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Case Study

Comorbid Risk Factors for an In-Hospital Fatal Outcome of Patients Hospitalized for Covid -19: A Case-control Study

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Abstract

Between 13 March - 31 July 2020, 2,529 Covid-19 cases were discharged from the Victor Babes 490 bed hospital recognized by the government as the primary Covid-19 hospital in the capital, Bucharest. Eighty six of these 2,529 patients died in hospital for a case fatality rate (CFR) of 3.4 % (95% CI: 2.8 % - 4.2 %). The CFR for males was 4.7 % (54/1127) while in women it was 2.4 % (33/1402). The difference between these two rates is statistically significant [(Relative Risk (RR): 2.04; 95%CI: 1.33 - 3.12; p: 0.00083)].

Among the 86 who died, 11 (12.8%) were previously healthy (no reported under lying medical condition), 77 (87.2%) had at least one under lying medical condition, and 47 (54.7%) had two or more under lying medical conditions. The prevalence of each of the individual under lying medical conditions in these 86 patients was as follows: hypertension (68.6 %), diabetes mellitus (40.7%), obesity (33.7%), chronic kidney disease (27.9 %), and COPD (7.0 %).

A 1:1 case control study was conducted after matching each case with one control of the same gender and age selected at random from the survivors list. Significant odds for death were identified for the presence of at least 2 under lying medical condition (OR:23.00; 95% CI (4.29 - 478.82);p: 0.0000),), chronic kidney disease (OR: 9.00; 95% CI(2.41 - 57.41); p: 0.0008), and obesity (Odds Ratio (OR): 6.75; 95%CI (2.53 - 22.59); p: 0.0001). These data suggest that individuals with 2 or more under lying disease processes, and either chronic renal disease or obesity should be included in the list of individuals recommended for priority vaccination with a COVID-19 vaccine to reduce the likelihood of death should they become infected with COVID-19.

Keywords: COVID - 19; Hospital Cases; Fatality Rates; Case-control Study

Abbreviations

CDC: Center for Disease Control; CFR: Cases Fatality Rate; OR: Odds Ratio; SD: Standard Deviation; COPD: Chronic Obstructive Pulmonary Disease; ICD: International Classification of Diseases

Introduction

On July 31, 2020, the World Health Organization recorded 17,106,007 cases of COVID-19 infection in 213 different countries resulting in 668,910 confirmed deaths [1]. An emerging issue has been to what extent to which individuals with specific disease processes are at greater risk of COVID-19 associated death. The US Centers for Disease Control (CDC) reported in their Morbidity and Mortality Weekly Report of April 17 that, for the period of March 1-30,2020, of 1482 individuals hospitalized for COVID-19, the highest rate of hospitalization was observed in adults aged ≥ 65 years (13.8 per 100 000 population compared with 4.6 overall) [2]. The CDC reported that for "…the 12% of adult patients with data, 89.3% had one or more underlying conditions; the most common being hypertension (49.7%), obesity (48.3%), chronic lung disease (34.6%), diabetes mellitus (28.3%) and cardiovascular disease (27.8%)(2). The prevalence of obesity is greater in older adults and its complications, such as hypertension, diabetes me-

llitus, and all types of cardiovascular disease, increase with increasing severity and duration of obesity. Importantly, a report of 4,103 patients with COVID-19 disease in New York City found that the most frequent clinical features leading to hospital admission were age > 65 years and obesity each of which was greater than hypertension, diabetes mellitus, or cardiovascular disease [3].

Aim of the Study

The goals of this investigation were to identify the most frequent comorbidities occurring in individuals with COVID-10 infection who died between March 13 and late July 2020 while hospitalized at the Hosptal Dr. Victor Babes in Bucharest, Romania a primary hospital idendified in Bucharest for COVID-19 infected patients, after adjusting for age and gender utilizing a case control analysis.

Materials and Methods

- The study cohort consisted of 2529 Covid-19 individuals, who were discharged from the hospital between March 13 and July 31, 2020 consisting of 1,127 (44.6%) men and 1,402 (55,4%) women. The mean age of the whole cohort was 44.11 years (IQR 0-98 years) with the mean age of the women being 45.2 years which was statistically significantly greater than for the men at 42.7 years: (Kruskal-Wallis H: 7.87; p: 0.0050.
- Deaths: 86 patients died in hospital for a case fatality rate (CFR) of 3.4 % (95% CI: 2.8 % - 4.2 %). The CFR in men was 4.7 % (53/1127) and in women was 2.4 % (33/1402), the difference between two rates being highly statistically significant [(RR: 2.00; 95%CI: 1.30 - 3.06; p: 0.0017533.)] The median age (SD) at death in men was 69.14 years (13.57 years) and in women of 74.18 years (11.94 years), the difference by rearegenders being statistically not significant : ANOVA; T-stat: 1.756; p: 0.0929.

