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Retrospective Analysis of Hematological Parameters in Covid Positive Pregnancy

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ABSTRACT

The newly identified SARS-CoV-2 virus and its ongoing implicated COVID-19 pandemic started off as pneumonia of unknown aetiology in Wuhan, China, in December 2019. Certain laboratory values that may be considered deranged in non pregnant states are normal physiological changes in pregnancy. An understanding of the normal haematological and immunologic parameters in pregnancy is necessary for the interpretation of COVID-19 severity. Considering the COVID-19 infection is still new, little is known about the clinical course of the disease in pregnancy. This is a retrospective observational study undertaken in the Department of Obstetrics and Gynaecology, Saveetha Medical College Hospital, Chennai, India, from April to November 2020. Out of the 50 women in the study, 19 women were anaemic with haemoglobin <11, accounting for 38% of the study population. A neutrophil to lymphocyte ratio greater than 4.5 was observed in 44% of the population. Thrombocytopenia was present in 12% of the population. D-dimer greater than 1000 was found in 12% of the study population. All of our patients were asymptomatic, had good maternal and fetal outcomes even though derangement of inflammatory markers were noted. The immunological changes of pregnancy make pregnant women more susceptible to pathogens. Though our patients had instances suggestive of critical prognosis like an increased neutrophil-lymphocyte-ratio and affirmative acute phase reactants and inflammatory markers, they were asymptomatic (category BNH) and stable in room air. However, further analysis of laboratory parameters and their correlation to clinical scenarios in the second wave of COVID19 infection is warranted.

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INTRODUCTION

The newly identified SARS-CoV-2 virus and its ongoing implicated COVID19 pandemic started off as pneumonia of unknown aetiology in Wuhan, China, in December 2019 (Syeda *et al.*, 2020).

The outbreak was declared a public health emergency of international concern by the World health organisation in January 2020 and was declared a pandemic in March 2020. The disease ranges across a wide spectrum, including asymptomatic states, flu like illnesses and the most dreaded severe infections that may require critical care. As of January 2021, the infection has crippled the world, leaving 100 million people in its wake (CDC, 2020).

Pregnancy is considered to be an immune-modulated state with suppression of various humoral and cell-mediated immunological functions. The foetus contains both ”foreign” paternal antigens and maternal host antigens; hence this shift to an anti inflammatory stage stops any potential rejection of the foetus and allows the pregnancy to continue.

However, this suppression of the natural immune response in pregnancy potentiates an increased susceptibility to infections. The pregnant women population are therefore included in the list of people at a moderate risk to COVID19 infections (clinically vulnerable) based on RCOG guidelines (Royal College of obstetricians and gynaecologists, 2020).

Considering the COVID19 infection is still new, little is known about the clinical course of the disease in pregnancy. Few literature studies are available on the interpretation of laboratory values in pregnancy (Qiao, 2020; Chen *et al.*, 2020a). Also, more data from other regions of the world are needed better to define laboratory abnormalities in pregnant women with COVID-19 infection (Novel Coronavirus, 2019). Pregnancy factors should also be considered when dynamically monitoring changes of laboratory indicators in pregnant women with COVID-19.

Certain laboratory values that may be considered deranged in non pregnant states are normal physiological changes in pregnancy (Chen *et al.*, 2020b; Vaught and Halscott, 2020). White blood cell counts up to 15000 are considered normal, and this value may go up to 25000 in labour and the immediate post-partum period. There is also an increase in inflammatory markers and acute phase reactants like C- Reactive protein and ESR. Pregnancy is also a pro-coagulant state with a higher level of fibrinogen when compared to the non pregnant population (range 300 to 600 mg/dl).

METHODOLOGY

This was a retrospective descriptive observational study undertaken in the Department of Obstetrics and Gynaecology, Saveetha Medical College Hospital. After receiving ethical clearance, medical records of COVID positive pregnant and postnatal women admitted to the Department of Obstetrics and Gynaecology, Saveetha Medical College Hospital were obtained. Women with chronic illnesses like liver and kidney diseases were excluded. A total of 50 women with COVID19 infection were included for the study and the following haematological parameters were analysed, including complete blood count, D-dimer, CRP, ESR and Ferritin with pregnancy specific values. Data were entered in Microsoft Excel and statistical analysis was done with SPSS version 17.

