

Characteristics Associated with COVID-19 Outcomes: A Population-Based Analysis Using SINAHR® Primary Care Data and Linked Hospital Care Monitoring System

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Abstract

Background: Identifying risk factors for severe COVID-19 outcomes is essential for shaping effective public health strategies. This study analyzed demographic, clinical, and comorbidity-related factors associated with hospitalization, ICU admission, mechanical ventilation, and mortality in a large Iranian population.

Methods: We conducted a population-based cross-sectional study of 405,397 individuals registered under the Mashhad University of Medical Sciences, combining primary care records with hospital monitoring data. Variables included age, sex, geographic region, diabetes, hypertension, cardiovascular disease, hyperlipidemia, pregnancy, obesity, and vaccination status. Logistic regression models were applied to examine associations with each outcome.

Results: Among 405,397 individuals (mean age 40.21±16 years; 46.30% female), 4.29% were hospitalized, 0.17% admitted to ICU, 0.42% required mechanical ventilation, and 0.67% died. Advanced age (≥80 years) was the strongest predictor across all outcomes, with adjusted odds ratios (AORs) ranging from 17.21 (95% CI, 15.37–19.28) for hospitalization to 283.31 (95% CI, 155.57–515.93) for mortality. Cardiovascular disease, diabetes, obesity, and pregnancy were also significant risk factors. In contrast, female sex (AOR for mortality: 0.63; 95% CI, 0.58–0.69), hypertension, and hyperlipidemia were associated with reduced risks. Vaccination demonstrated a strong dose-dependent protective effect, with three doses reducing the odds of mortality by 93% (AOR: 0.07; 95% CI, 0.05–0.12).

Conclusion: Advanced age, cardiovascular disease, diabetes, obesity, and pregnancy emerged as major risk factors for severe COVID-19 outcomes. The apparent protective associations of female sex, hypertension, and hyperlipidemia warrant further exploration. Most critically, the profound protective effect of vaccination highlights the urgent need to sustain and expand comprehensive immunization programs.

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Introduction

The COVID-19 pandemic has had a profound impact on global health, with disease severity and outcomes influenced by multiple demographic, clinical, and social factors. Identifying and understanding these determinants are essential for guiding public health strategies and optimizing patient management. Previous studies have highlighted age, sex, socioeconomic status, comorbidities, and pregnancy as key predictors of adverse outcomes such as hospitalization, ICU admission, and mortality.¹⁻⁴

Age has consistently emerged as one of the strongest risk factors for severe COVID-19. In the United States, approximately 80% of COVID-19-related deaths have occurred among individuals aged 65 years and older.⁵ This elevated risk is largely attributed to immunosenescence, the higher prevalence of chronic conditions, and increased exposure in settings such as long-term care facilities.^{6,7}

Gender also plays a role, with multiple studies reporting worse outcomes, including higher mortality rates, among males with COVID-19.^{1,2} This gender disparity may be attributed to biological factors, comorbidities, or behavioral differences. Socioeconomic status, often indicated by factors such as geographic region of residence, has also been linked to COVID-19 outcomes. Studies have demonstrated that individuals from areas with lower socioeconomic status or higher levels of deprivation experience worse outcomes, possibly due to limited healthcare access, higher comorbidity rates, or occupational exposure.^{1,2}

Comorbidities significantly influence COVID-19 outcomes. Conditions such as cardiovascular disease, diabetes, hypertension, obesity, and hyperlipidemia have been associated with increased risks of severe illness, hospitalization, and mortality.^{1,2,7,8} For example, a study conducted in the UK reported that individuals with cardiovascular disease had higher risks of both hospitalization and death due to COVID-19.⁶

Diabetes, in particular, has been identified as a significant risk factor, as it exacerbates inflammatory conditions in COVID-19 patients and is associated with increased risks of hospitalization, ICU admission, and death.⁹⁻¹¹ Similarly, obesity has been widely reported to increase the risk of severe COVID-19 outcomes, likely due to its association with pro-inflammatory states, diabetes, and cardiovascular disease.¹²⁻¹⁴ Pregnancy has also been recognized as a risk factor for severe COVID-19, with studies indicating that pregnant women are at higher risk for complications, including hospitalization and ICU admission.¹⁻⁴

