

2022

Hemoglobin As A Predictor For COVID-19 Disease Severity

Nicholas Sarcia

University of New England College of Osteopathic Medicine, nsarcia@une.edu

Dan Thai

University of New England College of Osteopathic Medicine, dthai@une.edu

Andrea M. Bodine MD

Berkshire Medical Center, bodineandrea@gmail.com

Follow this and additional works at: <https://scholar.rochesterregional.org/advances>



Part of the [Emergency Medicine Commons](#), [Infectious Disease Commons](#), and the [Virus Diseases Commons](#)



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](#)

Recommended Citation

Sarcia N, Thai D, Bodine AM. Hemoglobin As A Predictor For COVID-19 Disease Severity. *Advances in Clinical Medical Research and Healthcare Delivery*. 2022; 2(2). doi: 10.53785/2769-2779.1096.

ISSN: 2769-2779

This Article is brought to you for free and open access by RocScholar. It has been accepted for inclusion in *Advances in Clinical Medical Research and Healthcare Delivery* by an authorized editor of RocScholar. For more information, please contact Advances@rochesterregional.org.

Hemoglobin As A Predictor For COVID-19 Disease Severity

Abstract

Background: The dilemma of who is at highest risk for COVID-19 severe disease and death persists. Hemoglobin levels may be an indicator of COVID-19 disease severity. There is inconsistent data on Emergency Department (ED) hemoglobin levels and severity of disease. Our objective was to examine if COVID-19 patients presenting with abnormal hemoglobin levels have an increased risk of severe disease and in-hospital mortality.

Methods: We conducted a retrospective cohort study at Berkshire Medical Center in Pittsfield, MA to investigate the relationship of COVID-19 disease severity with hemoglobin level. Inclusion criteria consisted of ED patients over 18 years with a COVID-19 diagnosis from July 1, 2021, to November 1, 2021. Exclusion criteria consisted of duplicate visits and patients without a hemoglobin value recorded. Patients with anemia were stratified by severity. Disposition categories from most to least severe were: ICU/PCU, medical floor, or discharge from ED. In-hospital mortality was recorded. Backward linear regression followed by z-tests were used for each abnormal hemoglobin category versus normal hemoglobin category.

Results: The four-month period included 341 ED visits coded for COVID-19. After excluding 113 visits, 228 were eligible for analysis. There were 132 discharged from the ED, 64 admitted to the medical floor, 32 to ICU/PCU, and 19 deaths. Backwards linear regression showed hemoglobin category was a significant predictor of hospital disposition ($p < 0.0001$) and mortality ($p = 0.07$). Z-test showed a significant difference in disposition for normal hemoglobin versus mild anemia ($z = 2.1927$, $p = 0.03$) and normal hemoglobin versus moderate/severe anemia ($z = 3.6225$, $p = 0.0003$). Z-test showed a significant difference in death for normal hemoglobin versus moderate/severe anemia ($z = 3.2949$, $p = 0.001$). Normal hemoglobin versus elevated hemoglobin had no significant difference for disposition ($z = 0.356$, $p = 0.72$) or death ($z = 1.786$, $p = 0.07$).

Discussion: Abnormal hemoglobin is associated with severity of disease and death COVID-19 patients. Increasingly severe anemia is more associated with severity of disease and death. Elevated hemoglobin is not associated with severity of disease or death.

Keywords

COVID-19, Hemoglobin, Anemia, Delta Variant

Creative Commons License



This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/)

Conflict of Interest Statement

We do not have conflicts of interest or financial disclosures.

Cover Page Footnote

Acknowledgements Special thanks to Paul Johansen MA, Biostatistician.

ARTICLE

Hemoglobin as a Predictor for COVID-19 Disease Severity

Nicholas Sarcia ^{a,*}, Dan Thai ^a, Andrea M. Bodine ^b

^a University of New England College of Osteopathic Medicine, UK

^b Berkshire Medical Center, UK

Abstract

Background: The dilemma of who is at highest risk for COVID-19 severe disease and death persists. Hemoglobin levels may be an indicator of COVID-19 disease severity. There is inconsistent data on Emergency Department (ED) hemoglobin levels and severity of disease. Our objective was to examine if COVID-19 patients presenting with abnormal hemoglobin levels have an increased risk of severe disease and in-hospital mortality.

Methods: We conducted a retrospective cohort study at Berkshire Medical Center in Pittsfield, MA to investigate the relationship of COVID-19 disease severity with hemoglobin level. Inclusion criteria consisted of ED patients over 18 years with a COVID-19 diagnosis from July 1, 2021, to November 1, 2021. Exclusion criteria consisted of duplicate visits and patients without a hemoglobin value recorded. Patients with anemia were stratified by severity. Disposition categories from most to least severe were: ICU/PCU, medical floor, or discharge from ED. In-hospital mortality was recorded. Backward linear regression followed by z-tests were used for each abnormal hemoglobin category versus normal hemoglobin category.

