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Frequency of Megaloblastic Anemia with Thrombocytopenia in Pregnant Patients at Tertiary Care Hospital Karachi

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ABSTRACT

Objective: To determine the frequency of megaloblastic anemia with thrombocytopenia in pregnant patients at Tertiary Care Hospital, Karachi. **Study Design and Setting:** This cross sectional study was conducted at the Department of Gynecology and Obstetrics, JPMC, Karachi from June 2024 to December 2024. **Methodology:** This cross-sectional study was conducted after approval of a synopsis from the Research Department of the College of Physicians and Surgeons Pakistan and the institutional ethical review committee. Eligible patients at the Department of Gynaecology and Obstetrics, JPMC, Karachi, who meet the inclusion and exclusion criteria were enrolled in the study. Study was completed from June 2024 to December 2024 .All the findings of variables such as age, occupational status, parity, gravida, gestational age, educational status, chicken and beef consumption, vegetable consumption, serum hemoglobin, serum folic acid, vitamin B12, platelets, and megaloblastic anemia were noted. **Results:** In this study, patients with megaloblastic anemia with thrombocytopenia had a mean age of 27.51±6.18, gestational age of 33.46 ± 4.41, 22% were primipara and 78% were multipara, vitamin B12 deficiency was found in 36.6%, 46.3% were primi-gravid, 53.7% were multi gravida, MCV was 94.58±4.79, serum Hb 12.39 ± 1.07, platelet 117.22 ± 8.55, folic acid deficiency was observed in 80%, occupationally 46.3% were employed and 53.7% unemployed, and 36.6% were illiterate. It's reassuring to note that the consumption of green leafy vegetables was equally distributed among patients with megaloblastic anemia and those without. **Conclusions:** This study reveals 18.5% of pregnant women had megaloblastic anemia with thrombocytopenia. This study illustrates that severe megaloblastic anemia and thrombocytopenia caused by dietary deficiencies, such as folic acid and vitamin B12, have a favorable prognosis when correctly diagnosed and treated.

INTRODUCTION

Pregnancy imposes a period of heightened nutritional demand for both the mother and the fetus. During this time, physiological changes occur in the hematologic system to meet the needs of the developing fetus and placenta[1]. One significant alteration is the increase in plasma volume by approximately 40 to 45%, mediated by the hormones progesterone and estrogen, which affect kidney function and result in fluid retention. This increase typically accelerates during the late second trimester[2-3].

Concurrently, red blood cell mass increases by l5-20%, driven by enhanced erythropoietin production. However, since the increase in red cell mass is relatively smaller than that of plasma volume, the net result is a decrease in hemoglobin concentration by 1-2, leading to what is termed the physiological anemia of pregnancy[4,5].

Deficiencies in key nutrients like folate or vitamin B12 during pregnancy can result in megaloblastic anemia, characterized by macrocytic changes in the bone marrow, leading to anemia, neutropenia, and thrombocytopenia[6,7]. The earliest hematological change is macrocytosis, followed by significant reductions in red cell count. Thrombocytopenia in pregnant women is particularly concerning due to its association with increased maternal and neonatal complications, including impaired fetal development and more significant risks during delivery[8,9].

Unfortunately, there is a significant lack of data regarding the prevalence and concurrent management of megaloblastic anemia with thrombocytopenia among pregnant women, which poses substantial challenges in clinical decision-making- This study aims to address this

gap by establishing the prevalence of these conditions at a Tertiary Care Hospital in Karachi. The data derived from this research will illustrate the issue's magnitude and aid in refining and improving the existing management strategies for these conditions during pregnancy. Additionally, a clearer understanding of the association between megaloblastic anemia and thrombocytopenia will be sought, which is expected to guide more effective treatment approaches and improve patient outcomes.

METHODOLOGY

This cross-sectional study was conducted after approval of a synopsis from the Research Department of the College of Physicians and Surgeons Pakistan and the institutional ethical review committee. Eligible patients at the Department of Gynaecology and Obstetrics, JPMC, Karachi, who meet the inclusion and exclusion criteria, were enrolled in the study. Study was completed from June 2024 to December 2024 .A brief demographic history was collected from each patient. Patients were labeled as having megaloblastic anemia based on the following criteria: hemoglobin levels less than 11 g/dL, mean corpuscular volume (MCV) greater than 100 fL, and a peripheral smear demonstrating a megaloblastic picture characterized by anisopoikilocytosis, macrocytosis, hypersegmented neutrophils, macrocytes, and the presence of nucleated red blood cells. Patients with vitamin B12 levels below 200 pg/mL or folic acid levels less than two ng/mL were included. Thrombocytopenia was defined as a platelet count of less than 150,000/mm^3.

The required sample size came out to be 222 patients. By taking the frequency of megaloblastic anemia with thrombocytopenia to be 70.5%[10], the margin of error=67o and confidence level 'C.I':95%. This sample size was calculated using the WHO software. Women aged 20 to 45 years were included. Pregnant women with a gestational age of more than 6 weeks, as assessed by their last menstrual period (LMP) and dating scan, who were diagnosed with megaloblastic anemia, were eligible for the study.

