Section: General Medicine

Original Research Article

ETIOLOGICAL PROFILE OF CYTOPENIAS INPREGNANCY

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ABSTRACT

Background: Aim: To study the etiological profile of cytopenias in pregnancy.
Materials and Methods: This study was a hospital based Prospective observational study with single point contact. A total of 110 cases who met the inclusion criteria during the study period were included. The study was conducted in the Department of General Medicine and Department of Hematology at Nizam's Institute of Medical Sciences [NIMS], a multi-specialty tertiary care referral hospital in Hyderabad, Telangana.
Results: In this study population, 36.36% had anemia, 53.63% had thrombocytopenia, 6.36% had bicytopenia and 3.3% had pancytopenia. A case of bicytopenia secondary to isolated folate deficiency was seen. A total of 4 pancytopenia cases were seen in this study of which 2 cases were due to hypersplenism and one case each of aplastic anemia and systemic lupus erythematosus were seen. One case of hypersplenism was secondary to noncirrhotic portal fibrosis and the cause for other case was planned to evaluate after parturition with bone marrow biopsy. A total of four cases of splenomegaly were seen in this study. Two cases were due to noncirrhotic portal fibrosis, one case was due to sickle-HbD disease. In two cases of hypersplenism secondary to noncirrhotic portal fibrosis, one case presented with pancytopenia and the other case presented with isolated thrombocytopenia. A total of 9 subjects with previous history of abortion was seen in this study out of which 3 cases of antiphospholipid syndrome were seen. The prevalence of iron deficiency in our study was 22.72% and of vitamin B12 deficiency was 10.9% and of folate deficiency was 4.54%.
Conclusion: This study concludes that a complete hemogram should be made routine at first antenatal visit and if abnormal, a detailed evaluation of cytopenias that arise during pregnancy should be undertaken. This helps the clinician to initiate the appropriate treatment promptly that helps to avoid unwanted complications down the line.
Keywords: Thrombocytopenia, Hemogram, Cytopenias, sickle-HbD disease, pancytopenia.

INTRODUCTION

Blood, when centrifuged separates into a fluid plasma which constitutes 55% and the cellular elements (45%)-buffy coat and red cell mass. Each cell line serves a specific function: oxygen transport by the rbc, immunity by wbc and hemostasis by platelets.
The cellular elements of blood are produced from the hematopoietic stem cells and the process is known as hematopoiesis.[1] During the course of development, the sites of hematopoiesis vary, with the first hematopoietic cells arising during late gastrulation in the extraembryonic yolk sac. This initial hematopoiesis is termed primitive hematopoiesis.
Cytopenias are the reduction in number of cells in peripheral blood, which can affect only a single cell line or any two cell lines, termed bicytopenia, or all three cell lines, termed pancytopenia. The clinical

presentation is variable depending on the cell line involved.

In India this is expected to be even more given the high prevalence of nutritional deficiencies and infectious diseases.

Pregnancy is a state characterized by many physiological hematological changes, which may appear to be pathological in the non-pregnant state. During pregnancy, the total blood volume increases by about 1.5 liters, mainly to supply the demands of the new vascular bed and to compensate for blood loss occurring at delivery.[2] Of this, around one liter of blood is contained within the uterus and maternal blood spaces of the placenta. Red cell mass (driven by an increase in maternal erythropoietin production) also increases, but relatively less, compared with the increase in plasma volume, the net result being a dip in hemoglobin concentration. Thus, there is dilutional anemia.

White blood cell count is increased in pregnancy with the lower limit of the reference range being typically 6,000/mm^3. Leukocytosis, occurring during pregnancy is due to the physiologic stress induced by the pregnant state.[3] Neutrophils are the major type of leucocytes on differential counts.[4,5] This is likely due to impaired neutrophilic apoptosis.[4]

Gestational thrombocytopenia is partly due to hemodilution and partly due to increased platelet activation and accelerated clearance.[6] Gestational thrombocytopenia does not have complications related to thrombocytopenia and babies do not have severe thrombocytopenia (platelet count ≤20,000/ mm^3). It has hence been recommended that the lower limit of platelet count in late pregnancy should be considered as 1.15 lac/ mm^3.[2]

Anemia, in general, is defined as low hemoglobin concentration resulting in decrease in oxygencarrying capacity of the blood.

Statistical definition: Hemoglobin less than 2 standard deviations below the mean for a healthy matched population.

