Impact of Demography with Underlying Comorbidities in Mortality of Patients with COVID – 19: A Statistical Analysis of Observational Data in Tamilnadu, South India

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Abstract:

Background: India reported its first cases of COVID 19 in a group of returned Indian medical students from Wuhan to Kerala in January 30, 2020. Tamilnadu reported its first case on March 7, 2020 in Kanchipuram. Disease prognosis worsen when associated with various comorbidities. Understanding the impact of demography and various comorbidities on the disease outcome is a crucial public health issue. Aim: We aim to identify the patients hospitalized for COVID-19 that are associated with various comorbidities along with increased risk of death. Method: The study was a statistical analysis of observational data in Tamilnadu, South India. Patients admitted with COVID- 19 from May 1, 2021 to May 15, 2021 were enrolled. Electronic data records were analyzed for demography and comorbidities. Results: 2678 patients (Male = 1689 & Female = 989) were enrolled. Mean (average) age was 63 years (20 – 100). Death risk was significantly influenced by gender. Mean duration of hospitalization was 4.9 days (0 – 39) with older patients and men staying longer (P<0.05). Comorbidities of diabetes, hypertension, coronary artery disease, obesity, cancer, thyroid disorders, autoimmune disorders, other heart diseases, other kidney diseases and other comorbidities were associated with higher risk of mortality univariate, but Hypertension and obesity reached statistical significance after adjustment of age and gender. Conclusion: COVID-19 outcome was worse in older people and those with comorbidities. Males and older patients required longer hospitalization. Females were at higher risk of mortality due to their low survival period in hospitals.

Keywords: *COVID-19, Demography, Comorbidities, Mortality, Observational data, Statistical analysis*

1. Introduction

COVID – 19 (Coronavirus disease 2019) is caused by Severe Acute Respiratory Syndrome – Corona Virus – 2 (SARS-CoV-2) [1]. The disease was identified as a cause of outbreak of infection, originated at Wuhan city of China in early December 2019. Since then, the virus has rapidly widespread with confirmed cases in almost every country across the world and has become a new global public health crisis [2, 3]. The World Health Organization (WHO) coined the term COVID-19 and declared this novel coronavirus disease as a pandemic on March 11, 2020 [4]. First case of COVID 19 were reported in Kerala, India in a group of medical students who returned from Wuhan to their hometown in Kerala (Thrissur, Alappuzha and Kasaragod) in January 30, 2020 [5]. Tamilnadu reported its first case on March 7, 2020 in a resident from Kanchipuram in Chennai who had returned from Oman [6]. A total of 11,66,756 cases have been confirmed in Tamilnadu from first wave of COVID-19 as of April, 2021.

The onset of first surge of COVID – 19 in Tamilnadu was on March 7, 2020, with its first spike on June 30, 2020, affected by the virus originated from Wuhan (SARS-CoV-2 virus). The onset of second surge of COVID-19 in Tamilnadu was on April 11, 2021, with its first spike on May 13, 2021, affected by the mutated virus originated in Tamilnadu, India. (Delta – B.1.617.2 variant) [6, 7, 8]. The severity of disease was more severe in second surge than first surge of COVID – 19. During second surge, there was demand in oxygen supported beds and remdesivir drug for the management of COVID – 19 in patients [9, 10, 11]. During first wave, the vaccination was not available whereas during second wave, two vaccines (COVAXIN by Bharat biotech & COVISHIELD by Serum institute of India) were approved and available for persons above age 18 [12, 13].

Various comorbidities were found to be related to higher disease severity and risk of death. A meta-analysis by Emami *et al*, 2020 included 76,993 patients with COVID-19 showed that most common comorbidities associated with poorer prognosis were diabetes mellitus, hypertension, cardiovascular diseases, smoking, chronic obstructive pulmonary disease, malignancy, and chronic kidney disease [14]. Mortality rates were higher in patients with Diabetes which leads to a concern as Diabetes and Kidney disease had the highest prevalence of death rate in Tamilnadu [15, 16].

Demographic studies such as Age & Gender plays a significant role for the study of disease progression in patients with COVID – 19 along with other comorbidities. Disease prognosis worsen when associated with various comorbidities. Understanding the impact of demography and various comorbidities on the disease outcome is an important parameter to establish public health measures [3].

