"Impact of covid 19 pandemic on maternofetal outcome in pregnant women with severe anemia:a retrospective case control study"

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Abstract

Objective: To study the impact of COVID 19 pandemic on the prevalence, clinical profile, and pregnancy outcomes of women with severe anaemia. Design: Retrospective Case Control study Setting: Department of Obstertrics ,Tertiary care hospital of Delhi Population:Antenatal women >26 weeks and Hemoglobin<7 gm% Methods: After satisfying inclusion and exclusion criteria, cases were taken for a duration of six months during COVID pandemic, covid cases and controls from period six months post covid. Main outcome measures: Prevalence of anemia, Anemia indices and maternofetal outcome. Results: Total 4031 women delivered in study period compared to 6659 in control period. 74.7% and 51.6% were anaemic in study and control groups respectively ($p < 0.001$). Mean hemoglobin level was significantly lower in cases compared to the controls. Microcytic hypochromic anemia was most common morphological type of anemia in both groups. Serum ferritin, serum iron, serum B12 and folic acid levels among cases were significantly ($p<0.05$) lower as compared to controls. Odds of foetal growth restriction was 48% higher among cases as compared to controls. The odds ratio of new-born complications such as low birth weight 2.49 (95%CI: 1.04-5.91) and need for nursery or NICU admission 4.84 (95%CI: 0.48-48.24) was higher in cases as compared to controls. Low birth rate was higher in cases and was found to be statistically significant. Conclusion: India needs to focus on minimizing the indirect effects of the pandemic on the maternal and perinatal outcomes. Funding: none

TITLE: "Impact of covid 19 pandemic on maternofetal outcome in pregnant women with severe anemia:a retrospective case control study"

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ABSTRACT

Objective: To study the impact of COVID 19 pandemic on the prevalence, clinical profile, and pregnancy outcomes of women with severe anaemia.

Design: Retrospective Case Control study

Setting: Department of Obstertrics ,Tertiary care hospital of Delhi

Population: Antenatal women >26 weeks and Hemoglobin<7 gm%

Methods: After satisfying inclusion and exclusion criteria, cases were taken for a duration of six months during COVID pandemic, covid cases and controls from period six months post covid.

Main outcome measures : Prevalence of anemia, Anemia indices and maternofetal outcome.

Results : Total 4031 women delivered in study period compared to 6659 in control period. 74.7% and 51.6% were anaemic in study and control groups respectively ($p < 0.001$). Mean hemoglobin level was significantly lower in cases compared to the controls. Microcytic hypochromic anemia was most common morphological type of anemia in both groups. Serum ferritin, serum iron, serum B12 and folic acid levels among cases were significantly ($p<0.05$) lower as compared to controls. Odds of foetal growth restriction was 48% higher among cases as compared to controls. The odds ratio of new-born complications such as low birth weight 2.49 (95%CI: 1.04-5.91) and need for nursery or NICU admission 4.84 (95%CI: 0.48-48.24) was higher in cases as compared to controls. Low birth rate was higher in cases and was found to be statistically significant.

Conclusion : India needs to focus on minimizing the indirect effects of the pandemic on the maternal and perinatal outcomes.

Funding : none

BACKGROUND

Anemia is a major public health problem in developing countries. It is the most common nutritional disease in pregnancy with significant adverse impact on maternal and perinatal morbidity and mortality. In 2019,

the global prevalence of anemia in pregnant woman was estimated to be 36.5% (1). As per recent NFHS 5 report the prevalence of anaemia in pregnant women in India is 45.7% and 54.3% in urban and rural areas respectively(2) The important causes of anemia in developing countries include poor nutrition, inadequate iron in diet, poor absorption of iron due to hookworm infestation, diarrhea,, suboptimal screening and treatment and too early, too soon and too many child births. Routine antenatal and postnatal iron supplementation free of cost is an important Government initiative to reduce anemia in pregnancy. Despite this, anemia remains unabated due to poor compliance to iron supplementation by beneficiaries and lack of commitment among the health care providers to screen and treat pregnant women for anemia. Covid 19 pandemic further disrupted the antenatal care services due to lockdowns and related travel restrictions, loss of jobs and related financial constraints and reluctance of pregnant women to visit health facilities for the fear of contracting infection (3). The lower socioeconomic strata were the worst affected. As with previous epidemics there was a sudden increase in demand and redirection of the workforce towards the management of COVID pandemic and resultant reduction in provision of routine health services.(4) Although COVID-19 disease itself did not directly increase the maternal mortality but resulted in unsupervised pregnancies adversely affecting maternal health. (5, 6)

