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Original Research Article

Population Dynamics and Time Kinetics Of Recovery In Asymptomatic COVID -19 Patients

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Abstract

Introduction: The novel coronavirus (COVID-19) has created great havoc across the whole world and now developing its deep roots in India also. From major metropolitan cities, the disease has reached rural areas of the country. In India most of the patients are asymptomatic and the mortality rate is very low. **Objective**: To do retrospective data analysis and to study time kinetics of recovery in asymptomatic COVID-19 patients. **Methods:** A total of 118 patients of COVID-19 admitted at R.D.B.P. Jaipuria hospital, Jaipur were recruited for this study. All were subjected to a detailed history, the clinical examination required hematological and biochemical investigations along with repeated RT-PCR test on nasopharyngeal swab samples at a regular interval according to guidelines of ICMR to detect COVID-19 antigen. All types of data and reports were computerized and analyzed. **Results:** In our study male sex was found to be much more affected (about 2.3 times) by coronavirus disease than that of the female sex. This male predominance was also found in the pediatric age group. Young adults and middle-aged adults constitute 79% of our study population of COVID-19 patients. It is also concluded that most patients (60%) in all age groups recovered in the first week. As age advances, recovery takes longer time than younger age groups. Recovery is not affected by sex. Asymptomatic patients who do not have any comorbidity have faster recovery from coronavirus disease than that of older patients with some comorbid condition.

Keywords: Coronavirus disease, RT-PCR, SARS CoV- 2.

Introduction

Today the whole world is facing the pandemic of SARS CoV- 2 (COVID -19) which is the third and lethal outbreak of the corona virus group in the 21st century after SARS and MERS virus outbreaks in 2002 and 2012 respectively. Corona viruses are a large group of viruses that cause illness both in humans and animals. This outbreak of novel corona virus disease was initially noticed in a seafood market in Wuhan city Hubei Province of China in mid of December 2019.

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This outbreak was declared a Public Health Emergency of International Concern by the World Health Organization on 30 January 2020. On the same day, the first case of India of COVID-19 was detected in Kerala. Since then it has spread all over the country affecting the lacs of people and responsible for thousands of deaths in India till now. The currently available evidence for COVID-19 suggests that the causative virus has a zoonotic source and it is an enveloped RNA beta corona virus using angiotensin-converting enzyme-2(ACE-2) receptor for cell entry. COVID-19 is transmitted by respiratory droplets and fomites during close unprotected contacts between infector and infectee and also through contaminated surfaces. While around 80% of the patients of COVID-19 are either asymptomatic or with mild illness only, around 15% develop severe disease requiring

hospitalization and oxygen support and about 5% are critically ill. Globally, it has been observed that males are affected about three times more in number than that of females and the pediatric age group is less prone to this infection. Autopsy findings in China and European countries showed endothelial damage of pulmonary vasculature, microvascular thrombosis, and hemorrhage linked to extensive alveolar and interstitial inflammation that ultimately result in COVID-19 vasculopathy, pulmonary intravascular coagulopathy, ventilation-perfusion mismatch, and refractory ARDS. A reverse transcription-polymerase chain reaction (RT-PCR) test is recommended to detect viral RNA for making the diagnosis of COVID-19. Nasopharyngeal swab in viral transport medium (VTM) is the preferred sample with the maintenance of cold chain. The time duration in which patients of COVID-19 become negative for this swab test varies from person to person. This recovery time may be influenced by many factors like personal immunity, anemia, co-existence of any other infection, and presence of any co-morbidity like diabetes mellitus, hypertension, chronic heart diseases, and any addiction.

Review of literature

KS- CHAN, and colleagues have shown in their study conducted at United Christian Hospital, Hongkong in 2003 that "Age and comorbidity (eg: diabetes mellitus, heart disease) were consistently found to be significant independent predictors of various adverse outcomes in SARS."As mentioned in the report of the WHO-China Joint Mission on Corona virus disease 2019 (COVID-19)-using available preliminary data, the median time from onset to clinical recovery for mild cases is approximately 2 weeks and 3-6 weeks for patients with the severe critical disease [1]. A study conducted in Singapore in March 2020 by Monira Mollazehi and others shows that younger patients recover faster than elderly patients. The results tell that the hazard rate of recovery time from COVID-19 infection will increase by 1% as the age of patient increase by one year. In a study conducted at the University of California San-Francisco by Elizabeth Fernandez, it was found that among people infected with corona virus, the risk of disease progression in those who currently smoke or previously smoked was nearly double than of that of non- smokers.

Objectives

To do retrospective analysis of demographic data, hematological and biochemical investigation reports of asymptomatic COVID-19 patients.

To study time kinetics of recovery in COVID-19 asymptomatic patients.

To know the relation of co-morbidities with the recovery time of COVID-19 Patients.

Material and methods

Study design

This would be a Hospital-based retrospective data analytical and observational study. R.D.B.P. Jaipuria Government Hospital was declared as a designated treatment center for asymptomatic COVID-19 patients by the Government of Rajasthan. For symptomatic and critically ill patients of COVID-19 other hospitals were assigned in the city by the government (2). The study was approved by hospital administration and ethics committee clearance has been obtained for conduction of the study and publication of the report.

