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Original Article

Obstetrics and Gynaecology Section

Comparison of the Haematological and Psychological Parameters between COVID-19 Positive Pregnant and Non Pregnant Female: A Case-control Study from Tertiary Care Centre, Puducherry, India

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ABSTRACT

Introduction: Pregnancy is associated with lot of physiological and psychological changes, and it becomes important to study these changes in the background of COVID-19. A simple Complete Blood Count (CBC) can help to indicate the COVID-19 disease severity.

Aim: To understand the differences in the haematological and psychological parameters between COVID-19 infected pregnant females and age-matched non pregnant COVID-19 infected females.

Materials and Methods: This case-control study was conducted in Department of Obstetrics and Gynaecology, Indira Gandhi Medical College and Research Institute, Puducherry, India, from October 2020 to December 2020. Data collection was in an ambispective manner. Haematological values {Total Leukocyte Count, neutrophil, lymphocyte, Neutrophil-Lymphocyte ratio (NLR) and Red Cell Distribution Width (RDW)} were obtained from routine CBC and for the psychological component (scales-beliefs, practices for prevention of infection, fear, global) a pre-tested validated questionnaire was used. The questionnaire used the Likert scale and comprised of a total of 29 questions with a maximum score of 145. These scales analysed psychological apprehensions in general population and its impact on pregnancy and reproductive health of women. Categorical variables were expressed as mean±Standard Deviation (SD). Student t-test was used for comparison of means.

Results: The present study included 80 participants with 40 in each of the pregnant and non pregnant group. The total leukocyte count, neutrophil, lymphocyte, NLR and RDW were the haematological parameters with statistically significant difference between the two groups (p-value <0.001). While the mean total score of COVID-19 psychological impact in the COVID-19 pregnant women was 79.42±20.18 and higher in COVID-19 non pregnant women (88.92±20.77).

Conclusion: The significant difference in the haematological parameters of both the groups indicates the differential impact of COVID-19 in pregnant women. 'Coronaphobia' is on the rise and addressing this concern is important for holistic delivery of healthcare in patients.

Keywords: Behaviour-prevention practice, Caesarean section, Coronavirus disease-2019, Coronaphobia, Neutrophil-Lymphocyte ratio, Red cell distribution width

INTRODUCTION

The entire globe is fighting against the novel Coronavirus pandemic-Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Ideally, for any infectious condition, to contain its transmission, it is important to know the target populations for active interventions. One such secluded group is the cohort of pregnant women [1]. Pregnancy is known to have multitudes of physiological changes which make them to be disproportionately affected by respiratory infections there by increasing the morbidity and mortality profile. The previous pandemics by Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Symptoms (MERS) are a proof to this undoubted fact [2-4].

Coronavirus disease-2019 (COVID-19) infection has a congregation of symptoms reshaping all the blood parameters [5]. The most crucial and easily accessible change is the change in the haematological parameters in blood [6,7]. The haematological indices have been studied constructively and have been successfully used as early indicators of severity of COVID-19 infection and as early biomarkers for cytokine/inflammatory storms in such patients which are the most important cause of morbidity in COVID-19 patients. Bearing the background physiological changes in mind, it becomes absolutely important to study the differences in such parameters to frame and form distinct cut-off for such parameters in pregnant females infected with COVID-19 infection. So, studying these parameters is of paramount importance.

With the ongoing pandemic, there is a constellation of fears present in all the patients. Fear of social distancing, ongoing lockdowns, economic depressions, stigmas from the society and info emic fear instilled by media have all added to the apprehensions and a new terminology called 'Coronaphobia' is on the rise [8]. Studies have also suggested that these fears or the odds of developing such fears are more in the female gender than the male, making them a vulnerable population to mental stress and trauma [9]. When all of these are added with pregnancy, they reach a new high level. It is also documented that these fears and apprehensions could lead on to mediate depression and they could also trigger future career anxiety [10]. It is also a well-known fact that mental health during pregnancy affects foetal development and also hinders with physiological process of pregnancy including delivery and breast feeding. These apprehensions could be different between a pregnant and a non pregnant female. Thus, understanding those key raw areas and addressing those fears in the antenatal period is a crucial step in giving holistic approach to maternal and child health [11].

