THALASSEMIA IN PREGNANCY

by

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Thalassemia is a group of herditary disorders affecting haemoglobin synthesis. Thalassemia Minor is discussed and the effect of pregnancy on haematopoiesis is described. A review of 10 pregnant women of ß Thalassemia Minor is presented.

Anaemia is one of the biggest problems in the developing countries. Due to poverty, cooking habits and adulteration of food products, large percentage of anaemias are of nutritional deficiency. Parasitic infestation accounts for anaemia in villagers. While dealing with these factors in pregnant women an obstetrician should be aware of the existence of haemoglobinopathies like Thalassemia which may be the cause of anaemia.

Thalasemia is prevalent in the mediterranean races like Greeks, Italians and Armenians. It is also common in Chinese, South-east Asians i.e. the Malays, Asians and Indians. It also occurs in West-Indians and American negroes.

Normal Human Haemoglobin

Haemoglobin is the functional unit for oxygen transport. The haemoglobin molecule in the adult Hb-A consists of 4 sub-units, made up of 2 pairs of polypeptide chains, which consist of 141 and 146 aminoacid residues respectively. The aminoacid residues can be grouped into polar and non-polar types and this governs the conformation of the whole molecule.

Fig. 1

TABLE I

Haemoglobin — Heam + globin. Globin has two pairs of polypeptide chains. Adult Haemoglobin—A—has 2 alpha and 2 beta chains. Foetal Haemoglobin—F—has 2 alpha and 2 gamma chains. Haemoglobin—A_2—has 2 alpha and 2 delta chains.

Thus each of the three normal haemoglobins has a pair of common polypeptide chain (α).

Thalassemia is a genetic defect affecting the synthesis of polypetide chains of globin molecule. Defect in synthesis of ß chains results in ß Thalassemia. Thalassemia Major is homozygous inheritence, whereas Thalassemia Minor is the heterozygous inheritence of the genetic defect in ß chains. In these cases no abnormal haemoglobins are found in blood.

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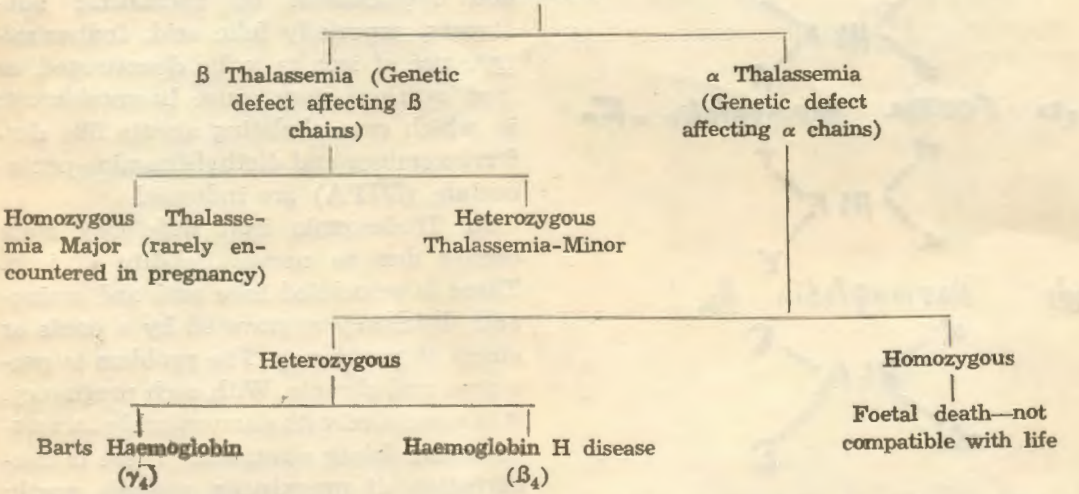
TABLE II
Normal

(a) At Birth:	Hb A	($\alpha_2\beta_2$)	= 30%
	Hb A_2	($\alpha_2\delta_2$)	= less than 1%
	Hb F	($\alpha_2\gamma_2$)	= 70%
(b) End of 1 year:	Hb A	($\alpha_2\beta_2$)	= 96-97%
	Hb A_2	($\alpha_2\delta_2$)	= 2-3.4%
	Hb F	($\alpha_2\gamma_2$)	= less than 2%

TABLE III
Thalassemia



Thalassemia Minor: (ß Heterozygous). This may be symptomless throughout life. It is a syndrome of moderate anaemia, intermittent jaundice, splenomegaly and changes in haemoglobin composition. It has following diagnostic findings.

(A) Peripheral blood smear reveals microcytosis, hypochromia, poikilocytosis, evalocytosis, anisocytosis with occasional basophillic stippling. Target cells are present.

