Section: Obstetrice & Gynaecology

Research

THROMBOCYTOPENIA IN PREGNANCY IN PANDEMIC ERA: AN OBSERVATIONAL STUDY

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Abstract

Background: Thrombocytopenia, defined as blood platelet count below 150,000/µL is the second leading cause of blood disorders in pregnancy after anemia. There is a physiological decrease in platelet count during normal pregnancy due to haemodilution, increased consumption in peripheral tissue and increased aggregation (higher levels of thromboxane A2). Interestingly, COVID-19 has some unique aspects interfering with the immune system which are rarely observed in other respiratory viral infections. Similar to other viral infections, SARS-CoV-2 can also trigger ITP and probably autoimmune hemolytic anemia. To study the prevalence of low platelet count in pandemic era in pregnant women; and to study correlation of low platelet count and maternal and fetal outcome in pandemic times. **Materials and Methods:** It was Observational and analytical study for a duration of 3months, which included 217 cases of pregnant women admitted to Lady Butler Hospital. **Result:** 217 were identified as having thrombocytopenia,54.37% were primigravidas. majority of cases belonged to 20-25yr age group.76.03% of identified had mild thrombocytopenia 2.76% had severe thrombocytopenia. 66.35% underwent vaginal delivery and rest 33.65% LSCS.33.18% of women were given tranexamic acid and 22.58% of cases required steroid coverage. Out of all 15.67% required whole blood,1.84% solely platelet and 4.15% required whole blood along with platelet rich plasma. Only 1.84% of patient required oxygen supplementation.6.45% of newborns were kept under NBSU and 8.75% had SNCU admission. 14.74% babies were low birth weight AND 1 was extremely low birth weight baby. **Conclusion:** Rapid recognition of thrombocytopenia can help to improvise maternal health, pregnancy and birth outcome.

INTRODUCTION

Zoonoses are diseases in which transmission from animals to humans can occur. The first stage of a pandemic caused by zoonotic agents, like SARS-CoV-2, is called spillover, when the virus jumps from wild animals to humans.[1-3] There are four stages that are required for zoonotic agents to emerge in humans: 1) human contact with the infectious agent; 2) cross-species transmission of the agent; 3) sustained human-to-human transmission and 4) genetic adaptation by the human host.[3,4] All these steps occurred when COVID-19 pandemic started in Wuhan, China on late December 2019,[5] and the possible initial source of the SARS-CoV-2 virus was a species of horseshoe bat found in caves in Yunnan Province.[3,4,6,7] It was also identified that secondary or intermediate hosts in which SARS-CoV-2 lived prior to reaching humans were likely the pangolins.[8] After the sustained human-to-human transmission was identified and the virus was adapted to humans, international outbreaks of COVID-19 were reported in South Korea, Iran, and Italy and the virus then rapidly spread worldwide.

Athough the overall risk of severe illness is low, pregnant people and recently pregnant people are at an increased risk for severe illness from COVID-19 when compared to non-pregnant people. Having certain underlying medical conditions, and other factors, including age, can further increase a pregnant or recently pregnant (for at least 42 days following end of pregnancy) person's risk for developing severe COVID-19 illness. Pregnant people with COVID-19 are also at increased risk for preterm birth (delivering the baby earlier than 37 weeks) and might be at increased risk for other poor

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pregnancy outcomes.(CDC)Pregnancy causes changes in the body that could make it easier to get very sick from respiratory viruses like the one that causes COVID-19. These changes in the body can continue after pregnancy. Pregnant women are not more affected by the respiratory complications of COVID-19, when compared to the outcomes described in the general population. It is also suggested that the important gestational shift Th1-Th2 immune response, known as a potential contributor to the severity in cases of viral infections during pregnancy, are counter-regulated by the enhanced-pregnancy-induced ACE2-Ang-(1-7) axis. Moreover, the relatively small number of reported cases during pregnancy does not allow us to affirm that COVID-19 is more aggressive during pregnancy. Conversely, it is also suggested, that down-regulation of ACE2 receptors induced by SARS-CoV-2 cell entry might have been detrimental in subjects with pre-existing ACE2 deficiency associated with pregnancy. This association might explain the worse perinatal outcomes described in the literature.

