Comparison of First and Second Wave of COVID-19 in Relation to Clinical Profile & Laboratory Investigations at a Single Centre in Northern India- A Retrospective Study

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Abstract

Introduction: SARS-CoV-2, a highly contagious virus, emerged and spread as a global pandemic in 2020. Its various mutants are continuously evolving though out the world. Repetitive waves of Covid-19 have drastically affected the whole world including India in terms of health and economy. The disease had a variable clinical course & laboratory investigation. Thus, in the present study, comparison was carried out between patients of first and second wave of Covid -19 regarding demographic profile, clinical severity, patients' outcome & laboratory findings.

Materials and Methods: 894 patients during first wave (01.08.2020 to 31.10.2020) & 367 patients during second wave (01.04.2021-01.06.2021) with laboratory confirmed diagnosis admitted at a tertiary care teaching Institute, in Northern India were enrolled in the study. Data was retrieved from Medical Records Department of the Institute.

Result: About 86 % of the people were symptomatic at the time of presentation in first wave while it was nearly 99% in case of 2nd wave. (P<0.0001). Most common symptoms were fever, cough and breathlessness. 53 % of the population had at least one-comorbidity in first wave while it was 67.30% in second wave. (P<0.0001). 13.4% & 44.10 % of the study subjects belonged to severe category in first & second wave respectively. (P<0.0001). On comparing lab investigations of two waves, leukocytes & neutrophils counts were more (P<0.0001) while lymphocytes & platelets were less in second wave (P<0.0001). Gender comparisons (first wave) of renal function tests, serum creatinine came out to be significantly higher (P<0.0001) in males. Similarly, liver function tests & CRP were significantly higher in males (P<0.0001, P<0.05). D-dimer & random blood sugar values were not significantly different. (P>0.05). Reduced lymphocytes count & increased neutrophils count were more in males (P<0.01). As against first wave, males & females exhibited almost similar values of lymphocytes & neutrophils in second wave (P>0.05). Platelets were decreased in males. (P<0.001). Number of deaths was significantly more in second wave (p<0.0001)

Conclusion: Second wave of Covid was significantly more aggressive. Significant laboratory findings differences in several parameters were observed in between two waves. Significant gender differences regarding lab investigations were also revealed in both the waves. Thus, knowledge of these differences is crucial for primary health care physicians to make the diagnosis and subsequent treatment strategies.

Keywords: Covid-19, comparison, first wave, second wave, demographic profile, laboratory investigations

Introduction

Severe Acute Respiratory Syndrome -Corona Virus-2 (SARS-CoV-2), a highly communicable virus, emerged and opened out as a global pandemic, declared by WHO virus on March 11, 2020 [1]. This pandemic resulted in huge mortality worldwide, which was witnessed by whole world This was labelled as First wave of Covid -19. India experienced three waves like this. Second wave hit the country in March, 2021 and this wave was much more devastating than the first wave, enormous mortality occurred [2].

As of 27 July 2023, according to Indian government figures, India has the second-highest number of confirmed cases in the world (after the United States

of America) with 44,994,955 [3] reported cases of COVID-19 infection and the third-highest number of COVID-19 deaths (after the United States and Brazil) at 531,915 deaths [4].

The first wave comparatively had a slow & prolonged course i.e, from January 2020 to approximately February 2021 whereas second wave had a very rapid course that started in March, 2021 & over few months , enormous cases & deaths were reported. [5]

The clinical presentation scenario ranged from asymptomatic [6] to highly symptomatic. Most common manifestations were fever, cough, myalgia & dyspnoea. Severity ranged from mild to critical illness having features of multiorgan failure [7,8] requiring ventilators. Similarly, laboratory investigations also varied from normal to highly abnormal where standard deviations were more than mean values stating high variations in the values. [9]

On the basis of scientific findings, WHO released updated treatment & diagnostic guidelines. Quarantine guidelines were also issued time to time by WHO. Accordingly, countries revised their management strategies.