(B) (i) Haemoglobin may be 2-3 gm% below normal.

(ii) Red blood cell count may be raised and red cells have a low mean corpuscular haemoglobin. Osmotic fragility is decreased.

(iii) Red cell span does not appear to be shorter than normal.

(vi) Serum iron levels are normal or elevated.

(C) Haemoglobin A_2 is raised to 3.4 to 7%. Foetal Haemoglobin is raised in 50% of the cases (2-6%). A small number of cases have Hb F ranging from 7-15% and Hb A_2 at normal level i.e. 2-3.4%.

Methods of Diagnosis

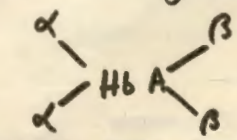
(a) Estimation of alkali resistant haemoglobin (Foetal $\alpha_2\gamma_2$).

(b) Osmotic fragility of RBC's to hypotonic saline i.e. increased resistance to haemolysis.

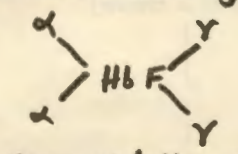
FIG 2:

(a) Haemoglobin = Haem + Globin
Globin has 2 pairs of polypeptide chains

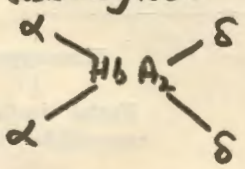
(b) ADULT Haemoglobin - A -



(c) FOETAL Haemoglobin - F -



(d) Haemoglobin A_2



(c) Electrophoresis of haemoglobin on paper, starch block, starch gel or agargel medias.

(d) Staining of foetal haemoglobin in erythrocytes.

(e) Staining of inclusion bodies in haemoglobin with brilliant cresyl blue.

(f) Haematological examination and family studies.

Management

At present there are no methods of treatment aimed at molecule levels directly. Supportive therapy is given by repeated blood transfusions of packed cells and replacement of haematinic substances, especially folic acid. Indiscriminate use of iron is to be discouraged, as iron overload may cause haemosiderosis in which case chelating agents like desferrioxamines and diethyl-triamine-pentaacetate (DTPA) are indicated.

In Thalassemia iron deficiency state occurs due to non-availability of iron. There is associated folic acid and amino-acid deficiency aggravated by a crisis or stress of pregnancy. The problem is persistent and chronic. With each pregnancy, it is associated with demonstrably increased serum folate clearance. There is exacerbation of preexisting anaemia partly relieved by high doses of folic acids. Megaloblastic changes have been observed to develop with alteration in ratios of affected haemoglobin. Usually there is normal or low serum B_{12} in pregnancy.

TABLE IV
Summary of Findings in Thalassemia

Condition	Hb Type	Sickling	Micro-cytosis	Hypo-chromia	Target cells	Haemo-lytic anemia	Spleno-megaly
Thalassemia Minor	AA_2	0	+	$+^I$	+	+	±
Thalassemia Major	AF	0	++	$++^I$	10-35	+++	+++
Sickle Cell-Thalassemia	SF	+	+	$+^I$	20-40	++	++
Hb H—Thalassemia	AH	0	++	++	++	++	±

The characteristics and significance of Thalassemia genes in regard to pregnancy and disease are mainly in their appearance in combination with other abnormal genes like those of sickle cell anaemia, presenting as Hb Thalassemia.

I Basophilic stippling in R.B.C.

Following is a review of 10 cases of Thalassemia Minor who were followed up during pregnancy and labour. The cases were detected during the first trimester of pregnancy at the antenatal clinics of Watford General Hospital, Watford and Bradford group of Hospitals Bradford, England over a period of 3 years i.e. (1972-1975).

TABLE V

Nationality	No. of pregnant patients
Italian	3
Greek	1
Cypriot	2
Pakistani	3
Indian (Sikh)	1

Four were known cases of ß Thalassemia Minor. Six were diagnosed in the antenatal clinic by electrophoresis as they reported with a haemoglobin less than 10 gm%.

Electrophoresis result of an Italian patient was as follows:—

Hb A_2 = 4.3%

Hb A = 95.7%

Foetal Hb F was not detected. She suffered from ß Thalassemia Minor.

All the 10 patients had reported to the antenatal clinic during first trimester. They were seen at 2 weekly intervals till 36 weeks after which check up was carried out weekly. Haemoglobin was repeated at every visit. Folic acid 5 mg. thrice daily was given throughout pregnancy. As serum iron levels were within normal limits, iron was not given. When haemoglobin result was below 7 gm% the patient was admitted to the antenatal ward for 2 days and 2 pints of packed cell transfusion was given. It was aimed to maintain Hb level of 10 gm% (Table VI).

