Assessment of mortality in correlation with comorbidities in COVID-19 patients of Telangana state.

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Abstract

Background The mortality data of COVID cases around the world has less explored in relation to comorbidities. The dogma/question to be answered is that the virus perse resulting or any comorbidities contributing to such frightened deaths. The aim of the study is to describe the clinical and epidemiological characteristics of 201 deceased from Telangana. We retrospectively collected all consecutive death cases with laboratory-confirmed COVID-19 infection admitted from March to mid-June at Gandhi Hospital the nodal centre designated for COVID-19 in Telangana. Clinical history, comorbidities, laboratory findings and treatment were recorded for each patient.

Results A total of 15394 patients with confirmed COVID-19 test were admitted at Isolation wards between March 2020 and June 2020 and 253 death cases were reported till the submission of this paper. The mean age of death is 57.0 ys in our study, 40.7% (88) deaths were above 60 years and 71.4% (147) were male. Several comorbid conditions existed with COVID-19 death cases among which hypertension being the most common comorbidity (60.1%). Lymphopenia was observed in 46% cases while lymphopenia with comorbidity was recorded in 63% cases.

Conclusion In this retrospective study, most of the COVID-19 deceased patients were elderly male aged with an age range from 50-60 yrs and above. Mortality rate and severity are higher in males than females. Our study indicated the importance of understanding comorbid conditions in COVID-19 cases especially Hypertension and Diabetes mellitus as they were more likely succumb to death.

Background

Coronaviruses have existed since ages but the presence of the virus was discovered in the year 1960 (Tyrrell and Bynoe 1966). Since then these viruses have evolved and effected humans by manifesting its harmless flu-like symptoms. In 2003, these viruses were isolated from the Severe Acute Respiratory Syndrome (SARS) cases which made the World Health Organization (WHO) declare “state of emergency” in various parts of the world (Organization 2004). In 2012, these evolved viruses strains, started showing its affect in the Middle East countries, disease called Middle East respiratory syndrome (MERS) (Zaki et al. 2012). In December 2019 novel coronavirus found its way to affect larger populations in the world starting from Wuhan, China (Wu et al. 2020) to become a global pandemic, affecting more than 10.4 million people including 5,08,228 deaths (World Health 2020). This disease was termed COVID 19 which is caused by a bat origin coronavirus named SARS-CoV-2. To understand the pathogenicity and effect of host factors in this morbidity, timely and effective data in mortality/fatality rate will be of considerable value for individuals who are at risk. Based on preliminary reports from different countries, the overall case fatality rate (CFR) of 2020 SARS CoV-2 pandemic was predicted to be 4.8% and there was considerable uncertainty over CFR in different places in the world (Onder et al. 2020, Wu et al. 2020). Since February 2020, various states in India and worldwide have experienced a steep increase in the COVID-19 positive cases, with substantial differences in the number of reported deaths among countries worldwide (Rothan and Byrareddy 2020). The first symptomatic case positive for the COVID-19 was
reported on 2 March 2020 and the first death was reported on 25 March 2020 from Hyderabad city, Telangana. Since then more than 15,000 cases of laboratory-confirmed COVID-19 positive have been identified. The purpose of the study is to assess the clinical and epidemiological characteristics of COVID-19 deceased patients from the first detection of the infection in Telangana in March 2020 up to June 2020. This is a retrospective observational study of Telangana's experience with COVID-19 with an emphasis on fatalities. We focused on the course of the disease, comorbid conditions and the risk factors and its impact on the severity and mortality of the disease. This will help in disease management and preparation for the possible subsequent waves.