Chief medical and health officer of Jaipur, Rajasthan appointed a team that has done cluster and random sampling at the community level in the containment zone and hot spot area of COVID-19 in Jaipur. Asymptomatic positive cases (RT-PCR test positive in nasopharyngeal swab) were referred to R.D.B.P. Jaipuria hospital for further evaluation and management.

Study size

A total of 118 patients of COVID-19 were taken for the study who were admitted in R.D.B.P. Jaipuria hospital, Jaipur in the month of April-May 2020. All these patients were included for demographic profile analysis. Out of these, 9 symptomatic patients were referred to a higher center. Rest 109 asymptomatic COVID-19 patients were recruited for further study.

Methodology

In this case series, asymptomatic 118 patients of COVID-19, admitted in the hospital were subjected to a detailed history, clinical examination, and routine investigations (complete blood counts, random blood sugar, blood-grouping, and urine complete examination). Required special investigations like liver function test, renal function test, chest X-ray, and blood sugar fasting and post-prandial were also done. Repeated RT-PCR tests for COVID-19 were performed on nasopharyngeal swab samples at the required interval for all 109 patients excluding referrals who became symptomatic and were excluded from further study. Hydroxychloroquine 400 mg and Azithromycin 500 mg daily were prescribed to all the Patients according to guidelines of the government of India (3). 'Recovery' from COVID-19 was confirmed when two consecutive swab samples taken at 24 hours interval were found negative for viral antigen by RT-PCR test. All types of data and investigation reports were computerized and analyzed by appropriate statistical methods.

Inclusion criteria

- All Patients below 70 years of age who were admitted to our hospital as asymptomatic cases of COVID-19.

Exclusion Criteria

- Pregnant women
- Symptomatic patients of COVID-19 (for purpose of studying time kinetics of recovery)

Observations

Table 1: Demographic Profile of COVID-19 Patients

Value	No.
Total patients	118
Patient referred	9
Patient treated	109
Sex Distribution	
Male	82
Female	36
Children (n)	12
(M)	10
(F)	2
Religion (n)	
Hindu	30
Muslim	88
Other	0

Table 2: Hematological profile and other variables of asymptomatic COVID-19 patients

Value	Mean	SD
Age (yrs.)	34.4.	13.3
Days of recovery (days)	7.21	5.82
Average days of Recovery (days)		
1st week	2.92	2.02
2nd week	12.34	1.91
3rd week	17.90	1.83
Hb (g/dL)	12.85	1.67
TLC (x 10^6/L)	7.288	2.124
Neutrophils (%)	55.80	8.93
Lymphocyte (%)	39.47	10.65
Platelets (x10^6/dL)	2.34	0.85
B. Sugar (g/dL)	94.4	40.5
SGOT (U/L)	29.2	10.9
SGPT (U/L)	29.72	18.9
S. Bilirubin (Total) (mg/dl)	0.84	0.36
S. Bilirubin (Direct) (mg/dl)	0.46	0.15
S. Urea (mg/dl)	21.34	5.5
S. Creatinine (mg/dl)	0.88	0.18
S. Total Protein (g/dl)	6.77	0.73
S. Albumin (g/dl)	4.44	1.57
S. BP (mmHg)	123	10
D. BP (mmHg)	80	6

Table 3: Age distribution of asymptomatic COVID-19 patients

Age	Total no of case	%
<1 yr	1	1%
1-5 yr	1	1%
6-10 yr	6	5%
11-15 yr	4	3%
16-20	7	6%
21-25 yr	10	8%
26-35 yr	35	30%
36- 45 yr	30	25%
46- 55 yr	19	16%
56-65 yr	4	3%
>65 yr	1	1%
	118	100%

