



Original Research

## Associated risk factors with COVID-19 and mortality in District Swat, Khyber Pakhtunkhwa Pakistan; A cross-sectional study

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### Abstract

The novel COVID-19 is associated with so many other diseases like diabetes, cardiovascular and cerebrovascular diseases, chronic lungs disease, sore throat and flu resulting serious health complications. Thus, we aimed to find the associated risk factors, comorbidities and mortality rate due to COVID-19 in the Northern area of Pakistan. A self-designed data entry sheet was used to collect patients' information. The study was conducted in Saidu group of teaching hospital in Swat, Khyber Pakhtunkhwa, Pakistan. Descriptive statistics and relevant analysis were calculated using SPSS software. P-value less than 0.05 was considered statistically significant. The current study involved 4057 subjects, with median age 42 years. COVID-19 was confirmed in 812 (20.01%) patients. The total death rate was 9.11% (74/812), with cardiovascular and diabetes being the most prevalent comorbidities 38 (4.7%) and 37 (4.6%), respectively, with a P-value of 0.001, followed by chronic lung disease (6 (0.7%) with a P-value of 0.013. The most common symptoms were cough 556 (68.5%), fever 573 (70.6%) and shortness of breath 209 (25.7%). We found that the mortality rate among patients was highest in older age. Those with comorbidities had a risk of fatality. These findings will assist the clinicians and healthcare providers to reduce the morbidity and mortality rates and combating the COVID-19 pandemic.

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**Introduction:** Coronaviruses (CoVs) are RNA viruses, belong to the family Coronaviridae (Order Nidovirales; subfamily Orthocoronavirinae). They have been divided based on antigenic characteristic and phylogenetic tree into four major groups: (a)  $\alpha$ -CoVs, which are mostly responsible for gastrointestinal illnesses or respiratory disorders; (b)  $\beta$ -CoVs, which include the severe acute respiratory syndrome virus (SARS) and the Middle Eastern respiratory syndrome virus (MERS); (c)  $\gamma$ -CoVs, which generally infect bird species such as owls and hawks; (d)  $\delta$ -CoV, which infects both animals and humans [1,2]. CoVs have the largest genomes size (26.4 to 31.7 kb) between all discovered RNA viruses [3]. Historically CoVs were supposed to be less risky and low pathogenic viruses. In 2019, the origination of the new beta coronavirus was recently revealed and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Currently, SARS-CoV-2 has caused a global health concern. CoVs infect many different wild and domestic animals including humans. CoVs are spherical in shape covered by a membrane and crown-like spike particle on their membrane after which they were named. Highly pathogenic and insane diseases in  $\beta$ -CoVs, SARS-CoV (severe acute respiratory syndrome corona virus) and MERS-CoV (Middle east respiratory syndrome corona virus) which affected pandemics in humans since 2002 [4,5]. SARS-CoV originated in China and infected 8000 people worldwide with a mortality rate of 10% during the 2002-2003 pandemic [4]. After 2012, MARS CoV spread over 27 countries in the world and confirmed cases were identified in 2249 laboratories with an average mortality rate of 35.5% [5]. Which is a significantly lower mortality rate compared with MERS that of 35.5%, which might be due to cross-protective immunity against SARS-CoV-2 in that population because of an earlier exposure of MERS-CoV [6]. Moreover,  $\alpha$ -CoVs 229E, NL63, and  $\beta$ -CoVs HKU1, OC43 can also infect the human respiratory system [7,8]. The SARS-CoV-2 is newly discovered which is responsible for this pandemic and high-scale outbreak in China and around worldwide. SARS-CoV-2 is a highly pathogenic single, positive-strand RNA virus that belongs to the  $\beta$ -CoV family because of antigenic and phylogenetic similarities, which emerged in late 2019 [9]. SARS-CoV-2 targets the respiratory system of mammals, including humans being. According to the world health organization (WHO), more than 219 million confirmed cases have been reported worldwide, with 4.55 million deaths. Almost half of these cases (48% and 55% deaths) are still being recorded in the regions mostly in the United States of America, Argentina, and Brazil. In Pakistan, 4316 cases of COVID-19 have been recorded in the previous 7 days, totaling 1.26 million confirmed positive cases, with 28228 deaths. There are 177k cases only in KPK and 5673 deaths, which are increasing every day. In other countries, the number of infected people contentiously increases every day while some countries were not yet diagnosed. A systematic evaluation of 14 studies indicated that smoking, diabetes, and lung disease were major risk factors for poorer disease, while another 14 studies discovered that obesity was also a predictor of death [10]. Although SARS-CoV-2 cause-specific respiratory disorder also causes multiple organ system failures (e.g., lungs, heart, liver, and kidney), and even death [9,11]. This study aimed

to find the mortality rate and risk associated with COVID-19 in confirmed cases in district Swat.