Methods

This is the first mortality study which is hospital-centred and carried out in Gandhi Medical College and Hospital, which is the only Government Hospital designated as a nodal centre for COVID-19 treatment and one of the six Government centres for COVID-19 testing. There were 15394 positive cases admission between March and June 2020 out of which 253 had died (till the time of manuscript preparation). Of the total COVID-19 positive death cases, 52 cases were excluded due to lack of sufficient data and 201 cases were retrieved from the official electronic notifying system in Gandhi Hospital, Telangana, India and entered in predesigned format (by Indian Council for Medical Research, Government of India). It included information of epidemiological characteristics like age, gender, residential address, the time lag for positive detection of COVID-19, comorbidities, laboratory findings etc. The trend of occurrence of positive cases and death from mid-March, 2020 to June 2020, was drawn. The study was initiated only after the clearance from the Institutional Ethical Committee (VIDE RC NO. IEC/GMC/2020/05/24 -Dated; 23/May/2020). Clinical characteristics and outcomes including length of the hospital stay, symptoms onset and death are presented in tables. Categorical measures are presented as percentages, continuous measures are presented as means and standard deviations or median and Inter quartile ranges (IQRs). Non-parametric test like Chi square test was also done to test for significance. All analysis were conducted with the use of SPSS Statistics for Windows version 22 (IBM).

Results

There were 15394 positive cases admission between mid-March to June 2020 out of which 253 had died (Till the time of submission). The CFR among SARS CoV -2 positive cases in India is 3% (GOI 2020), whereas in Telangana CFR was 1.64 %. The current paper discusses the clinical data of 201 death cases retrieved from March to mid-June, 2020. Demographic details of COVID-19 positive cases and deaths are shown in Table 1. Of the total COVID-19 positive cases, 2.5% (201) accounted for the deceased, 6 (2.98%) were non-ICU deaths and 195 (97.01%) died in Intensive care unit (ICU). The Six non-ICU death cases had a sudden cardiac arrest. The death cases were in age groups spanning 2 months to 80 years. Age-wise distribution of the death cases showed that 2% (4) were 0-20 years, 10% (20) were between 21-40years, 41% (95) in 40-60 years and 41% (82) were more than 60 years. The mean age among COVID-19 positive mortality cases was 56.8 (± 14.9) years. The detailed age-wise occurrence along with the case fatality
rate of COVID-19 deaths is given in Table 2 which showed that among the death cases majority were between the age ranges of 50-60 years. Considering the gender, males were in preponderance among the COVID-19 death cases ie., 73.1% (147) when compared to females 26.9% (54). Distribution of COVID-19 positive deaths per residential area showed that 93% (187) deaths were in urban, with 7% (14) deaths in rural. Of the reported death cases, 167 (83.1%) patients reported a history of contacts with SARS-CoV-2 infected patients.

Among the symptoms recorded, the most common symptoms at the onset of illness were breathing difficulty/ dyspnea (87%) followed by fever (63.1%) cough (54%), cold/ loss of smell (15.4%) and myalgia or fatigue (8.4%); Least common symptoms were diarrhoea (5.4%), headache (4.4%), and sore throat (4.4%); (Table 1). Dyspnea was common respiratory symptoms and fever was the common non-respiratory symptom.

The overall median time from onset of symptoms to death is 6.5 days (IQR 4-10) Figure 2. The clinical manifestations, outcomes and duration of illness onset to death in these cases are described in Figure 3. The median duration from illness onset to dyspnea was 4.23 days (IQR 2-9). Onset of illness to acute respiratory distress syndrome (ARDS) was 8 days (IQR 8–14), to mechanical ventilation was 10·5 days (IQR 7–14), and to first hospital admission was 5 days (IQR 3-7); the median time from onset of symptoms to ICU admission was 7 days (IQR 5–11).

Radiological findings (Table 3) reported 34.8% abnormal chest radiography in COVID-19 death cases whereas the majority (65.2%) of the cases had minor to normal radiographic changes. Among the abnormal findings, bilateral pulmonary infiltration was highest 33.8% (68) followed by consolidation. No ground glass opacity was recorded in this study group.

Of the death cases, 76.6% of cases had comorbid conditions, 23.4% had no comorbidity. In the group with comorbidity, males showed higher preponderance (70.8%) than females. Comorbidities recorded include the presence of hypertension (HTN), diabetes mellitus (DM), chronic kidney disease (CKD), coronary artery disease (CAD), hypothyroidism, malignancy, chronic obstructive pulmonary disease (COPD), dyslipidemia, asthma and other diseases as shown in Table 4. Multiple comorbidities were observed in 23.4% of death cases while one in 25.9% cases and two comorbid conditions in 27.4%.

