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Original Article

Prediction of Disease Severity with Initial Symptoms in SARS-CoV-2 Infection- A Single Center Study

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Abstract

Objective: The objective of this study was to predict disease severity with the help of initial symptoms in Covid-19 patients.

Methods: Ninety Nine coronavirus positive cases were recruited for the study. Their initial symptoms were recorded and correlated with parameters of disease severity like chest CT Severity Scores and laboratory parameters like C-reactive protein, serum Lactate dehydrogenase and serum ferritin. They were followed up over the period of 20 days and their initial symptoms were also correlated with mortality at 20th day.

Results: Fever was found to be the most common initial symptom in 58(59%) of patients, followed by sore throat 11 (11%) and shortness of breath 8(8%). Fever was also the first symptom in individuals with greatest mortality at 20th day among all age groups. Similarly, older age, greater CT severity scores (OR 8.14, 95% CI 1.82-36.25), raised CRS markers and lower oxygen saturations at room air (RR 1.18, 95% CI 1.07-1.30) were independently related to severe disease and higher mortality.

Conclusion: Fever as the first symptom was the most sensitive indicator of severe covid-19 infection especially in older population. Dyspnea followed by fever is the second most common symptom related to acute respiratory distress syndrome and severe covid infection.

Keywords: Covid, Symptoms, Severity, Prediction.

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Introduction

The outbreak of coronavirus disease 2019 quickly gained the status of pandemic due to its rapid spread around the globe. It is known to spread through respiratory droplets while sneezing and coughing. The novel coronavirus 2 (SARS-CoV-2) is a beta coronavirus that enters human cells through the membrane-bound angiotensin-converting enzyme 2 (ACE2).[1]

Clinical features of this infection are variable. Patients might be asymptomatic or may show symptoms such as loss of smell, fever, sore throat, shortness of breath, fatigue, myalgia or diarrhea. In some cases, disease progresses rapidly into severe illness either with or without acute respiratory distress syndrome (ARDS).[2] After its spread to all corners of the world, preventive measures were adapted including lockdowns, mass testing and later on country wide vaccinations. To tackle its effects on limited health care resources, patients were triaged on basis of their symptoms and severity of their disease. Interest also developed in predicting severity of disease with the help of initial symptoms, age, co-morbidities, social background and days of illness.[3] Age was found to a risk factor for severe COVID-19 infection along with co morbidities. In many instances, patients initially with mild symptoms later progressed to severe disease and vice versa. Therefore, development of screening tools for severe SARS-COV-2 infection are still being formulated.

The objective of this study was to predict disease severity in individuals infected with SARS CoV-2 virus on basis of their initial symptom onset and disease progression with relation to symptom progression. Mortality at

Table 1: *Regression analysis*

Factors		Disease Severity(CTSS >20)		Univariate logistic regression			Multivariate logistic regression		
		Yes	No	p-value	Un-adj OR	95% CI for UOR	p-value	Adj. OR	95% CI for AOR
Gender	Male	41 (45.2)	32(43.8)		1				
	Female	9(64.3)	5(35.7)	0.575	0.712	0.217–2.333	0.344	0.522	0.136–2.009
Mortality at 20thDay	Yes	9 (90)	1 (10%)	0.055	0.127	0.015–1.048	0.143	0.189	0.020–1.756
	No	41 (53.2)	36 (46.8)		1.00				
D-dimer Levels	<200	19 (39.6)	29 (69.4)		1.00			-	
	>200	28(82.4)	6(17.6)	0.000	7.123	2.481–0.447	0.001	0.143	0.048–0.430

95% CI: 0.03–4.05; p = 0.409) were not statistically significant predictors of severe disease.

had higher mean HRCT scores (29.4 ± 7.8) compared to those without dyspnea (23.8 ± 10.0), but the difference was not statistically significant (p = 0.092). The mean HRCT severity score among patients presenting with fever as the initial symptom was slightly higher (24.8 ± 9.1) compared to those without fever (23.5 ± 11.2). However, this difference was not statistically significant (t(88) = 0.589, p = 0.558; 95% CI: −3.03 to 5.58).