In pregnancy, there are physiological variations in normal values. According to the WHO, anemia in pregnancy is defined as a hemoglobin value of less than 11gms/dl. Anemia is further graded as mild, moderate or severe as given below.[7] Mild anemia :10.0 - 10.9 g/dl Moderate anemia: 7.0 - 9.9g/dl Severe anemia :<7.0g/dl

Thrombocytopenia, defined as a platelet count of under 150 x 10^9/L, is the second most common haematological abnormality in pregnancy.[8] Thrombocytopenia in pregnancy occurs either due to obstetric conditions like gestational thrombocytopenia, pre-eclampsia/eclampsia or secondary to systemic disorders like thrombocytopenic thrombotic purpura, immune thrombocytopenia.[9] Other less common causes of thrombocytopenia in pregnancy include coagulopathy related to sepsis/disseminated intravascular coagulation (DIC), microangiopathic hemolyticanemia and kidney injury. Thrombocytopenia is categorized into mild (platelet count between 1 lakh/ mm3 to 1.49 lakh/ mm^3), moderate (50000/cumm-1 lakh/ mm3) and severe (<50000/ mm^3).[10]

Pancytopenia is the reduction in all three major cellular elements of blood, hence it is the simultaneous presence of anemia, leukopenia and thrombocytopenia.[11] It is a triad which involves bone marrow primarily or secondarily depending on the various pathogenesis. The various etiology of pancytopenia includes aplastic anemia, megaloblastic anemia, infections, nutritional deficiencies and malignancies.[12]

Bicytopenia is the reduction of any of the two cell lines of blood: erythrocytes, leukocytes or platelets. Malignancies and Megaloblastic anemia are the most frequently reported causes.[13]

Purpose of The Study

Most of the studies performed till now regarding cytopenias in pregnancy did not take into consideration of all the cell lines as a combined study. Very few case reports and studies were performed on bicytopenia and pancytopenia that occurred during pregnancy.

In this study conducted at NIMS, a tertiary care center, all the pregnant women who are referred from other hospitals for evaluation of various cytopenias were included. This constitutes a heterogenous group of patients with various possible causes. We aim to find the etiology of the various causes of cytopenias that arise during pregnancy which includes isolated cytopenias as well as with various combination of cytopenias in the form of bicytopenia and pancytopenia and include in the single study and contribute to the existing literature in this field.

Aims and Objectives

Aim:

To study the etiological profile of cytopenias in pregnancy.

Objectives

1. To study the incidence of anemia, thrombocytopenia, bicytopenia and pancytopenia in the study population.
2. Study the various clinical presentations of the cytopenias in pregnancy.

MATERIALS AND METHODS

Study Design

This study was a hospital based Prospective observational study with single point contact.

Sample Size

A total of 110 cases who met the inclusion criteria during the study period were included.

Setting of the Study

The study was conducted in the Department of General Medicine and Department of Hematology at Nizam's Institute of Medical Sciences [NIMS], a multi-specialty tertiary care referral hospital in Hyderabad, Telangana.

Study Period

July 2023 to June 2024

Study Population

Pregnant females who are referred from various hospitals to Nizam's Institute of Medical Sciences [NIMS], for the evaluation of various newly detected cytopenias. Written informed consent was taken from all subjects. Approval from Institutional Ethical committee was obtained.

Inclusion Criteria

1. Age Group: 18 to 45 years
2. Pregnant females
3. Diagnosed to have cytopenia during pregnancy irrespective of the trimester or gravida.

Exclusion Criteria

1. Known cases of Hemoglobinopathies.
2. Patients who refused to take part in the study.

Statistical Analysis

- The collected data was entered into a MS excel sheet.
- Data was analyzed as percentages and categories and presented as tables and diagrams.

RESULTS

- This study included a total of 110 patients who attended the outpatient department of Hematology and General medicine.
- This study was conducted at Nizam's Institute of Medical Sciences, a tertiary care hospital in Telangana.

Table 1: Age wise distribution of the patients

AGE	No. of patients (n=110)	%
< 20 years	4	3.63
20-30 years	89	80.9
>30 years	17	15.4

A total of 110 pregnant subjects were included in this study. The mean age was 25.3 ± 4.11 years. The majority of the subjects belonged to 20-30 years cohort (80.9%) followed by >30 years cohort(15.4%). Only 3.6% subjects are in <20 years cohort.

Table 2: Distribution according to gestational age

TRIMESTER	No. of patients (n=110)	%
1ST	10	9.09
2ND	30	27.27
3RD	70	63.63

Out of 110 subjects, 70 (63.6%) subjects were referred in third trimester followed by 30 (27.2%) subjects who were referred during second trimester. Only 10 (9.09%) subjects were referred in first trimester.

Table 3: Gravida wise distribution of the subjects

GRAVIDA	No. of patients (n=110)	%
1ST	76	69.09
2ND	20	18.18
3RD	9	8.18
4TH	5	4.54

Out of 110 subjects, 76(69.09%) subjects belonged to primi gravida followed by 20(18.18%) subjects who belonged to second gravida. 9 (8.18%) subjects belonged to third gravida and 5 (4.5%) subjects belonged to fourth gravida.

Table 4: Distribution of symptoms

SYMPTOMS	No. of patients (n=110)	%
ASYMPTOMATIC	88	80
EASY FATIGABILITY	19	17.27
GENERALISED WEAKNESS	18	16
PURPURIC RASH	3	2.72
MUCOSAL BLEED	2	1.81
JAUNDICE	1	0.9

Out of 110 subjects, 88 (80%) subjects were asymptomatic at the time of referral. 19 (17.27%) subjects had easy fatigability, 18 (16%) subjects had generalised weakness, 3
(2.72%) subjects had purpuric rash. Only 2 (1.81%) subjects had mucosal bleed and 1 (0.9%) subject had jaundice.

