



## PATTERN OF HEMATOLOGICAL DISORDERS IN VARIOUS TRIMESTERS OF PREGNANCY

### Pathology

**Vinodkumar S**

Department of Pathology, Trichy SRM Medical College Hospital and Research Centre, Tamilnadu Dr. MGR Medical University, Chennai, Tiruchirapalli, India

**Suganya R\***

Department of Pathology, Trichy SRM Medical College Hospital and Research Centre, Tamilnadu Dr. MGR Medical University, Chennai, Tiruchirapalli, India \*Corresponding Author

**Sarada V**

Department of Pathology, Trichy SRM Medical College Hospital and Research Centre, Tamilnadu Dr. MGR Medical University, Chennai, Tiruchirapalli, India

### ABSTRACT

Pregnancy is a state of many physiologic changes affecting the hematologic indices like anemia, neutrophilia and thrombocytopenia where it requires earliest treatment. The objective is to study the various hematological patterns in different trimesters in pregnancy and to correlate the clinical manifestations and possible etiology. Blood samples were collected for analyzing complete hemogram, peripheral smear and coagulation profile. In this study, out of 100 pregnant women, 43%, 30% and 27% were from 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> trimesters. From this most of them are from reproductive age group of less than 25 years. Many are suffering from the microcytic hypochromic anemia during the 1<sup>st</sup> trimester. About 12 cases presenting in the 3<sup>rd</sup> trimester are in the need of blood transfusion and 12 cases are suffering from macrocytic anemia so they should be scanned for neural tube defects. Thrombocytopenia was observed in 7 cases out of which 5 were identified as immune thrombocytopenic purpura and were mostly among the primi from the first trimester. Pregnancy causes a number of physiologic changes in the blood. Recognizing and treating them during pregnancy is difficult owing to the paucity of evidence to guide consultants.

### KEYWORDS

Pregnancy, trimesters, hemogram

### INTRODUCTION

Hematological variations and fluctuations in pregnancy is one of the main health problems and affects the results of pregnancy negatively. The prevalence of anemia is still in question in our country. It is important to recognize and treat hematologic disorders occurring during pregnancy at the earliest. But due to paucity of studies, the consultants felt difficult to identify them and require guidelines and policies.<sup>[1]</sup>

Anemia secondary to iron deficiency is the most frequent hematologic complication and is easily treated with oral iron formulations; however care must be taken not to miss other causes of anemia such as Sickle cell disease,<sup>[2]</sup> thalassemia, aplastic anaemia and autoimmune haemolytic anaemia. Anaemia due to folic acid deficiency causes neural tube defects in fetus which has to be diagnosed early as it is a preventable cause.<sup>[3]</sup>

Next to anaemia, thrombocytopenia is the other reason to approach the haematologist. Though gestational thrombocytopenia (GTP) is common, it needs to be distinguished from Immune Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura (TTP), eclampsia or HELLP (Hemolysis, elevated liver enzymes and low platelets) syndrome in addition to those caused by viral infections, malaria or drugs as the treatment plan varies.<sup>[4]</sup> Occasionally the management of mother and infant involves the expeditious recognition of neonatal alloimmune thrombocytopenia (NAIT), a condition that is responsible for severe life-threatening bleeding of the newborn.<sup>[5]</sup>

Pregnancy is a procoagulant state, however inherited and acquired bleeding disorders are also common necessitating early diagnosis and careful monitoring of coagulation parameters to prevent bleeding both intrapartum and postpartum. Additionally, venous thromboembolism (VTE) during pregnancy is still largely responsible for mortality during pregnancy and puerperium. Hence the diagnosis, treatment options and guidelines for prevention of VTE during pregnancy are explored.<sup>[6]</sup>

Although neutrophilic leucocytosis is a feature of pregnancy, moderate to marked increase with qualitative changes alert towards severe infections like urinary tract infection and even chorioamnionitis, few of which may predispose to abortion. Similarly lymphocytosis favors viral infections like Toxoplasmosis, Others, Rubella, Cytomegalovirus and Herpes (TORCH) which also has to be given due importance. Even

the less common leukemias, systemic lupus erythematosus (SLE), antiphospholipid syndrome (APLS) have to be identified.<sup>[7]</sup> The aim of this present work is to study the prevalence and evaluate the etiology of various haematological disorders among pregnant women who are attending the antenatal care clinic at a tertiary care teaching hospital, Tiruchirapalli, India.