#### **Materials and Methods:**

**Study area:** Swat is a district in the Malakand division, which located between 34° 34' and 35° 55' North scopes and 72° 08' and 72° 50' East longitudes, limited by Ghizer and Chitral on the North, Indus Kohistan and Shangla on the East, Buner and Malakand are situated on toward the South and Dir, shielded it from the West and situated in the lap of precipitous reaches. The all-out zone of locale Swat is 5337.0 km square and establishes populace around 2,309,570.0 as per the 2017 evaluation, making it the 3rd biggest region of Khyber Pakhtunkhwa after Peshawar and Mardan districts.

**Ethical Approval:** This study was approved by the Institutional Ethical Committee (IEC), Islamia College Peshawar, Peshawar for ethical consideration. Written permission was also obtained from head of department of pathology, public health Lab. and hospital administration.

**Study design and duration:** A cross-sectional epidemiological study was designed from March 24th to August 6th, 2020 at Saidu group of teaching hospital in Swat, Khyber Pakhtunkhwa, Pakistan. A self-designed data entry sheet was used to collect patient's information. A total of 4057 subjects were enrolled in the current study. These data were compiled from Saidu group of teaching hospital, Swat and removed the personally identifiable information of all cases during the analysis to protect the personal privacy. The samples were collected using a nasopharyngeal swab and an oropharyngeal swab, and the confirmed cases were identified using RT-PCR.

**Data Collection:** Demographic information was gathered, including the age and gender of the patients, chronic comorbidities and key travel information such as travel history while symptomatic in 14 days, travel history to China, Iran or other Country, travel by airplane or by road, departure from Peshawar or Islamabad. the confirmation of the COVID-19 infection and death or discharged, were collected. The research did not include any labels that suggested the cases were critical, severe, or under treatment. Among COVID-19 participants, risk variables for mortality were assessed, including age, non-modifiable sex, and modifiable chronic disorders.

**Statistical analysis:** Confirmed cases were used in descriptive statistical and clinical characteristics of the subjects. The crude mortality rate was the number of confirmed cases (numerator) divided by the total positive number of confirmed cases (denominator) listed as percentage. The collected data was analyzed through SPSS version 25.0 (SPSS Inc., Chicago, III, USA). Univariate analysis of categorical variables was performed, while an independent sample t-test was used for continuous data. For all statistical analyses,  $P < 0.05$  was considered significant and means for the continuous variables were compared through independent group t-test when the data were normally distributed. The frequencies mean standard deviation of data was performing by descriptive statistics in SPSS.

**Results:** The flowchart of patients in Figure 1 show that all 4057 cases were diagnosed for SARS-CoV 2 in which 3245 cases were not confirmed cases and 812 were confirmed cases of COVID-19. Out of 812 cases of COVID-19, 738 cases were recovered, and 74 cases were

expired and the median age were 62 years old. In which 36 were Diabetic patients, 36 were cardiovascular disease patients and 6 were chronic lung disease. One case has chronic lung disease with diabetes, 3 cases have chronic lung disease with cardiovascular disease and 2 have only chronic lung disease. The mean of these 74 patients ages were 62.36 (range,  $\leq 60 > 60$  years), and 51 (68.9%) were male; the details were presented in table 2. The median age of 812 cases were 42 years' old (IQR, 1-80 above years), and 601 (74%) were male. Sixty-one patients (7.5%) had one or more co-existing chronic medical disorders. Cardiovascular and diabetes were the most common comorbidities 38 (4.7%) and 37 (4.6%), followed by chronic lung disease 6 (0.7%). The most common symptoms were cough 556 (68.5%), fever 573 (70.6%) and shortness of breath 209 (25.7%) and Sore throat 194 (23.9%). Less common symptoms included Flu, Dizziness and headache, and Diarrhea (Table 1). One hundred sixteen (14.3%) who were in close contact with confirmed COVID-19 cases were asymptomatic while RT-PCR results positive in their Nasopharyngeal or Oropharyngeal swab samples. As fever and cough were the most common symptoms among these patients with COVID-19, The total of 641 (78.9%) had clear fever and symptoms during their test. On admission, including 116 (14.3%) were asymptomatic patients. Therefore, a total of 573 (70.6%) had fever. As high as an average of 78.25% of the patients in this study, including those how to survive and non-survive patients (Table1). All of these patients were isolated and give him supportive treatment after admission. A total of 617 (76%) patients were home isolated, 36 (4.4%) patients were admitted in ICU and 30 (3.7%) are put on the ventilator they critical in condition. In a total of 812 patients, 728 (89.7%) were recovered, 9 (1.1%) are still positive. A total of 74 patients expired (9.1%). In the ICU out of 30 patients, 3 patients were recovered and 33 died in ICU at Saidu Group of Teaching hospital.

