacteria such as Streptococcus pneumoniae and Haemophilus influenzae and require lifelong prophylaxis with penicillin (250 mg twice daily) or erythromycin (250 mg twice daily) if allergic to penicillin.

5. Vaccination: Antibody titres to diseases for which childhood vaccination is performed decline after SCT. Revaccination is therefore recommended, particularly in allograft recipients, and most centres commence such a programme 12 months after transplantation or after stopping all immunosuppressive medicines.

Primary Prevention of Thalassemia

Dr. Sangeeta Gupta

Thalassemia is most common inherited autosomal recessive blood disorders. The incidence of beta thalassemia in different regions of India varies from 3% to 17% with a mean prevalence of 4%

Haemoglobin is a tetramer composed of of 2α globin and 2β globin chains. Thalassemia results in microcytic anaemia caused by mutation of the alpha and beta-globin gene leading to decreased or absent synthesis of β globin, resulting in ineffective erythropoiesis. Thalassemia major manifest with severe anaemia and regular blood transfusion. Community control programmes are the only way to reduce this burden. Screening for identification of carriers forms an integral component of a prevention programme

Genotypic classification: - a) Heterozygous thalassemia (thalassemia trait)
b) Homozygous thalassemia

Phenotypic classification

Silent carrier: Completely asymptomatic with normal hematologic parameters.

Thalassemia minor: Usually asymptomatic and diagnosis is based on screening when there is a positive family history, or during a workup for mild anaemia

Thalassemia intermedia: Usually a similar presentation to beta-thalassemia major, less pronounced and the course is usually more insidious.

Thalassemia major: Complete absence of haemoglobin A; often presents at a few months of age with progressive pallor and abdominal distension; perinatal history is most often uneventful, and the infant may be pale, possibly with poor feeding and decreased activity; hepatosplenomegaly and bony abnormalities are often present at presentation, most often of the skull (frontal and parietal bossing, and chipmunk facies).

PREVENTION OF THALASSEMIA

Thalassemia is an autosomal recessive disease due to point mutations in one of globin change. It is possible to prevent new disease with proper education, carrier screening and timely prenatal diagnosis.

AIM: To prevent the birth of patients with thalassemia

FOCUS

1**) Education:** Mainstay of prevention programs. Its aim is to improve awareness and knowledge

a) Education of healthcare providers: Education is provided in the form of regularly scheduled meetings amongst physicians (primary care provides, paediatricians, obstetricians), nurses, social workers, and other healthcare team members.

b). Education of large-scale population: Can achieve via distribution of information booklets, use of social media, and printing of posters. These materials are typically placed in strategic sites where patients are most likely to read them, including family planning clinics, counselling rooms, and marriage registries.

2). Carrier screening:

a) Especially in high risk groups and pregnant women

Investigation	Normal	Thalassemia carrier	Special consideration
Haematology	MCH (pg) >27 MCV(fl)->80	MCH < 27 MCV < 80	Iron deficiency anemia to be ruled out
RBC count		RBC count > 5.0 $\times 10^6/\mu L$)	-Only 70.5% specificity & 65.3% -RBC alone is not a reliable tool for distinguishing thalassemia from IDA. -Elevated RBC count might be associated with erythrocytosis.
Haemoglobin electrophoresis	HbA2(%) <3.3, Hb A+A2	Hb A2(%) >3.5 A+(F)+A2	-Normal HbA2 level in α thalassemia trait* -In rare cases of concurrent severe iron deficiency, an increased Hb A2 level may not be observed, although it becomes evident with iron repletion
Red cell distribution width index (RDWI)= (MCV x RDW /RBC).	>220	< 220	-Better and more accurate predictive marker for β-TT as a screening tool in comparison to Mentzer index. -Sensitivity & specificity of RDWI is 80.7% and 84.7%, respectively.
Mentzer index(MCV/RBC count)	>13	<13	- RDWI and Mentzer index both are screening methods, can be used to determine the patients who are the best candidates for Hb electrophoresis. -sensitivity (80- 90%), specificity (80%)