Studies have also shown that, minor surgical interventions can provoke severity in the course of COVID-19 infection [12]. Though,

caesarean section is reserved only for obstetric indications in COVID-19 infected mothers, these could trigger the severity of the illness. One of the early predictors of severity of the illness is the Neutrophil Lymphocyte Ratio (NLR) and Red Cell Distribution Width (RDW). So, it becomes important to study the salient effect of a surgical intervention on these parameters [13]. Thus, the study aimed to understand the differences in the haematological and psychological parameters between antenatal COVID-19 infected pregnant female and age-matched non pregnant COVID-19 infected females.

MATERIALS AND METHODS

This case-control study was conducted in Department of Obstetrics and Gynaecology, Indira Gandhi Medical College and Research Institute (tertiary healthcare government hospital, designated as the state exclusive COVID-19 hospital), Puducherry, India, from October 2020 to December 2020. Institute Human Ethics Committee (IEC) clearance was obtained prior to start of the project (Reference No: 265/IEC No.-29/PP/2020). Convenience sampling was followed and a total of 80 participants, with 40 in each group (pregnant and non pregnant, respectively) were included in the study.

Inclusion and Exclusion criteria: All COVID-19 positive participants who gave the consent to participate in the study were included. Patients with known psychiatric illness and any co-morbidities which would affect the basic Complete Blood Count (CBC) parameters like patients with hypertensive disorders, chronic kidney disease and chronic liver disease were excluded from both the groups.

Parameters

The study tools included a participant record form to collect data on their socio-demographic details, menstrual history. For the non pregnant women only previous obstetric history (if applicable) and menstrual history were obtained.

Haematological parameters: Red Blood Cells, Total leukocyte count, Neutrophils, Lymphocytes, Neutrophil/Lymphocytes ratio, Basophils, Monocytes, Eosinophils, Haemoglobin, Mean corpuscular volume, Red cell distribution width, Mean corpuscular haemoglobin, Mean corpuscular haemoglobin concentration, Platelets, Packed Cell Volume.

Psychological evaluation: A pretested questionnaire was used after validating with a pilot test. The questionnaire comprised of a total of 30 questions with 29 on various components and one general question on feedback of participation:

a) Belief scales with regards to COVID-19 information-4 [3],

b) Behaviour scales for COVID-19 infection prevention control practices and information-8 [3],

c) Fear of COVID-19 scale or apprehension factor-10,

d) Global question relating to COVID-19 infection [14], pregnancy and women health-7,

e) Feedback question-1.

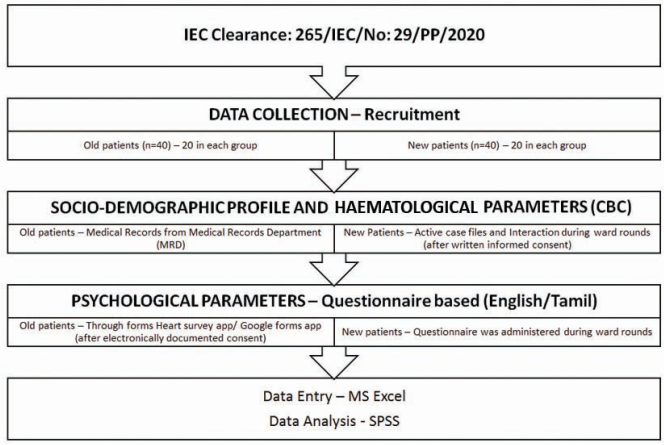
Each of the questions had five options in Likert scales with a maximum score of 5 and a minimum score of 1.

The study tools were prepared taking into view the previously published literatures on the topic of interest along with incorporating inputs from the subject experts [14]. Face and content validity were ensured. The pilot study comprised of a total of 30 participants with 15 in each group. The results of the pilot study were not included in the present study.

Of the 80 participants, we had 40 previously treated patients and 40 new patients with 20 each in the pregnant and non pregnant groups of both the cohorts.

