THALASSEMIA PREVENTION PROGRAMME - BLOOD BANK PERSPECTIVE

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INTRODUCTION

- The thalassemia syndromes are a heterogeneous group of inherited anemias characterized by defects in the synthesis of one or more of the globin chain subunits of the hemoglobin (Hb) tetramer.
- The clinical syndromes associated with thalassemia arise from the combined consequences of inadequate Hb production and imbalanced accumulation of globin subunits.
- The former causes hypochromia and microcytosis; the latter leads to ineffective erythropoiesis (IE) and hemolytic anemia.

BURDEN OF THALASSEMIA

- Thalassemia is not a disease of '' Just a few people''.
- **WORLDWIDE:** According to WHO 4.5 % of population is affected by thalassemia and allied diseases.
- 56,000 conceptions would have a major thalassemia disorder and among them around 30,000 would have β thalassemia major, the majority of babies being born in middle and low income countries.

(Reference :-(1)Cao A, Kan YW. The prevention of thalassemia. Cold Spring Harb Perspect Med 2013;3. a011775. (2) Verma IC, Choudhary VP, Jain PK. Prevention of thalassemia: a necessity In India. Indian J pediatr. 1992;59:649-54).

- **INDIA:** The average prevalence of β-thalassemia carriers is 3-4% which translates to 35 to 45 million carriers in our multi-ethnic and culturally and linguistically diverse population of 1.21 billion people. Several ethnic groups have a much higher prevalence (4-17%).

Reference :-(1)Madan N, Sharma S, Sood SK, Colah R, Bhatia HM. Frequency of b thalassemia trait and other hemoglobinopathies in northern and western India. Indian J Hum Genet 2010;16:16e25. (2) Colah RB, Gorakshakar AC. Thal Reports. Control of thalassemia in India, 4; 2014. p. 1955.)

COMMUNITIES WITH A HIGH PREVALENCE OF β-THALASSEMIA

(Reference: Pediatric Hematology Oncology Journal Volume 2, Issue 4, December 2017, Pages 79-84)

Communities with a high prevalence of β thalassemia.

Communities	Prevalence of β thalassemia
Sindhis, Lohanas, Bhanushalis, Vellalas	8–17%
Vasava, Chaudhry, Gamit, Kokana tribes from Surat, south Gujarat	12–15%
Aroras, Khatris, Jaths,	6–10%
Prajapatis, Banias, Jains, Patels, Mayavanshis	6–8%
Bhuyan, Pik, Dudh Kharia tribes from Sundargarh, Odisha and Rohit tribe from Surat, south Gujarat	6–8%
Kayastha, Mandols	5–9%
Menons, Shiyas, Fakirs	5–7%
Neobuddhists, Mahars	4–6%

Burden of Thalassemia in GUJARAT : Based on study published by Indian red cross society Gujarat state branch on 3,17,539 samples in a study period of 4 year

(Reference: National Journal of Community Medicine Vol 3 Issue 1 Jan-March 2012)

Prevalence of Common Haemoglobinopathies in tribal districts

Name of District	Number	ß-thalassemia trait (%)	Sickle cell trait (%)
Banaskantha	9489	423(4.45)	486 (5.12)
Baroda	31608	381(1.2)	5018 (15.87)
Bharuch	19373	330(1.7)	2737 (14.12)
Dahod	15975	410(2.57)	2079 (13.1)
Narmada	31966	464(1.45)	5377 (16.82)
Panchmahal	23077	422(1.83)	2189 (9.49)
Sabarkantha	37007	505(1.37)	1268 (3.43)
Total	168495	2935 (1.76)	19154 (11.4)

Prevalence of Common Haemoglobinopathies in non-tribal districts

District	Number	ß-Thalassemia trait (%)	Sickle cell trait (%)
Ahmedabad	19825	678 (3.4)	138 (0.7)
Anand	24329	482 (1.98)	273 (1.1)
Gandhinagar	3165	71 (2.24)	30 (0.95)
Bhavnagar	1009	28 (2.77)	10 (0.99)
Amreli	468	14 (2.99)	4 (0.86)
Jamnagar	864	30 (3.47)	5 (0.58)
Kheda	1812	45 (2.48)	7 (0.39)
Kutch	2476	102 (4.1)	2 (0.08)
Navsari	12175	230 (1.89)	328 (2.7)
Mehsana	31161	432 (1.36)	51 (0.16)
Patan	12691	173 (1.36)	20 (0.15)
Rajkot	2284	70 (3.1)	25 (1.1)
Surat	31368	732 (2.33)	596 (1.9)
Porbandar	725	21(2.89)	10 (1.38)
Surendranagar	1042	8 (0.77)	33 (3.17)
Valsad	3625	145 (4)	72 (1.97)
Total	149044	3261 (2.18)	1604(1.1)

Prevalence of β-thalassemia and expected annual births of β-thalassemia major babies in the districts of Gujarat.

(Reference: British Journal of Hematology, 149, 739-747)

District	Population (millions)	Crude Birth Rate	Total annual births	Number tested	Prevalence of heterozygotes No (%)	Marriages at risk per 1000 marriages	Expected annual births of homozygotes
South Gujarat							
Valsad	1·41	22·7	32 019	200	7 (3·5)	1·2	10·2
Dang	0·19	32·8	6124	141	4 (2·8)	0·8	1·3
Navsari	1·23	17·9	22 007	137	3 (2·2)	0·5	2·7
Surat	5·0	23·2	115 888	552	12 (2·2)	0·5	14·0
Central Gujarat							
Bharuch	1·37	22·3	30 565	432	9 (2·1)	0·4	3·4
Narmada	0·51	24·6	12 654	41	0	0	0
Anand	1·86	21·7	40 294	300	10 (3·3)	1·4	11·8
Ahmedabad	5·82	20·5	119 238	504	18 (3·6)	1·3	39·4
Vadodara	3·64	21·3	77 570	2194	67 (3·1)	1	18·7
Kheda	2·02	23·1	46 759	353	13 (3·7)	1·4	16·5
Gandhinagar	1·33	22·1	29 491	51	1 (2·0)	0·1	2·9
Panchmahal	2·03	27·7	56 100	258	10 (3·9)	1·5	21·9
Dahod	1·64	34·2	55 966	119	4 (3·7)	1·4	16·4
Saurashtra							
Porbandar	0·54	21·8	11 703	105	10 (9·5)	9·0	29·4
Jamnagar	1·82	21·7	39407	185	6 (3·3)	1·1	10·7
Rajkot	2·57	16·9	43433	309	16 (5·2)	2·7	30·7
Surendranagar	1·52	27·6	41 818	92	5 (5·4)	2·9	32·7
Amreli	1·39	21·1	29 411	144	9 (6·3)	4·0	30·7
Bhavnagar	2·47	25·3	62 481	379	17 (4·5)	2·0	32·9
Junaghad	2·45	23·1	56 553	304	25 (8·2)	6·7	104·4
Kuchchh	1·58	25·4	40 214	603	27 (4·5)	2·0	21·1
North Gujarat							
Patan	1·18	26·1	30 869	74	2 (2·7)	0·7	5·8
Banaskantha	2·50	31·3	78 383	74	0	0	0
Mehsana	1·84	22·4	41 169	307	4 (1·3)	0·2	1·8
Sabarkantha	2·08	25·1	52 271	146	1 (0·7)	0	0·6
Total	49·9			8004	280 (3·5)		460