Peripheral blood smear	Normocytic normochroic	Microcytes , hypochromia,target cells, poikilocyte & Heinze body	
Naked eye single tube red cell osmotic fragility test (NESTROFT)- detects the osmotic fragility of red cells	Negative	Positive (pronounced decrease in osmotic fragility of red cells in β thalassemia)	-High sensitivity (90-95%) & negative predictive value along with low cost and simplicity, this is suitable for mass screening of high-risk population in a low resource country like India - False positive report in the 4 -5 % patients with IDA -If combined with red cell indices using MCV & MCH ,only 1.8 % b-thalassemia carrier may be missed -In population with Hb S & Hb E NESTROFT test is not sufficient as it may miss 25%–40% of carriers

* Definitive diagnosis of α thalassemia trait requires measuring either the alpha-beta chain synthesis ratio or performing genetic tests of the alpha-globin cluster (using Southern blot or polymerase chain reaction [PCR] assay tests).

b). DNA analysis- used to confirm mutations in the alpha and beta globin-producing genes. DNA testing is not routinely done but can be used to help diagnose thalassemia and to determine carrier status, if indicated.

c). Family study: Blood samples to from family members of patient

d). Molecular diagnosis: Molecular analysis (ARMS, Sequencing etc.)

3). **Genetic counselling**: - It is an important component of prevention programs for thalassemia. It should be comprehensive and include diagnostic as well as clinical aspect of disease, mode of inheritance, risk estimation and possible preventive measures. Genetic counselling is aimed about informing carrier about issues as reproductive options, partner selection, birth control and prenatal diagnosis. This is especially important in patients who are heterozygous for globin gene mutations, since mating with another heterozygote can result in the birth of a baby with a significant disease burden. Consanguinity increases the risk of having affected child as there is higher possibility of two carriers getting married.

4). Prenatal Diagnosis and selective termination of affected pregnancy-

It is mainly part of secondary prevention-

Prenatal diagnosis is the only effective way to prevent the birth of a fetus with severe thalassemias, which include hemoglobin Bart's hydrops fetalis and thalassemia major. It is based on determination of the mutations in the α- or β-globin genes of foetus if both partner are thalassemia carrier, and selective termination of pregnancy of fetus with homozygous or compound heterozygous mutations. Most critical issue in prenatal diagnosis is maternal cell contamination (MCC), especially when a fetus is found to inherit a particular mutation from the mother.The recent successful studies of fetal DNA in maternal plasma may allow future prenatal testing that is non-invasive for the fetus and result in significant reduction of invasive diagnostic procedures.

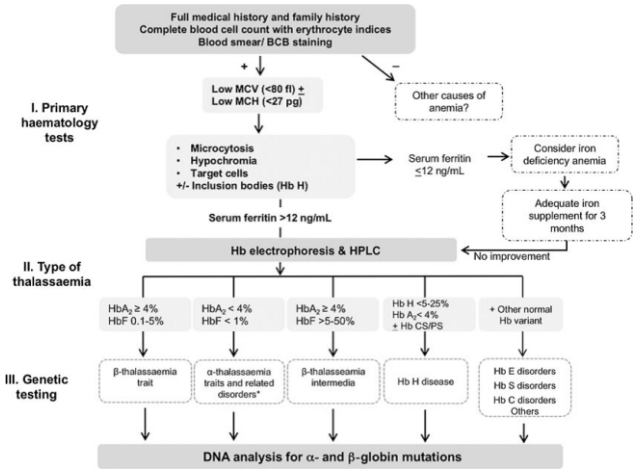
PGD (Pre Implantation)

CVS (1st Trimester)

Amniocentesis (2nd Trimester)

Barriers to Primary prevention-

Lack of awareness and poor understanding related to thalassemia propagation results in poor carrier screening. There is also lack of quality genetic counselling. Cost and religious beliefs are also the barrier for prenatal diagnosis and termination of affected foetus.



providers and patients, encouraging better communication and limiting the chances of misdiagnosis.