Results: The four-month period included 341 ED visits coded for COVID-19. After excluding 113 visits, 228 were eligible for analysis. There were 132 discharged from the ED, 64 admitted to the medical floor, 32 to ICU/PCU, and 19 deaths. Backwards linear regression showed hemoglobin category was a significant predictor of hospital disposition ($p < 0.0001$) and mortality ($p = 0.07$). Z-test showed a significant difference in disposition for normal hemoglobin versus mild anemia ($z = 2.1927$, $p = 0.03$) and normal hemoglobin versus moderate/severe anemia ($z = 3.6225$, $p = 0.0003$). Z-test showed a significant difference in death for normal hemoglobin versus moderate/severe anemia ($z = 3.2949$, $p = 0.001$). Normal hemoglobin versus elevated hemoglobin had no significant difference for disposition ($z = 0.356$, $p = 0.72$) or death ($z = 1.786$, $p = 0.07$).

Discussion: Abnormal hemoglobin is associated with severity of disease and death COVID-19 patients. Increasingly severe anemia is more associated with severity of disease and death. Elevated hemoglobin is not associated with severity of disease or death.

Keywords: COVID-19, Hemoglobin, Anemia, Delta variant

1. Introduction

The dilemma of who is at highest risk for COVID-19 severe disease and death persists. In July 2021, the Delta variant became the dominant strain in the United States causing more severe disease and vaccine breakthrough. Through October 2021, there had been over 233 million cases and 4.8 million deaths worldwide.¹ Multiple comorbid conditions and risk factors have been linked

to more severe disease such as increased age, hypertension, cardiovascular disease, diabetes, obesity, and chronic lung disease.^{2,3} Worse outcomes have been associated with abnormal laboratory values of liver enzymes, kidney function, and inflammatory markers.⁴ COVID-19 association with comorbidities and laboratory values may present in a similar fashion to other acute and chronic respiratory conditions. Patients with severe acute respiratory diseases, such as community-acquired

Accepted 9 May 2022.
Available online 31 May 2022

* Corresponding author.

E-mail addresses: nsarcia@une.edu (N. Sarcia), dthai@une.edu (D. Thai), bodineandrea@gmail.com (A.M. Bodine).

Acknowledgements Special thanks to Paul Johansen MA, Biostatistician.

<https://doi.org/10.53785/2769-2779.1096>

2769-2779/© 2022 Rochester Regional Health.



pneumonia have an increased risk of mortality if anemia is present.⁵ Hemoglobin levels may be an indicator or precursor of COVID-19 disease severity.

There is inconsistent data on hemoglobin levels in Emergency Department (ED) visits and severity of disease in COVID-19 patients. Some studies have shown an association of severity of anemia and worse outcomes in the hospital,^{6,7} while others have shown no significant difference.^{8,9} One study observed an increase in mortality with elevated hemoglobin levels.¹⁰ Worse outcomes have been defined as ICU admission rate and mortality, although data has shown that these two parameters do not always accompany each other.^{6,7} Hemoglobin is commonly measured in the ED during hospital visits. If altered hemoglobin on initial blood work is predictive of more severe disease, it could be used as an early risk stratification tool for patients who first arrive at the ED. This could also be used to classify patients who have a known anemia to be at higher risk.

The purpose of this study was to investigate hemoglobin levels on initial blood work and determine whether it could be used as a tool to predict outcomes for COVID-19 patients. Our objective was to examine if COVID-19 patients presenting with abnormal hemoglobin levels have an increased risk of severe disease and in-hospital mortality. We hypothesized that COVID-19 patients who present with an abnormal hemoglobin would have more severe disease and a higher in-hospital mortality rate than COVID-19 patients with normal hemoglobin.

2. Methods

We conducted a retrospective cohort study at Berkshire Medical Center (BMC) in Pittsfield, MA to investigate the relationship of COVID-19 disease severity and in-hospital mortality with hemoglobin (Hgb) levels. IRB exemption was obtained.

Inclusion criteria consisted of patients 18 years and older presenting to the ED with a diagnosis of COVID-19 from July 1, 2021, to November 1, 2021. Records were reviewed for demographics of age, sex, race, and vaccination status which was positive if documented on ED record. Exclusion criteria consisted of duplicate visits and patients who did

not have a recorded hemoglobin value. Duplicate visits greater than or equal to 48 days were considered a new infection and counted as an additional subject. Visits less than 48 days were subjected to selection of the most severe presentation requiring the highest level of care and exclusion of the other visit(s) in the following order: in-hospital death, highest level of care, lowest abnormal hemoglobin value, highest abnormal hemoglobin value, all other things being equal, choose the earliest visit.

