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CASE SERIES

Pancytopenia in pregnancy: a case series

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ABSTRACT

Pregnancy is a state of high metabolic demand. Anaemia and thrombocytopenia are common during pregnancy, which is the result of normal dilutional effect of increased plasma volume seen during pregnancy. These are frequently seen in pregnant women but are not severe enough to require interventions unless aggravated by deficiency of micronutrients. Anaemia due to nutritional deficiency is common in developing countries.

Keywords: Pancytopenia, vitamin B12, folate.

Pancytopenia is the reduction in all three major cellular elements of blood, hence it is the simultaneous presence of anaemia, leukopenia and thrombocytopenia[1]. It is a traid which involves bone marrow primarily or secondarily depending on the various pathogenesis. The various etiology of pancytopenia includes aplastic anaemia, megaloblastic anaemia, infections, nutritional deficiencies and malignancies [2]. Vegetarians are at serious risk of Vitamin B 12 deficiency an essential micronutrient that plays a specific role in DNA synthesis and in one carbon metabolism.

Vitamin B 12 deficiency is common in pregnancy due to increased foetal demand over gestation, an essential micronutrient that plays an important role in nucleic acid synthesis. Deficiency of which leads defective erythropoiesis and neuronal myelinisation. 38 % of women have low B12 levels at the time of delivery[3]. Pancytopenia is associated with many maternal and foetal complications during pregnancy like maternal sepsis, postpartum haemorrhage, pre eclampsia and preterm labour , IUGR and intrauterine foetal demise.

Materials and methods

The study will be conducted at BLDE (Deemed to be) University, Shri.B.M.Patil Medical College from November 2019 to April 2020. All pregnant women with pancytopenia at admission will be enrolled in the study. The participants will be subjected for further clinical and laboratory evaluation and followed for fetomaternal outcome.

Cases

Case A: A 25 year old primigravida with 35 weeks of gestation complaining of leaking per vaginum (PV) was referred in view of anaemia. On obstetrical examination, patient was in active stage of labour. Complete haemogram on admission was done, haemoglobin: 7.1gm/dl; platelet: 60,000/cumm; total leucocytic count (TLC): 4610/cumm; peripheral blood smear (PBS) showed pancytopenia. On dietary history patient was vegetarian and had protein calorie deficiency. Renal and liver function tests were in normal limits. Further she was evaluated for Vitamin B12 level which was 136pg/ml (Normal 200-900pg/ml) and folic acid level was 2.13 ng/ml which too was decreased. After evaluation she was advised blood transfusion. Prophylactic antibiotics and steroids were given. Patient delivered a male

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baby weighing 2.2 kg with no intrapartum and postpartum complications. Baby was in neonatal intensive care unit (NICU) in view of early onset sepsis. Patient received parentral iron and multivitamin supplementations. No blood transfusion was done. Patient was discharged on 8th postnatal day. Patient was advised weekly follow up in out patient department (OPD).

Case B: A 22 year old, G2P1L1 with previous lower segment caesarean section (LSCS) with 39 weeks of gestation, referred from Government hospital in view of severe anaemia and was in labour. On routine obstetrical examination, patient was in labour with features of impending uterine scar rupture and was taken up for emergency LSCS in view of threatened scar rupture with laboratory values of Hb: 6.1 g/dl, platelet : 41000/ cumm, total leucocyte count (TLC): 2920. Renal and liver profile normal and peripheral blood smear (PBS) showed pancytopenia. On detailed history patient was vegetarian in diet and had protein calorie deficiency. Patient delivered a female baby with birth weight: 2.6 kg , baby was shifted to NICU in view of foetal distress. Patient received 1 unit of whole blood transfusion. Patient developed fever with chills on postoperative day 4 for which complete haemogram and fever profile was done , Hb: 7.7 g/dl , TC: 2460/cumm; platelet: 31000/cumm, dengue: negative , Weilfelix test : negative, ESR: 58 mm1st hour. Patient was evaluated for vitamin B12 level which was 140 pg/ml and folate level was 2.13ng/ml which was decreased. Baby developed neonatal sepsis and was treated with vancomycin intravenously for 10 days. Patient received iron sucrose, and parenteral vitamin B 12 supplementations and oral multivitamin supplementations. Patient was discharged on postoperative day 15 with discharge Hb:8.2gm/dl, platelet count: 45000/cumm and TLC: 1790. Patient was advised for follow up weekly in OPD.

