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Prevalence and impact of comorbidities in hospitalized patients with COVID-19: a study from Saudi Arabia

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Abstract

Background In this study, we aimed to address the prevalence of comorbidities and their impact on the outcomes of hospitalized COVID-19 patients admitted to a large tertiary Saudi Arabian hospital.

Methods This is a retrospective study that included all adults with COVID-19 admitted to a large tertiary Saudi Arabian hospital, between January 1, 2021, and September 30, 2022. The study outcomes were the prevalence of comorbidities among hospitalized COVID-19 patients and the effects of these comorbidities on all-cause hospital mortality.

Results A total of 1118 /1853 (60.3%) patients had one or more comorbidities. The most prevalent comorbidity was diabetes mellitus (48.5%), followed by hypertension (12.5%), and chronic renal disease (10.3%). Age (OR 3.032 (95% CI 0.006 – 0.029, $p=0.002$), clinical status (8.194, 0.0350 – 0.709, $p<0.001$), the presence (versus absence) of comorbidities (3.167, 0.042—0.233, $p=0.002$), the number of comorbidities (2.972, 0.027 – 0.133, $p=0.003$), and the 4C score (2.894, 0.010 – 0.054, $p=0.004$), were independent significant predictors of mortality.

Conclusions A total of 60.3% of hospitalized COVID-19 patients had one or more comorbidities, the most prevalent of which were diabetes mellitus, hypertension, and chronic renal disease. The presence and the number of comorbidities, but not the individual ones, together with age, clinical status at admission, and the 4C mortality score were significant independent predictors of mortality.

Keywords Prevalence, Impact, Comorbidities, Hospitalized, COVID-19, Outcomes, Clinical, Saudi Arabia

Introduction

Since November 2019, the rapid outbreak of coronavirus disease 2019 (COVID-19), which arose from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, has contributed to an enormous adverse impact globally [1] knowing the risk factors and the underlying diseases in COVID-19 patients is of crucial importance for healthcare professionals, particularly for immunocompromised people and the elderly. The clinical operators should consider the risk factors and underlying diseases for critical cases of COVID-19, correctly assign medical resources, and identify severe patients

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in the early stages of the disease, to reduce the mortality rate and improve the effectiveness of the treatment [2, 3]. Thus, the evaluation of the prevalence of chronic diseases, such as hypertension, kidney disease, cardiovascular disease, chronic respiratory diseases, and diabetes mellitus, is considered one of the most important measures to reduce negative outcomes in COVID-19 patients [2–4].

Several studies had addressed the prevalence of comorbidities in patients with COVID-19, however, the results were highly variable [2–8]. The effects of comorbidities on outcomes of COVID-19 patients have been previously studied [2–6, 8–10]. Yang, et al. [2] observed that underlying diseases, including hypertension, respiratory system disease, and cardiovascular disease, may be risk factors for severe patients compared with non-severe patients. On the contrary, Baradaran and coworkers [11] found that comorbidities do not seem to be the prerequisite for symptomatic and severe COVID-19 infection, except hypertension.

There is, still a need to address the prevalence and impact of comorbidities in COVID-19 patients. This would be of particular importance if large numbers of COVID-19 patients are admitted into large tertiary referral centers. Therefore, in the current study, we aimed to address the prevalence of comorbidities and their impact on the outcomes of hospitalized COVID-19 patients admitted to a large tertiary Saudi Arabian hospital.

Methods

Study setting, design and population

The Armed Forces Hospital Southern Region (AFHSR) is situated in the city of Khamis Mushait, which is part of the Asir Province in the southern region of Saudi Arabia. It serves as a tertiary care referral center for military personnel, their families, and civilians in the region. It receives patients who require specialized medical care from other healthcare facilities within the southern region or from other parts of the country. It has advanced medical capabilities and expertise to handle complex cases and provide advanced treatments [12].

The current study is a retrospective study that included all adults (>14 years old) with COVID-19 admitted to the AFHSR, between January 1, 2021, and September 30, 2022. COVID-19 was confirmed by nasopharyngeal reverse transcription–polymerase chain reaction (RT-PCR). The criteria for admission were as per the COVID-19 management recommendations of the Saudi Ministry of Health [13].

