Prevalence of anemia and mortality among anemic patients with COVID-19 in a tertiary care setting in Nepal

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Abstract

Introduction: The COVID-19 pandemic first detected in December 2019 has claimed so many lives globally as well as in Nepal. Inflammatory changes in SARS-CoV-2 infection can lead to anemia. This study aims to find the prevalence of anemia and mortality among anemic patients in COVID patients admitted to a tertiary care centre in Nepal.

Method: A descriptive cross-sectional study with data collected retrospectively between May 2021 to February 2022 on patients with proven COVID-19 admitted to Patan Hospital.

Result: Among 890, anemia was prevalent in 296(33.25%) (CI 95%, 30.17-36.35) patients which was more among the female population. The mean hemoglobin was 10.68±1.62 g/dl in anemic patients. Mild anemia was present in 215(72.6%) patients followed by moderate in 64(21.6%) patients and severe in 17(5.8%) patients. The mortality in anemic patients was 43(14.5%).

Conclusion: One third of COVID-19 patients admitted to Patan Hospital had anemia which was found to be similar to studies done in similar setting. One in four COVID-19 patients with anemia had died was found to be lower than other studies done in similar settings.

Keyword: anemia, COVID-19, hemoglobin, prevalence

Introduction

The COVID-19 pandemic first detected in December 2019 has so far claimed 6,539,077 lives out of 619,722,666 known infections globally. In Nepal 999,506 infections have been reported with 12,016 deaths as of October 2022.[1] Cardiovascular disease, diabetes, chronic respiratory disease, and hypertension are among the known risk factors that can exacerbate the impact of SARS-CoV-2 infection on erythropoiesis and hemoglobin levels, further increasing the susceptibility of individuals with these comorbidities to complications associated with COVID-19.[2] Respiration is crucial for oxygenation and SARS-CoV-2 infection can interfere with erythropoiesis by inducing the production of interferons (IFNs) that promote the iron uptake by macrophages limiting the availability of iron that leads to decreased hemoglobin levels, iron overload in tissue, and hypoxemia.[3-5] IFNs, along with interleukin 1 (IL-1) and tumor necrosis factor α (TNF-α) also inhibits production of erythropoietin in the kidney hindering the differentiation and proliferation of erythroid-progenitor-cells interfering the erythropoiesis.[6] This disruption in oxygen transport and homeostasis can have profound implications in clinical outcomes of COVID-19 patients, potentially exacerbating respiratory distress and complicating the management of the disease.[4] Prevalence of anemia is reported to be 35.3% in patient with COVID-19.[7] Studies done in China have shown that anemia in COVID-19 patients increases the risk of severe pneumonia.[8] COVID-19 is also associated with lower hemoglobin levels and higher mortality rates.[9-11] This study aims to determine the prevalence of anemia and mortality among COVID patients at a tertiary care centre in Nepal.

Method

A descriptive cross-sectional study was conducted in Patan Hospital. We performed a retrospective review of electronic records of COVID-19 patients admitted to fever clinic and COVID Intensive Care Unit (ICU) of Patan Hospital from May 2021 to February 2022. We received ethical approval from Institutional Review Committee of Patan Hospital with reference number: std2212091695 after getting approval from head of department of Internal medicine for the conduction of research. We used structured proforma to extract data which includes age, gender, hemoglobin level and discharge outcome of cases of COVID-19. Research participant name was not be disclosed and a unique code was assigned for their identification. Confirmed cases of the SARS-COV 2 infection whose hemoglobin measured within 24 hours of admission were included in the study and children of age <14 years were excluded from the study.