Black and Hispanic race, obesity, advanced maternal age, medical comorbidities, and antepartum admissions related to coronavirus disease 2019 are risk factors for associated morbidity. (ACOG) the response to viral infections during pregnancy relies mostly on the immunological changes that occur before and during gestation, in order to accommodate the developing fetus, so that the fetal tissues are not rejected by the maternal immune system.[9] These changes are characterized mostly by elevation of humoral immune responses and suppression of cell-mediated immunity, referred to as the T-helper lymphocyte type 1-type 2 (Th1-Th2) shift.[10] Pregnancy-induced alterations in immune cells and their cytokines, disparity between maternal-fetal glycosylation of IgG, and immunoregulatory pathways have important roles in the immunomodulation during pregnancy, which might explain clinical improvements of severe COVID-19 infected pregnant women after delivery.[11-14]

MATERIALS AND METHODS

This is Observational and analytical study done in department of Obstetrics and gynaecology of NSCGMC Khandwa & lady butler Hospital, Khandwa over a period of 3months from April to June 2021. Total 1500 pregnant ladies antenatal records were reviewed out of which 217 cases of pregnant women with thrombocytopenia were identified.

Inclusion Criteria

All pregnant women admitted to LHK for delivery with low platelet count,willing to participate in study.

Exclusion Criteria

- Hypertensive disorder of pregnancy
- Abruptio placentae
- Dengue
- Patient not willing to participate in study.

Outcome Measured Were

- Maternal: age, parity, booking status, mode of delivery, platelet counts prior to delivery and in puerperium, component therapy requirement and monitoring
- Fetal: birth weight, baby status, admission to nbsu/sncu.

RESULTS

The demographic data such as age, parity, booking status were studied. Total 150 cases records were reviewed of which 217 were identified as having thrombocytopenia. Out of 217 cases,54.37% were primigravidas,42.85%multigravida and rest 2.76% grandmultis. majority of cases belonged to 20-25yr age group.in our study,48.38% were booked,29.03% unbooked and 22.58% referred.76.03% of identified had mild thrombocytopenia,21.19% had moderate and 2.76% had severely low platelet levels. Out of total cases identified,66.35% underwent vaginal delivery and rest 33.65% LSCS.33.18% of women were given tranexamic acid during antenatal or intrapartum or postnatal period and 22.58% of cases required steroid coverage. Out of all 15.67% required whole blood, 1.84% solely platelet and 4.15% required whole blood along with platelet rich plasma.10 out the study subjects were given FCM in puerperal period. Only 1.84% of patient required oxygen supplementation.

Out of total babies delivered, majority were alive and healthy, whereas 6.45% were kept under observation in New born stabilisation unit and 8.75% had SNCU admission while 3 babies were IUFDs. 32 of the babies (14.74%) were low birth weight ,1.84% belonged to very low birth weight and 1 was extremely low birth weight baby.

Table 1: distribution according to age

Age	No. Of cases	Percentage
<20yrs	3	1.38
20-25yrs	154	70.96%
26-30yrs	55	25.30%
>30	4	1.84%

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Table 2: distribution of patients according to booking status.

Booking status	No. Of cases	Percentage
Booked	105	48.38%
Unbooked	63	29.03%
Referred	49	22.58%

Table 3: distribution of patients according to platelet count

Platelet count	No. Of cases	Percentage
1-1.499 LAC/CUMM	165	76.03%
0.5-0.99LAC/CUMM	46	21.19%
<0.5 LACLCUMM	6	2.76%

Table 4: Distribution of patients according to thrombocytopenia

Thrombocytopenia	No. Of cases	Percentage
Mild	165	76.03%
Moderate	46	21.19%
Severe	6	2.76%

Table 5: distribution of patients according to parity

Parity	No. Of cases	Percentage
PRIMI	118	54.37%
MULTI	93	42.85%
GRANDMULTIPARA	6	2.76%

Table 6: Distribution of patients according to mode of delivery

Mode of delivery	No. Of cases	Percentage
VAGINAL	144	66.35%
LSCS	73	33.65%

Table 7: Distribution of babies according to sex

Baby sex	Number	Percentage
Female	97	44.70%
Male	120	55.30%

Table 8: Distribution of babies according to health status

Baby status	Number	Percentage
ALIVE & HEALTHY	181	83.41%
NBSU	14	6.45%
SNCU	19	8.75%
IUD	3	1.38%

Table 9: Distribution of babies according to weight

Weight status	Cases	Percentage
Normal weight	180	82.94%
LBW(<2.5KG)	32	14.74%
VLBW(<1.5KG)	4	1.84%
ELBW	1	0.48%

Table 10: Percentage of women required tranexamic acid.