Amongst the comorbidities, hypertension (60.7%) was highest in the death cases followed by diabetes mellitus (48.3%). Data were distributed according to age group 0-40, 41-60 and above 60 years, it was observed that hypertension and diabetes mellitus was significantly associated in above 40 years COVID-19 deaths (p<0.01*) (Table 5). Age was distributed based on the number of comorbidities present (Figure 4) compared with younger patients, patients above 40 years had a higher proportion of comorbidities.

The radiological and haematological findings were distributed based on the presence and absence of comorbidities. Table 6 shows higher proportion of abnormal radiological findings in COVID-19 death cases with comorbidity, suggesting the extensive lung involvement. The basic haematological examination was done on the admission day which showed that the lymphocytopenia occurred in 93 (46%) patients (lymphocyte count <1·0 × 10^3/μl) while leucopenia was reported in (11%) (white blood
cell count less than $4 \times 10^3/\mu I$); Based on the comorbidities, 63% of patients with comorbidity had lymphopenia while 25% of patients with comorbidity had leucopenia. Lymphopenia was seen in higher proportion when compared to a patient without comorbidities.

Most pertinent reason for death in COVID-19 patients found and associated in this study is acute respiratory distress syndrome (ARDS) (77%) with underlying comorbid conditions. Based on the ratio of the partial pressure of arterial oxygen (PaO2) to the fraction of inspired oxygen (FiO2) the disease severity was classified as mild (PaO2/FiO2 >200), Moderate (PaO2/FiO2 =100-200) and Severe ARDS (PaO2/FiO2 <100) (Table 7). A chi square independent test was performed to analyse the relationship between severity of ARDS and the presence of comorbidities. The relation between these two variables was statistically significant $\chi^2 =24.9$ $p=0.0003$ ($p<0.05$*) indicating the presence of multiple comorbidities increases the risk of severe ARDS leading to death.

**Discussion**

The present study provides an insight on the clinical and laboratory characteristics of 201 telangana death cases, mostly primary or secondary contacts of infected COVID-19 patients, treated in Gandhi Hospital, Telangana. The mean age of the study group was 56.7 years. Earlier two studies from China reported an average age in non-survivors respectively of 65.8 and 70.7 years-old ([Du et al. 2020, Du and Tu 2020](#)) whereas a recent European study by Baigi et al. stated that the overall average age in COVID 19 non-survivors was 78.0 years ([Biagi et al. 2020](#)). A study by Chen et al (2020) indicated that advanced age is one of the strongest predictors of death in patients with SARS-CoV-2 ([Chen et al. 2020](#)). In our study, it was observed that 74.1 % (149) patients were $\geq$ 50 years and the mean age of the COVID-19 death cases was lower when compared to the above studies indicating that the age group $\geq$ 50 years having a low survival rate in Telangana in comparison to world scenario.

Few studies suggested that though men and women have the same prevalence, men with COVID-19 are more at risk for worse outcomes and death, independent of age ([Jin et al. 2020, Li et al. 2020](#)). Male preponderance was observed in our study (147, 71.4%) with 3:1 male-female ratio, reaffirming that COVID-19 was more prevalent in males ([Biagi, Rossi et al. 2020, Li et al. 2020](#)).

In a recent study, shortness of breath or dyspnea was found as an independent risk factor leading to death in 74% of fatal patients with COVID-19 ([Chen, Liang et al. 2020](#)). Similarly in our study, increased hypoxemia led to dyspnea which may have resulted in 85% COVID-19 deaths. Sore throat was observed in only 4.4% death cases making them least common respiratory symptom. Among the Non-respiratory symptoms, fever (63.1%) was the most common symptom presented which was also observed as common symptoms in various studies in different regions in the world ([Guan et al. 2020, Li et al. 2020](#)). Few death cases had underlying comorbidities like asthma and COPD which is in concordance with existing study by Guan et al (2020) which stated that patients with COVID-19 rarely reported as having comorbid respiratory diseases (particularly COPD and asthma) ([Guan, Liang et al. 2020](#)). Majority of studies suggested that unlike H1N1 infection, there is no known impact of COVID-19 on mortality in
pregnant women with few exceptions (Hantoushzadeh et al. 2020, Pierce-Williams et al. 2020, Schwartz 2020, Zaigham and Andersson 2020). In our study, only one pregnant woman was reported as COVID positive deaths making it difficult to comment on the mortality rate in pregnant women in our population. In our study we also found one death who had preexisting myasthenia gravis (MG). The impact of the presence of this disease on mortality was unclear (Anand et al. 2020).

