# ORIGINAL ARTICLE

# Hospital Acquired Decline in Hemoglobin in Non-Bleeding Patients Admitted to General Medical Wards of a Public Hospital in Northern India

Fayaz A Wani, Vani Kapoor, Rakesh Bahl, [1] Vagmi Kapoor, Saransh Bahl , Abdul Hamid

### Abstract

**Background** A decline in hemoglobin levels with no apparent cause is known to occur in ICU patients during their hospital stay. Less information is available about patients admitted in general medical wards. In countries like India, having high overall prevalence of anemia, further decrease in hemoglobin due to hospital related factors can have a pronounced effect on patient recovery and prognosis. To the best of our knowledge, this is the first study which aims to determine the decrease in hemoglobin in general medical ward patients during their hospital stay in a tertiary care public hospital in India, and to explore related variables. **Methods** A prospective observational study carried out in a tertiary care public hospital in northern India, including 100 patients with no obvious cause for hemoglobin decline. Hemoglobin difference between admission and discharge was determined and association with various factors was studied.**Results** A total of 67 patients showed a decline in hemoglobin with average decline being 0.37 gm%. Significant decline (>1.5 gm %) was observed in 13 patients. Statistically significant association was obtained between hemoglobin decline and sex, discharge diagnosis and IV fluid units infused.**Conclusion** A majority of patients showed a definite decline in hemoglobin. The average overall decline as well as the proportion of patients showing significant decline was much less than what was previously observed in ICU patients and in western settings.

### Key Words

Non-bleeding patients, Hemoglobin, Hospital Acquired Decline

## Introduction

Advances in medical science have had a monumental role in improving lives worldwide. Improved diagnostic techniques, better monitoring, high-tech surgeries and advanced blood tests have contributed greatly to better patient care. However, these practices suffer from certain disadvantages; one of those being Hospital Acquired Anemia (HAA).The etiology of HAA appears to be multifactorial. Repeated phlebotomies [1,2,3], blood loss secondary to invasive diagnostic procedures, hemodilution following IV infusions [4], surgical losses, occult bleeding, anemia of inflammation etc. could possibly lead to HAA. Small decrements in hemoglobin level may not affect healthy individuals but can have adverse implications for hospitalized patients with co-morbid conditions.

HAA has been reported to cause a significant increase in morbidity and mortality for certain disease groups like acute coronary syndrome.[5,6] It has also been observed to prolong the duration of hospital stay [7] which may secondarily decrease hemoglobin levels further. This can necessitate blood transfusion and compromise patient recovery.

The effects of HAA are not limited to the in-hospital course, but deteriorate the post discharge recovery of the patient as well. Study conducted by Makam *et al* has shown increased 30 day readmission and death rates due to HAA. [8] Consequentially, an increased burden on

**PG Department of Medicine and SPM** [1] **, Government Medical College Jammu-J&K India.**
**Correspondence to**: **Dr Fayaz A Wani, Professor , Department of Medicine, Government Medical College, Jammu (J&K), India.**

healthcare facilities and resources is evident.[6, 7]

In populations having high overall prevalence of anemia, like that of developing nations, the consequences of HAA can be of a greater magnitude.Ironically,in India , which has the maximum burden of anemia in the world, hardly any studies have been conducted to determine the incidence and effects of HAA.

Most studies conducted worldwide have focused on consequences of HAA in ICU patients. Its effects on general ward admitted patients, who form the majority of the inpatient population of a hospital, remains to be established.

To the best of our knowledge, this is the first study on hospital acquired decline in hemoglobin among patients in general medical wardsof a public hospital in India.

## Material and Methods

Presuming prevalence of HAA as 50%, the proposed sample size was derived at 100 patients using the formula $4PQ/L^2$ [where P is prevalence of HAA, Q is (100-P) and L is allowable error, kept at 20% of prevalence]. Hundred patients, aged above 18 years were enrolled in the study.

Patients with the following characteristics were excluded:
a)Patients having acute medical conditions that may cause or contribute to decrease in hemoglobin (e.g. gastrointestinal bleeding, hemolysis, hemorrhagic stroke, retroperitoneal bleed, chronic kidney disease/dialysis or any hematological malignancy).
b)Patients on treatment that may alter hemoglobin levels (e.g. Iron , erythropoietin or chemotherapy)
c)Patients admitted specifically for the evaluation of anemia.
d)Patients with hospital stay less than 3 days.
e)Pregnant women

Given the high overall prevalence of anemia in India(53.1% for females and 22.7% for males) [9] as well as in the union territory of Jammu and Kashmir (49.4% in females and 20.6% in males) [10] ,the present study did not exclude patients who were anemic at the time of admission.

