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Acute kidney injury and COVID-19; incidence, risk factors, and mortality

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Abstract

Introduction: Acute kidney injury (AKI) is a common complication among patients infected with SARS-CoV-2, particularly in intensive care unit (ICU) settings. Understanding the incidence, risk factors, and outcomes associated with AKI in COVID-19 patients is crucial for optimizing clinical management and improving patient outcomes.

Objectives: The main goal of our study was to investigate the impact of AKI on the mortality rates of COVID-19 patients. We achieved this by determining the incidence of AKI and mortality in COVID-19 patients, and by comparing mortality rates between patients with and without acute renal failure. Our aim is to highlight the importance of kidney function in hospitalized COVID-19 patients, which could lead to timely diagnosis and improved management of those who develop AKI.

Patients and Methods: We conducted a retrospective observational study to investigate the incidence of AKI and its association with mortality in COVID-19 patients. A total of 125 patients diagnosed with COVID-19 were included in the study, with 93 patients who had recovered and were discharged am 32 patients who were deceased. Data was collected from 2 referral medical centers during one year. Demographic, clinical, and laboratory data were collected and analyzed to assess the incidence of AKI and its impact on patient outcomes.

Results: The study found that 48.8% of COVID-19 patients developed AKI during or shortly before their hospitalization, with 57.4% requiring ICU admission. Older age was identified as a significant risk factor for AKI development, with patients in the AKI group having a significantly higher mean age compared to those without AKI (55.54 vs 65.33, $P<0.001$). Additionally, male gender, obesity, tobacco/opium addiction, prior tuberculosis infection, ischemic heart disease or chronic kidney disease as an underlying disease and history of kidney transplantation were shown as significant risk factors for AKI development in COVID-19 patients. After adjusting for and removing all confounding variables, two variables emerged as predictors of mortality; high creatinine levels ($P=0.005$) and hospitalization in the ICU ($P<0.001$).

Conclusion: This study highlights the high incidence of AKI among COVID-19 patients, particularly in older individuals and those requiring ICU care. Importantly, AKI was associated with increased mortality, underscoring the need for early detection and management of renal complications in COVID-19 patients to improve clinical outcomes.

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Introduction

Since late 2019, a novel respiratory disease caused by SARS-CoV-2 spread worldwide, leading to a global pandemic known as COVID-19, as declared by the World Health Organization. This unprecedented pandemic has impacted millions of individuals across the globe. Numerous studies have underscored the multifactorial nature of mortality rates among COVID-19 patients, with underlying and chronic comorbidities playing a significant role in exacerbating the severity of the disease (1).

Given the ongoing effects of global pandemic and the challenges associated with the SARS-CoV-2 virus, including the absence of complete eradication or definitive treatment, it is evident that potential complications may arise, posing significant consequences for healthcare systems worldwide. These complications can impose substantial costs and strain on healthcare infrastructure. Consequently, accurate identification of such complications and implementation of preventive measures are crucial for mitigating their impact (2).

Key point

This retrospective study investigates the incidence and impact of acute kidney injury (AKI) in COVID-19 patients. We analyzed data from 125 patients admitted to our university hospital, focusing on AKI occurrence, associated risk factors, and outcomes. Our findings reveal a substantial prevalence of AKI among COVID-19 patients, particularly in older individuals and those requiring ICU care. Importantly, AKI correlates significantly with higher mortality rates, underscoring the critical importance of early detection and management of renal complications in COVID-19 management strategies.

In December 2019, the initial clinical manifestations of COVID-19 patients were identified in Wuhan, China. Initially, the number of cases remained low but rapidly escalated, reaching a peak in mid-January 2020. Subsequently, with exponential growth, the disease spread to other countries, prompting a global health crisis. By May 2020, the cumulative number of reported cases worldwide had surged to 4 819 372, with 316 961 recorded deaths and 1 864 629 documented recoveries (3). Notably, a mortality rate of 6.6% was reported (4).

Based on available evidence, individuals with additional risk factors, such as advanced age or pre-existing chronic conditions like cardiovascular disease, chronic renal failure, diabetes, or chronic rheumatic diseases with a history of immunosuppressive drug administration, demonstrate a higher incidence of COVID-19 (5).