An inverse correlation was found between age and oxygen saturation levels at room air (SPO levels), indicative of severe disease with lower oxygen levels in more aged individuals (r=-0.359, p<0.001). A positive correlation was found between age of our patients and their HRCT chest severity scores, indicating a direct relationship between both revealing that individuals with higher age, had higher CTSS scores leading to a more severe disease (r=+0.298, p<0.001). Comparison of means for age showed that individuals with higher age showed greater rates of mortality at 20th day.

On multivariable logistic regression analysis, age was identified as a significant independent predictor of severe disease (adjusted OR: 1.05; 95% CI: 1.01 – 1.10; p = 0.010), indicating a 5% increase in odds of severe disease with each additional year of age. Similarly, lactate dehydrogenase (LDH) was identified as a significant independent predictor of severe disease (adjusted OR: 1.002; 95% CI: 1.000–1.004; p = 0.046). Other variables, including CRP (OR: 1.00; 95% CI: 0.99 – 1.01; p = 0.747), ferritin (OR: 1.00; 95% CI: 0.99 – 1.00; p = 0.956), presence of fever (OR: 0.68; 95% CI: 0.23 – 2.01; p = 0.484) and dyspnea (OR: 0.36; 95% CI: 0.03 – 4.05; p = 0.409) were not statistically significant predictors of severe disease.

The Kruskal–Wallis H test was applied to compare oxygen saturation at room air among patients presenting with different initial symptoms of COVID-19. A total of 99 patients were divided into 10 groups based on their first reported symptom: fever (n=58), sore throat (n=10), dyspnea (n=8), headache (n=2), rhinorrhea (n=2), myalgia (n=2), and one each with chills, malaise, abdominal pain, and arthralgia. The median oxygen saturation did not differ significantly across the symptom groups, $\chi^2(9) = 3.483$, p = 0.942. Although not statistically significant, patients who presented first with dyspnea had the lowest mean rank of oxygen saturation (mean rank = 32.19), while those presenting with chills had the highest mean rank (mean rank = 57.50). This suggests a possible trend towards lower oxygenation in patients initially presenting with dyspnea compared to other symptoms.

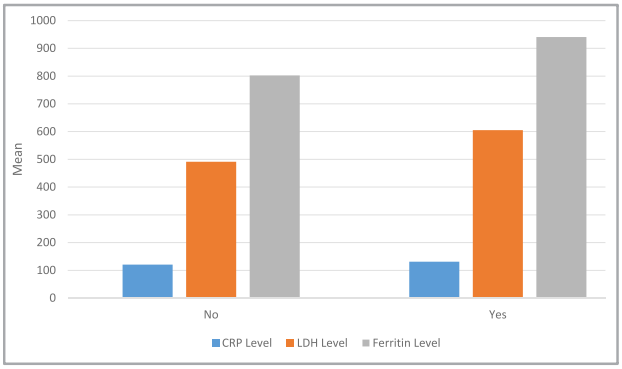

Figure 2: *Shows the different parameters with respect to mortality at 20th day.*

The distribution of ferritin, LDH, and CRP levels was compared across patients stratified by their first reported symptom using the Kruskal-Wallis test. Patients who initially presented with abdominal pain and myalgia showed the highest mean ranks for ferritin (88.00 and 81.33, respectively), while rhinorrhea was associated with the lowest (22.50). For LDH, myalgia (63.67) and headache (51.75) showed higher ranks, with rhinorrhea again having the lowest (6.50). Similarly, CRP levels were highest in patients with arthralgia (76.50), chills (72.00), and headache (66.50), and lowest in those with rhinorrhea (6.25). However, the Kruskal-Wallis test did not demonstrate statistically significant differences among the groups for ferritin ($\chi^2(9) = 13.172$, p = 0.155), LDH ($\chi^2(9) = 9.679$, p = 0.377), or CRP ($\chi^2(9) = 12.083$, p = 0.209).

20th day was also recorded.