Distribution of Sickle cell trait and β-thalassemia trait in different castes of Gujarat

Caste	Sickle cell trait (%)	ß-thalassemia trait(%)
General Caste		
Barot	1.68	3.5
Brahmin	1.98	3.49
Bhanusali	-	8.1
Bhakta	-	7.93
Bhavsar	-	2.59
Chaudhary	15.63	1.97
Lohana	-	6.5
Patel	3.6	1.43
Parmar	10.4	2.6
Patil	-	4.35
Rajput	7.7	2.9
Rabari	1.03	1.52
SC		
Chamar	10.52	3.49
Chauhan	9.39	-
Harijan	8.1	3.52
Solanki	9.22	2.64
Vankar	8.7	2.94
ST		
Adivasi	15.25	2.42
Bamaniya	6.9	-
Bariya	16.5	1.12
Gamit	17.64	
Koli	16.87	
Nayka	15.38	2.19
Rathva	18.65	
Tadvi	16.95	

Need for comprehensive programme for prevention and control of thalassemia

(Reference: Prevention and Control of Hemoglobinopathies in India, National Health Mission, Ministry of Health & Family Welfare, Govt. of India, 2016)

- It is estimated that around 10,000-15,000 babies with thalassemia major are born every year.
- Most of the thalassemia major children resort to palliative treatment by blood transfusions which is eventually compromised by the concomitant problem of iron overload, alloimmunization and blood borne infections.


Time for a national policy on thalassaemia
As the number of thalassaemics grows in India, ...
www.thehindu.com
https://www.thehindu.com/sci-tech/health/time-for-a-national-policy-on-thalassaemia/article18401885.ece

- The only cure available for these children with thalassemia major is bone marrow transplantation (BMT) more appropriately called hematopoietic stem cell transplant (HSCT).
- However, this can help only a few patients because of cost, paucity of BMT centers, or non-availability of a suitable HLA matched donor.
- Therefore, the mainstay of treatment is a regimen of regular blood transfusions followed by adequately monitored iron chelation therapy to remove the excessive iron overload- as a consequence of the multiple blood transfusions.
- Thus it is a transfusion dependent disorder and places a great burden on healthcare services. In India 2 million units of packed red cells are required for transfusion to thalassemic patients.

(REF: Marwaha N. Whole blood and component use in resource poor settings. Biologicals 2010; 38 : 68-71.)

- In India, the cost of transfusing and chelating a 30 kg body weight child for one year was estimated at Rs. 200,000 for one year in 2008.
- With an estimated birth of 10,000 children with Thalassemia Major every year, and survival for 50 years, the cost of managing 500,000 children (10,000 x 50) works out to Rs.10000 crores, and Rs.100 crores even if only 1% were to survive to 50 years of age.

- Birth rates of homozygous β-thalassemia have reduced considerably in different parts of the world.
- Cyprus, Sardinia Italy and Greece have been able to control thalassemia with their extensive screening programs at various levels along with prenatal diagnosis. Iran has an antenatal diagnostic program and it has reduced birth of Thalassemia major children.
- Therefore there is an urgent requirement for starting a thalassemia screening and control program at national level.

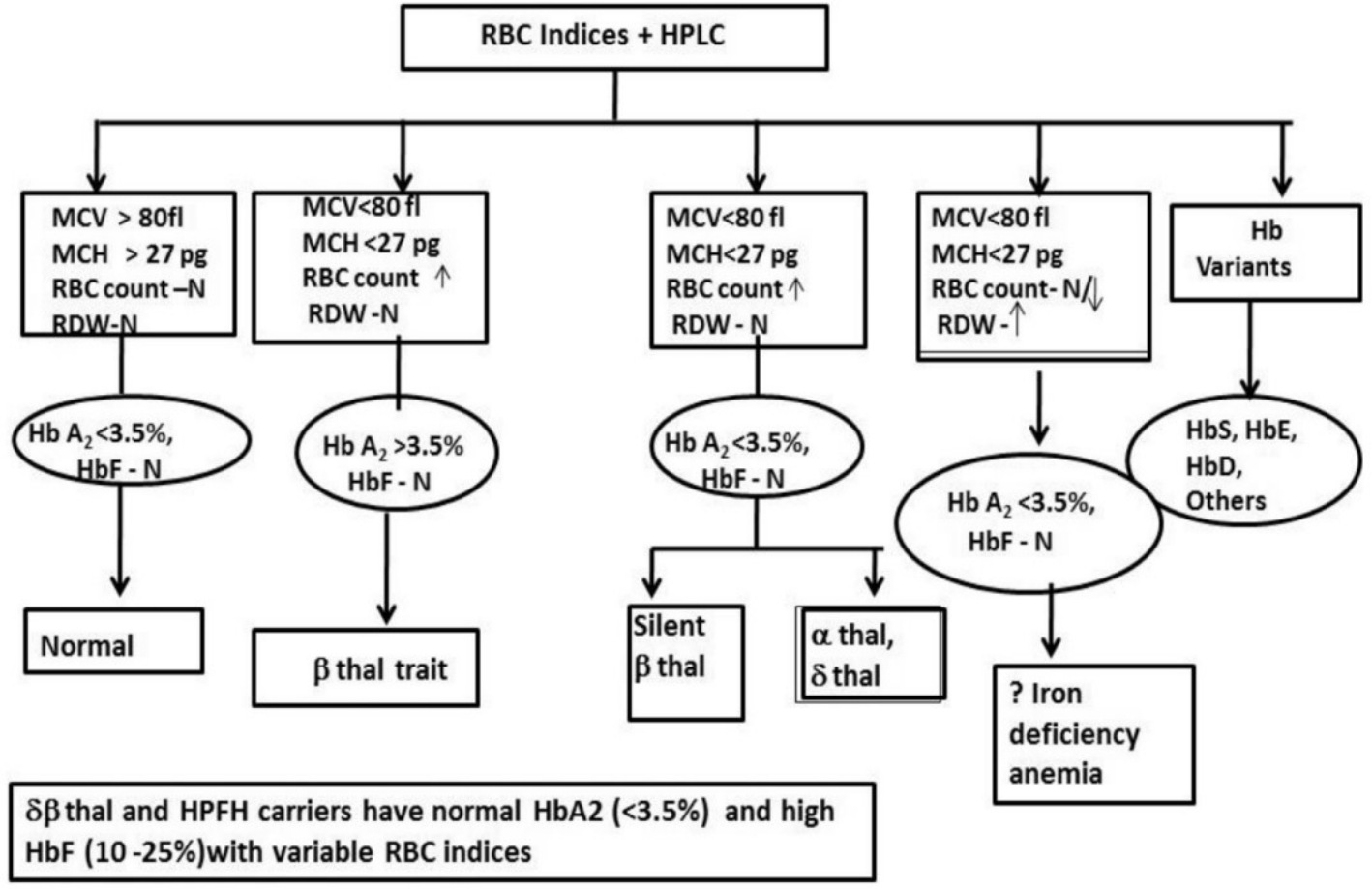
- **Component of comprehensive thalassemia prevention and control:**
- public awareness and education,
- carrier screening, and counseling,
- information on prenatal diagnosis
- preimplantation diagnosis.