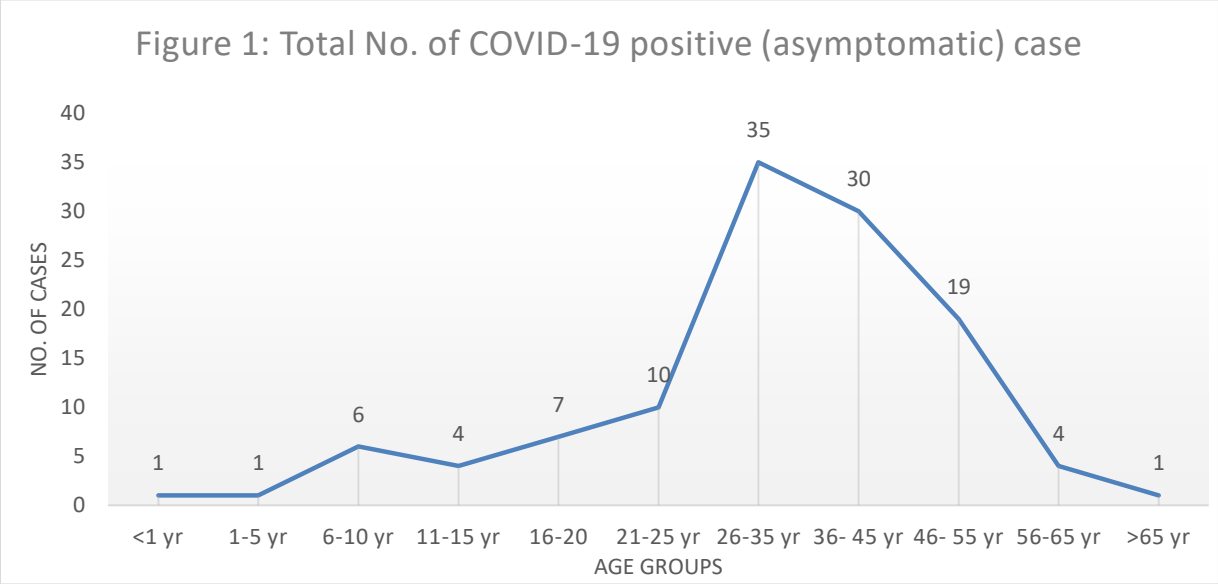


Table 4: Sex distribution of COVID-19 (asymptomatic) patients

	No.	%
Male	82	70%
Female	36	30%
Total	118	100%

Table 5: Sex Distribution of COVID-19 (children) patients

Table 5: Sex Distribution in COVID-19 children (asymptomatic)		
	No.	**%**
Male	10	83%
Female	2	17%
Total	12	100%

Table 6: Time kinetics of recovery in Asymptomatic COVID-19 patients

Table 6: Time of virus recovery in COVID-19 patients (asymptomatic)		
Time	**No. of patients**	**Percentage %**
≤1 week	66	60%
≤2 week	32	30%
≤3 week	11	10%
Total	109	100%

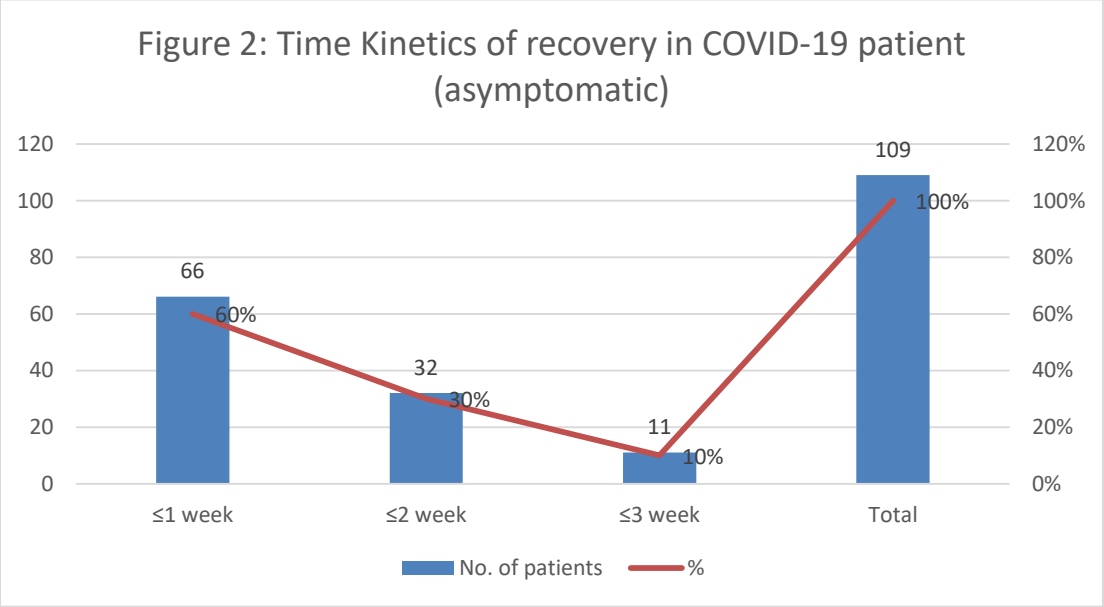
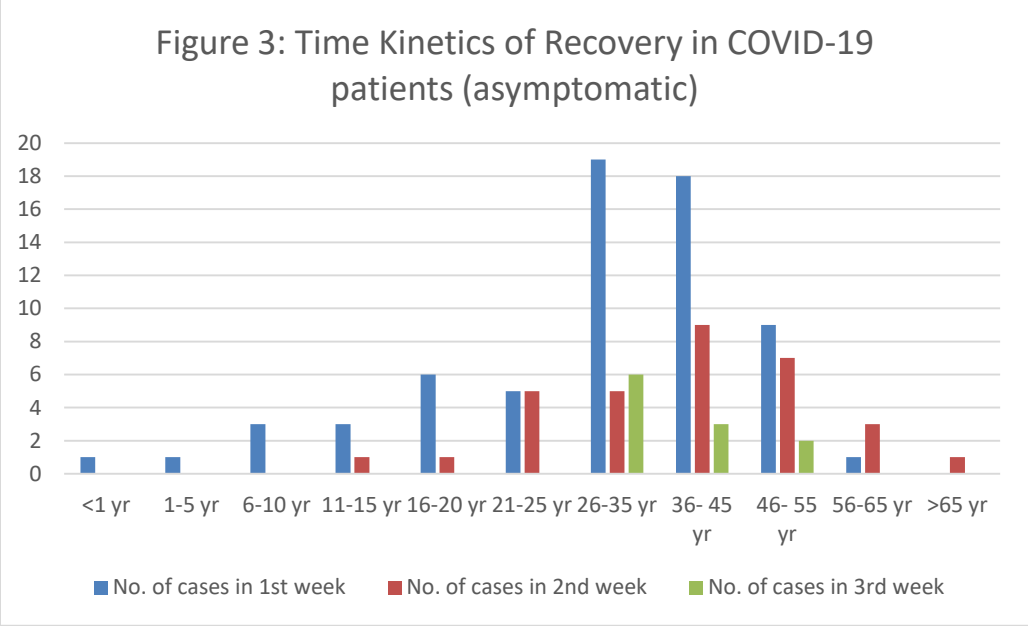


