Annals of Community Health (AoCH) pISSN 2347-5455 | eISSN 2347-5714

An Indexed (Index Medicus, DOAJ and More), Peer Reviewed, Quarterly, International Journal focusing exclusively on Community Medicine and Public Health

ORIGINAL ARTICLE

A Cross-sectional Study on Coronavirus Disease-19 Deaths without any Known Comorbidities in Tamil Nadu, 2020

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ABSTRACT

Introduction: The coronavirus disease (COVID)-19 has turned out to be a pandemic* posing a great burden to humanity and involving all seven continents. Understanding the factors involved in COVID-19 deaths* without underlying comorbidities are essential to know about the trend and to contain the spread of the disease. **Methodology:** The data were taken from www.stopcorona.tn.gov.in (official COVID-19 website of the state) which is a publicly available secondary data source. The details of the deaths without any underlying comorbidity were extracted from the daily media bulletin till October 2020. The results were expressed as proportion, mean, median, and standard deviation. Fisher's exact test and Mann–Whitney U*-test were used and $P < 0.005$ was considered statistically significant. **Results:** Among the 912 COVID-19 deaths without any underlying comorbidities, 78% were male and 61.9% were above 50 years of age. The median time interval between symptom onset and admission, between admission and death was 4 days and 3 days, respectively. Other than the respiratory and cardiac causes of death, sepsis and thromboembolic causes amount to 6.2% and 4.5%, respectively. Nearly 46.2% had a combination of fever, cough, and breathing difficulty symptoms. About 77.6% of COVID-19 deaths occurred because of delayed presentation to the hospital. Male gender and the symptomatic patients had a greater time interval between hospital admission and death ($P < 0.05$). **Conclusion:** The study will help in future anticipation of deaths without comorbidities*, take appropriate actions, reduce the pressure on the health system, and future researches. A systematic well-coordinated public health* actions are essential to control this pandemic.

Key words: COVID-19 deaths, Mann–Whitney U, *pandemic, public health, without comorbidities

INTRODUCTION

The coronavirus disease-19 (COVID-19) is an infectious disease caused by a newly discovered variant of coronavirus (severe acute respiratory syndrome coronavirus 2 virus) in humans. The disease was identified in December 2019 in Wuhan, China.[1] On January 31, 2020, the WHO announced it as a Public Health Emergency of International Concern and now it has turned into a worldwide pandemic posing a great burden to humanity. Population migration, international transitions, trade, and airborne transmission, and communal spread have resulted in the rapid spread of the disease. On December 21, 2020, scientists working in the Chilean research base at Antarctica tested positive for COVID-19.[2] Now, the disease has not spared any continent on the planet.

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The high rate of transmission, increasing number of cases, and deaths have severely ravaged the health system, and the development of the countries. The entire world has made efforts to take stringent measures such as the use of personal protective measures, practicing social distancing, travel restrictions, disinfection, advanced diagnostics, and proper treatment. High-level coordination between national and international agencies with pharmaceutical companies has now resulted in the invention of vaccines effective for COVID-19.

Many developed and developing countries had a second wave of the pandemic. Several mutations have occurred overtime

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How to cite: Anand VV, Yogaraj GA, Raj PP. A Cross-sectional Study on Coronavirus Disease-19 Deaths Without Any Known Comorbidities In Tamilnadu, 2020. Ann Community Health 2021;9(2):34-39.

and recently a new variant (VOC – 202012/01) with a high rate of transmission is identified in the United Kingdom.[3] With all these threats taunting us, it is important to understand the disease and mortality of this new virus on the human body. Many studies have been published regarding COVID-19 deaths in the old age group associated with other risk factors. Very limited studies have analyzed the cause of death due to COVID-19 without any underlying comorbidity. This study will be very helpful in analyzing the trend of deaths due to COVID-19 without comorbidity and the results might help in health system planning, formulating guidelines, preventing future deaths, and further scientific researches.