Procedure

For the previously treated patients, list of COVID-19 infected pregnant females and age matched COVID-19 positive non pregnant females were obtained from the hospital census/statistical department. The socio-demographic data, haematological parameters were obtained from their case files in the Medical Records Department (MRD). For the psychological analysis, the questionnaire was administered through the computerised electronic channel system. A proper electronic documented informed consent form and an e-questionnaire were prepared in both, local vernacular language and English, using the Google forms app/Forms Heart survey app. All these participants were contacted over phone and after explaining the procedure, a verbal consent was obtained to share the questionnaire evaluating the psychological component. Based on their convenience, the e-questionnaire and e-consent form was sent to them through e-mail/WhatsApp. The choice of language was given to the participants and each participant was given a total time of 45 minutes to fill the form. For participants who lacked technological support, a trained interviewer received their responses after due consent through voice calls [Table/Fig-1].



[Table/Fig-1]: Flowchart depicting the methodology of data collection.

For the new patients, 20 each in both the pregnant and the non pregnant group, an informed written consent was obtained, and their basic data was obtained using the participant record form during the routine rounds. All the haematological parameters were procured from the routine CBC's done for these patients. The vitals at the time of admission were documented. For the psychological component, a questionnaire in the pen and paper format was given to the participants to receive their response. Help from the trained interviewers were sort for participants finding difficulty.

STATISTICAL ANALYSIS

All the responses were entered and analysed in Microsoft Excel software version 2020 and were analysed using Statistical Package for the Social Sciences (SPSS) software version 16.0. Continuous variables were expressed as Means±SD and categorical variables as percentages and proportions. Student t-test was used for comparison of means.

RESULTS

In the present study, total 40 participants each from the pregnant and the non pregnant cohort was taken. The mean age of the pregnant group was 23.8±3.2 years and of the non pregnant group was 25±4.1 years (p-value 0.213, non significant). With regards to the presenting symptomatology, 40% (n=32) of the total population presented with cough and 40% (n=32) were asymptomatic [Table/Fig-2].

[Table/Fig-3] shows neutrophil, lymphocyte, NLR and total leucocyte count are the parameters with statistical significance (p-value ≤0.05).

Interestingly, the fear of COVID-19 seemed to predominate in the non pregnant group (29.05±12.89) in comparison to the pregnant group (24.72±13.33) [Table/Fig-4].

Parameters		Pregnant women N (%)	Non pregnant women N (%)	Total N (%)
Asymptomatic	Yes	21 (52.5)	11 (27.5)	32 (40)
	No	19 (47.5)	29 (72.5)	48 (60)
	Total	40 (100)	40 (100)	80 (100)
Sore throat	Present	15 (37.5)	10 (25)	25 (31.3)
	Absent	25 (62.5)	30 (75)	55 (68.8)
	Total	40 (100)	40 (100)	80 (100)
Cough	Present	11 (27.5)	21 (52.5)	32 (40)
	Absent	29 (72.5)	19 (47.5)	48 (60)
	Total	40 (100)	40 (100)	80 (100)
Cold	Present	8 (20)	15 (37.5)	23 (28.8)
	Absent	32 (80)	25 (62.5)	57 (71.3)
	Total	40 (100)	40 (100)	80 (100)
Headache	Present	3 (7.5)	11 (27.5)	14 (17.5)
	Absent	37 (92.5)	29 (72.5)	66 (82.5)
	Total	40 (100)	40 (100)	80 (100)
Fever	Present	5 (12.5)	20 (50)	25 (31.3)
	Absent	35 (87.5)	20 (50)	55 (68.8)
	Total	40 (100)	40 (100)	80 (100)
Diarrhoea	Present	0 (0)	5 (12.5)	5 (6.3)
	Absent	40 (100)	35 (87.5)	75 (93.8)
	Total	40 (100)	40 (100)	80 (100)
Chest pain	Present	0	2 (5)	2 (2.5)
	Absent	40 (100)	38 (95)	78 (97.5)
	Total	40 (100)	40 (100)	80 (100)
Breathlessness	Present	0	4 (10)	4 (5)
	Absent	40 (100)	36 (96)	76 (95)
	Total	40 (100)	40 (100)	80 (100)
Contact history	Present	5 (12.5)	11 (27.5)	16 (20)
	Absent	35 (87.5)	29 (72.5)	64 (80)
	Total	40 (100)	40 (100)	80 (100)

[Table/Fig-2]: Distribution of symptoms of COVID 19 among the study population.