### MATERIALS AND METHODS

This is a cross sectional observational study which was conducted between June 2018 and August 2018 among the patients who are attending outpatients and inpatients department of Obstetrics and Gynecology in Trichy SRM Medical college hospital and Research Centre, Tiruchirapalli, India for their regular and routine check-up. A total of 100 pregnant women of all the trimesters are randomly selected for the study. After obtaining approval from Institutional Research Board and the Institutional Ethics committee (Ref. No. CMCH&RC/IEC/ 95/ dated 05.12.2017), the study was conducted. Written informed consent was also obtained from all participants. All the pregnant women with the following criteria attending the tertiary care hospital were included.

1. Pregnant women in all three trimesters
2. Age group between 18 - 45 years
3. Pregnant women of any gravida
4. Normal or complicated pregnancies

Cases of haematological disorders who are already diagnosed or on treatment and hematological disorders diagnosed prior to pregnancy were excluded. About five ml of intravenous blood was collected from all the patients and were sent to Pathology laboratory for haematological analysis. The data including socio demographic data, economic and educational status of various stages of pregnancy were collected. Further types, severity and pattern of any specific gynecological or obstetric illness were recorded. Diagnostically, the blood samples were collected for analyzing complete hemogram, peripheral smear and coagulation profile and the data were correlated and compared with the clinical manifestations and various trimesters using descriptive analysis.

### RESULTS

In this study, 49% were primigravida and 51% were multigravida. Out of this 51% multigravida, 23% were second gravida, 20% were third gravida and 8% were fourth and fifth gravida and the details were depicted in figure 1. The age group distribution among the subjects included in this study was analyzed and the same was impregnated in figure 2.

Figure 1: Comparison of parity of patients

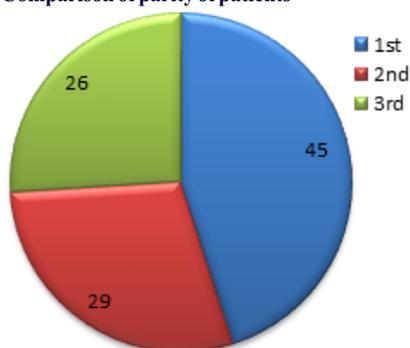
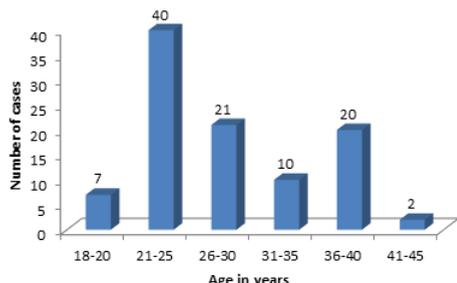


Figure 2: Age wise distribution of the subjects (n=100)



As the decade progressed, fertility decreased significantly for most women and also showed an increase in complication. In this study out of 100 patients, 68% were suffering from anemia; among them, 68% of anemia, 43%, 12%, 12% and 1% were observed with microcytic hypochromic anemia, macrocytic anemia, normocytic anemia and hemolytic anemia respectively. This anemia is further classified into mild anemia, moderate anemia, and severe anemia based on the levels of the hemoglobin. About 38% are suffering from conditions such as leukocytosis and Thrombocytopenia. From this 37%, 31% of the women are having leukocytosis and 7% women are suffering from the ITP and HELLP. The remaining 11% women are normal and the same were tabulated in table 1.

Complications of the pregnant women were the major factor causing mortality and morbidity. Out of the 100 pregnant women 63% were suffering from anemia, 7% had bleeding disorders, 12% had pregnancy induced hypertension (PIH), 8% had gestational diabetes mellitus (GDM) and 10% were normal uncomplicated pregnancies. The complications during the pregnancy compromise both the maternal and the fetal outcome.

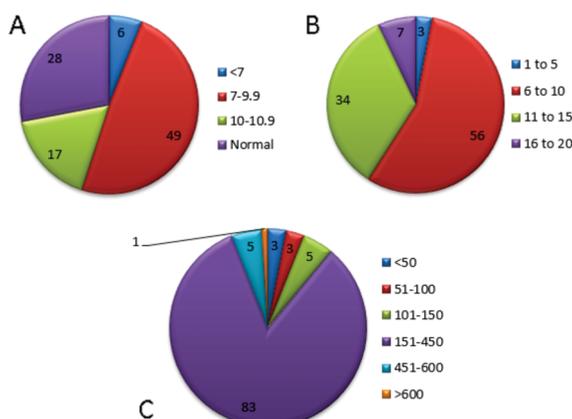
Table 1: Comparison of major haematological complications in various trimesters