2. Aim

We aim to identify the patients hospitalized for COVID-19 that are associated with various comorbidities along with increased risk of death and also to assess whether Gender is correlated with increased risk of death due to COVID – 19 in Tamilnadu.

3. Method

The analysis was an observational study in Tamilnadu, South India. Patients with the age (20 – 100) who were admitted with COVID-19 from May 1, 2021 to May 15, 2021 were included. Electronic data from government source were reviewed [17]. Records were studied for patients' Age, Gender, Duration of hospitalization and comorbidities. The

comorbidities include diabetes mellitus, hypertension, coronary artery disease, cerebrovascular accident, chronic kidney disease, HIV/AIDS, obesity (body mass index of more than 25 kg/m^2), cancer, thyroid disorders, respiratory diseases, neurological disorders, liver diseases, auto immune disorders, other heart diseases, other kidney diseases and other comorbidities.

3.1. Statistical method

Sample size was determined by the total number of comorbid (death) patients. Statistical analysis was carried out using bivariate methods to compare groups, such as independent sample t-test and multivariate analysis such as Cox-reg for main death parameters. SPSS v.16 was used for all analyses. Throughout the study, 0.05 was taken as significance level. The Mantel-Cox (log rank) test was used to compare "survival" rate. Kaplan-Meier curves were used to present duration of hospitalization graphically.

4. Results

2678 adult patients were included from the source during the study period. 1689 were males and 989 were females. Mean (average) duration of hospitalization was 4.9 days (0 – 39). Overall mean (average) age was 63 years (20 – 100).

4.1. Duration of hospitalization

Deceased patients stayed on average of 4.9 days (SD.4.4) in hospital. Among deceased patients, the duration of hospitalization depended on age and gender. The probability of getting a death at initial days was 0.891 and at 1^{st} day was 0.758 and at the end of the 30^{th} day of hospitalization was found to be 0. This shows that the probability of getting death was found to be very high at beginning days. A linear regression of duration of stay on gender showed that men stayed on average 0.664 (se .024, $P < 0.05$) days longer than women. Duration of hospitalization for females (log rank $P < 0.05$) was significantly shorter than those of males (Figure 1).