Table 5: Reason for referral

REASON	No. of patients (n=110)	%
ANEMIA	47	42.72

LEUKOPENIA	0	0
THROMBOCYTOPENIA	66	60
PANCYTOPENIA	4	3.63

Out of 110 subjects in this study, 47 subjects (42.7%) subjects were referred in view of anemia and 66 (60%) subjects were referred in view of thrombocytopenia. Only 4 (3.63%) subjects were referred in view of pancytopenia. No referrals were done for leukopenia.

Table 6: Previous history of cytopenias

CYTOPENIA HISTORY		No. of patients (n=110)	%
ABSENT		**99**	**90**
PRESENT	ANEMIA	6	5.45
	THROMBO CYTOPENIA	5	4.54

Out of 110 subjects, 99 (90%) subjects did not have any history of cytopenias. Only 6 (5.45%) subjects had prior history of anemia and 5 (4.54%) subjects had history of thrombocytopenia.

Table 7: Prior history of blood products transfusion

TRANSFUSION		No. of patients (n=110)	%
ABSENT		**103**	**93.63**
PRESENT	PRBC	6	5.45
	RDP	1	0.9

Out of 110 subjects, 103 (93.63%) never had any history of any blood products transfusion. Only 6 (5.45%) subjects had history of PRBC transfusion and only 1 (0.9%) subject had prior RDP transfusion.

Table 8: Distribution of clinical signs

SIGNS	No. of patients (n=68)	%
PALLOR	51	46.36
ICTERUS	4	3.63
PERIPHERAL EDEMA	6	5.45
PURPURA	1	0.9
MUCOSAL BLEED	2	1.81
SPLENOMEGALY	4	3.63

Out of 110 subjects, 51 (46.36%) subjects had pallor on examination. Only 6 (5.45%) subjects had peripheral edema and 4 (3.63%) subjects had icterus. Another 4 (3.63%) subjects had splenomegaly, 2 (1.18%) subjects had mucosal bleed and 1(0.9%) subject had purpura on examination.

Table 9: Hemogram analysis

HEMOGRAM ANALYSIS	No. of patients (n=110)	%
ANEMIA	40	36.36
LEUKOPENIA	0	0
THROMBOCYTOPENIA	59	53.63
ANEMIA+THROMBOCYTOPENIA	7	6.36
PANCYTOPENIA	4	3.63

Out of 110 subjects, hemogram analysis showed 59 (53.63%) subjects having thrombocytopenia and 40 (36.36) subjects having anemia. 7 (6.36%) subjects had anemia + thrombocytopenia and only 4 (3.63%) subjects had pancytopenia.

Table 10: Distribution of anemia based on MCV

ANEMIA	No. of patients (n=51)	%
MICROCYTIC	43	84.31
NORMOCYTIC	3	5.88
MACROCYTIC	5	9.8

Out of 110 subjects, 51 subjects had anemia out of which 43 subjects (83.31%) had microcytic anemia. Only 3 (5.88%) subjects had normocytic anemia and 5 (9.8%) subjects had macrocytic anemia. This graph includes subjects having isolated anemia(n=40) as well as anemia as a part of bicytopenia(n=7) and pancytopenia(n=4).

Table 11: Etiology of isolated anemia

ANEMIA	No. of patients (n=40)	%
IRON DEFICIENCY	18	45

Vit.B12 DEFICIENCY	2	5
Vit.B12 + FOLATE DEFICIENCY	1	2.5
SICKLE CELL TRAIT	2	5
SICKLE- β THALASSEMIA	1	2.5
SICKLE-HbD DISEASE	1	2.5
β-THALASSEMIA TRAIT	15	37.5

Table 12: Etiology of isolated thrombocytopenia

THROMBOCYTOPENIA	No. of patients (n=59)	%
GESTATIONAL THROMBOCYTOPENIA	37	62.71
ANTI PHOSPHOLIPID SYNDROME	13	22.03
Vit.B12 DEFICIENCY	6	10.16
Vit.B12 + FOLATE DEFICIENCY	1	1.69
IMMUNE THROMBOCYTOPENIC PURPURA	1	1.69
NONCIRRHOTIC PORTAL FIBROSIS	1	1.69

Table 13: Distribution of bicytopenia

BICYTOPENIA	No. of patients (n=7)	%
ANEMIA+LEUKOPENIA	0	0
ANEMIA+THROMBOCYTOPENIA	7	100
LEUKOPENIA+THROMBOCYTOPENIA	0	0

In this study, only combination of bicytopenia seen was anemia + thrombocytopenia. Anemia +leukopenia or leukopenia+thrombocytopenia was not seen.

Table 14: Distribution of pancytopenia

PANCYTOPENIA	No. of patients (n=4)	%
APLASTIC ANEMIA	1	25
SYSTEMIC LUPUS ERYTHEMATOSIS	1	25
HYPERSPLENISM	2	50

In this study, a total of 4 subjects had pancytopenia. 2 subjects had pancytopenia because of hypersplenism, 1 subject had SLE and 1 subject had aplastic anemia.