Tranexamic acid	Number	Percentage
Given	72	33.18%
Not given	145	66.82

Table 11: percentage of women given steroids

Steroid	Cases	Percentage
Given	49	22.58%
Not given	168	77.42%

Table 12: percentage of women requiring blood products

Blood product given	Cases	Percentage
Whole blood	34	15.67%
Platelet	4	1.84%
WB +PRP	9	4.15%
WB+FFP	1	0.46%
FCM	10	4.61%
Nil	159	73.27%

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Table 13: Percentage of women requiring oxygen support

Oxyegen support	Percentage	Cases
Required	1.84%	4
Not required	98.16%	213

DISCUSSION

The coronavirus disease-19 (COVID-19) pandemic has directly and indirectly impacted pregnant women with co-morbidities or antenatal medical complications, through vulnerability to the severe effects of COVID-19 and service reconfiguration. Women with diabetes or hypertension in pregnancy are at higher risk of admission to intensive care, need for invasive ventilation and death from COVID-19. Suggested service modifications specific to maternal medicine services include home measurement of blood glucose or blood pressure, the use of risk calculators, adaptations to screening criteria for gestational diabetes and monitoring of obstetric cholestasis. Neither the added risk of COVID-19 on pregnant women with medical comorbidities nor the impact of maternal medicine service modifications has yet been established.

The increased use of heparin during the current COVID-19 pandemic has highlighted the risk of a rare but potentially serious complication of heparin therapy, viz. heparin-induced thrombocytopenia (HIT). This is a short review on the pharmacology of heparin and its derivatives, and the pathophysiology of HIT. Guidance on laboratory testing for and clinical management of HIT is presented in accordance with international guidelines. There are important similarities and differences between HIT and the new entity of vaccine-induced immune thrombotic thrombocytopenia, also known as thrombosis with thrombocytopenia syndrome, which clinicians need to be aware of.

Eltemamy E et al did assessment of fetal growth and anomalies in the era of COVID-19 pandemic. Results revealed no significant difference between both groups regarding fetal biometry, estimated fetal weight, amniotic fluid index, Doppler scan, and gross anomaly scan throughout all visits. According to the results of pilot study, SARS-CoV-2 infection in pregnancy was not found to increase the risk of fetal growth restriction or possible fetal gross anomalies. Nevertheless, larger-scale studies are needed to confirm those findings. Perhaps, post-SARS-CoV-2 infection pregnancies may run an uncomplicated course regarding fetal parameters.

Borhany M et al in a similar study like us did a study. The study aimed to evaluate the causes of thrombocytopenia in pregnancy and its management along with the outcome in the COVID-19 era. Causes of thrombocytopenia were gestational thrombocytopenia (GT) 72 (48%), acute fatty liver five (3.3%), pre-eclampsia in 11 (7.3%), and eclampsia seven (4.6%). Causes not specific to pregnancy included 30 (20%) cases of ITP, hepatitis C, and nutritional deficiency was reported in nine (6%) patients each. 72/150 received supportive care treatment to manage thrombocytopenia and were closely monitored and given supplements. Twenty (66.6%) ITP patients received treatment with steroids, with complete response in 70% of them seen. Overall, 38 (25.3%) women with bleeding symptoms and platelet count <50x109/L received platelet transfusions. The study shows that pre-eclampsia and eclampsia are serious conditions with a high risk for complications, while GT is a benign and the most common cause of thrombocytopenia in pregnancy which requires no active treatment. The other causes such as ITP and infections require individualized management.

Rodeghiero F et al gave practical recommendations for the management of patients with ITP during the COVID-19 pandemic. This report describes an updated version of consensus-based practical guidelines on the management of ITP, adapted to the Italian health system and social context. It highlights the role of the hematologist in offering guidance for choosing differentiated approaches in relation to specific circumstances and is intended to provide them with a useful tool for sharing the decision-making process with their patients.