RESULTS

Table 1: Descriptive Analysis

Variable	Mean	Std. Deviation	N
Hb	11.330	1.4293	50
TLC	10662.80	3760.201	50
Neutrophil	74.332	7.6949	50
Lymphocyte	20.096	7.0636	50
D-dimer	1141.27	1088.662	22
CRP	44.07	36.444	14
Ferritin	48.96	64.450	11
ESR	54.32	27.480	14

Out of the 50 women in the study population, 38% were primigravidas and 62% were multigravidas (Figure 1). 34% of the population had gestational age below 37 weeks (6% first trimester, 4% second trimester, 24% third trimester). 66% were term gestation.

6% of women had gestational diabetes mellitus (GDM), 4% women had gestational hypertension (GHTN) and 4% women had GDM and GHTN. Of the total 50, 1 patient was diagnosed with obstetric cholestasis and 1 patient had a history of hypothyroidism.

Out of the 50 women in the study, 19 women were diagnosed to be anaemic with haemoglobin less than 11g/dL, accounting for 38% of the study population (Figure 2). The mean Hb was 11.33g/dL

24% were diagnosed with mild anemia (Hb10.9-10g/dL) and 14% were diagnosed with moderate anemia (Hb 7.1-9.9g/dL) (Figure 3).

The total leucocyte count was found to be greater than 11000 cu. mm in 21 patients accounting for 42% of the population. 10% of the population had total counts greater than 15000 cu. mm. 44% of the population (22 of 50) had a Neutrophil to lymphocyte ratio greater than 4.5 (Figure 4). The average neutrophil to lymphocyte ratio in COVID positive patients was found to be 4.514.

Thrombocytopenia (platelets <150000 cu.mm) was found in 12% of the population (6 of 50). The D-dimer level was greater than 1000ng/ml in 6 women, 12% of the study population.

C reactive protein was evaluated and 28% of women (14 of 50) had values greater than 5mg/L (CRP positive). One patient had CRP >100mg/L, which

Table 2: Correlations

		Hb	TLC	Neutrophil	Lymphocyte	D-dimer	CRP	Ferritin	ESR
Hb	Pearson correlation	1	-.154	-.173	.202	.121	.174	.285	-.199
	Sig. (2 tailed)		.285	.230	.160	.592	.552	.396	.494
	N	50	50	50	50	22	14	11	14
TLC	Pearson correlation	-.154	1	.475**	-.482	.339	-.173	.046	.303
	Sig. (2 tailed)	.285		.000	.000	.123	.555	.892	.293
	N	50	50	50	50	22	14	11	14
Neutrophil	Pearson correlation	-.173	.475**	1	-.973**	.279	-.450	-.118	.121
	Sig. (2 tailed)	.230	.000		.000	.208	.107	.730	.681
	N	50	50	50	50	22	14	11	14
Lymphocyte	Pearson correlation	.202	-.482**	-.973**	1	-.258	.438	.136	-.140
	Sig. (2 tailed)	.160	.000	.000		.245	.118	.689	.632
	N	50	50	50	50	22	14	11	14
D dimer	Pearson correlation	.121	.339	.279	-.258	1	-.404	.160	-.020
	Sig. (2 tailed)	.592	.123	.206	.245		.218	.639	.953
	N	22	22	22	22	22	11	11	11
CRP	Pearson correlation	.174	-.173	-.450	.438	-.404	1	.637	.019
	Sig. (2 tailed)	.552	.555	.107	.118	.218		.248	.961
	N	14	14	14	14	11	14	5	9
Ferritin	Pearson correlation	.285	.046	-.118	.136	.160	.637	1	.179
	Sig. (2 tailed)	.396	.892	.730	.689	.639	.248		.671
	N	11	11	11	11	11	5	11	8
ESR	Pearson correlation	-.199	.303	.121	-.140	-.020	.019	.179	1
	Sig. (2 tailed)	.494	.293	.681	.632	.953	.961	.671	
	N	14	14	14	14	11	9	8	14

**Correlation is significant at the 0.01 level (2 tailed)

Table 3: Socio demographic data

Parity	Percentage
Primigravida	19
Multigravida	31
Gestational age	
Below 37 weeks	17
Above 37 weeks	33
No. of gestation	
Singleton	49
DCDA twins	1
Chronic disease	
Gestational diabetes mellitus	3
Gestational hypertension	2
Both GDM and GHTN	2
Hypothyroid	1
Obstetric cholestasis	1

