

Predictors of illness severity in COVID-19 cases

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Research

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Abstract

Background

Multiple studies worldwide reported the clinical and epidemiological features of coronavirus disease 2019 (COVID-19) with limited reports from the Middle East area.

Methods

This is an observational study to describe the clinical and epidemiological features of 341 COVID-19 cases in the Eastern Province of Saudi Arabia over the first three months from reporting the first case in the country and identify factors associated with severity of the illness.

Results

The median age was 45 years and males were twice as affected as females (p value < 0.0001). The duration of viral shedding ranged from 9 to 36 days. The most common clinical presentations include fever, shortness of breath, cough, myalgia, sore throat, vomiting, and headache. Severe and critical cases were significantly higher in males compared to females (23% vs 8.7%), senior adults (> 65 years), Bengali ethnicity, and in patient with com-morbidities including diabetes, hypertension, and dyslipidemia (p -value = 0.001). Furthermore, case fatality rate was found to be 10% and was significantly higher in male gender compared to female (13.8%vs 2.6%), and in Asian ethnicity (17.9%) compared to Arabs (6%) and African counterparts (0) (p -value = 0.002). No association was found between viral load represented by the RT-PCR cycle threshold (Ct) values and severity of illness.

Conclusion

Age, gender and ethnicity are important predictors of COVID-19 severity while Cycle threshold (Ct) of SARS-CoV-2 RT-PCR test cannot be used as a predictor of criticality of illness.

Background

In late December 2019, a cluster of pneumonia of unknown etiology emerged in Wuhan, China [1] that was believed to be a zoonotic disease [2,3] linked to a local animal market [4]. Few weeks later the disease showed a sustained transmissibility among human [5] and the etiology was identified as a novel member of the *Coronaviridae* named later as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) due to its genetic homology (82%) to the previously identified member of the coronavirus family, SARS-CoV [4]. Rapidly thereafter, the virus started to spread beyond China signaling an impending pandemic. On January 30th, the World Health Organization declared the novel coronavirus outbreak as a Public Health Emergency of International Concern (PHEIC).

The disease caused by the virus was called coronavirus disease-2019 (COVID-19) [6]. Individuals infected with SARS-CoV-2 can be asymptomatic, or more commonly present with a wide spectrum of clinical manifestations ranging from mild illness to life-threatening pneumonia with a median incubation period of 6.4 days [7]. Symptomatic patients commonly present with fever, cough, fatigue, and shortness of breath [8], and sometimes gastrointestinal manifestations in the form of diarrhea, anorexia, nausea, vomiting and abdominal pain [9]. Children have been shown to manifest mild features of the disease compared to adults [10] although certain studies suggested an increase in the incidence of multisystem inflammatory disease in children with COVID-19 [11,12]. In addition, pregnant women and their newborns seems to be mildly affected by COVID-19 with no reports of teratogenicity or severe illness [13]. On the 26th of November 2020, the World Health Organization indicated that COVID – 19 cases exceeded 59.8 million cases and multiple studies reported that the virus evolved gradually [14, 15] and this genetic evolution was thought to impact the severity and infectivity of COVID-19 [16, 17].

This study describes the epidemiological and clinical features of COVID-19 of the first 341 cases diagnosed in a university teaching hospital in the Eastern Province of Saudi Arabia over the first three months period of the pandemic in the country, and identify the spectrum of clinical presentation in different age groups. In addition, demographic data and comorbidities were analyzed and correlated to identify predictors of severity and prognosis.

Methods

A combined retrospective and prospective single-centered observational study was conducted at a university teaching hospital, which is a 550-bed hospital, which serves patients from the Eastern Province of Saudi Arabia and was authorized, among other hospitals, by the Saudi Ministry of Health to hospitalize and manage COVID-19 patients. The study describes the epidemiological and clinical features of COVID-19 for the first 341 SARS-CoV-2 positive cases diagnosed in the hospital since the start of the spread of the pandemic in the Eastern Province for three months (March 10th -June 13th).

During the study period, 3146 individuals were tested for SARS-CoV-2 infection using nucleic acid detection tests, of which 341 were positive. The indications for testing included clinical suspicion of symptomatic COVID-19, contact with confirmed cases, health care worker screening, and screening for all elective admissions to the hospital.

Testing for SARS-CoV-2 infection was done using either the RealStar SARS-CoV-2 RT-PCR kit (Altona diagnostics, Hamburg, Germany) or the Xpert Xpress SARS-CoV-2 kit (Cepheid, California, USA) according to the available and following the manufacturer's recommendations. Samples from all positive cases were sent to the National Health Laboratory for confirmation. Cycle thresholds were retrieved from the instruments software as shown in the final report.