While these risk factors have been well documented, the impact of vaccination in mitigating them remains an area of ongoing research. Early studies suggest that

vaccination substantially reduces the risk of severe outcomes, even among high-risk groups.^{15,16}

In this study, we aim to provide a comprehensive analysis of demographic variables and comorbidities associated with various COVID-19 outcomes, including hospitalization, ICU admission, mechanical ventilation, and death. By combining primary healthcare data with hospital records, we capture a broad spectrum of patients, ranging from those with mild symptoms to severe cases. This population-based approach enables a more accurate estimation of the impact of risk factors and vaccination status on COVID-19 outcomes, thereby offering valuable insights for public health strategies and patient care.

Methods

Data source: The ‘Sina’ electronic health record (EHR) database at the primary healthcare level contains patient-related information, including demographic data (age, gender, nationality, education level, and occupation) and clinical information (diagnoses, treatments, and tests). This database encompasses approximately 5.2 million individuals affiliated with Mashhad University of Medical Sciences, accounting for about 8% of Iran’s total population. Established in 2015 with support from the Iranian Ministry of Health and Medical Education, the database has been widely used for research, particularly studies related to COVID-19.

Data extraction was conducted with the approval and supervision of the Research Ethics Committee. Primary data were extracted from the Sina EHR system, which registers all cases with positive SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test results, including individuals from comprehensive health service centers, laboratories, and private clinics. Data were aggregated from three sources:

1. Medical Care Monitoring Center (MCMC): Registers suspected and confirmed COVID-19 cases in all hospitals nationwide.

2. National Infectious Disease Surveillance System: A national portal managed by the Ministry of Health and Medical Education. Data are sent daily to the local health center in Mashhad by hospital infection control specialists.

3. Private and Government Imaging Centers: Data related to suspected and confirmed patients undergoing CT scans are sent to the university’s central service.

Individual-level data from these sources were linked using national identification numbers. This study was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Outcomes: The study considered four COVID-19 outcomes:

1. Hospital Admission: Patients with a positive PCR result, classified under ICD-10 codes U07.1 or U07.2, registered in the MCMC system.

2. ICU Admission: Determined based on information in the MCMC system and the national disease management portal.

3. Mechanical Ventilation: Based on information in the MCMC system and the national disease management portal.

4. Mortality: Determined using disease classification and data from the MCMC system, the national disease portal, and the mortality cause registration and classification system.

Risk Factors: The variables included:

- **Age:** Categorized into groups (0-17, 18-29, 30-59, 60-79, ≥ 80 years).

- **Gender:** Male, female.

- **Place of Residence:** Categorized as rural, urban areas (population < 1 million), suburban areas, and major cities (e.g., Mashhad).

- **Comorbidities:** Only conditions previously associated with COVID-19 outcomes were considered:

- o Diabetes: ICD-10 codes E10 and E11

- o Hypertension: Codes I10 and I15

- o Cardiovascular diseases: Codes I20, I21, I24, I25, I63, and I70

- o Hyperlipidemia: Code E78

- o Obesity: BMI ≥ 30

- o Pregnancy

- **Vaccination Status:** Extracted from the national TITAC service (Food and Drug Administration, Ministry of Health), and recorded in the Sina EHR system by doses (first, second, third).

Statistical Analysis

Logistic regression was used to investigate associations between patient characteristics and each of the four COVID-19 outcomes (hospitalization, ICU admission, mechanical ventilation, and death). All models were adjusted for demographic factors (age, sex, geographic region) and relevant comorbidities (diabetes, hypertension, cardiovascular disease, hyperlipidemia, pregnancy, and obesity). Statistical analyses were performed using Stata version 14.0 (StataCorp). Variance inflation factors (VIFs) were calculated to assess potential multicollinearity among independent variables. Two-sided P-values < 0.05 were considered statistically significant.

