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Original Research Article

Spectrum of Haematological Parameters and Haemoglobinopathies (Sickle Cell and Thalassaemia) In Antenatal Cases

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Abstract: The haemoglobinopathies are autosomal recessive inherited disorders of haemoglobin synthesis (thalassaemia) or structure (sickle cell disorders) that is responsible for significant morbidity and mortality. Maternal hematological parameters influence health and survival of infant. Hence we need a powerful infrastructure in the form of screening methods, where we can detect pathology before-hand like the genetic disorders and prevent the newborn from many diseases. The present study was designed to study hematological profile in Antenatal care patients attending OPD, to compare the hematological parameters in normal pregnant women with those having Haemoglobinopathies and identifying the communities at risk. Total 500 pregnant women were screened. Out of 500 cases 4% are affected by haemoglobinopathy. Category wise distribution and prevalence of haemoglobinopathies in different castes along with number of cases screened of each caste was studied. Hematological parameters in all the 500 antenatal cases showed that anemia is prevalent in pregnancy i.e. known as physiological anemia of pregnancy. Also other parameters like Hematocrit, MCV, MCH, and MCHC are at lower normal limits in pregnancy. Haemoglobin values along with HCT, MCV, MCH and MCHC are found to be decreased in all the cases with Haemoglobinopathies while RDW is increased in all cases. Primary screening should be undertaken in all pregnant women. Blood indices can be used as cost effective method in pregnancy in resource limited settings. Due to high prevalence rate of haemoglobinopathies in India, a Universal Antenatal care screening programme for haemoglobinopathies should be adopted.
Keywords: Blood indices, Haemoglobinopathies, hematological parameters

INTRODUCTION:

It is truly said that "PREGNANCY" is the most precious thing and the turning point of life for a women. As the moment a child is born, the mother is also born. Thus, as the quote rightly state that birth is not only about making babies but it is about making women stronger, capable and competent. This is a proven fact that a healthy mother can only bring a healthy child and to have a healthy mother, we need a powerful infrastructure in the form of screening methods, where we can detect pathology before-hand like the genetic disorders and prevent the newborn from many diseases. Screening for haemoglobinopathies is one such tool to aid this process. Haemoglobinopathies are a complex group of red cell disorders [1], which constitute a major burden of genetic diseases [2] and one of the major public health problems in India[1]. Haemoglobinopathies have a highly variable clinical manifestation [3]. At one end of the spectrum there is incompatibility with life and, at the other end, the patient under a stress, such as pregnancy, may experience some deterioration in her normal healthy state [3]. Both the abnormal haemoglobin and the thalassaemia give rise to health problems of immense proportions [3]. The haemoglobinopathies are autosomal recessive inherited disorders of haemoglobin synthesis (thalassaemia) or structure (sickle cell disorders) that are responsible for significant morbidity and mortality on a worldwide scale [1]. Individuals with trait (carriers) are healthy and unaware of their carrier status unless specifically screened. Maternal hematological parameters influence health and survival of infant.Hence, a joint venture of antenatal and inductive screening seems to be the most fruitful strategy for haemoglobinopathy in India [4]. The present study was designed to study hematological profile in Antenatal care (ANC) patients attending OPD, to compare the hematological parameters in normal pregnant women with those having

Haemoglobinopathies and identifying the communities at risk.

MATERIAL AND METHODS

The present study was carried out in a tertiary care hospital in Maharashtra for a period of 2 years from 2008 to 2010. 500 Antenatal patients attending Obstetric-OPD for routine check-up were included in study. Antenatal checkups (ANCs) with clinical suspicion of anaemia, attending the ANC clinics (Routine checkup) were included in study group**.** Blood was collected in EDTA anticoagulant bulbs from the anticubital vein, with all aseptic precaution for different types of laboratory investigations. Complete blood counts (using Mythic18, Orphee SA counter) and smears stained by using Standardised Romanowsky stain, Leishman stain for peripheral blood smears and Brilliant cresyl blue stain for reticulocyte count of all the patients were studied. Finally a very standardized method to detect HbA_2 and HbF, also presence of some abnormal Hb was done by using HPLC (using VARIANT^{TM} of Bioradcompany). A final correlation of CBC and evaluation of HPLC was done in detection of sickle cell disorders and thalassaemia in Antenatal cases.