Irrespective of management of COVID-19 cases, apart from the virus, other factors are also contributing to the death. To understand this, the patterns leading to death in COVID-19 cases are listed in this paper. The median duration from illness onset to dyspnea was 4.23 days (IQR 2–9) which was lower when compared to the latest retrospective study from China which showed median time from illness onset to dyspnea of 5.5 days (IQR 1–9). Grasselli et al (2020) reported a median ICU length period of 9 days (Grasselli et al. 2020) but in our study, we observed that the median ICU stay was 7 days (IQR: 5–11) which was shorter. An overall time taken for a COVID-19 patient to lead to death was published by different research groups who reported that COVID-19 patients had died at an average of 18.5- 28 days, and few reported the median duration from admission to the intensive care unit (ICU) to death as 7 days (IQR 3–11) (Yang et al. 2020) while others reported as 12 days (IQR 8–15) (Zhou et al. 2020). In our study, early deaths have been reported; 2.5% of cases died in 10 days (IQR 5-15) from the time of onset of symptoms, yet the death rate was observed to be lower.

Radiological findings in a recent study by Naem et al (2020) suggested that chest radiography was more appropriate to follow the progression of the disease (Naeem K 2020). In this study, 65.5% cases presented with a normal chest radiograph while 35.5% showed abnormal findings. A study by Zhou et al (2020) reported the most common finding in COVID-19 non-survivors to be bilateral infiltrates (72%) followed by ground-glass opacity (67%) (Zhou, Yu et al. 2020). In our study, bilateral infiltrates (34.3%) was most common finding.

Among the death cases, several comorbidities recorded of them, three fourth of the patients (76.6%) presented one or more associated disease, whereas only 47 patients (23.4%) had no comorbidities. Earlier studies reported similar findings showing a higher prevalence of coexisting chronic illness in death cases when compared to survivors (Biagi, Rossi et al. 2020, Yang et al. 2020). Considering co-existing conditions, studies by Li et al. and Biagi et al. stated that among that reported comorbidities, hypertension was a common condition among the death cases (Biagi, Rossi et al. 2020, Li et al. 2020). In our study, HTN (60.7%) was the most common condition followed by DM (48.3%). The higher prevalence of hypertension can be attributed to the role of ACE2. The SARS-CoV-2 virus uses the ACE2 receptor to enter in human alveolar epithelial cells (Sakoulas 2020). The altered expression of ACE2 should increase patient susceptibility to viral host cell entry and may partially explain the high prevalence of hypertension in deceased patients. This indicates that investigation of host factors like ACE 2 receptor gene.

According to literature, DM inhibits neutrophil chemotaxis, phagocytosis, and intracellular killing of microbes. Impairments in adaptive immunity, delay in the activation of Th1 cell-mediated immunity and a late hyper-inflammatory response is often observed in diabetics (Hodgson et al. 2015). In our study, DM
was the second leading comorbidity recorded. Thus, it is likely that COVID-19 patients with DM may have dull immune responses leading to severe disease condition and may lead to high mortality in this group of people. A study by Kulcsar et al (2020) examined the effects of DM in a humanized mouse model of MERS-CoV infection (Kulcsar et al. 2019). Following MERS-CoV infection, the disease was more severe and prolonged in diabetic male mice and was characterized by imbalances in lymphocyte counts. We also found Lymphopenia in 63% of the cases with comorbidity which is consistent with this finding where patients with COVID-19, peripheral counts lymphocytes were low (Hussain et al. 2020). More death cases need to be assessed to understand the radiological significance in COVID-19 death cases.

A meta-analysis study reported that presence of more than one pre-existing comorbidities were closely related to ARDS, severity and mortality (Hu et al. 2020). According to the New York State Department of Health (Franki 2020), 86% of reported COVID-19 deaths involved at least one comorbidity. In present study, it was observed that pre-existing comorbidities increased risk of mortality which was similar to other studies (Ferrando et al. 2020). Considering COVID-19 ARDS patients, this study showed presence of multiple comorbidities in severe ARDS when compare to mild. In this context, the underlying diseases in ARDS COVID-19 patients increases the severity especially those with hypertension and diabetes being the most significant risk factors.