Table 7: Time kinetics of recovery of COVID-19 patients (asymptomatic) in Weeks: Age-wise distribution

Age	1st Week	% (cases in age group)	2nd week	% (cases in age group)	3rd week	% (cases in age group)	Total Patients
<1 yrs.	1	100%	0	0%	0	0%	1
1-5 yrs.	1	100%	0	0%	0	0%	1
6-10 yrs.	3	100%	0	0%	0	0%	3
11-15 yrs.	3	75%	1	25%	0	0%	4
16-20 yrs.	6	86%	1	14%	0	0%	7
21-25 yrs.	5	50%	5	50%	0	0%	10
26-35 yrs.	19	63%	5	17%	6	20%	30
36- 45 yrs.	18	60%	9	30%	3	10%	30
46- 55 yrs.	9	50%	7	39%	2	11%	18
56-65 yrs.	1	25%	3	75%	0	0%	4
>65 yrs.	0	0%	1	100%	0	0%	1
Total	66		33		11		109



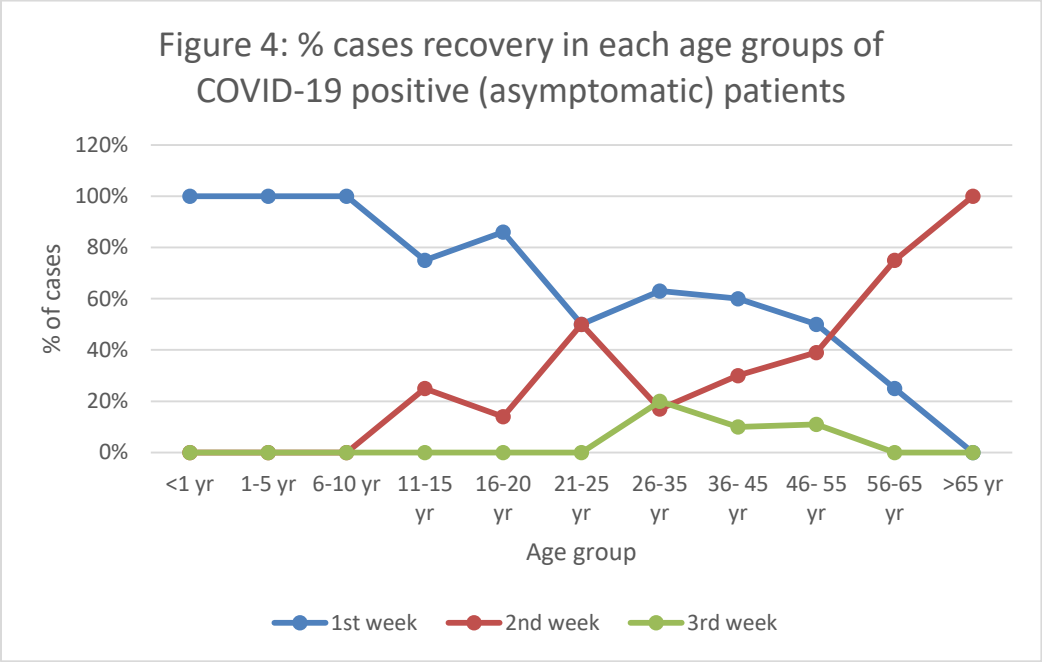


Figure 4: % cases recovery in each age groups of COVID-19 positive (asymptomatic) patients
120%
100%
80%
60%
40%
20%
0%
% of cases
<1 yr
1-5 yr
6-10 yr
11-15 yr
16-20 yr
21-25 yr
26-35 yr
36- 45 yr
46- 55 yr
56-65 yr
>65 yr
Age group
1st week
2nd week
3rd week