All laboratory confirmed COVID-19 cases were included in the study. Clinical, demographic, and SARS-CoV-2 test results for all patients were obtained from the computerized hospital data system. Patients were stratified by age groups into infants (≤ 1 year), children (> 1 years-19 years), adults (20–65 years) and senior adults (> 65 years) for analysis according to the WHO classification. In addition, patients were also grouped based on clinical presentation as described by the Saudi Ministry of health into 4 groups: asymptomatic, mild to

moderate, severe, and critical cases [18]. Serial RT-PCR results were recorded for all confirmed cases which were followed up for clearance using a test-based strategy. Clearance duration was defined by the duration between the first positive RT-PCR and the first negative RT-PCR samples when the negative sample was confirmed by another negative RT-PCR sample collected ≥ 24 hours later.

Statistical analysis:

All data were tabulated in Excel spread sheets to calculate frequencies. Data grouping and calculation of chi square for linear trend were performed by the IBM SPSS software version 26. Graphpad software was used to calculate the correlation between Ct values and the disease severity. P value of less than 0.05 was considered significant.

Results

Epidemiological features of COVID-19

The total number of patients with laboratory confirmed COVID-19 infection was 341. The male to female ratio was 2:1 (225:116) (p value < 0.0001). The mean age of patients was 44.19 ± 18.03 years (median = 45 years and range = 4 months to 96 years). There was no significant difference in mean age between males and females (p value= 0.958).

With regards to mode of acquisition of infection, 67.2 % of patients (n = 229) did not report contact with a suspected or a confirmed COVID-19 case nor was there any clear epidemiological link with the source of infection. On the other hand, 20.2 % (n = 69) reported positive household contact with COVID-19 cases, and 3.2% (n=11) reported contact with suspected cases not confirmed by laboratory test, while only 7.3% (n=25) and 2.1% (n=7) of patients reported positive contact at work or travel history, respectively.

Case fatality rate (CFR), which is the proportion of death among cases, was 10% (n= 34). Male patients exhibited a higher mortality rate (13.8%, n= 31) than their female counterparts (2.6%, n= 3), and this difference was found to be statistically significant ($\text{Chi}^2 = 10.68$, p value = 0.001). In addition, the CFR was higher among patients with Asian descents demonstrated (n=21, 17.9%) compared to Arabs (n=13, 6%) and African counterparts (n=0) (p-value =0.002). Mortality rate was highest among patients older than 65 years old (24.32%) followed by patients between 41 and 65 years old (12.84%).

Clinical features of COVID-19

Out of the 341 COVID-19 cases, 52 (15.2%) were completely asymptomatic. Of the majority symptomatic cases, 153 (44.9%) had mild to moderate disease, 74 (21.7%) had severe disease and 62 (18.2%) were critically ill (Figure.1). Symptomatic patients presented with a wide variety of clinical manifestations including systemic manifestations in the form of fever, headache, and myalgia in addition to respiratory symptoms such as cough, shortness of breath, rhinorrhea and 3 patients reported loss of smell and taste. In addition, patients also reported gastrointestinal manifestation in the form of nausea, vomiting, anorexia and diarrhea. The most common clinical features were fever, shortness of breath, cough, myalgia, vomiting, sore throat, and headache (Table 1).

Table 1. Clinical features of COVID-19 cases between March and June 2020 according to age groups.

Clinical features	Infant (≤ 1 year)		Children ($>1-19$ years)		Adults ($>19-65$)		Senior adults ($65+$)		Total N=341	P-value
	N=5	%	N=18	%	N=280	%	N=38	%		
Fever	5	2.16	12	5.19	189	81.82	25	10.82	231	0.296
Shivering	0	0.00	0	0.00	22	95.65	1	4.35	23	0.936
Shortness of Breath	2	1.31	4	2.61	127	83.01	20	13.07	153	0.106
Chest pain	0	0.00	1	7.14	12	85.71	1	7.14	14	0.598
Wheezes	0	0.00	0	0.00	3	75.00	1	25.00	4	0.683
Cough	1	0.53	6	3.19	158	84.04	23	12.23	188	0.038
Sputum production	0	0.00	0	0.00	17	80.95	4	19.05	21	0.179
Hemoptysis	0	0.00	1	25.00	2	50.00	1	25.00	4	0.511
Rhinorrhea	0	0.00	3	30.00	6	60.00	1	10.00	10	0.057
loss of taste/smell	0	0.00	0	0.00	3	100.00	0	0.00	3	0.470
Sore Throat	0	0.00	3	9.68	26	83.87	2	6.45	31	0.336
Headache	0	0.00	3	10.00	24	80.00	3	10.00	30	0.576
Myalgia	0	0.00	3	5.56	41	75.93	10	18.52	54	0.122
Vomiting	0	0.00	4	11.76	30	88.24	0	0.00	34	0.035
Diarrhea	1	2.63	1	2.63	32	84.21	4	10.53	38	0.823
Abdominal pain	0	0.00	1	14.29	6	85.71	0	0.00	7	0.168
Nausea	0	0.00	0	0.00	7	77.78	2	22.22	9	0.376
Anorexia	0	0.00	0	0.00	1	16.67	5	83.33	6	<0.001

