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ORIGINAL ARTICLE

Effects of Novel Coronavirus 2019 Infection on Antenatal Hematological Parameters in Pregnant Women

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ABSTRACT

Background: Disturbance of haematological parameters is prevalent in pregnancy globally leading to a range of feto-maternal complications. Covid-19 infection has potential to enhance the severity of and complications impending due to anaemia in pregnancy.

Objective: To determine the effects of Covid-19 infection on haematological parameters during antenatal care among pregnant women in rural Sindh.

Study Design: Cross sectional study.

Setting: Shaikh Zaid Institute, Chandka Medical College, Larkana.

Duration: From March 1, 2021, and May 31, 2021.

Materials and Method: A sample of 110 pregnant women, of 18-50 years of age, presenting in first through third trimester with single alive pregnancy, were included in the study after taking a valid written consent. The Research Evaluation Committee of SMBBMU- Larkana granted approval. Women having any haemoglobinopathy were excluded. Covid-19 test conducted through rt-PCR method. A standard questionnaire was used to collect data of two groups. Analysis was performed through SPSS Version-23. Descriptive and inferential statistics were calculated.

Results: Mean ± SD age was 30.3 ± 6.99 (Range: 19 to 45) years. Both groups were identical in age. Mean ± SD gestational age was 28.12 ± 4.66 weeks (Range: 20-38). Covid-19 positive women had lower mean Hb (9.7 ± 2.11) than the covid-19 negative (10.54 ± 2.51; P = 0.158). Other haematological parameters like MCV, serum ferritin, TIBC, TLC & platelets were statistically different between groups.

Women of eldest group i-e; in 41-50 years, from urban areas, second trimester (gest. age 13-24 weeks), and nulliparous had been affected more from covid-19 (P = 0.271, 0.748, 0.290 & 0.053). Frequency and severity of anaemia was more among Covid-19 positive women.

Conclusion: Covid-19 demands maternal healthcare to be extra vigilant to the haematological parameters of pregnant women during antenatal care till delivery.

Keywords: Antenatal care, pregnancy, anaemia, haemoglobin, Covid-19.

INTRODUCTION

Abrupt appearance in December 2019 in China and rapid spread of novel coronavirus 2019 (SARS COV-2) or n-covid-19 within a few months throughout the world, has affected all age groups.[1] The pandemic has put millions of pregnancies occurring annually- at an insurmountable risk. [2] Many aspects of which are yet to be explored and measured in their intensity and severity against mothers and their neonates. [3,4] The caution raises and warrants through research because previously; other coronavirus infections like severe acute respiratory syndrome and Middle East respiratory syndrome severely affect the pregnancies. [5,6]

Uptil now; with a mixture of picture; some suggest women with covid-19 remain asymptomatic or develop very non-significant flu-like clinical features. Others found that pregnant women who contract Covid-19 are 22 times more likely to die and have 50% more chances of experiencing pregnancy-related complications than pregnancies without Covid-19 as found in a study of over 2,100 pregnant women across 18 countries, including Pakistan, published in JAMA Paediatrics.[7] A t least 10% of required admission to intensive care unit while 50% of those could not survive. [8]

World Health Organization recommends care of covid-19 affected pregnancies including; regular antenatal visits and check-ups/ scans. [9] All pregnant women should be screened for covid-19 during ANC specially their haematological status. [10] Covid-19 tends to lower hemoglobin levels in almost 50% of patients [6,11] indicating the presence of anemia, and pathologically increased levels of ferritin.[2,12] Anaemia in pregnancy has long been a prevalent and dangerous affecting upto 40% pregnancies. Covid-19 infection may worsen as it is associated with first trimester miscarriage wherein the woman was having mild anaemia. [13] Studies conducted in China, showed that anemic patients were more likely to have severe disease and higher mortality. [14,15] while other did not. [16] Similarly, in a study in Italy, Cecconi et al. did not observe any association between anemia and poor outcomes of covid-19. [17] Unfortunately, no local study provides clear evidence regarding the link between anemia and covid-19.

The covid-19 is a rapidly evolving and emerging situation. There is a dearth of information for people with

hemoglobin disorders in the context of covid-19. In our daily practice, we noticed a relatively increased proportion of hospital admission to intensive care units of pregnant women with covid-19 therefore; investigated the association and its course in antenatal period as we could not find sufficient evidence from our local population on relation and effects of covid-19 on pregnancy and feto-maternal well-being. Therefore; the current study was conducted with the objective to investigate covid-19 infected pregnancies in antenatal phase. The generated evidence and the knowledge gained will be used to devise strategies for improving antenatal/ maternity care.