Parameters	Group	N	Mean±SD	t-value	p-value
Red blood cells (10^6/uL)	Pregnant woman	40	4.41±1.53	0.409	0.684
	Non pregnant woman	40	4.51±0.37		
Total leukocyte count (10^3/uL)	Pregnant woman	40	10080.00±3571.76	3.391	0.001*
	Non pregnant woman	40	7835.20±2183.27		
Neutrophils (%)	Pregnant woman	40	75.82±6.85	5.005	0.001*
	Non pregnant woman	40	64.75±12.20		
Lymphocytes (%)	Pregnant woman	40	18.02±6.36	6.325	0.001*
	Non pregnant woman	40	30.15±10.31		
Neutrophil/ Lymphocytes ratio (%)	Pregnant woman	40	5.30±4.16	3.580	0.001*
	Non pregnant woman	40	2.70±1.96		
Basophils (%)	Pregnant woman	9	1.55±0.72	-	-
	Non pregnant woman	0	-		
Monocytes (%)	Pregnant woman	40	3.40±2.09	0.830	0.409
	Non pregnant woman	34	3.05±1.25		
Eosinophils (%)	Pregnant woman	36	2.44±1.05	0.042	0.967
	Non pregnant woman	37	2.43±1.38		
Haemoglobin (g/dL)	Pregnant woman	40	11.69±1.19	1.111	0.270
	Non pregnant woman	40	11.97±1.01		
Mean corpuscular volume (fL)	Pregnant woman	40	85.00±10.40	1.125	0.264
	Non pregnant woman	40	82.83±6.41		
Red cell distribution width (fL)	Pregnant woman	40	12.53±2.64	11.001	0.001*
	Non pregnant woman	40	7.79±0.68		
Mean corpuscular haemoglobin (pg)	Pregnant woman	40	28.63±3.15	3.134	0.002
	Non pregnant woman	40	26.57±2.71		
Mean corpuscular haemoglobin concentration (g/dL)	Pregnant woman	40	32.38±0.86	2.579	0.012
	Non pregnant woman	40	31.74±1.31		
Platelets (10^3/ uL)	Pregnant woman	40	195827.50± 72487.07	1.757	0.083
	Non pregnant woman	40	221275.00± 55982.13		
Packed cell volume (%)	Pregnant woman	40	36.75±3.14	2.001	0.049
	Non pregnant woman	40	38.09±2.87		

[Table/Fig-3]: Haematological parameters and the variations between the pregnant and the non pregnant group.
*Statistically significant p-value of less than <0.05; p-value was calculated by using t- score and z-score using online algorithms and was cross verified by hand method using t-distribution

Parameter	Group	Mean±SD	t-value	p-value
Belief scales	Pregnant woman	13.50±4.43	1.073	0.287
	Non pregnant woman	14.50±3.88		
Behaviour-prevention practice	Pregnant woman	20.80±4.96	0.942	0.349
	Non pregnant woman	21.85±5.00		
Fear scales	Pregnant woman	24.72±13.33	1.474	0.144
	Non pregnant woman	29.05±12.89		
Global question relating to COVID-19 infection	Pregnant woman	20.40±9.95	1.455	0.150
	Non pregnant woman	23.52±9.24		
Total	Pregnant woman	79.42±20.18	2.074	0.041
	Non pregnant woman	88.92±20.77		

[Table/Fig-4]: Various Psycho-social parameters assessed in the study group and their mean values.

DISCUSSION

The present study included 80 participants with 40 in each cohort. The most common disorder associated with pregnancy in the present population was identified as hypothyroidism (n=11, 27.5%). The other disorders noted in the pregnant women included malpresentations (n=3, 7.5%). Though Pregnancy Induced Hypertension (PIH) and Gestational Diabetes Mellitus (GDM) are commonly spoken off in the context of medical disorders complicating pregnancy, hypothyroidism is equally a medical disorder encountered in pregnancy. The present study agrees with the conclusion of the study by Yadav V et al., in recommending universal screening for thyroid dysfunctions among the antenatal population, considering maternal hypothyroidism is a preventable cause of mental retardation/sub normality in the offspring [15]. In the present study the total leukocyte count, neutrophil, lymphocyte, NLR and RDW were the haematological parameters with statistical significance (p-value <0.005). The total of COVID-19 psychological impact scale is higher in non pregnant group.

