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A CASE SERIES

PANCYTOPENIA IN PREGNANT MOTHERS FROM EASTERN SHOA ZONE OF ETHIOPIA: A CASE SERIES

Sisay Teklu, MD,[1*] Amaha Gebremedhin, MD,[2] Alula Meressa, MD,[3] Buruhan Feki, MD[1]

ABSTRACT

Pregnancy is a state of high metabolic demand. Anemia and thrombocytopenia, commonly as a result of the normal dilutional effect of increased plasma volume during pregnancy, are frequently seen in pregnant women but are not severe enough to require intervention unless aggravated by deficiency of micronutrients. Nutritional deficiency related anemia is often seen in developing countries. In this study, we describe seven cases of severe thrombocytopenia, anemia and leukopenia (pancytopenia) from the same geographic locality and similar clinical presentation. The cases were referred to the Tikur Anbessa Specialized Hospital (TASH) for investigation and treatment. Potential causes, methods of prevention and treatment options are discussed along with relevant clinical and laboratory findings of the cases.

Key words: *Pancytopenia, Pregnant mothers, East Shoa Zone*

INTRODUCTION

The physiological change of pregnancy results in a disproportionate increase in plasma volume(40-50%) compared with cell mass (20-30%), leading to a drop in hematocrit. Values up to 10gm/dl are tolerable and do not lead to clinical anemia; however, if hemoglobine drops below this level, an evaluation for iron deficiency anemia should be initiated as this is the commonest cause of anemia diagnosed during pregnancy (1). An increased hematopoietic demand during pregnancy leads to an increased daily iron requirement from 18mg/day to 27mg/day (2).

Nutritionally related iron deficiency is the main cause of anemia worldwide. It is especially common in women of reproductive age and particularly during pregnancy. The demand for iron increases about six to seven times from early to late pregnancy (3). Folate deficiency was known since the 1960s and B12 vitamin deficiency since the 1990s to contribute to nutritional anemia and these deficiency states may also impact anemia during pregnancy(4). Folate deficiency is the most common and carries a more negative prognosis for both mother and the fetus than iron deficiency(5).

Megaloblastic anemia during pregnancy begins most often in either the third trimester or shortly after delivery (6). Folate requirements increase during pregnancy and the diets of many pregnant mothers are insufficient to meet the increased need (7,8).

Similarly, thrombocytopenia is also common during pregnancy, occurring in approximately 8–10% of pregnancies. It is usually secondary to physiologic changes during gestation, namely the aforementioned increase in blood plasma volume, platelet activation, and increased platelet clearance(9). Gestational thrombocytopenia accounts for the majority of thrombocytopenia during pregnancy and most cases are mild, with platelet count of100,000–150,000/µL and often not associated with any adverse events for either the mother or the baby. Although thrombocytopenia may worsen as the pregnancy progresses, the platelet count rarely drops below 70,000–80,000/µL and typically resolves within days to weeks postpartum(10).

In addition to the nutritional deficiencies, the presence of widespread infectious diseases like malaria, hook worm infestation and other water-born diseases contribute to the very high prevalence of anemia in Ethiopia compared to other developing countries (11). Over the past year, many pregnant mothers were referred to Tikur Anbessa Specialized Hospital (TASH) from around the rift valley area of Eastern Shoa Zone of the

[1] Department of Obstetrics and Gynecology, Addis Ababa University, School of Medicine
[2] Department of Internal Medicine, Addis Ababa University, School of Medicine
[3] Center for International Reproductive Health Training-Ethiopia
* Corresponding author: siteet@yahoo.com, sisay.teklu1@aau.edu.et

Oromia region with diagnoses of severe anemia, low platelet and low white cell counts. The consecutive cases reported here came from the same geographic location; they had similar clinical presentation and laboratory findings. This raised questions as to whether the cases were coming from the same locality, had the same underlying cause, exposure risk or any recent lifestyle change. The objective of this case series study is to bring this phenomenon to the attention of the medical community and policy makers, and recommend follow-up measures to be taken.

MATERIALS AND METHODS

Cases of severe anemia and thrombocytopenia referred to TASH from Eastern Shoa Zone during the month of May and June of 2015 were reviewed. Those cases whose charts were complete were identified and information was abstracted from the charts. Important and relevant findings are summarized in the table. Investigations such as serum folate and vitamin B12 were not available and were not determined in this series.

RESULT

A total of seven mothers were included in the case series study. Their demographic features and clinical profile are summarized in Table 1. All the mothers were either pregnant or immediately postpartum. The gravidity range was from 1 to 9, and three of the seven were pregnant for the fifth time. The average age of cases was 26.5 years while the range was between 17 to 38 years. Regarding their geographic location, all were residing within a 100 kilometer radius of Adama town in East Shoa Zone.