Anemia was classified according to the World Health Organization (WHO) definition (Table 1), as hemoglobin (Hb) levels <13.0 g/dL in males and <12.0 g/dL in females. Severity of anemia was defined in males by: mild 11–12.9 g/dL, moderate 8–10.9 g/dL, and severe <8 g/dL. Severity of anemia was defined in females by: mild 11–11.9 g/dL, moderate 8–10.9 g/dL, severe <8 g/dL.¹¹ Elevated hemoglobin in males and females was defined as ≥ 16 g/dL. These categories comprised the abnormal hemoglobin groups. Severity of disease was measured by hospital disposition with the most severe to mild as ICU/PCU (intensive care unit/progressive care unit), medical floor, or ED discharge. In-hospital mortality was defined as patients who died before discharge. ICU admission was made based upon the clinical judgment of the ICU attending physician and ED provider. Patients who required intubation and ventilation or had refractory hypoxia were generally admitted to the ICU. When no beds were available in the ICU, patients were admitted to the PCU, which is an intermediate level of care between the medical floor and ICU at BMC.

Data was obtained from BMC Medical Records Department using ICD-10 codes for COVID-19 and patients who presented initially through the ED. Electronic medical records were reviewed for hemoglobin on initial CBC, in-hospital mortality, and disposition to ICU/PCU, medical floor, or ED discharge. Demographics of age at initial presentation, sex, race, and vaccination status were also recorded independently. Patients with anemia were then stratified by severity. Backward linear regression was used for analysis followed by z-tests to compare each abnormal hemoglobin category to the normal hemoglobin category. All data was de-identified.

Table 1. Hemoglobin categories.

	Severe	Moderate	Mild	Normal	Elevated
Male	<8 g/dL	8–10.9 g/dL	11–12.9 g/dL	13–15.9 g/dL	≥ 16 g/dL
Female	<8 g/dL	8–10.9 g/dL	11–11.9 g/dL	12–15.9 g/dL	≥ 16 g/dL

3. Results

During the four-month period there were 341 ED visits coded for COVID-19 in patients 18 and older. After excluding 70 subjects who did not have a hemoglobin value and 45 repeat visits with two subjects in both exclusion criteria, there were a total of 228 subjects for analysis. One patient had a repeat visit greater than 48 days which was counted as a separate visit. There were a total of 132 discharged from the ED, 64 admitted to the medical floor, and 32 to the ICU/PCU. Of the 228 subjects, 19 died during their hospital stay (Fig. 1).

Ages ranged from 18 to 97 with an average age of 56. Average age in normal Hgb was 53, mild 62, moderate 73, severe 78, and elevated 54. Males were 46% of the subjects. Males for each hemoglobin category consisted of 64% normal Hgb, 39% mild,

58% moderate, 29% severe, and 50% elevated. Of the subjects 53% were vaccinated. Vaccination status for each hemoglobin category consisted of 48% normal Hgb, 71% mild, 75% moderate, 50% severe, and 39% elevated (Table 2).

Hemoglobin levels ranged from 7.9 to 18.6. There were a total of 154 normal Hgb, 36 mild, 17 moderate, 2 severe, and 19 elevated (Table 3). Distribution of each hemoglobin category for disposition () and death () are shown. Due to the small number of subjects in the severe anemia group, the moderate and severe categories were combined for analysis.

Five variables were used in backwards linear regression to predict disposition: Age, Vaccination status, Sex, Race, and Hemoglobin category. Of these five variables, two remained significant at the alpha = 0.10 level: Hemoglobin category (p < 0.0001) and Age (p = 0.002). Z-test compared normal