A preformed questionnaire containing the following information was filled for each patient: Patient's biodata; date of admission; brief diagnosis of the patient's condition; treatment provided; number of blood samples drawn, number of units(500ml)of parenteral fluids administered, if any; invasive diagnostic procedures performed,if any; other apparent causes that can contribute to the change in hemoglobin; date of discharge etc.Two blood samples, one at admission and the other at discharge (or transfer to a critical care unit) were collected from each patient. These were in addition to the other blood samples that the patient might have given for other diagnostic purposes during his/her hospital stay. Venous blood (2 ml) was collected in EDTA tubes with all aseptic precautions. The hospital automated analyzer was used for hemoglobin analysis.

Patients were characterized on the basis of their sex, age, religion, duration of hospital stay (in days), number of blood samples collected (other than the ones collected for this study), numberof units of i/v fluids administered and discharge diagnosis. Discharge diagnosis were classified as infectious diseases, respiratory, neurologic, gastrointestinal, cardiovascular disorders and others(*Table 1*).

The WHO Criteria for diagnosing anemia was used i.e.,<13g/dL for men,<12g/dL for non-pregnant women. Akin to previous studies, a fall of >1.5 g/dL was considered to be a significant fall [11-13]

The study was approved by the Institutional ethical committee.

## Results

A total of 100 patients above the age of 18 years were included in the study (males:57, females:43). Age distribution ranged between 18-90 years(mean age: 46.56years, SD =18.159). Sixty patients were anemic at the time of admission.

During the hospital stay, the average hemoglobin level of the study population declined from 12.07g/dL to 11.69g/dL amounting to a difference of 0.37g/dL.The average hematocrit decline was 1.052.

A decline in hemoglobin level was observed in 67 out of 100 patients. A decline of > 1g/dL was noted in 24 patients. Of these, 13 showed a more significant decline of >1.5g/dL. A total of17 non anemic patients(13 male and 4 female) became anemic at discharge (*Fig 1*).

The study showed some gender bias. Among those showing a decrease, 40 were males and 27 were females. In males, hemoglobin dropped from 12.91g/dL to 12.23g/dL with an average drop of 0.67g/dL.However, in females, the average hemoglobin change was negligible(from 10.96g/dL to 10.97g/dL).The association of hemoglobin change with gender was found to be statistically significant(p=0.007) with a definite decrease seen in males(*Fig 2* ).

The percentage of patients showing hemoglobin drop was maximum in the age group 85-95 years(100%), followed by 72.72% in 15-25 years age group.The age groups lying between these extremes had relatively lesser percentage of patients showing decline. However, the association between age and hemoglobin decline was not found to be significant statistically. Patients werecategorized and

*Table1 Baseline Characteristics of Patients*

| | N | % | Mean(SD) | Median | Min;Max |
|---|---|---|---|---|---|
| **Age(years)** | | | 45.5(18.1) | 45 | 18;90 |
| 15-35 | 28 | 28 | | | |
| 35-55 | 36 | 36 | | | |
| 55-75 | 27 | 27 | | | |
| 75-95 | 9 | 9 | | | |
| **Gender** | | | | | |
| Male | 57 | 57 | | | |
| Female | 43 | 43 | | | |
| **Religion** | | | | | |
| Hindu | 64 | 64 | | | |
| Muslim | 29 | 29 | | | |
| Sikh | 7 | 7 | | | |
| **Diagnosis** | | | | | |
| Infections | 46 | 46 | | | |
| Respiratory | 6 | 6 | | | |
| Neurological | 24 | 24 | | | |
| Gastrointestinal | 12 | 12 | | | |
| Cardiovascular | 8 | 8 | | | |
| Others | 4 | 4 | | | |
| **Length of stay(days)** | | | 4.2(1.8) | 4 | 3;12 |
| **No. of blood samples taken** | | | 5.3(2.0) | 5 | 2;16 |
| **No. of i/v fluids infused(units)** | | | 5.3(5.8) | 5 | 0;28 |
| **Hb at admission** | | | 12.0(2.0) | 12.3 | 6.1;18.3 |
| **Hb at admission(males)** | | | 12.9(2.0) | 13.1 | 6.1;18.3 |
| **Hb at admission(females)** | | | 10.9(1.5) | 10.9 | 7.7;13.7 |
| **Anemia at diagnosis** | 60 | 60 | | | |