A retrospective analysis of clinical profile (baseline characteristics, clinical severity, comorbidities & association between the clinico-epidemiological factors and clinical severity & outcome of indoor Covid-19 patients at the same centre has already been done [10] . There are very studies in India who compared the clinical & lab investigations of the two waves. Therefore, in the present study , the authors aimed to compare the First wave & Second wave patients' baseline characteristics, clinical severity, comorbidities, laboratory investigations & their outcomes at the very centre by retrieving the data from Medical Records Department so that future understanding of management could become easier.

Objectives-The study was conducted with the following Objectives: -

- To compare the clinico-demographic profile of Covid-19 patients of First wave & Second wave admitted in the Institute.
- To compare the clinical severity of the Covid patients at the time of presentation/ admission in the hospital and outcome of the patients of First & Second wave admitted in our Institute
- To compare the laboratory investigations of Covid patients of First & Second Wave admitted in our Institute
- To compare gender wise laboratory findings in both the waves separately

Methodology-

- The present study is a retrospective analysis. The data was retrieved from Medical Records at a tertiary care teaching Institute, which was approved as a 'Dedicated COVID health facility' in Lucknow. The periods of study were from 1st August 2020 to 31st October 2020 (First Wave) and 1st April, 2021 to 1st June 2021 (Second Wave) among laboratory confirmed Covid patients admitted in the hospital during these periods.
- Sample Size- 903 patients during first wave (Confirmed by laboratory testing) were admitted in the hospital. Out of these , 894 patients records were enrolled in the study as these patients' records were complete. During second wave , 367 patients were admitted with laboratory confirmed diagnosis and these all were enrolled in the study.
- Inclusion Criteria- All the lab confirmed Covid patients admitted during the study period were included
- Exclusion criteria- Admitted Patients whose complete records could not be retrieved were excluded.
- The data was collected from the triage forms and case files.
- At the triage, the patients were classified for the clinical severity according to Clinical Management Protocol: COVID 19 version 5 by the MOHFW as mild, moderate & severe & accordingly sent to respective wards. SpO_2 & temperature were measured using a pulse oximeter & thermal scanner respectively.
- Ethical approval was obtained from the Institutional Ethics Committee (IEC). There was no breach in the confidentiality of the patients.

Statistical Analysis

Comparison of first wave & second wave were made between demographic profile, clinical severity & laboratory parameters. The retrieved data was managed in a Microsoft Excel spreadsheet. The results of descriptive statistics , continuous variables & normal distribution were presented as mean ± standard deviation, analyzed by unpaired t test. Categorical data were presented as frequencies & percentages as proportions & analyzed by Z score for two proportions. All p values presented were two tailed & significance level calculated at p<0.05.

Results-

The mean age of study subjects (n=894) was 47.68 ± 17.62 years in first wave while it was 55.42 years ± 14.50 yrs in second wave. (P<0.0001) Gender wise comparison showed almost similar pattern in both the waves. (nearly 2/3rd are male).The difference between male & female in both the waves was significant. (P<0.05) . Maximum number (55.80 %) of patients belonged to 31-60 years of age. (First wave), almost similar findings were obtained in second wave. (**figure 1**) (P>0.05)