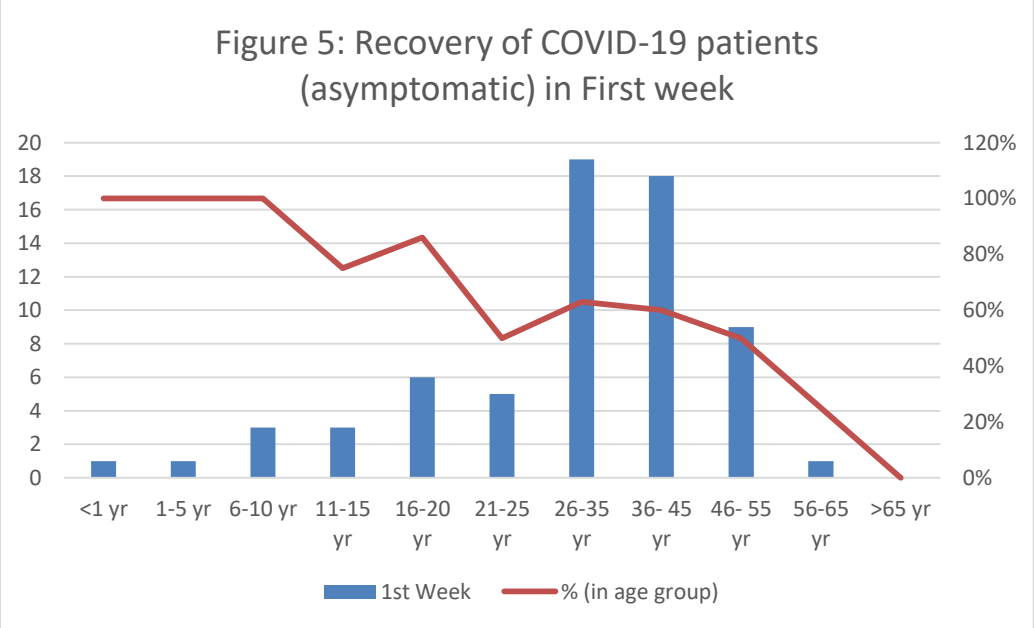


Figure 5: Recovery of COVID-19 patients (asymptomatic) in First week
20
18
16
14
12
10
8
6
4
2
0
120%
100%
80%
60%
40%
20%
0%
<1 yr
1-5 yr
6-10 yr
11-15 yr
16-20 yr
21-25 yr
26-35 yr
36- 45 yr
46- 55 yr
56-65 yr
>65 yr
1st Week
% (in age group)

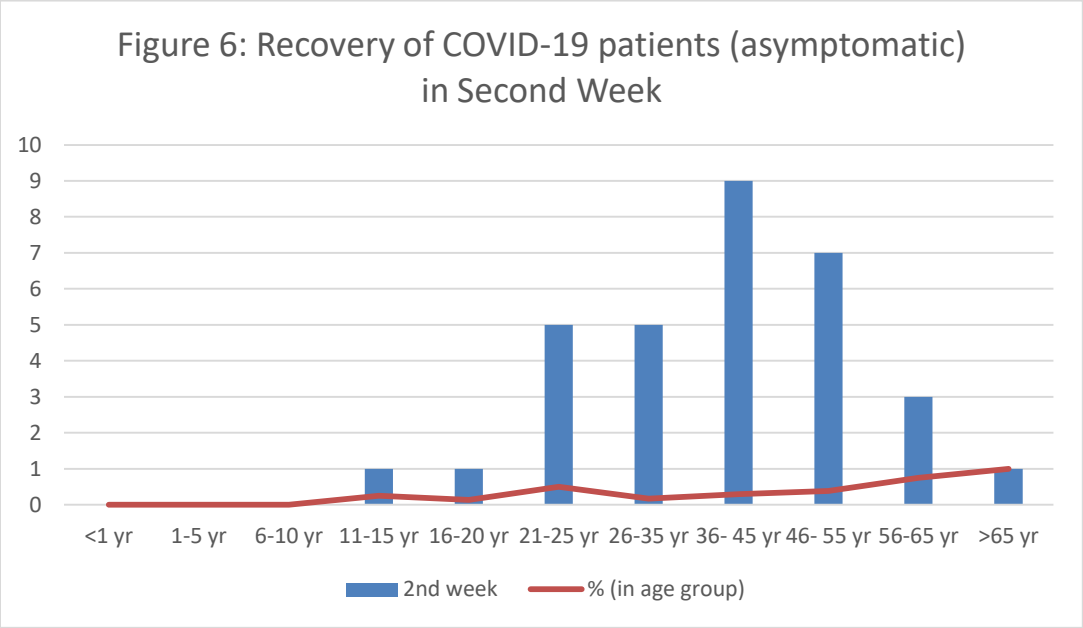


Figure 6: Recovery of COVID-19 patients (asymptomatic) in Second Week
10
9
8
7
6
5
4
3
2
1
0
<1 yr
1-5 yr
6-10 yr
11-15 yr
16-20 yr
21-25 yr
26-35 yr
36- 45 yr
46- 55 yr
56-65 yr
>65 yr
2nd week
% (in age group)