All infant cases described in this study (5/5) showed fever yet there was no significant difference in the clinical presentation among different age groups except for cough and vomiting which were reported more frequently in adults (16-65 years) (p value <0.05) and anorexia which was mainly reported in senior adults (>65 years) (p -value- <0.001)

The COVID-19 was found to be more severe in males, senior adults, and patients of Bangladeshi nationality while less severe in females, infants, children, and Saudi and Egyptian nationalities (Table 2). Furthermore, patient with diabetes mellitus, hypertension and dyslipidemia were more likely to have severe illness (Table 2).

No significant association was found between bronchial asthma, heart disease, cancer, and sickle cell disease with severity of COVID-19 (Table 2)

Table 2. The distribution of COVID-19 cases based on gender, age, co-morbidities, and nationality relative to the disease severity

Variables	Asymptomatic		Mild to Moderate		Severe		Critical		Total	p-value
	N	%	N	%	N	%	N	%		
	52		153		74		62			
Gender										
Female	22	19.30	60	52.63	22	19.30	10	8.77	114	<0.001
Male	29	12.83	93	41.15	52	23.01	52	23.01	226	
Age groups										
Infant (<=1year)	2	40.00	2	40.00	1	20.00	0	0.00	5	0.08
Children (>1- 19 years)	4	21.05	12	63.16	3	15.79	0	0.00	19	0.017
Adults (>19-65)	43	15.36	128	45.71	59	21.07	50	17.86	280	0.52
Senior adults (>65)	3	8.11	11	29.73	11	29.73	12	32.43	37	0.004
Co-morbidity										
Diabetes Mellitus	4	4.04	26	26.26	32	32.32	37	37.37	99	<0.001
Hypertension	5	6.17	23	28.40	32	39.51	21	25.93	81	<0.001
Smoking	0	0.00	1	20.00	3	60.00	1	20.00	5	0.23
Heart Failure	1	12.50	2	25.00	5	62.50	0	0.00	8	0.96
Cancer	1	16.67	3	50.00	0	0.00	2	33.33	6	0.97
Dyslipidemia	1	3.23	8	25.81	12	38.71	10	32.26	31	<0.001
CAD	1	14.29	4	57.14	1	14.29	1	14.29	7	0.55
CKD	5	14.71	8	23.53	8	23.53	12	35.29	34	0.23
Bronchial Asthma	0	0.00	4	57.14	3	42.86	0	0.00	7	0.84
SCD*	0	0.00	4	80.00	1	20.00	0	0.00	5	0.44
Nationality										
Saudi	37	19.9	93	50.0	36	19.4	20	10.8	186	<0.001
Bahraini	0	0.0	0	0.0	1	100.0	0	0.0	1	-
Egyptian	7	43.8	4	25.0	4	25.0	1	6.3	16	0.025
Jordanian	0	0.0	0	0.0	0	0.0	2	100.0	2	0.05
Yemeni	1	11.1	4	44.4	1	11.1	3	33.3	9	0.56
Bengali	2	5.1	8	20.5	12	30.8	17	43.6	39	<0.001

Indian	1	2.5	23	57.5	7	17.5	9	22.5	40	0.26
Pakistani	0	0.0	10	52.6	4	21.1	5	26.3	19	0.18
Philippine	3	13.6	8	36.4	8	36.4	3	13.6	22	0.8
Somalian	0	0.0	1	100.0	0	0.0	0	0.0	1	-
Sudanese	1	20.0	1	20.0	1	20.0	2	40.0	5	0.52

*SCD= sickle cell disease

Clinical features of COVID-19 in pregnant women

During the three-months study period, three pregnant women were diagnosed as SARS-CoV-2 positive. Two cases were 32 and 29 years old, at 36 and 40 weeks of gestation, respectively. Both reported household contact with COVID-19 cases. The first patient was gravida 2 para 1, asymptomatic case presented at the time of labor, had uneventful vaginal delivery and discharged home with her baby in good conditions. The second lady was primigravida, who reported runny nose 5 days prior to presentation, was discharged home and readmitted 10 days later with labor which was also uneventful with a healthy newborn baby. Both newborns were isolated in single cribs, initially tested by nasopharyngeal PCR twice, 24 hours apart, and closely monitored in the neonatal intensive care unit for 14 days as per the institution policy followed by a 3rd PCR prior to discharge. The third case was 27 years old primigravida at 11th gestational week who presented with fever and cough after acquiring the infection from a household contact. The lady was sent home for home isolation and care with no complications. The newborns were kept under observation for 14 days during which serial PCR testing was performed; none of the three cases was infected.