OBSERVATIONS:

Out of total 500 pregnant women, 20 (4%) women were having haemoglobinopathies, whereas rest 480 (96%) women had normal haemoglobins. Out of these 20 cases, maximum no. of cases i.e. 11 (2.2%) were of β –Thalassemia trait, followed by Sickle cell trait cases 06 (1.2%), sickle cell disease 1 (0.2%), δβ Thalassemia case 1 (1.2%), and double heterozygous 1 (0.2%). [Table 1] Prevalence of haemoglobinopathies in different castes along with number of cases screened of each caste, out of total 500 cases studied. Maximum number of cases screened are of Muslim community (114), followed by Mahar (98) and Maratha (64). It is evident that haemoglobinopathies are most prevalent in Walmik and Kathar community (20% each) followed by Matang (16.6%), Sonar (14.2%), Mahar (9.1%), Dhangar (9.09%), Mali (5.5%), Maratha (4.6%) and Muslim (0.8%). Category wise distribution shows maximum 39.7% cases belonging to other backward castes (OBC) category followed by scheduled castes (SC) category i.e. 29.1% cases; scheduled tribes (ST) category - 16.6% cases; Nomadic tribes (NT) category – 9.09% and General category - 5.4% cases. Caste-wise distribution of thalassemia cases which includes β- thal trait cases and δβ thalassemia. Thalassemia is found to be more prevalent in Walmik and Kathar community (20% each) followed by Sonar (14.2%), Dhangar (9.09%), Matang (8.33%), Mali (5.5%), Maratha (4.6%) and Mahar (3.06%). Category wise distribution shows maximum 39.7% cases belonging to OBC category followed by SC category i.e. 23.06% cases; NT category – 9.09%; S.T category – 8.33% cases and General category – 4.69% cases. Sickle cell disorders are more prevalent in Matang- 8.33% followed by Mahar- 5.10%. Also a case of sickle was found in Muslim community accounting for 0.87%. Category wise distribution shows that sickle cell disorder is most prevalent in ST (8.33%) followed by SC (5.10%) and General Category (0.87%). [Table 2]

Hematological parameters in all the 500 antenatal cases showed that anemia is prevalent in pregnancy i.e. known as physiological anemia of pregnancy. Also other parameters like Hematocrit, MCV, MCH, and MCHC are at lower normal limits in pregnancy. Thus it shows a wide variation in all hematological parameters. Haemoglobin values <7gm% i.e. severe anaemia are found in 19 antenatal cases. Haemoglobin values in the range of 7-9gm% i.e. moderate anemia are found in 88 cases. Maximum number of cases is with mild grade of anemia i.e 320 cases. Also it is found that haemoglobin values >10gm% are found in 71.2 % cases. [Table 3] Haemoglobin values along with HCT, MCV, MCH and MCHC are found to be decreased in all the cases. While as RDW is increased in all cases.

Screening for β-thalassemia trait can be effectively done by examining the red blood cell indices. In all the cases of β- Thalassemia trait, haemoglobin values are decreased with MCV levels < 75 fl and MCH levels < 27 pg. Also RDW values are < 19 %. However RBC indices cannot be used as lone indicator for diagnosis of β-thalassemia trait and needs further confirmation. MCV and RDW values show a statistically significant difference amongst normal pregnant women and β- Thalassemia trait cases. Hence MCV and RDW can be reliably used as primary indicator in differentiating β- Thalassemia trait cases even in pregnancy, along with cutoff values of MCV <75fl, MCH <27pg and MCHC <33g/dl. [Table 4].

There was no statistically significant difference recorded in the blood cell indices between normal and sickle cell trait in pregnant women except Hb and RBC count which is significantly decreased. Similar picture can be seen in iron deficiency anaemia. Hence patient blood indices cannot be used as primary screening tool in sickle cell traits, in pregnancy. A significant difference was noted in Hb values, HCT values and RBC counts, amongst normal pregnant women and sickle cell disease case. Hence significantly reduced Hb, HCT and RBC counts can be used as a primary screening tool in case of sickle cell disease in pregnancy. MCV values and RBC counts are significantly decreased in δβ- thalassemia cases while RDW values are significantly increased in double heterozygous cases. Hence these parameters can aid in primary screening of δβ- thalassemia and double heterozygous cases in pregnancy.