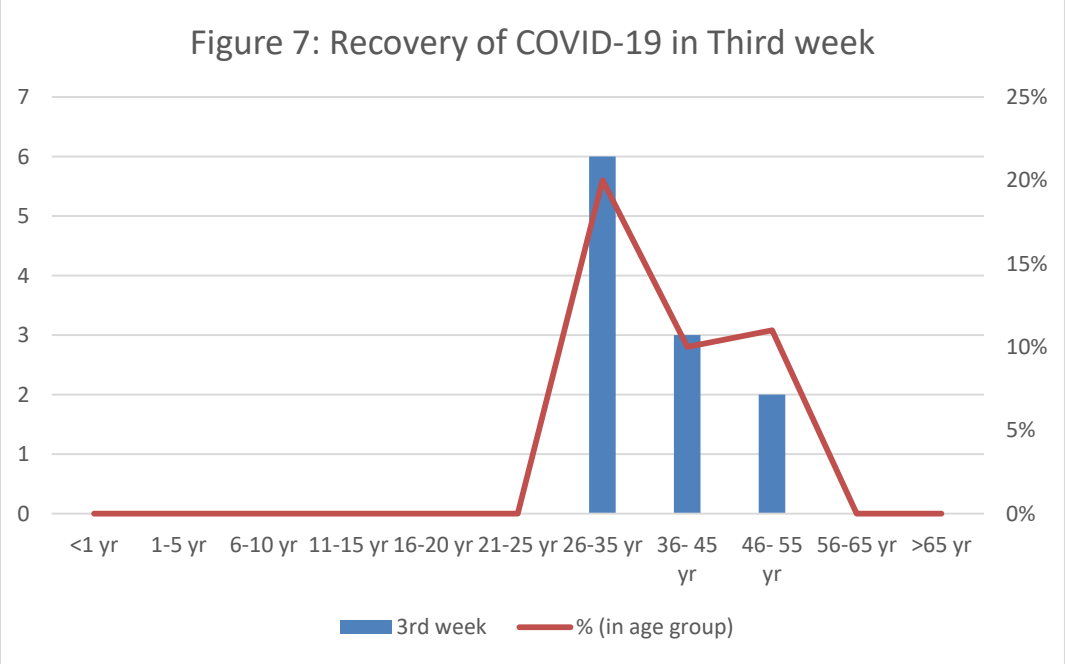


Figure 7: Recovery of COVID-19 in Third week
7
6
5
4
3
2
1
0
25%
20%
15%
10%
5%
0%
<1 yr
1-5 yr
6-10 yr
11-15 yr
16-20 yr
21-25 yr
26-35 yr
36- 45 yr
46- 55 yr
56-65 yr
>65 yr
3rd week
% (in age group)

Table 8: Time recovery of asymptomatic COVID-19 patients according to Sex

Table 8: Time of Recovery of COVID-19 patients (asymptomatic) according to sex							
	1st week	% (1 week)	2nd week	% (2nd week)	3rd week	% (3rd week)	Total
Male (n=78)	48	62%	24	31%	6	8%	78
Female (n=31)	18	58%	8	26%	5	1%	31
Total	66		32		11		109