Data collection

Demographic, clinical, laboratory, and outcome data were collected from electronic medical records. The clinicodemographic data included age, gender, the main presenting symptoms, signs, admission data (ICU versus non-ICU), the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) 4C mortality score, and comorbidities. Included comorbidities were hypertension, cardiovascular disease, chronic respiratory disease, chronic kidney disease, chronic liver disease, diabetes mellitus (type 1 or 2), chronic neurological disease, connective tissue/rheumatological disease, malignant neoplasm, dementia, and HIV/AIDS. Laboratory data included basic investigations and inflammatory markers. Outcome data included mortality during hospitalization.

The ISARIC 4C mortality score [14]

The International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) 4C mortality score is a risk stratification tool that was developed by Knight et al., [14] to allow early identification of COVID-19 patients at higher risk of mortality, using readily available objective criteria at the patient admission.

For calculating the ISARIC score, the following variables were collected: age; gender; number of comorbidities; respiratory rate (RR), peripheral oxygen saturation (SpO2) on room air, and Glasgow coma scale (GCS) at hospital admission; first available blood urea level (mmol/L); and C-reactive protein (CRP) (mg/L). The 4C Mortality Score ranges from 0 to ≥15 and it divides patients into four risk groups: low (0–3), intermediate (4–8), high (9–14), and very high-risk groups (≥15) [14].

Study outcomes

The study's primary outcome was the prevalence of comorbidities among hospitalized COVID-19 patients. The secondary outcome was to address the impact of comorbidities in terms of their effects on the all-cause hospital mortality outcome.

Ethical considerations

Ethical approval was obtained from the institutional review board of the hospital (; approval no; AFHSRMREC/2022/PULMONOLOGY-INTERANL MEDICINE/603).

Statistical analysis

Descriptive statistics: Means, standard deviations (SD), medians, inter-quartile range (IQR) and percentages were calculated. Significance test: Chi-square/Fisher's exact test was used to compare the differences in frequency between groups. Test of normality, Shapiro–Wilk or Kolmogorov Smirnoff was used to test the normality of continuous variables. For continuous variables with two categories, independent sample t-test/Mann Whitney U

test was used to compare the difference in means/median as appropriate. A multivariable regression analysis was performed to analyse the impact of clinicodemographic factors, the presence versus absence of comorbidities, and individual comorbidities on the patient's outcomes. The confounders used were age, gender, clinical status, the presence or absence of comorbidities, individual comorbidities, number of comorbidities, and the ISARIC 4C mortality score. A p-value of 0.05 or less was considered to indicate statistical significance. Statistical analysis was performed using the Statistical Package for Social Science (SPSS) Software (version 24).

Results

Demographic and clinical features

The average age of the study subjects was 57.2 ± 21.6 years. Males represented 56.4% of the patients. A total of 1118 /1853 (60.3%) patients had one or more comorbidities. With regards to comorbidities, 39.6%, 31.2%, and 29.2%, had 0, 1, and ≥ 2 comorbidities, respectively. Among the study cohorts, 18.8% needed ICU admission. During the study period, 1541 (83.2%) survived, while 312 (16.8%) patients died.

Table 1 depicts the demographic and clinical characteristics of the cohort.

Prevalence of comorbidities

The most prevalent comorbidity was diabetes mellitus (48.5%), followed by hypertension (12.5%), and chronic renal disease (10.3%). With regards to other comorbidities,7.9%, and 6.3% were reported for chronic neurological diseases and both cardiovascular disease and chronic respiratory disease, respectively Table 2.

Impact of Comorbidities on the Patients' Outcomes

Effects of various comorbidities as well as the presence versus absence of comorbidities, the number of comorbidities, and other clinicodemographic factors (age, gender, clinical status, 4C score) were compared between survivors and non-survivors (Table 3).

Results revealed that there were significant differences between survivors and survivors with regard to age, gender, clinical status, and 4C score. For individual comorbidities, non-survivors were significantly higher than survivors in COVID-19 patients with hypertension, cardiovascular disease, chronic respiratory disease, chronic renal disease, dementia, chronic neurological disease, diabetes mellitus, and malignancy.

There were significant differences between survivors and non-survivors with regards to patients with comorbidities versus those with no comorbidities (56.4% vs 79.5%, $p < 0.001$), as well as those with ≥ 2 comorbidities (25.2% vs 48.7%, $p < 0.001$), respectively Table 3.