Case-control study

- **Cases:** The study population consisted of 86 patients with COVID - 19, who died while in hospital between March 13 and July 30, 2020. Each case assigned a unique code number
- **Controls:** The list of Covid-19 survivors was sorted in descendent order of age; from this list for each case a similar age and gender control was selected consecutively from the top to the bottom without replacement. Each control was assigned the same code as its matched case.
- **Exposures:** 5 medical conditions identified in the discharge summaries: Chronic kidney disease, diabetes mellitus, hypertension, obesity, and COPD were examined for an effect on mortality.
- **Analysis:** Discordant pairs [Case/Yes Control/No] vs [Case/No Control/Yes] were examined for statistical significance using EpiInfo 7 . A p-value of 0.05 was set as the cutoff for statistical significance.

Results and Discussion

Of the 86 who died, 11 (12.8%) had no pre-existing comorbid disease, 77 (87%) had one pre-existing disease process while 47 (54.7 %) had 2 or more pre-existing conditions that could affect the outcome of interest, death. The prevalence of the 5 underlying comorbid conditions of interest was as follows: hypertension 68.6%, diabetes mellitus 40.7%, obesity 33.7%, chronic renal disease 27.9%, and COPD 7.0%.

Underlying medical conditions (Exposure)	Odds ratio			
	Estimate	Lower	Upper	P value
Chronic kidney disease	9.00	2.41	57.41	0.0008
Diabetes	1.76	0.90	3.59	0.1336
Hypertension	1.73	0.92	3.35	0.1184
Obesity	6.75	2.53	22.59	0.0001
COPD	6.00	0.88	138.96	0.1306
With ≥ 2 comorbidities	23.00	4.29	478.82	0.0000

Table 1: Results of case control study regarding the association between underlying medical conditions and an in hospital fatal outcome.

The odds ratios that were significant for death were in order: the presence of 2 or more comorbid diseases: OR: 23; 95% CI: 4.29-478.8, p = 0.000), chronic renal disease: OR 9.00; 95% CI: 2.41 - 57.41, p= 0.0008), obesity: OR: 6.75 ; 95% CI: 2.53-22.59, p=0.0001, and COPD : OR: 6.00; 95% CI: 0.88-18.96, p 0.1306.

The present findings are consistent with the uncontrolled associations between COVID-19 and those previously reported for age and gender [4-11]. They are also consistent with the reports examining the association between chronic renal disease and death in COVID-19 infected individuals [12,13]. In addition they provide statistical data to support the relationship with death in COVID-19 infected individuals [14-21]. Most surprising was the failure to identify a statistically significant relationship between COPD and death with COVID-19 disease despite the well- recognized clinical finding of pulmonary disease as a predominant clinical manifestation of COVID-19 infection in all age groups and a pulmonary disease presentation being the most frequent indication for hospitalization of individuals with COVID-19. Of note is that of the 17163 patients discharged from our hospital in 2019 1928 (11%) had

COPD as an identified diagnosis (ICD-10: J44.0) included in their discharge summary.

Several mechanisms might explain why obesity predisposes individuals with COVID-19 to more severe disease and subsequently an increased death rate in obese COVID-19 infected individuals [18]. First, an increase body weight decreases the individual's expiratory reserve volume, functional capacity and respiratory system compliance findings associated with a poor outcome with a COVID-19 infection [22]. Secondary, obesity is associated with type 2 diabetes mellitus and hypertension, both of which are recognized risk factors for cardiovascular disease and are prevalent in COVID-19 infected individuals particularly those that are hospitalized [23,24]. Thridly, obesity per se is a pro- inflammatory disorder characterized by increased blood levels of "toxic" cytokines that are responsible for the adverse manifestations of COVID-19 infection [25,26]. Fourthly, excess visceral fat is associated with insulin resistance as well as a heightened activity of the renin induced aldosterone system both of which are linked to a more severe outcomes reported in cases of COVID-19 infection [27-29]. Finally, obesity enhances the risk of vascular thrombosis [30-32]; COVID-19 has been noted to be associated with pro-thrombotic disseminated intravascular coagulation and an increased rate of venous thromboembolism [28].

Conlusion

Irrespective of age and gender, the present study adds statisitical evidence consistent with prior findings that both obesity and chronic renal disease in hospitalized COVID-19 infected individuals are predictors of an increased risk of a fatal outcome.

In lieu of the current pandemic of COVID-19, public health planners should consider adding both obese individuals and those with chronic renal disease to the list of individuals with underlying medical conditions recommended to receive COVID-19 vaccination early following those that are first responders and essential workers.

Conflict of Interest

None declared.

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