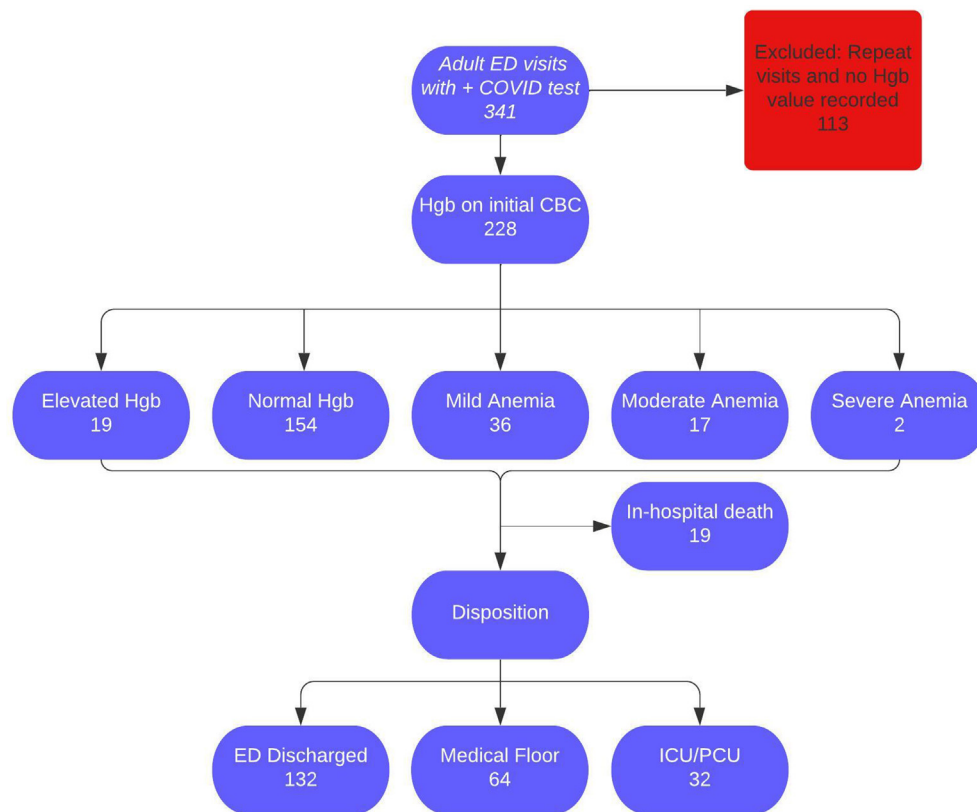


Fig. 1. Study population.

Table 2. Demographics for hemoglobin categories.

	Normal	Mild	Moderate	Severe	Elevated	Total
Age (mean)	53	62	73	78	54	56
Males (%)	64	39	58	29	50	46
Race (white %)	91	92	94	100	89	91
Vaccinated (%)	48	71	75	50	39	53

Table 3. Hgb Category for disposition and death.

	Normal	Mild	Moderate	Severe	Elevated
Discharge	99	16	4	0	13
Floor	42	13	4	2	3
ICU/PCU	13	7	9	0	3
Death	8	3	5	0	3

Number of patients in each disposition and deaths.

hemoglobin versus mild anemia, moderate/severe anemia, and elevated hemoglobin for disposition with a significance level of $p \leq 0.05$. There was significant difference in disposition for normal hemoglobin versus mild anemia ($z = 2.1927$, $p = 0.03$) and normal hemoglobin versus moderate/severe anemia ($z = 3.6225$, $p = 0.0003$). There was no significant difference in disposition for normal hemoglobin versus elevated hemoglobin ($z = 0.356$, $p = 0.72$).

Five variables were used in backwards linear regression to predict death: Age, Vaccination status, Sex, Race, and Hemoglobin category. Of these five variables, three remained significant at the $\alpha = 0.10$ level: Patient Age ($p < 0.0001$), Vaccination status ($p = 0.022$), and Hemoglobin category ($p = 0.07$). Z-test compared normal hemoglobin versus mild anemia. Moderate/severe anemia, and elevated hemoglobin for death with significance level at $p \leq 0.05$. There was a significant difference in death for normal hemoglobin versus moderate/severe anemia ($z = 3.2949$, $p = 0.001$). There was no significant difference in death for normal hemoglobin versus mild anemia (z -score = 0.7259 , $p = 0.47$) or normal hemoglobin versus elevated hemoglobin ($z = 1.786$, $p = 0.07$).

4. Discussion

We found COVID-19 patients who presented to the ED with an abnormal hemoglobin had a significant association with severity of disease measured by disposition, and death by in-hospital mortality. For disposition, there was increasing significance with severity of anemia, particularly at the moderate-severe levels and no significance with elevated hemoglobin. For death, there was significance with moderate/severe anemia and no significance with mild anemia or elevated hemoglobin. We satisfied our hypothesis that COVID-19 patients with abnormal hemoglobin had more severe disease only with the anemic groups and for in-hospital mortality only with moderate/severe anemia. We were unable to satisfy our hypothesis for severity of disease in the elevated hemoglobin group and in-hospital mortality in mild anemia and elevated hemoglobin groups.