SCREENING CARRIERS OF βTT (universal Vs target group)

- Ideal is to screen every individual for βTT, but cost of screening is the prohibitive to this approach.
- Based on the experience of a pilot project funded and implemented under National Health Mission in Uttarakhand, the cost of screening one lakh adolescents was estimated at Rs.1 crore.
- **Target group for screening**
  - Eligible couples- Increase awareness of the disease, and motivate for screening for carrier status.
  - Youth - Increase the awareness on the prevention and care of the disease.
  - Affected families- Encourage voluntary screening for thalassemia in the relatives (cascade screening).
  - Children who have thalassemia major- Inform about care and prevention of complications.
  - General community- Reduce myths and misconceptions.

Screening for carriers of hemoglobinopathies

(Reference: Pediatric Hematology Oncology Journal 2 (2017) 79-84)



TIMING OF SCREENING FOR HEMOGLOBINOPATHIES

Adolescence	Most suitable for carrier screening, as a long term sustainable strategy.
Premarital	Carrier screening at this stage is effective in a well-informed community
Preconception	Carrier screening is effective in communities where termination of pregnancy in case of affected fetus is permitted. Married couples can also seek pre-implantation genetic diagnosis if available
Antenatal screening & Prenatal diagnosis (PND)	Serves as a net to screen those who have not been screened at earlier stages. If both parents are carriers i.e. "at-risk" couple : then the status of the fetus for Thalassemia disease or sickle cell disease can be ascertained through prenatal diagnosis

First line screening tests for βTT

Differentiation of βTT from Iron deficiency Anaemia

	RESULTS	
CALCULATION	IRON DEFICIENCY	THALASSEMIA MINOR
MCV – (5 x Hb) – RBC – 3.4	>0	<0
MCV/RBC	>13	<13
MCH/RBC	>3.8	<3.8
RBC	<5.0	>5.0
MCH x $(MCV)^2/100$	>1530	<1530

NESTROFT Test (Naked Eye Single Tube Red cell Osmotic Fragility Test)

For Beta thalassemia trait

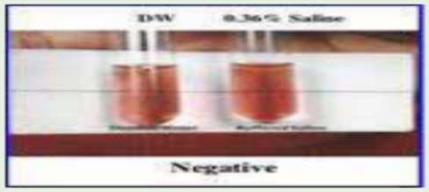
This test has a high specificity and sensitivity and is easy to perform. The positive test has to be followed by a confirmatory test

Sensitivity of 91-100%, specificity of 85.47%.