The success of a patient engagement is solely determined by transparency in the information conveyed to them, in order for them to make informed decisions with their health providers. Hence empowering patients with the right information about their health, ways to care for themselves and divulging information regarding their treatment will go a long way in ensuring continued engagement with health providers.

Patient and family engagement may begin with educating and empowering people to recognize their health needs and to seek health care in a timely manner. Encouraging people to ask questions or speak about their concerns is important. Informed patients are more likely to feel confident to report both positive and negative experiences and have increased concordance with mutually agreed care management plans. This not only improves health outcomes, but also advances learning and reducing adverse events.

The term **"patient engagement"** refers to the process of building the capacity of patients, families, carers, as well as health care providers, to facilitate and support the active involvement of patients in their own care, in order to enhance safety, quality and people-centeredness of health care service delivery.

The move from empowerment to engagement means that providers are no longer giving patients their information and allowing them to control the outcome, but rather providers are now actively working to engage patients in their healthcare. The patient is a participant, but they are no longer viewed as really the owner and driver of the process. Engaged patients are better able to make informed decisions about their care options.

Essential strategies to improve patient engagement:

1. Keep the information simple. Do not use jargon and acronyms.
2. Be as specific as possible.
3. Get patients involved in setting their goals.
4. Ensure everyone is on the same page.
5. Make information sharable.
6. Create accountability.

Ways to Engage:

Patients

- Be part of the organization's leadership or government team, as board members.
- Care Partner or family member be present and engaged for all conversations.
- See and contribute to your medical record. If you don't understand, ask questions.
- Come to doctor's appointments prepared. Bring a notepad with questions, your medication list and any other pertinent personal healthcare information.

Engagement and Empowerment

-Dr. J.S. Arora

Like any relationship, a provider-patient relationship also requires good communication and trust in order to work towards a common goal. In healthcare, the goal would be to ensure better health outcomes. This is why patient empowerment and engagement is exceedingly becoming a necessity in healthcare today. In fact, health policies in several countries around the world are implementing strategies to increase patient empowerment & engagement and in order to get them more involved in their health care.

Engagement and empowerment are two tossing words. Their meaning and impact are overlying

Empowerment – making the patients aware of their condition and putting the information in their hands and giving them control of their destiny.

Engagement means that providers are not just giving patients their information and allowing them to control the outcome, but providers actively work to engage patients in their healthcare.

What is patient empowerment?

Patient empowerment is a process that helps people gain control over their own lives and increases their capacity to act on issues that they themselves define as important. The best way to define patient empowerment would be to describe it as an inclusive practice that encourages patients to be actively involved in their providers' health services. The aim of empowering patients is to help them develop self-awareness, self-care and promote the confidence in their healthcare decisions. Patient empowerment puts the patient in the heart of services. It is about designing and delivering health and social care services in a way, which is inclusive and enables patients to take control of their health care needs, understands their health condition and its effect on their body.

Why is it important for providers?

Meaningful engagement with patients helps them understand and participate in their care more proactively. This, in turn, improves treatment compliance and adherence, meaning patients end up getting healthy and as a result, they are more satisfied with their health provider.

Many argue that there are pitfalls to empowering patients as it promotes self-care and reduces dependence on healthcare providers. While that may be true in some respects, it is still debatable whether empowerment is detrimental to better healthcare. On the contrary, it can also be argued that empowering patients will ensure that they engage better with their providers.

The success of engagement lies in empowerment

It isn't just about health outcomes, patient empowerment also improves engagement between

- Create a medical biography about yourself. What conditions and medications have you had in the past? What are you currently experiencing?
- Be a teammate, not a subject.

Healthcare Providers & Policy Makers:

At an organizational level, patients and families can be engaged in the design and development of patient-centred processes and system, for example as members of advisory committees. Health care services have engaged patients in planning committees, patient and public engagement groups, patient advisory committees or in prospective surveys to encourage change.