METHODOLOGY

The study is based on a secondary data source, taken from www.stopcorona.tn.gov.in which is a publicly available, COVID-19 official website of the State Government of Tamil Nadu.[4] The details of the deaths without any underlying comorbidity were available in the daily media bulletin release. Data such as age, gender, date of admission, date of death, date of symptom onset, and symptoms were collected from March to October 2020. Among the 11,122 COVID-19-positive deaths that had occurred in Tamil Nadu till October 2020, complete details were not available for 470 deaths. Finally, 912 COVID-19 deaths without any known underlying comorbidities were included for the analysis.

For analysis, categorical variables were expressed as frequency, percentage, and 95% confidence interval (CI) and the continuous variable as mean, median, standard deviation, and interquartile range (IQR). For inferential analysis, the Chi-squared test (χ^2) or the Fisher's exact test and Mann–Whitney U-test were used and $P < 0.005$ was considered as statistically significant. SPSS software version 21.0 (IBM) was used for analysis.

RESULTS

In Table 1, nearly 78% (n = 713, 95% CI =75.4–80.8%) of the deceased without any comorbidities were male. About 61.9% of the COVID-19 deaths without any known comorbidities (n = 564, 95% CI =58.6–65.0%) were above 50 years of age and 74.2% died in public sector hospitals (n = 677, 95% CI =71.3–77.0%). A total of n = 337 (36.9%, 95% CI =33.9–40.2%) deaths belonged to Chennai and Chengalpattu districts of Tamil Nadu state. Nearly 99% (N = 912, n = 902, 95% CI: 97.9–99.5%) had died due to respiratory cause, among them, majority had bronchopneumonia (98.6%), acute respiratory distress syndrome (ARDS) and respiratory failure (68.9%). Cardiovascular cause accounts for about 12.3% (n = 112, 95% CI: 10.2–14.5%) with cardiorespiratory arrest (10.9%) being common. Other than the respiratory and cardiac causes, sepsis and coagulopathy/thromboembolic cause amounts to nearly 6.2% (n = 57, 95% CI: 4.7–8.0%) and 4.5% (n = 41, 95% CI: 3.2–6.0%), respectively. Central nervous system involvement (with hypoxic encephalopathy n = 12, 1.3%) amounts to 1.6% (n = 15, 95% CI: 0.9–2.7) and acute kidney injury/renal failure accounts for 1.3% (n = 12, 95% CI: 0.7–2.3) of total COVID-19 deaths without any underlying comorbidities.

In Table 2, nearly 55.26% (n = 504, 95% CI =51.9–8.5%) of the deceased without any comorbidities belonged to the age group of 46–60 years and the age-specific death rate per 1 lakh population was 4.37 (95% CI: 4.01–4.77).[5]

Table 1: Descriptive analysis

Sociodemographic details of COVID-19 deaths without any comorbidities (n=912)		
Description	**Frequency, n (%)**	**95% CI of proportion**
Gender		
Male	713 (78.2)	75.4-80.8
Female	199 (21.8)	19.2-24.6
Age		
<50 years	348 (38.2)	34.9-41.4
>50 years	564 (61.9)	58.6-65.0
Hospital admission		
Public sector	677 (74.2)	71.3-77.0
Private sector	235 (25.7)	22.9-28.7
Geography		
Chennai and Chengalpattu	337 (36.9)	33.9-40.2
Other districts	575 (63.1)	59.8-66.2
Cause of death without any underlying comorbidities (N=912)		
Cause of death	**Frequency n (%)**	**95% CI of proportion**
Respiratory cause	902 (98.9)	97.9-99.5
Bronchopneumonia	899 (98.6)	97.6-99.2
ARDS/respiratory failure	629 (68.9)	65.8-71.9
Others	12 (1.3)	0.7-2.3
Cardiovascular cause	112 (12.3)	10.2-14.5
Cardiorespiratory arrest	99 (10.9)	8.9-13.1
Acute coronary syndrome/CAD	6 (0.7)	0.2-1.4
Myocarditis	4 (0.4)	0.1-1.1
Others	11(1.2)	0.6-2.1
Sepsis/septic shock	57 (6.2)	4.7-8.0
Thromboembolic cause/coagulopathy	41 (4.5)	3.2-6.0
Central nervous system involvement	15 (1.6)	0.9-2.7
Hypoxic encephalopathy	12 (1.3)	0.7-2.3
Acute meningoencephalitis	3 (0.3)	0.1-0.9
Acute kidney injury/renal failure	12 (1.3)	0.7-2.3
Gastrointestinal tract involvement	5 (0.5)	0.2-1.2
Perforation peritonitis	3 (0.3)	0.1-0.9
Acute pancreatitis/ gastroenteritis	2 (0.2)	0.03-0.79
Metabolic disorder	3 (0.3)	0.1-0.9
Incidental COVID-19 positive	21 (2.3)	1.4-3.5