Positive predictive value of 66% and negative predictive value of 97-100%

References: 3,4,6,14,15,

NESTROFT test : Negative

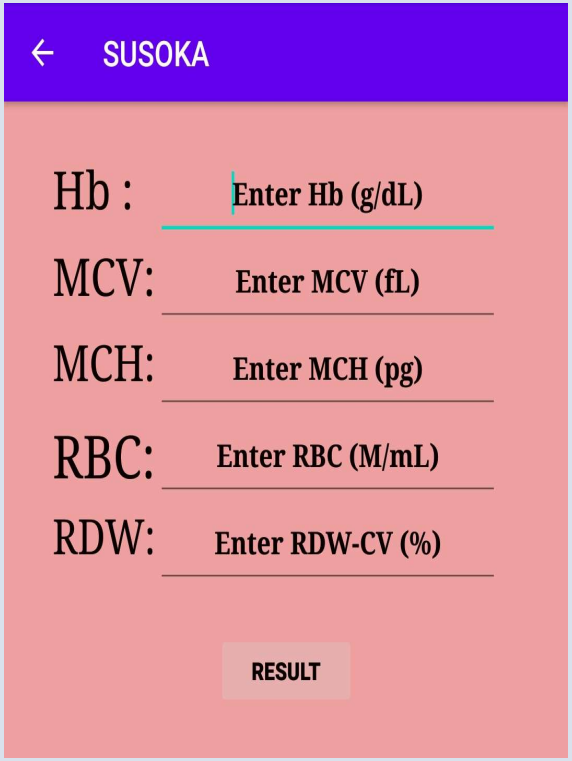


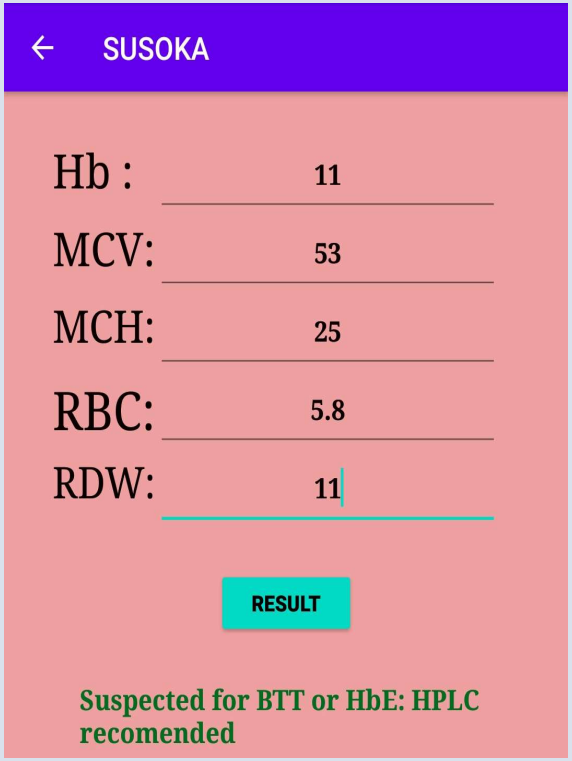
NESTROFT test Positive

Limitation of first line screening methods

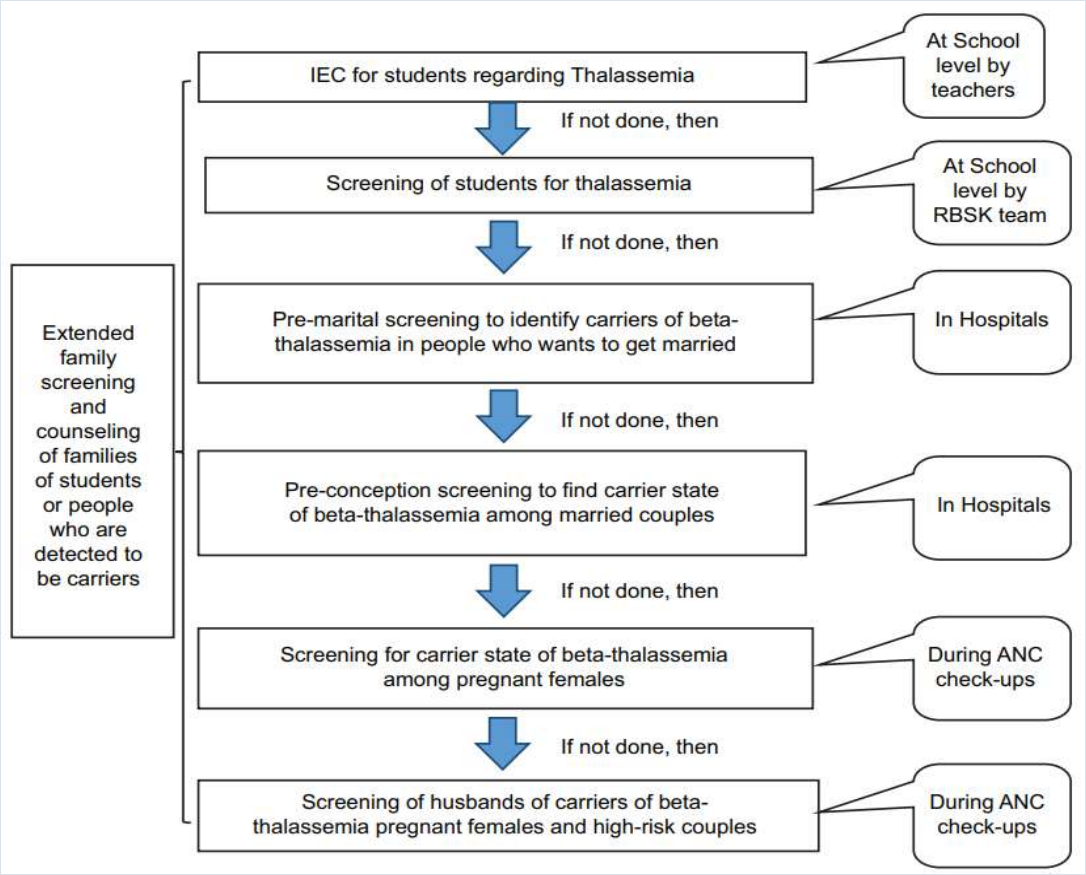
- The Jai Vigyan project experience showed that NESTROFT missed an average of 13% of ß thalassemia carriers. This was due to certain lacunae like non maintenance of water quality used at different centers, variations in preparation and dilution of the buffer due to frequent change of technicians who put up the test.
- When the NESTROFT buffer was prepared centrally and sent to the different centers; the results improved considerably. Red Blood Cell (RBC) indices also missed around 3 to 4 % of beta thalassemia carriers at different centers.
- However, if NESTROFT and RBC indices were taken together in the first step, less than 2% of beta thalassemia carriers were missed.
- β-thalassemia carrier genotypes referred to as 'silent' carriers will not be detected on screening or by HPLC.
- Only carrier states with clear diagnostic cut off values are detectable.
- Some of the values will fall in equivocal range and may lead to missed detection.

SUSOKA is a Beta-thalassemia and HbE carrier screening mobile application. Please click the "Next" button and enter five haematological parameters (as mentioned in the next page) from your blood report to check whether you are a possible carrier of beta thalassemia or HbE or not.





Recommended algorithm for thalassemia screening at different levels



Quality Assurance and Quality Control for the First line screening tests

- CBC report showing an MCV of <80 fl & MCH <27 pg is regarded as a positive screening test for βTT, and the sample is taken up for diagnostic testing by HPLC.
- It is recommended that if a sample with normal MCV and MCH and Hb >8 gm/dl shows a positive NESTROFT, it should also be taken up for further testing by HPLC as combined screening with CBC and NESTROFT has been shown to be more effective.
- The success of the screening program depends on the results of Hematology cell counter and NESTROFT.
- Utmost care must be taken to provide reliable results from the first line screening tests using appropriate & regular IQC and participation in EQAS/PT programme.

IQC material for cell counters

Hematology Controls

Hematology Controls

My eInserts Overview

For monitoring the precision of hematology test procedures, these controls contain blood parameters at various levels

Category Products

Liquichek Hematology Control (A)

Assayed hematology control for evaluating the precision of Abbott CELL-DYN® analyzers with 3- and 5-part differential technology

Liquichek Reticulocyte (A) Control

An assayed hematology control for evaluating the precision of automated methods of reticulocyte counting

Liquichek Reticulocyte Control (A-I)

An assayed reticulocyte control for use with the Abbott CELL-DYN Sapphire® hematology analyzers.

Liquichek Hematology Control (C)

An assayed hematology control for evaluating the precision of the Beckman Coulter® hematology instruments with complete CBC and VCS 5-part differential technology

ACUSERA

Combining 45 parameters in total the Randox Acusera Haematology quality control completely covers the commonly tested full blood profile in a single control. Providing a true third party solution for Sysmex and Mindray haematology analysers with 5-part differential technology an unbiased, independent assessment of analytical performance is guaranteed.

Features & Benefits

- Liquid ready-to-use
- Assayed target values for parameters
- Barcoded samples enabling quick and easy recognition and increased productivity
- Open vial stability of 14 days 2°C – 8°C