MATERIAL AND METHODS

This prospective study was conducted at Shaikh Zaid Medical Institute, CMC-Larkana between March 1, 2021, and May 31, 2021. The Research Evaluation Committee of SMBBMU- Larkana approved it and data collection permission was taken from the Obs/ Gynaecology department. Pregnant women who present to the OPD for their antenatal check-up/ delivery were enrolled in the study after taking a valid written consent.

A consecutive sample of 110{sample calculated by taking incidence of pregnancy complications with covid-19 at rate of 10% with 6% margin of error, 95% confidence interval and using single proportion formula. The sample size came to by 100 ~ 110} pregnant women, of 18-50 years of age, presenting in first through third trimester with single alive pregnancy, were included. Women having any haemoglobinopathy were excluded. Covid-19 test conducted was done through rt-PCR method and data was collected in two groups. Anemia was defined according to the World Health Organization (WHO) definition as Hb concentration of <11 g/dL. [18]

The data was collected by the researcher team working at site of data collection on demographic variables (maternal age, parity, weight, height, BMI, gestational age, gravida, parity, and address) and the haematological parameters. Patients were followed if they continued to visit for ANC. Status of covid-19 infection was recorded. The data was entered and analyzed through SPSS version 25. The continuous variables like age, Hb%, were expressed in mean & standard deviation (Mean ± SD). Categorical variables like presence and severity anemia were expressed in frequencies and percentages. To evaluate the relationship/ effect modification, study variables were stratified followed by application of chi-square or students'-test with a p value <0.05 taken as significant.

RESULTS

A sample of 110 pregnant women coming for antenatal visit were enrolled in this study. Their covid-19 test through rt-PCR performed and were categorized into two groups viz; covid-19 positive and covid-19 negative. Cumulatively; their mean ± SD age was 30.3 ± 6.99 years ranging from 19 to 45 years and both groups were identical in age. Mean ± SD gestational age was 28.12 ± 4.66 weeks (Range: 20-38). Women having covid-19 positive had presented slightly earlier i-e; 27.55 ± 5.41 gestational age compared to covid-19 negative which presented at 30.19 ± 5.05 weeks. (Table: 1). Regarding parity, height & weight there were only minor and not significant difference found between the two groups. However; the BMI of covid-19 negative was significantly (P = 0.0089) lower than the covid-19 positive women (26.55 ± 3.08 versus 28.45 ± 2.23). (Table: 1).

The details of haematological parameters of these pregnant women shows in table: 2, differences in the haemoglobin values of the two groups. Covid-19 positive women had lower mean Hb (9.7 ± 2.11) than the covid-19 negative (10.54 ± 2.51; P = 0.158). Other haematological parameters like MCV, Serum Ferritin, TIBC, TLC & Platelets were statistically different between the two groups. (Table: 2).

Stratified analysis revealed that pregnant women were eldest group i-e; in 41-50 years, from urban areas, presented in their second trimester (gest. age 13-24 weeks), and having no children- nulliparous had been affected more from covid-19 (P = 0.271, 0.748, 0.290 & 0.053). Spread of infection through covid-19 contact tracing was present among 57.14% of +ve while 42.86% of covid-19 –ve pregnant women (P = 0.09). (Table: 3).

Further; it was noted that 23.17% of covid-19 +ve pregnant women while 76.83% of the covid-19 –ve women had completed all three ANC visits till term (P = 0.256). (Table: 3).

Finally; it was noted that moderate and severe anaemia was more frequently presented among covid-19 +ve pregnant women than the covid-19 –ve (33.33% & 19.05% versus 30.34% & 13.48%; P = 0.884). Overall; anaemia was more among covid-19 +ve pregnant women than the covid-19 –ve (32.58% & 28.57%; P = 0.884). (Figure: 1).

Table: 1. Descriptive statistics of all enrolled pregnant women (n= 110).

Characteristics/ variables	Mean ± Standard Deviation			Range	t-statistic & P value
	All women	Covid-19 +ve	Covid-19 -ve		
Age (years)	30.3 ± 6.99	31.04 ± 7.65	29.1 ± 7.12	19 - 45	t = -1.107 P = 0.2706
Gestational age (weeks)	28.12 ± 4.66	27.55 ± 5.41	30.19 ± 5.05	20 - 38	t = 2.126 P = 0.0358
Parity	3.4 ± 1.4	3.5 ± 1.5	3.3 ± 1.1	0 - 5	t = -0.696 P = 0.4879
Height (cms)	167.64 ± 14.4	160.19 ± 15.9	159.23 ± 18.7	145 - 189	t = -0.217 P = 0.8284
Weight (Kgs)	81 ± 12.5	86.2 ± 11.1	81.4 ± 13.79	67 - 104	t = -1.484 P = 0.1407
BMI (Kg/ m^2)	27.4 ± 2.31	28.45 ± 2.23	26.55 ± 3.08	21-34	t = -2.663 P = 0.0089
Monthly family income	21399 ± 3490	25100 ± 3545	22031 ± 3003	15000 - 30000	t = -4.067 P < 0.0001

Table: 2. Haematological characteristics of pregnant women (n= 110).

