Original Article

Anemia as a Predictor of Poor Outcome in Hospitalized Patients of COVID-19

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ABSTRACT

Objective: To find an association between anemia & outcome of COVID-19 in hospitalized patients.

Methodology: This retrospective cross-sectional study was conducted at The University of Lahore Teaching Hospital, Lahore. Two hundred and ten patients with age ≥18 years and who tested positive for COVID-19 on polymerase chain reaction (PCR) were included. These patients were admitted to the COVID-19 ward and intensive care unit (ICU) of The University of Lahore Teaching Hospital from January to December 2021. Complete blood count reports at the time of admission were evaluated and hemoglobin (Hb) & mean corpuscular volume (MCV) levels were noted. COVID-19 outcomes of these patients in terms of discharge from the hospital, ICU admission, and death were recorded.

Results: In this study, the mean age of the patients was 61.60±13.39 years. The majority of the patients [109(51.9%)] were greater than 60 years of age. There were 94(44.8%) anemic patients. Out of 210, 43(20.1%) patients died and 167(79.5%) were discharged. Out of 43 mortalities, 30(69.8%) patients were anemic. So, there was a significant association noted between anemia & outcome in hospitalized COVID-19 patients in terms of mortality (p=0.00).

Conclusion: The majority of COVID-19 affected patients were anemic at the time of hospitalization and it was associated with poor COVID-19 outcomes in terms of mortality

Keywords: *Anemia. COVID-19. Mortality.*

INTRODUCTION

COVID-19 caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in the city of Wuhan, China, and spread all over the world. It was declared a pandemic by World Health Organization. The COVID-19 disease presents with a variety of symptoms ranging from mild flu and anosmia to severe pneumonia leading to thromboembolism, respiratory failure, and death. It has been observed that male gender, obesity, and elderly patients have increased morbidity and mortality.[1]

Literature showed that anemic patients had a greater risk of disease and mortality. Various recent studies have observed a relationship between COVID-19 mortality and anemia, with varied outcomes.[2,3] According to the World Health Organization (WHO), anemia is defined as a Hb concentration of less than 13 g/dL in males and 12 g/dL in females. The prevalence of anemia was 22.8% globally in 2019, a decrease from 27.0% in 1990. However, anemia is still a major health issue worldwide, accounting for 60,534 deaths and affecting 3.4 percent of women aged 15-49 years globally.[4] Infection caused by novel coronavirus causes increased release of interleukins and inflammatory biomarkers such as ferritin, C-reactive protein, and lactate dehydrogenase along with a deranged coagulation profile. This inflammation can decrease intestinal absorption of iron in COVID-19 patients leading to reduced iron availability for erythropoiesis and hemoglobin production causing anemia which further decreases oxygen delivery to peripheral tissues in COVID-19 patients who already have an increased oxygen demand due to interstitial pneumonia.[5]

It was observed in a study of 67 COVID-19 patients in Singapore that serious patients who were admitted to the ICU had lower hemoglobin levels compared to relatively less serious patients who were admitted to wards.[6] Another research on COVID-19 elderly patients revealed that the majority of these patients had hemoglobin levels below the normal limit, but the study did not find a significant association between anemia and mortality.[7]

COVID-19 is currently a global public health problem. Some studies showed an association of COVID-19 morbidity & mortality in admitted patients and low hemoglobin levels at the time of admission but few studies in Pakistan correlate anemia and mortality in COVID-19 hospitalized patients. Therefore, the rationale of the current study was to find a relationship between anemia & COVID-19 in hospitalized patients in Lahore, Pakistan.

METHODOLOGY

This retrospective cross-sectional study was conducted at The University of Lahore Teaching Hospital, Lahore. Institutional review board approval was taken (Letter No: ERC/106/22/4, 13-04-2022). Two hundred and ten patients with age ≥18 years and who tested positive for COVID-19 on PCR were included. These patients were admitted to the COVID-19 ward and

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ICU of The University of Lahore Teaching Hospital from January to December 2021. Patients diagnosed with COVID-19 infection having a breathing rate of 30/min or more at rest and room air oxygen saturation (SpO2) of ≤93% were admitted. A questionnaire was used to record patients' demographic data, complete blood count reports, and hospital stay in all COVID-19 related units. Data with incomplete information was excluded. Complete blood count reports at the time of admission were evaluated and Hb & MCV levels were noted. Male patients with hemoglobin levels below 13 g/dL and females with hemoglobin less than 12 g/dL were considered anemic. The outcomes of COVID-19 in terms of discharge from the hospital, ICU admission, and death were recorded.

STATISTICAL ANALYSIS

Data was analyzed in Statistical Package for the Social Sciences (SPSS) version 24. Age, Hb level, and mean corpuscular volume (MCV) level were presented as mean and standard deviation (SD). Gender, admission in the ward, discharge, and ICU admission were presented as frequency and percentage. Chi-square test was used to find association and a p-value of ≤0.05 was taken as significant.

RESULTS

Out of 210 patients, 130(61.9%) were males and 80(38.1%) were females. The mean age was 61.60±13.39 years. There were only 31(14.8%) patients between the ages of 20 to 40 years. The majority of the patients 109(51.9%) were older than 60 years of age. There were 94(44.8%) anemic patients. Out of 210, 43(20.1%) patients died and 167(79.5%) were discharged (Table 1).

The mean oxygen saturation level at admission was 85.10±14.62%. There were 51(24.28%) patients hospitalized at room air and 159(75.72%) required oxygen. The mean Hb level was 13±1.91 g/dL and MCV was 81.2±7.41 fL. Data showed that only MCV had a significant relationship with anemia ($p < 0.05$)

In COVID-19 patients, more males were anemic as compared to females. There was a significant association between anemia & gender observed (p=0.026). Above 60 years of age, patients were mostly anemic but there was no significant association observed between age & anemia (p=0.16).