Methods

This study was a prospective cross-sectional study conducted at a Pak-Emirates Military Hospital turned into COVID facility over the period of 3 months from October till December 2021. Sample size was calculated using WHO sample size calculator taking confidence level 95%, margin of error 5%, reported prevalence of COVID 6.5%. Study participants were selected through non probability convenience sampling technique from a field of nearly 500 potential candidates who presented to COVID screening desk. Informed consent was taken from all participants.

Inclusion criteria included all individuals from 2 till 90 years of age, symptomatic with confirmed positive real time Reverse Transcriptase-Polymerase Chain Reaction for COVID-19. Exclusion criteria included COVID 19-PCR negative patients with similar presenting symptoms, and patients who had positive COVID-PCR but were asymptomatic. Study was initiated after formal approval from Institutional Ethical Board via (Letter number EC/360/2021).

Patient demographics, oxygen saturations at room air and CT severity scores on admission were noted. Patient's highest CRP, LDH and ferritin levels were also collected after admission their trends followed and mortality at 20th day was recorded. Symptoms and their sequence were recorded individually by interviewing the admitted patients. Grouping of age was done as per WHO guidelines for better assessment of the disease symptoms and progression. Grouping was as follows, Group 1: 1-19 years; Group 2: 20-38 years; Group 3: 39-57 years; Group 4: 58-76 years; Group 5: 77-95 years.

Data was analyzed in statistical package for social sciences version 22.0. Continuous variables were expressed as mean ± standard deviation (SD) after checking for normality of distribution using the Shapiro–Wilk test. Categorical variables were presented as frequencies and percentages (n, %).

To assess correlations between continuous variables (e.g., age and oxygen saturation, age and HRCT severity score), the Pearson correlation coefficient (r) was computed. Group comparisons of continuous variables (e.g., HRCT scores between different symptom groups) were performed using the Independent Samples t-test. Statistical significance was set at $p < 0.05$.

To identify independent predictors of severe disease, multivariable binary logistic regression analysis was performed. Severe disease was defined as [e.g., HRCT severity score ≥20, oxygen saturation ≤90% and mortality at 20th day]. The dependent variable was coded as 1 for non severe disease and 2 for severe. Independent variables included age (continuous), gender, initial presenting symptoms (fever and dyspnea; coded as 1 =present, 0=absent), and biomarkers (C reactive protein, lactate dehydrogenase, and ferritin; all continuous). Variables were entered simultaneously into the model. Model fit was assessed using the Hosmer–Lemeshow goodness of fit test. Adjusted odds ratios (ORs) with 95% confidence intervals (CI) and corresponding p values were reported for each predictor. The distribution of ferritin, LDH, and CRP levels was assessed for normality using the Shapiro-Wilk test, which showed non-normal distributions. Therefore, the Kruskal-Wallis test, a non-parametric alternative to one-way ANOVA, was applied to compare the distribution of ferritin, LDH, and CRP levels across groups stratified by the first reported symptom. The results were presented as mean ranks for each group. A p-value <0.05 was considered statistically significant.

Results

Total of Ninety nine patients were recruited to participate in the study. Males comprised of 79(79%) of the total sample size while females were 20 (21%). Mean age of sample population was 60.63 ± 16.91 years. Average day of illness was 8 ± 3.74 days. Average saturation at room air was 86.10 ±10.18 % with minimum saturation till 50% and maximum till 99%. Mean CTSS came out to be 24.32±9.92 out of 40, with mild disease in 21(21%), moderate disease in 19(19%) and severe disease in 47(48%) of patients. In terms of laboratory parameters, mean values of CRP(Q), LDH and Ferritin to be 125 ± 91µg/mL 506 ± 329 U/L and 819 ± 918 µg/mL respectively.