Characteristics/ variables	Mean ± Standard Deviation			Range	t-statistic & P value
	All women	Covid-19 +ve	Covid-19 -ve		
Haemoglobin (g/dL)	9.3 ± 1.71	9.7 ± 2.11	10.54 ± 2.51	6.81 - 13.5	t = 1.419 P = 0.158
MCV (fl)	81.88 ± 5.59	75.52 ± 4.21	83.98 ± 3.41	67.4 – 92.2	t = 9.763 P < 0.0001
Serum Ferritin (ng/mL)	124.9 ± 42.1	151.5 ± 22.15	90.25 ± 10.59	76.41 - 189	t = -18.702 P < 0.0001
TIBC (µmol/L)	38.11 ± 7.71	27.29 ± 5.55	49.90 ± 8.6	39 - 137	t = 11.475 P < 0.001
TLC (/mm^3)	7.11 ± 2.35	11.86 ± 2.21	4.24 ± 1.79	3.84 - 14.44	t = -16.753 P < 0.0001
Neutrophils (%)	77 ± 12.1	84.65 ± 7.23	53.70 ± 5.88	51-95	t = -22.076 P < 0.001
Lymphocytes	23.34 ± 4.41	15.10 ± 2.5	21.31 ± 3.03	31.31 - 5.89	t = 8.709 P < 0.0001
Basophils	0.12 ± 0.04	0.10 ± 0.02	0.14 ± 0.06	0.10 - 0.16	t = 3.007 P < 0.0033
Eosinophils	0.01 ± 0.04	0.10 ± 0.11	0.06 ± 0.01	0.01 - 0.1	t = -3.421 P < 0.0009
Platelets (/mm^3)	175800 ± 23650	160500 ± 12505	189100 ± 39560	15500 ± 20050	t = 21.584 P < 0.0001

Table: 3. Demographic and antenatal characteristics (n = 110).

Characteristic	Covid-19 +ve		Covid-19 -ve		Total	P value
	n	%	n	%		
Age categories						
Upto 20 years	1	14.29	6	85.71	7	chi-square = 3.9047 P = 0.271
21-30 years	6	23.08	20	76.92	26	
31-40 years	8	13.56	51	86.44	59	
41-50 years	6	33.33	12	66.67	18	
	21		89		110	
Residence						
Rural	7	17.50	33	82.50	40	chi-square = 0.103 P = 0.748
Urban	14	20	56	80	70	
	21		89		110	
Gestational age						
Upto 12 weeks	11	18.03	50	81.97	61	chi-square = 2.469 P = 0.290
13-24 weeks	8	27.59	21	72.41	29	
25-36 weeks	2	10	18	90	20	
	21		89		110	
Parity						
Nulliparous	2	50	2	50	4	chi-square = 7.675 P = 0.053
1-2 children	17	23.29	56	76.71	73	
3-4 children	1	3.57	27	96.43	28	
> 5 children	1	20	4	80	5	
	21		89		110	
Covid-19 contact traced						
Yes	20	57.14	15	42.86	35	chi-square = 48.120 P < 0.0001
No	1	1.33	74	98.67	75	
	21		89		110	
Completed ANC visits till term						
1	1	6.67	14	93.33	15	chi-square statistic is 2.718 P = 0.256
2	1	7.69	12	92.31	13	
3	19	23.17	63	76.83	82	
	21		89		110	

Table 4:

Anaemia	Covid-19 +ve		Covid-19 -ve		Total	Test value
	n	%	n	%		
Nil	6	17.14	29	82.86	35	chi-square =0.6517 P value= 0.884
Mild	4	16	21	84	25	
Moderate	7	20.59	27	79.41	34	
Severe	4	25	12	75	16	
Total	21		89		110	

