

## EXPERIENCE OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS-2 (SARS-COV-2) - COVID-19 AT A TERTIARY CARE HOSPITAL IN QUETTA, BALUCHISTAN

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### ABSTRACT

**Objective:** To share the experience of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)-COVID-19 at a tertiary care hospital in Quetta, Baluchistan.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Department of Pathology, Combined Military Hospital Quetta, from Mar to Dec 2020.

**Methodology:** This study included 14,741 study participants presenting to CMH Quetta with signs and symptoms of Coronavirus Disease-19 (COVID-19) and others undergoing COVID-19 PCR for screening purpose. Nasopharyngeal swab collected from these study participants were tested for COVID-19 viral RNA by real-time Reverse Transcription Polymerase Chain reaction (RT-PCR) assay.

**Results:** Out of these 14,741 study participants, 1886 (12.7%) were found to be SARS-CoV-2 PCR positive. Among 1886 study participants, 1503 (80%) were males while 383 (20%) were females. Mean age of the study participants was  $36 \pm 14$  years. Most frequent clinical presentations were body aches (96.5%), fever (94.1%), cough (66.8%) and loss of appetite (68.2%). Around 67 (3.5%) positive study participants were asymptomatic.

**Conclusion:** In this study, we observed male predominance but severity of signs and symptoms among female study participants. SARS-COVID-19 caused disease with wide range of clinical spectrum and disease can be fatal as well.

**Keywords:** Coronavirus disease-19, Novel coronavirus pneumonia, Nasopharyngeal swabs, Reverse transcription polymerase chain reaction.

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### INTRODUCTION

SARS-CoV-2 also commonly known as COVID-19, first emerged as a cluster of cases of pneumonia with unknown etiology from Wuhan, Province Hubei in city of China. It was a new threat to global health. Later on, it was found out to be Novel Coronavirus as the causative agent, because of which it was initially called "Novel Coronavirus Pneumonia (NCP)".<sup>1</sup> It is an RNA virus and has the same genus and receptor as SARS Virus.<sup>2,3</sup> SARS-CoV which is Severe Acute Respiratory Syndrome Coronavirus and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) are the previous two Coronavirus outbreaks.<sup>4</sup> Different patterns have been observed in the disease with the virus mainly affecting the respiratory system. Diagnostic strategies range from molecular testing like RT-PCR to various serological tests.<sup>5</sup> High Resolution Computerized Tomography (HRCT) chest has also been used as useful adjunct in the early diagnosis of the disease

serving as a more sensitive modality.<sup>6</sup>

Till date, there are 115, 289, 961 confirmed cases of COVID-19 globally including 2,564,560 deaths as reported by WHO.<sup>7</sup> This third outbreak of Coronavirus has affected the population in 209 countries worldwide including Pakistan. First case of Coronavirus was reported in Pakistan Karachi, on 26<sup>th</sup> February, 2020.<sup>8</sup> Initially reported cases of Pakistan had travel history from Iran by road and then they travelled to Baluchistan. Some of the initial cases were first quarantined in Baluchistan at Taftan Border. Cases with travel history were the main source of infection in the initial phases of the pandemic in Pakistan. However, there has been an exponential rise by local transmission nowadays.<sup>9</sup>

Baluchistan province has been lagging behind in research studies regarding COVID-19 situation. According to SIR (Susceptible-Infected-Recovered) model, based on the spread of the virus in Baluchistan, under the assumptions mentioned in Model parameters, the estimated number of infected people was 30,00000. Twenty five percent of total population of Baluchistan was estimated to be affected with a recovery rate of 98%.<sup>10</sup>

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Keeping in view the lack of studies on COVID-19 in the province and also such huge number of affected individuals, this study was planned to take an insight in the current situation of COVID-19 within Baluchistan province.

## METHODOLOGY

This was a cross-sectional study carried out in Department of Pathology Combined Military Hospital, Quetta from March 2020 to December 2020. Sampling technique was non-probability convenient. Study was approved from the Hospital Ethical Committee (No CMH QTA/Trg/IRB/049 dated 20 Aug 2020). A total of 14741 study participants reporting to CMH Quetta with symptoms suggestive of SARS-Cov-2 viral infection, pre-surgical screening, history of exposure to COVID-19 patients, health care professionals and travelers from endemic areas were considered for PCR testing. Informed written consent was obtained from all the participants of this study. A total of 14741 study participants were tested.