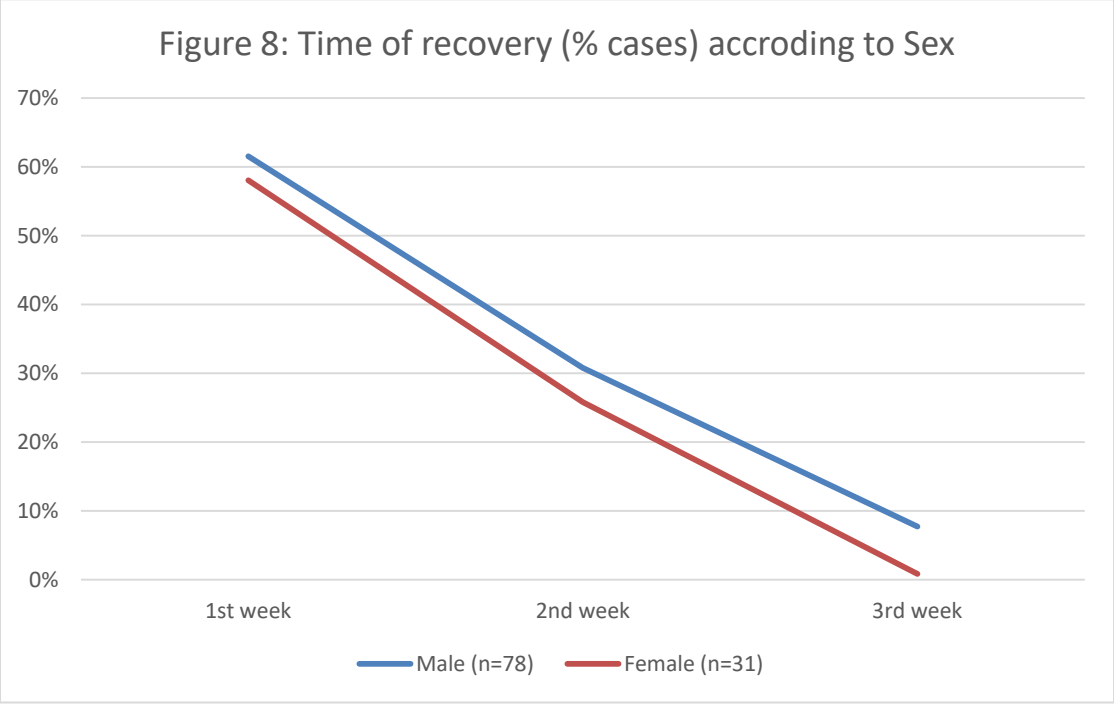
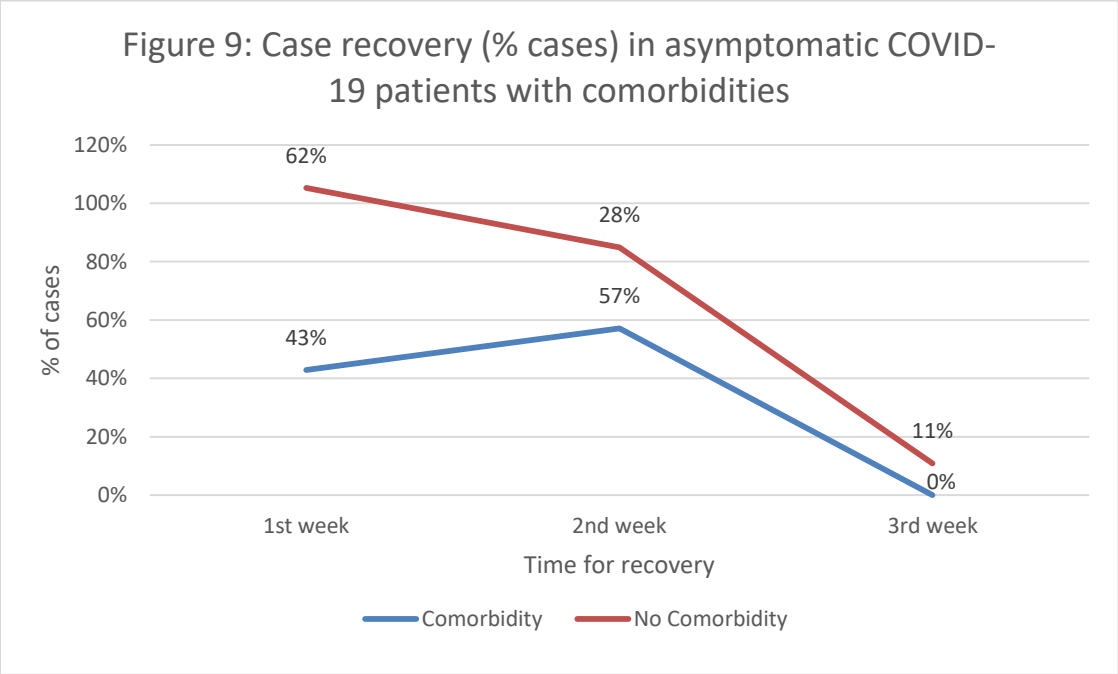


Table 9: Time kinetics of recovery in COVID-19 patients (asymptomatic) with comorbidities

Table 9: Time recovery in (asymptomatic) COVID-19 patients with comorbidities							
	n	1st week	% cases 1st week	2nd week	% cases 2nd week	3rd week	% cases 3rd week
Comorbidity	7	3	43%	4	57%	0	0%
No Comorbidity	102	63	62%	28	28%	11	11%
Total	109	66		32		11	
Comorbidity: Hypertension, Diabetes Mellitus, Hypothyroidism, alcoholism							



Discussion

In our study of demographic profile, out of a total of 118 patients, 82 patients (70%) were males while 36 patients (30%) were females (Table 1&5). It has been observed worldwide that males are much more affected in number than that of females by COVID-19. Chang D and Lin M have shown in their study that 77% of COVID-19 patients are males [4]. In our study population, 12 patients were of the pediatric age group. Among them, 2 (17%) were females while 10 (83%) were males (Table 4), so in children also male predominance is found. Wei M and colleagues have resulted in his study that among children, the male infection rate (60.95%) is higher than that of females (39.05%) [5]. The mean age of the affected population was 34.4 (± 13) years in our study (Table 1). In our study population, different age groups were- Children 0-20years (16% of the total study group), Young adults 21-25 years (8%), 26-35 years (30%), middle-age adults 36-55 years (41%), and >55 years (old adults) were only 4% of the study population (Table 3 & Figure 1). Lechien et.al reported the initial experience of 1420 patients in Europe from France, Belgium, Spain, and Switzerland. The mean age was 39±12 years, 94% were less than 60 years of age [6]. It is observed that young adults (38% of our study population) and middle-aged adults (41% of the study population) are more affected by COVID-19 than that of children and old age people. This can be explained by the reason that these age groups are more exposed because they tend to work outside the home, go out to fulfilling domestic requirements, etc. In hematological findings of asymptomatic COVID-19 patients (Table 2), their mean hemoglobin was 12.85gm% (±1.67), and the mean WBC count was 7,200 (±2,124) and was in the normal range. These results are synchronous with the study of De Chang[7]. In our study lymphocytosis was found only in 34% of patients while in differential leukocyte count, the mean lymphocyte percentage was 39.47% (±10.65). These results are contradictory to findings of Sina Vaqili and others who have found lymphopenia in COVID-19 patients in their literature review[8]. Thrombocytopenia was found only in 17% cases of our study group and the mean value of platelet count in our study was 2.34 lacs/c.mm (±0.85). Panyang XU has mentioned in his article note that statistics from 41 patients of COVID-19 at a designated hospital in Wuhan, 5% of patients had thrombocytopenia on admission [9].

