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Covid Prognostic Score (CoPs) to Predict Prognostic Outcome in Patients with Severe Covid-19 Pneumonia

Rizwan Qazi[1], Saad Shakil[2], Hafsa Atique[3]

[1]HOD, Department of Medicine, Dr. Akbar Niazi Teaching Hospital, Islamabad
[2]Medical Officer, Department of Medicine, Dr. Akbar Niazi Teaching Hospital, Islamabad
[3]Final Year MBBS, Islamabad Medical and Dental College, Islamabad

Author`s Contribution

[1,2]Conceptualized the study and contributed in data collection and aided in drafting the article
[3]data collection, drafting of the article and statistical analysis

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Address of Correspondent
Dr Saad Shakil
Medical Officer, Department of Medicine, Dr. Akbar Niazi Teaching Hospital, Islamabad
saad_shakil7@live.com

ABSTRACT

Objectives: To assess the degree of medical intervention needed for treatment and its application in areas with low resources and testing facilities.

Methodology: A Retrospective Cohort study was conducted on 141 patients from June 2020 to May 2021. All PCR positive covid patients were included; excluding those who died or left within 24 hours of admission. Data was obtained from hospital record. (HIMS), incorporating sociodemographic details, history of co-morbids and presenting complaints.

A Covid-Prognostic Score was developed to predict hospital outcome and severity of covid disease. It comprised of age, comorbidity (diabetes and ischemic heart disease), chest-x ray score, neutrophil- lymphocyte ratio (NLR) and ferritin score.

Using SPSS version 23, descriptive means were analyzed; Chi-square test was applied along with Mann- Whitney U and linear regression. P-value less than 0.05 was considered significant.

Results: A significant association was found between health status (i.e., alive or dead) and diabetes (p=0.045) and ischemic heart disease (p=0.004), which reinforced their importance in the CoPS score. Association between CoPS and gender health status was highly significant; (p=0.003) (p=0.000) respectively. A positive correlation was found between CoPS and duration of hospital stay (R = 0.495) (p=0.216).

Conclusion: The continuous surge of Covid-19 is causing hospital resource and facility burn out. The CoPS score aims to pave way for triage therapy from the point of admission. A multi-center approach and scoring of "severity strata" of disease would further corroborate the relevance of the CoPS scoring system.

Keywords: Covid-19, prognostic score, age, diabetes, IHD, NLR, x-ray score, ferritin.

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Introduction

December 2019 marked the emergence of many cases of unknown pneumonia in Wuhan city, Hubei Province, China. After respiratory sampling and investigation, a new type of corona virus was found, named severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). It was a typical RNA virus, belonging to the β-coronavirus family.[1]

The corona virus disease 2019, as dubbed by the World Health Organization (WHO), was declared as the 6th public health emergency of international concern (PHEIC) on 30th January 2020. Soon, the disease crossed borders and affected areas other than China. On 11th March 2020, WHO confirmed its status as a global pandemic.[2]

Covid-19 also affected Pakistan with a toll of 287,300 confirmed cases, and 6153 deaths reported as of August 14th,2020.[3] The first cases of the pandemic were reported on 26th February 2020, in Karachi and Islamabad. On 18 March 2020, cases had been registered in all the four provinces, the two autonomous territories, and Islamabad Capital Territory, and by 17th June, each

district in Pakistan had recorded at least one confirmed case of COVID-19.[4]

Worldwide, Covid-19 has affected more than 10 million people, causing mortality in >5 lac. This widespread is credited to the mode of transmission and contagious nature of the virus with an Ro (basic reproduction number) of 2-2.5. Another factor leading to this outspread is the asymptomatism of 50% of the infected cases.[5]

In addition to 23% mortality6, Pakistan has also faced a massive loss in terms of finance and economy. With the constant increase in the number of Covid cases, the global health structure has also faced resource insufficiencies.[7]

Sudden surge of cases occurred again in Pakistan in July 2020 after a period of relative control on the pandemic. On October 29, over 10,000 positive cases were reported nationwide. Authorities said that the health facilities were unable to cope with the pace. Hospitals were short of beds, Covid testing facilities lacked and the infection rate in health care workers was increasing swiftly.[8]