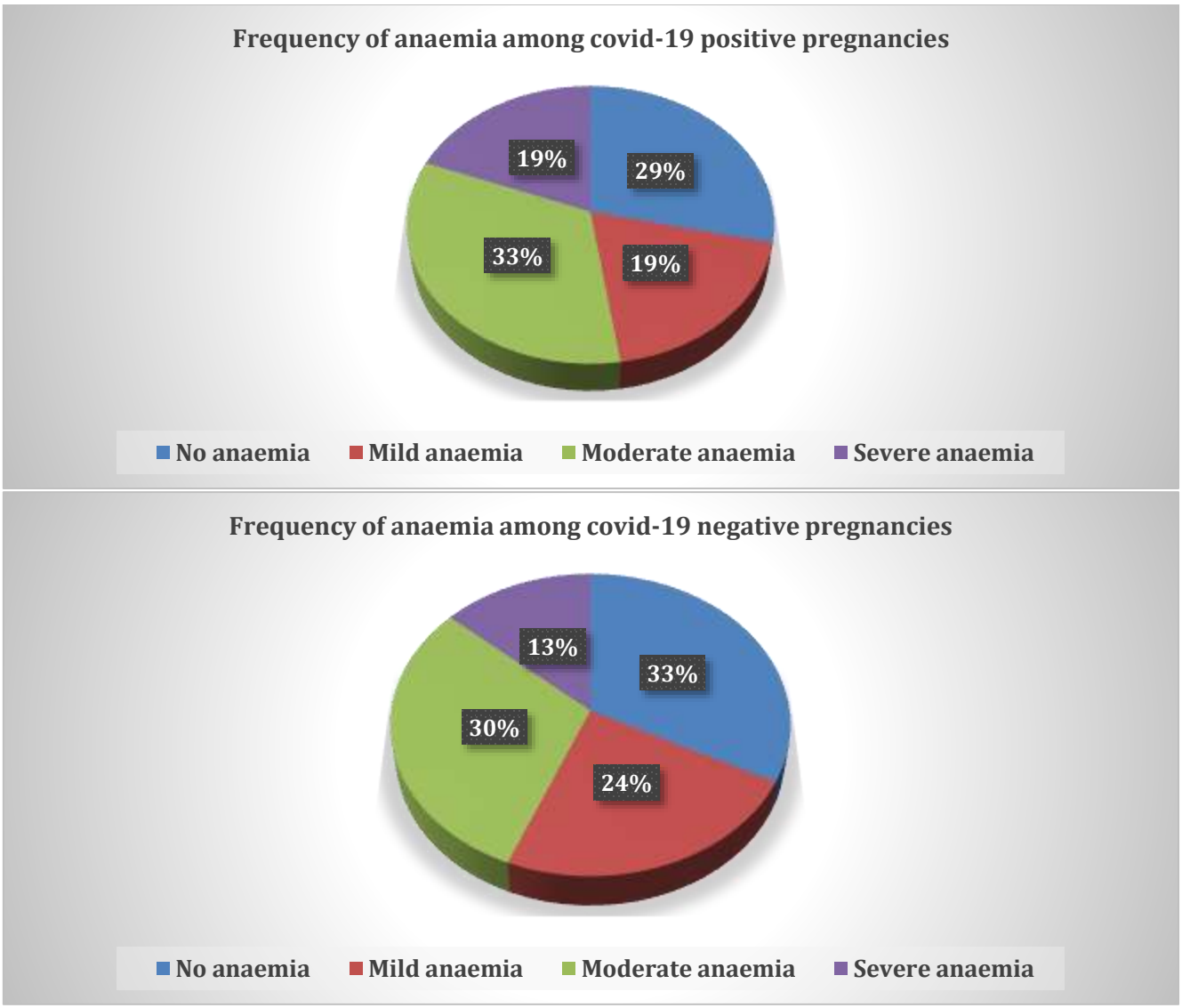

Figure: 1. Frequency of anaemia among pregnant women presenting with or without covid-19 infection (n = 21).

DISCUSSION

Disturbances of haematological parameters especially anemia affects an estimated 1.62 billion people, almost 25% of the world's population. [19,20] Prior to the emergence of the current COVID-19 pandemic, the anaemia was very common and affected two fifths of all pregnancies globally. The current pandemic of covid-19 has increased the extent and ways of this risk especially among developing countries. Therefore, it is crucial to understand the relation between anemia, and progression of COVID-19. Haematological parameters during antenatal care is best part of pregnancy course for this investigation. The current study has focused the prevalence and effects of covid-19 infection on haematology of pregnancy in our local population.

