# A Prospective Observational Study about Prevalence, Comorbidities, Treatment Modalities, and Drug-drug interactions among Anaemic Inpatients at a Government Medical College Hospital in Tamil Nadu

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## ABSTRACT

**Objectives:** Anaemia is a well acknowledged nutritional deficiency disorder in the world. This study is pivoted on to examine the prevalence of anaemia among hospitalized inpatients and classifying them according to WHO's severity index with little insight on drugs used to treat anaemia and drugs interacting with haematinics. **Materials and Methods:** A study of prospective observational nature was carried out between July 2022 and September 2022 in a government district headquarters medical college hospital of Tamil Nadu. The demographic and other data collected for this study includes age, sex, clinical laboratory profiles, diagnostic findings, drugs administered etc. Among lab profiles, hemoglobin, red blood cells, and packed cell volume were segregated. The collected data were segregated with the help of Microsoft Excel 2007 spreadsheets. Drug interactions in prescriptions were found using Micromedex drug interactions checker application. **Results:** Totally hundred inpatients diagnosed with anaemia were there in our study. Out of 70 female inpatients, 36 (51.42%) were women in child-bearing age (15 - 49 years). Among 100 inpatients, 36 were mildly anaemic, followed by 30 in moderate index, 22 in severe index, and 12 in life-threatening anaemia index. Chronic kidney disease is the most common co-morbidity. Fluroquinolone antibiotics (ofloxacin and ciprofloxacin) were the most common drugs interacting with prescribed iron products in our study. **Conclusion:** Growing global burden of anaemia is threatening. Drug-drug interactions are often double-edged swords. Educating health-care practitioners about drug-drug interactions and making them aware about clinical management strategies in order to eschew from untoward effects of interactions is an absolute requisite.

**Keywords:** Anaemia, Haemoglobin, Co-morbidities, Haematinics, Drug-drug interactions, Fluroquinolones.

## INTRODUCTION

Anaemia is a well acknowledged nutritional deficiency disorder in the world. It is a condition in which erythrocytes are not able to carry over enough oxygen to the tissues.[1] World Health Organization designate anaemia as a drop in haemogloblin concentration. It is a public health plight affecting low, middle, and high-income nations and has momentous adverse health ramifications, as well as adverse repercussions on socio-economic status of a nation.[2] Anaemia is a major public health hurdle which affects 1.62 billion people globally. The prevalence of anaemia is said to be at 9% in developed nations and the prevalence is said to be 43% in developing countries. Children and women of child-bearing age are at higher risk. At present the worldwide anaemia prevalence estimates are 47% in

children younger than 5 years, 42% in pregnant women, and 30% in non-pregnant women aged 15-49 years.[3] The common etiologies for the clinical manifestations and diagnosis of anaemia are deficiency of iron, thalassemia, hemoglobinopathies, folic acid deficiency, and parasitic infections (especially malaria, hookworm infestations, and schistosomiasis).[4] Anaemia is generally ruled out by a low haemoglobin level or a decreased haematocrit. It can also be manifested using erythrocytes counts. The role of haemoglobin to transport oxygen to tissues explains the most common subjective evidences of anaemia like fatigue, dyspnoea, palpitations and pallor.[5]

Threshold haemoglobin concentrations used to rule out anaemia in people living at sea level according to the World Health Organization guidelines is presented below,[6]

| Age or Gender Group | Haemoglobin Threshold (g%) |
|---|---|
| Children (6 months to under 5 years) | 11.0 |
| Children(5 years to under 12 years) | 11.5 |
| Children (12 years to under15 years) | 12.0 |
| Non pregnant women (15 years and over) | 12.0 |
| Pregnant women | 11.0 |
| Men (15 years and over) | 13.0 |