COVID: Coronavirus disease, CI: Confidence interval

In Table 3, the mean age among COVID-19 deaths without any comorbidities was 52.16 years (95% CI=51.45–52.86, SD-1.084), without any significant difference between males (52.44 years, SD-1.043) and females (51.14 years, SD-1.219). The median time interval between symptom onset and admission was 4 days (IQR-4) and the median time interval between admission and death was 3 days (IQR-6).

In Table 4, FEVER, 83.5% (n = 264, 95% CI: 78.99–87.46%), was the most common symptom associated COVID-19 deaths without any underlying comorbidities. Breathing difficulty 79.43% (n = 251, 95% CI: 74.55–83.75%) was the second most common symptom followed by cough 62.97% (n = 199, 95% CI: 57.39–68.31%). Nearly 46.2% had combination of fever, cough, and breathing difficulty (n = 146. 95% CI: 40.61–51.87%) symptoms.

In Table 5, a Fisher's exact test showed 62.2% (n = 561) of the COVID-19 deaths without comorbidity having a respiratory cause of death belonged to the age group >50 years (n = 564) when compared with age group <50 years (n = 348) and P value was statistically significant. Furthermore, 66.6% (n = 10) of the COVID-19 deaths without comorbidity having central nervous system as a cause of death belonged to the age group of <50 years (n = 348), when compared with age group >50 years (n = 564) and P value was statistically significant.

Table 2: Details of age groups and age-specific death rate (ASDR) of COVID-19 deaths without any comorbidities (n=912)

Age group in years	Frequency, *n* (%)	95% CI of proportion	ASDR per 1 lakh population* (95% CI)
0-15	4 (0.44)	0.12-1.12	0.02 (0.00-0.06)
16-30	28 (3.07)	2.05-4.41	0.14 (0.10-0.21)
31-45	203 (22.26)	19.6-25.1	1.21 (1.06-1.39)
46-60	504 (55.26)	51.97-58.52	4.37 (4.01-4.77)
61-75	161 (17.65)	15.23-20.29	2.65 (2.28-3.10)
>75	12 (1.32)	0.68-2.29	0.79 (0.45-1.39)

*Reference population for individual age groups are taken from 2011 census data (5). COVID: Coronavirus disease, CI: Confidence interval

Table 3: Age- and hospital-specific time intervals

Details	Mean	95% CI of mean	SD	Median	IQR
Age (n=912)	52.16 years	51.45-52.86	1.084	54 years	15
The time interval between symptoms onset and hospital admission (n=273)	5.11 days	4.70-5.52	3.45	4 days	4
The time interval between hospital admission and death (n=908)	5.06 days	4.72-5.39	5.15	3 days	6

IQR: Interquartile range

In Table 6, a non-parametric test (Mann–Whitney U-test/ Wilcoxon signed-rank test) was performed for non-normally distributed continuous variables. It indicated that among COVID-19 deaths without any underlying comorbidity, age was greater for patients with COVID-19 bronchopneumonia (n = 899, mean rank 459.25) than without COVID-19 bronchopneumonia and the results were statistically significant (U = 3.372, P < 0.05). Similarly, among COVID-19 deaths without comorbidity, the male gender had a greater time interval between hospital admission and death (n = 709, larger mean rank 474.37) as compared with females and the results were statistically significant (U = 5.646, P < 0.05). Furthermore, symptomatic had a greater time interval between hospital admission and death as compared with asymptomatic and the results were statistically significant (P < 0.05).