**Inclusion Criteria:** Patients with positive PCR results were included in the study.

**Exclusion Criteria:** Patients with negative results were excluded from the study.

Nasopharyngeal swabs were taken from around 2-7 days of presentation. Samples were transported to laboratory in 2-3 ml of Viral Transport Medium (VTM) at 2-8°C within 24-48 hours as per hospital standard operative procedures (SOP). Qualitative detection of nucleic acid of SARS-CoV-2 in nasopharyngeal swabs was done by using Coronavirus Real-Time Reverse Transcriptase PCR kit. Extraction, amplification and detection of nucleic acid of SARS-CoV-2 were done according to manufacturer's guidelines. Extraction was carried out in biosafety cabinet Class II A 2 as per guidelines. Internal control was used in RT-PCR to ensure integrity of PCR run, identification of any PCR inhibition and to assess the purity of extraction.

After RNA extraction, 12 µl of reaction mixer was prepared (by mixing: 10 µl Oasig Master Mix & 2 µl Primer and Probe). RT-qPCR plate was prepared by loading reaction mixture 12 µl per well and adding RNA sample or control (8µl). After sealing reaction plate, it was placed in thermal cycler and analyzed. Results were interpreted on basis of cycle threshold value (Ct value). A Ct- value of less than 34 was taken positive, 34-37 was considered Indeterminate while Ct-value of more than 37 was taken as negative. Samples of study participants with indeterminate results were

again analyzed after 48 hours and reported after clinical correlation. Follow-up PCR was done one week after patient became asymptomatic or about 2 weeks after initial testing.

Data analysis was done on Statistical Package for the social sciences (SPSS) version 24. Descriptive statistics mean and  $\pm$  SD and frequencies were computed. Chi Square was applied for age and co morbidities and *p*-value of  $\leq 0.05$  was taken as significant.

## RESULTS

A total of 14741 study participants were tested for SARS COV-2 infection from March to December 2020. Out of these 14741 study participants, 1854 (12.5%) were COVID PCR positive, while 145 (0.9 %) had Indeterminate results. Samples of study participants with indeterminate results were again analyzed after 48 hours and reported after clinical correlation. Out of these 145 (0.9%) study participants with indeterminate results, 32 came out to be positive on repeat testing, thus making an overall positivity rate of about 12.7%. Among 1886 study participants finally included in study, 1503 (80%) were males while 383 (20%) were females. Out of these 383 females, 11 (2.87%) were pregnant. Mean age of the study participants was  $36 \pm 14$  years. Mean age of male study participants was  $36 \pm 13.8$  years, while that of female study participants was  $36.0 \pm 13.8$  years. Study participants were divided according to the age into nine main groups as shown in Table-I.

**Table-I: Age group distribution of SARS COV-2 PCR positive study participants.**

Age Groups (Years)	n (%)
<11	44 (2.3)
11-20	81 (4.3)
21-30	541 (28.7)
31-40	671 (35.6)
41-50	279 (14.8)
51-60	141 (7.5)
61-70	102 (5.4)
71-80	19 (1.0)
> 80	8 (0.4)

Majority of study participants were from 31-40 years of age. Minimum age of 2 months to maximum age of 85 years was noted. Most frequent clinical presentations were fever, body aches, cough and loss of appetite. These symptoms were more severe in female study participants. Around 67 (3.5%) positive study participants were asymptomatic (Table-II). About 289 (19.5%) males were smokers. Majority of study participants were indoor cases i.e., 1433 (76%), while 453 (24%) study participants were from outdoor. Out of

453 outdoor patients, 275 (14.8%) underwent pre surgical screening for SARS COV-2. Various comorbidities were observed in COVID positive study participants. About 104 (5.5%) study participants were suffering from diabetes mellitus while hypertension was found in 181 (9.6%) study participants. Other comorbidities included bronchial asthma in 22 (1.2%) study participants, liver disease in 72 (3.8%) and kidney diseases were present in 32 (1.7%) study participants.