Compared with comorbidity and its effect on patients with COVID-19. The most common comorbidities found were diabetes chronic lung disease and cardiovascular disorder. Patients with cardiovascular disease were very older an age. (Mean [range] age), 42.5 [ $\leq 60 > 60$ ] years vs 62.36 [ $\leq 60 > 60$ ] years;  $P < .001$ . (No [%] survive), 2 [0.3%] survive vs 36 [48.6%] were not survive and they have more likely to have fever 65 (87.8%), cough 66 (89.2%) and breathing issue 64 (86.5%)  $P < .001$ . Moreover, comorbidity, including diabetes (No [%] survive), 1 (0.1%) survive vs 36 (48.6%) were not survive;  $P < .001$  and chronic lungs disease patients 1 (0.1%) survive vs 6 (8.1%) were not survive; 0.013 (Table 2).

**Discussion:** For the first time, we evaluated the associated risk factors with COVID-19 and mortality in Northern Pakistan in the current study. We found that the mortality rate (9.11%) among hospitalized patients, could be explained by more severe disease in different reporting methods, or by geographic variation. According to this study, first it is provided the mortality while precious research has focused on the clinical characteristic, signs and symptoms of the COVID-19. Current findings show that there are additional risk factors associated with in-hospital mortality and comorbidity patient numbers.

According to current statistics and information, people of any age with a serious medical condition are at a higher risk of contracting COVID-19. A population, with chronic disease such as chronic lung disease, diabetes and cardiovascular disease are at greater risk of death if they become ill [12]. In present study, out of 812 cases, 74 were not surviving in which 39 (52%) were older than their age and 51 (68.9%) cases were male. The most common signs and symptoms were cough 66 (89.2%) P-Value of  $< 0.001$ , and fever 65 (87.8%) P-Value of  $< 0.001$ , and breathing problems 64 (86.5%) P-Value of  $< 0.001$ . In addition, a total of 74 COVID-19 patients passed away; 34 of them were admitted to the intensive care unit, 30 were placed on a ventilator, and 4 were isolated in the home. The data contributes a clearer understanding that those patients who died and admitted to ICU had severe COVID-19 symptoms, were older in age, had at least one kind of chronic condition, and were more likely to die in hospital. One study shows that patients admitted for AMI with COVID-19 disease had higher risk scores and hospital mortality [13]. COVID-19 is an independent risk factor for both in hospital and high GRACE score mortality. The severity of SARS-CoV-2 in humans has already been characterized and many researchers have concluded that this infection activates the immune system, stress cell cycle, metabolic pathways. Evaluating the biological pathways and functions involved in virus replication and outcome will be critical and not well understood [14]. It is beyond the scope of this study to assess the biological function of these pathways, but our study confirms that associated risk factors including age, immunological response, comorbidities and organ dysfunction predict worse outcomes [15]. However, the difficulty of predicting COVID-19 disease severity remains diversified and complicated. Older COVID-19 patients with at least one kind of chronic disorder are at significantly higher at risk. The data suggests that diabetic and cardiovascular disorders are widespread among hospitalized COVID-19 patients and are associated with higher risk of mortality.

**Conclusion:** This study revealed that the mortality rate among COVID-19 patients was highest in the older age. Those with comorbidities, such as diabetes and cardiovascular disease, were at a higher risk of fatality. These are the common conditions among hospitalized COVID-19 patients associated with higher risk factor of mortality were observed in district Swat. The current study findings are extremely important and will assist physicians and healthcare providers in lowering morbidity and mortality rates and combating the COVID-19 pandemic.

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**Conflict of interest:** The authors declare no conflict of interests.