Our findings of abnormal hemoglobin predicting more severe disease and death are partially consistent with other studies that have shown a significant association in either severity of disease or death, but not both.^{6,7} Our data is inconsistent with other studies that have shown no association of anemia and severe illness or death,^{8,9} and an association of death with elevated hemoglobin which we found to be non-significant.¹⁰ These inconsistencies may be related to our limitations which include a lack of subject racial diversity thereby decreasing the generalizability of the study, and a small sample size, especially in the severe anemia category which was combined with moderate anemia for analysis. We were unable to determine if patients who were discharged to another facility or home later died from disease. It may be useful to record death out of the hospital within a certain time frame. This study also has several confounding variables such as chronic diseases or other abnormal laboratory values that may have placed certain patients at higher risk. Patients with chronic disease may have had a chronic abnormal hemoglobin or have multiple diseases that would subject them to placement at a higher level of care such as the ICU/PCU or death. These confounding factors can only be controlled for by a more extensive study design and analysis. The disposition of the patient is also dependent on the provider which adds subjectivity to the analysis of severity of disease.

Future studies that have a larger and diverse sample size controlling for confounding variables would be able to give a more precise interpretation on severity of disease and death. Follow-up of patients after discharge may provide a better representation of the actual mortality rate. It also may be useful to analyze data from different time periods to compare with the delta variant, which was the dominant source of infection in this study, versus other strains.

The strengths of our study include addition of the elevated hemoglobin category which fewer studies have assessed, and the study population which was concentrated during the delta variant outbreak. The data from our study provides clinical relevance as it suggests patients with abnormal hemoglobin to be at higher risk for severe disease and death which can be considered in assessing risk for COVID-19 disease in the ED. We can also emphasize the importance of vaccination and additionally the risk of death in the older population as it was a more significant predictor of death than the hemoglobin category in our analysis.

5. Conclusion

Within the limitations of the study, abnormal hemoglobin appears to be associated with severity of disease and death COVID-19 patients. Increasingly severe anemia is more associated with severity of disease and death. Elevated hemoglobin is not associated with severity of disease or death.

Conflict of interest

We do not have conflicts of interest or financial disclosures.

Author contribution

Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing

References

1. Who coronavirus (COVID-19) dashboard. World Health Organization. <https://covid19.who.int/>. Accessed October 31, 2021.
2. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ*. 2020:m1966. <https://doi.org/10.1136/bmj.m1966>.
3. Sanyaolu A, Okorie C, Marinkovic A, et al. Comorbidity and its impact on patients with covid-19. *SN Comprehensive Clinical Medicine*. 2020;2(8):1069–1076. <https://doi.org/10.1007/s42399-020-00363-4>.
4. Henry BM, de Oliveira MH, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (covid-19): a meta-analysis. *Clin Chem Lab Med*. 2020;58(7):1021–1028. <https://doi.org/10.1515/cclm-2020-0369>.
5. Reade MC, Weissfeld L, Angus DC, Kellum JA, Milbrandt EB. The prevalence of anemia and its association with 90-day mortality in hospitalized community-acquired pneumonia. *BMC Pulm Med*. 2010;10(1). <https://doi.org/10.1186/1471-2466-10-15>.
6. Oh SM, Skendelas JP, Macdonald E, et al. On-admission anemia predicts mortality in COVID-19 patients: a Single Center, retrospective cohort study. *Am J Emerg Med*. 2021;48:140–147. <https://doi.org/10.1016/j.ajem.2021.03.083>.
7. Tao Z, Xu J, Chen W, et al. Anemia is associated with severe illness in Covid-19: a retrospective cohort study. *J Med Virol*. 2020;93(3):1478–1488. <https://doi.org/10.1002/jmv.26444>.
8. Bergamaschi G, Borrelli de Andreis F, Aronico N, et al. Correction to: anemia in patients with covid-19: pathogenesis and clinical significance. *Clin Exp Med*. 2021;21(2):247. <https://doi.org/10.1007/s10238-021-00699-8>.
9. Benoit JL, Benoit SW, Oliveira MH, Lippi G, Henry BM. Anemia and Covid-19: a prospective perspective. *J Med Virol*. 2020;93(2):708–711. <https://doi.org/10.1002/jmv.26530>.
10. Kuno T, So M, Takahashi M, Egorova NN. U Shape Association of hemoglobin level with in-hospital mortality for COVID-19 patients. *J Thromb Thrombolysis*. 2021. <https://doi.org/10.1007/s11239-021-02516-1>.
11. WHO. *Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity*. Vitamin and Mineral Nutrition Information System. Geneva: World Health Organization; 2011. <http://www.who.int/vmnis/indicators/haemoglobin.pdf>. Accessed October 12, 2021.