This study was initiated to study the impact of COVID 19 pandemic on the prevalence, clinical profile and pregnancy outcomes of women with severe anaemia

MATERIALS and METHODS

This record based retrospective comparative observational study was conducted in the department of Obstetrics and Gynaecology at LHMC and SSK Hospital, Delhi for a duration of six months from July 2020 to December 2020 during COVID pandemic (study group) and a six month Pre COVID period from July 2019 to December 2019 (control group). The study included all antenatal women admitted at a gestational age >26 weeks (third trimester) with severe anaemia that is haemoglobin level of <7 gm% for delivery as per ICMR classification for grading of anemia in pregnancy. The case records of patients having severe anaemia due to acute blood loss like antepartum haemorrhage were not included in the study.

After obtaining ethical clearance from institutional ethics committee eligible subjects were identified from birth entry register and case records were retrieved. A proforma was used to record the relevant demographic details including maternal age, registration status of pregnancy, parity, gestational age in weeks at admission, inter-conception period, gestational age in weeks at delivery, presence of factors contributing to anaemia (such as intolerance to iron, non-availability and lack of antenatal care) ; clinical complaints at admission (exercise intolerance, easy fatiguability, breathlessness etc); clinical data on management (such as injectable iron, Vit B12, blood transfusion); complications (like abruption, postpartum haemorrhage, ICU admission, need of intubation , maternal death, foetal growth restriction); mode of delivery (vaginal delivery, LSCS); laboratory investigations (hemoglobin level, peripheral smear, serum ferritin, serum B12 and folic acid levels and foetal outcome (gestational age, live or still birth, birth weight, APGAR score and need of nursery/NICU admission).

Statistical analysis: The data collected during the study was entered in Microsoft Excel spreadsheet. The statistical analysis was performed using the Statistical Package for the Social Sciences for Windows version 18 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as mean ± standard deviation for continuous variables and frequencies or percentages for categorical variables. Normality of the data distribution were assessed with the Kolmogorov-Smirnov test. Depending upon normality of data, appropriate tests were used. Chi-square test and students t-test were applied to see the difference between study and control groups for baseline clinical and laboratory characteristics and outcomes. Univariate logistic regression models were used to assess the association between year and maternal/perinatal outcomes. Odds ratios and 95% confidence intervals were presented. A p value of less than 0.05 was considered statistically significant.

RESULTS

In the present study, 4031 women delivered in study period compared to 6659 in control period. Of these (3010/4031) 74.7% and (3446/6659) 51.6% were anaemic in study and control groups respectively. ($p < .001$).

The overall prevalence of severe anemia was (51/4031) 1.27 % and (77/6659) 1.16% respectively amongst all deliveries in the study and control groups respectively **(p value =0.616).** (Table 1).

In the present study a total of 51 case records from study group and 77 case records from control group were analysed. Table no 2 shows the comparison between the epidemiological details including mean age of the pregnant women, their antenatal registration status, inter-conception period, mean gestational age at delivery and antenatal prophylactic iron supplementation.

Table no 3 describes the clinical presentation at the time of admission in the study and control groups. Majority of women were asymptomatic in both the groups at the time of admission. Of the symptomatic women breathlessness was the commonest symptom in both the groups. There was no difference in the clinical presentation in both the groups.

All patients received blood transfusion in both the groups in view of severe anemia whereas 5.9% and 2.6% in study and control groups received platelet transfusion. Parenteral iron was administered to 9.8% patients in study group compared to none in control group whereas parenteral Vit B12 was given to 19.6% and 26.8% patients in the study and control groups respectively.

The vaginal delivery rates were higher among control group (83.1%) as compared to study group (76.5%) however the difference was statistically not significant.

Mean hemoglobin level was significantly lower in study group than the control group. Microcytic hypochromic anemia was the most common morphological type of anemia in both study and control groups. Serum ferritin, serum iron, serum B12 and folic acid levels among study group were significantly ($p<0.05$) lower as compared to control group .