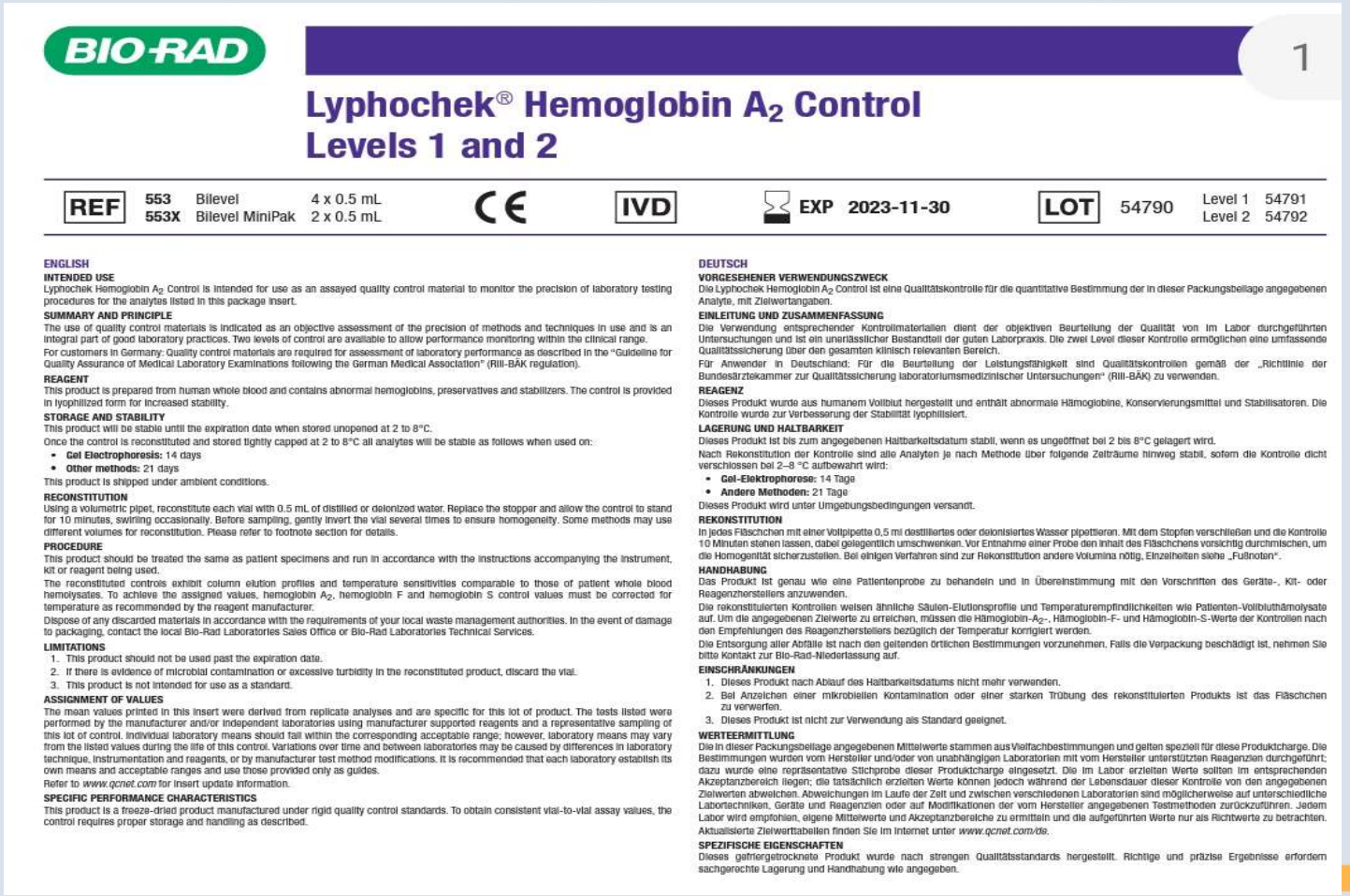
	Description	Size	Analytes	Cat No
+	Haematology Tri-Level	3 x 2 x 4.5 ml	45	HM5162

The RIQAS Haematology EQA programme is designed to monitor the performance of 11 haematology parameters. All samples are supplied liquid ready-to-use in primary tubes for ease-of-use and convenience.

- Accredited to ISO/IEC 17043:2010
- Liquid ready-to-use
- 100% whole blood
- Flexible options available with bi-weekly and monthly reporting
- Register up to five instruments per programme (volume permitting) at no extra cost for comparative performance assessment
- Samples provided in primary tubes with penetrable septums

	Cat No	Kit Size	Frequency	Cycle Start	Paramete
+	RQ9118	6 x 2ml (primary tubes)	Bi-weekly (2 x 6 monthly cycles)	March / Sept	11 parameters
+	RQ9140	12 x 2 ml	Monthly Programme	January	11 pa (monthly

IQC material for HbA_2



BIO-RAD

1

Lyphochek® Hemoglobin A_2 Control Levels 1 and 2

REF					IVD		LOT		
553	Bilevel	4 x 0.5 mL		EXP 2023-11-30		54790	Level 1	54791
553X	Bilevel MiniPak	2 x 0.5 mL					Level 2	54792

ENGLISH

INTENDED USE
Lyphochek Hemoglobin A_2 Control is intended for use as an assayed quality control material to monitor the precision of laboratory testing procedures for the analytes listed in this package insert.

SUMMARY AND PRINCIPLE
The use of quality control materials is indicated as an objective assessment of the precision of methods and techniques in use and is an integral part of good laboratory practices. Two levels of control are available to allow performance monitoring within the clinical range.
For customers in Germany: Quality control materials are required for assessment of laboratory performance as described in the "Guideline for Quality Assurance of Medical Laboratory Examinations following the German Medical Association" (RiII-BÄK regulation).

REAGENT
This product is prepared from human whole blood and contains abnormal hemoglobins, preservatives and stabilizers. The control is provided in lyophilized form for increased stability.

STORAGE AND STABILITY
This product will be stable until the expiration date when stored unopened at 2 to 8°C.
Once the control is reconstituted and stored tightly capped at 2 to 8°C all analytes will be stable as follows when used on:
- **Gel Electrophoresis:** 14 days
- **Other methods:** 21 days

This product is shipped under ambient conditions.

RECONSTITUTION
Using a volumetric pipet, reconstitute each vial with 0.5 mL of distilled or deionized water. Replace the stopper and allow the control to stand for 10 minutes, swirling occasionally. Before sampling, gently invert the vial several times to ensure homogeneity. Some methods may use different volumes for reconstitution. Please refer to footnote section for details.

PROCEDURE
This product should be treated the same as patient specimens and run in accordance with the instructions accompanying the instrument, kit or reagent being used.
The reconstituted controls exhibit column elution profiles and temperature sensitivities comparable to those of patient whole blood hemolysates. To achieve the assigned values, hemoglobin A_2, hemoglobin F and hemoglobin S control values must be corrected for temperature as recommended by the reagent manufacturer.
Dispose of any discarded materials in accordance with the requirements of your local waste management authorities. In the event of damage to packaging, contact the local Bio-Rad Laboratories Sales Office or Bio-Rad Laboratories Technical Services.

LIMITATIONS
1. This product should not be used past the expiration date.
2. If there is evidence of microbial contamination or excessive turbidity in the reconstituted product, discard the vial.
3. This product is not intended for use as a standard.

ASSIGNMENT OF VALUES
The mean values printed in this insert were derived from replicate analyses and are specific for this lot of product. The tests listed were performed by the manufacturer and/or independent laboratories using manufacturer supported reagents and a representative sampling of this lot of control. Individual laboratory means should fall within the corresponding acceptable range; however, laboratory means may vary from the listed values during the life of this control. Variations over time and between laboratories may be caused by differences in laboratory technique, instrumentation and reagents, or by manufacturer test method modifications. It is recommended that each laboratory establish its own means and acceptable ranges and use those provided only as guides.
Refer to *www.qcnet.com* for insert update information.