Among the complications observed in COVID-19 patients, acute renal failure stands out as a significant concern. It represents a contributing factor to elevated mortality rates, particularly when coupled with other risk factors. Indeed, it may emerge as the foremost determinant of mortality within this patient population (6).

Various studies have provided compelling evidence of direct invasion of renal parenchymal tissue by the SARS-CoV-2 virus, leading to the development of acute kidney injury (AKI). Despite the predominant targeting of the respiratory and immune systems by COVID-19 (7), cases of acute renal impairment and proteinuria have been documented in affected patients. However, comprehensive pathological examinations of kidney damage in severe COVID-19 cases remain limited.

To elucidate this aspect, Su et al conducted postmortem analyses of renal abnormalities in 26 autopsies of COVID-19 patients using light microscopy. The patients, with an average age of 69 years (19 males and 7 females), exhibited respiratory failure associated with multiple organ dysfunction syndrome as the primary cause of death. Notably, nine out of 26 patients exhibited clinical indicators of kidney damage, such as elevated serum creatinine levels or proteinuria.

Light microscopy revealed proximal tubular damage characterized by epithelial cell destruction, non-isometric vacuolization, and necrosis. Additionally, the presence of hemosiderin granules and pigments was observed in certain areas. Notably, prominent erythrocyte accumulation was evident within capillary lumens, devoid of platelets or fibrinoid deposits. Importantly, no evidence of vasculitis, interstitial inflammation, or hemorrhage was detected.

Electron microscopic examination unveiled clusters of coronavirus particles with distinctive surface protrusions within tubular epithelial cells and podocytes, providing direct evidence of SARS-CoV-2 invasion of kidney tissue. These findings significantly contribute to our understanding of SARS-CoV-2 infection, highlighting the potential for viral attack on kidney tissue and subsequent development of proteinuria (8).

Objectives

The objective of this study was to assess the impact of acute renal failure on mortality among patients with COVID-19. Additionally, we investigated the influence of other variables, including age, gender, hospitalization status, and the presence of comorbidities associated with renal complications, on mortality rates in individuals with COVID-19.

Patients and Methods

Study design

This case-control study assessed patients admitted to Shahid Modarres and Dr. Masih Daneshvari hospitals in Tehran in 2021. One hundred twenty-five patients with the mean age of 60.35 ± 15.67 years ranging from 28 to 92, were included in the study. 83 of the patients (66.4%) were male and 42 (33.6%) were female. Ninety-three of the patients had recovered from COVID-19 and were discharged from the hospital whereas 32 were deceased. These patients were confirmed to have COVID-19 based on their medical history, clinical examinations, laboratory criteria (polymerase chain reaction-restriction fragment length polymorphism), and imaging (computed tomography scan). The study specifically focused on individuals who developed acute renal failure during their hospitalization.

The diagnostic criteria for COVID-19 included clinical signs such as fever, chills, cough, shortness of breath, body aches, weakness, lethargy, anosmia, diarrhea, or abdominal pain, alongside laboratory confirmation through the SARS-CoV-2-specific polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) test. Pulmonary involvement may be confirmed using computed tomography (CT) scans interpreted by a radiologist.

The diagnostic criteria for acute renal failure included an increase in serum creatinine greater than or equal to 0.3 mg/dL within 48 hours, or an increase in creatinine greater than or equal to 1.5 times the patient's baseline creatinine within the last seven days, or a decrease in urine volume to less than 0.5 ml per kg of body weight per hour for at least 6 hours (9).

Exclusion criteria encompassed the absence of clinical and laboratory evidence confirming COVID-19 infection, as well as the presence of chronic kidney disease.

Patients were categorized into two groups: deceased COVID-19 patients and discharged COVID-19 patients. Demographic and anthropometric data were collected from patient files or through questionnaires administered during hospitalization. Confounding variables, including underlying diseases such as diabetes, chronic kidney failure, and cardiovascular disease, which could potentially impact patient mortality, were assessed and analyzed in both the deceased and discharged groups. These variables were controlled for using multivariate logistic regression analysis.

Statistical analysis

For statistical analysis, we conducted both descriptive and analytical statistics. In descriptive statistics, quantitative variables such as age were presented as mean ± SD, while nominal and qualitative variables were expressed as numbers and percentages. Analytical statistics began with univariate analysis tests, where the *t* test was employed to compare means of variables between the case and control groups. To assess the relationship between qualitative or nominal variables, the chi-square test was utilized. Subsequently, multivariate tests, such as logistic regression, were performed to evaluate the independent effects of variables on the outcome (mortality).