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**Table 1.** Baseline Clinical characteristics of the 812 COVID-19 patients

Clinical characteristics	No of Patients/ %
<b>Age years (N, %)</b>	
Median (interquartile rang)	42 (≤60->60)
<b>Sex (N, %)</b>	
Male	601 (74%)
Female	211 (26%)
<b>Comorbidities</b>	
Comorbidity (N, %)	61 (7.5%)
Cardiovascular and cerebrovascular diseases	38 (4.7%)
Chronic lungs disease	6 (0.7%)
Diabetes	37 (4.6%)
Pregnancy	0 (0%)
Is there travel history while symptomatic in 14 days	1 (0.1%)
History of travel to China, Iran or any other Country	1 (0.1%)
Travel mode by Air	2 (0.2%)
Travel mode by road	1 (0.1%)
Departure from Peshawar	1 (0.1%)
Departure from Oman	1 (0.1%)
Departure from Panjab, Lahore	1 (0.1%)
<b>Specimen information</b>	
Nasopharyngeal swab	265 (32.6%)
Oropharyngeal swab	547 (67.4%)

**Table 2.** Demographics and Clinical Characteristics of Hospitalized Patients with COVID-19

Variables	Total (n= 812)	Survivors (n = 741)	Non-Survivors (n = 74)	P-value
Age, mean (IQR)	42 (≤60->60)	42.5	62.36	<0.001
≤60	591 (72.5%)	612 (82.5%)	35 (46.7%)	
>60	224 (27.5%)	129 (17.4%)	39 (52%)	
Gender				0.379
Male	603 (74%)	552 (747.4%)	51 (68.9%)	
Female	212 (26%)	189 (25.5%)	23 (31.1%)	
<b>Occupation</b>				
Health worker	98 (12%)	97 (13.1%)	0 (0%)	<0.001
<b>Work designation</b>				
Class-IV	3 (0.4%)	3 (0.4%)	0 (0%)	
Doctor	65 (8%)	65 (8.8%)	0 (0%)	
IT staff	1 (.1%)	1 (1%)	0 (0%)	
Nurse	23 (2.8%)	23 (3.1%)	0 (0%)	
Para-medic	6 (0.7%)	5 (0.7%)	1 (1.4%)	
Others	717 (88%)	644 (86.8%)		
<b>Signs and symptoms</b>				
Fever	575 (70.6%)	510 (68.7%)	65 (87.8%)	<0.001
Flu	162 (19.9%)	150 (20.2%)	12 (16.2%)	0.377
Sore throat	195 (23.9%)	183 (24.7%)	12 (16.2%)	0.067
Cough	558 (68.5%)	492 (66.3%)	66 (89.2%)	<0.001
Diarrhea	22 (2.7%)	15 (2%)	7 (9.5%)	0.035
Breathing issue	210 (25.8%)	146 (19.7%)	64 (86.5%)	<0.001
<b>Comorbidities</b>				
Cardiovascular disease	38 (4.7%)	2 (0.3%)	36 (48.6%)	<0.001
Diabetes	37 (4.5%)	1 (0.1%)	36 (48.6%)	<0.001
Chronic Lungs disease	6 (0.7%)	1 (0.1%)	6 (8.1%)	0.013
Is home isolated	619 (76%)	615 (80.9%)	4 (5.4%)	
Admitted in ICU	36 (4.4%)	2 (0.3%)	34 (45.9%)	
Is on ventilator	30 (3.7%)	1 (0.1%)	30 (40.5%)	

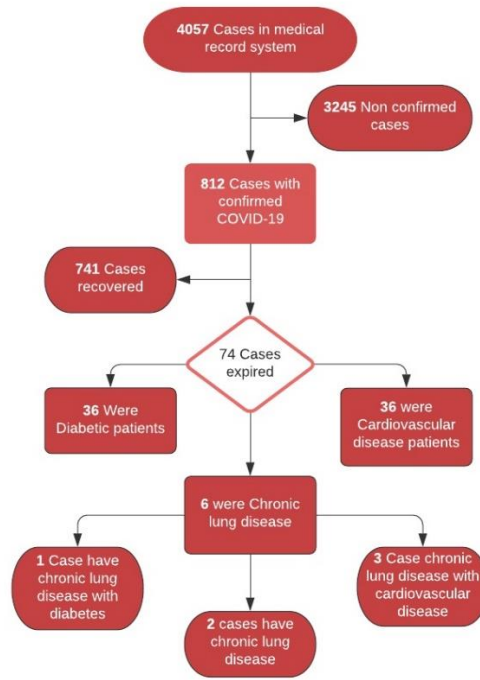


Figure 1. Flowchart of patient enrollment.