The odds ratio of maternal death in study group was 6.46 (95%CI: 0.70-59.63) as compared to control group. The odds ratio of maternal complications was such as abruption 2.34 (95%CI: 0.37-14.54), postpartum haemorrhage 2.65 (95% CI: 0.99-7.04) and ICU admission 3.29 (95% CI: 0.78-13.80) in study group compared to control group but the difference was statistically not significant as the confidence intervals were very wide. Odds of foetal growth restriction was 48% higher among study group as compared to control group (Table 4).

The odds ratio of neonatal deaths in study group was 4.84 (95%CI: 0.48-48.24) compared to control group. The odds ratio of new-born complications such as low birth weight 2.49 (95%CI: 1.04-5.91) and need for nursery or NICU admission 4.84 (95%CI: 0.48-48.24) was higher in study group as compared to control group. Low birth rate was higher in study group and was found to be statistically significant. Odds of still birth was 5% higher in study group as compared to control group (Table 6).

DISCUSSION

Main findings

Anemia is the second most common cause of maternal death in India and contributes to about 80% of the maternal deaths in Southeast Asia. (7,8,9) Anemia is also an established risk factor for intrauterine growth restriction, leading to perinatal and neonatal mortality and morbidity. Anaemia during pregnancy increase the risk of hemorrhage, labor complications and puerperal sepsis to the mother. The gestational complications, maternal mortality, low birth weight and, adverse birth outcome is among the major adverse impacts of anaemia in pregnancy in most developing countries, particularly in south-east Asia. (10,11)

Though COVID-19 has not affected maternal and fetal outcomes directly, the present study highlights the indirect effects of COVID-19 on pregnancy outcomes. Overall prevalence of anemia as well as severe anemia was more in study group that is during the pandemic compared to control group in the pre pandemic period. Two-third of pregnant women with severe anemia (60.8%) did not have any contact with health care provider as they were asymptomatic and due to pandemic related factors like lack of transport, finances, or fear of contagion from health care centres. The reduced number of antenatal visits and increased unregistered pregnancies contributed to an increase in pregnancy complications and related morbidity and mortality. In

the study by Davis et al (12), it was found that women preferred home deliveries instead of institutional deliveries in the fear of contagion from delivery institutes. It is possible that the number of cases of severe anaemia during pandemic in the study group are not reflective of the actual numbers. The inter-conception period <2 years was significantly higher in study group compared to control group. This difference is likely due to an increase in sexual exposure consequent to couples staying home due to lock down coupled with inaccessibility to family planning services both with respect to contraception and safe abortion services. In present study 47.1% of women in study group did not receive routine iron and folic acid supplementation during pregnancy, with resultant anemia and related complications. A decreased mean hemoglobin level was observed in study group as compared to control group. Similar observation has been reported in other Indian studies. (13, 14)

In a study by Justman et al., the rate of caesarean deliveries, including emergency cesarean deliveries, was similar between the two periods: 22.1% (164/742) in control group vs. 24.1% (147/610) during the pandemic group (15). However, contrast to this the caesarean section rates were higher in study group (23.5%) compared to control group (16.9%) but the difference was statistically not significant. The factors contributing to an increased caesarean section rate in study group might be due to the difficulty in close fetal monitoring in PPE and unexpected delays in decision delivery interval due to COVID protocols .

More patients in study group required ICU admission due to an increase in complications like abruption and postpartum haemorrhage. An increase in the maternal mortality rate was also observed. In the present study, the odds ratio of maternal deaths among study group was higher as compared to control group OR 6.46 (95% CI 0.70-59.63). Similar findings have been reported in the studies by Kumari et al., (1·54 95% CI: 0·56–4·25) and Lumbreras-Marquez et al., (1·36 95% CI: 1·22–1·53) (16,17). In present study the odds ratio for preterm birth before 37 weeks' gestation was 1.22 times (95% CI: 0.59-2.51) in study group as compared to control group. Similar findings were observed in the studies by Khalil et al., Main et al., McDonnell et al., and Sun et al, where odds ratio for pandemic group was higher than control group such as 1·11 (95% CI: 0·85–1·44), 1·01 (95% CI: 0·99–1·03), 1·18 (95% CI: 0·91–1·54), 1·03 (95% CI: 0·30–3·51) respectively (18,19,20,21)

In present study, odds of still birth was 5% higher among pandemic as compared to control group which was similar to pattern found in study by Kumar et al., (1·26, 955 CI: 1·00–1·58) but opposed to the study by Caniglia et al., where odds of stillbirth were higher in control groups as compared to pandemic group (0·96, 95% CI: 0·73–1·26) [22,23]. In the study by KC et al., the institutional stillbirth rate increased from 14 per 1000 total births before lockdown to 21 per 1000 total births during lockdown (p=0·0002), and institutional neonatal mortality increased from 13 per 1000 livebirths to 40 per 1000 livebirths (p=0·0022) [24).