Table 15: Distribution of anemia+thrombocytopenia

CAUSE	No. of patients (n=7)	%
ITP+IRON DEFICIENCY	2	28.57
IRON+Vit.B12+FOLATE DEFICIENCY	1	14.28
IRON+Vit.B12 DEFICIENCY	1	14.28
IRON+FOLATE DEFICIENCY	1	14.28
IRON DEF. ANEMIA + GTP	1	14.28
FOLATE DEFICIENCY	1	14.28

Out of 110 subjects, 7 subjects had bicytopenia with combination of anemia+thrombocytopenia out of which 2 subjects had bicytopenia because of ITP+iron deficiency. Remaining causes are GTP+iron deficiency, iron+folate deficiency, iron+Vit.b12 deficiency, iron+Vit.b12+Folate deficiency and Folate deficiency in rest of each 5 subjects.

Table 16: Severity of anemia

SEVERITY (Hb levels)	No. of patients (n=51)	%
MILD (9-10.9 g/dL)	13	25.49
MODERATE (7-8.9 g/dL)	26	50.98
SEVERE (<7 g/dL)	12	23.52

Out of 51 subjects who had anemia, 26 (50.98%) subjects had moderate severity of anemia followed by 13 (25.49%) subjects who had mild anemia and 12 (23.52%) subjects had severe anemia.

Table 17: Severity of thrombocytopenia

SEVERITY (Platelet count)	No. of patients (n=70)	%

MILD (1,00,000-1,50,000)	21	30
MODERATE (50,000-1,00,000)	39	55.71
SEVERE (<50,000)	10	14.28

Out of 70 subjects of thrombocytopenia, 39 (55.71%) subjects had moderate thrombocytopenia and 21 (30%) subjects had mild thrombocytopenia. Only 10 (14.28%) subjects had severe thrombocytopenia.

Table 18: Distribution of cytopenias in primigravida

CYTOPENIAS	No. of patients (n=76)	%
ANEMIA	30	39.47
THROMBOCYTOPENIA	41	53.94
BICYTOPENIA	2	2.63
PANCYTOPENIA	3	3.94

Out of 76 primi subjects, 41 (53.94%) subjects had thrombocytopenia followed by 30(39.47%) subjects who had anemia. Only 3 (3.94%) subjects had pancytopenia and 2 (2.63%) subjects had bicytopenia.

Table 19: Distribution of cytopenias in second gravida

CYTOPENIAS	No. of patients (n=20)	%
ANEMIA	5	25
THROMBOCYTOPENIA	10	50
BICYTOPENIA	4	20
PANCYTOPENIA	1	5

Out of 20 second gravida subjects, 10 (50%) subjects had thrombocytopenia followed by 5 (25%) subjects had anemia. Only 4 (20%) subjects had bicytopenia and 1 (5%) subject had pancytopenia.

Table 20: Distribution of cytopenias in third gravida

CYTOPENIAS	No. of patients (n=9)	%
ANEMIA	2	22.22
THROMBOCYTOPENIA	6	66.66
BICYTOPENIA	1	11.11
PANCYTOPENIA	0	0

Out of 9 third gravida subjects, 6 (66.66%) subjects had thrombocytopenia followed by 2 (22.22%) subjects having anemia. Only 1 (11.11%) subject had bicytopenia. No subject had pancytopenia.

Table 21: Distribution of cytopenias in fourth gravida

CYTOPENIAS	No. of patients (n=5)	%
ANEMIA	3	60
THROMBOCYTOPENIA	2	40
BICYTOPENIA	0	0
PANCYTOPENIA	0	0

Table 22: Distribution of pregnancy interval in multigravida

PREGNANCY INTERVAL	No. of patients (n=34)	%
<1 YEAR	22	64.7
1-2 YEAR	10	29.41
>2 YEARS	2	5.88

A total of 34 multigravida subjects were referred. Out of them, 22 (64.7%) subjects had duration of pregnany interval of < 1 year and 10 (29.41%) subjects had interval of 1-2 years. Only 2 (5.88%) subjects had pregnancy interval of >2 years.

Table 23: Distribution of pregnancy interval and iron deficiency in multipara

PREGNANCY INTERVAL	No. of patients	No. of subjects with iron deficiency	%
<1 YEAR	22	5	22.72
>1 YEAR	12	4	33.33

Out of 34 multigravida patients, 22 subjects have pregnancy interval of <1 year and 5 cases of iron deficiency anemia were seen in those subjects. 12 multigravida subjects who had pregnancy interval >1 year, 4 cases of iron deficiency anemia were seen.

Table 24: Gravida wise distribution of anemia

GRAVIDA	No. of patients (n=51)	%
PRIMI	35	68.62

2ND GRAVIDA	10	19.6
3RD GRAVIDA	3	5.8
4TH GRAVIDA	3	5.8

A total of 51 cases of anemia were seen in this study, out of which 35 (68.62%) cases were seen in primi gravida subjects followed by 10 (19.6%) cases were seen in second gravida subjects. Only 3 (5.8%) cases each were seen in third and fourth gravida subjects.