Case C: A 24 year old primigravida with 38 weeks period of gestation, was refereed to our hospital in view of pregnancy induced hypertension and history of generalized weakness since 1 week prior. Patient blood pressure on admission was 160/110 mmhg with urine albumin of 4+ with no imminent signs. Her complete haemogram revealed Hb: 7.1 gm/dl , platelet count : 20000 /cumm :TLC: 4170; renal profile within normal limits and deranged liver function test with LDH: 5650, PBS showing pancytopenia. On detailed history patient was vegetarian in diet and had protein calorie deficiency. Patient received whole blood and random donor platelet (RDP) transfusion. Patient went in to spontaneous labour and delivered vaginally a female baby of birth weight 2kg. Patient had postpartum haemorrhage which was managed medically. Postnatally patient was transfused with 2 pint fresh whole blood and 4 pint platelet. Repeat complete blood count (CBC) was done on alternate days. Patient was managed initially as HELLP syndrome. Later patient was evaluated for vitamin B 12 and folate levels which was 146pg/ml and 2.13ng/ml. Patient was given 3 doses of iron sucrose and multivitamin supplementations and was discharged on postnatal day 6 with Hb: 8.3 gm/dl, platelet count: 41000/cumm : TLC: 3250 and follow up in opd every week.

Case D: A 24 year old primigravida with 36 weeks period of gestation in active labour referred to our hospital in view of pregnancy induced hypertension (PIH) and thrombocytopenia. On admission patient laboratory values are as follows: Hb: 5.2 gm/dl; platelet: 48000/cumm , TLC:2020 / cumm ; PBS : normocytic normochromic blood picture with pancytopenia. On detailed history patient was vegetarian in diet and had protein calorie deficiency. Renal and liver profile in normal limits and lactate dehydrogenase (LDH): 1125IU/I. Patient was transfused with one pint whole fresh blood intrapartum. Patient delivered vaginally a live male baby of birth weight 1.5kg. Baby was shifted to NICU in view of low birth weight. Patient had postpartum haemorrhage (PPH) which was managed medically. On detailed history patient was vegetarian by diet with no history any drug intake. Patient vitamin B12 level 159 pg/ml; folic acid level 2.13 ng/ml. Patient received multivitamin supplementation and parenteral iron. Patient was discharged on postnatal day 10 with Hb: 8.1 gm/dl; platelet: 53000/cumm , TLC: 3450/cumm. Patient was advised for weekly follow up in OPD.

Case E: A 26 years old G2P1L1 with 27 weeks period of gestation, came with complain of giddiness and bilateral swelling of lower limbs since 4 days and sudden onset shortness of breath on the day of admission. On admission complete haemogram was done with Hb: 2.1 gm/dl; platelet count: 31000/cumm; TLC: 7000/cumm; LDH: 2487IU/L. PBS showed pancytopenia. On detailed history patient was vegetarian in diet and had protein calorie deficiency. Liver function test (LFT) was deranged and renal profile was normal. ECG and 2D –Echo was done and was normal. Further patient was evaluated for Vitamin B 12 and folate levels which were decreased i.e 163 pg/ml and 2.16 ng/ml. She transfused with 3 pint of whole blood and 2 pint of single donor platelet (SDP). Labour was induced in view of

intra uterine foetal demise of the baby. Labour was induced medically with vaginal misoprostol and delivered a intrauterine death (IUD) baby of weight 800gms. Patient had no intrapartum and postpartum complications. Her Hb: 8.1 gm/dl, platelet (PLT): 27000/cumm; TLC: 4190/cumm on day 4 postnatally. Patient was supplemented with parental iron and multivitamins and was discharged for follow up in OPD every week.

Case F: A 19 year old primigravida with 22 weeks period of gestation, referred in view of fever and generalised weakness. On admission complete haemogram Hb: 2.9gm/dl, PLT:29000/cumm, TLC: 3850/cumm, normal renal and liver profile with negative fever profile. PBS showed pancytopenia with Vitamin B 12 levels of 159pg/ml and folate levels of 2.13ng/dl. Patient was transfused with pack cell volume (PCV) 5 units and SDP. She was also supplemented with parenteral iron and multi vitamins. Patient had no obstetrical indication for termination of pregnancy. Patient was allowed to continue the pregnancy with fortnightly follow up in to the OPD.