Ethical Consideration

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Mashhad University of Medical Sciences

Table 1: COVID-19 and Outcomes by characteristics

Characteristic	Total patient	Admitted to primary health care	Hospital contact	ICU admission	Ventilation	Death
Total population	405397	387996(95.71)	17401(4.29)	679(0.17)	1697(0.42)	2722(0.67)
Sex						
Male	217718	208423(95.73)	9295(4.27)	386(0.18)	897(0.41)	1645(0.76)
Female	187679	179573(95.68)	8106(4.32)	293(0.16)	800(0.43)	1077(0.57)
Age, median (IQR), y	40(31-52)	39(31-51)	56(41-69)	59(44-70)	55(42-69)	69(59-79)
Age categories						
1-17	22092	21660(98.04)	432(1.96)	7(0.03)	19(0.09)	11(0.05)
18-39	177964	174597(98.11)	3367(1.89)	114(0.06)	329(0.18)	139(0.08)
40-59	141822	135977(95.88)	5845(4.12)	227(0.16)	609(0.43)	557(0.39)
60-79	55223	49331(89.33)	5892(10.67)	251(0.45)	573(1.04)	1343(2.43)
≥ 80	8296	6431(77.52)	1865(22.48)	80(0.96)	167(0.42)	672(8.10)
Type of Region						
Rural	47302	44262(93.57)	3040(6.43)	80(0.17)	301(0.64)	396(0.84)
City under 1 million population	54997	50945(92.63)	4052(7.37)	78(0.14)	516(0.94)	365(0.66)
Slum area	79022	76333(96.60)	2689(3.40)	150(0.19)	231(0.29)	483(0.61)
Metropolitan	224076	216456(96.60)	7620(3.40)	371(0.17)	649(0.29)	1478(0.66)
Comorbidities						
Diabetes	9609	7038(73.24)	2571(26.76)	130(1.35)	324(3.37)	495(5.15)
Hypertension	13145	11746(89.36)	1399(10.64)	64(0.49)	141(1.07)	289(2.20)
cardiovascular	4779	2517(52.67)	2262(47.33)	145(3.03)	288(6.03)	409(8.56)
yperlipidemia	23560	21487(91.20)	2073(8.80)	64(0.27)	219(0.93)	316(1.34)
Pregnancy	6885	6533(94.89)	352(5.11)	13(0.19)	42(0.61)	44(0.64)
Obesity	45744	42757(93.47)	2985(6.53)	112(0.24)	314(0.69)	407(0.89)
Vaccination						
1 dose	338784	326357(96.33)	12427(3.67)	461(0.14)	1235(0.36)	399(0.12)
2 doses	306556	295401(96.36)	11155(3.64)	409(0.13)	1109(0.36)	201(0.07)
3 doses	78587	295996(96.36)	3973(5.06)	154(0.20)	389(0.49)	21(0.03)

(approval number: IR.MUMS.REC.1399.129). Data were de-identified before analysis to ensure patient privacy. Individual consent was waived due to the retrospective design and use of anonymized data.

Results

Study Population

In this study, 405,397 individuals under the coverage of Mashhad University of Medical Sciences were examined, with a mean age of 40 ± 16.21 years (Table 1). Approximately 46.30% (187,679 individuals) were female, and 78.88% were between 18 and 59 years old.

COVID-19 Hospitalization

Among hospitalized patients, 53.42% were male and 46.30% were female. Comorbidities were present in a substantial proportion of hospitalized patients: 22.08% had diabetes, 12.01% had hypertension, 19.42% had cardiovascular disease, 17.80% had hyperlipidemia, and 25.63% were obese. In the adjusted logistic regression model, controlling for age, gender, geographic region, and comorbidities, the odds ratio for COVID-19 hospital admission in females was (AOR, 0.92; 95% CI, 0.88-0.96), age ≥ 80 years (AOR, 17.21; 95% CI, 15.37-19.28), city under 1 million inhabitants (AOR, 1.21; 95% CI, 1.14-1.27), diabetes (AOR, 6.06; 95% CI, 5.70-6.44), hypertension