Progress in Pregnancy and Labour: Patients complained of weakness and backache, particularly those with Hb less than 7 gm%. Pallor was present, although it was difficult to comment on some Europeans due to complexion. Weight gain during pregnancy was satisfactory. No signs of congestive heart failure were present despite low haemoglobin.

Labour

Duration of first stage was between 2-8 hours. Labour remained uncomplicated except in 2 patients who had forceps delivery for foetal distress. Cord was round the neck in 1 case. Both babies had apgar score 8/10 and 9/10 at 5 mts.

Intravenous injection of Ergometrine (0.5mg) was given at the birth of anterior shoulder. Third stage had been unremarkable.

Weight of the babies varied between 6.2 to 8 lbs.

Weight of placenta varied between 450-640 gms.

Puerperium was uneventful. Haemoglobin on 2nd postpartum day remained between 8-10%. None of the 10 patients needed blood transfusion after delivery. The babies of these Thalassemia mothers were being investigated for Thalassemia trait by the paediatric departments.

Patient No. 5 (Italian), the baby (with birth weight of 7 lbs) was discharged home with the mother. Two weeks later he was admitted to childrens' ward.

TABLE VI

Blood Picture During Pregnancy

Patients Blood Picture	1	2	3	4	5	6	7	8	9	10	Remarks
Blood (gm. 100 ml) at 36/52	6.5	9	8.5	7	6	9	8.5	10	10	9.5	Varied between 6-10 gm%
Blood Transfusion required in pregnancy	4	Nil	1	2	4	0	3	0	0	0	50% needed blood transfusion
RBC 10^6/Cu mm	3.30	4.30	4.50	4.10	3.00	5.20	4.80	4.80	5.20	3.80	Between 3-5.2
MCV Cubic microns	71	76	78	68	67	71	76	78	80	68	Below normal (78-94)
MCN Micrograms	20	22	21	22	20	24	20	24	26	20	Below normal (27-32)
MCMC Per cent	28	30	29	28	27	28	30	30	30	26	Lower limit of normal (30-36)
Serum Bilirubin mg/100 ml	0.2	0.4	0.8	0.8	0.7	0.1	0.6	0.2	0.1	0.3	Within normal limits
Reticulocytes Per cent	4	2	3	3	4	2	3	2	2	4	Higher than normal (0.2.2%)
Serum Iron mg/100 ml	130	136	140	134	132	134	136	142	155	142	Normal range (80-150)

Anaemia was microcytic hypochromic with marked poikilocytosis.
There was slight to moderate Basophilic stippling, alongwith some target cells in all the cases.

(Baby's Hb 67% (9.5 gm%) Electrophoresis showed:
Hb A 35%
Hb F 65%

Many target cells were present in blood smear. Investigation of Baby's relatives was as follows:—

Italian Father:
Hb A 98%
Hb A_2 2%
Normal

Brother
Hb A 98.5%
Hb A_2 1.5%
Normal

Sister:

Showed heterozygous trait and suffered from Thalassemia Minor.
Hb A 94.6%
Hb A_2 5.4%
Her Hb was 8 gm%.

In conclusion

Thalassemia Minor is uncommon but not rare. In normal life these patients are well adapted to a state of chronic anaemia (8-9 gm%). Due to increased demands of foetus in pregnancy and to allow for the complications of haemorrhage and sepsis in labour, Haemoglobin level of 9-10gm% should be maintained as far as possible. Excess of iron does not raise the haemoglobin levels due to constant haemolysis of red blood cells. The only possible treatment to raise haemoglobin is blood transfusion. Overloading with iron or excessive blood transfusion may result in haemosiderosis of the reticulo-endothelial system which presents as enlarged spleen. Like most cases of anaemia labour is usually short and if prophylactic measures are taken, third stage remains uncomplicated. If antenatal care is not adequate or haemoglobin levels are lower than 8

gm%, even normal loss of blood during third stage may deteriorate the patient's condition.

The babies of Thalassemia mothers have not been found to be smaller by weight or size in relation to the particular race. It is advisable to investigate these babies for Thalassemia trait and if possible, rest of the family should also be investigated.

In diagnosis, absence of foetal haemoglobin does not always exclude Thalassemia Minor. Haemoglobin electrophoresis is a definitive method of diagnosis. Patients of ß Thalassemia Major rarely live to the reproductive age and thus do not present problem in obstetrics. Thalassemia Minor is difficult to diagnose in adults.

Considering that anaemia is one of commonest diseases of pregnancy in India, measures should be taken to detect Thalassemia in the antenatal patients presenting with low haemoglobin.

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