SPECIFIC PERFORMANCE CHARACTERISTICS
This product is a freeze-dried product manufactured under rigid quality control standards. To obtain consistent vial-to-vial assay values, the control requires proper storage and handling as described.

DEUTSCH

VORGESEHENER VERWENDUNGSZWECK
Die Lyphochek Hemoglobin A_2 Control ist eine Qualitätskontrolle für die quantitative Bestimmung der in dieser Packungsbeilage angegebenen Analyte, mit Zielwertangaben.

EINLEITUNG UND ZUSAMMENFASSUNG
Die Verwendung entsprechender Kontrollmaterialien dient der objektiven Beurteilung der Qualität von im Labor durchgeführten Untersuchungen und ist ein unerlässlicher Bestandteil der guten Laborpraxis. Die zwei Level dieser Kontrolle ermöglichen eine umfassende Qualitätssicherung über den gesamten klinisch relevanten Bereich.
Für Anwender in Deutschland: Für die Beurteilung der Leistungsfähigkeit sind Qualitätskontrollen gemäß der „Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen" (RiII-BÄK) zu verwenden.

REAGENZ
Dieses Produkt wurde aus humanem Vollblut hergestellt und enthält abnormale Hämoglobine, Konservierungsmittel und Stabilisatoren. Die Kontrolle wurde zur Verbesserung der Stabilität lyophilisiert.

LAGERUNG UND HALTBARKEIT
Dieses Produkt ist bis zum angegebenen Haltbarkeitsdatum stabil, wenn es ungeöffnet bei 2 bis 8°C gelagert wird.
Nach Rekonstitution der Kontrolle sind alle Analyten je nach Methode über folgende Zeiträume hinweg stabil, sofern die Kontrolle dicht verschlossen bei 2–8 °C aufbewahrt wird:
- **Gel-Elektrophorese:** 14 Tage
- **Andere Methoden:** 21 Tage

Dieses Produkt wird unter Umgebungsbedingungen versandt.

REKONSTITUTION
In jedes Fläschchen mit einer Vollpipette 0,5 ml destilliertes oder deionisiertes Wasser pipettieren. Mit dem Stopfen verschließen und die Kontrolle 10 Minuten stehen lassen, dabei gelegentlich umschwenken. Vor Entnahme einer Probe den Inhalt des Fläschchens vorsichtig durchmischen, um die Homogenität sicherzustellen. Bei einigen Verfahren sind zur Rekonstitution andere Volumina nötig, Einzelheiten siehe „Fußnoten".

HANDHABUNG
Das Produkt ist genau wie eine Patientenprobe zu behandeln und in Übereinstimmung mit den Vorschriften des Geräte-, Kit- oder Reagenzherstellers anzuwenden.
Die rekonstituierten Kontrollen weisen ähnliche Säulen-Elutionsprofile und Temperaturempfindlichkeiten wie Patienten-Vollbluthämolysate auf. Um die angegebenen Zielwerte zu erreichen, müssen die Hämoglobin-A_2-, Hämoglobin-F- und Hämoglobin-S-Werte der Kontrollen nach den Empfehlungen des Reagenzherstellers bezüglich der Temperatur korrigiert werden.
Die Entsorgung aller Abfälle ist nach den geltenden örtlichen Bestimmungen vorzunehmen. Falls die Verpackung beschädigt ist, nehmen Sie bitte Kontakt zur Bio-Rad-Niederlassung auf.

EINSCHRÄNKUNGEN
1. Dieses Produkt nach Ablauf des Haltbarkeitsdatums nicht mehr verwenden.
2. Bei Anzeichen einer mikrobiellen Kontamination oder einer starken Trübung des rekonstituierten Produkts ist das Fläschchen zu verwerfen.
3. Dieses Produkt ist nicht zur Verwendung als Standard geeignet.

WERTEERMITTLUNG
Die in dieser Packungsbeilage angegebenen Mittelwerte stammen aus Vielfachbestimmungen und gelten speziell für diese Produktcharge. Die Bestimmungen wurden vom Hersteller und/oder von unabhängigen Laboratorien mit vom Hersteller unterstützten Reagenzien durchgeführt; dazu wurde eine repräsentative Stichprobe dieser Produktcharge eingesetzt. Die im Labor erzielten Werte sollten im entsprechenden Akzeptanzbereich liegen; die tatsächlich erzielten Werte können jedoch während der Lebensdauer dieser Kontrolle von den angegebenen Zielwerten abweichen. Abweichungen im Laufe der Zeit und zwischen verschiedenen Laboratorien sind möglicherweise auf unterschiedliche Labortechniken, Geräte und Reagenzien oder auf Modifikationen der vom Hersteller angegebenen Testmethoden zurückzuführen. Jedem Labor wird empfohlen, eigene Mittelwerte und Akzeptanzbereiche zu ermitteln und die aufgeführten Werte nur als Richtwerte zu betrachten.
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EQAS/PT programme for HbA_2

Bio-Rad EQAS programs are fully accredited to help meet the regulatory needs of today's clinical laboratories.

External quality assessment programs are accepted around the world as invaluable tools used by laboratories to periodically monitor the performance of their test systems. Results are objectively compared to other laboratories using the same methodologies, instruments and reagents. When used in conjunction with daily quality controls, these external programs can give laboratories added confidence in reporting their patient test results.

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Bio-Rad EQAS programs provide an independent and confidential external assessment of individual laboratory performance.

- Large international database with participants from over 110 countries
- Fully accredited to ISO/IEC 17043:2010 "Conformity assessment–General requirements for proficiency testing"
- Comprehensive, easy-to-read reports
- Technical support from experienced professionals
- Convenient electronic reporting options: EQAS Online and EQAS Mobile
- Each cycle includes 12 high quality samples together in one convenient shipment (except Hematology and Blood Typing Programs)
- Comprehensive analyte menus covering a wide range of diagnostic tests suitable for clinical labs and blood banks
- Analyte levels that challenge both normal and abnormal ranges
- Reference Method Values provided for select programs

Hematology Program*

- Liquid product with human RBCs
- Choice of 11 basic hematology parameters
- For use on manual or automated analyzers
- Convenience of primary pierceable tubes
- 12-month cycle consisting of 4 separate shipments
- Submit results for the appropriate sample every month

Parameters

Hematocrit (HCT)
Hemoglobin
Mean Corpuscular Hemoglobin (MCH)
Mean Corpuscular Hemoglobin Concentration (MCHC)
Mean Corpuscular Volume (MCV)
Mean Platelet Volume (MPV)
Platelets (PLT)
Red Blood Cells (RBC)
Red Blood Cell Distribution Width (RDW)
Red Blood Cell Distribution Width-SD (RDW-SD)
White Blood Cells (WBC)

Hemoglobin Program

- Lyophilized, human whole blood based
- Includes HbA1C and HbA_2
- 12-month cycle
- Submit results for the appropriate sample every month
- Reference Method Values provided for Hemoglobin A1C

Analytes

Hemoglobin A1C
Hemoglobin A_2
Hemoglobin (Total Glycated)

PRENATAL DIAGNOSIS-PREVENTING THE BIRTH OF AN AFFECTED CHILD OF "AT RISK COUPLE"

- The biochemical and molecular methods to identify the particular phenotype/genotype is the key to PND.
- There are 22 common mutations and as well as other rare ones causing β-thalassemia in Asian Indians, the point mutation detection by reverse dot blot (RDB), allele-specific oligonucleotide hybridization for common mutations along with the amplification refractory mutation system (ARMS) technique was developed for PND.
- Development of early and safe CVS has enabled PND to be undertaken in the first trimester of pregnancy. Though there is still a margin of error and precautions to prevent maternal contamination and other stringent care is necessary to not miss an affected child.