(AOR, 0.54; 95% CI, 0.51-0.59) cardiovascular disease (AOR, 10.94; 95% CI, 10.23-11.71), hyperlipidemia (AOR, 0.76; 95% CI, 0.71-0.80), pregnancy (AOR, 2.12; 95% CI, 1.89-2.37), obesity (AOR, 1.30; 95% CI, 1.30-1.37), one dose vaccination (AOR, 0.59; 95% CI, 0.55-0.66), two dose vaccination (AOR, 0.68; 95% CI, 0.64-0.72), three dose vaccination (AOR, 0.76; 95% CI, 0.70-0.77) (Figure 1).

COVID-19 ICU Admissions

In the adjusted regression model, odds ratios for COVID-19 ICU admission were: female (AOR, 0.84; 95% CI, 0.72-0.98), age ≥ 80 years (AOR, 22.31; 95% CI, 10.21-48.73), slum area (AOR, 1.23; 95% CI, 0.93-1.63), diabetes (AOR, 3.91; 95% CI, 3.12-4.91), hypertension (AOR, 0.80; 95% CI, 0.60-1.08) cardiovascular disease (AOR, 9.07; 95% CI, 7.34-11.21), hyperlipidemia (AOR, 0.60; 95% CI, 0.46-0.80), pregnancy (AOR, 2.29; 95% CI, 1.31-4.01), obesity (AOR, 1.29; 95% CI, 1.04-1.60), one dose vaccination (AOR, 0.66; 95% CI, 0.50-0.88), two dose vaccination (AOR, 0.65; 95% CI, 0.49-0.85), three dose vaccination (AOR, 0.83; 95% CI, 0.67-1.03) (Figure 2).

COVID-19 Ventilation

In adjusted regression model odds ratio for COVID-19 ventilation in female (AOR, 0.96; 95% CI, 0.86-1.06), age ≥ 80 years (AOR, 20.96; 95%