Odds ratio (OR) and confidence interval (CI) were reported for both univariate and multivariate tests. It is worth noting that certain characteristics may have exhibited different distributions between the deceased and discharged groups from the onset of data collection, which were neutralized as confounding variables using logistic regression. The significance level in statistical tests was set at 0.05 (5%).

Results

Demographic data, incidence of AKI, risk factors and applicable laboratory tests were compared between COVID-19 patients who had recovered from the disease and those who were deceased.

A significant relationship was found between increased serum creatinine levels and mortality in COVID-19 patients ($P = 0.023$). The frequency of elevated serum creatinine levels was 65.625% among deceased patients and 42.22% among discharged patients (Table 1).

A statistically significant relationship was observed between intensive care unit (ICU) admission and mortality ($P < 0.001$). The frequency of ICU admission among deceased patients was 90.3%, whereas it was 43.4% among discharged patients (Table 2).

Older age was found to have a significant association with higher mortality rate (Table 3).

No significant association was observed between gender and mortality ($P = 0.381$). Similarly, weight ($P = 0.983$), hospitalization duration ($P = 0.307$), and non-steroidal anti-inflammatory drug (NSAID) use ($P = 1.00$) did not show a statistically significant relationship with mortality. The mean weight of the patients was 82.61 kg in total, with 82.65 kg in the deceased group, and 82.52 kg in the discharged group. The patients had an average hospitalization period of 10.0 ± 8.21 days; The average duration of hospitalization for deceased patients was 11.1935 days, compared to 9.4186 days for discharged patients. The frequency of NSAID use in the deceased group was 12.5%, while it was 14.44% in the discharged group.

CT scans revealed signs of pulmonary involvement in 100% of deceased patients and 97.75% of discharged patients. This difference did not reach statistical significance ($P = 0.620$).

A significant relationship was observed between smoking tobacco, opium consumption, and mortality in COVID-19 patients ($P = 0.051$). The frequency of smoking alone in deceased and discharged patients was 12.5% and 31.82%, respectively. Similarly, the frequency of opium use alone in deceased and discharged patients was 21.875% and 17.04%, respectively. Additionally, the frequency of simultaneous use of tobacco and opium in deceased and discharged patients was 9.375% and 1.14%, respectively (Table 4).

There was no significant relationship observed between the frequency of diabetes in deceased patients (53.125%) and discharged patients (38.89%) ($P = 0.212$). Similarly, the frequency of obesity did not differ significantly

Table 1. Relationship between increased serum creatinine level and mortality in COVID-19 patients

		Patient population		*P* value
		Deceased	Recovered	
Increased serum creatinine levels	Yes (%)	65.62%	42.22%	0.023
	No (%)	34.37%	57.78%	

Table 2. Relationship between ICU admission and mortality in COVID-19 patients

		Patient population		*P* value
		Deceased	Recovered	
ICU admission	Yes (%)	90.32%	43.42%	<0.001
	No (%)	9.68%	56.58%	

Table 3. Relationship between age and mortality in COVID-19 patients

	Patient population	Mean (years)	Std. deviation	*P* value
Age	Deceased	67.96	14.76	0.002
	Recovered	57.70	15.43	

Table 4. Relationship between tobacco or opium consumption and mortality in COVID-19 patients

		Patient group		*P* value
		Deceased	Recovered	
Tobacco/Opium use	No use	56.25%	50%	0.051
	Tobacco only	12.5%	31.82%	
	Opium only	21.87%	17.04%	
	Tobacco and Opium	9.37%	1.14%	

between patients who died (15.625%) and those who were discharged (20%) ($P=0.617$).

Tuberculosis was observed in three deceased patients, while none of the discharged patients had tuberculosis, indicating a significant difference in the relationship between tuberculosis and mortality in COVID-19 patients in our study ($P=0.017$).

Furthermore, the frequency of ischemic heart disease (IHD) in deceased patients was nearly three times higher than that in discharged patients (25% versus 7.78%), highlighting a significant relationship between IHD and mortality in COVID-19 patients ($P=0.016$; Table 5).