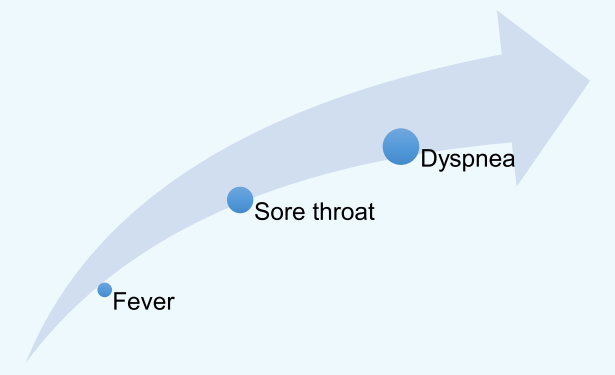

Figure 1: *The appearance of symptoms in individuals effected by Covid19 disease.*

Among all age groups, fever was reported as the first symptom in 58(59%) of the patients while only 11(11%) reported sore throat and 8(8%) had dyspnea as their first symptom. Dyspnea, a classic symptom of severe Cov-2 virus disease appeared to be the 'third' most common symptom among all age groups, in 14(14%) of patients. Patients with dyspnea as their first symptom

Discussion

In a systematic review done on 148 studies from 9 countries, fever was found to be the most common symptom followed by cough and fatigue which is consistent with the findings of our study where fever was the most commonly occurring first symptom followed by sore throat among hospitalized patients.[4,5] Presence of dyspnea as the third most common symptom in our study is contrary to this meta-analysis.

A study from Catalonia which included data from nursing homes showed a positive predictive value of mortality for some variables like age and symptoms like fever and dyspnea in older individuals.[6] Findings of our study are also in accordance with the findings of recent studies, which showed that increasing age was directly proportional to the greater disease severity with older individuals having greater CT severity scores and lower oxygen saturations at presentation. Another study showed age to be strongest predictor of death, surpassing abnormal vitals or laboratory parameters and comorbidities[7]. Similar facts were reported from studies done in different parts of the world.[8] All these findings are suggestive of a more proactive approach in older patients in terms of an early diagnosis, staging and treatment of the severe Covid disease.

In a study done in Wuhan China, dyspnea and expectoration were found to be the most common symptoms associated with death.[9] Just as increasing age, shortness of breath has also been found to be an independent risk factor contributing towards mortality.[10] Shortness of breath indicates that the patient has developed lung damage and the infection has progressed to respiratory distress syndrome which is the severe category of the disease.[9] Shortness of breath was also a prevalent symptom in older population whereas cough was more prevalent in younger individuals with good recovery.[11] This study also found shortness of breath to be a symptom of severe disease as it was associated with lower oxygen saturation levels at room air, higher CTSS scores, higher levels of CRP and LDH, all of which are markers of severe disease.[12,13,14] Our study also found cough to be a more prevalent symptom in younger patients and dyspnea among older patients.

Relationship of fever and dyspnea with disease severity and poor clinical outcomes has been interesting as one systematic analysis showed both dyspnea and fever to be associated with severe disease.[12] In another study, fever rather than dyspnea was found to be associated with greater disease severity however, a case series from Henan province declared presence of fever not to be associated with disease severity.[15] Our study showed fever as the initial symptom progressing to dyspnea in later stages to be linked with severe disease and higher mortality which is consistent with studies showing fever as the most prevalent symptom in hospitalized patients.[16,17,18]

One thing common in all studies world over was the presence of high grade fever as the most prevalent symptom. Our study also found fever to be the most common first symptom in all age groups. Another important aspect is the fact that none of the studies found in literature recorded sequence of symptom onset in Covid patients. With regards to the sequence of symptoms, this study was able to show that fever followed by dyspnea as the second or third symptom was associated with respiratory distress syndrome. Therefore, it can be inferred that fever followed by dyspnea is associated with increased mortality whereas fever alone or in combination with symptoms other than dyspnea was not associated with increased mortality. More research is required in order to better understand the temporal association of symptoms in COVID infection in order to better predict disease severity.

The current study is a single center study with limited number of admitted cases. More studies are required at multiple centers as increased sample size can provide with better results. Population with mild symptoms was not included in this study as they did not undergo extensive laboratory work up nor were offered hospital admission. More studies are required to be done on population with mild symptoms which shall help in better understanding of the disease.

Conclusion

Fever as the first symptom was the most sensitive indicator of severe covid-19 infection especially in older population. Dyspnea followed by fever is the second most common symptom related to acute respiratory distress syndrome. Onset of fever as the first symptom along with other risk factors is the most sensitive indicator of severe disease.