Table 1 Demographic and clinical features of the study cohort ($n = 1853$)

Feature	Number (%)
Age (years)	
Mean ± SD	**57.20 ± 21.6**
Median (Range)	**28.6 (15—109)**
Gender	
Male	**1045 (56.4%)**
Female	**808 (43.6%)**
Comorbidities	
Yes	**1118 (60.3%)**
No	**735 (39.7%)**
No of comorbidities	
0	**735 (39.6%)**
1	**578 (31.2%)**
≥ 2	**540 (29.2%)**
Clinical status	
Stable (non-ICU)	**1505 (81.2%)**
Critical (ICU)	**348 (18.8%)**
Outcome	
Alive	**1541 (83.2%)**
Dead	**312 (16.8%)**
4C score	
0–3	**316 (17.1%)**
4–8	**638 (34.4%)**
9–14	**814 (43.9%)**
≥ 15	**85 (4.6%)**

Table 2 Prevalence of comorbidities among the study cohort ($n = 1853$)

Comorbidity	Number (%)
Hypertension	232 (12.5%)
Cardiovascular disease	116 (6.3%)
Chronic respiratory disease	116 (6.3%)
Chronic renal disease	199 (10.3%)
Chronic liver disease	32 (1.7%)
Dementia	45 (2.4%)
Chronic neurological disease	146 (7.9%)
Connective tissue disease	30 (1.6%)
Diabetes mellitus	899 (48.5%)
HIV/AIDS	1 (0.1%)
Malignancy	39 (2.1%)

The multivariable regression analysis revealed that age (OR 3.032 (95% CI 0.006 – 0.029, $p = 0.002$), clinical status (8.194, 0.0350 – 0.709, $p < 0.001$), the presence (versus absence) of comorbidities (3.167, 0.042—0.233, $p = 0.002$), the number of comorbidities (2.972, 0.027 – 0.133, $p = 0.003$), and the 4C score (2.894, 0.010 – 0.054,

Table 3 Determinants of Mortality among the studied Cohort

	Alive (*n* = 1541, 83%)	Dead (*n* = 312, 17%)	*P*-value
Age/years (Median, IQR)	55 (30)	73.5 (19)	< 0.001*
Gender (Male/Female)	849/692	196/116	0.012**
Status (Critical)	87 (5.6%)	261 (83.9%)	< 0.001**
Comorbidity			
Hypertension	174 (11.3%)	58 (18.5%)	0.021**
Cardiovascular Disease	257 (16.7%)	92 (29.5%)	< 0.001**
Chronic Respiratory Disease	87 (5.6%)	29 (9.3%)	0.015**
Chronic Renal Disease	143 (9.3%)	56 (17.9%)	< 0.001**
Chronic Liver Disease	27 (1.8%)	5 (1.6%)	0.853**
Dementia	32 (2.1%)	13 (4.2%)	0.029**
Chronic Neurological Disease	103 (6.7%)	43 (13.8%)	< 0.001**
Connective Tissue Disease	24 (1.6%)	6 (1.9%)	0.641**
Diabetes Mellitus	699 (45.4%)	200 (64.1%)	< 0.001**
HIV/AIDS	1 (0.1%)	0 (0%)	0.832***
Malignancy	25 (1.6%)	14 (4.5%)	0.001**
Comorbidities			
Yes	870 (56.4%)	248 (79.5%)	< 0.001***
No	671 (43.5%)	64 (20.5%)	
No. of comorbidities			< 0.001**
0	671 (43.5%)	64 (20.5%)	
1	482 (31.3%)	96 (30.7%)	
≥ 2	388 (25.2%)	152 (48.7%)	
4 C Score			< 0.001**
0–3	314 (20.4%)	2 (0.6%)	
4–8	577 (37.4%)	61 (19.6%)	
9–14	613 (39.8%)	201 (64.4%)	
> 15	37 (2.4%)	48 (15.4%)	

* Mann Whitney U-test was used to compare the differences in Median between groups

** Chi-square test was used to compare the differences in frequency between groups

*** Fisher's exact test was used to compare the differences in frequency between groups

$p = 0.004$), were independent significant predictors of mortality. None of the individual comorbidities was a significant predictor of mortality. Table 4 shows these results.