Only 2 out of 55 women among cases were COVID-19 positive and none of them required intensive care and had live births implying that COVID-19 infection itself did not contribute substantially to an increase in maternal or fetal morbidity or mortality in the study population.

Strengths and limitations

The present study was carried out in a government setup of a developing country reflecting the true face of disrupted antenatal care during the covid pandemic.Despite the set up catering free of cost services to the pregnant woman ,the pandemic hindered adequate service provision.

Few limitations of the study include that it is a single-center study at a tertiary hospital so the results cannot be generalized. Second, the analysis includes only those women who were admitted to the facility, while pregnant women with anaemia attending outpatient department were not included. Lastly, as it is a retrospective, observational study with a small sample size it does not take in to account other independent factors affecting delay in patient seeking antenatal care and influencing maternofetal outcomes. Large multicentric studies and worldwide surveys are needed to identify and guide management of antenatal women during pandemics to optimize outcomes .

Interpretation

As in other pandemics, the healthcare system faced a great challenge during the COVID- 19 pandemic, showing its indirect effects on the vulnerable antenatal group and an increase in pregnancy-related complications.

CONCLUSIONS

The indirect effects of COVID-19 on maternal and perinatal outcomes were observed. Although it is likely that other factors might have been at play,the lower mean Hb levels,lower iron reserves and B12 levels, increased caesarean section rate, increased perinatal mortality rate, increased number of stillbirths together with the increased likelihood of abruption point towards disruptions in the provision of antepartum care and compromised quality of intrapartum care. As India continues to implement public health measures to curb the spread of COVID-19, there is need to reduce the indirect effects of the pandemic on the maternal and perinatal outcomes. The country is presently battling the third wave of the COVID-19 pandemic, therefore these results may be useful for local, provincial, and national program planning.

Disclosure of interests: none

Contribution to authorship :

Author's contribution: MS contributed in planning, carrying out, analysing, and writing up of the work, MP contributed in the conception and final proof check of the manuscript ,VC ,AK,TG,G,MP and VK contributed in data collection and analysis.

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TABLES

Table 1. Grading of severity of anemia in women admitted in pandemic and control group

Grading of severity of anemia of delivered women	Study group (n=4031)	Control group (n=6659)	P value
No anemia (Hb>=11g%)	1021 (25.3%)	3223 (48.4%)	<0.001
Anaemia	3010 (74.7%)	3436 (51.6%)	
Mild anemia (Hb 10-10.9 g%)	1750 (43.4%)	1820 (27.3%)	<0.00001
Moderate anemia (Hb 7 -9.9g%)	1207 (29.9%)	1539 (23.1%	<0.0.0001
Severe anemia (Hb <7 g%)	51 (1.27%)	77 (1.16%)	0.616

Table 2. Comparison of the epidemiological characteristics of pregnant women with severe anaemia in pregnancy

Variable	Study group (n=51)	Control group (n=77)
Age (in years)	27.9±3.1	24.8±4.0
Parity		
Primigravida	36(70.6%)	50(64.9%)
Multigravida	15(29.4%)	27(35.1%)
Antenatal registration	**Antenatal registration**	**Antenatal registration**
Yes	20 (39.2%)	43 (55.8%)
No	31 (60.8%)	34 (44.2%)
Inter-conception period#	(N=15/51)	(N=27/77)
< 2 years	13(86.6%)	7(25.9%)
>2 years	2 (13.3%)	20 (74.1%)
Gestational age (in weeks) at delivery	36.9±1.6	37.0±2.1
Preterm birth (< 37 weeks of gestation)		
Yes	31 (61.8%)	43 (55.8%)
No	20 (38.2%)	34 (44.2%)
Antenatal iron supplementation	**Antenatal iron supplementation**	**Antenatal iron supplementatio**
Yes	27 (52.9%)	65 (84.4%)
No	24 (47.1%)	12 (15.6%)