Fig 1 Comparison of number of Patients in Different Age –Groups of First & Second Wave of Covid-19
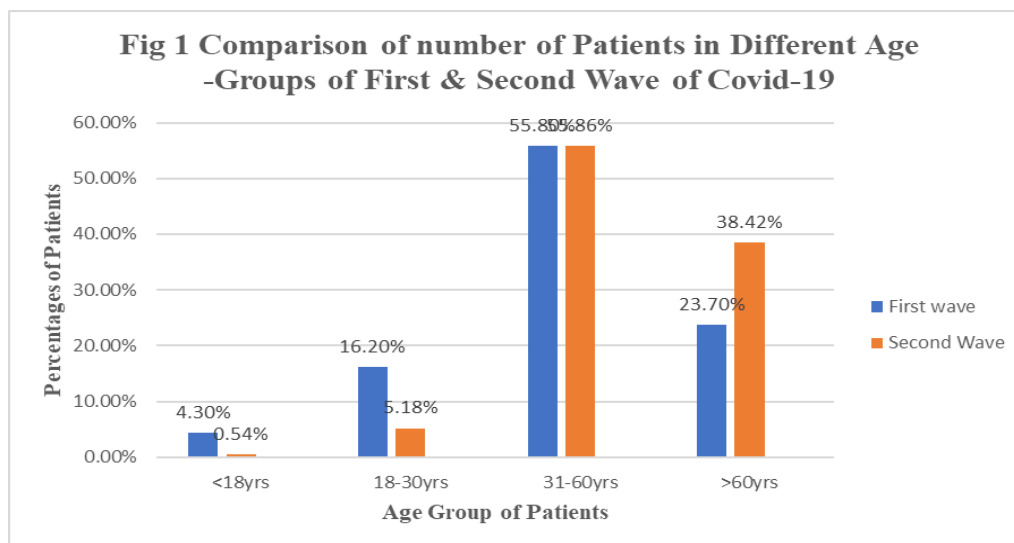
About 86 % of the people were symptomatic at the time of presentation to hospital in first wave while it was nearly 99% in case of 2nd wave. (P<0.0001).Most common symptoms were fever, cough and breathlessness. 53 % of the population had at least one-comorbidity in first wave while it was 67.30% in second wave. (P<0.0001) Diabetes and hypertension were the most common co-morbidities with more preponderance in first wave**. (Table 1)**

Table-1 Camparison of Socio-demographic & Clinical characteristics of study participants in first & second wave of Covid-19

P value calculated by Z score in two tailed Z test, NS-Non significant , S-significant

Socio-demographic and Clinical Characteristics	First Wave		Second Wave		P-Value	Level of Significance at <0.05
	Frequency	**Percentage**	**Frequency**	**Percentage**		
Mean Age (in years) (mean ± SD)	47.68± 17.62		55.42 ±14.50		<0.00001	S
Gender						
Male	600	67.10%	223	60.76	0.031	S
Female	294	32.90%	144	39.24	0.031	S
Clinical profile						
Asymptomatic	126	14.10%	4	1.09	<0.00001	S
Symptomatic	768	85.90%	363	98.91	<0.00001	S
Ever Reported Symptoms*(*Multiple Choice)						
Fever	491	63.80%	279	76.02	<0.00001	S
Cough	346	44.90%	166	45.23	0.748	NS
Breathlessness	334	43.40%	225	61.31	<0.00001	S
Sore Throat	109	14.20%	32	8.72	0.003	S
Diarrhea	12	1.60%	4	1.09	<0.00001	S
Others	320	41.60%	142	38.69	0.322	NS
Comorbidities						
No	420	47.00%	120	32.70	<0.00001	S
Yes	474	53.00%	247	67.30	<0.00001	S
Comorbidities(if any)						
Diabetes	278	59.70%	164	44.69	<0.00001	S
Hypertension	254	54.50%	155	42.23	<0.0001	S
Cancer	6	1.30%	1	0.27	0.0949	NS
COPD	11	2.40%	20	5.45	0.00578	S
Others	185	39.70%	96	26.16	<0.00001	S

There was a significant difference between first & second wave regarding the number of patients in different categories of clinical severity. In first wave, around three fourth of patients (75.70%)

belonged to mild category while it was 43.60% in second wave. 13.4% & 44.10 % of the study subjects belonged to severe category in first & second wave respectively.(P<0.0001) Only 5.5% of the population reported at the triage area of the hospital with a basic life support in first wave while it was 38.82% in second wave. (P<0.0001) (**figure 2**) .