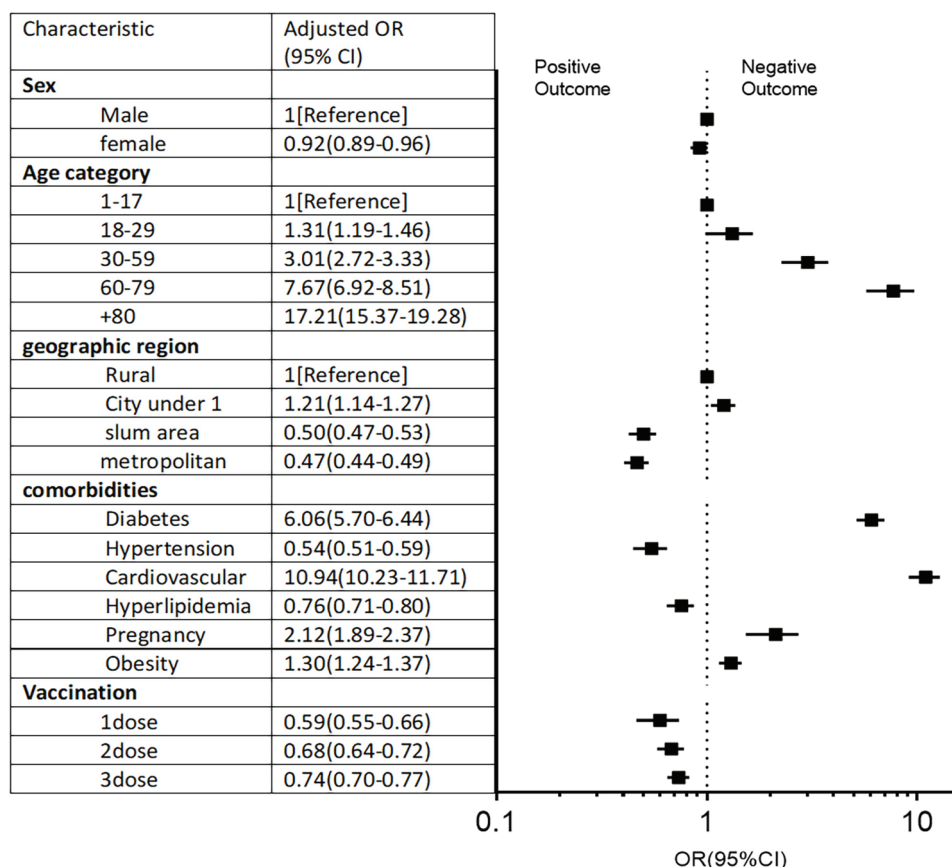


Figure 1: Adjusted regression analysis for association between characteristic and Hospital Admission

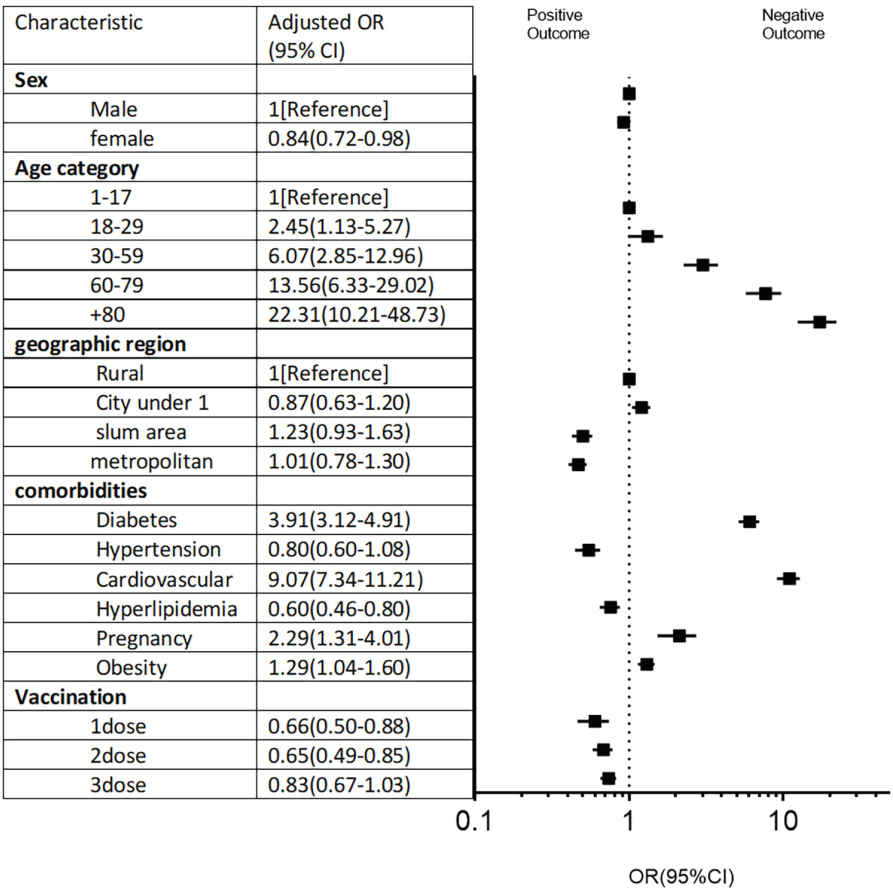


Figure 2: Adjusted regression analysis for association between characteristic and ICU Admission