**Table-II: Clinical presentations of SARS COV-2 PCR positive study participants.**

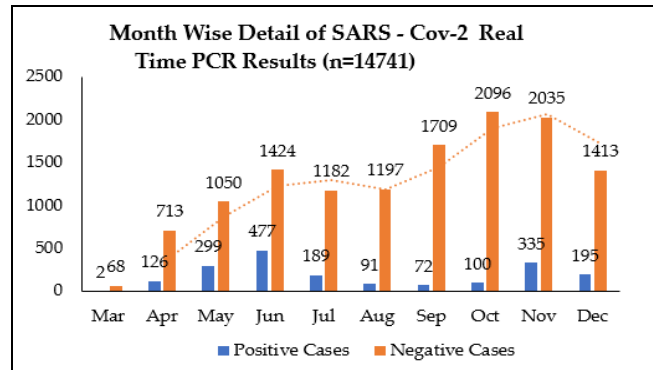
Signs & Symptoms	n (%)
Fatigue/Generalized Body Aches	1819 (96.5)
Fever	1774 (94.1)
Loss of Appetite	1286 (68.2)
Cough	1259 (66.8)
Headache	958 (50.8)
Loose Motions	603 (32.0)
Chest Pain	320 (17.0)
Decreased Sleep	301 (16.0)
Myocardial Infarction	11 (0.6)
Cerebrovascular Accidents (CVA including Stroke)	9 (0.5)

PCR positive study participants were classified into asymptomatic/mildly symptomatic, moderately symptomatic and severe or critical disease patients on the basis of severity of clinical symptoms, based on oxygen saturation, HRCT CO-RADS score, CRP and ferritin levels. Unfortunately, 27 (1.4%) of positive study participants never reported for any treatment from hospital. Out of remaining 1859 positive study participants, 426 (23%) were classified as asymptomatic/mildly symptomatic, 1247 (67%) as moderately symptomatic and 186 (10%) as having severe or critical disease. Asymptomatic/mildly symptomatic study participants were quarantined at home and prescribed oral Hydroxychloroquine (HCQ) initially. As the data on efficacy of various treatment modalities emerged, HCQ was stopped and Ivermectin along with azithromycin was introduced. Moderately symptomatic and critical patients were admitted to hospital in high dependency unit and Intensive Care Units (ICU) respectively. However, 276 (14.6%) patients admitted in high dependency unit and ICU required oxygen therapy. Only 58 (3%) patients admitted in ICU were placed on ventilator support. All the study participants in these two groups received methyl prednisolone or dexamethasone along with broad spectrum antibiotics and prophylactic heparin for venous thromboembolism prophylaxis. Four novel therapies were used in 72 (3.8%) moderately symptomatic and critical patients. These

included convalescent plasma in 32 (44.4%) patients, tocilizumab in 24 (33.3%) patients, therapeutic plasma exchange in 21 (29.1%) patients and Remdesivir was used in 16 (22.2%) patients. Out of these 72 patients who received novel therapy, 14 (10.08%) of the patients received two novel therapies while 5 (3.6%) received three novel therapies (including convalescent plasma, Tocilizumab and therapeutic plasma exchange). Remaining 53 patients received single novel therapy.

Out of 1886 positive study participants, unfortunately 38 (2.0%) participants died. Among these 38 cases, 28 (73.6%) were males while 10 (26.4%) were females. Average age of participants who died was 59.1 years. In addition to advanced age and co morbidities, higher CO-RADS score (more than 50%), raised serum ferritin (greater than 1500 ng/ml), raised CRP (above 50 mg/l) and higher oxygen requirement (10 L by non-rebreather oxygen mask) at the time of admission were associated with increased mortality.

Disease pattern throughout this period was assessed showing a peak of cases in month of June (477 positive cases) and then around November (355 positive cases), signifying the occurrence of a severe second wave of pandemic in second half of year 2020 (Figure). Relationship of co-morbidities with PCR positive cases was found to be significant ( $p$ -value <0.001) (Table-III).



**Figure: Month wise detail of SARS-Cov-2 real time PCR positive cases.**

**Table-III: Association of different comorbidities with COVID-19 polymerase chain reaction (PCR) positive cases.**

Comorbidities	No of PCR Positive cases with DM (%)	No of PCR Positive cases without DM (%)	$p$ -value
Diabetes Mellitus	104 (5.5%)	1782 (94.5%)	<0.001
Hypertension	181 (9.6%)	1705 (90.4%)	<0.001
Bronchial Asthma	22 (1.2 %)	1864 (98.8%)	<0.001
Liver Disease	72 (3.8%)	1814 (96.2%)	<0.001
Renal Disease	32 (1.7%)	1854 (98.3%)	<0.001