Fig 2: Comparison of Clinical severity of Patients in First & Second Wave Patients of Covid-19
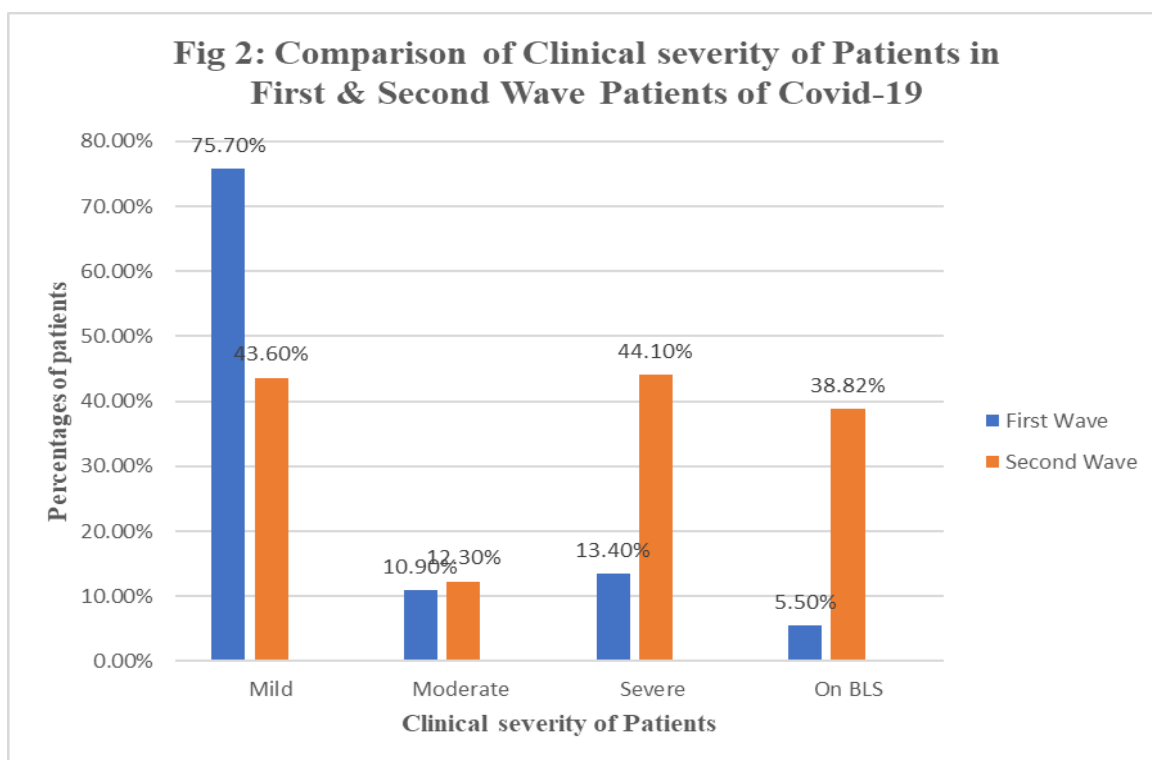
Fever was recorded at the triage area with a thermal scanner and 38% & 3.50% of the patients had fever on presentation in First & Second wave respectively.(P<0.0001) Among the patients ≥ 10 years (n=876), 63% & 74.10% did not have a respiratory difficulty (RR < 24 breaths/min) in first & second wave respectively. (P<0.0001) The oxygen saturation (SpO2) as measured by pulse oximeter was more than 94% in about three fourth of the subjects in first wave while it was 32.40% in second wave. (P<0.0001) **(Table 2)**

Table 2: Vitals Comparison of study subjects at presentation at Triage in first& second wave of Covid-19