Viral shedding dynamics and Predictors of severe COVID-19

Of the 341 cases, one hundred and thirty-five (39.6%) confirmed cases underwent clearance following a test-based strategy with other cases being followed on a time-based clearance. The duration of viral shedding ranged between 9 and 36 days, with a median of 13.5 days \pm 5.66 (Figure 2). Association between duration of shedding and severity of illness was not possible because asymptomatic cases were following time-based clearance with no repeated testing. No association was found between cycle threshold (Ct values) of Xpert Xpress SARS-CoV2 test and severity of illness (Figure 3)

Discussion

This study of the first COVID-19 cases diagnosed in a university teaching hospital in eastern Saudi Arabia showed that out of 3,146 individuals tested for SARS-CoV-2, 341 were positive with an overall 10.8% detection rate. Majority of COVID-19 cases were adults (19–65 years) followed by senior adults (> 65 years), which most probably reflects the frequency of Covid-19 diagnosis in the described settings rather than an incidence in various age groups. Furthermore, males were more commonly affected than females and this is consistent with a recent multi-variate analysis study that identified male gender as an independent risk factor for acquisition of Covid-19 infection [19]. However, this could also be attributed to local social factors with males being more exposed by leaving homes to fulfil their work and family commitments during the lockdown periods.

The mode of acquisition was not known for most cases indicating a huge impact of asymptomatic spreaders of the disease and the need to improve contact tracing measures. This also may indicate the possibility of contacting the virus with means other than close contact such as the long distance migrating micro-aerosols, which is getting a growing acceptance among experts in the field [20]. The later hypothesis is supported by the fact that only one fifth of the cases in our study reported household contact with COVID-19 confirmed cases and 3% reported contact with suspected cases. Population-level studies are still limited for comparisons and most data available to date regarding the source of infection represent institutional experiences.

Case fatality rates (CFR) was found to be 10%, which is double that reported from Wuhan, China (5.6%) the epicenter of the pandemic [21]. This could be explained by multiple reasons including the study settings, a university hospital that was authorized to receive COVID-19 cases from other regional hospitals, which might lead to selection bias in the severity of cases included. Additionally, heterogeneity in the ethnicity and other demographics might also contribute to this difference in the case fatality across different studies. Most importantly, that case fatality rate does not take into consideration all individuals affected by SARS-CoV2 infection but only considers those cases who presented for testing as symptomatic, contact, or health care workers. This is also evident by the proportion of asymptomatic cases (15.2%) in our cohort that is less than that described in many similar studies [22]. Thus, the overall infection mortality rate among individuals with Covid-19 infections is likely to be considerably lower as it has been estimated by the CDC and WHO to be around 0.5- 1% [23,24]. On the other hand, the reported case fatality rates may have been underestimated considering that several fatal Covid-19 infections remain undiagnosed [25].

In our study, case-fatality was significantly associated with male gender, which can be explained by a possible genetic predisposition and also justified by the random and heterogeneous nature of the study sample where nationality being a significant confounding factor similar to earlier reports [26,27]. In addition, fatality was also found to be affected by the ethnic origin, being higher in Asian particularly Bengalis compared to Arabs (17.9–6%) ($p = \text{value } 0.002$), and also by the age factor, with higher rates in older age groups [28].

Clinically, COVID-19 confirmed patients were classified into four categories of severity, based on the local national protocol [18]. These categories include asymptomatic, mild to moderate, severe, and critical. This classification was made based on the clinical features, evidence of pneumonia, oxygen requirements, and the presence of serious complications. In addition to respiratory symptoms, patients also reported gastrointestinal symptoms in the form of vomiting, diarrhea, abdominal pain, nausea, and anorexia which is in line with other reports from different countries [29]. Fever also was reported in 100% of infants, a feature that was well documented in other studies, despite the low number of cases in our study [30]. It is interesting that only three patients reported the lack of smell/taste in the study. Whether this is a feature of the disease in the region or a lack of reporting needs further investigation.

Severe and critical COVID-19 illness was significantly higher in male gender, senior adults age groups, and Bengali ethnicity. On the other hand, severe and critical illness was significantly lower in Saudis and Egyptians (Arab ethnic groups) compared to other groups. The severity of the disease in various patient populations needs to be interpreted with cautions taking account for the full burden of the pandemic including delayed care and social determinants of health. Severity was also affected by co-morbidities, particularly diabetes mellitus, hypertension, and dyslipidemias as it was found in other studies [31]. The study included three pregnant cases

in whom the disease was mild to moderate in severity since pregnancy has not been identified as a risk factor for acquiring SARS-CoV-2 infection or worsening the prognosis [32–33].