The calculated sample size was 384. However, 890 samples were taken from the study. A confirmed case of SARS-CoV-2 infection is defined by the World Health Organization (WHO) based on two distinct criteria. The first criterion encompasses individuals who have tested positive for the virus through the Nucleic Acid Amplification Test (NAAT), regardless of whether they present clinical symptoms or meet specific epidemiological criteria. The second criterion includes individuals who, while potentially meeting clinical or epidemiological criteria suggestive of COVID-19, have further confirmed their infection through the professional use of a self-test SARS-CoV-2 Antigen-Rapid Diagnostic Test (Antigen-RDT).[12] According to WHO, anemia was defined as hemoglobin <13 g/dl in male and <12 g/dl in female and severity of anemia was categorized into mild, moderate and severe, mild anemia 10-12.9 g/dL in male and 10-11.9 g/dL in female, moderate and severe anemia 8- 9.9 g/dL and <8 g/dl respectively for both genders.[13] The data which was collected and analyzed, were securely stored on a password-protected computer, thereby safeguarding the integrity and confidentiality of information. Data were entered in Microsoft excel 2007 and analyzed in descriptive statistics using IBM SPSS Statistics version 16.0. The point estimate was calculated at 95% CI.

Result

A total of 890 patients were included in our study. Males were 439(49.3%) and females were 451(50.7%). The mean age of patients was 50.83 years ± 2.32 years. There were maximum number COVID-19 patients from age group 21-30 years and minimum patients from age 91 or above (Table 1). In our study the prevalence of anemia in COVID-19 patients was 296(33.26%) (30.17-36.35, 95%

Confidence Interval). Anemia was more prevalent in female compared to male (Table 2). In our study, anemia was more prevalent in female than male and maximum anemia was found in age group 71-80 years. Majority of the anemic patients had mild anemia followed by moderate and severe anemia. Seventy-three (8.20%) out of 890 COVID-19 patients had expired. The mortality in COVID-19 in anemic was 43(14.5%) and the mortality in non-anemic patients was 30(5.1%).

Table 1. Characteristics of COVID-19 patients (N=890)

Variables	ƒ (%)	Variables	ƒ (%)
Gender		**Age group (in years)**	
Male	439(49.33%)	41-50	121(13.60%)
Female	451(50.67%)	51-60	125(14.04%)
Age group (in y)		61-70	109(12.25%)
<21	57(6.40%)	71-80	130(14.61%)
21-30	156(17.53%)	81-90	61(6.85%)
31-40	119(13.37%)	91 or more	12(1.35%)
		Mean age, SD	**50.83±2.32 y**

Table 2. Distribution of anemia in COVID-19 patients according to demographic variables (N=296)

Variables	ƒ (%)	Variables	ƒ (%)
Gender		**Age group**	
Male	128(43.24%)	61-70	43(14.53%)
Female	168(56.76%)	71-80	57(19.26%)
Age group		81-90	30(10.14%)
< 21	23(7.77%)	91 or more	5(1.69%)
21-30	34(11.49%)	**Severity**	
31-40	28(9.46%)	Mild anemia	215(72.64%)
41-50	38(12.84%)	Moderate anemia	64(21.62%)
51-60	38(12.84%)	Severe anemia	17(5.74%)

Discussion

Our study found that 33.26% patients with COVID-19 had anemia. Various mechanisms between virus and human body interplay when a patient gets infected to COVID-19. One of the mechanisms is COVID binding the S1 Spike protein and Band-3 protein, causing a decrease in protective enzymes against oxidative stress.[14] Similarly the ORF8 protein and surface glycoprotein of virus bind to porphyrin, attacking the heme on the 1-beta chain of hemoglobin, and creating dysfunctional hemoglobin.[4] Another mechanism is the formation of immunoglobulin against the RBC due to

similarities in viral and erythrocyte proteins. Complement deposition on RBCs and a hyperinflammatory immunological response follows the COVID infection.[15] Also the virus mimics the action of hepcidin, causing internalization of ferroportin and concurrently causing serum iron deficit and hemoglobin insufficiency.[6] All these mechanisms eventually cause lysis of RBC and thus precipitates anemia.