## DISCUSSION

SARS COVID-19 is one of the main pathogens of human respiratory tract infection. Two extremely pathogenic viruses, SARS-COVID and MERS-COVID, have caused severe respiratory syndrome in humans, while other four human Coronaviruses (HCoV-OC43, HCoV-229E, HCoV-NL63, HCoV-HKU1) have induced minor upper respiratory infection. Major SARS-COVID outbreak which involved 8422 patients had occurred during 2002-03 and involved approximately 29 countries worldwide. MERS-COVID had emerged in Middle Eastern countries in 2012 but later on spread to China.<sup>12,13</sup> Sequence of establishment and progression of SARS COVID-19 has been found relatively different from other six Coronaviruses but all can be classified as a single class, Betacoronavirus. SARS-COVID and MERS-COVID have ability to transmit directly to SARS COVID-19, which is an enveloped virion measuring 50-200 nm in diameter with a single RNA genome. Virus has 16 club-shaped glycoprotein spikes in the envelope, giving the virus a crown-like or coronal appearance and makes it able to attach with respiratory epithelium.<sup>14</sup>

Present study was conducted in a tertiary care hospital of Quetta, Baluchistan. In this study samples of 14741 study participants were included. RT-PCR for SARS-CoV-2 had been performed on these samples and our preliminary results were noteworthy for providing substantiation of SARS-CoV-2 dynamic profile in infected patients.

In our study, study participants had mean age of  $36 \pm 14$  years and 1886 (12.7%) were found positive on RT-PCR for SARS COVID-19. Around 1503 (80%) study participants were male and 383 (20%) were female including 20 pregnant ladies. Majority of the study participants predominantly presented with respiratory tract infections and had history of smoking. Mean age for study participants ( $36 \pm 14$  years), which we determined in our study population is quite less than populations of some studies from different regions of globe like China and other international studies.<sup>15,16</sup> Another fact which has been revealed in our study is that out of total 1886 positive cases, 1433 (76%) of study participants had been managed in indoor settings while 186 (13%) study participants required ICU facility. Findings of indoor study participants were found to be comparable to studies conducted in China and US but study participants who required ICU facilities were lesser in our population as compared to popu-

lations in other studies, which could be because of more young population in our study.<sup>17,18</sup>

Among the symptoms of presentation, fever and cough were the most common symptoms in study participants of our population. Similar findings were also found in other studies.<sup>15-17</sup> Around 67 (3.5%) positive study participants were asymptomatic in our study, which is comparable to a study conducted in Japan.

Similarly, co-morbidities like hypertension, diabetes mellitus, cardiovascular diseases, liver and kidney disease found in our study were comparable to multiple international studies.<sup>20,21</sup> Outcome of co-morbidities were found to be associated with more lethal disease, Intensive Care Unit (ICU) admission and greater mortality. Severity of disease and mortality has been even more common in study participants with more than one comorbidity. This finding was also comparable to other international studies.<sup>22</sup>

Requirement of invasive ventilation of our study {58 study participants (4%)} was compared with different studies and findings were comparable in some studies but lesser in other studies.<sup>23,16</sup> Association of severity of disease, admission in ICU, ventilator support requirement and increased age had been clearly identified in our study and this association became more stronger when age of study participants was more than 55 years. Severity of symptoms with gender was also identified in our study. Another important finding of our study is that females had more severe symptoms as compared to male study participants but number of female study participants presented to us were less. Therefore, such findings cannot be generalized. These findings are consistent with other international studies.<sup>24,25</sup>

In our study 426 (23%) of asymptomatic/mildly symptomatic study participants were prescribed oral Hydroxychloroquine (HCQ) initially, followed by Ivermectin along with azithromycin.

## CONCLUSION

We concluded that Baluchistan province like other areas of the world is badly hit by COVID-19. In this region SARS-COVID-19 caused disease with wide range of clinical spectrum. Male gender in middle age group needs to be extra careful as this group was the maximum affected group in Baluchistan. Severity of disease, requirement of ICU care and mortality were directly linked to age of the patient and underlying comorbidities.

**Conflict of Interest:** None.

**Authors' Contribution**

NA: Direct contribution to conception, design, analysis, data interpretation, SAS: Intellectual contribution to analysis, literature review, manuscript preparation & final approval, AY: Intellectual contribution to analysis, literature review, manuscript preparation & final approval, MG: Manuscript preparation & data analysis, WS: Intellectual contribution to analysis, literature review, QUA: Intellectual contribution to analysis, data interpretation & final approval.

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