In our study of asymptomatic COVID-19 patients, random blood sugar levels, liver function tests, and kidney function tests were in normal limits. We didn't measure s. ferritin level, IL-6 levels, and S. procalcitonin levels.

In the analysis of time kinetics of recovery of 109 asymptomatic COVID-19 cases, 66 patients (60%) became RT-PCR test negative in one week, 32 patients (30%) recovered in two weeks and the rest of the 11 patients (10%) had their recovery during the third week of admission (Table 6 & Figure 2). The mean recovery time of our study group of asymptomatic patients of COVID-19 was 7.2 (±5.8) days (Table 2). In the study of De Chang, the median recovery time (days from virus positivity to virus negativity) was 5.5 days (7). Irena Voinsky and et.al. have mentioned in their study the average recovery time of between 13 to 14 days in symptomatic patients of COVID-19, lowest for women under 19 years and highest for men aged 50-59 years respectively [10]. As mentioned in table 7 and Figure 3,4,5,6&7 among all asymptomatic patients, most of the children (0-15 years) recovered within one week (89%). In the age group 16-20 yrs., 86% recovered during the first week. Similarly, 50% of patients of 21-25 years age gr.,63% of 26-35 years age gr, 60% of 36-45 years of age gr,50% of 46-55 age gr and 25% of 56-65 years age group recovered with-in one week of treatment. On the other hand, the percentage of patients recovering during the second-week were 11% in children (0-15 yrs), 14% of age group 16-20 yrs., 50% of 21-25 yrs age, 17% in the age group 26-35 yrs., 30% in the age group 36- 45 yrs., 39% in 46- 55 yrs., 75% in the age group 56-65 yrs. and in >65 yrs. 100% gained recovery in the second week. We also observed that patients recovered in the third week are mostly young adults (26-35 yrs.) and middle age groups (36-55 yrs.) patients. Based on these observations, it can be concluded that as the age advances patients of COVID-19 take a longer time to recover from the disease. This recovery pattern is synchronous with the findings of Irena Voinsky in his study (10). However, this trend was not found in elderly patients >65 yrs., maybe because only one patient of this age was there in our study. This may be due to the fact that we were admitting only asymptomatic cases and most of the patients suffering from COVID-19 of the elderly age group tend to have symptoms.

As depicted in table 8 and figure 8, we have not found any significant difference in the recovery time of males and females. However, this finding is contradictory to the results of Irena Voinsky who found early recovery in females [10]. The impact of comorbidities (hypertension, diabetes mellitus, hypothyroidism, alcoholic liver disease) over the recovery time of asymptomatic COVID-19 patients is evident in our study as shown in table 9 & figure 9. In our study 43% of patients belonging to comorbid groups recovered in the first week while 62% of patients without any co-morbidities recovered in the first week. 57% of patients with comorbidities recovered in the second week while in the non-comorbid group 28% recovered in two weeks. And rest 11% of patients with no comorbidity recovered in the third week. Thus, it can be understood that even asymptomatic comorbid patients of COVID-19 take a longer time for recovery than that of non-comorbid patients. Sanyaolu A. et al. concluded that diabetes, hypertension, and hyperlipidemia were the most common comorbidities associated with COVID-19[11]. Wei-Jie Guan and et al. have observed in their study that among laboratory-confirmed cases of COVID-19 patients with any comorbidity yielded poorer clinical outcomes than those without[12]. A big limitation of our study is that only asymptomatic COVID-19 patients are recruited for the study. The small sample size is also a limiting factor. Thus, there is a need for a larger and vast study including symptomatic and critically ill patients to explore the less understood areas of this novel coronavirus disease.

Conclusion

It is concluded from our study that among patients of COVID-19 disease, male patients are affected more than that of female patients (males 2.3 times more affected than females). Similarly, male children are more prone to COVID-19 disease than female children (males 5 times more than females). Young adults and middle-aged persons are the most affected age group by this disease. Hematological and biochemical profiles of asymptomatic COVID-19 patients are not altered, however, thrombocytopenia and lymphocytosis are found in a small percentage of patients which may not be statistically significant. It has been observed in our study that younger patients recover faster than that of older patients. Recovery from COVID 19 is not affected by the sex of the patient. Presence of comorbidity slower the speed of recovery even in asymptomatic COVID-19 patients. The comorbidities had not affected and caused severity with multi-organ dysfunctions in our patients thus it has not compounded the natural course of the virus and its disease in humans. Our analysis was done on asymptomatic COVID-19 positive patients (confirmed by RT-PCR), hence time kinetics of recovery in these patients has revealed the dynamics of this emerging SARS-CoV2 virus in humans as a natural progression of infection in humans.

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