Table 1: Summary of clinical profile of enrolled cases

Serial no.	Age in years	Gravidity	Gestation (weeks)	Complaints at presentation
1.	25	1	35	Leak per vaginum
2	22	2	39	Labour pain
3	24	1	38	High blood pressure
4	24	1	36	Labour pain
5	27	2	27	Giddiness
6	22	1	22	Fever

Table 2: Summary of laboratory profile of cases

Sl. no	Haemoglobin (gm/dl)	Platelet count	White blood cell count	Vitamin B 12 (pg/ml)	Folate (ng/ml)	Peripheral blood smear
1	7.1	60000	4160	136	2.20	Pancytopenia
2	7.7	31000	2460	140	3.50	Pancytopenia
3	7.1	20000	4170	146	2.50	Pancytopenia
4	5.2	48000	2020	159	2.04	Pancytopenia
5	2.1	31000	4000	163	4.01	Pancytopenia
6	2.9	29000	3850	159	2.10	Pancytopenia

Discussion

Anaemia during pregnancy is apublic health problem especially in developing countries and is associated with adverse pregnancy outcomes [4]. Globally 56% of pregnant women in low and middle income countries have anaemia. The prevalence of anaemia is highest among pregnant women in Sub – Saharan Africa (57%) followed by pregnant women in south east Asia (48%) [5]. The causes of anaemia are multifactorial in which micronutrient deficiencies like iron and vitamin B12 plays an important role. Anaemia during pregnancy vary due to geographical location, dietary practice and season. Pancytopenia is a clinical phenomenon characterized by the reduction in all three major elements of blood. Pancytopenia may go undetected initially due to mild impairment in the bone marrow and may become apparent only during times of stress or during increased demand, (eg pregnancy, bleeding, infection)[6]. Bone marrow failure syndromes and malignancies are important causes for pancytopenia and non-malignant conditions like infections (HIV, EBV, Tuberculosis) and nutritional anaemia (severe vitamin B12 and folate deficiency) are also the major causes [7].

Table 3: Summary of maternal and foetal complications

Sl no	Maternal complications	Neonatal complications
1	Nil	Early onset sepsis
2	Puerperal sepsis	Early onset sepsis
3	PIH, PPH	LBW
4	PPH	LBW
5	Nil	IUD
6	Pyrexia of unknown origin	**

PIH – Pregnancy induced hypertension, PPH – Postpartum haemorrhage, LBW – Low birth weight, IUD – Intrauterine death.
** Patient has not yet delivered

A systematic review and meta analysis of individual participant data in associations of maternal vitamin B 12 concentrations in pregnancy with the risks of preterm birth and low birth weight conducted by Tormad Rognen et al observed that vitamin B 12 deficiency in pregnancy was associated with higher risk of preterm birth. A study by Pawlak R et al, shows that there is a high prevalence of vitamin B 12 deficiency among pregnant vegetarians [8]. Low maternal serum concentration of vitamin B 12 during the first trimester is a risk factor for neural tube defect (NTD) and poor maternal outcomes such as preeclampsia and neurological impairment. Shravya Govindappagari et al, reported a case of severe vitamin B12 deficiency in pregnancy mimicking HELLP syndrome and emphasised the importance of screening for vitamin B12 deficiency in pregnancy. A study done by Koebnick C et al showed that the prevalence of B12 deficiency increased between second and third trimester from 8-35%. Van de Velde et al concluded that severe pancytopenia caused but ineffective haematopoiesis because of folate and vitamin B 12 deficiency.

In our study, 6 of the patients enrolled, 4 of them presented with preterm delivery (table 1) with one or the other obstetric complications. 2 patients presented in term with HELLP syndrome and one has to be followed. All the participants enrolled in the study where vegetarian in diet and had protein calorie deficiency and on laboratory evaluation had low levels of vitamin B 12 and folic acid levels. Mean vitamin B12 levels of our patients were 150.5 pg/ml (Normal range 195-950 pg/ml). Mean folate levels of

our patients were 2.725 ng/ml (Normal range 2-20 ng/ml). Further the patients were not subjected to bone marrow studies as the cause of pancytopenia in all our cases was diagnosed with blood investigations and dietary history. Maternal and neonatal complications are as explained in table 3.

Conclusion

Association of pancytopenia with pregnancy is a rare entity yet it has increased risk of poor maternal and foetal outcome. Early diagnosis and intervention brings favourable maternal and foetal outcome. Our study observed that all the participants had Vitamin B12 and folate deficiency leading to pancytopenia were vegetarian by diet. Hence, proper dietary counselling and well balanced dietary plans even with plant originate food can prevent the micronutrients deficiency and avoid the deleterious consequences like pancytopenia.

Conflict of interest: None. **Disclaimer:** Nil.

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