Health care providers and policy-makers need to create opportunities for engaging patients and their families in a dialogue at all levels: in direct care at an individual level, in organizational governance and systems design and at the level of policy development & implementation through education, research, regulation and standard setting

A patient's greater engagement in healthcare contributes to improved health outcomes. Patients want to be engaged in their healthcare decision-making process, and those who are engaged as decision-makers in their care tend to be healthier and have better outcomes.

Openness and transparency strengthen the patient-provider relationship.

Life Stages: Adolescence in Thalassemia

-Ms. Sangeeta Wadhwa

"many parents find it hard to understand their adolescent children" Why ?
--BECAUSE ITS FULL OF MANY CHALANGES

Adolescence, is an intermediate phase between childhood and adulthood, where takes place a permanent change in the body. Furthermore, adolescence is accompanied by many challenges, such as social, personal and career-

Lay Man Definition ---Many parents and patients say that the teen years are the most difficult time for families. Families struggle with the shift of responsibility and control over the disease, academic progress, and social activities.

The main factors involved in psychiatric disorders -are family (overprotective, negligent, or hostile parents), social (uncompassionate peers) and the burden of disease (complications, blood transfusions, iron chelation).

Thalassemic adolescents experience feelings of shame or denial, uncertainty about the outcome of the disease and the fear of stigmatization or the imminent death that impose restrictions on social life, many feel protected from negative consequences; this can lead towards risk-taking behaviors, including experimenting with drugs and alcohol, sex and aggressive behavior.

Common issues in adolescence age -- social withdrawal, complain of psychosomatic symptoms, such as headache, abdominal pain or show irritability, poor school performance, feeling aloof , lethargic social isolation and inability to handle frustration depression.

On the contrary, thalassemic adolescents, being already affected by the chronic illness and having realized the impact of its' chronicity, are more vigilant of their illness progression and potential health hazards. Accordingly, they face significant problems in all facets of life that contribute to the onset of depression.

Thalassemic adolescents were having higher scores in neuroticism. Some behavioral problems are also found to exist along with neurotic manifestations.(as per research reference)

What we can do ? a need to improve the management of thalassemia in terms of psychological aspects in order to improve the mental health of this group

deficits and providing help to plan and actualize their educational, personal and career goals thus leading fulfilling lives.

What you can do as a parent:

1. Continue to negotiate with your child around disease responsibility.
2. understand in accurate terms about the nature of the disease, the need for treatment,
3. The new medical protocols, has beneficial effects both on the outcome of thalassemia and depression.
4. Have your teen start to develop independent relationships with his or her health care providers; this can help you negotiate the transfer of care to your child and give him/her a private and safe place to voice concerns.
5. Get support and information from other parents going through this difficult time. (Talk and share your emotions with other sufferers .)
6. Do not hesitate to ask for your family to meet with a psychosocial provider to help you manage these years
7. Stop blaming yourself and others .

What you can do as a patient:

1. Share your emotions and feelings with other thalassmics
2. If you feel you require counseling withoght hesitation go and explore yourself
3. believe in yourself , your doctors and your Parents .
4. Meet your mentors , try to cherish all the movement of life
5. Focus on bright side of life
6. Learn to harness the power of positive thoughts .
7. Explore and update yourself with new treatments and your medical requirements

Rajkot – An example of community control of thalassemia.

Dr. Ravi Dhanani

Thalassemia is heredity blood disorder and one of the commonest single gene disorders representing a major health burden in India and in the world. It is estimated that more than 200 million people are carriers of the thalassemia gene in the world and about 50 million of them are in India. Every year about 10,000 children are born with thalassemia major in India accounting for 10% of thalassemia major births worldwide. While bone marrow transplant (BMT) is the only curative option, the available remedy for managing thalassemia is lifelong blood transfusion and removal of high cost involved Rs. 12 to 15 lacs for BMT and a recurrent annual cost of about Rs. 2 lacks for transfusion and iron chelation. Only 5 to 10% of children born with thalassemia in India receive optimal treatment due to non-affordability.