Individuals who did not consent to participate were excluded. Patients with known chronic medical conditions such as diabetes mellitus, hypertension, cardiac diseases, chronic obstructive pulmonary disease (COPD), asthma, renal diseases, or thyroid dysfunctions (both hypothyroidism and hyperthyroidism) were excluded.

Patients with a history of epilepsy who were actively taking anti-epileptic medications were omitted. Those with hematological disorders were also excluded, including thalassemia, acute leukemia, hemoglobinopathies, or other clotting disorders. Participants with systemic lupus erythematosus (SLE), complicated pregnancies such as preeclampsia and eclampsia, or other conditions that could compromise the study results were excluded. Additionally, patients with infectious diseases affecting hematologic status, such as HIV, tuberculosis (TB), Epstein-Barr virus (EBV), or conditions leading to hypersplenism, were omitted. Those with chronic aplastic anemia were also excluded.

Blood samples were drawn using a 5cc disposable syringe; approximately 5 ml of blood was collected from a peripheral vein and placed into a specific tube to analyze CBC, serum vitamin B12, and folic acid levels. Based on the Laboratory reports, patients were categorized as having megaloblastic anemia with thrombocytopenia according to the operational definitions used in this study. All the findings of variables such as age, occupational status, parity, gravida, gestational age, educational status, chicken and beef consumption, vegetable consumption, serum hemoglobin, serum folic acid, vitamin B12, platelets, and megaloblastic anemia were noted.

Data was analyzed using SPSS version 26.0. The mean + SD (standard deviation) was reported for normally distributed quantitative variables. In contrast, numerically distributed variables, such as gestational age, serum vitamin Bl2, folic acid, and gestational age, as well as the median and interquartile range (IQR), were presented. The Shapiro-Wilk test was applied to assess the normality of the data. Frequencies and percentages were calculated for categorical variables, including parity, gravida, educational status, occupational status, frequency of chicken/beef consumption per week, frequency of green leafy vegetable consumption per week, and presence of megaloblastic anemia with thrombocytopenia (yes/no).

RESULTS

In this comprehensive study, we included 222 patients. In this study, patients with megaloblastic anemia with thrombocytopenia had to have mean age of 27.51±6.18, gestational age of 33.46±4.41, 22% were primipara and 78% were multipara, vitamin B12 deficiency was found in 36.6%, 46.3% were primi gravid, 53.7% were multi gravida, MCV was 94.58±4.79, serum Hb 12.39±1.07, platelet 117.22±8.55, folic acid deficiency was observed in 80%, occupational ly 46.3% were employed and 53.7% unemployed, and 36.6% were illiterate. They were equally distributed among patients with megaloblastic anemia and those without. This comprehensive analysis, with a p-value of less than 0.050, ensures that all aspects were considered (Table. 1).

It's reassuring to note that the consumption of green leafy vegetables was equally distributed among patients with megaloblastic anemia and those without. This finding, with a p-value of 0.828, provides a sense of

balance and normalcy in the dietary habits of the two groups (Table. No. 2).

Figure 1

Presence of thrombocytopenia among the study patients

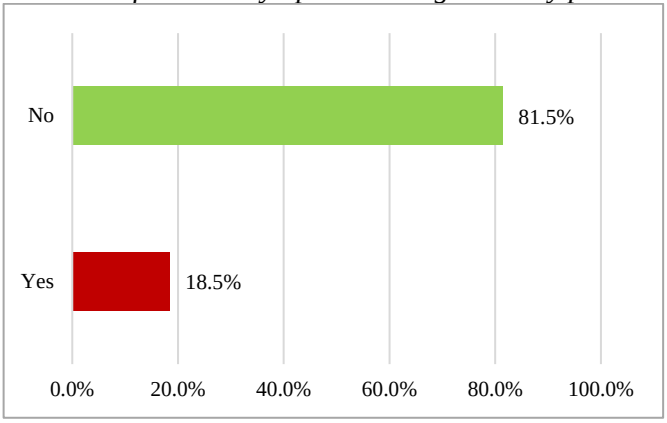

Table 1

Demographic profile according to thrombocytopenia

Variable	Megaloblastic anemia with thrombocytopenia		p-value
	Yes	No	
Age (years)	27.51±6.18	26.78±5.39	0.446
Gestational age (weeks)	33.46±4.41	33.10±4.16	0.623
Parity distribution			
Primipara	9 (22.0%)	33 (18.2%)	0.583
Multipara	32 (78.0%)	148 (81.8%)	
Vitamin B12 deficit	15 (36.6%)	64 (35.4%)	0.882
Gravida			
Primi gravid	19 (46.3)	103 (56.9)	0.220
Multigravida	22 (53.7)	78 (43.1)	
MCV	94.58±4.79	94.40±4.55	0.821
Serum Hb	12.39±1.07	12.58±1.21	0.378
Platelet	117.22±8.55	119.19±9.08	0.987
Folic acid deficit	33 (80.5)	120 (66.3)	0.076
Occupational status			
Employed	19 (46.3)	65 (35.9)	0.214
Unemployed	22 (53.7)	116 (64.1)	
Educational status			
Illiterate	15 (36.6)	53 (29.3)	0.414
Primary	21 (51.2)	92 (50.8)	
Secondary	3 (7.3)	11 (6.1)	
Higher	2 (4.9)	25 (13.8)	