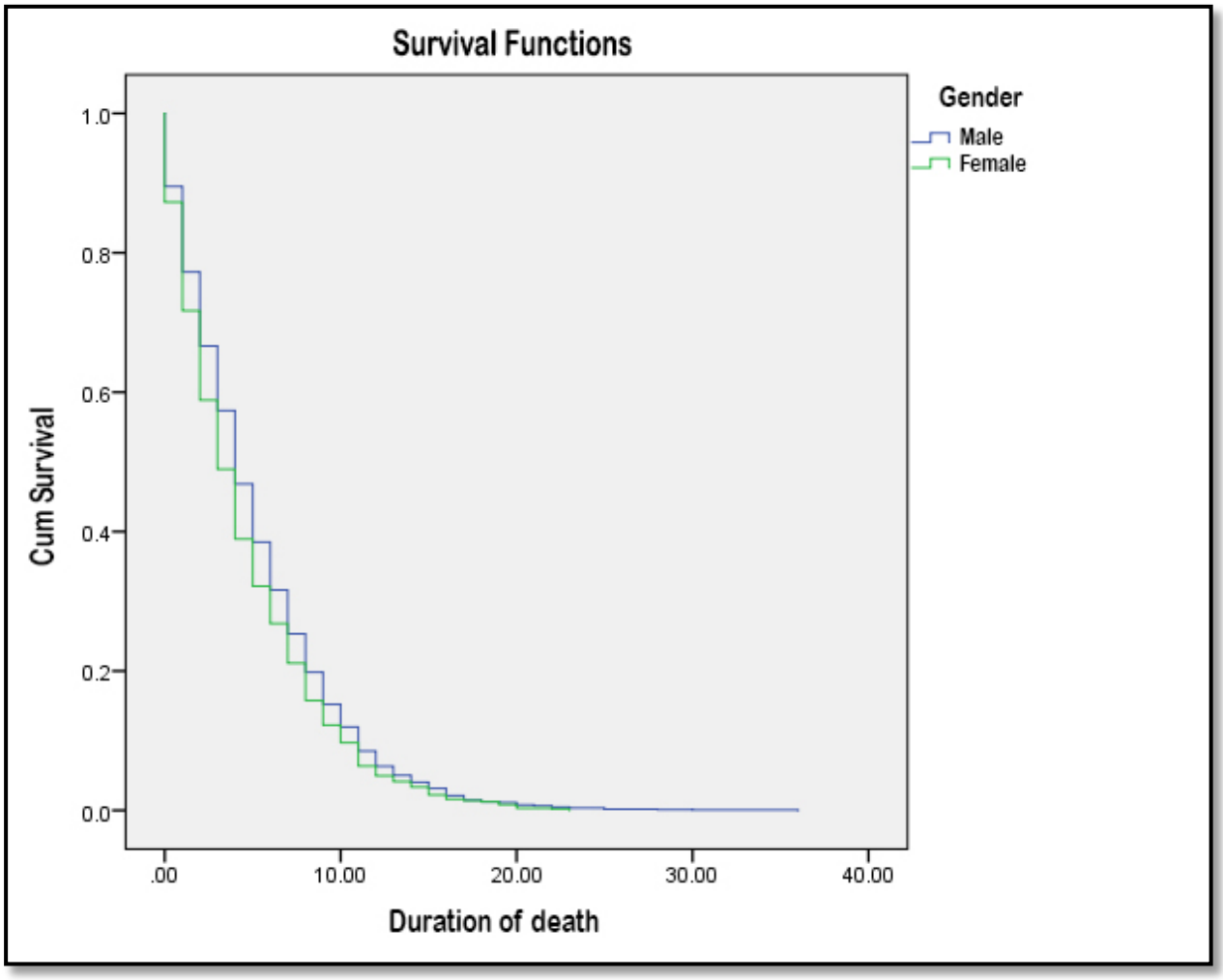

Figure 1. Kaplan – Meier curves of gender difference of hospitalization duration among deceased patients.

4.2. Age, Gender and Risk of Death

Out of 2678 adult patients, 1689 were males and 989 were females. Overall mean (average) age was 63 years (SD.12.5) among the diseased patients. The survival time for both males and females were estimated at 5.168 and 4.504 respectively. There was a significant difference between both male and female (log rank test P = 0.000) since the P – value is less than 0.05.

4.3. Comorbidities and Risk of death

1994 patients were diabetic, while 684 were non diabetic out of 2678 deceased patients. Similarly, 1513 were hypertensive whereas 1165 were non hypertensive patients. 373 patients (out of 2678) had coronary artery disease. 63 patients were obese, while 2615 were non obese patients died out of 2678. 52 patients (out of 2678) had neurological disorders. 8 patients (out of 2678) had liver disorders. 116 patients (out of 2678) had thyroid disorders (Table 1). The dependent variable was considered as death. Other variables such as age, gender, and Comorbidities are taken as independent variable. Most of the deceased patients were found to have diabetes. Comorbidities of diabetes, hypertension, coronary artery disease, obesity, cancer, thyroid disorders, autoimmune

disorders, other heart diseases, other kidney diseases and other comorbidities were significantly associated with higher risk of mortality after adjustment of gender, but Hypertension (P = 0.046) and obesity (P = 0.038) were found to be significant predictors of death.

Table 1. Comorbidities among Deceased Patients.

Comorbidity (Y/N)		Number (%)*	P value
Diabetes	Y	1994 (74.5)	> 0.05
	N	684 (25.5)	
Hypertension	Y	1513 (56.5)	< 0.05
	N	1165 (43.5)	
CAD	Y	373 (13.9)	> 0.05
	N	2305 (86.1)	
CVA	Y	43 (1.6)	< 0.05
	N	2635 (98.4)	
CKD	Y	121 (4.5)	< 0.05
	N	2557 (95.5)	
HIV/AIDS	Y	4 (0.1)	< 0.05
	N	2674 (99.9)	
Obesity	Y	63 (2.4)	< 0.05
	N	2615 (97.6)	
Cancer	Y	11 (0.4)	> 0.05
	N	2667 (99.6)	
Thyroid disorders	Y	116 (4.3)	> 0.05
	N	2562 (95.7)	
Respiratory disorders	Y	102 (3.8)	> 0.05
	N	2576 (96.2)	
Neurological disorders	Y	52 (1.9)	< 0.05
	N	2626 (98.1)	
Liver disorders	Y	8 (0.3)	< 0.05
	N	2670 (99.7)	
Autoimmune disorders	Y	17 (0.6)	> 0.05
	N	2661 (99.4)	
Other heart disorders	Y	49 (1.8)	> 0.05
	N	2629 (98.2)	
Other kidney disorders	Y	9 (0.3)	> 0.05
	N	2669 (99.7)	
Other Comorbidities	Y	15 (0.6)	> 0.05
	N	2663 (99.4)	