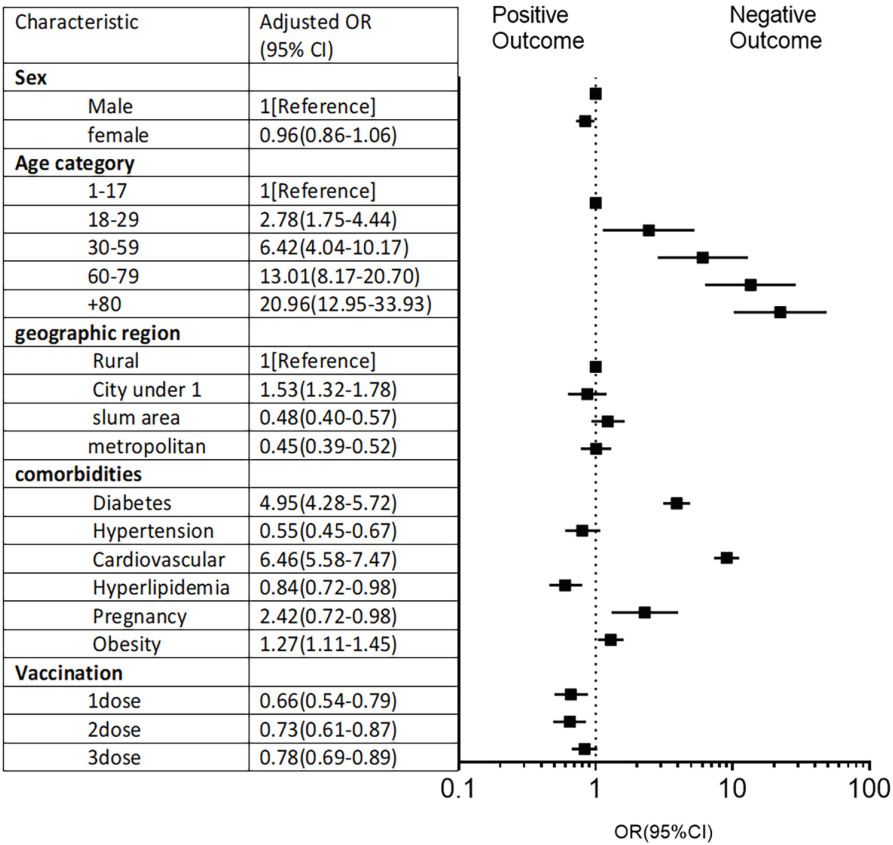


Figure 3: Adjusted regression analysis for association between characteristic and ventilation in hospital

CI, 12.95-33.93), city under 1 million inhabitant (AOR, 1.53; 95% CI, 1.32-1.78), diabetes (AOR, 4.95; 95% CI, 4.28-5.72), hypertension (AOR, 0.55; 95% CI, 0.45-0.67) cardiovascular disease (AOR, 6.46; 95% CI, 5.58-7.47), hyperlipidemia (AOR, 0.84; 95% CI, 0.72-0.98), pregnancy (AOR, 2.42; 95% CI, 1.76-3.32), obesity (AOR, 1.27; 95% CI, 1.11-1.45), one dose vaccination (AOR, 0.66; 95% CI, 0.54-0.79), two dose vaccination (AOR, 0.73; 95% CI, 0.61-0.87), three dose vaccination (AOR, 0.78; 95% CI, 0.69-0.89) (Figure 3).

COVID-19 Death

In adjusted regression model odds ratio for COVID-19 death in female (AOR, 0.63; 95% CI, 0.58-0.69), age ≥ 80 years (AOR, 283.31; 95% CI, 155.57-515.93), city under 1 million habitant (AOR, 0.87; 95% CI, 0.74-1.03), diabetes (AOR, 4.20; 95% CI, 3.66-4.82), hypertension (AOR, 0.68; 95% CI, 0.58-0.80) cardiovascular disease (AOR, 4.96; 95% CI, 4.29-5.73), hyperlipidemia (AOR, 0.86; 95% CI, 0.75-1), pregnancy (AOR, 3.95; 95% CI, 2.82-5.53), obesity (AOR, 1.59; 95% CI, 1.40-1.81), one dose vaccination (AOR, 0.22; 95% CI, 0.19-0.25), two dose vaccination (AOR, 0.10; 95% CI, 0.08-0.13), three dose vaccination (AOR, 0.07; 95% CI, 0.05-0.12) (Figure 4).

Discussion

In this study, we leveraged a unique combination of primary

care and hospital data to conduct a population-based analysis of individual-level factors and comorbidities associated with COVID-19 outcomes. Our findings indicate that advanced age, cardiovascular disease, diabetes, obesity, and pregnancy are consistently associated with higher risks of hospitalization, ICU admission, mechanical ventilation, and mortality. In contrast, vaccination exhibited significant protective effects across all outcomes, particularly in reducing mortality.