Table 2

Meat and vegetables consumption of the study patients

Variable	Megaloblastic anemia with thrombocytopenia		p-value
	Yes	No	
Chicken and beef consumption			
<l day/week	9 (22.0)	45 (24.9)	0.030
2-3 day/week	19 (46.3)	110 (60.8)	
>4 day/weeks	13 (31.7)	26 (14.4)	
Green leafy vegetables consumption			
<l day/week	14 (34.1)	64 (35.4)	0.828
2-3 day/week	14 (34.1)	68 (37.6)	
>4 day/weeks	13 (31.7)	49 (27.1)	

DISCUSSION

Megaloblastic anemia results from the inhibition of DNA synthesis during erythropoiesis, preventing cells from progressing into the cell cycle's mitotic (M) phase. As a result, the cells grow without dividing, leading to a clinical manifestation known as macrocytosis[11]. Megaloblastosis is frequently associated with increased polymorphonuclear leukocytes (PMNs) exhibiting a high degree of nuclear segmentation, a condition known as hypersegmentation. Additionally, patients with megaloblastosis may develop neutropenia, with neutrophil counts occasionally dropping as low as 1,000 cells per cubic millimeter. Thrombocytopenia can also occur in rare cases, with platelet counts falling to critically low levels, sometimes as low as 50,000 platelets per cubic millimeter[12].

Tran et al.[13] highlighted that megaloblastic anemia is predominantly caused by vitamin deficiencies, particularly folic acid and vitamin B12, resulting from inadequate dietary intake, impaired gastrointestinal absorption, or abnormalities in metabolic processes. Our study observed that 36.6% of female participants were affected by this condition, underscoring the significant prevalence of vitamin-related deficiencies as a contributing factor to megaloblastic anemia in this demographic.

Megaloblastic anemia with thrombocytopenia was found to have developed in 18.5% of the cases, highlighting a complex condition that requires further investigation, as it is strongly influenced by factors such as educational status and unemployment. Studies such as those by Vyas et al.[14] and Elgari et al.[15], who evaluated hematological parameters of Sudanese pregnant women at Omdurman Al Saudi Maternity Hospital, demonstrate significant regional variations in hematological health. This study found notable differences in maternal Hemoglobin levels influenced by dietary and socio-economic factors, providing valuable insights into hematological health disparities. Similarly, Townsley et al.[16] discuss the hematologic complications of pregnancy, focusing specifically on the impact of gestational changes on blood volume and composition, which is critical for understanding conditions like megaloblastic anemia at the Tertiary Care Hospital in Karachi. These variations underscore the need for region-specific data to manage pregnancy-related hematological disorders better.

Meanwhile, Ijaz et al.[10] reported a prevalence rate of 70.5% for anemia and thrombocytopenia in pregnant females in Lahore, highlighting the severity of these conditions in local populations. Another regional study by Ujjan et al.[17] reported a frequency of 26.660% for megaloblastic anemia among patients with pancytopenia admitted at Isra University Hospital in Hyderabad, further emphasizing the regional variability and the critical nature of these hematological challenges.

Boehlen et al.[18] reported that the prevalence of maternal thrombocytopenia, defined as a platelet count of less than 150 × 10^9/L, was observed to be 11.6%. Additionally, they found that the mean platelet count in

healthy nonpregnant women was significantly higher at 248 × 10⁹/L compared to 213 × 10⁹/L in pregnant women. Similarly, the 2.5th percentile of platelet counts was notably greater in nonpregnant women, measuring 164 × 10⁹/L, as opposed to 116 × 10⁹/L in pregnant women. These findings highlight the physiological differences in platelet levels between pregnant and nonpregnant women.

Khan et al.[19] and Sally et al.[20] reported that women in developing countries will likely experience Vitamin B12 and folic acid deficiencies, making them more susceptible to developing megaloblastic anemia. This disorder is particularly prevalent in these regions, especially among children. Additionally, the older population in developing countries is often economically disadvantaged, with limited income, which increases their likelihood of Vitamin B12 and folic acid deficiencies and, consequently, their risk of developing megaloblastic anemia. In our study, meat and green leafy vegetable consumption was notably low.

CONCLUSIONS

This study reveals 18.5% of pregnant women had megaloblastic anemia with thrombocytopenia. This study illustrates that severe megaloblastic anemia and thrombocytopenia caused by dietary deficiencies, such as folic acid and vitamin B12, have a favorable prognosis when correctly diagnosed and treated.

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