***Percentage indicated in relation to total group within individual comorbidity.**

5. Discussion

According to Global evidence, specific characteristics such as older age, male gender, obesity and comorbidities [18, 19] has shown a greater COVID-19 burden on people. Enormous data shows that influence of age had become an adverse outcome of disease. Older patients had more probability of a severe disease and had a higher mortality rate [20, 21]. A similar study by Grasselli *et al*, 2020 described 1591 patients referred for intensive care treatment in Milan, Italy. The majority were older men who required mechanical ventilation and had a mortality rate of 26% [22]. A multivariate analysis by Chen *et al*, 2020 concluded that older patients, male gender, comorbidities, and time of

hospitalization were significantly associated with death [23]. We found that most of the deceased patients were older (63, SD.12.5) than the other age groups.

Influence of gender on COVID-19 had been extensively studied. A meta-analysis by Zhu *et al*, 2020 included 38 studies with 3062 COVID-19 patients showed that a higher proportion of infected patients were male in whom the incidence rate of respiratory failure was 19.5% and the fatality rate was 5.5% [24, 25]. A similar study by Biswas *et al*, 2021 shows that male patients were associated with increased risk of mortality compared to females [35]. In our study, male patients presenting with the disease are higher than females. There was a significant difference between male and female mortality statistically (log rank test $P = 0.000$) since the P – value is less than 0.05. The survival time for both males and females were estimated at 5.168 and 4.504 respectively. Females were at higher risk of mortality due to their low survival period in hospitals.

Studies showed an average duration of hospitalization for COVID-19 of 12 ± 4 days [26, 27, 28] with longer duration of hospitalization for critically sick patients and those who died [29]. Among deceased patients, the duration of hospitalization (4.9, SD.4.4) depended on age and gender. A linear regression of duration of stay on gender showed that men stayed on average 0.664 (se .024, $P < 0.05$) days longer than women. We found that duration of hospitalization for females (log rank $P < 0.05$) was significantly shorter than those of males.

Several comorbidities were found to be predisposing factors for disease severity and death. A meta-analysis by Emami *et al*, 2020 included 76,993 patients with COVID-19 showed that the most common comorbidities associated with poor prognosis were hypertension, cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease, malignancy, and chronic kidney disease [14, 30]. A meta-analysis by de Almeida-Pititto *et al,* 2020 included 18,012 COVID-19 patients concluded that diabetes, hypertension and cardiovascular disease are important risk factors for severity and mortality in COVID-19 patients [31]. Another meta-analysis by Wang *et al*, 2020 shows that hypertension, diabetes, COPD, cardiovascular disease and cerebrovascular disease are major risk factors for COVID-19 patients [34]. In a large cohort of 1305 COVID-19 patients by Imam *et al*, 2020, it was found advanced age and an increasing number of comorbidities are independent predictors of inhospital mortality for COVID-19 patients [29]. Higher mortality rate was seen in patients with diabetes [32]. We found a significant difference in deceased patients who had diabetes, but it disappeared after adjustment of gender. Besides diabetes, obesity was also noted to be associated with severe disease requiring intensive care admission and mechanical ventilation [26, 33]. In our study, we found that Obesity was a statistically significant contributory factor to death. Apart from obesity, hypertension was found to be statistically significant predictors of death. We found a significant difference in risk of death in patients with diabetes, hypertension, coronary artery disease, obesity, neurological disorders, liver disorders, and thyroid disorders, but some of the disorders seem to be confounded by age and gender.

6. Conclusion

We conclude that COVID-19 outcome was worse in older patients and with those patients having comorbidities. Males and older patients required longer hospitalization. Females were at higher risk of mortality due to their low survival period in hospitals. We also conclude that gender was correlated with increased risk of death among those hospitalized for the disease.

7. Conflicts of Interest

None of the authors here have any conflict of interest to declare.

8. Acknowledgement

We acknowledge the contribution of Mr. G. Saravanan, Research Scholar, Centre for Statistics, SRM Institute of Science and Technology (SRM IST) for his support and guidance in this work.

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