The virus hit yet again with a new strain on February 22nd, 2021 with the highest rate of infectivity and severity of symptoms, taking a toll of 15,872 in a minimum period of two months.[9]

It is to note that considering the rapid decline of basic health resources and testing facilities with the sudden surges in the pandemic, it is essential to identify patients at high risk for covid and its complications and its prognosis before any confirmatory testing. This is to effectively utilize and prioritize PCR tests, containment facilities and provision of personal protective equipment (PPE) in hospitals.[10]

Patients need to be triaged according to their clinical severity. Early risk stratification and mortality prediction is needed[11] to provide early medical intervention and assess prognosis timely. Here, we have developed a score to predict the mortality of covid-infected patients early on. The aim of this score is to assess the degree of medical intervention needed for treatment and its application in areas with low resources and testing facilities.

Methodology

A Retrospective Observational Cohort study was conducted on 141 patients in the Department of Medicine at Dr. Akbar Niazi Teaching Hospital, Islamabad, Pakistan. The study lasted for a year from June 2020 to May 2021. Ethical approval was obtained from the Ethical Review Board of the hospital.

The study included all those patients who had tested positive for Covid-19 on real-time polymerase chain reaction (RT-PCR). Most of the patients admitted were already suffering from severe Covid disease and were ICU-admitted. Patients who died within 24 hours of admission (i.e., 3) and did not receive any laboratory testing or left against medical advice (i.e., 4) were excluded from our study.

During the study period, due to limited testing facilities and affordability issues, the patients were admitted on the basis of either suggestive or confirmatory laboratory findings or the severity of their presenting complaints. Any patients who presented with shortness of breath or an un-resolving fever, unresponsive to anti-pyretic medications or a positive HRCT or PCR were admitted in the hospital.

Regular vital sign monitoring was followed by baseline investigations. These included complete blood picture, arterial blood gases, chem-7 blood test, liver function tests, ferritin or C-reactive protein and D- dimer levels. All these gave us information about the intensity of their inflammatory processes and body's immune status against the disease.

Treatment protocol for all the admitted patients included a regime of antibiotics and antivirals, followed by steroids. Amoxicilin, remdesivir and dexamethasone were used along with a cover of clexane or heparin. Further, oxygen supplementation was also provided to patients in acute respiratory distress.

All the data was obtained from the hospital-based health information management system (HIMS). This included their name, age, sociodemographic history, history of presenting complaint and presence of any co-morbidities. It further included their length of hospital stay and hospital outcome i.e., if they died or were healthy and discharged by the attending physician.

We developed a score to predict the hospital outcome and severity of Covid disease in these patients. It consisted of their age,[12] comorbidity, which mainly included diabetes[13] and ischemic heart disease[14] due to their reported severe impact on covid in previous studies; neutrophil-lymphocyte ratio (NLR)[15], chest x-ray score[16] and ferritin levels[17]. Each factor was

calculated from a total of 1 and they were summed up to 5.

- Age of all the patients was recorded and scored according to the set values.
- Patients were inquired about any existing co-morbidities at the time of admission. Then they were categorized and scored based on the type of co-morbidity present.
- All patients were screened through blood tests and chemical analysis for their disease severity. Their complete blood pictures at admission recorded neutrophil and lymphocyte levels. Then their ratio was calculated and scored according to the CoPS scoring system.
- Ferritin levels of all the patients were tested at admission and then classified and scored.
- The x-ray was divided into six zones, based on a literature-based scoring system. Each zone was further scored from 0-3 based on the degree of interstitial or alveolar infiltrates. All x-rays were then graded out of 16 and classified into mild, moderate and severe and finally scored out of 1.

Statistical Analysis: SPSS-version 23 was used. Descriptive means and frequencies were calculated and Chi-square test was applied to compare the health status with comorbidities and presenting complaints of the patients. Mann-whitney U was used to compare CoPS score with the gender and health status of patients. Linear regression was also applied to compare CoPS with the duration of hospital stay, as the data was non-parametric. Results with p-value less than 0.05 were considered significant.