DISCUSSION

The case fatality rate of Tamil Nadu for COVID-19 as on October 31, 2020, was 1.54% (95% CI: 1.51–1.56%). Among the COVID-19 deaths without any comorbidity, crude death rate (CDR) was 1.26/1 lakh population (95% CI:

Table 4: Symptoms among COVID-19 deaths without comorbidities (n=316)

Symptoms	Frequency, *n* (%)	95% CI of proportion
Fever	264 (83.54)	78.99-87.46
Breathing difficulty	251 (79.43)	74.55-83.75
Cough	199 (62.97)	57.39-68.31
Myalgia/headache/fatigue	18 (5.69)	3.41-8.85
Other symptoms	31 (9.81)	6.76-13.64
Fever + cough + breathing difficulty	146 (46.2)	40.61-51.87

COVID: Coronavirus disease

Table 5: Inferential analysis

Age limit	Respiratory cause of death - present (n=902)	Respiratory cause of death - absent (n=10)	*P*-value* (Fisher exact)
Age group <50 years (n=348)	341 (37.8%)	7 (70%)	0.049 (sig.)
Age group >50 years (n=564)	561 (62.2%)	3 (30%)	
	CNS cause of death - present (n=15)	**CNS cause of death - absent (n=897)**	***P*-value* (Fisher exact)**
Age group <50 years (n=348)	10 (66.6%)	338 (37.7%)	0.022 (sig.)
Age group >50 years (n=564)	5 (33.3%)	559 (62.3%)	

*P<0.05 is considered to be statistically significant

1.18–1.35%). The CDR of males (1.97/1 lakh population, 95% CI: 1.83–2.12%) was greater than females (0.55/1 lakh population, 95% CI: 0.48–0.63%). Ioannidis *et al*. conducted a cross-sectional survey on COVID-19 deaths <65 years without underlying conditions in France, Italy, Mexico, the Netherlands, Sweden, Georgia, and New York city and the results showed a prevalence of 0.7–3.6% of all COVID-19 deaths.[6] The same study showed Mexico having a higher prevalence of 17.7% COVID-19 deaths without underlying comorbidities.[6] Estimates of these mortality rates are important as they have greater implications in public health. Especially COVID-19 deaths of young age group without any underlying comorbidity have a greater impact on the future development of our country.

Until October 31, 2020, 11,122 COVID-19 deaths had occurred in Tamil Nadu. After scrutinizing the data source, 912 (8.19%) COVID-19 deaths had occurred without any known comorbidities. A data from Mexico said that among the population aged <65 years, one in six COVID-19 deaths occurred without underlying comorbidities.[7]

In our study, nearly 78% of the deceased without any comorbidities were males and 61.9% of them were above 50 years of age. About 55.26% of the deceased without any comorbidities belonged to the age group of 46–60 years and their age-specific death rate was 4.37/1 lakh population. The Centers for Disease Control of the United States reported a 12 times higher deaths among COVID-19 patients with underlying conditions as compared with those without any underlying conditions (19.5% vs. 1.6%).[8]

Furthermore, the mean age affected was 52.16 years (SD-1.084), without any significant difference between males and females. The median time interval between symptom onset and admission, and between admission and death was 4 days and 3 days, respectively. A similar study done by Asirvatham *et al*. showed that both the time intervals were 4 days.[9] Studies from China, Singapore, and Italy indicated a time interval between symptoms and admission with a range of 3–10 days.[10-12] The duration may change because of the rapid programmatic interventions of the public health authorities and the government.

A report from Wuhan stated that 16.7% of the hospitalized and 44.4% of the patients admitted in the intensive care unit with COVID-19 had arrhythmias.[13] This could have contributed to the COVID-19 deaths due to cardiovascular causes. Furthermore, several studies showed life-threatening arrhythmias in 10–16% of hospitalized COVID-19 patients.[14-16] However, our study showed that other than the respiratory and cardiac causes of deaths in COVID-19