Table 25: Trimester wise distribution of anemia

TRIMESTER	No. of patients (n=51)	%
1ST	9	17.64
2ND	16	31.37
3RD	26	50.98

Out of 51 cases of anemia, 26 (50.98%) cases presented in third trimester followed by 16 (31.37%) cases in second trimester. Only 9 (17.64%) cases of anemia are presented in first trimester.

Table 26: Gravida wise distribution of iron deficiency anemia

GRAVIDA	No. of patients (n=25)	%
PRIMI	16	64
2ND GRAVIDA	6	24
3RD GRAVIDA	2	8
4TH GRAVIDA	1	4

Out of 25 cases of iron deficiency anemia, 16 (64%) cases are seen in primi gravida subjects followed by 6 (24%) cases in second gravida subjects. Only 2 (8%) cases are seen in third gravida and 1 ($%) case was belonged to fourth gravida subject.

Table 27: Trimester wise distribution of iron deficiency anemia

TRIMESTER	No. of patients (n=25)	%
1ST	7	28
2ND	4	16
3RD	14	56

Out of 25 cases of iron deficiency anemia, 14 (56%) cases are seen in third trimester and 7 (28%) cases are seen in first trimester. Only 4 (16%) cases are seen in second trimester.

Table 28: Trimester wise distribution of gestational thrombocytopenia

TRIMESTER	No. of patients (n=37)	%
1ST	1	2.7
2ND	3	8.1
3RD	33	89.18

A total of 37 cases of gestational thrombocytopenia were seen, out of which 33 (89.18%) cases were seen in third trimester. Only 3 (8.1%) cases were seen in second trimester and 1 (2.7%) case was seen in first trimester.

Table 29: Gravida wise distribution of gestational thrombocytopenia

GRAVIDA	No. of patients (n=37)	%
PRIMI	27	72.97
2ND GRAVIDA	6	16.21
3RD GRAVIDA	4	10.81

Out of 37 gestational thrombocytopenia cases, 27 (72.97%) cases were seen in primi gravida subjects and 6 (16.21%) cases are seen in second gravida subjects. Only 4 (10.81%) cases were seen in third gravida subjects.

Table 30: Trimester wise distribution of antiphospholipid syndrome

TRIMESTER	No. of patients (n=13)	%
1ST	0	0
2ND	9	69.23
3RD	4	30.76

In this study, a total of 13 cases of antiphospholipid syndrome were seen out of which, 9 (69.23%) cases were seen in second trimester and 4 (30.76%) cases were seen in third trimester. No cases were recorded in first trimester.

Table 31: Gravida wise distribution of antiphospholipid syndrome

GRAVIDA	No. of patients (n=13)	%
PRIMI	7	53.84
2ND GRAVIDA	2	15.38
3RD GRAVIDA	2	15.38
4TH GRAVIDA	2	15.38

Table 32: Distribution of cytosis

CYTOSIS	No. of patients (n=110)	%
ERYTHROCYTOSIS	0	O
LEUCOCYTOSIS	24	21.81
THROMBOCYTOSIS	7	6.36

Out of 110 subjects in this study, 24 (21.81%) subjects had leucocytosis and 7 (6.36%) had thrombocytosis. None of the subjects showed erythocytosis.

Table 33: Distribution of pregnancy related causes of cytopenias

CAUSES	No. of patients (n=70)	%
GESTATIONAL THROMBOCYTOPENIA	38	54.28
IRON DEFICIENCY ANEMIA	18	25.71
Vitamin B12 DEFICIENCY	8	11.42
FOLATE DEFICIENCY	1	1.42
IRON + Vitamin B12 + FOLATE DEFICIENCY	1	1.42
IRON + Vitamin B12 DEFICIENCY	1	1.42
IRON + FOLATE DEFICIENCY	1	1.42
Vitamin B12 + FOLATE DEFICIENCY	2	2.85

In this study of 110 subjects, a total of 70 cases of cytopenias were related to pregnancy. Majority of the cases were due to gestational thrombocytopenia which constituted 38 (54.28%) cases followed by iron deficiency anemia in 18 (25.71%) cases. 8 (11.42%) cases are due to vitamin B12 deficiency and 2 (2.85%) cases are due to combined vitamin B12 and folate deficiency. 1 (1.42%) case each of folate deficiency, combined iron with vitamin B12 and folate deficiency, combined iron with vitamin B12 deficiency and iron with folate deficiency were seen.