Table 4 Independent Predictors of Mortality: Multivariable Logistic Regression

	OR (95% CI)[a]	*P*-value
Age/years (Median (IQR))	3.032 (0.006 -0.029)	0.002
Gender (Male/Female)	0.941 (0.014 – 0.092)	0.347
Status (Critical)	8.194 (0.350 – 0.709)	< 0.001
Hypertension	1.123 (0.033 – 0.224)	0.201
Cardiovascular Disease	1.263 (0.042 – 0.116)	0.207
Chronic Respiratory Disease	0.516 (0.096 – 0.240)	0.606
Chronic Renal Disease	0.208 (0.053 – 0.243)	0.835
Dementia	0.524 (-0.056 – 0.096)	0.600
Chronic Neurological Disease	0.170 (-0.046–0.054)	0.865
Diabetes Mellitus	0.834 (0.039–0.128)	0.405
Malignancy	1.633 (-0.014–0.151)	0.103
Comorbidities (Yes)	3.167 (0.042—-0.233)	0.002
No. of comorbidities (≥ 2)	2.972 (0.027 – 0.133)	0.003
4 C Score (high)	2.894 (0.010 – 0.054)	0.004

[a] *OR* Odds Ratio, *95%CI* Confidence Interval

Discussion

The current study was carried out at a large tertiary Saudi Arabian hospital to address the prevalence and impact of comorbidities in hospitalized patients with COVID-19.

Our results showed that 60.3% of COVID-19 patients had one or more comorbidities. This prevalence is remarkably higher than those reported by other studies [3, 4, 15]. This may reflect the higher prevalence of chronic medical diseases, like diabetes mellitus, in Saudi Arabia [16]. It may also reflect the transmission dynamics within particular age groups, case detection or testing practices or hospital admission policies during the different phases of the epidemic.

The transmission dynamics describe the process of transmission of an infectious agent (e.g. SARS-CoV-2) between hosts (humans, animals and/or vectors) in a population. Mathematical transmission dynamics models can be used by epidemiologists to better understand these emerging infections [17].

Our findings add to the existing worldwide literature on the spectrum of comorbidities [2–8] in patients with COVID-19 based on the large sample size and representativeness of the population at a large tertiary Saudi Arabian center. Previous studies from Saudi Arabia had highlighted the importance of comorbidities in patients with COVID-19 [18–23]. Despite the relatively large number of publications from Saudi Arabia, still, the results from these publications have similarities and differences with our data. Remarkably, none of these studies addressed the prevalence and impact of comorbidities in COVID-19 patients in the Southern Region of Saudi Arabia.

Our results showed that diabetes mellitus constituted the most prevalent comorbidity (48.5%), followed by hypertension (12.5%), and chronic renal disease (10.3%). These findings may be different from those reported by other studies and meta-analyses which found that hypertension was the most prevalent comorbidity in patients with COVID-19 [2–6, 8–10, 24]. Epidemiological population differences and the prevalence

of such chronic diseases among the study target could be attributable factors [16, 25].

The World Health Organization (WHO) has reported that Saudi Arabia ranks the second highest in the Middle East and is seventh in the world for the rate of diabetes. It is estimated that around 7 million of the population are diabetic and almost around 3 million have pre-diabetes [16]. A number of existing literature reports have pointed out that chronic disorders such as hypertension, diabetes, cardiovascular and respiratory disease, and their susceptibility conditions may be linked to the pathogenesis of COVID-19 [3, 4, 7, 16, 21]. Chronic diseases share several standard features with infectious disorders, such as the proinflammatory state, and the attenuation of the innate immune response. Notably, diabetes mellitus occurs in part because the accumulation of activated innate immune cells in metabolic tissues leads to the release of inflammatory mediators, especially IL-1β and TNFα, which promote systemic insulin resistance and β-cell damage [21, 26]. Additionally, metabolic disorders may lead to low immune function by impairing macrophage and lymphocyte function, which may make individuals more susceptible to disease complications [27]. Except for diabetes, no other comorbidities were identified to be predictors of poor clinical outcomes in patients with MERS-CoV infections [28].

Recently, it was observed that serum levels of inflammation-related biomarkers such as IL-6, C-reactive protein, serum ferritin, and coagulation index, D-dimer, were significantly higher ($P<0.01$) in diabetic COVID-19 patients compared with those without, suggesting that patients with diabetes are more susceptible to an inflammatory storm eventually leading to rapid deterioration of COVID-19 [16]. On the other hand, chronic kidney disease (CKD) has been associated with inflammation and dysregulation of immune function which may explain the increased risk of mortality in COVID-19 patients with kidney disease [29]. It has been reported in a recent study that the ACE2 receptor is overexpressed in the tubular cells of COVID-19 patients with kidney disease characterized by increased serum creatinine and urea nitrogen [29, 30]. Taken together, the alterations in ACE2 receptor expression and dysregulation of immune function may answer why the highest significantly increased risk of mortality was found in COVID-19 patients with kidney disease.