The cycle threshold (Ct) refers to the number of cycles in a PCR assay needed to amplify viral nucleic acid to a detectable level. To the best of our knowledge, there are no clinical studies that validated use of Ct to estimate the disease burden in case of Covid-19. Although cycle threshold (Ct value) of the RT-PCR has often been considered a surrogate semi-quantitative measure for viral load estimation. In our study the initial Ct value on presentation did not correlate with the severity of illness. This can be attributed to variability in timing of sample collection with regards to onset of clinical features since many cases with severe illness commonly present late. On the contrary, asymptomatic contacts commonly present within few days of exposure and demonstrate variable Ct values. Therefore, Ct value should not be used as an indicator of viral loads in respiratory samples of Covid-19 cases. Furthermore, the Ct values are not standardized across various diagnostic platforms, therefore, results cannot be compared between different assays. Given the uncertainty of the role of Ct values in estimating the relative viral RNA level in a specimen, our study does not support its use for guiding a clinical decision.

The minimum duration for viral clearance from respiratory samples in our cohort was found to be 9 days and the maximum reported duration was 36 days. The duration of viral shedding has been reported to be variable and influenced by the severity of the illness [34–37]. Nevertheless, detectable viral RNA does not necessarily correlate with the presence of live infectious virus as more accumulative evidence suggests that viral RNA detected after 8 days is unlikely to be infectious [34]. Additionally, the virus has been detected in other types of specimens even after respiratory clearance with unlikelihood of clinical or infection control significance [38,39]. Therefore, the time-based strategy for clearance has been widely adopted in various institutions. Nonetheless, recent reports described the transmission of infectious virus later than 10 days from severely infected patients and therefore caution should be considered for vulnerable patient populations [35,40]. Further data are needed to conclude the period of infectivity in cases of critical and severe illness.

Our study is not without limitations, nevertheless, it contributes to the growing evidence of variable Covid-19 presentation and illness severity in relation to other factors and provided an insight about the lack of usefulness of Ct values as a predictive clinical tool.

Conclusions

Patients with COVID-19 manifest wide range of clinical presentations ranging from asymptomatic infection to severe and critical cases. Adult males were found to be twice as affected as females, and severity of COVID-19 was significantly associated with male gender, senior age group, and Asian ethnicity particularly Bengali ethnicity. On the other hand, for the first time, milder form of the disease was found to be significantly associated with Arab ethnic groups (Saudi and Egyptian), demonstrating the impact of ethnicity on disease severity. Furthermore, CFR was also found to be three times higher in Asian compared to Arabs. Cycle threshold (Ct) of Xpert Xpress SARS-CoV2, a surrogate measure of viral load, was not found to correlate with severity of illness and therefore is not recommended to be used as a predictor tool.

Declarations

Ethics approval: Ethical approval for the study was obtained from the Institutional Review Board at Imam Abdulrahman Bin Faisal University (IRB-2020-01-150)

Availability of data and materials: All data analyzed in the study are available upon reasonable request from the corresponding author

Competing interest: The authors declare no conflict of interest. The funding body did not contribute to the conceptualization, design, analysis, data interpretation, writing or publication choice.

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References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med.* 2020;382(8):727-33.
2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579(7798):270-3.
3. Ji W, Wang W, Zhao X, Zai J, Li X. Cross-species transmission of the newly identified coronavirus 2019-nCoV. *J Med Virol.* 2020;92(4):433-40.

4. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerg Microbes Infect.* 2020;9(1):221-36.
5. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223):514-23.
6. Dong L, Li Z, Fung ICH. A Call for Consistency in the Official Naming of the Disease Caused by Severe Acute Respiratory Syndrome Coronavirus 2 in Non-English Languages. *Disaster Med Public Health Prep.* 2020:1-2.
7. Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20-28 January 2020. *Euro Surveill.* 2020;25(5).
8. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395(10223):497-506.
9. Tian Y, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Aliment Pharmacol Ther.* 2020;51(9):843-51.
10. Song W, Li J, Zou N, Guan W, Pan J, Xu W. Clinical features of pediatric patients with coronavirus disease (COVID-19). *J Clin Virol.* 2020;127:104377.
11. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, et al. Kawasaki-like multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. *BMJ.* 2020;369:m2094.
12. Rauf A, Vijayan A, John ST, Krishnan R, Latheef A. Multisystem Inflammatory Syndrome with Features of Atypical Kawasaki Disease during COVID-19 Pandemic. *Indian J Pediatr.* 2020.
13. Yang H, Sun G, Tang F, Peng M, Gao Y, Peng J, et al. Clinical features and outcomes of pregnant women suspected of coronavirus disease 2019. *J Infect.* 2020;81(1):e40-e4.
14. Phan T. Genetic diversity and evolution of SARS-CoV-2. *Infect Genet Evol.* 2020;81:104260.
15. Biswas SK, Mudi SR. Genetic variation in SARS-CoV-2 may explain variable severity of COVID-19. *Med Hypotheses.* 2020;143:109877.
16. Hoehl S, Ciesek S. [The virology of SARS-CoV-2]. *Internist (Berl).* 2020;61(8):789-92.
17. de Lusignan S, Dorward J, Correa A, Jones N, Akinyemi O, Amirthalingam G, et al. Risk factors for SARS-CoV-2 among patients in the Oxford Royal College of General Practitioners Research and Surveillance Centre primary care network: a cross-sectional study. *The Lancet Infectious Diseases.* 2020;20(9):1034-42.
18. Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infect Dis.* 2020;20(7):773.
19. Oran DP, Topol EJ. Prevalence of Asymptomatic SARS-CoV-2 Infection : A Narrative Review. *Ann Intern Med.* 2020;173(5):362-7.
20. Weinberger DM, Chen J, Cohen T, Crawford FW, Mostashari F, Olson D, et al. Estimation of Excess Deaths Associated With the COVID-19 Pandemic in the United States, March to May 2020. *JAMA Intern Med.* 2020.
21. Mantovani A, Byrne CD, Zheng M-H, Targher G. Diabetes as a risk factor for greater COVID-19 severity and in-hospital death: A meta-analysis of observational studies. *Nutrition, Metabolism and Cardiovascular Diseases.* 2020;30(8):1236-48.

22. Li N, Han L, Peng M, Lv Y, Ouyang Y, Liu K, et al. Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study. *Clin Infect Dis*. 2020.
23. Qiancheng X, Jian S, Lingling P, Lei H, Xiaogan J, Weihua L, et al. Coronavirus disease 2019 in pregnancy. *Int J Infect Dis*. 2020;95:376-83.
24. Kragholm K, Andersen MP, Gerds TA, Butt JH, Østergaard L, Polcwiartek C, et al. Association between male sex and outcomes of Coronavirus Disease 2019 (Covid-19) - a Danish nationwide, register-based study. *Clin Infect Dis*. 2020.
25. Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A, et al. Clinical Characteristics and Morbidity Associated With Coronavirus Disease 2019 in a Series of Patients in Metropolitan Detroit. *JAMA Netw Open*. 2020;3(6):e2012270.
26. Bonanad C, Garcia-Blas S, Tarazona-Santabalbina F, Sanchis J, Bertomeu-Gonzalez V, Facila L, et al. The Effect of Age on Mortality in Patients With COVID-19: A Meta-Analysis With 611,583 Subjects. *J Am Med Dir Assoc*. 2020;21(7):915-8.
27. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious SARS-CoV-2 from diagnostic samples. *Clin Infect Dis*. 2020.
28. Liu WD, Chang SY, Wang JT, Tsai MJ, Hung CC, Hsu CL, et al. Prolonged virus shedding even after seroconversion in a patient with COVID-19. *J Infect*. 2020;81(2):318-56.
29. Perera R, Tso E, Tsang OTY, Tsang DNC, Fung K, Leung YWY, et al. SARS-CoV-2 Virus Culture and Subgenomic RNA for Respiratory Specimens from Patients with Mild Coronavirus Disease. *Emerg Infect Dis*. 2020;26(11).
30. Wolfel R, Corman VM, Guggemos W, Seilmaier M, Zange S, Muller MA, et al. Virological assessment of hospitalized patients with COVID-2019. *Nature*. 2020;581(7809):465-9.
31. Cheung KS, Hung IFN, Chan PPY, Lung KC, Tso E, Liu R, et al. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples From a Hong Kong Cohort: Systematic Review and Meta-analysis. *Gastroenterology*. 2020;159(1):81-95.
32. Zheng S, Fan J, Yu F, Feng B, Lou B, Zou Q, et al. Viral load dynamics and disease severity in patients infected with SARS-CoV-2 in Zhejiang province, China, January-March 2020: retrospective cohort study. *Bmj*. 2020;369:m1443.