Table 1: Summary of demographic and clinical profile of the seven cases

	Age	Gravidity	Parity	Gestation (Weeks)	Complaints at Presentation	Hemoglobin (gm/dl)	Platelet Count*	White Blood Cell Count *
1	25	9	5	38	Epistaxis Headache	5.5	43	17
2	17	1	0	36	Fatigue, palpitation, dizziness	6.2	6	1.5
3	28	Postpartum	4	Postpartum	Epistaxis	2.7	33	4.6
4	38	5	4	Term	Shortness of breath and easy fatigability	2.9	6	7.5
5	25	Postpartum	4	Postpartum	Epistaxis	4.2	6	1.6
6	28	4	3	36	Body swelling	3.6	5	1.48
7	25	2	0	34	Epistaxis, fatigue	6.5	15	2.7

($\times 1000/mm^3$)**;** lowest value recorded

All seven cases were married and their means of living was farming. All had a similar staple diet comprised of corn and wheat, two to three meals per day, including occasional animal products such as meat and milk. None of the women had a similar illness in the past. Five of the seven cases had past history of malaria, one of them had recent treatment for malaria although blood films were negative for parasites. All had an acute onset disease developing in less than two weeks. Four of the seven cases' initial presentation was nasal bleeding, while three presented with generalized body weakness and one with body swelling. There were no reports of chronic diarrhea or vomiting. All had tachycardia, pale conjunctiva and non-icteric sclera. Four cases had evidence of epistaxis in one of the nostrils and areas of echymosis present on the up-

per extremities. None of the seven cases exhibited hepatosplenomegaly.

The mean hemoglobin (Hgb) level recorded in the series was 4.5gm/dl (range 2.7-6.5gm/dl), with five having Hgb levels less than 6gm/dl. The lowest platelet recorded was 5,000/mm^3 while the average was 16,200/mm^3(range 5,000-43,000/mm^3). White cell count ranged from 1,500-17,000/mm^3. All cases received blood transfusion therapy while six of them received additional platelet and fresh frozen plasma transfusions. There was no significant post-partum hemorrhage PPH) recorded. All except one had bone marrow examinations performed before or after delivery and all examinations revealed megaloblastic marrow changes, hence all cases were treated with folic acid and vitamin B12. All cases showed clinical improvement upon discharge.

DISCUSSION

The present case series described pregnant mothers with pancytopenia among a number of patients referred to TASH for better care. The cases in this case series appear to be unusual in that all patients resided within a 100 km radius of Adama. All had apparent acute onset of disease manifestations which primarily consisted of fatigue and epistaxis, all were otherwise stable pregnant mothers who did not report any chronic illness, impaired appetite or gastrointestinal losses from diarrhea or vomiting. Although the areas of residence were malaria endemic, there was no recent history of proven malaria attacks. Although there were differences in the levels of the three blood lineages, all patients exhibited anemia and thrombocytopenia well beyond physiological changes expected due to pregnancy alone. These concerns prompted a bone marrow evaluation.

All cases revealed megaloblastic bone marrow changes upon bone marrow examination. Although megaloblastic bone marrow morphology is most commonly associated with anemia due to folate and vitamin B12 deficiency, it is also known that these deficiency, in severe cases, may lead to thrombocytopenia as well as leukepenia. Although we did not directly measure folate and B12 levels in our patients, the pancytopenia observed in our small case series are consistent with these earlier findings of pancytopenia among patients with megaloblastic anemia (13). The commonest cause of anemia in developing countries is nutritional, iron and folate deficiencies contributing the major share. Megaloblastic anemia during pregnancy begins most often in either the third trimester or shortly after delivery, consistent with our cases(6).Our patients all showed clinical improvement with RBC, plasma and platelet transfusions, folate and B12 treatment.

None of our cases in this case series are different from the majority of Ethiopian rural dwellers in terms of their income, nutritional history and medical history. This demands a very reasonable hypothesis for the potential cause of this unique clinical scenario in one geographic locality of the country. Although our results are most consistent with folate and/or B12 deficiency, it is important to realize that derangement in the metabolism of these nutrients can have similar clinical presentation as deficiency state. As reported in the literatures, environmental factors related to air, water, food or toxins could have contributed to derangement in metabolism and manifestation of the disease in our cases(2). Regardless, it is important to determine whether this cluster of cases are isolated, exceptional cases within this geographic region, or rather the tip of the iceberg representing a much larger problem. We thus suggest a need for more well designed epidemiological studies to determine the scope of this problem. This in turn can lead to appropriate public health interventions.

Conclusion and recommendation: Many pregnant mothers with clinical and laboratory evidence of pancytopenia and megaloblastic bone marrow changes have been referred from health facilities in the East Shoa Zone of Oromia region to TASH for better care. Based on the demographic and clinical findings in this case series, we recommend a well-designed epidemiological study in the East Shoa Zone and the neighboring vicinity to determine the magnitude of the problem, identify potential cause (s) and to recommend appropriate interventions.

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