Spectrum of β-Thalassemia mutations

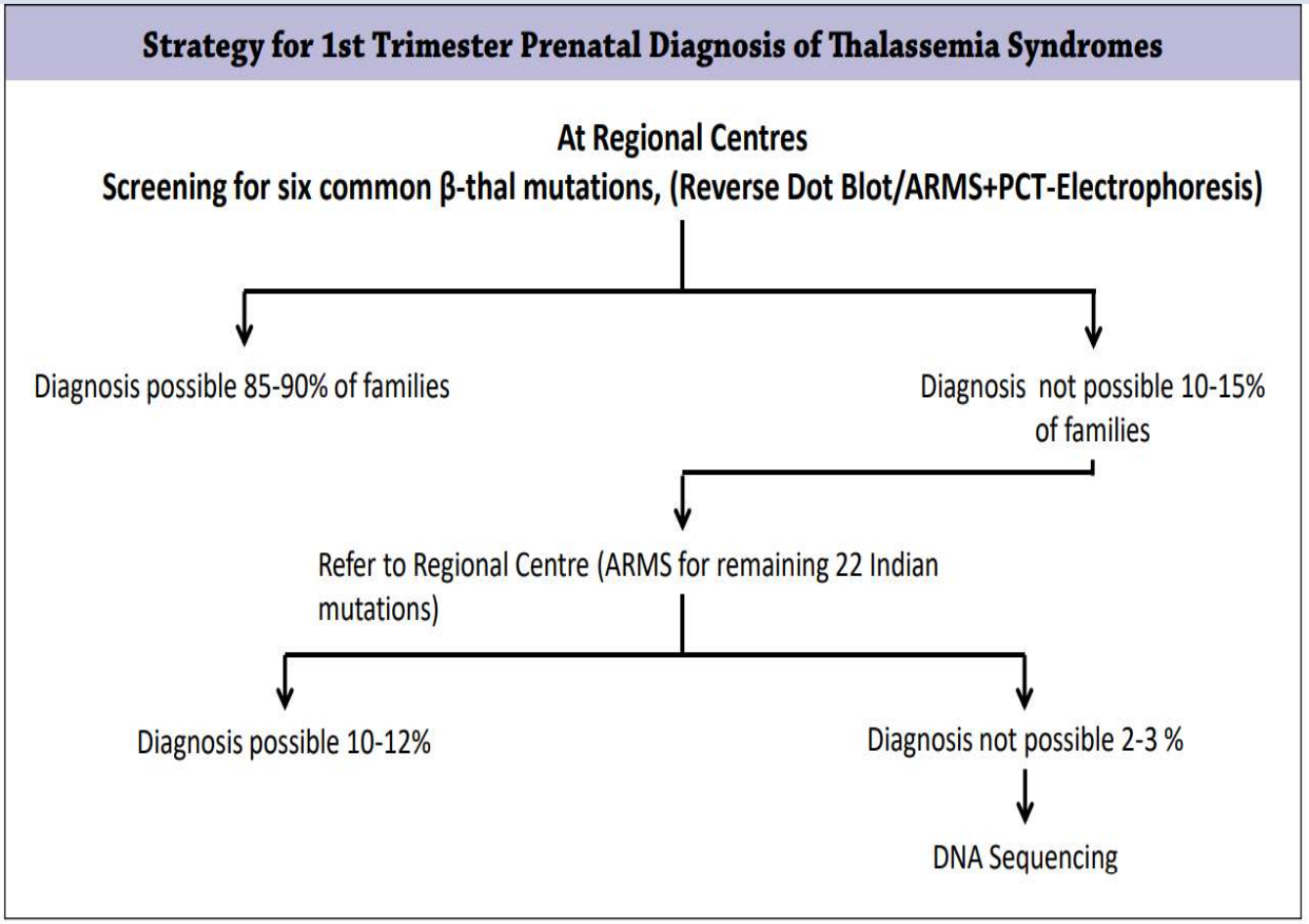
(Reference: British Journal of Hematology, 149, 739-747)

- Around 80 mutations have now been characterized with IVS 1-5 (G>C) being the predominant mutation in most regions. 6 or 7 common mutations account for 80-90% of the mutant alleles and many rare and novel mutations are continuously being reported.

	IVS 1-5 (G → C)	619 bp del	IVS 1-1 (G → T)	CD 8/9 (+G)	CD41/42 (–CTTT)	CD 15 (G → A)	CD 30 (G → C)	Cap site (+1) (A → C)	CD 5 (-CT)	Others	Uncharacterized	Total no. of alleles
South Gujarat	41 (47·7%)	5 (5·8%)	3 (3·5%)	2 (2·3%)	13 (15·1%)	13 (15·1%)	2 (2·3%)	1 (1·2%)	4 (4·7%)	CD 30 (G → A)-1, poly A (T → C) – 1 Total: 2 (2·8%)	–	86
Central Gujarat	49 (38·6%)	25 (19·7%)	8 (6·3%)	11 (8·7%)	2 (1·6%)	7 (5·5%)	1 (0·8%)	3 (2·4%)	17 (13·4%)	CD 30 (G → A)-1, IVS 1 –130 (G → C) – 1, poly A (T → C) – 1 Total: 3(2·4%)	1	127
Saurashtra	178 (55·7%)	31 (9·8%)	21 (6·6%)	16 (5·1%)	19 (6·0%)	15 (4·7%)	6 (1·9%)	5 (1·6%)	19 (6·0%)	CD 30 (G → A)-1, IVS 1 –1 (G → A) – 1, CD 16 (-C) – 1, IVS II – 654 (C->T)– 1, CD 47/48 (+ATCT) -1 Total : 5(1·6%)	3	318
Kuchchh	7 (29·0%)	5 (20·8%)	5 (20·8%)	0	1 (4·2%)	0	1 (4·2%)	2 (8·3%)	3 (12·5%)	0	–	24
North Gujarat	8 (44·4%)	8 (44·4%)	1 (5·6%)	0	0	0	0	1 (5·6%)	0	0	–	18
Region not specified	2 (15·4%)	–	–	–	5 (38·5%)	1 (7·7%)	1 (7·7%)	1 (7·7%)	–	IVS 1-1 (G → A) – 2, CD 16 (-C) – 1 Total: 3 (23·0%)		13
Total	285 (48·6%)	74 (12·6%)	38 (6·5%)	29 (5·0%)	40 (6·9%)	36 (6·1%)	11 (1·9%)	13 (2·2%)	43 (7·3%)	13 (2·2%)	4 (0·7%)	586

Districts under each region:
South Gujarat – Valsad, Dang, Navsari, Surat.
Central Gujarat – Bharuch, Narmada, Anand, Ahmedabad, Vadodara, Kheda, Gandhinagar, Panchmahal, Dahod.
Saurashtra – Porbandar, Jamnagar, Rajkot, Surendranagar, Amreli, Bhavnagar, Junaghad.
Kuchchh – Kuchchh.
North Gujarat – Patan, Banaskantha, Mehsana, Sabarkantha.