In line with global trends,⁷⁻¹⁰ our study highlights the heightened vulnerability of older adults to severe COVID-19 outcomes. Individuals aged 80 and older faced substantially higher risks: 17.21 times for hospitalization, 22.31 times for ICU admission, and an alarming 283.31 times for mortality compared to those under 17. These findings align with reports indicating that approximately 80% of COVID-19 deaths occur among individuals aged 65 and older.⁵ The increased susceptibility in older adults is likely driven by factors such as immunosenescence and a higher prevalence of comorbid conditions.^{7, 12}

Our findings on gender differences partially align with previous studies. While many studies report worse outcomes in males,^{1, 2} our analysis found that females experienced reduced risks across all outcomes, most notably for mortality (AOR, 0.63; 95% CI, 0.58-0.69). This discrepancy suggests a need for further investigation into potential gender-specific

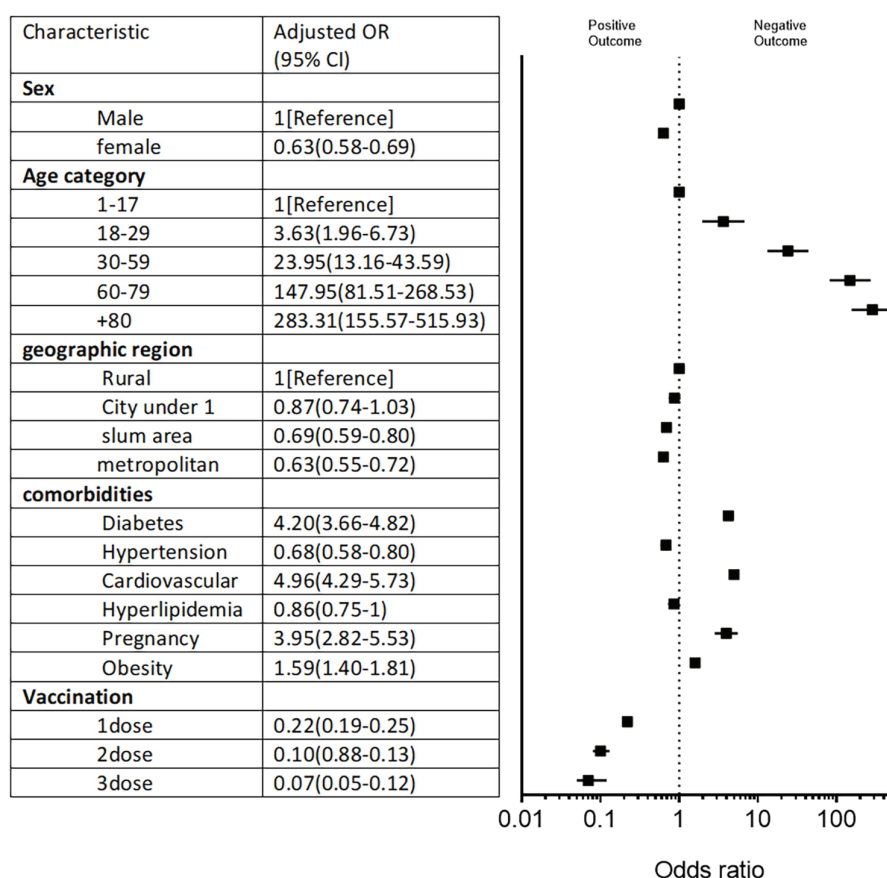


Figure 4: Adjusted regression analysis for association between characteristic and death

differences in immune responses or healthcare access patterns within our population.

The geographic region of residence, often serving as a proxy for socioeconomic status, also influenced the outcomes. Residents of cities with populations under one million had higher risks of hospitalization and mechanical ventilation, possibly reflecting disparities in healthcare resources or COVID-19 management strategies. However, unlike some prior studies,^{1, 2} we did not consistently observe elevated risks in rural or low-income areas.