Table 34: Distribution of causes of cytopenias unrelated to pregnancy

CAUSES	No. of patients (n=40)	%
β-THALASSEMIA TRAIT	15	37.5
ANTIPHOSPHOLIPID SYNDROME	13	32.5
IMMUNE THROMBOCYTOPENIC PURPURA	3	7.5
HYPERSPLENISM	3	7.5
SICKLE CELL TRAIT	2	5
SICKLE-β THALASSEMIA	1	2.5
SICKLE-HbD DISEASE	1	2.5
SYSTEMIC LUPUS ERYTHEMATOSIS	1	2.5
APLASTIC ANEMIA	1	2.5

In this study of 110 subjects, a total of 40 cases of cytopenias unrelated to pregnancy were seen. Majority of cases were seen due to β-thalassemia trait in 15 (37.5%) cases followed by antiphospholipid syndrome in 13 (32.5%) cases. 3 (7.5%) cases each were due to immune thrombocytopenic purpura and hypersplenism while 2 (5%) cases due to sickle cell trait were seen. 1 (2.5%) case each due to sickle-β thalassemia, sickle-HbD disease, systemic lupus erythematosus and aplastic anemia were seen.

DISCUSSION

We included a total of 110 patients who attended the outpatient department of Hematology and General Medicine. This study was conducted at Nizam's Institute of Medical Sciences, a tertiary care hospital in Telangana.

Out if 110 subjects in this study, 59 (53.63%) subjects had thrombocytopenia and 40 (36.36%) subjects having anemia. 7 (6.36%) subjects had anemia + thrombocytopenia and only 4 (3.63%) subjects had pancytopenia.

The age distribution ranged from 19-38 years. Patients <20 years of age constitute 3.63%(n=4) of cases, 20-30 years was 80.9%(n=89) and >30 years was 15.4%(n=17).

The mean age in our study was 25.3 ± 4.11 years. The mean age reported was 22.4 years in a study by Ravishankar Suryanarayana et al(113), 29.42 ± 4.87 years in a study by Huifengshi et al(114).

In our study group, 70 (63.6%) subjects were referred in third trimester followed by 30 (27.2%) subjects

who were referred during second trimester. Only 10 (9.09%) subjects were referred in first trimester.

Out of 110 subjects, 76(69.09%) subjects belonged to primigravida followed by 20(18.18%) subjects who belonged to second gravida. 9 (8.18%) subjects belonged to third gravida and 5 (4.5%) subjects belonged to fourth gravida.

Easy fatigability was the most common symptom of presentation. A total of 19 (17.27%) subjects had easy fatigability, 18 (16%) subjects had generalised weakness and 3 (2.72%) subjects had purpuric rash. Only 2 (1.81%) subjects had mucosal bleed and 1 (0.9%) subject had jaundice. Majority of the study population, 88 (80%) subjects, were asymptomatic at the time of referral.

Out of 110 subjects in this study, 47 (42.7%) subjects were referred in view of anemia and 66 (60%) subjects were referred in view of thrombocytopenia. Only 4 (3.63%) subjects were referred in view of pancytopenia. No referrals were done for leukopenia.

In this study population, 99 (90%) subjects did not have any history of cytopenias. Only 6 (5.45%) subjects had prior history of anemia and 5 (4.54%) subjects had history of thrombocytopenia. Only 6(5.45%) subjects had history of PRBC transfusion and only 1(0.9%) subject had prior RDP transfusion. 103 (93.63%) never had any history of any blood products transfusion.

On physical examination, pallor was the most common finding present in 51 (46.36%) subjects. A study by Bably sabina et al,[14] pallor was seen in 27.6% of subjects. Of the 110 subjects, 6 (5.45%) subjects had peripheral edema and 4 (3.63%) subjects had icterus.

Another 4 (3.63%) subjects had splenomegaly, 2 (1.18%) subjects had mucosal bleed and 1(0.9%) subject had purpura on examination.

Anemia

Out of 110 subjects, 51 subjects had anemia out of which 43 subjects (83.31%) had microcytic anemia. Only 3 (5.88%) subjects had normocytic anemia and 5 (9.8%) subjects had macrocytic anemia. When isolated cytopenias were assessed, 40 (36.36%) subjects had anemia and 59 (53.63%) subjects had thrombocytopenia.

The prevalence of anemia in our study was 46.36%. In study conducted by Yuting Quio et al,[15] the prevalence of anemia was 43.59% while 44.4% was seen in study by Ramla Hussein et al.[16] In a study done by Gretchen et al,[17] the prevalence of anemia was 38% which was lower than our study while it was 62.3%. In a study done by Periyasamy Kuppusamy et al,[18] which are higher than our study. The prevalence of anemia in pregnancy according to WHO(120) was 36.5%.

Iron deficiency was the most common cause of isolated anemias, accounting for 18 (45%) cases. 15 (37.5%) cases were due to β- thalassemia trait and 2 (5%) cases each were due to vitamin B12 deficiency and sickle cell trait. 1 (2.5%) case each were due to combined Vitamin B12 and folate deficiency, sickle-β thalassemia and Sickle-HbD disease were seen.

Our study showed that the prevalence of anemia was highest in third trimester while compared to second and first trimester. These findings agree with that of study by Bably sabina et al.[14] The anemia risk increases with the age of a pregnancy (trimester), as iron demand reaches 6.6 mg/day in the third trimester.[21]

In our study, 26 (50.98%) subjects had moderate severity of anemia followed by 13 (25.49%) subjects who had mild anemia and 12 (23.52%) subjects had severe anemia. In the study done by Huifeng Shi et al(114), the prevalence of mild, moderate and severe anemia are 22.7%, 27.5% and 47.05% respectively.