Algorithm for Prenatal diagnosis



Why blood centres are central to Thalassemia prevention & Management Programmes

- Blood Centres have to offer Transfusion support to Thalassemia Major children at regular intervals.
- **Challenges faced by Blood Centres:**

(Reference: (1)Farrukh T. Shah, Farzana Sayani, Sara Trompeter, Emma Drasar, Antonio Piga. Challenges of blood transfusions in β-thalassemia, Volume 37, 2019, https://doi.org/10.1016/j.blre.2019.100588. (2) Chapter 2 Blood Transfusion Therapy in β-Thalassaemia Major.)

1. Arrange on time blood units from voluntary non remunerated blood donors on regular basis.
2. Prevent red cell alloimmunisation in multiply transfused thalassemia major children by giving phenotype matched blood.
3. Reduce rates of Adverse Transfusion Reactions especially FNHTR using Saline washed & Leukoreduced units.
4. Reduce risk of TTI by possibly issuing NAT tested units.

Why Blood Centers are better placed to manage Thalassemia Prevention & Control

1) Already into counselling through Donor Motivator & Donor Counsellor. So Counselling about screening for β-Thalassemia would be an easier task.
2) Blood center has already contacts with many other Non Governmental charitable & social organizations, Education & Industrial institutes, through their voluntary Donor programme & Blood camps. Blood center can easily outreach these groups & convince them for either universal or targeted group screening for β-thalassemia trait.
3) Already have a list of Thalassemia children enrolled with them for regular transfusions. Their contacts can be used for cascade screening.

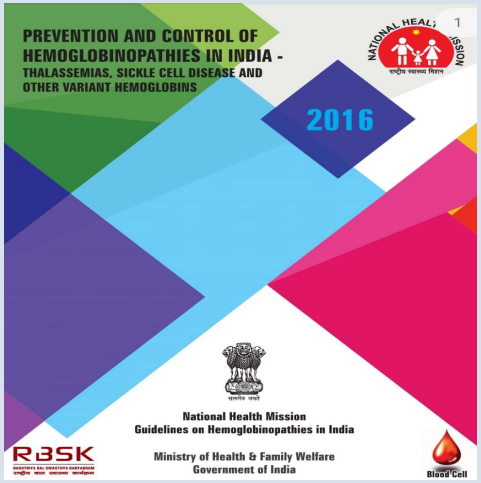
4) Most blood canters are now headed by M.D. in Transfusion Medicine & such experts can properly manage the programme by evaluating CBC & HPLC reports. The Experts are in a position to look after the Preanalytical, Analytical and Postanalytical aspects of these screening tests and bring out quality assured results from first line screening tests.

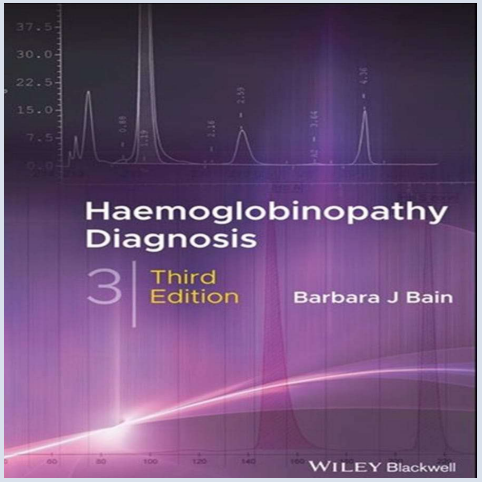
5) Such experts can also be instrumental in making a team of Obs & Gynec, Geneticists and Molecular Pathology laboratory specialist guiding the collection & transportation of samples for prenatal diagnosis of Thalassemia.

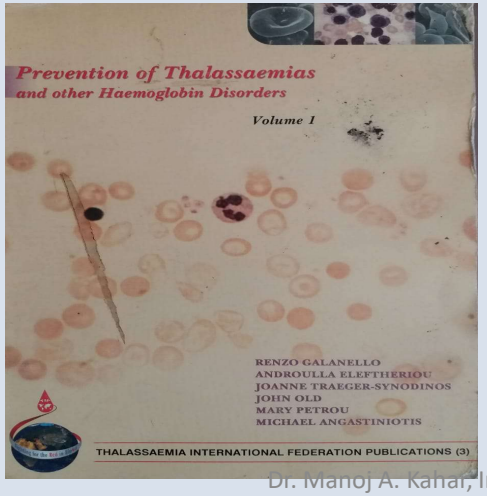
CONCLUSION

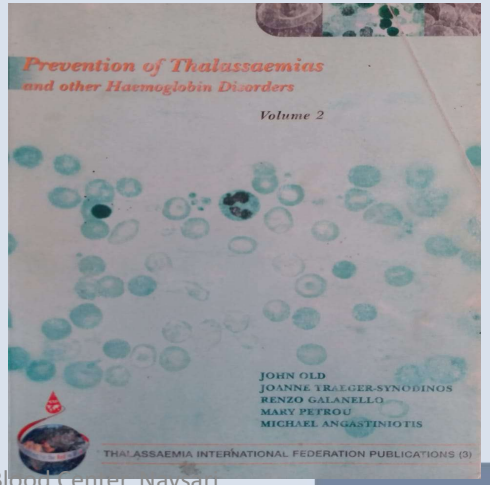
- Hemoglobinopathies are one of the major public health problems in India.
- To achieve success in their prevention and control, an on-going holistic approach is required. It is feasible to establish centers for awareness, screening and counselling in blood centers.
- Blood centers should establish linkage with higher centers for prenatal genetic testing and help in timely detection and thus prevention of birth of Thalassemia major babies.
- It is expected that with optimal collaboration and support from community, effective prevention and control of thalassemia can be achieved. This will lead to a healthier new generation which enjoys a better overall quality of life.

IMPORTANT RESOURCES FOR THE PROGRAMME









THANK YOU FOR YOUR ATTENTION