Vitals and Clinical Severity at Triage	First Wave		Second Wave		P-Value	Level of Significance at p<0.05
	Frequency	Percentage	Frequency	Percentage		
Temperature						
≤ 100 °F	556	62.20%	354	96.50	<0.00001	S
> 100 °F	338	37.80%	13	3.50	<0.00001	S
Respiratory Rate						
<24/min	563	63.00%	272	74.10	<0.00001	S
24 -30/min	300	33.6%%	67	18.30	<0.00001	S
≥ 30/ min	13	1.50%	28	7.60	<0.00001	S
SpO$_2$						
>94%	672	75.20%	176	32.40	<0.00001	S
90-94%	128	14.30%	72	19.60	0.019	S
<90%	94	10.50%	119	32.40	<0.00001	S
On BLS						
No	845	94.50%	221	58.78	<0.00001	S
Yes	49	5.50%	146	38.82	<0.00001	S

P value calculated by Z score in two tailed Z test; NS-Non significant , S-significant

Comparison of routine haemogram of patients of first & second wave is depicted in **table 3**.

Table 3: Laboratory profile of study subject of first & second wave of Covid-19

Investigation	First Wave		Second Wave		P-Value	Level of Significance at p<0.05
	Mean	SD	Mean	SD		
Hb (gm %)	12.11	2.06	11.97917526	5.346865907	0.501	NS
TLC(cu/mm)	7172.38	4311.95	10295.2009	6536.68664	<0.0001	S
Neutrophils(%)	63.92	13.52	68.96868557	13.25983853	<0.0001	S
Lymphocytes(%)	30.14	11.98	26.80154639	12.2580901	<0.0001	S
Eosinophils(%)	4.19	2.88	2.422938144	1.772221668	<0.0001	S
Monocytes(%)	1.59	1.04	1.806365979	1.237262729	0.002	S
RBC(*10/ul)	4.3	1.77	4.205360825	0.668312019	0.29	NS
HCT(%)	36.57	6.59	35.83293814	5.640487739	0.05	NS
MCV(fl)	87.12	9.52	85.17881443	9.057382138	<0.0008	S
MCH(pg)	28.86	3.22	27.84639175	2.908479072	<0.00001	S
MCHC(g/dl)	32.99	1.6	32.49005155	1.312986417	<0.00001	S
RDW(%)	13.61	2.18	13.57427835	1.436213708	0.77	NS
Platelet(lac/cumm)	2.26	2.63	2.171056701	1.087690898	0.526	NS

P value calculated by unpaired t test, NS-Non significant , S-significant

In this comparison , some findings were significantly different in two waves like TLC, Neutrophils, Lymphocytes, Eosinophils, Monocytes, MCV, MCH, MCHC (P<0.01) while others like RDW, Platelets. RBCs & hematocrit were not.(P>0.05) Kidney function tests , liver function tests. Random blood sugar, C-reactive protein , D-dimer records of patients of only first wave available & depicted in **Table 4**.

Table 4: Gender wise Comparison of laboratory parameters of Study Subjects in First Wave