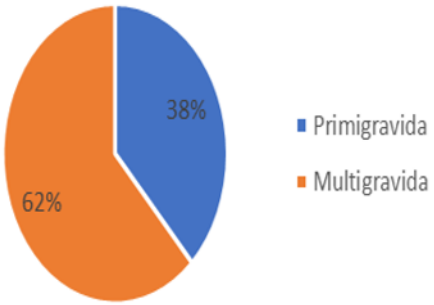

Figure 1: Parity

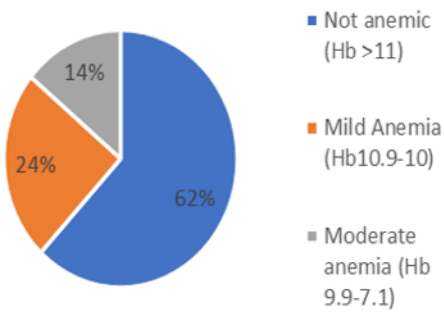

Figure 2: Prevalence of Anemia

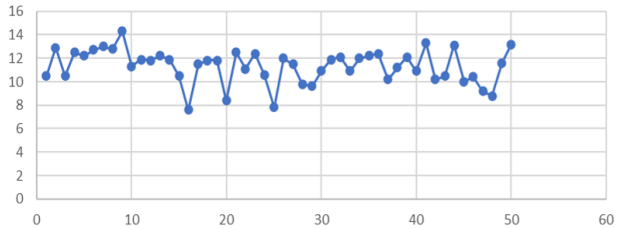

Figure 3: Haemoglobin Range

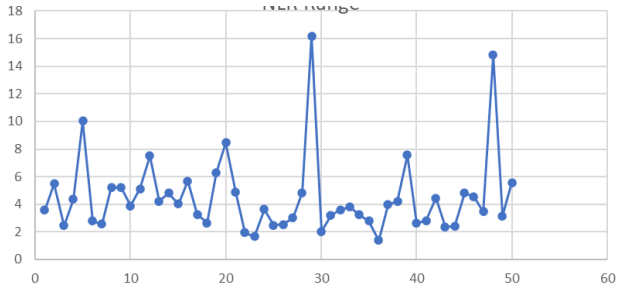

Figure 4: NLR Range

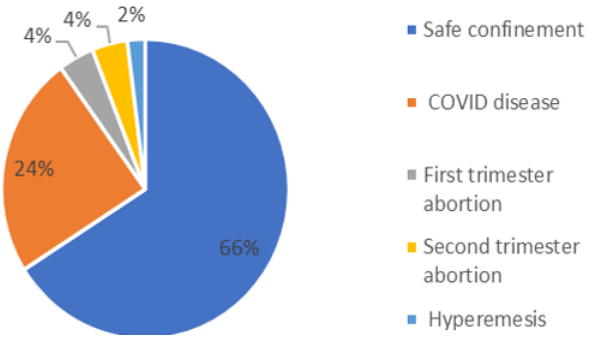

Figure 5: Reason for Admission

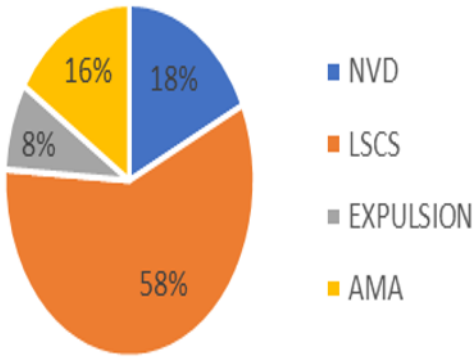

Figure 6: Outcome of Pregnancy

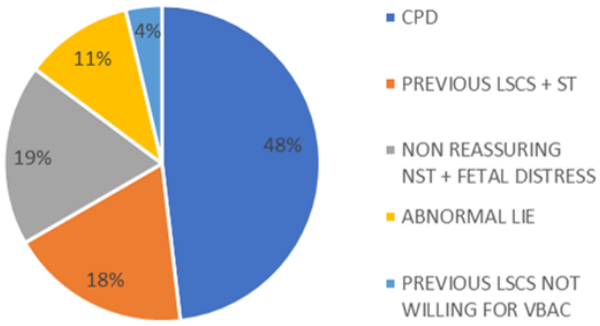

Figure 7: Indication for LSCS

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denoted increased severity of infection but was asymptomatic. ESR was elevated (>20mm/hr) in 24% of population (12 of 50). Ferritin >15 was found in 10% of the population (5 of 50), (Tables 1 and 2)

66% population was admitted for safe confinement, 24% for management of COVID19 disease, 4% for first trimester abortion, 4% for second-trimester abortion and 2% for management of hyperemesis Figure 5.