Complications	Trimesters (n=100)		
	1 <sup>st</sup> (n=45)	2 <sup>nd</sup> (n=29)	3 <sup>rd</sup> (n=26)
Microcytic anemia	18 (40)	13 (44.8)	12 (4.6)
Macrocytic anemia	1 (2.2)	5 (17.2)	6 (2.3)
Normocytic anemia	6 (13.3)	1 (3.4)	5 (19.2)
Hemolytic anemia	-	1 (3.4)	-
Leucocytosis	6 (13.3)	2 (6.9)	4 (15.4)
Neutrophilia	7 (15.6)	5 (17.2)	5 (19.2)
Eosinophilia	-	1 (3.4)	-
Lymphocytosis	1 (2.2)	-	-
Thrombocytopenia	-	1 (3.4)	1 (3.8)
ITP	4 (8.9)	1 (3.4)	-

[Figure in parenthesis denoted percentages; the total of the percentage did not tallied due to the multiple complications in the same subject or absence in some cases]

The detailed description of hemoglobin ranges from <7 to 11 (g/dL) and normal was depicted in figure 3A. The various ranges of white blood cells in 10<sup>3</sup>/μL was picturized in figure 3B and the platelet count in 10<sup>3</sup>/μL was also impregnated in figure 3C.

Figure 3: Observation of haemoglobin, WBC and platelet counts



Severe anemia is noted in the multigravida in second and third trimester. Moderate anemia is seen more in primi in the first trimester itself. The difference is statistically significant among the haemoglobin and platelet levels and same was depicted in table 2.

Table 7: Comparison of Hemoglobin and platelet in various trimesters and gravida

Hemoglobin (g/dl) and platelet (10 <sup>3</sup> /μl)		Trimester			Total	
		1st	2nd	3rd		
<7 and <50	Parity	Primi	- / 3	1	-	1 / 3
		2nd	-	2	-	2
		3rd	-	2	1	3
	Total	- / 3	5	1	6 / 3	
7 - 9.9 and 51 - 150	Parity	Primi	19 / 2	5 / 1	1	25 / 3
		2nd	4 / 1	2 / 1	2 / 2	8 / 4
		3rd	-	4 / 1	6	10 / 1
		>3	-	1	5	6
	Total	23 / 3	12 / 3	14 / 2	49 / 8	
10-10.9 and 151 - 450	Parity	Primi	4 / 30	2 / 7	1 / 3	7 / 40
		2nd	3 / 8	3 / 8	- / 3	6 / 19
		3rd	-	2 / 8	1 / 9	3 / 17
		>3	-	-	1 / 7	1 / 7
	Total	7 / 38	7 / 23	3 / 22	17 / 83	
> 11 and 451 - 600	Parity	Primi	13 / 1	1 / 1	2 / 1	16 / 3
		2nd	2	2	3	7
		3rd	-	2 / 1	2 / 1	4 / 2
		>3	-	- / 1	1	1 / 1
	Total	15 / 1	5 / 3	8 / 2	28 / 6	
Total	Parity	Primi	36	9	4	49
		2nd	9	9	5	23
		3rd	-	10	10	20
		>3	-	1	7	8
	Total	45	29	26	100	

In the present study, there was an increase in PT among 24% of cases and most of them are mild except for those with HELLP and ITP. Similarly APTT was increased in 46% which was not much significant except for HELLP, PIH and ITP. Acute increase in the coagulation profile alerts the clinician to impending DIC and hence needs to be monitored in complicated pregnancies especially preeclampsia.

DISCUSSION

The hematological disorders in pregnancy are among the leading causes of the maternal and fetal morbidity and mortality. New guidelines and findings from clinical trials must be taken into account so that the diagnosis and treatment of the hematological disorders like anemia, thrombocytopenia, gestational diabetes mellitus, pregnancy induced hypertension and many others can be diagnosed.<sup>[3,4]</sup>

In this study, the pregnant women were selected from all the three trimesters with 43% from first trimester, 30% from the second trimester and 27% from the third trimester. Most of the patients were from the reproductive age group out of which 47% are having age less than 25 years and 32% were above 30 years. Generally with increase in age there was increase in complications as well as there a steep decline in the fertility of the women.<sup>[5]</sup>