Table 6: Inferential analysis with continuous variables

Variable	Grouped variable	*n*	Mean rank	Mann-Whitney U	Wilcoxonsigned-rank	*P*-value*
Age (*n*=912)	COVID-19 bronchopneumonia present	899	459.25	3.372	3.462	0.009 (sig.)
	COVID-19 bronchopneumonia absent	13	266.35			
Time interval between symptom on set and admission (*n*=276)	Public sector admission	78	117.71	6.100	9.181	0.006 (sig.)
	Private sector admission	198	146.69			
Time interval between symptom onset and admission (*n*=276)	Fever present	239	142.20	3.536	4.240	0.048 (sig.)
	Fever absent	37	114.58			
Time interval between symptom onset and admission (*n*=276)	Myalgia/headache/fatigue present	15	185.60	1.251	3.544	0.018 (sig.)
	Myalgia/headache/fatigue absent	261	135.79			
Time interval between admission and death (*n*=908)	Male gender	709	474.37	5.646	7.636	0.000 (sig)
	Female gender	199	383.70			
Time interval between admission and death (*n*=908)	MODS - Cause of death	33	586.23	1.009	3.933	0.003 (sig.)
	MODS - Not a cause of death	875	449.53			
Time interval between admission and death (*n*=908)	Thromboembolism/coagulopathy - Cause of death	41	555.95	1.361	3.899	0.011 (sig.)
	Thromboembolism/coagulopathy - Not a cause of death	867	449.70			
Time interval between admission and death (*n*=908)	Symptoms present	313	553.75	6.205	2.394	0.000 (sig.)
	Symptoms absent	595	402.29			
Time interval between admission and death (*n*=908)	Fever+ cough + breathing difficulty present	18	648.69	4.514	4.010	0.001 (sig.)
	Fever+ cough + breathing difficulty absent	890	450.37			

*$P<0.05$ is considered to be statistically significant. COVID: Coronavirus disease

(such as bronchopneumonia, ARDS and respiratory failure, and cardiorespiratory arrest), sepsis (6.2%), thromboembolic cause (4.5%), central nervous system involvement (1.6%), and acute renal failure (1.3%) were most common. Conway and Pryzdial in their article have given satisfactory evidence of complement activation and thromboembolic phenomenon causing COVID-19 catastrophe.[17]

Nearly 46.2% of the deaths without comorbidities had a combination of fever, cough, and breathing difficulty ($n = 146.$ 95) symptoms. A similar study done by Asirvatham *et al*. showed 35.8% of COVID-19 deaths showed the combination of all three symptoms.[12] Among the COVID-19 deceased patients without any comorbidities ($n = 273$) who sought hospital care, 22.34% ($n = 61$, 95% CI: 17.54–27.76%) were admitted within the first 2 days of symptom onset and 77.66% ($n = 212$, 95% CI: 72.24–82.46%) were admitted after 2 days of symptom onset. This indicates that the majority of COVID-19 deaths without any known comorbidities had occurred because of delayed presentation. Furthermore, 26.65% ($n = 908$, $n = 242$, 95% CI: 23.8–29.6%) COVID-19 deaths without comorbidities had occurred within 1 day of hospital admission. A Mann–Whitney U-test showed that among COVID-19 deaths without comorbidity, the male gender had a greater time interval between hospital admission and death compared with females, and also symptomatic had a greater time interval between hospital admission and death as compared with asymptomatic. Both the results were statistically significant ($P < 0.05$).

Very limited data and journal articles discussed COVID-19 deaths without any underlying comorbidities. Maximum efforts were put by the government to save every life. Still, lack of timely access to the hospitals and other health-care facilities, the sudden surge of cases, delayed health-seeking behavior might have resulted in these unexpected mortalities due to COVID-19.

CONCLUSION

The study provides evidence regarding the current trend of deaths due to COVID-19 without any underlying comorbidity, their most common causes of death, time trends that had caused these deaths, and other factors. The modifiable risk factors like the delayed presentation despite having the combination of symptom triad could be avoided to reduce these deaths. Knowledge of the trend of COVID-19 deaths without underlying comorbidities will help and guide the different management strategies, health system planning, and further research in the field of public health. Strict infection control measures travel restrictions, increasing the diagnosing rate and appropriate treatments, and finally vaccination, in coordination with different stakeholders only can end this pandemic.

Limitation

Complete death details were not available for 474 deaths (444 deaths were included in the report of Death Reconciliation Committee in Greater Chennai Corporation and complete details of the first 30 deaths were not released). The details of a comparison group were not available for further analysis.

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