Out of 43 mortalities, 30(69.8%) patients were anemic. So, there was a significant association between anemia & mortality (p=0.00). The frequency of ICU admission (anemic: 29(48.3%) versus nonanemic: 31(51.7%)), had an insignificant association with anemia (p=0.510) (Table 2).

DISCUSSION

COVID-19 is a rapidly spreadable disease with high morbidity and mortality.[8] Various factors are related to poor outcomes in COVID-19 patients.[9] This study focused on the relationship between anemia and the outcome of COVID-19. Anemia frequently increases the severity of respiratory diseases and has been linked to poor outcomes.[1,5] It's an independent risk factor for COVID-19, thus healthcare providers should pay more attention to the hemoglobin levels of COVID-19 patients on admission.[6]

Our results showed that lower hemoglobin levels are associated with an increased risk of death in COVID-19 patients, regardless of age & gender. The majority of the patients [30(69.8%)] who died due to COVID-19 were anemic. There was a significant association between anemia & mortality (p=0.00). Anemia had an insignificant association with ICU admission (p=0.510). So, anemia may serve as an early indicator of poor outcomes in COVID-19 diseased patients. Similar results were found in other studies. Bellmann-Weiller et al. reported in their study conducted in Austria that 24.7% of patients were anemic on admission. Anemia was associated with high mortality

Table 1: Demographic Information of the Admitted Patients with COVID-19

Study Variables		Frequency & Percentage
Gender	**Male**	130(61.9%)
	Female	80(38.1%)
Age (Years)	**Mean±SD**	61.60±13.39
	20-40	31(14.8%)
	41-60	70(33.3%)
	>60	109(51.9%)
Anemia	**Yes**	94(44.8%)
	No	116(55.2%)
Outcome	**Died**	43(20.5%)
	Discharged	167(79.5%)

Table 2: Comparison of Anemia with Gender, Age Group, and Outcome

Study Variables		Anemia		p-value
		Yes Frequency & Percentage	No Frequency & Percentage	
Gender	Male	66(50.8%)	64(49.2%)	0.026*
	Female	28(35%)	52(65%)	
Age Groups (Years)	20-40	16(51.6%)	15(48.4%)	0.16
	41-60	36(51.4%)	34(48.6%)	
	>60	42(38.5%)	67(61.5%)	
Outcome	Died	30(69.8%)	13(30.2%)	0.001*
	Discharged	64(38.3%)	103(61.7%)	
COVID-19 Inpatients Areas	ICU	29(48.3%)	31(51.7%)	0.510
	Ward	65(43.3%)	85(56.7%)	

**Significant p-value*

(p=0.001) but it was not associated with increased ICU admissions.[5] Faghih Dinevari et al. showed a prevalence of anemia in 48% of hospitalized COVID-19 patients. They also reported that ICU admissions were significantly more in anemic patients (p <0.001).[10] Another study conducted in Italy found no relationship between anemia & poor COVID-19 outcomes.11 Similarly, Yang et al. also observed no link between anemia and morbidity & mortality associated with COVID-19 patients.[12]

In this study, we found a significant association of gender with anemia. Our results showed that the majority of COVID-19 male patients were anemic and the association of anemia with age is not significant. In contrast to these results, another study reported that the prevalence of anemia in COVID-19 positive patients is high in females and the association of age & gender with anemia is significant.[12]

Furthermore, our findings revealed that anemic patients were much more vulnerable to critical care ICU admissions. A meta-analysis conducted by Henry et al. reported that anemia is a significant factor in ICU admissions and mortality.[13]

Another study found anemia in 59.8% of patients which led to ICU admission and mortality.[14] Tremblay et al. found anemia in 30.9% of patients in their study and they also concluded that anemia is an independent predictor of morbidity and mortality in patients of COVID-19.[15]

Anemia is a major comorbidity in almost 25% of COVID-19 patients and is also associated with a significantly increased rate of mortality. From a pathophysiological point of view, Hb concentration exemplifies a vital component of oxygen-carrying capacity in the blood. Thus, anemia can further decrease oxygen delivery to peripheral tissue in COVID-19 patients who already have an increased oxygen demand due to interstitial pneumonia.[16] A study conducted by Jha et al. in India, observed a significant correlation between anemia and the severity of COVID-19. The study stated that anemia can be considered a single independent prognostic factor in COVID-19 patients.[17] Another study by Chen et al. comprehensively described a close relationship between anemia and the severity of COVID-19. They showed that patients of COVID-19 with concurrent anemia had an 8.2 times greater possibility of developing severe pneumonia.[18] All these studies potentiate the findings of our study.

CONCLUSION

The majority of COVID-19 affected patients were anemic at the time of hospitalization, and it was associated with poor COVID-19 outcomes in terms of increased mortality.

LIMITATIONS & RECOMMENDATIONS

There were several limitations to this study. Anemia was noticed at the time of admission but previous Hb levels were not noted. Other markers of inflammation like D-dimer and lactate dehydrogenase were not included in this study. This was a single-centered study, so it may not be an accurate reflection of the Pakistani population. Multi-centered study with hemoglobin levels known before COVID-19 at the time of presentation and during the hospital stay is recommended. Other inflammatory markers should be measured to accurately judge how anemia affects morbidity and mortality associated with COVID-19.

Our findings may have an important impact on daily clinical practice as the early identification of patients with anemia in COVID-19 assists in identifying at-risk patients who would require prioritization in treatment, close monitoring, and rectification of anemia.

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