Figures

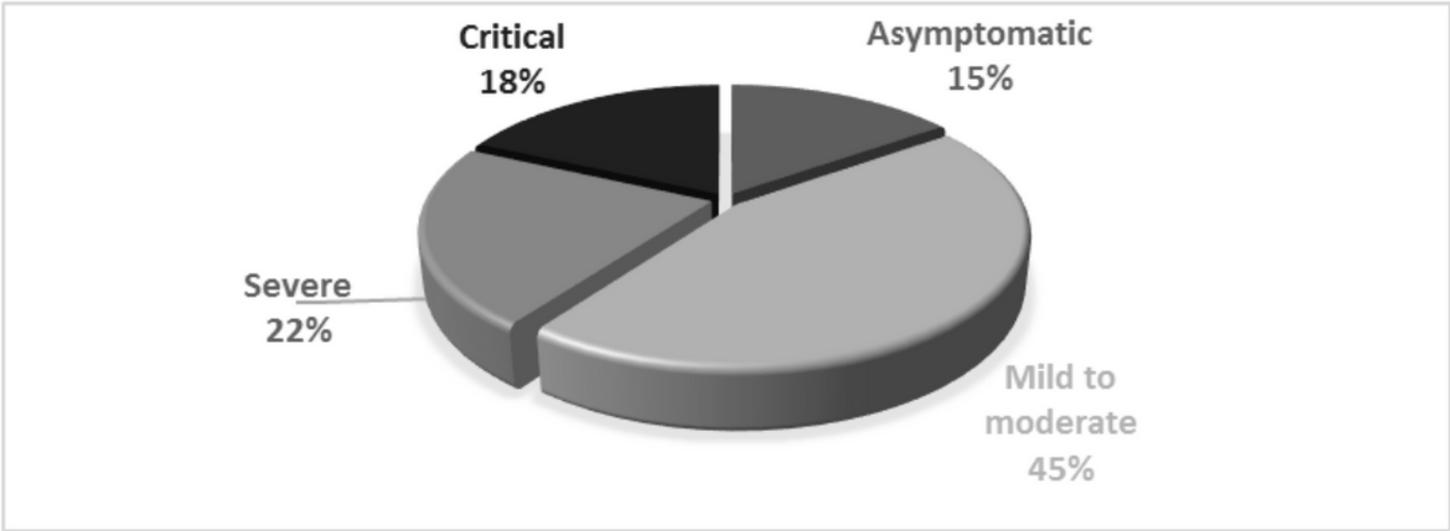


Figure 1

The spectrum of the severity of illness among the 341 COVID-19 cases

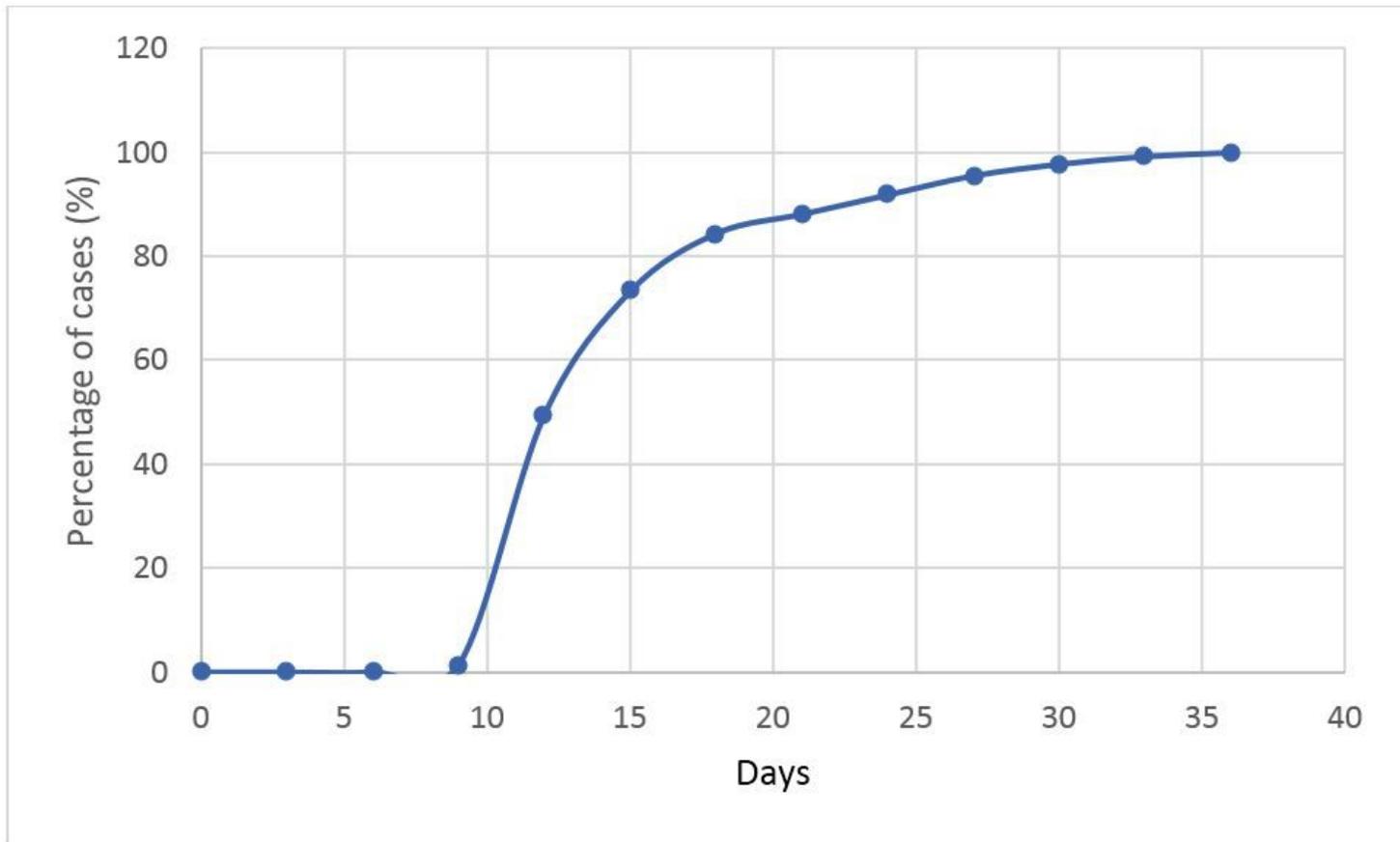


Figure 2

Dynamics of SARS-CoV2 viral clearance