Majority of mild anemia cases were because of β-thalassemia trait and majority of moderate and severe anemia cases due to iron deficiency were seen in this study.

A total of 51 cases of anemia were seen in this study, out of which 35 (68.62%) cases were seen in primigravida subjects followed by 10 (19.6%) cases in second gravida subjects. Only 3 (5.8%) cases each were seen in third and fourth gravida subjects.

In our study, 26 (50.98%) cases anemia presented in third trimester followed by 16 (31.37%) cases in second trimester. Only 9 (17.64%) cases of anemia were presented in first trimester. Similar proportions with majority being in third trimester were seen in studies done by Bably sabina et al.[14]

In this study, a total of 25 cases of iron deficiency cases were seen out of which 16 (64%) cases are seen in primigravida subjects followed by 6 (24%) cases in second gravida subjects. Only 2 (8%) cases are seen in third gravida and 1 (4%) case was belonged to fourth gravida subject. Similarly, 14 (56%) cases of iron deficiency anemia were seen in third trimester and 7 (28%) cases were seen in first trimester. Only 4 (16%) cases were seen in second trimester.

Thrombocytopenia

The prevalence of isolated thrombocytopenia in our study was 53.63% while the combined prevalence of isolated thrombocytopenia along with thrombocytopenia in cases of bicytopenia and pancytopenia was 63.63%. In a study by Jigyasa singh et al,[22] the prevalence of thrombocytopenia was 34%. The prevalence was much lower in studies conducted by Sumathy et al,[23] which showed 7.7% while a study by Sangeetha et al,[24] reported 3%. In a study by Nisha singh et al,[25] reported the prevalenceof 8.8%. The higher prevalence seen in our study when compared to other mentioned studies is because of inclusion of subjects with already diagnosed cytopenias while other studies calculated prevalence in general pregnant population.

Gestational thrombocytopenia was the most common cause of isolated thrombocytopenia which accounted for 37 (62.71%) cases followed by antiphospholipid syndrome in 13 (22.03%) cases. 6 (10.16%) cases of thrombocytopenia due to vitamin B12 deficiency were seen and 1 (1.69%) case each of combined vitamin B12 and folate deficiency, immune thrombocytopenic purpura and noncirrhotic portal fibrosis were seen.

Gestational thrombocytopenia was seen in 37 cases, out of which, majority of cases are seen in third trimester which constituted 33 (89.18%) cases followed by 3 (8.1%) cases in second trimester. Only 1 (2.7%) case was seen in first trimester. Maximum number of gestational thrombocytopenia cases were seen in primigravida subjects which constituted 27 (72.97%) cases followed by 6 (16.21%) cases in second gravida subjects. Only 4 (10.81%) cases were seen in third gravida and no cases in fourth gravida subjects.

The prevalence of immune thrombocytopenia in our study was 2.8%. Sumathy et al,[23] reported the prevalence of 1.6% while Anitha et al(128) reported 5.26%. Sangeetha et al(24) reported 8% of cases, Sainio et al,[26] reported 3% and Jigyasa singh et al(22) reported 11.1% of cases. Nisha singh et al,[25] reported 5.26%. In this study, a total of 13 cases of antiphospholipid syndrome were seen out of which, 9 (69.23%) cases were seen in second trimester and 4 (30.76%) cases were seen in third trimester. No cases were recorded in first trimester. Gravida wise, 7 (53.84%) cases were seen in primigravida subjects and 2 (15.38%) cases each are seen in second, third and fourth gravida subjects.

When severity of thrombocytopenia was assessed, moderate thrombocytopenia accounted for 39 (55.71%) of cases which is a majority. Mild thrombocytopenia was seen in 21 (30%) cases and severe thrombocytopenia was seen in 10 (14.28%) cases.

The prevalence of antiphospholipid syndrome was 22.03% in our study while no other studies reported the cases of thrombocytopenia in pregnancy secondary to antiphospholipid syndrome.

While other studies reported cases of thrombocytopenia due to hypertensive disorders of pregnancy (preeclampsia, eclampsia, HELLP syndrome) and due to infections, none of such cases were seen in our study.

Bicytopenia

In our study, only 7 cases of bicytopenia were seen and all cases were in anemia and thrombocytopenia combination. 2 (28.57%) cases were because of combined immune thrombocytopenia with iron deficiency. 1 (14.28%) case each of combined iron with vitamin B12 and folate deficiency, combined iron with vitamin B12 deficiency, combined iron and folate deficiency, combined iron deficiency with gestational thrombocytopenia and isolatedfolate deficiencies were seen. To our knowledge, there were no studies performed to evaluate bicytopenia in pregnancy.

Pancytopenia

A total of 4 cases of pancytopenia were seen in this study. 2 (50%) cases are due to hypersplenism out of which one case of hypersplenism secondary to noncirrhotic portal fibrosis was noted. 1(25%) case each of systemic lupus erythematosus and aplastic anemia were seen as the cause of pancytopenia.