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Conflict of Interest: None

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Authors' Contribution

ARA: Conception.

FA, AR: Design of the work.

MZAQ, MA, STHG: Data acquisition, analysis, or interpretation.

MZAQ, MA, STHG, FA: Draft the work.

ARA, FA: Review critically for important intellectual content.

All authors approve the version to be published.

All authors agree to be accountable for all aspects of the work.

References

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020; 395(10229): 1054 – 62.
2. Pietrobon AJ, Teixeira FM, Sato MN. Immunosenescence and Inflammaging: Risk Factors of Severe COVID-19 in Older People. Front Immunol. 2020; https://doi. org/ 10.3389/fimmu.2020.579220.
3. 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.
4. 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.
5. Grant MC, Geoghegan L, Arbyn M, Mohammed Z, McGuinness L, Clarke EL, et al. The prevalence of symptoms in 24,410 adults infected by the novel coronavirus (SARS-CoV-2; COVID-19): A systematic review and meta-analysis of 148 studies from 9 countries. PLOS ONE. 2020;15(6):e0234765.
6. Meis-Pinheiro U, Lopez-Segui F, Walsh S, Ussi A, Santaeugenia S, Garcia-Navarro JA, et al. Clinical characteristics of COVID-19 in older adults. A retrospective study in long-term nursing homes in Catalonia. PLOS ONE. 2021;16(7):e0255141.
7. Jackson BR, Gold JAW, Natarajan P, Rossow J, Neblett Fanfair R, da Silva J, et al. Predictors at Admission of Mechanical Ventilation and Death in an Observational Cohort of Adults Hospitalized with Coronavirus Disease 2019. Clin Infect Dis. 2020; 73(11):e4141-51.
8. Gemcioglu E, Davutoglu M, Catalbas R, Karabuga B, Kaptan E, Aypak A, et al. Predictive values of biochemical markers as early indicators for severe COVID-19 cases in admission. Future Virol 2021; 16(5): 353 – 67.
9. Deng Y, Liu W, Liu K, Fang YY, Shang J, Zhou L, et al. Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 in Wuhan, China: a retrospective study. Chin Med J. 2020;133(11):1261.
10. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated with Acute Respiratory Distress Syndrome and Death in Patients with Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med. 2020;180(7):934–43.
11. Singhal S, Kumar P, Singh S, Saha S, Dey AB. Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis. BMC Geriatrics. 2021;21(1):1–9.
12. Khan JA, Asmat F, Siddiqi FA, Tareen TB, Hassan F, Mehreen S, et al. High-Resolution Ct (Hrct) Chest Findings in PCR Positive Patients of COVID19 at Combined Military Hospital Rawalpindi. Pak Arm Forces Med J. 2021;71(3):951–4.
13. Javed MW, Anwar M, Bangash TM, Satti RU, Rehman M, Malik UI. C-reactive protein levels and the severity of COVID-19. Pak Arm Forces Med J. 2020; 70(2): S603-07.
14. Adil M, Baig ZF, Amir M, Chatha SS, Habib A, Majid M. Neutrophil to lymphocyte ratio vs platelets to lymphocyte ratio: biomarkers to predict severity of disease and their comparison in patients of COVID-19. Pak Arm Forces Med J. 2020;70(6):1609–15.
15 Chidambaram V, Tun NL, Haque WZ, Gilbert Majella M, Kumar Sivakumar R, Kumar A, et al. Factors associated with disease severity and mortality among patients with COVID-19: A systematic review and meta-analysis. PLOS ONE. 2020;15(11):e0241541.
16. Li J, Chen Z, Nie Y, Ma Y, Guo Q, Dai X. Identification of Symptoms Prognostic of COVID-19 Severity: Multivariate Data Analysis of a Case Series in Henan Province. J Med Internet Res. 2020;22(6): e19636.
17. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J. 2020;133(9):1025–31.
18. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. New Eng J Med. 2020;382(18):1708–20.
19. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAm Med Assoc. 2020; 323(11): 1061–9.