Results

Overall, 68% males and 45% females, with a mean age of 61±13.381 were analyzed. Q-Q plot was used to determine the data as non-parametric. Frequential data revealed that 23% patients only had reported of no comorbidities. Amongst the rest, 50% patients were diabetic, 49% hypertensive and 20% had an underlying ischemic heart disease.

To account for the presenting complains, 80% participants presented with fever, 85% with shortness of breath, 66% with cough and 81% with other complaints like anosmia, altered state of consciousness, myalgias, chest pain, collapse, drowsiness, dyspnea, sore throat, tonic-clonic fits, urinary symptoms and generalized body weakness.

The patients underwent the basic covid-19 treatment protocol, which included measurement of basic cell levels and inflammatory markers, like platelets, lymphocytes, neutrophils and d-dimers and ferritin etc. It also included administration of drugs like remdesivir, solumedrol, dexamethasone etc. A descriptive analysis was run to assess the frequency of all these factors. The patients had a mean platelets level of 234517.73±180928.818 per microliter and they stayed in the hospital for an estimate of 7±7 days. Table I show frequencies of patients who received solumedrol and remdesivir and also their definitive health status.

Table I: Number of Remdesivir doses administered

No. of Doses	No. of Patients	Percent
0	43	30.5
1	16	11.3
2	19	13.5
3	14	9.9
4	13	9.2
5	13	9.2
6	6	4.3
7	5	3.5
8	1	.7
9	1	.7
10	9	6.4
11	1	.7
Total	**141**	**100.0**

Chi-square test was applied to compare the health status with comorbidities and presenting complaints of the patients. A significant association was found between health status (i.e., alive or dead) and diabetes (p=0.045) and ischemic heart disease (p=0.004) (table II), which reinforced their importance in the CoPS score. Association between health status and presenting complaints (fever, cough, shortness of breath and others) was insignificant (p>0.05). Duration of hospital stay was also compared with the presenting complaints and comorbidities, which did not amount to any statistical significance (p>0.05).

Mann-whitney U was used to compare the numeric variables. The CoPS score was compared with the gender and health status (alive or dead) of all the admitted patients. This turned out to be highly significant; (p=0.003) (p=0.000) (table III) respectively.

Further, linear regression was applied to compare CoPS with the duration of hospital stay. The analysis was statistically insignificant (p>0.05). However, a positive correlation was seen between the two (B = 0.067) (p=216) (table IV). CoPS was also compared with

solumedrol and the no.of Remdesivir doses received, which were also statistically insignificant (p>0.05).

Table II: Comparison of Health Status with Ischemic Heart Disease

				Total	P value
		alive	dead		
Ischemic Heart Disease	yes	13	16	29	0.004*
	no	87	32	119	
Total		100	48	148	

Table III: Comparison of CoPS with Health Status

Health Status		N	Mean Rank	Sum of Ranks	P value
CoPS total	alive	96	57.34	5505.00	0.000*
	dead	45	100.13	4506.00	
	Total	**141**			

Table IV: Comparison of CoPS with Duration of Hospital Stay

Descriptive Statistics				
	Mean	Std. Deviation	N	P value
Duration of Hospital stay	7.2482	6.96641	141	.216
CoPS total	2.741	.9385	141	.216

Discussion

In this study, we developed a covid prognostic score (CoPS) to accurately identify the severe disease outcome, i.e, requiring intensive treatment protocol and ventilatory support during the course of stay in the hospital, and the ultimate outcome of the disease, i.e., discharge or death. The aim was to predict the expected disease severity early on, based on the individual CoPS of the patient and devise an efficient management plan accordingly.

The predictive factors included age, comorbidities like diabetes and ischemic heart disease, ferritin levels, neutrophil-lymphocyte ratio and x-ray scores. Since almost all these factors are routinely measured at admission globally, the score aimed to provide effective patient triaging even in low resource and high flow areas.