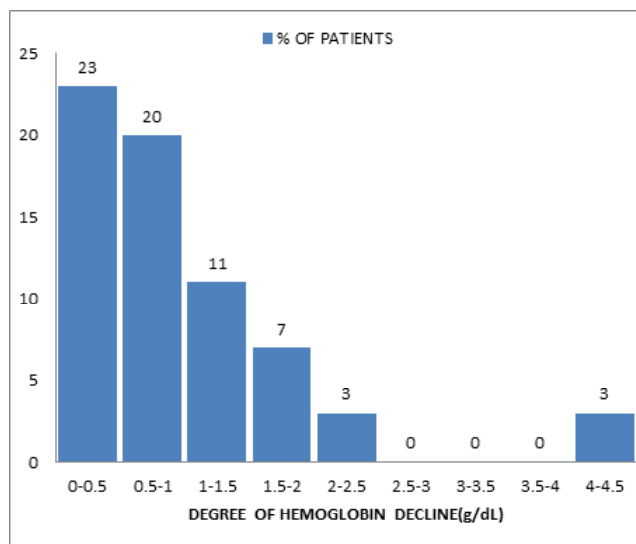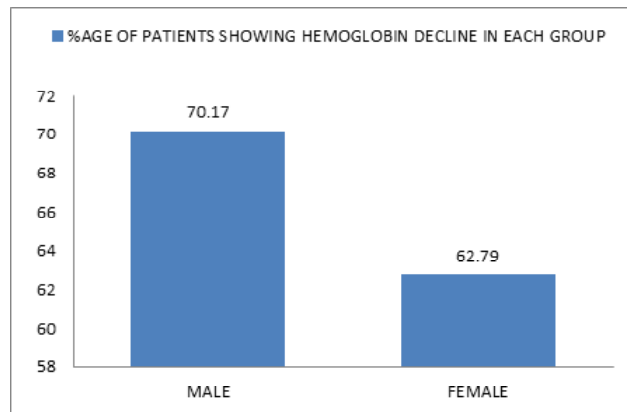*Fig 1. Degree of Decline in Hemoglobin levels*



*Fig. 2 Relation Between Hemoglobin Decline and Gender*



studied on the basis of their discharge diagnosis. A decline in hemoglobin was seen in 83.33%,79.16% and 58.69% of patients admitted for gastrointestinal diseases, neurological diseases and infections respectively. Groups of patients admitted for respiratory and cardiovascular diseases showed a decline in 50% patients each(*Fig 3*).The association of discharge diagnosis and hemoglobin decline was seen to be statistically significant(p=0.01). Hemoglobin decline was also studied in relation with the quantity of intravenous fluids administered. The quantity ranged from 0 to 30 units(500 ml each) .With increasing number of IV fluid units received, a rising trend in the number of patients showing decline was observed (*Fig 4*). The maximum percentage showing decline was in the group being administered between 20 and 25 units of fluid. More than 25 units did not lead to further rise in

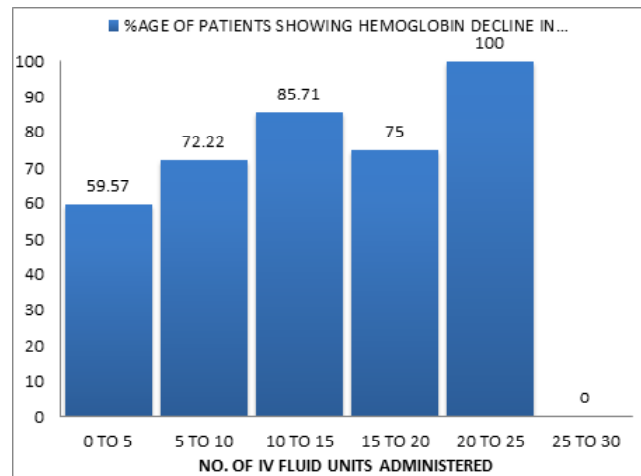*Fig 3. Relation Between Hemoglobin Decline and Disease Category*



*Fig 4. Relation betweenhemoglobin decline and IV fluid*
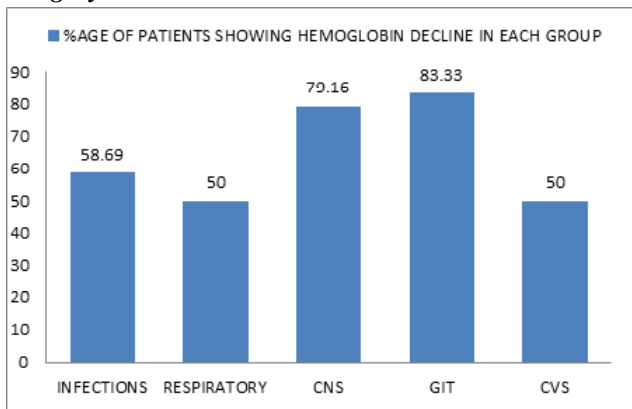
percentage of patients showing decline.The association was found to be statistically significant(p=0.015).