Our findings confirm that comorbidities such as diabetes, hypertension, cardiovascular disease, and chronic renal disease predispose to adverse clinical outcomes in patients with COVID-19.

Importantly, comorbidities have an impact on the mortality of hospitalized patients with COVID-19. Our data showed that age, clinical status, comorbidities, number of comorbidities, and the 4C score were independent significant predictors of mortality in our cohorts.

In COVID-19 prognostic models, comorbidities were handled differently; they might be included individually [31], given equal weight [32], or found to have no predictive effect [33].

In the current study, it has been shown that the presence of comorbidities (versus their absence), and the number of comorbidities (as an overall count), but not the individual comorbidities, were predictive factors of mortality. Our data are in agreement with those of Guan and coworkers [4] who analyzed data from 1590 COVID-19 hospitalized patients from 575 hospitals across mainland China. The risk of reaching the composite end-points (which consisted of admission to an ICU, invasive ventilation or death) was compared according to the presence and number of comorbidities. The authors concluded that patients with any comorbidity yielded poorer clinical outcomes than those without, and a greater number of comorbidities correlated with poorer clinical outcomes [4].

On the contrary, our results are not in agreement with those observed by Baradaran, et al. [11] who concluded that comorbidities do not seem to be the prerequisite for symptomatic and severe COVID-19 infection, except hypertension.

In daily clinical practice, our results have important implications. The proper triage of patients should be implemented by carefully inquiring about the medical history because this will help identify patients who would be more likely to develop serious adverse outcomes of COVID-19. Moreover, better protection should be given to patients with COVID-19 who had comorbidities upon confirmation of the diagnosis.

Strengths and limitations

Strengths of the current study include: First, despite, it seems that the results of the current study are "apparently" "non-novel" they; they- to the best of our knowledge—represent "the first" data coming from the Southern Region of Saudi Arabia. Although many studies came from Saudi Arabia [18–23], none came from the Southern region. The current study data are the "nucleus" for continuous database and innovative future research for Saudi populations in the Southern region. In this instance, it is worthy to mention the importance of the AFHSR as a large tertiary referral center that serves all populations from the Southern Region [12].

Second, taking into consideration the importance of the 4C ISARIC mortality score in risk assessment of COVID-19 patients [14], the current study is the first Saudi Arabian study that includes that score in predicting (together with the use of the comorbidities) mortality of hospitalized Saudi Arabian patients with COVID-19.

Third, despite other Saudi Arabian studies [18, 19] enrolled results for mixed populations (Saudi and

non-Saudi COVID-19 patients), our data were representative of "only Saudi" patients. This gives the study its statistical robustness and validation. Fourth, the current study highlighted the impact of "less common but important" comorbidities on COVID-19, like malignancy and HIV/AIDS. Mentioning these comorbidities was lacking among other studies from Saudi Arabia [18–20].

Fifth, the current study is the first Saudi Arabian study that highlights the importance of the presence (versus absence) of comorbidities and their number (as an overall count), but not the individual ones, as significant independent predictors of mortality.

On the other hand, this study had some potential limitations to be considered while interpreting the results. First, the inherent limitations of the retrospective study design are applicable. Second, our study was performed in a single medical center, limiting the generalizability of the results. Further prospective multi-center studies with larger sample sizes and including those with varied comorbidities and severities are required to confirm the effects of comorbidities in the larger Saudi population.

Conclusion

A total of 60.3% of hospitalized COVID-19 patients had one or more comorbidities. The most prevalent comorbidities were diabetes mellitus, hypertension, and chronic renal disease were the most prevalent comorbidities. The presence and the number of comorbidities, but not the individual ones, together with age, clinical status at admission, and the 4C mortality score were significant independent predictors of mortality. Further prospective multicenter studies are warranted.

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Authors' contributions
The idea of the research and conceptualization : A.A.A., A.H., U.E.A. Writing of the manuscript: S.M.A.A., N.S. A, U.E.A: Editing and revision: B.A.A. D., N.A.S.M. Collection of data: A.S.K., M.A.Q., N.A.A., A.S.Y.A., M.A.A., F.A.A. Methodology: A.A.A., Y.A.A., A.A., S.A.S.A., I.M.A.M, U.E.A.

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Declarations

Ethics approval and consent to participate
Ethical approval was obtained from the institutional review board of the AFHSR (approval no; AFHSRMREC/2022/PULMONOLOGY-INTERANL MEDICINE/603).

Consent for publication
Not applicable.

Availability of data and material
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests
The authors have no competing interests.

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