The finding of the present study is on a cross with the report by Dashraath P et al., [4]. Fever (84%) was the most common symptom reported among their study group while in the present study asymptomatic women topped the list alongside cough as

a presenting symptom. Also, in his study, 38% of the population had leukocytosis and in the present study 40% of the pregnant women had leukocytosis (total leukocyte count >11,000 cells/mm^3). Similarly, 13% had thrombocytopenia in his study while its 15% in the current study (platelets <1,50,000 cells/ mm^3). Despite a larger sample size in the present study, the percentages remain similar, which indicates that the presentation in a pregnant COVID-19 infected female with regards to haematological parameters is strikingly unique from a non pregnant female and despite geographic and racial changes in the study settings, the blood picture remains similar.

Further, majority of pregnant women in the present study were asymptomatic which is on a cross with the findings of Liu Y et al., study, where fever was the most common symptom (77%) [7].

In the study conducted by Shi S et al., NLR has been found to be an indicator for severity of infection [16]. The values between severely infected patients and non severe group were statistically significant. Similarly, the mean value of NLR of severe group (9.95) was found to be higher than the non severe group (2.24). Even in the present study, the mean NLR of pregnant group (5.30) was found to be higher than the non pregnant group (2.70). It is interesting to note that, the non pregnant group and the non severe group of their study are on consensus. This indirectly reflects, pregnancy can be considered a group with plausible severity of infection. The present study seconds the finding of haematological changes appreciated in the study by Liu Y et al., and Ponti G et al., [7,8]. There is a statistical significance in the NLR. This means separate cut-offs for pregnant women is necessary and these finding mandates further evaluation in this regard.

Also, in the study taken up by Wang C et al., NLR and RDW have been found to be promising severity markers for COVID-19 infection. Both these markers are quintessential severity indicators in accordance to the present study [11].

In the study conducted by Broche-Pérez Y et al., about the fear of COVID-19 amongst the population in Cuba, the total score mean was found to be 17.9 [2]. In the present study, the mean is proportionately higher. This difference could be because of change in the geographical setting, small sample size of the present study. Also, a small difference in the mean score between pregnant and non pregnant group is identified. The non pregnant group seems to have more fear of COVID-19 than the pregnant. This difference could be attributed to acceptance among pregnant women about COVID-19, as they knew somewhere down the line that they had to visit a hospital for their antenatal management and that they would come across COVID-19 during their visits to hospital. From the other corner, this could be because of the fact that pregnant women have a timely concern about their foetus, while non pregnant women have families which are of larger concern to them. So, timely priorities vary along with which the fear and apprehension keep changing.

In comparison to the study conducted by Chang KC et al., the individual means of the three scales in the present study are slightly different [3]. The mean of the fear scales is lower in the present study, than 2.63±1.02 in their study. The mean of belief scales is slightly higher in the present study, than 3.31±0.74 in their study. The prevention of infective behaviour 3.54±0.92 is more in their study, than in the present study. All these could be because of the difference in the study setting. Also, huge difference in the sample size and geographic setting could be reasons for variations in the psychological perceptions.

One of the future plans is to compare the same parameters between pregnant COVID-19 positive females and age matched COVID-19 negative pregnant females. This would help get a vivid picture and help eliminate pregnancy as a confounder from the study.

Limitation(s)

The peak of first wave of COVID-19 in the union territory of Puducherry was observed in the months of August and September, 2020. With beginning of October 2020, the total number of inpatient admissions had reduced as the curve began to flatten. Owing to this logistic limitation, we had to recruit 20 previously treated patients and had to retrospectively collect the data. While the haematological records were from their time of admission, we were unable to fully comprehend the magnitude of psychological impact that the participants would have undergone as a result of being COVID-19 positive. Due to logistic and technical constraints other inflammatory markers and their coherence with pregnant state could not be ascertained. The present study setting was also a limitation. The study was conducted in an exclusively designated COVID-19 hospital with no access to non COVID-19 Patients.

CONCLUSION(S)

Pregnancy per say is subject to plethora of constitutional and physiological changes. COVID-19 infection could add to the morbidity profile of pregnant women. In the study, the majority of positive pregnant women were asymptomatic, had a distinct change in their neutrophil, lymphocyte, NLR and RDW-SD values. With regards to the psychological parameters, apprehensions were noted, and predominantly non pregnant group is affected and is down with 'Coronaphobia'. Thus, studying the haematological and psychological changes and setting up appropriate interventions could avert severity of COVID-19 infection.

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