Variables affecting mortality in COVID-19 patients in a multivariate study

In the multivariate analysis, after adjusting for and removing all confounding variables, only two variables emerged as predictors of mortality: creatinine level disorder ($P=0.005$) and hospitalization in the ICU ($P<0.001$). The other variables assessed, including age, Tuberculosis, or IHD were not shown as significant predictors of mortality in COVID-19 patients.

Discussion

Recent studies have highlighted the potential side effects of COVID-19, including its propensity to induce various organ failures such as kidney failure. However, there remains limited information regarding the association between AKI incidence and COVID-19, and subsequently, its impact on mortality in affected patients.

In this study, we sought to investigate the incidence of AKI among COVID-19 patients and its correlation with mortality.

Diagnosis index of acute renal failure

The diagnosis index of acute renal failure is characterized by an increase in serum creatinine greater than or equal to 0.3 mg/dL within 48 hours, an increase in creatinine greater than or equal to 1.5 times the patient's baseline creatinine in the last 7 days, or a decrease in urine volume to less than 0.5 mL/kg of body weight in every hour for at least 6 hours (9).

Table 5. Relationship between mortality and underlying diseases in COVID-19 patients

		Patient group		*P* value
		Deceased	Recovered	
Comorbidities (Count, %)	DM	17 (53.12%)	35 (38.89%)	0.212
	Obesity	5 (15.62%	18 (20.0%)	0.617
	CVA	2 (6.25%)	2 (2.22%)	0.572
	CKD	3 (9.37%)	4 (4.44%)	0.377
	Cancer	0 (0%)	1 (1.11%)	1.000
	COPD	3 (9.37%)	4 (4.44%)	0.377
	Asthma	0 (0%)	2 (2.22%)	0.610
	TB	3 (9.37%)	0 (0%)	0.017
	Transplant	0 (0%)	1 (1.11%)	1.000
	HTN	15 (46.87%)	37 (41.11%)	0.678
	HLP	1 (3.12%)	2 (2.22%)	1.000
	IHD	8 (25.0%)	7 (7.78%)	0.016
	CABG	2 (6.25%)	4 (4.44%)	1.000
	MI	1 (3.12%)	0 (0%)	0.262

DM, Diabetes mellitus; CVA, Cerebrovascular accident; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; TB, Tuberculosis; HTN, Hypertension; HLP, Hyperlipidemia; IHD, Ischemic heart disease; CABG, Coronary artery bypass grafting; MI, Myocardial infarction.

In our study, the frequency of AKI was determined to be 48.8%. Several other studies have also explored the relationship between AKI and COVID-19, yielding varying outcomes. For instance, Yang et al examined 52 patients with COVID-19 and reported an AKI incidence of 29% (10). Pei et al, in a study involving 333 COVID-19 patients, reported an AKI incidence of 6.6% and categorized AKI into three stages, with incidences of 18.2%, 31.8%, and 50% for stages 1, 2, and 3, respectively (11).

Similarly, Chan et al investigated 3993 COVID-19 patients and found an AKI incidence of 45.9%. They also staged AKI, reporting incidences of 21%, 10.8%, and 26.7% for stages 1, 2, and 3, respectively (12,13). In another study by Hirsch et al, which included 5449 COVID-19 patients, the incidence of AKI was 36.6%, with incidences of stages 1, 2, and 3 reported as 46.5%, 22.4%, and 31.1%, respectively (13).

In a study conducted by Costa et al, involving 102 COVID-19 patients, the incidence of AKI was reported as 55.9%, with stage 1, 2, and 3 incidences of 17.5%, 15.8%, and 66.7%, respectively (14). Conversely, Ferlicot et al examined 47 COVID-19 patients and found a lower AKI incidence of 2.2%, with stage 1, 2, and 3 incidences of 6.4%, 4.3%, and 87.2%, respectively (15).

A recent study by Moledina et al observed 22 122 suspicious cases, with 2600 patients testing positive for SARS-CoV-2 and 19 522 testing negatives. The incidence of AKI was higher in the SARS-CoV-2 positive group compared to the negative group (30.6% versus 18.2%). This suggests that COVID-19 significantly increases the risk of developing AKI (16).