**Conclusion**

Through our study, we can suggest that age group 40 and above COVID-19 males with comorbidities like hypertension and diabetes mellitus are more susceptible to succumb with severe symptoms than people younger than 40 years. This can be attributed to the presence of underlying diseases in this population. Hence improving the protection against COVID-19 in persons with chronic disorders is essential in management of the disease.

**Abbreviations**

COVID-19- coronavirus disease 2019, MERS CoV- Middle East respiratory syndrome-related coronavirus, SARS-CoV-2-Severe acute respiratory syndrome coronavirus 2, CFR- Case Fatality Rate, SDs- standard deviation, IQR- interquartile range, ICU- Intensive Care Unit, ARDS- Acute respiratory Distress Syndrome, HTN-Hypertension, DM-Diabetes Mellitus, CKD-Chronic Kidney Disease, CAD-Coronary Artery Disease, COPD-Chronic Obstructive Pulmonary Disease, PaO2-Partial pressure of arterial oxygen, FiO2-fraction of inspired oxygen, MG- Myasthenia Gravis, ACE-2- Angiotensin Converting Enzyme-2

**Declarations**

Ethics approval and consent to participate: Name of the Ethics Committee: Institutional Ethics Committee, Gandhi Medical College, Secunderabad.

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Informed consent is waived due to pandemic and urgent need of data collection.

**Consent for publication:** Not applicable

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests

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**Authors' contributions:** AKM, HK, KTR, JV, RKS, Collected the clinical data, NK, MM and WT, analyzed and interpreted the patient data regarding mortality and COVID-19. RM, VA, TC, RS, SI, SV, DP, and SB performed the clinical examination of COVID-19 patients. TB, AKM, MM and WT were a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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### Tables

**Table 1: Demographics and baseline characteristics of COVID-19 death cases**
| Variable                        | Data N (%)          |
|--------------------------------|---------------------|
| All positives N=15394,         | Death cases included in the study N=201 |
| Death cases=253                |                     |
| Over all Case fatality rate (%)| 1.64                |
| Mean age (X±SD)                | 56.8 ±14.9 years    |
| Gender                         |                      |
| Male                           | 57.5±14.8           |
|                                | 147 (73.1)          |
| Female                         | 55.1±15.4           |
|                                | 54 (26.9)           |
| Deaths                         |                      |
| Non ICU deaths                 | 6 (3.0)             |
| ICU deaths                     | 195 (97)            |
| Age group                      |                      |
| 0-20 years                     | 4 (2.0)             |
| 21-40 years                    | 20 (10)             |
| 41-60 years                    | 95 (47)             |
| > 60 years                     | 82 (41)             |
| Residential area               |                      |
| Urban                          | 187 (93)            |
| Rural                          | 14 (7.0)            |
| Contact history                |                      |
| Yes                            | 167 (83.1)          |
| No                             | 34 (16.9)           |
| Symptoms at onset of illness   |                      |
| Type                           |                      |
| Dyspnea/breathing difficulty   | 175 (87.1)          |
| Fever                          | 127 (63.2)          |
| Cough                          | 108 (53.7)          |
| Cold/ loss of smell            | 31 (15.4)           |
| Myalgia                        | 17 (8.4)            |
| Diarrhea/ vomiting             | 11 (5.5)            |
| Sore throat                    | 9 (4.5)             |
| Headache                       | 9 (4.5)             |
| Onset of illness to death      | 6.5 days            |
| (median)                       | IQR=(4-10)          |
Table 2: Age-wise occurrence of COVID-19 death cases along with case fatality rate (CFR)

| Age range | No of deaths=201 | Death cases (%) | Case fatality rate (%) |
|-----------|------------------|-----------------|------------------------|
| 0–9       | 3                | 1.49            | 0.02                   |
| 10–19     | 1                | 0.50            | 0.01                   |
| 20–29     | 2                | 1.00            | 0.01                   |
| 30–39     | 18               | 8.96            | 0.12                   |
| 40–49     | 28               | 13.93           | 0.18                   |
| 50–59*    | 55               | 27.36           | 0.36                   |
| 60–69     | 46               | 22.89           | 0.30                   |
| 70–79     | 39               | 19.40           | 0.25                   |
| ≥80       | 9                | 4.48            | 0.06                   |