Investigation	Female (n=294, 32.88%)		Male(n=600, 67.11%)		P-Value	Level of Significance at <0.05
	Mean	SD	Mean	SD		
Hb (gm %)	11.1	1.63	12.76	2.04	<0.0001	S
TLC(cu/mm)	7129.16	3250.25	7200.71	4887.09	0.8	NS
Neutrophils(%)	62.17	10.97	65.07	14.85	0.003	S
Lymphocytes(%)	32.1	9.88	28.85	13.02	0.0002	S
Eosinophils(%)	4.05	2.12	4.28	3.29	0.27	NS
Monocytes(%)	1.46	0.99	1.67	1.07	0.0048	S
RBC(*10/ul)	4	0.55	4.49	2.21	0.0002	S
HCT(%)	33.78	4.69	38.39	7.01	<0.0001	S
MCV(fl)	85.1	6.58	88.45	10.83	<0.0001	S
MCH(pg)	27.95	2.56	29.45	3.45	<0.0001	S
MCHC(g/dl)	32.73	1	33.16	1.87	0.0002	S
RDW(%)	13.91	2.14	13.41	2.19	0.0013	S
Platelet(lac/cumm)	2.33	0.98	2.22	3.29	0.574	NS
S Urea(mg/dl)	38.36	35.67	40.2	31.26	0.43	NS
S. Creatinine(mg/dl)	1	0.79	1.57	1.24	<0.0001	S
S. Bilirubin(mg/dl)	0.68	1.38	0.87	0.57	0.0038	S
Alanine transaminase (ALT) (IU/L)	48.24	33.96	76.15	60.2	<0.0001	S
Aspartate transaminase (AST) (IU/L)	45.74	25.13	63.9	63.27	<0.0001	S
Alkaline Phosphatase(mg/dl)	115.5	68.54	102.49	57.72	0.003	S
CRP	(n=151), 37.95	29.85	(n=332), 50.51	47.77	0.003	S
D-Dimer	(n=143), 1226.39	1153.29	(n=294), 1235.44	1295.82	0.943	NS
RBS	(n=40), 166.97	99.98	(n=81). 160.07	89.2	0.699	NS

P value calculated by unpaired t test, NS-Non significant , S-significant

Statistically significant differences in s parameters were observed between males & females in first wave. In renal function tests, the value of serum urea was almost same (P>0.05) but serum creatinine was significantly higher (P<0.0001) in males. Similarly, liver function tests were significantly higher in males (P<0.0001). C-reactive protein was also higher in males(P<0.05) while D-dimer & random blood sugar values were not significantly different.(P>0.05).

While comparing, lab investigations of patients of second wave, statistically significant differences in some parameters were observed between males & females. As against first wave, lymphocytes & neutrophils were not significantly different in males (P>0.05). No thrombocytopenia was observed but the difference between the genders was significant being low in males.(P<0.001) **(Table 5)**

**Table 5: Gender wise Comparison of Laboratory Parameters in Second Wave**

Investigation	Female (n=144, 39.23%)	Male (n=223, 60.76%)	P- Value	Level of Significance at <0.05	Investigation	Female (n=144, 39.23%)
	Mean	SD	Mean	SD		
Hb (gm %)	10.91	1.76	12.74	6.75	0.0016	S
TLC(cu/mm)	9835.99	6562.67	10624.37	6512.60	0.25	NS
Neutrophils(%)	68.06	13.58	69.62	13.02	0.189	NS
Lympho-cytes(%)	27.26	12.49	26.47	12.10	0.546	NS
Eosinophils(%)	2.52	1.83	2.36	1.73	0.39	NS
Monocytes(%)	1.97	1.29	1.69	1.18	0.03	S
RBC(*10/ul)	4.07	0.64	4.30	0.67	0.0012	S
HCT(%)	33.63	5.23	37.41	5.40	<0.0001	S
MCV(fl)	83.20	8.63	86.59	9.11	0.0004	S
MCH(pg)	27.00	3.21	28.45	2.51	<0.0001	S
MCHC(g/dl)	32.21	1.30	32.69	1.29	0.0006	S
RDW(%)	13.77	1.50	13.43	1.37	0.026	NS
Plate-let(lac/cumm)	2.35	1.36	2.04	0.82	0.0068	S

P value calculated by unpaired t test, NS-Non significant , S-significant

Regarding final outcome of patients' , significantly more no of patients were cured in first wave as compared to second wave(P<0.0001). Similar differences were observed in patients who could not be saved in both the waves.(P<0.0001). No significant difference was noticed in number of referred patients. (P>0.05). No of patients who absconded, discharged on patients' request (DOPR) or left against medical advice (LAMA) were also significantly more in second wave. (P>0.05) **(Figure 3)**