Other retrospective studies found that the prevalence of anemia among COVID-19 patients ranging from 25% to 38%.[7,16-18] Anemia is known to be poor prognostic marker in several other respiratory diseases

and has recognition that extends beyond the confines of the COVID-19 pandemic. It had been identified as an independent risk factor capable of precipitating exacerbated morbidity and unfavorable clinical outcomes in COVID-19 infection.[19–21] Anemia aggravates the severity of respiratory disease which in combination with anemia associated with poor outcomes such as ventilator need, ICU admission and death.[22] It is, therefore, imperative to underscore that the confluence of anemia with COVID-19 portends a precarious trajectory, often characterized by heightened requirements for ventilatory support, augmented rates of intensive care unit admissions, and an elevated mortality risk, collectively manifesting as a complex interplay between anemia and COVID-19 infection with far-reaching implications for clinical management and patient prognosis.

A multicentric study in Bangladesh showed higher prevalence of anemia in male COVID-19 patients than female (71.42% vs 36.36%).[23] However, our study showed that the prevalence of anemia was higher among female COVID-19 patients as opposed to males (56.76 % vs 43.24%). Data from the National Demographic Health Survey 2022 indicates that 34% of women in Nepal suffer from anemia.[24] Poor nutrition and menstrual blood loss are believed to be the main causes of anemia among women in Nepal.[25] This disparity in the prevalence of anemia among female COVID-19 patients might be related to pre-existing anemia in women. Similarly, studies done in Italy and China also reported higher prevalence of anemia in female COVID-19 patients compared to male.[8,26]

In our study, 72.64% of COVID-19 patients had mild anemia, while 21.62% had moderate anemia and 5.74% had severe anemia. A study done in Italy reported mild anemia in 72%, and moderate/severe in 16.99% of COVID-19 patients.[26] Several studies revealed a higher prevalence of mild anemia in comparison to moderate and severe anemia.[7,8,16]

In our study, the mortality in COVID-19 in anemic was 43(14.5%) and the mortality in non-anemic patients was 30(5.1%). Similar results were found in a study done in Italy which showed that the one-month mortality of anemic patients with COVID-19 was 39% while that of non-anemic patients was 36%. In a study done in Israel in 2020 showed that COVID-19 patients with low hemoglobin levels had a higher mortality rate compared to those with normal hemoglobin levels.[27] A multicentric study done in Italy showed lower hemoglobin associated with increased mortality risk.[28] A study done in South Korea found anemia to be associated with increased mortality due to infection.[29]

In COVID-19 infection, there is increased oxygen demand due to the high metabolism. COVID-19 virus infected cell expresses angiotensin converting enzyme-2 (ACE-2) throughout the body (that leads to septic shock and multiple organ dysfunction which may reduce the availability of ACE-2 receptors preventing the vasodilation.[30-32] In addition to that anemia further reduce the oxygen supply to the peripheral tissues that causes significant tissue ischemia. Anemia also activates the sympathetic nerve fibres that increases the heart rate, blood pressure and pulmonary capillary leakage causing acute respiratory distress.[10] As COVID-19 virus has hepcidin-mimetic action that cause the depletion of extracellular iron, which withhold the iron from invading pathogen by promoting iron sequestration in macrophages.[5,29] However, that causes the detrimental effect to the cellular defence making person more susceptible to infection thus increasing the mortality.[29] Iron has an important role in immunity which includes the bactericidal activity of macrophages, formation of peroxide- and nitrous oxide-generating cellular enzymes, as well as T-cell numbers and function.[33] Because of these reasons anemic patients likely to have high morbidity as well as mortality.

There were some limitations to our study. Firstly, the results of this study was based on the hospital records of patients collected

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retrospectively which might have led to incomplete data, Secondly, there can be confounding factors, which was not considered in our study, such as presence of pre-existing diseases, medications, and socioeconomic factors might have an effect in mortality outcome. Selection bias is a prominent concern, as our study includes hospitalized patients, potentially excluding asymptomatic or mildly affected individuals. This might have impacted on the reliability and quality of our findings. Our study was conducted in a single centre which might not be representative of the whole population. Our study used convenience sampling which might have resulted in sampling bias. Finally, the absence of baseline hemoglobin data presented a significant limitation in our analysis.

Conclusion

This study showed that one third of COVID-19 patients admitted to Patan Hospital had anemia, and majority of them are in mild category. The mortality in COVID-19 patients with anemia was more than that the non-anemic group.

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Conflict of Interest
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