Of the 50 COVID positive patients, 18% underwent labour natural with episiotomy, 58% underwent Lower segment Caesarean section, 8% had missed miscarriage followed by suction evacuation and 16% were discharged against medical advice Figure 6. The indications for LSCS were CPD in labour (44%), Non reassuring NST and fetal distress (17%), previous LSCS with scar tenderness (17%), Abnormal lie (10%) and Previous LSCS not willing for VBAC (2%) Figure 7.

DISCUSSION

The analysis of the laboratory value in COVID19 infected pregnant women and its proper interpretation is essential when following the course of the disease, keeping a watchful eye for rapid deterioration and formulating better management plans (Syeda *et al.*, 2020). Even interpreting basic haematological parameters becomes a challenge when two dynamic variables play; both pregnancy itself and then superimposed COVID19 infection

Anaemia in pregnancy (Hb<11) is a public health problem in India, affecting 63% of the gravid population. In our study, 24% were diagnosed with mild anaemia (Hb10.9-10g/dL) and 14% were diagnosed with moderate anaemia (Hb 7.1-9.9g/dL) Considering COVID19 infection, which is an inflammatory state could further precipitate anaemia due to abnormalities in iron metabolism, shunting of body iron stores for production of pro inflammatory cytokines. These cytokines further cause inhibitory action on myeloid and especially erythroid precursors, which manifests as anaemia (Bergamaschi *et al.*, 2021). The literature review on the incidence of anaemia in COVID19 positive pregnancy was limited Table 3.

Leukocytosis, is a normal physiological response in pregnancy. The stress of pregnancy accounts to increased bone marrow drive that promotes both leukopoiesis and erythrocytes. There is a further spike in leukocyte count during parturition as labour is a pro inflammatory state (Molberg *et al.*, 1994). The viral infection in COVID19 precipitates a systemic inflammatory response and cytokine storm, which manifests as Leukocytosis (Yang *et al.*, 2020). In contrast to the literature review, a retrospective analysis of haematological parameters revealed leukocytosis above 15,000 was observed only in 10% of COVID19 positive women (Yang *et al.*, 2020) and all were asymptomatic.

The Neutrophil: Lymphocyte ratio is a biomarker that can easily be derived by dividing the total number of neutrophils by the total number of lymphocytes (Imran *et al.*, 2021).

The Neutrophil: Lymphocyte ratio (NLR) is an indication of the body's systemic inflammatory response and hence can signify the severity of COVID19 infection (Li *et al.*, 2020).

For the purpose of our study, we took NLR> 4.5 as our cutoff value (low threshold). Increased neutrophil: lymphocyte ratio is indicative of adverse prognosis. In our study, despite the N/L ratio was more than 4.5 in 44% of the patients, all were asymptomatic. This is in accordance with the literature (Cheng *et al.*, 2019).

The exact cause of thrombocytopenia in COVID19 infection is not known. One theory is that the SARS-CoV-2 virus causes bone marrow suppression and reduces platelet production (megakaryocytosis). Our results were comparable to the study done by (Gouez *et al.*, 2020).

The elevated D-dimer in COVID19 infection signifies a hyperfibrinolysis and increased inflammatory burden state (Yao *et al.*, 2020). The above parameters are indicative of the prothrombotic state of the COVID infection. Literature review showed corresponding elevated levels of D-dimer in COVID19 infection (Lokken *et al.*, 2021). In our study, during the first wave, even though 12% of women had Ddimer > 1000, all were asymptomatic.

Acute phase reactants are increased in both pregnancy and COVID19 Infection (Waites *et al.*, 2019; Yormaz *et al.*, 2020).

Increased C Reactive protein level indicated increased severity. Even though one patient had CRP >100mg/L, she was asymptomatic.

The increased incidence of LSCS as a mode of delivery in our COVID19 population is similar to other studies (Giaxi *et al.*, 2020).

CONCLUSIONS

The immunological changes of pregnancy make pregnant women more susceptible to pathogens and complications. Though our patient's population had instances suggestive of critical prognosis

like increased neutrophils: lymphocyte ratio and affirmative acute phase reactants and inflammatory markers, our patient population was asymptomatic (category BNH) and stable in room air. A similar severity scale for assessment of pregnant patients with COVID 19 (mild, moderately severe and critical) was put forth by the Society of Maternal and Fetal Medicine. However, further analysis of laboratory parameters and its correlation to clinical scenarios in the second wave of COVID19 infection is warranted.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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