of 135 cases based on SARS-CoV-2 RNA detection

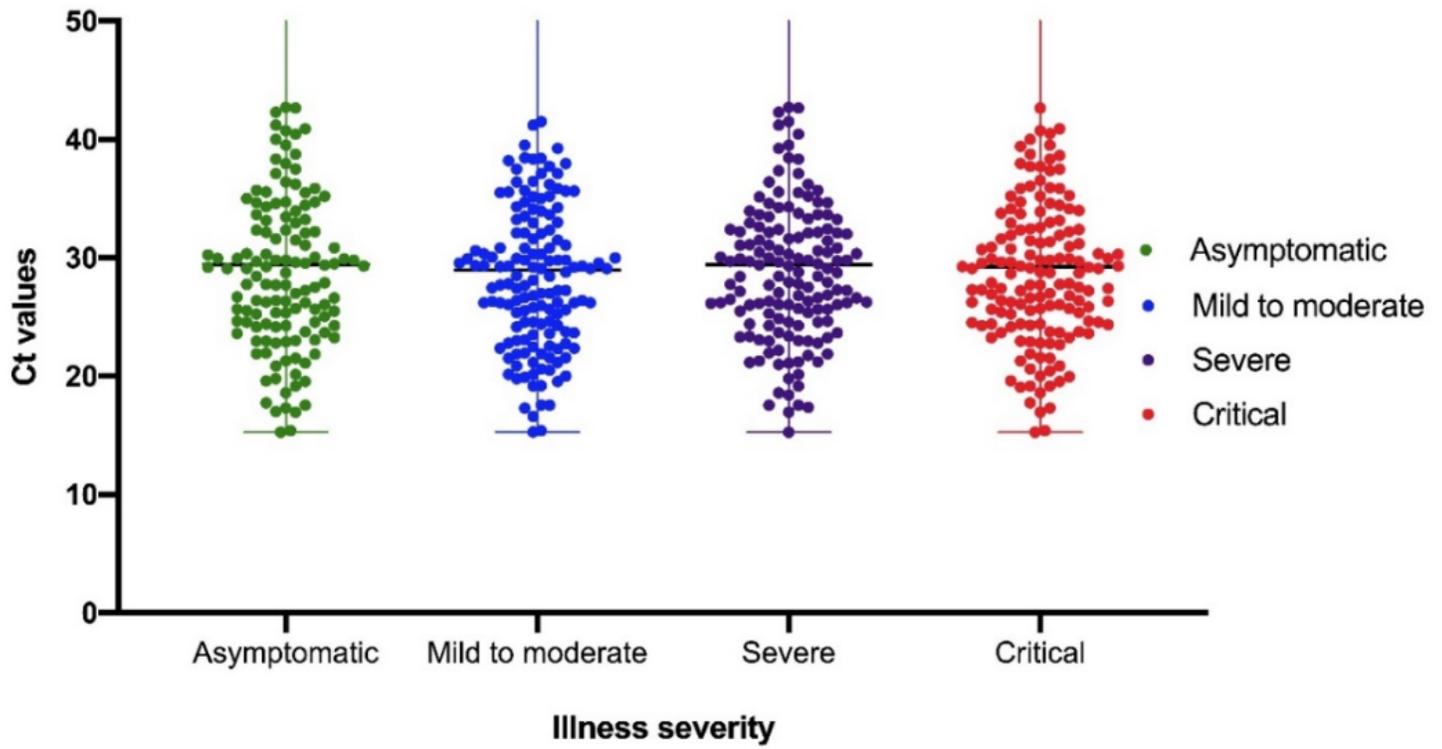


Figure 3

Frequency of cycle threshold (Ct) values for the E and N2 gene targets relative to COVID-19 severity (p value 0.65).