Table 1: Distribution of all cases studied

Case Distribution		**No. of cases**	**Percentage**
Normal Cases	NAD	480	96%
Affected Cases	B- Thalassemia trait	11	2.2 %
	Sickle cell trait	06	1.2 %
	Sickle cell disease	01	0.2 %
	δβ Thalassemia	01	0.2 %
	Double Heterozygous	01	0.2 %
Total Cases		**500**	**100 %**

Table 2: Caste/Category wise distribution of haemoglobinopathy cases

Caste	**Category**	**Thalassemia trait**	**Sickle cell trait**	**Sickle cell disease**	**δβ Thalassemia**	**Double Heterozygous**	**Total No. of affected Cases**	**Cases screened out of 500**	**% of affected cases**
Mahar	S.C	2	4	1	1	1	9	98	9.18
Maratha	G	3	-	-	-	-	3	64	4.68
Matang	S.T	1	1	-		-	2	12	16.6
Mali	O.B.C	1	-	-	-	-	1	18	5.5
Walmik	S.C	1	-	-	-	-	1	5	20
Sonar	O.B.C	1	-	-	-	-	1	7	14.2
Dhangar	N.T	1	-	-	-	-	1	11	9.09
Muslim	G	-	1	-	-	-	1	114	0.87
Kathar	O.B.C	1	-	-	-	-	1	5	20
Total Cases	**-**	**11**	**6**	**1**	**1**	**1**	**20**	**334**	**100**

Table 3: Grading of Anaemia

Hb (gm %)	**No. of cases**	**Percentage (%)**
< 7(severe)	19	3.8
7-9 (moderate)	88	17.6
9-11 (mild)	320	64
>11(normal)	73	14.6
Total cases	500	100

Table 4: Complete blood count in all pregnant women

		HB Gm%	**HCT %**	**MCV fl**	**MCH Pg**	**MCHC g/dl**	**RDW %**	**RBC Count Mill/mm^3**
All pregnant women (500)	Mean+1 S. D	9.7 +1.4	28.2 +4.5	75.8 +8.6	25.3 +11.5	34.3 +4.7	16.6 +2.9	4.0 +0.7
Thalassemia trait (11)	Mean+1 S. D	8.9 +1.6	27.7 +5.0	67.5 +4.6	24.6 +4.4	30.2 +3.5	14.7 +1.5	4.4 +0.6
	P value	>0.05	> 0.05	< 0.05*	> 0.05	> 0.05	< 0.05*	> 0.05
Sickle cell trait (06)	Mean+ 1S.D	8.4 +1.5	22 +4.1	75.7 +16.9	28.9 +9.7	32.4 +5.6	15.9 +1.4	3.3 +0.9
	P value	<0.05*	>0.05	>0.05	> 0.05	> 0.05	> 0.05	<0.05*
Sickle cell disease (01)	Single Case CBC Values	6.8	19.2	74	26.3	35.4	16.9	2.5
Δβ Thalassemia (01)	Single Case CBC Values	8.9	25.4	52	18.1	35	20.8	4.9
Double Heterozygous (01)	Single Case CBC Values	8.8	23.2	70	26.7	37.6	22.5	3.3
Mean CBC in all affected cases (20)		8.6	26.1	68.5	22.9	32.7	16.7	3.7

* - Statistically significant

DISCUSSION:

Study by Kate *et al.;* [5] shows that sickle cell gene harbor amongst different caste groups but very high prevalence amongst SC, ST and OBC. Thus, in present study also the sickle cell gene is highly prevalent in SC, ST categories however no cases are found in the OBC category. According to study by Sinha *et al.;* [2] which gives ethnic distribution of haemoglobinopathy in Varanasi region, overall prevalence of haemoglobinopathy in General category is 43.3%, in SC/ST category is 34.1% while in OBC and others is 10.8% and 5.8% respectively. Thus in contrast to this study, present study shows maximum 39.7% cases belonging to OBC category followed by S.C category i.e. 29.1% cases and S.T category16.6% cases; NT category – 9.09% and General category-5.4% cases. Study by Gupta [6] shows prevalence of sickle cell trait in ST category ranging from 12.0 to 28.6% and 5.1% in SC category. About 0.6-30 per thousand population of SC/ST is expected to suffer from sickle cell disease (SCD). While present study shows prevalence in ST (8.33%) followed by SC (5.10%) and General Category (0.87%). Thus, prevalence rate in SC in both studies are similar. Also the expected sufferer for SCD in this study i.e.0.3-15% and SCD rate in present study i.e.5% matches well.