Rajkot city is the small town which is situated in Gujarat state. It is heart of the Saurashtra region. Saurasthra region covers 150 lacks population and Rajkot covers more than 13 lacks population. More than 650 thalassemia patients are registered in Rajkot city and more than 3000 are in Saurashtra region. Due to lack of awareness average 30 children with thalassemia are born in Saurashtra region.

PRENTIVE STEPS AT RAJKOT

Thalassemia is completely preventable. It is one such disease which can be prevented by pre-marriage counseling, thalassemia screening, prenatal genetic diagnosis and generating awareness among the general masses. In Rajkot Vivekanand Youth Club, Shree Blamukund Seva Sansthan Cheritable Trust, Thalassemia Jan Jagruti Abhiyan Trust and Jain Sa Dhrmik Seva Samiti Trust works for thalassemia prevention and optimal care for patients. We believe in **"PREVENTION IS BETTER THAN CURE"** and we work for prevention.

Our preventable steps are

- Organized thalassemia screening camps at more than 7200 school students with cooperation of Rajkot Municipal Corporation.
- Counseled more than 10,000 youth for the thalassemia.
- Thalassemia test is mandatory for every first year college students.
- Patients, parents and volunteers stand at various traffic points with play card every Saturday for last 2 years for the thalassemia awareness.
- A rally is organized for thalassemia awareness in major area of the city on the last Saturday of every month for last one year.

- Sindhi and Lohana community makes thalassemia test mandatory before marriage.
- Life NGO has done more than 7 lacks thalassemia screening tests in Saurashtra region.
- Free thalassemia test is done in Rajkot civil hospital for last one year.
- Daily we send thalassemia awareness message through social media.
- Thalassemia awareness message is also spread through "AKILA" evening newspaper daily for last 10 years.
- Putting hoardings of thalassemia awareness at home of the patients.

Our effort is to achieve "0" thalassemia at Rajkot.

Patients' role in decision-making

Mrs. Anubha Taneja Mukherjee

Decision making is an inherently complicated procedure, which by its very nature requires the decision-maker to co-opt all the stakeholders concerned. The procedure of decision-making may vary from country to country, depending on its size, culture, history and special demographic circumstances. Around the world, key decision-makers include the executive, the legislature and the judiciary. While the distribution of powers between these three may vary in tandem with their relation to each other, their roles remain the same. While the legislature enacts laws for its citizens, the executive, popularly known as the government, implements these laws and while doing so promulgates policies that are in alignment with the said laws. Mostly, the executive is also authorised to promulgate some laws of its own. The judiciary, on the other hand, comes into the picture when there is a dispute with regard to such laws. It also steps in on its own at times. While settling such disputes, the judiciary also ends up setting what we know as precedents, which also become a part of the legal fabric of a society. In a nutshell, these three are the key decision makers in any country.

As mentioned above, while making decisions, these authorities are mostly required to co-opt all the stakeholders concerned, thereby making decision making a consultative process. These stakeholders include think tanks, research bodies, media and most importantly the affected party. The reason for having such a consultative procedure in place is that the decision makers are not experts in every subject or issue that comes their way. For instance, when a need to promulgate a national policy on thalassemia presents itself to a certain government, whether it be owing to media reportage or representations from the civil society, the decision makers will look towards people considered to be the experts in the subject to come forward and be a part of the policy making. One could say that this sounds like an ideal situation where the government actually invites people concerned with thalassemia to come forward and share views about it for the purpose of policy making. It is, however, true! It is as true for India as it is for any developed country. What we must ensure then is that the government or the decision maker considers us, the patients, as the experts. While it does sound obvious that those impacted with the disorder would be the ones with the first-hand knowledge about the disorder, the very fact that there is a topic in this conference on the role of patients in decision making speaks volumes about the distance that remains to be covered by the patients of thalassemia as far as participation in decision-making is concerned.