In a study conducted by Sridevi et al,[27] and Sangamesh Mahapati et al,[28] showed prevalence of 3%. The prevalence of aplastic anemia in our study was 25%. A study conducted by Shobana singh et al,[29] reported the prevalence of 29.05% cases of aplastic anemia.

No cases of pancytopenia secondary to vitamin B12 and folate deficiency were reported in our study while 100% of cases of pancytopenia were due to Vitamin B12 and folate deficiency in studies done by Sridevi et al,[27] and Sangamesh Mahapati et al,[28] while 23.64% was seen in study by Shobana et al.[29]

In our study, 100% of pancytopenia cases were seen in age group of 20-30 years. Sangamesh Mahapati et al(134) reported 94.8% of cases in age group of 20-30 years and 5.3% cases in<20 years age group. In our study, 75% of cases were seen in primigravida subjects and 25% cases in multigravida while Sangamesh Mahapati et al,[28] reported 31.6% of cases in primigravida and 68.4% cases in multigravida.

In 76 primigravida cases seen in this study, majority of cases had thrombocytopenia which constituted 41 (53.94%) cases followed by anemia in 30 (39.47%) cases. A total of 3 (3.94%) cases were due to pancytopenia and 2 (2.63%) cases were due to bicytopenia.

In this study, 20 second gravida cases were seen out of which, majority of cases were due to thrombocytopenia which constitute 10 (50%) cases. Anemia was seen in 5 (25%) cases, bicytopenia was seen in 4 (20%) cases and pancytopenia was seen in 1 (5%) case.

A total of 9 third gravida subjects were referred and majority of cases were due to thrombocytopenia which is seen in 6 (66.66%) cases. Anemia was seen in 2 (22.22%) cases and bicytopenia was seen in 1 (11.11%) case. No pancytopenia cases were seen in third gravida patients.

There were 5 fourth gravida cases seen in this study out of which 3 (60%) cases were due to anemia and 2 cases were due to thrombocytopenia. No bicytopenia or pancytopenia cases were seen in fourth gravid subjects.

Out of 110 cases, 76 subjects belonged to primigravida and 34 subjects are multigravida. Out of 34 multigravida patients, 22 subjects have pregnancy interval of <1 year and 5 cases of iron deficiency anemia were seen in those subjects. Among 12 multigravida subjects who had pregnancy interval >1 year, 4 cases of iron deficiency anemia were seen.

In this study of 110 subjects, a total of 70 cases of cytopenias were related to pregnancy. Majority of the cases were due to gestational thrombocytopenia which constituted 38 (54.28%) cases followed by iron deficiency anemia in 18 (25.71%) cases. 8 (11.42%) cases are due to vitamin B12 deficiency and 2 (2.85%) cases are due to combined vitamin B12 and folate deficiency. 1 (1.42%) case each of folate deficiency, combined iron with vitamin B12 and folate deficiency, combined iron with vitamin B12 deficiency and iron with folate deficiency were seen.

In this study of 110 subjects, a total of 40 cases of cytopenias unrelated to pregnancy were seen.

Majority of cases were seen due to β-thalassemia trait in 15 (37.5%) cases followed by antiphospholipid syndrome in 13 (32.5%) cases. 3 (7.5%) cases each were due to immune thrombocytopenic purpura and hypersplenism while 2 (5%) cases due to sickle cell trait were seen. 1 (2.5%) case each due to sickle-β thalassemia, sickle-HbD disease, systemic lupus erythematosus and aplastic anemia were seen.

Out of 110 subjects in this study, 24 (21.81%) subjects had leukocytosis and 7 (6.36%) had thrombocytosis. Out of seven thrombocytosis cases, six subjects had iron deficiency and one subject is a case of sickle cell anemia with normal iron profile with history of blood transfusions. None of the subjects showed erythrocytosis.

CONCLUSION

According to the WHO's criteria based on the prevalence for the severity of an anemia problem, an anemia prevalence of 5–19.9% is a mild public health problem, 20–39.9% is a moderate public health problem, and ≥40% is the standard of a severe public health problem. The prevalence of anemia in our study was 46.36%, which according to WHO is a severe public health problem. Anemia in pregnancy affects the maternal outcome as well as fetal outcome. Early diagnosis and treatment of preventable conditions is one of the better ways to reduce the health impacts on both the mother and the child. This study concludes that a complete hemogram should be made routine at first antenatal visit and if abnormal, a detailed evaluation of cytopenias that arise during pregnancy should be undertaken. This helps the clinician to initiate the appropriate treatment promptly that helps to avoid unwanted complications down the line. A multidisciplinary approach is necessary and a timely consultation with a Hematologist should be sought for further evaluation of resistant cytopenias for rare causes of cytopenias in pregnancy.

Limitations

- This was a prospective, single point contact, outpatient based study with limited number of patients.
- This study was done in a tertiary care hospital and so cannot be represented for general population as mostly rare and treatment resistant cases will be referred for evaluation.
- Since this study is not a follow-up study, definitive diagnosis of such conditions which require follow-up evaluation cannot be established.

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