Study by Deshmukh *et al.;* [7] for prevalence of sickle cell disorder in Rural Wardha shows maximum prevalence in Matang (15.8%). Prevalence in Mahar (4.6%) and OBC (5.3%). While present study shows prevalence in Matang- 8.33% followed by Mahar- 5.10%. Also a case of sickle was found in Muslim community accounting for 0.87%. Study by Panda *et al.;* [8] shows prevalence of haemoglobinopathies among general category, SC and OBC category of Southern Orissa in pregnant women. The present study is in accordance with this study. The mean values of all hematological parameters in present study correlates well with the values of Study by Panda *et al.;* [8].

The incidence of anemia in pregnancy ranges widely from 40 to 80 % in the tropics compared to 10 to 20 % in developed countries [5]. A typical iron deficiency anemia shows following blood values HB < 10 gm %, RBC < 4 million/mm^3, PCV < 30%, MCHC < 30%, MCV < 75 fl, MCH < 25 pg and considering the lower limit for Hb as 10gm%, the prevalence of anaemia in present study is 71.2%, matches well with Basu [9] and Dutta [10] reference values. In studies of Gupta [6] and Panda *et al.;* [8] majority of normal pregnant women were under mild grade anemia. Thus all the parameters in the present study match well with Panda *et al.;* [8] and Sanchaisuriya *et al.;* [11] studies.

Various indices utilizing these CBC components have been developed with a view of providing a mathematical derivation to reliably differentiate iron deficiency from thalassemia minor. The RBC count is also useful as a diagnostic adjunct because the thalassemia's produce a microcytic anemia with an associated increase in the RBC [8]. Thalassemia individuals have a reduced MCV; and one study has suggested that an MCV of 72 fL is maximally sensitive and specific for presumptive diagnosis of thalassemia syndromes [8].

In present study no statistical difference was noted in the haematological parameters like Hb, HCT, MCH, MCHC and RBC counts except the MCV and RDW values, which shows a statistically significant difference amongst normal pregnant women and β-Thalassemia trait cases. Hence MCV and RDW can be reliably used as primary indicator in differentiating β-Thalassemia trait cases even in pregnancy. The hematological parameters for sickle cell trait and sickle cell disease in present study are similar to study of Panda *et al.;* [6]. There is statistically significant difference found in the blood cell indices as compared to the values in the normal pregnant women except the Hb and RBC count which is calculated to be significant due to very low values in sickle cell trait and sickle cell disease cases as compared to normal pregnant women. Hence significantly reduced Hb, HCT and RBC counts can be used as primary screening tool in case of sickle cell disorder in pregnancy. No comparative studies for hematological values in δβ-Thal and double heterozygous in pregnant women are found so far done.

CONCLUSION:

Very few studies are done in India for spectrum and prevalence of haemoglobinopathies in pregnancy. Haemoglobinopathies are highly prevalent in OBC (39.7%), SC (29.1%), and ST (16.6%) categories followed by NT (9.09%) and General Category (5.4%) Caste-wise distribution of cases showed that haemoglobinopathies are most prevalent in Walmik and Kathar (20% each) followed by Matang 16.6%, Sonar 14.2%, Mahar 9.1%, Dhangar 9.09%, Mali 5.5%, Maratha 4.6% and Muslim 0.8%. Haematological profile showed that anemia is prevalent in pregnancy. Also other parameters like Haematocrit, MCV, MCH, and MCHC are at lower normal limits in pregnancy. Haemoglobin values along with HCT, MCV, MCH and MCHC are found to be decreased in all the cases while RDW is increased in all cases. Screening for β-thalassemia trait can be effectively done by examining the red blood cell indices. However RBC indices cannot be used as lone indicator for diagnosis of β-thalassemia trait and needs further confirmation. However MCV and RDW can be reliably used as primary indicator in differentiating β-Thalassemia trait cases even in pregnancy, along with cutoff values of MCV <75fl, MCH <27pg and MCHC <33g/dl. Significantly reduced Hb, HCT and RBC

counts can be used as a primary screening tool in case of sickle cell disease in pregnancy. Decreased MCV values and RBC counts in δβ- thalassemia cases while increased RDW values in double heterozygous cases can aid in primary screening of δβ- thalassemia and double heterozygous cases in pregnancy. Primary screening should be undertaken in all pregnant women. Blood indices can be used as cost effective method in pregnancy in resource limited settings. Due to high prevalence rate of haemoglobinopathies in India, a universal ANC screening programme for haemoglobinopathies should be adopted.

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