No decipherable pattern was seen between hemoglobin decline and dietary practices(vegetarian/ non-vegetarian), duration of hospital stay and frequency of diagnostic blood sampling.

## Discussion

This study involved patients admitted to the general medical wards of a tertiary care public hospital in northern India.A significant proportion of patients (67%) did show a decline in hemoglobin level. However, the average drop in hemoglobin(0.37g/dL) as well as the proportion of patients showing asignificant drop(13%) is considerably lower than what was reported in previous studies. [11,14,15] Significant association between higher admission hemoglobin levels and greater decline in hemoglobin during hospitalization has been reported previously. [11] Since average admission hemoglobin levels are lower in Indian populations, this could be a possible reason for the relatively less decline. Interestingly, since 60% of our study population was already anemic at admission,it is also plausible that a significant hemoglobin drop had already occurred prior to admission due to late presentation of the patient.This drop, apart from other underlying causes like nutritional deficiencies, might have been secondary to the disease itselfi.e. anemia of inflammation, which in its own right is a proposed mechanism of HAA. [11,16]

Also, less frequent diagnostic testing and monitoring in a general ward of a typical public hospital in India as compared to a private set up, an ICU setting or a hospital in a developed country could be a possible cause, although diagnostic sampling was not shown to have a significant association with hemoglobin decline in this study.

The number of patients developing new onset anemia was also less in our study than studies performed in the West. [14] This could be possibly because of the greater proportion of patients in non-anemic hemoglobin range in western settings while in our study 60% patients were already anemic at admission. A total of 17% patients developed new onset anemia.

The difference in results of our study vis-a-vis previous studies is in line with Salisbury et al who noted persistent variability in incidence of HAA across hospitals suggesting the role of unmeasured procedural and protocol differences in different hospitals. [17] This may also be attributed to the different genetic and demographic profiles of different populations.

In this study, it was noted that being a male was more often associated with having a decline in hemoglobin level .This might be due to a higher average admission hemoglobin level in males.

Longer duration of hospital stay was seen to be an associated factor with HAA [5] but statistical significance for the same was not obtained in this particular study. It may be because, for most patients (86%) in our study, the duration of stay was in the narrow range of 3 to 5 days (average: 4.22 days).Insufficient variation limits our ability to determine its effect. Pertinently, it has also been observed in previous studies that the maximum hemoglobin decline occurred in the first days of hospitalization and in non-septic patients, the decline was not substantial beyond 3 days. [11,12] Increased inflammatory mediators as well as more diagnostic sampling in the initial days might be some of the related mechanisms. Being admitted for gastrointestinal, neurological or infectious diseases was seen to have greater decline in hemoglobin level which is akin to results obtained by Agustin *et. al.*[11]

The effect of intravenous hydration has been less

described in literature. In our study, it was observed that with increasing number of IV fluid units administered, greater proportion of patients developed a hemoglobin decline.Though, beyond 25 units of IV fluids, none of the patients showed a decline. This ambiguity however may not hold much worth as only 2 patients fell in this category. Notably,a previous study involving myocardial infarction patients reported greater evidence of congestion in patients developing in-hospital anemia, suggesting a possible causal role of hemodilution. [4]

There were several limitations of this study. The small sample size limited our capability to detect other possible factors and generalize this to larger populations.The study considered the decrease in hemoglobin with respect to admission and discharge levels only .It is possible that if serial monitoring of hemoglobin had been done and nadir levels also taken into account, the proportion of patients acquiring HAA would have been more.

The effect of severity of the disease was not studied. Finally, the patients were not followed up after discharge and therefore any prognostic significance of the decline was not determined. However, our study did not aim to find out mechanisms behind HAA or its prognostic value, but to determine its incidence and explore related variables.These results can be useful for further studies to determine hemoglobin variations and new onset HAA in general ward admitted patients. Multimodal techniques must be devised to prevent and further reduce the magnitude of HAA. More studies evaluating its possible causal factors and effect on disease prognosis in Indian population are required.

## Conclusion

Our study showed an average hemoglobin decline of 0.378 g/dL during hospitalization. A total of 67 % patients showed a decline with 17 % developing new onset anemia and 13% patients showed a drop > 1.5 g/dL. Being a male, being admitted for gastrointestinal, neurological or infectious diseases and receiving greater quantities of IV fluids were significantly associated with the hemoglobin decline.

**Conflicts of Interest**
There are no conflicts of interest.

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