Anaemia is linked with escalating morbidity and mortality, and can lead to cardiovascular and neurological complications.[7] Anaemia is caused by multi-factorial conditions that requires a multi-frontal approach for its prevention and treatment. Iron deficiency anaemia is the most common type of anaemia. Recent evidences said that proportion of anaemia due to iron deficiency is less than 50% and varies, in different population in developing countries.[8] Other causes of anaemia include, blood loss during menstruation, ulcer, haemorrhoids; decreased or faulty production of RBC; destruction of RBC, improper growth and maturation of RBC, and Vitamin-$B_{12}$, folate deficiency which are essential for growth of RBC.[9] Anaemia is an indice of both poor nutrition and poor health. The most dramatic health effect of severe anaemia such as increased maternal and foetal mortality have been well documented.[10] This study is pivoted on to examine the prevalence of anaemia among hospitalized inpatients in various departments and classifying them according to WHO's severity index with little insight on drugs used to treat anaemia and drugs interacting with haematinics. Clinical management and mechanisms of these interactions were also presented.

## MATERIALS AND METHODS

### Study design and site

A study of prospective observational nature was carried out between July 2022 and September 2022 in a Government District Headquarters Hospital of Tamil Nadu which is now uplifted as medical college hospital. The case records of hospitalized patients needed for this study was gathered during our internship which was duly permitted by dean and other authorities of the hospital.

### Ethical clearance

This study was duly permitted by the institutional human ethical committee of the hospital. The reference number of the ethical committee certificate provided by them for performing this study is R.No 110 / HS /GHQH - VNR / SEP 2019.

### Sample size

This study includes hundred (100) in-patients whom were diagnosed with anaemia. It includes both men and women inpatients, and pediatric patients from various departments like general medicine, orthopedics, pediatrics, of the concerned hospital. Patients with severe illness and those who were unwilling to give consent were excluded from this study. The sampling was made by systematic random sampling method upon taking the margin of error of ±5% with a confidence interval of 95% even though data sample was collected sufficiently enough for the study.

### Data collection and analysis

The data gathered for this study includes age, sex, clinical laboratory profiles, diagnostic findings, drugs administered etc. Among lab profiles, hemoglobin, red blood cells, and packed cell volume were segregated. These data were gathered from case records. Separate data collection proforma was used for this purpose Informed consent was administered for every study participant. The collected data were segregated using Microsoft Excel 2007 spreadsheets. Drug interactions in prescriptions were found using Micromedex drug interactions checker application and drug reference application in android mobile.

## RESULTS

Totally hundred inpatients diagnosed with anaemia were there in our study. The patients were further segregated into adults and paediatrics. Gender wise demographic distribution shows the preponderance of women in adult

**Table 1: Gender wise prevalence of anaemia among hospitalized patients.**

| Category | Male | Female | Total (*n*=100) |
|---|---|---|---|
| Adults | 22 | 65 | 87 |
| Pediatrics | 8 | 5 | 13 |
| | 30 | 70 | 100 |

Out of 70 female inpatients, 36 (51.42%) were women in child-bearing age (15 - 49 years).

**Table 2: Classification of anaemia among study participants based on severity criteria of WHO.**

| WHO categorisation of haemoglobin | Male | Female | Male children | Female children | Total patients (*n*=100) | % |
|---|---|---|---|---|---|---|
| Mild (10-11.5 g%) | 5 | 26 | 4 | 1 | 36 | 36 |
| Moderate (8-9.9g%) | 6 | 22 | 1 | 1 | 30 | 30 |
| Severe (6.5-7.9g%) | 9 | 7 | 3 | 3 | 22 | 22 |
| Life-threatening (below 6.5g%) | 2 | 10 | 0 | 0 | 12 | 12 |

**Table 3: Comorbidities associated with severe Anaemia in Adults.**

| Comorbidities | No of patients |
|---|---|
| Chronic kidney disease | 7 |
| Cerebro vascular attack | 1 |
| AIDS | 1 |
| Tuberculosis | 1 |
| Fever | 3 |
| Acute Gastroenteritis | 1 |
| Fracture | 2 |