Le Gouez A et al studied thrombocytopenia in pregnant patients with mild COVID-19. They describe three pregnant patients, each presenting with a mild form of COVID-19 in which thrombocytopenia was observed. The patients presented to the emergency department during pregnancy because of fever and dry cough. Two were diagnosed with COVID-19 using reverse transcription-polymerase chain reaction (PCR) assay on nasopharyngeal swab. The PCR was negative in the third patient, but her chest computed tomography scan showed pulmonary lesions that were strongly linked to COVID-19. The first patient presented at 40 weeks' gestation and had a platelet count nadir of 94×109/L. The second patient presented at 31 weeks' gestation and had a platelet count nadir of 79×109/L. Both these patients had a normal prothrombin time (PT), activated partial thromboplastin time (aPTT) and plasma fibrinogen concentration. The third patient, at a gestation of 37 weeks, had a lowest platelet count of 40×109/L and a prolonged aPTT, but normal values of Factors VIII, IX and XI.

Bhattacharjee S, Banerjee M et al did a systematic review on immune thrombocytopenia secondary to COVID-19. A comprehensive approach is essential for diagnosing COVID-19-associated ITP after excluding several concomitant factors that can cause thrombocytopenia in COVID-19. Majority of ITP cases (71%) were found to be elderly (> 50 years) and 75% cases had moderate-to-severe COVID-19. Three patients (7%) were in the pediatric age group.

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Reports of ITP in asymptomatic COVID-19 patients (7%) underscore the need for COVID-19 testing in newly diagnosed patients with ITP irrespective of COVID-19 symptoms amid this pandemic. Good initial response to short course of glucocorticoids and intravenous immunoglobulin has been found with the exception of delayed lag response in one case. Thrombopoietin receptor agonist usage as a second-line agent has been noted in few cases for short duration with no adverse events. In the relatively short follow-up period, four relapses of ITP were found.

Liu Y ennumerated effects of initial COVID-19 outbreak during first trimester of pregnancy outcome in Wuxi, China. The initial COVID-19 outbreak might increase the incidence rates of HDP and GDM among pregnant women whose first trimesters were during that period, resulting in higher percentages of premature delivery and low birth weight. These results should be confirmed by studies from other hospitals or cities.

Rasmussen SA et al studied coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. Overall case fatality rate appears to be ~1%; however, early data may overestimate this rate. In 2 reports describing 18 pregnancies with coronavirus disease 2019, all were infected in the third trimester, and clinical findings were similar to those in nonpregnant adults. Fetal distress and preterm delivery were seen in some cases. All but 2 pregnancies were cesarean deliveries and no evidence of in utero transmission was seen.

Vlachodimitropoulou Koumoutsea E et al studied COVID- 19 and acute coagulopathy in pregnancy. They saw a putative link between maternal COVID-19 infection in the peripartum period and rapid maternal deterioration with early organ dysfunction and coagulopathy. The current pandemic with SARS-CoV-2 has already resulted in high numbers of critically ill patients and deaths in the non-pregnant population, mainly due to respiratory failure. During viral outbreaks, pregnancy poses a uniquely increased risk to women due to changes to immune function, alongside physiological adaptive alterations, such as increased oxygen consumption and edema of the respiratory tract. The laboratory derangements may be reminiscent of HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, and thus knowledge of the COVID-19 relationship is paramount for appropriate diagnosis and management. In addition to routine measurements of D-dimers, prothrombin time, and platelet count in all patients presenting with COVID-19 as per International Society on Thrombosis and Haemostasis (ISTH) guidance, monitoring of activated partial thromboplastin time (APTT) and fibrinogen levels should be considered in pregnancy, as highlighted in this report. These investigations in SARS-CoV-2-positive pregnant women are vital, as their derangement may signal a more severe COVID-19 infection, and may warrant pre-emptive admission and consideration of delivery to achieve maternal stabilization.

CONCLUSION

Covid 19 disease 2019 pandemic is one of the biggest healthcare crises faced globally. Pregnant patient poses a higher challenge due to concerns of an already altered immune system during pregnancy and the disease's effect on fetus. Thrombocytopenia is an established marker of worsening of disease. Thus rapid recognition of severe thrombocytopenia highlight the importance of careful monitoring of platelet count of pregnant women with covid 19 infection even if asymptomatic and can help to improvise maternal health, pregnancy and birth outcome.

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