Table 3: Radiological findings by chest radiography

| Type of radiological findings in COVID 19 death cases | No of cases (%) |
|-------------------------------------------------------|-----------------|
| Consolidation                                          | 2 (1)           |
| Ground glass opacity                                  | 0               |
| Bilateral pulmonary infiltration                       | 68 (33.8)       |
| Minor changes                                          | 131(65.2)       |

Table 4: Pre-existing comorbidities in COVID-19 positive death cases
| N= 201 | No comorbidities | Comorbidities |
|-------|------------------|---------------|
|       | N=47 (23.4%)     | N=154 (76.6%) |
| Gender | Male/ 147 (73.1) | 38 (80.9) | 109 (70.8) |
|        | Female/ 54 (26.9)| 9 (19.1)  | 45 (29.2)  |
| Type   | Mean Age (X±SD) years | N=154   |
| Hypertension (HTN) | 59.7±11.8 | 122 (60.7) |
| Diabetes mellitus (DM) | 60±11.8  | 97 (48.3)  |
| Chronic kidney disease (CKD) | 58.9±13.7 | 32 (15.9)  |
| Coronary artery disease (CAD) | 58.5±12.5 | 28 (13.9)  |
| Hypothyroidism (HYT) | 55±15 | 19 (9.5)  |
| Malignancy | 56.4±15.3 | 8 (4.0)   |
| Chronic obstructive pulmonary disease (COPD) | 63.8±10.1 | 5 (2.5)   |
| Asthma | 63.8±11 | 4 (2.0)  |
| Dyslipidaemia | 30 | 1 (0.5)   |
| Patients without comorbidities | 49.5±19 | 47 (23.4) |
| Patients with 1 comorbidity | 56.8±12.3 | 52 (25.9) |
| Patients with 2 comorbidities | 62.5±11.6 | 55 (27.4) |
| Patients with more than 2 comorbidities | 57.7±12.5 | 47 (23.4) |

Table: 5 Distribution of Comorbidities according to age groups
### Table 6: Radiological and Haematological findings with respect to the presence and absence of comorbidity

| Radiological findings | Type | No Comorbidities | Comorbidities |
|-----------------------|------|------------------|---------------|
|                       |      | N=47 (23.4%)     | N=154 (76.6%) |
| Consolidation         | 0 (0)| 2 (1.3)          |
| Ground glass opacity  | 0 (0)| 0 (0)            |
| Bilateral pulmonary infiltration | 8 (17.0) | 60 (39.0) |
| Other findings        | 39 (83) | 92 (59.7) |

| Haematological findings | Lymphocytes $<1\times10^3/\mu l$ | Leucocytes $<4\times10^3/\mu l$ |
|-------------------------|----------------------------------|----------------------------------|
|                         | N (%)                            | N (%)                            |
|                         | 69 (74.2)                        | 24 (11.9)                        |
|                         | 93 (46.2)                        | 9 (37.5)                         |
|                         | 24 (11.9)                        | 15 (62.5)                        |

* indicates significance (p<0.05), NS indicates not significant.
Table 7: COVID-19 disease severity categories (ARDS) with respect to the presence and absence of comorbidities

|               | No comorbidities | One Comorbidity | Two comorbidities | >2 comorbidities | *Significance (p<0.05). |
|---------------|------------------|-----------------|-------------------|------------------|-------------------------|
| Mild ARDS (>200) | 13 (27.7)        | 2 (4.4)         | 14 (25.5)         | 21 (44.7)        | χ² = 24.9 p = 0.0003*   |
| Moderate ARDS (100-200) | 9 (19.1)        | 20 (39.1)       | 17 (30.9)         | 8 (17.0)         |                         |
| Severe ARDS (<100)   | 25 (53.2)        | 29 (56.5)       | 24 (43.6)         | 18 (38.3)        |                         |