**Table 4: Comorbidities associated with severe Anaemia in Paediatrics.**

| Co morbidities | No of patients |
|---|---|
| Seizure disorder | 1 |
| Acute Gastroenteritis | 3 |
| Thalassemia | 1 |
| Fever | 1 |

**Table 5: Comorbidities associated with life threatening Anaemia in Adults.**

| Co morbidities | No of patients |
|---|---|
| Chronic kidney disease | 3 |
| Gastro oesophageal reflux disease | 2 |
| Oesophagitis | 1 |
| Menorrhagia | 1 |
| Congestive cardiac failure | 1 |
| Systemic hypertension | 1 |
| Fracture | 1 |
| Hypothyroidism | 1 |
| Gastroenteritis | 1 |

category and male children in pediatrics category. It is mentioned in Table 1.

Among 100 inpatients, 36 were mildly anaemic, followed by 30 in moderate index, 22 in severe index, and 12 in life-threatening anaemia index. This classification of anaemia according to haemoglobin level and severity index which was put forth by WHO is enlisted in Table 2.

16 adult patients were severely anaemic in this study. Chronic kidney disease is the most common comorbidity. Anaemia in chronic kidney disease is known as anaemia of chronic disease. The comorbid diseases interlinked with these severely anaemic adult inpatients were enlisted in Table 3.

Totally 6 paediatrics were found to be severely anaemic. Among them the most common comorbidity is acute gastroenteritis. The co-morbid diseases interlinked with these severely anaemic paediatric inpatients were enlisted in Table 4.

Twelve adult inpatients alone are with life-threatening anaemia in our study. There is no paediatric in this severity index. Among patients with life threatening anaemia, the most commonly found comorbid condition is chronic kidney disease followed by gastro oesophageal reflux disease. Comorbidities associated with life-threatening anaemia are enlisted in Table 5.

The most commonly prescribed haematinics in this hospital were iron sucrose, ferrous sulphate, Vitamin-C, Vitamin-B complex, Vitamin-B$_{12}$, desferoxamine, erythropoietin, folic acid, and albendazole. Albendazole was prescribed only in anaemia associated with warm infestations. Desferoxamine was prescribed in paediatric patient with thalassemia to reduce iron overload as a result of repeated blood transfusions. Among the above haematinics, the most commonly prescribed haematinics are iron sucrose and ferrous sulphate. Prescribed medications interacting with these two products with their respective severity, management, and mechanism were provided in Table 6.

## DISCUSSION

This study includes 100 hospitalized patients with varied severity of anaemia. Among them 70 were women. This includes female children also. This female predominance is customary in anaemia. This trend is similar to another cross-sectional study which was conducted in Nepal in which prevalence of anaemia in women was 70.9%.[11] Among 70 female inpatients, 36 (51.4%) were women of

**Table 6: Commonly found drug-drug interactions with haematinics.**

| Sl.NO | Haematinics | Interacting drugs | Severity | Clinical management | Mechanism of interaction |
|---|---|---|---|---|---|
| 1. | Iron sucrose | Omeprazole | Moderate | Use iron sucrose only as parenteral. | increased gastric acid $_pH$ and decreased absorption of non heme iron. |
| | | Doxycycline | Moderate | Separate the administration of iron products and doxycycline by at least 4 hr. | Decreased iron effectiveness. |
| | | Ofloxacin | Moderate | Ofloxacin should be administered two hours before or two hours after a dose of iron salts. | Decreased ofloxacin effectiveness. |
| 2. | Ferrous sulphate | Omeprazole | Moderate | Consider Parenteral administration of iron if concurrent omeprazole and iron administration is avoidable. | Reduced non heme iron bioavailability. |
| | | Ciprofloxacin | Moderate | Separate the administration of iron products and ciprofloxacin by at least 4 hr. | Decrease ciprofloxacin exposure. |
| | | Thyroxine | Moderate | Separate the administration of iron products and levothyroxine by at least 4 hr. | Reduced levothyroxine absorption. |
| 3. | Vitamin- $B_{12}$ | Omeprazole | Minor | Separate the administration of vitamin-$B_{12}$ and omeprazole by atleast two hours. | Reduced vitamin-$B_{12}$ absorption. |