With the massive strides in the field of medical science and the unflinching support of organisations like Thalassemia International Federation (TIF), we have now reached the stage where we must step out of the victim mode and represent ourselves before the decision-makers, whether by forming Patients Advocacy Groups or otherwise. One may take cue from various associations around the world. Global HD Organisations are a good example. They are known to have got together to give patients a voice in clinical research. The most popular strategy for reaching out to the decision makers is to unite, engage, and partner both in private meetings and consultative fora like events, task forces and projects. “Unite, Engage & Partner” can therefore be the most successful *mantra* for engaging with the decision makers.

Talking of examples of advocacy and participation by patients, while there are numerous examples in Europe and North America of the power of patient advocacy so much so that patients are on the same level as doctors when it comes to voicing opinions in policy making, TIF on an international level has created since 2009 the Expert Patients Programme, and is now moving forward in giving patients a voice through its educational platform. Recently, India also launched its first Thalassemia Patients Advocacy Group (PAG) in the august presence of the Deputy Chief Minister of the capital of the country. The India PAG has seven patients from the fields of law, psychology, education and IT. The Group is already involved with the government on the formulation of the National Thalassemia Policy. This is a great start and this should give enough and more encouragement to thalassemics across the world to UNITE, ENGAGE AND PARTNER in the process that impacts them the most – decision-making!

Bihar vs Thalassemia

Mr. N.N. Vidhyarthi

Children are the gifts of God but what if they themselves get gifted with Thalassemia. Definitely, with today's medical advancement, a thalassemic patient can live a normal life if they take proper medicines and regular blood transfusion. But then, there are places where there is no proper availability of medical treatment and most importantly, awareness.

Such a place in India is Bihar, where the thalassemic patients become a curse to the family when parents find themselves completely hopeless on what to do. Around 33.74 percent of Bihar's population is below poverty line where the people already have hard time in fulfilling their basic requirements. If in such a family, a child is born with Thalassemia, the family has no other option but to pray and leave everything to the time. The thalassemic patients and their parents suffer from mental pressure when the people around start treating them as untouchables thinking the disease to be contagious. Further, there is gender inequality. If any girl child happens to be thalassemic, they are not taken care of.

Actually, the people in Bihar don't know what Thalassemia is. Not even the doctors (particularly in rural areas) could make out what the disease is. And so, it's completely useless to think that any proper medical treatment would be available here. The doctors are arrogant and don't do what is required. They consider themselves as God and could not think out of their ego. There is no haematologist to treat the patients.

Only few districts in Bihar have Blood unit separators. However, they don't seem to be helping the people. As per the law, the thalassemic patients should get the blood for free and without exchange. But, only the rich people or the people with power get it. The most renowned state hospital in Bihar, the P.M.C.H issues blood to the thalassemic patients with a haemoglobin around 5gm and the second largest hospital, the D.M.C.H is completely reluctant in issuing blood to the patients. And so, it is not at all possible for the patients to maintain their haemoglobin level to 10gm. On the other hand, those who get blood by any means, don't get what they want. Thalassemic patients need packed red blood cells (PRBCs), but sometimes, they have to use the whole blood.

Medicines and tests are very costly for the poor families. The family whose annual income is below 1 lakh, cannot spend everything on their children and so the patients quietly wait for their deaths. Blood transfusion is done with normal pipes. The leukocyte filters are not available anywhere in Bihar. MRI scan to diagnose the iron stored in Liver, Kidney, Heart and Pancreas is not done anywhere in Bihar not even in the newly established AIIMS, Patna. Serum Ferritin test, which is the most important test for thalassemic patients, is very costly and

so cannot be done on every three months by the patients.

So, all of this have a serious impact on Bihar. Only 2 to 3 percent of the patients survive and rest of them just pass away. There is no help to the people by the government. The government should run some awareness programs in the rural areas in the same way as it was done for the HIV, AIDS and Polio drops. Doctors should be able to advise the couples on the possibility of having a thalassemic child if both of them happens to be the carriers of thalassemia. The medicine should be made available to the people for free and strict implementation of the law should be made so that the patients get blood easily.

It's not me crying for these demands but the thalassemic patients of Bihar who are in a queue of death.

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