Fig 3: Comparison of Outcome of Patients in First & second Wave of Covid-19
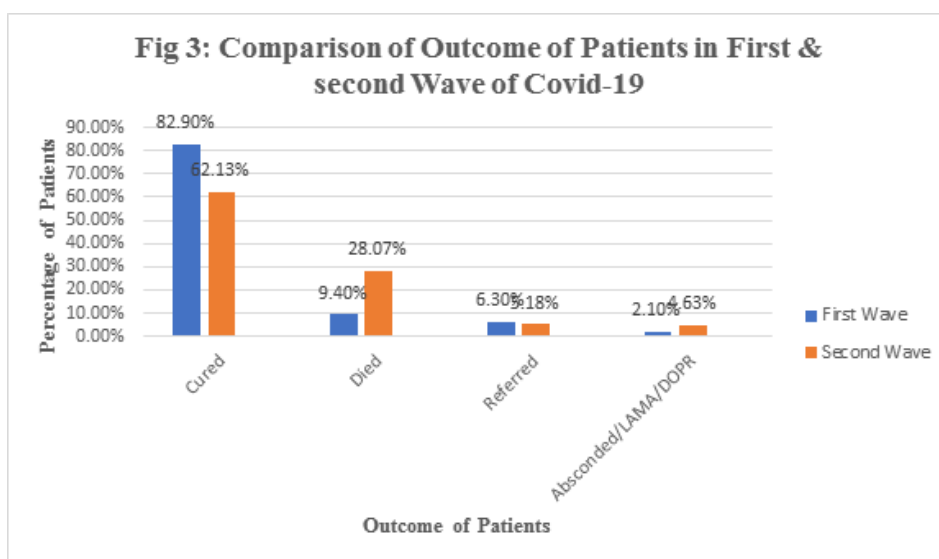
Discussion

To our knowledge, this is the first study in India to compare demographic profile, clinical severity , outcome of patients & laboratory investigations between first & second wave of Covid 19 . Our findings exhibit significant variation between the two waves regarding the said parameters.

There was significant difference in mean age of patients between the two waves which was more in second wave (55.4 yrs vs 47.6yrs). This was in accordance with a previous study conducted by Tendulkar et al., 2023, India [11]. More mean age was observed in second wave though it was not significantly different. In contrast to our study, Nausad VA et al., 2022, Qatar (9) found no difference in the mean age of patients between two waves (65.9 vs 65.8) while Iftimie et al.,2021 from Spain [12] concluded that patients in second wave were significantly younger than first wave (58 vs 67 yrs) . Environmental effects may be the reason for these findings.

The age group most affected was 31-60 yrs in both the waves (P>0.05). Similar findings were observed by another study [9] while Tendulkar et al., 2023, India [11] confirmed more patients belonged to >60 years of age in both the waves.

In both the waves, the number of male patients were significantly more as compared to females in our study. (p<0.05). This is in confirmation with the findings concluded by a study. [9, 11]. This finding may be explained on the basis of hormonal & prevalence.

In our study, percentage of symptomatic patients were significantly higher in second wave as compared to first wave. Tachypnoea & hypoxia requiring oxygen was significantly more in second wave basic life support was needed in 38.8% in second wave while it was only 5.5% in first wave This is in accordance with Naushad VA et al., Qatar 2023 [9].

In our study, Diabetes Mellitus & Hypertension were the common comorbidities as also evidenced by another study [9]. Patients of both Diabetes & Hypertension were higher in second wave in our study . On contrary to this, the authors in Qatar, 2023 [9] these were more in first wave. Iftimie et al., 2021 [12] reported no difference between the two waves in comorbidities.