child-bearing age. Anaemia in women of child bearing age leads to both maternal and foetal complications. World Health Organisation's 2019 prevalance estimate of anaemia among child bearing women in India was 50.1%.[12] This is more or less equal to our study finding. Among 87 adults, 30 were geriatrics (60 and above years of age). In geriatrics, anaemia is interconnected with poor performance status, increased weakness, memory problems, depression, decreased movements, increased risk of accidental falls, and poor prognosis.[13]

This study utilized WHO's severity criteria for classification of anaemia among these inpatients. Among 100 hospitalized patients, majority of patients (36) were mildly anaemic. This is in line with another study which was conducted in Raichur, Karnataka in which 36.6% of study participants were with mild anaemia.[14]

Chronic kidney disease is the most common co-morbidity associated with severe and life-threatening anaemia in this study. Anaemia in patients with CKD is attributed to decreased erythropoietin levels and increased hepcidin levels.[15] Gastroenteritis and gastro oesophageal reflux disease is the next common co-morbid condition linked with anaemia. This may be due to gastro-intestinal blood loss associated with gastroenteritis and GERD.[16]

Fluroquinolone antibiotics (ofloxacin and ciprofloxacin) were the most common drugs interacting with prescribed iron products in our study. This should be avoided carefully as fluroquinolones' effectiveness is found to be decreased due to these interactions which in turn results in poor prognosis in the treatment of various bacterial infections.[17] The other drugs which were found to be interacting with iron products are doxycycline, omeprazole, and thyroxine. Interaction of ferrous sulphate with thyroxine will severely affect the clinical outcome of hypothyroidism. It can even lead to recurrent hypothyroidism in women.[18] Omeprazole was found to be interacting with both iron products and Vitamin $-B_{12}$ in our study. Long-term use of proton pump inhibitors results in iron and Vitamin- $B_{12}$ deficient state in many cases. It is therefore recommended to constrain long-term use of proton pump inhibitors and to critically appraise this in the differential diagnosis of iron deficiency and Vitamin $-B_{12}$ deficiency anaemia.[19]

## LIMITATIONS OF THE STUDY

This is a observational study not a case-control study. Physicians of the hospital were not intimated about these results and findings. Lack of pharmacist intervention component is yet another limitation.

## CONCLUSION

Growing global burden of anaemia is threatening. Anaemia in women of child-bearing age leads to both maternal and foetal complications. In countries with poor nourishment for female children like India, it is further worrisome. Anaemia in hospitalized patients occurs due to myriad complications like comorbid diseases and drug-drug interactions. Chronic kidney disease is the foremost co-morbidity that upshots into life threatening anaemia. Drug-drug interactions are often double-edged swords. It negatively impacts the clinical outcomes of treatment provided for both presenting illness and comorbid diseases. Educating health-care practitioners and workers about drug-drug interactions and make them aware about clinical management strategies in order to eschew from

untoward effects of interactions is an absolute requisite.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**RBC:** Red Blood Cells; **WHO:** World Health Organization; **AIDS:** Acquired Immunodeficiency Syndrome; **CKD:** Chronic Kidney Disease; **GERD:** Gastro Oesophageal Reflux Disease.

## SUMMARY

Anaemia is a haematological disorder which results in decreased oxygen carrying capacity of the blood. Examining the prevalence of anaemia among hospitalized inpatients and classifying them according to WHO's severity index with little insight on drugs used to treat anaemia and drugs interacting with haematinics are the key objectives of this study. Chronic kidney disease is the foremost co-morbid condition associated with anaemia in this study. The most commonly prescribed haematinics are iron sucrose and ferrous sulphate. Antibiotics like fluroquinolones, and doxycycline; omeprazole, and thyroxine are the drugs which interact frequently with iron sucrose and ferrous sulphate.

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