The results of these studies are consistent with our findings. In our study, the frequency of AKI among COVID-19 patients was 48.8%, which aligns with some of the reported incidences in the literature. It is apparent that various factors such as sample size, timing of patient referral to the hospital, disease severity, age, and underlying diseases can influence the frequency or incidence of AKI in these patients, potentially accounting for the observed differences among the aforementioned studies.

The relationship between various risk factors and the incidence of AKI in COVID-19 patients was investigated in our study. Our findings revealed a significant association between AKI and age. The mean age of patients with AKI was significantly higher compared to the control group (65.32 years versus 55.53 years). This suggests that increasing age in patients with COVID-19 elevates the risk of developing acute renal failure. Therefore, assessing renal function in older COVID-19 patients is crucial for the early detection and prevention of AKI during the course of the disease.

Another crucial finding in our study pertained to the relationship between AKI and mortality in COVID-19 patients. Notably, a significant association was observed between AKI and mortality in this patient cohort. Our study revealed that the prevalence of mortality among patients in the AKI group (35.6%) was significantly higher compared to the control group (17.5%). These results strongly suggest that the incidence of acute renal failure in COVID-19 patients significantly elevates the risk of mortality. This underscores the importance of AKI prevention and its potential role in mitigating mortality rates among individuals with COVID-19.

AKI has been recognized as a predictor of poor prognosis across various medical contexts. Studies have highlighted its association with increased mortality rates among patients with coronary heart disease. For instance, Chan et al conducted a study revealing a stark contrast in mortality rates between coronary heart disease patients with and without AKI. Specifically, the mortality rate among coronary heart disease patients with AKI was reported at 50%, whereas those without AKI experienced a substantially lower mortality rate of 8%. Additionally, the study unveiled significant differences in the need for ventilation and ICU hospitalization between the two groups. Coronary patients with AKI demonstrated a higher requirement for ventilation (44%) and ICU hospitalization (41%) compared to those without AKI, where the corresponding figures were notably lower at 6% and 11%, respectively (12).

In the study conducted by Hirsch et al, the mortality rate among coronary heart disease patients with AKI was reported at 34.8%, whereas those without AKI had a notably lower mortality rate of 5.6%. Furthermore, there were significant disparities in the need for ventilation and ICU hospitalization between the two groups. Coronary patients with AKI exhibited a higher requirement for ventilation (53.2%) and ICU hospitalization (53%) compared to those without AKI, where the corresponding figures were substantially lower at 3.5% and 9.7%, respectively (13).

Similarly, Fisher et al reported comparable findings, with a mortality rate of 33.7% among coronary heart disease patients with AKI, while those without AKI had a mortality rate of 8.6%. Interestingly, there was no significant difference in ventilation requirements between coronary patients with and without AKI (2.9% and 3.8%, respectively). However, there was a notable discrepancy in the need for ICU hospitalization, with coronary patients with AKI having a significantly higher requirement (20%) compared to those without AKI, where the need was substantially lower at 3.9% (17).

In a study by Pei et al, the mortality rate among coronary patients with AKI was strikingly high at 86.4%, whereas those without AKI had a markedly lower mortality rate of 8.7% (11).

Similarly, in a study by Costa et al, coronary patients with AKI exhibited a mortality rate of 33.3%, while those without AKI had a mortality rate of 8.9%. Additionally, there were significant differences in the need for ventilation between the two groups, with coronary heart disease patients with AKI requiring ventilation at a much higher rate (71.9%) compared to those without AKI (17.8%) (14).

These findings to some extent align with the results of our research. In our study, the mortality rate among patients in the AKI group was 35.6%, while in the group without AKI, it was 17.5%. However, it's noteworthy that no significant difference was observed in the length of hospital stay between the two groups of patients.

In our study, we found a significant relationship between serum creatinine levels and the duration of ICU admission with the mortality of COVID-19 patients. Specifically, our findings indicated that an increase in creatinine above the baseline was associated with a 26.2% increase in the risk of death, while hospitalization in the ICU was associated with a 45.2% increase in mortality among these patients.