In the current study; the covid-19 infection was detected among 21 (19.09%) pregnant women getting antenatal care. It is also a high alarming rate of covid-19 in pregnancy. Other studies noted that covid-19 infected very high proportion pregnancies.[10,15] In the current study; mean haemoglobin was 9.7 ± 2.11 g/dL in covid-19 +ve women which was lower than the 10.54 ± 2.51 g/dL of covid-19 -ve (P = 0.158). Few other studies also noted that the covid-19 infection was associated with a lower Hb among pregnant women.[6,12,15,21] Further; we noted that overall; anaemia was more frequent and more severe among covid-19 +ve pregnancies than the covid-19 –ve (32.58% & 28.57%; P = 0.884). A study from Iran reported that among covid-19 positive patients there was a higher prevalence of anaemia which increased the morbidity and eventually led to poor outcomes. [22] A study by Tao Z, et al., found that the odd ratio of anemia related to the severe condition of covid-19 was 3.47 (95% confidence interval: 1.02-11.75; P = 0.046).[16] It is estimated that there will be an additional 2.1 million pregnancies with any form of anaemia in the 118 countries in 2020-2022 compared with 2019. [23] This raises the significance of alarming situation which can come across the healthcare systems.

Serum ferritin level tend to increase in covid-19 infection and similar was observed in current study where; a very significant difference of serum ferritin was noted among covid-19 +ve and covid-19 -ve women (151.5 ± 22.15 versus 90.25 ± 10.59; P < 0.0001). A meta-analysis suggests that hemoglobin and ferritin levels vary according to the severity of COVID-19 as well as age, gender and presence of comorbidity among COVID-19 patients. Taneri PE, et al., also noted change in serum levels ferritin was noted between the covid-19 positive and negative patients however; Hb did not differed much. [24] Whether hemoglobin and ferritin can be used for prognostic purposes, or have further implications for identifying novel treatment targets, needs further investigation.

It was an expected finding that mean levels of leucocyte/ neutrophils counts were significantly much higher among covid-19 positive pregnant women compared to covid-19 negative (P < 0.0001). Furthermore; lymphocytes, basophils, eosinophils and platelets counts differed significantly between the two groups. Other studies have found similar finding of increased leucocyte/ neutrophils counts among covid-19 positive patients.[25,26,27]

There was no any significant difference in mean ± SD age of the two groups (30.3 ± 6.99 years) however; it was noted that mainly 41-50 years of age group was more affected with covid-19. One reason to this may be elder age however; it needs more exploration. Urban women were more affected. Covid-19 was more frequent in the second trimester and the nulliparous women.

More the women completed all ANC visits more was the chance of being detected covid-19 +ve. This may be due to their repeated testing.

It was noted that more cases of severe anaemia were found to have Covid-19 +ve which re-iterates the findings that covid-19 infection has some negative affect on haemoglobin level in pregnancy. Studies have reported that presence of anaemia superimposed with covid-19 infection leads to elevated risk of ICU admission (27.8% vs. 14.71%) and death (23.9% vs. 13.8%) than the non-anaemic covid-19 positive patients (P < 0.001).[20] Therefore; it highlights the importance of fact that these women should be monitored and supported throughout the course of pregnancy.

In current study we found that; mean BMI of covid-19 negative was significantly (P = 0.0089) lower than the covid-19 positive women (26.55 ± 3.08 versus 28.45 ± 2.23). The projected calculations by Osendarp S, et al., reported that an additional 2.1 million children will be born to women with a low BMI (optimistic = 1.4 million; pessimistic = 3.0 million) in 2020-2022 which to some extent may be due to covid-19 effects.[21]

The most frequent type of obstetric anaemia is iron deficiency anaemia (IDA), both worldwide and in developed countries. Covid-19 increases the chances of it as well as severity of impending complications. Therefore; the diagnosis of iron deficiency should be made according to local protocols and managed with oral iron supplementation. In the current study we have highlighted a number of potential biomarkers of anemia and iron metabolism that may help identify those patients at greatest risk for severe COVID-19 outcomes. Future studies should explore the impact of iron metabolism and anemia in the pathophysiology, prognosis, and treatment of covid-19.

The study was designed as a cross sectional, single center study where majority of participants were from rural areas therefore; the results of this study may be referred carefully as might not be generalizable to larger populations.

CONCLUSION

Pregnancies are always threatened by presence of anaemia. Appearance of pandemic covid-19 has increased this risk. Women in developing countries and living in rural areas are facing the synergistic effect of these two conditions. Pregnant women presenting with convid-19 have more deepened level of anaemia than those who are not infected from covid-19. Already prevalent anaemia during pregnancy tends to worsen in women getting infected of covid-19. Maternal healthcare professionals need to be extra vigilant to the hemoglobin levels of pregnant women during antenatal care till delivery in the era of covid-19.

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