From the complications recorded, many of them were suffering from microcytic hypochromic anemia of which most of them were from the first trimester itself. Though anemia is a complication of pregnancy, it worsens the condition of an already anemic patient, so it has to be given due importance and should be treated as early as possible. About 12 cases presented in the third trimester necessitating blood transfusion. Twelve cases of macrocytic anemia were observed of which two cases were from the first trimester, they should be screened for neural tube defects and should be given folic acid supplements. Others presented in the second and third trimester, suggestive of combined nutritional deficiency.<sup>[4,6]</sup>

Few of them have associated complications like gestational diabetes mellitus, hypertension, preeclampsia, etc. The 12 cases with normocytic anemia may be early iron deficiency anemia or physiological anemia due to hemodilution in pregnancy. One of the cases was diagnosed as hemolytic anemia with thrombocytopenia, a classic case of HELLP syndrome, the worst complication of preeclampsia. Hence peripheral smear and complete blood count could guide for early diagnosis and intervention.<sup>[8,9,10]</sup>

About 46% presented with mild anemia, 5% were having severe anemia and the rest with moderate anemia which was the highest. The screening in the early trimester and treatment in previous pregnancy would have prevented the complications and morbidity in the current pregnancy. Hence hemoglobin estimation becomes mandatory.<sup>[11]</sup> Other study had the significance and factors and revealed that in second and third trimester, anemia was more common. This finding correlated with this study where anemia progressed with gestational age.<sup>[10]</sup>

This was comparable with the study conducted by previously where it was found that 66.6% of iron deficient mothers with reduction in two or more of the haematological indices [mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC)]. They further stated that a combined reduction of MCV and MCH was more sensitive to detect iron deficiency anaemia.<sup>[11]</sup> It was observed that lower levels of pregnancy hemoglobin were associated with low birth weight and premature birth. Relevant risks are 2.52 for more than 13gm/dl and it increased to 3.73 for hemoglobin between 6 to 9 gm/dl.<sup>[9]</sup>

Normally there is mild neutrophilia in pregnancy. In this study, about 44% showed leucocytosis of which only 18% showed neutrophilia and 1% showed eosinophilia. Hence leucocytosis, rather than the neutrophilia alerts towards infection. Moreover, severe neutrophilia also point towards infection or sepsis. One of the cases presented with eosinophilia, who was an asthmatic patient with acute exaggeration. One case showed lymphocytosis with normal WBC count. With retrospective analysis, the history of viral fever was observed for the past one week, and it was recorded that the patient had self medication. Among platelet disorders, thrombocytopenia was observed in seven cases. Five cases were diagnosed as ITP and were primi mostly in the first trimester of pregnancy. One case was a second gravida with 28 weeks gestation, a known case of PIH progressed to HELLP syndrome. The peripheral smear showed hemolytic anemia with thrombocytopenia. The last case was Gestational thrombocytopenia presenting in a multigravida of third trimester. About 6% cases showed thrombocytosis of more than five lakhs platelet count. This may be attributed to reactive thrombocytosis secondary to anemia. Reactive thrombocytosis can be caused by severe anemia with marrow response, severe infections and hemorrhage.<sup>[12,13]</sup>

In the coagulation profile, the cases in which the prothrombin time (PT) and activated partial thromboplastin time (APTT) increased were 24% and 46% respectively. There was only a mild increase; most of them did not have any manifestations. Five out of seven were observed with thrombocytopenia and one case of hemolytic anemia presented with disseminated intravascular coagulation (DIC) and showed marked increase in coagulation profile.

The other study analyzed that thrombocytopenia complicated about 10% of all pregnancies. The common causes were gestational thrombocytopenia (74%), preeclampsia and HELLP (21%), ITP (5%). In this study we observed 70% of ITP, 15% of gestational thrombocytopenia and 15% of HELLP syndrome.<sup>[12]</sup> It was discussed that platelet count was lower in pregnancy with 10% decrease in the third trimester. Gestational thrombocytopenia was the commonest. Only few cases of ITP in pregnancy need intervention (30%).<sup>[13]</sup> Some

study demonstrated that there is no change or only a minimal decrease in coagulation tests like PT, international normalized ratio (INR) and APTT. But monitoring was mandatory in case of preeclampsia and thrombocytopenia.<sup>[14]</sup>

## CONCLUSION

Pregnancy causes a number of physiologic changes in the blood. Recognizing and treating hematologic disorders that occur during pregnancy is difficult owing to the paucity of evidence available to guide consultants. In this study, we have attempted to recognize few of the abnormal hematological disorders with the use of common basic investigations. These investigations can be done with point of care devices making it feasible even at the under resourced areas. Though this study has some limitations and caveats because of short term cross sectional study, the follow up of patients will add on to its significance.

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