#Multigravida (n=42)

Table 3. Comparison of clinical characteristics of severely anaemic pregnant women in the two groups

Variable	Study group (n=51)
Clinical complaints and presentation at time of admission*	**Clinical complaints and presentation at time o**
Breathlessness (n=27)	11 (21.6%)
Pedal oedema	0 (0.0%)
Dizziness	0 (0.0%)
Anasarca	2 (3.9%)
Asymptomatic	41 (80.4%)

***Multiple responses**

Table 4: Laboratory parameters related to Anemia

Variable	Study group N=51
Mean Hb (g/dl)	5.4±0.8
Peripheral smear (Morphological type of anaemia)	**Peripheral smear (Morphological type**
Microcytic hypochromic	27 (52.9)
Dimorphic anaemia	9 (17.6)
Macrocytic	15 (29.4)
Serum ferritin and iron levels in microcytic +dimorphic anaemia	**Serum ferritin and iron levels in micro**
Serum ferritin (ng/ml)	5.6±5.2
Serum iron (µg/dl)	25.3±6.5
Serum B12 and folate levels in macrocytic and dimorphic anaemia	**Serum B12 and folate levels in macroc**
Serum B12 (pg/ml)	110.4±34.5
Serum Folic acid (ng/l)	4.1±1.7

***Multiple responses**

Table 5. Comparison of pregnancy outcome in study and control groups

Pregnancy outcomes	Study group (n=51)	Control group (n=77)	OR, 95% CI, P value
Abruption	**Abruption**	**Abruption**	**Abruption**
Yes	3 (5.9%)	2 (2.6%)	2.34, 0.37-14.54, 0.914
No	48 (94.1%)	75 (97.4%)	
Postpartum haemorrhage	**Postpartum haemorrhage**	**Postpartum haemorrhage**	**Postpartum haemorrhag**
Yes	12 (23.5%)	8 (10.4%)	2.65, 0.99-7.04, 0.050
No	39 (76.5%)	69 (89.6%)	
ICU admission	**ICU admission**	**ICU admission**	**ICU admission**
Yes	6 (11.8%)	3 (3.9%)	3.29, 0.78-13.80, 0.103
No	45 (88.2%)	74 (96.1%)	
Need of intubation	**Need of intubation**	**Need of intubation**	**Need of intubation**
Yes	6 (11.8%)	3 (3.9%)	3.29, 0.78-13.80, 0.103
No	45 (88.2%)	74 (96.1%)	
Maternal death	**Maternal death**	**Maternal death**	**Maternal death**
Yes	4 (7.8%)	1 (1.3%)	6.46, 0.70-59.63, 0.099
No	47 (92.2%)	76 (98.7%)	
Foetal growth restriction	**Foetal growth restriction**	**Foetal growth restriction**	**Foetal growth restrictio**
Yes	22 (43.1%)	26 (33.8%)	1.48, 0.71-3.08, 0.284
No	29 (56.9%)	51 (66.2%)	

Table 6. Perinatal outcome in Pregnant women with severe anemia

Outcome	Study group (n=51)	Control group (n=77)	OR, 95% CI, P value
Birth	**Birth**	**Birth**	**Birth**
Still birth	9 (17.6%)	13 (16.9%)	1.05, 0.41-2.68, 0.910
Live birth	42 (82.4%)	64 (83.1%)	
Neonatal death*	N=42/51	N=64/77	
Yes	3 (7.1%)	1 (1.6%)	4.84, 0.48-48.24, 0.178

Outcome	**Study group (n=51)**	**Control group (n=77)**	**OR, 95% CI, P value**
No	39 (92.9%)	63 (98.4%)	
Baby birth weight< 2500 grams*	N=42/51	N=64/77	
Yes	32 (76.2%)	36 (56.3%)	2.49, 1.04-5.91, 0.038
No	10 (23.8%)	28 (43.8%)	
5 min APGAR score < 7 *	N=42/51	N=64/51	
Yes	3 (7.1%)	1 (1.6%)	4.84, 0.48-48.24, 0.178
No	39 (92.9%)	63 (98.4%)	
Need of nursery/ NICU admission*	N=42	N=64	
Yes	3 (7.1%)	1 (1.6%)	4.84, 0.48-48.24, 0.178
No	39 (92.9%)	63 (98.4%)	

* Percentages are calculated out of live borns in each group