Importance of each of these factors as predictors of covid severity has been well documented in literature. A study conducted in USA studied the correlation of all three types of adaptive immunity, i.e., specific $CD4^+$ and $CD8^+$ T cell and neutralizing antibody responses, and SARS-Covid 19 disease. It determined a failed coordination of the antigen-specific adaptive immune response (ADIM) in association with aging and scarce native T cells. According to this study, individuals above 65 years of age displayed a poor association of all three immune responses, thus resulting in increased susceptibility to severe covid-19.[12]

A meta-analysis conducted by Kumar A et.al. concluded that diabetic patients with Covid-19 disease were twice more susceptible to disease severity and mortality, with an odds ratio close to 2.[18] An analysis done by researchers in Italy confirmed that amongst the 44,672 covid cases in Wuhan, China, case-fatality rate was increased by 10.5% in presence of cardiovascular diseases.[19]

Yang AP et.al concluded from their study that high NLR was a significant prognostic marker for pneumonia progression in covid patients. They also emphasized its importance and benefit of integration into the prognostic nomograms.[20] As in our study, another group of researchers from Italy also developed a prognostic score which included chest x-ray score as a predictive factor and claimed to be the first study to assess the effectiveness of this score in predicting mortality.[21] A meta-analysis done by researchers in China pointed out that increased levels of circulating ferritin indicate a viral infection and its replication. They also pointed out the role of ferritin in cytokine storm and inflammation process, thus playing a major role in exaggeration of the body's immune response and development of severe covid disease.[22]

Thus, all the above evidence supports the importance of our score components and their role as prognostic markers for Covid-19 severity and their likelihood of developing ARDS, need for ICU care, ventilatory support and vulnerability to mortality.

We analyzed the importance of CoPS through comparison with different factors. Significant associations were found between the CoPS and gender and mortality. A similar study assessed 30-day mortality risk through covid mortality risk score. According to this study, as the score increased, the risk of 30-day mortality also increased.[23] Another systematic review from Italy reported that even though no striking difference was appreciable among disease susceptibility of males and females, a minute difference of 0.1 was noticed. This difference was owed to the significant association

between male gender and high risk of mortality coupled with low chances of recovery.[24]

Although no promising association was witnessed among CoPS and the duration of hospital stay in our study, a positive correlation was achieved. This indicated that with every 1 point increase in the CoPS, the duration of hospital stay is likely to increase by 0.495 days (R = 0.495) (p=216).

Further, in our study sample, the patients stayed in the hospital for an average of seven days, ranging from 1 day to 35 days. According to the patient data analyzed at the Renmin Hospital of Wuhan University, the mean length of patients' hospital stay was 22 days, ranging from 9 to 46 days for pneumonia patients while patients suffering from severe pneumonia stayed to an average of 25 days, with a range of 14 to 44. Thus, this study concluded that the duration of hospital stay was prolonged for the patients experiencing severe covid disease symptoms, intensive management techniques and related disease complications.[25] These results were therefore consistent with the ones deduced by our prognostic score.

We also aimed to deduce the importance of CoPS related to the need for intensive treatment. The main two drugs analyzed were Remdesivir and steroids (solumedrol). However, the result was inconclusive; the main reason at hand being that most the patients admitted in our study were hospitalized late in the course of their ailment and were already suffering from a severe covid disease. The exact role and benefit of these two drugs is still questionable. A study by Beigel JH et.al. highlighted that administration of remdesivir for 5 days did improve the disease course as compared to other patients on standard therapy.[26] Similarly, another study reported that patients on remdesivir for 10 days or less did improve their symptoms in comparison of a placebo drug.[27] Carlet J et.al. discussed the controversial role of corticosteroids in their study. Their article discussed that although steroid administration in the first 28 days did increase ventilator-free days significantly, no such benefit was seen after 28 days.[28] Thus further research is warranted to explore the possibilities of such medical interventions.

Conclusion

With the ever-increasing reports of new covid-19 cases, the resources and hospital facilities continue to burn out. The CoPS score aims to dictate the intensity of therapy from the point of admission.

Considering the nature of patients that our center receives, a multi-center approach and scoring all "severity strata" of disease would further corroborate the relevance of the the CoPS scoring system.

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