Regarding laboratory parameters, no significant difference was observed in mean haemoglobin levels in two waves in our study . This is in accordance with study conducted by Tendulkar et al., 2023 , [11] while significant difference was observed by the authors of an another study. Total leucocyte count was significantly higher in second wave in our study ($10.3*10^3$ vs $7.2*10^3$) (P<0.001). This finding is in line with the study conducted by Tendulkar et al., 2023.(11) On contrary, this was significantly high in first wave in study conducted in Qatar(9). Neutrophil counts were higher than normal in both the waves , second wave showed more rise in counts (63% vs 68% , P<0.0001) . A meta –analysis [13] also concluded Neutrophils to be raised in severe group. Monocytes were slightly towards lower side in both the waves with more reduction in first wave (1.6% vs 1.8 %, P<0.01), the meta- analysis [13] also reported the same. Lymphocytes & eosinophils were within normal range in both the waves in the present study (30% & 4% and 27% vs 2.4% in first & second wave respectively), while these parameters were reduced in the meta-analysis(13) Therefore, only neutrophil counts were raised indicating cytokines release & disease severity rest other cells are normal in both the waves. However, NLR was mild (2.1 vs 2.5). This is in accordance with the a study [14] . NLR was found to be increased in meta-analysis(13). Platelets count was nearly normal in both the waves.(P>0.05). Study conducted by Ucar et al., 2021 [14] & Chen et al., 2020 [15] also exhibited the same while Tendulkar et al., 2023 [9], Guan et al., 2020 [16] reported thrombocytopenia in both the waves & significant difference was observed between the two. Study done in Qatar also did not show thrombocytopenia but platelet values were significantly different in two waves being higher in first wave.

We could find random blood sugar level, renal function tests , liver function tests, C-Reactive Protein, D-dimer data for first wave only.

While comparing laboratory parameters gender wise in first wave patients, we found that except for serum creatinine , CRP & D-Dimer levels, rest other parameters were within normal limits in both the groups. Serum creatinine levels were significantly high in males as compared to females (P<0.0001). However, there was significantly different higher values observed in males as compared to females in relation to neutrophils, lymphocytes, monocytes, red blood cells, haematocrit, , MCV, MCH, MCHC, RDW, serum creatinine, serum total bilirubin, AST, ALT, Alkaline phosphatase & CRP (P<0.001) This was in accordance with other studies [17-19] where AST , ALT, serum urea & creatinine were significantly higher in males than in females. These lab findings predispose males as more susceptible for organs dysfunction during the course of the disease.

C-Reactive Protein (CRP) levels were significantly higher in males as compared to females (P<0.0001) indicating severe inflammation suggesting infectious lung disease. High D-dimer values indicate critical illness suggestive of coagulopathy. Its levels were raised by 3 times the higher value in both the groups. No significant difference was observed between the two genders (P>0.05).

Random blood sugar levels were also not significantly different between two groups.

Gender wise comparison of lab investigations in second wave exhibited some different pattern. Levels of lymphocytes & neutrophils were slightly high, but not significantly different in males. (P>0.05) . Platelets, though , within normal range but exhibited more fall in males as compared to females.(P<0.001). Rest of the differences in lab findings of two genders were same as first wave patients.

Regarding final outcome of patients' in our study, more number of patients were cured in first wave as compared to second wave (P<0.0001). Percentage of died patients was also significantly more in second wave indicating the aggressiveness of second wave , similar results were also concluded by Tendulkar et al., 2023 [9] and Bogam et al., 2022(20)

Conclusion

This study , apart from comparing demographic features, clinical severity, patients outcome in terms of cured, death, referred, LAMA, DOPR and laboratory investigations , also throws some light on the gender differences in relation to laboratory investigations in presentation of COVID-19 disease of both waves. The study concluded that mean age of patients was significantly high in second wave as compared to first wave (55yrs vs 48yrs). Both the waves witnessed that males were affected significantly more, maximum number of patients belonged to 31-60yrs of age and fever, cough & breathlessness were the major symptoms . Comorbidities were significantly more in second wave. Patients in severe category and on basic life support were more in second wave while mild category patients formed the bulk in first wave. Significant laboratory findings differences in several parameters were observed in between two waves. Significant gender differences regarding lab investigations was also revealed in both the waves. Knowledge of these differences is crucial for primary health care physicians to make the diagnosis and subsequent treatment strategies.

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