Comorbidities were a significant determinant of COVID-19 outcomes, consistent with previous research.^{2, 7, 13} Cardiovascular disease substantially increased risks across all outcomes, most prominently for hospitalization (AOR, 10.94; 95% CI, 10.23–11.71) and ICU admission (AOR, 9.07; 95% CI, 7.34–11.21). These findings align with studies highlighting the role of cardiovascular complications in severe COVID-19 cases.^{1, 14, 15} Similarly, diabetes—even present in only 3.2% of our cohort—markedly increased risks, consistent with its known role in exacerbating inflammatory responses in COVID-19 patients.^{16–19}

Obesity, another pro-inflammatory condition often associated with diabetes and cardiovascular disease,^{20–22} was linked to elevated risks, particularly for mortality (AOR, 1.59; 95% CI, 1.40–1.81). This association may be explained by factors such as difficulties with intubation, reduced mobility,²³ and impaired immune responses to viral infections.²⁴ Pregnancy also emerged as a significant risk factor across all outcomes, with the strongest effect observed for mortality (AOR, 3.95; 95% CI, 2.82–5.53).

Interestingly, hypertension and hyperlipidemia were associated with reduced risks in our study, which contrasts with findings from several meta-analyses identifying these conditions as risk factors for severe COVID-19 outcomes.²⁵ Several explanations may account for this discrepancy. First, our study specifically examined diagnosed hypertension and hyperlipidemia, conditions that are likely to be under treatment in Iran's primary care system. The use of statins for hyperlipidemia and ACEIs/ARBs for hypertension may have contributed to this protective effect, as suggested by other studies.^{26–32} Second, variations in the definition and measurement of these conditions across studies may lead to inconsistent results. Finally, the interplay between blood pressure, lipid metabolism, and COVID-19 outcomes is likely complex and may be influenced by underlying inflammation and metabolic dysfunction, factors not fully captured in our study. Further research is warranted to clarify the precise role of blood pressure and lipid regulation in COVID-19 severity, particularly in populations with well-managed chronic conditions.

The most striking finding was the robust protective effect of vaccination. Consistent with other studies,^{28, 29} we observed a clear dose-dependent reduction in risk, with the most pronounced effect on mortality. Three vaccine doses reduced the odds of mortality by 93% (AOR, 0.07; 95% CI, 0.05–0.12), underscoring the critical importance of comprehensive vaccination programs in mitigating the pandemic's impact.

This study has several limitations. Underreporting is likely to have occurred during peak periods in Khorasan Razavi due to shortages of testing kits, potentially affecting the completeness of our dataset. By including only PCR-confirmed cases, we may have excluded clinically diagnosed or CT-based cases. Additionally, data from five universities within the Mashhad University of Medical Sciences catchment area were not included due to access constraints, which may limit generalizability. These factors should be taken into account when interpreting our results.

Conclusion

This population-based study provides strong evidence on risk factors for severe COVID-19 outcomes in Iran. Advanced age, cardiovascular disease, diabetes, obesity, and pregnancy consistently emerged as major risk factors. The apparent protective effects of female gender, controlled hypertension, and hyperlipidemia warrant further investigation. Most importantly, our findings highlight the life-saving potential of vaccination, particularly in reducing mortality. These insights should inform public health strategies, with a focus on comprehensive vaccination and targeted interventions for high-risk groups.

Authors' Contribution

Conceptualization and study design: Ehsan Mosa Farkhani and Ali Taghipour; Data extraction and validation: Mehdi Norouzi, Zahra Amiri, and Fatemeh Taghipour; Data analysis and interpretation: Ehsan Mosa Farkhani, Mehdi Norouzi, and Mohammad Hossein Madahali; Manuscript drafting: Ehsan Mosa Farkhani and Mehdi Norouzi; Critical revision and editing: Ali Taghipour and Fatemeh Taghipour. All authors reviewed and approved the final version of the manuscript.

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Conflict of Interest

The authors declare no conflicts of interest related to this study.

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