Similar results have been reported in several other studies. For instance, Cheng et al conducted a study involving 701 COVID-19 patients in Wuhan, China, where they observed elevated serum creatinine levels in 14.4% of patients. This elevation in creatinine levels was found to increase the risk of death by 2.1 times in affected patients. Furthermore, patients with elevated creatinine levels were predominantly male, older, and experienced more severe manifestations of the disease. The researchers concluded that the prevalence of AKI in COVID-19 patients is high and is closely related to the mortality rate in these individuals. They emphasized that implementing effective interventions to mitigate kidney complications could significantly reduce the mortality of COVID-19 patients (18).

These findings underscore the importance of monitoring serum creatinine levels and providing prompt ICU care for COVID-19 patients to improve clinical outcomes and reduce mortality rates.

Moreover, in the study conducted by Pineiro et al on 237 COVID-19 patients in the ICU of a hospital in Barcelona, Spain, it was observed that 52 (21.4%) of the patients developed AKI. This complication led to a decrease in SOFA score, increased liver function test results, and elevated inflammatory factors. Interestingly, the administration of corticosteroids in 69.2% of patients reduced the need for dialysis. The study highlighted a significant association between AKI and mortality, as well as the length of hospitalization. The authors concluded that the prevalence of AKI in COVID-19 patients admitted to the ICU is high and strongly correlates with mortality and length of hospital stay (19).

In our study, we also found noteworthy associations between AKI and comorbidities such as chronic renal failure and hypertension. Specifically, the incidence of chronic renal failure and hypertension among AKI patients was higher (11.5% and 54.1%, respectively) compared to the control group patients (0% and 32.8%, respectively). These findings further emphasize the importance of monitoring and managing comorbidities in COVID-19 patients, particularly those at risk of developing AKI, to optimize clinical outcomes and reduce mortality rates.

Recent studies have provided insights into the incidence of chronic renal failure among Crohn's disease patients with AKI, ranging from 0% to 37.5% (20). For instance, Aggarwal et al reported a notably high incidence of chronic renal failure at 37.5% among Crohn's disease patients with AKI (21). Additionally, Wang et al reported a relatively lower incidence of chronic renal failure at 4.3% among coronary heart disease patients with AKI (22).

These findings underscore the vulnerability of coronary heart disease patients with acute renal impairment to develop chronic renal failure, along with hypertension. Such insights are crucial for comprehensive management strategies aimed at mitigating the risk of long-term renal complications among patients with AKI, especially those with underlying conditions such as Crohn's disease or coronary heart disease.

Conclusion

Acute renal failure emerges as a prevalent complication among individuals afflicted with SARS-CoV-2 infection, particularly among those in ICUs and older patients, and is unequivocally linked to heightened mortality rates. Therefore, vigilant monitoring of kidney function in COVID-19 patients, particularly those in ICU settings, holds paramount importance. Such proactive monitoring can aid in averting acute renal failure or facilitating its early detection, thereby enabling prompt and appropriate treatment interventions. Ultimately, these measures have the potential to curtail mortality rates among COVID-19 patients, underscoring the critical role of renal function assessment in the comprehensive management of this infectious disease.

Limitations of this study

While our study offers valuable insights into the relationship between acute renal failure and mortality in COVID-19 patients, several limitations warrant consideration. Firstly, the retrospective nature of the study design may introduce inherent biases and limitations in data collection and analysis. Additionally, the study was conducted at 2 centers, which may limit the generalizability of our findings to broader patient populations. Moreover, the sample size of the study may have influenced the statistical power and precision of our results. Future studies with larger, multicenter cohorts and prospective designs are warranted to validate and expand upon our findings.

Authors' contribution

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Writing–review & editing: Aidin Shahilooy, Sahar Tavakoli Shiraji.

Conflicts of interest

The authors declare that they have no conflicts of interest related to this research study. No financial or non-financial interests, direct or indirect, influenced the design, conduct, interpretation, or reporting of this study. Additionally, the authors have not received any funding, grants, or support that could be perceived as influencing the outcomes or conclusions presented in this paper.

Ethical issues

The research adhered to the principles outlined in the Declaration of Helsinki. Approval for this study was obtained from the Ethics Committee of Tehran University of Medical Sciences (Ethical code #IR.SBMU.MSP.REC.1400.020). It is noteworthy that this study was derived from the internal medicine residency thesis of Sholeh Tavakoli at Tehran University of Medical Sciences (Thesis #25593). Moreover, ethical issues (including, double publication, data fabrication, plagiarism) have been completely observed by the author.

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