A PROSPECTIVE OBSERVATIONAL STUDY OF CLINICAL PROFILE IN ETIOLOGY OF ANEMIA IN ELDERLY-A HOSPITAL BASED STUDY IN A TERTIARY CARE CENTRE IN SOUTH INDIA

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Introduction:
Anaemia is often considered as a normal physiological process that occurs with aging, but recently since past 2 decades anemia of any degree is being recognized as significant independent contributor to morbidity, mortality and frailty in elderly patients. It is easy to overlook anemia in elderly as symptoms of anemia like fatigue, SOB etc are often attributed to aging process itself. Many evidences accumulated states that anemia of any degree reflects poor health and increased vulnerability to poor outcomes.

Materials and methods: This study was conducted in the department of internal medicine in a tertiary care hospital over a period of one year with sample size of 362 subjects satisfying the inclusion and exclusion criteria after taking the consent form.

Results: Moderate degree anaemia was the commonest around, 65.6% followed by severe degree anemia 20.1%. Easy fatigability was the commonest symptom and pallor was the commonest sign of anaemia in elderly. Anemia is not always a consequence of aging. Anemia of unexplained etiology constituted 15.97% of total study population.

Conclusion: Anaemia in elderly is a challenge and has to be approached in an organized manner for appropriate diagnosis and evaluation to look into its cause and plan management to improve the quality of life of the elderly persons. An effort should always be made to reach etiological diagnosis before instituting specific therapy.
associated with longer hospital stays, prolonged recovery, risk of acquiring infections etc. It is also said to be associated with cognitive decline, depression, recurrent falls and overall quality of life (4).

It is easy to overlook anaemia in elderly as symptoms of anaemia like fatigue, SOB etc. are often attributed to aging process itself. Though the prevalence of anaemia increases with age, healthy aging is not always associated with anaemia and it is not considered as an inevitable consequence of aging as some cause which is often multifactorial is usually identified in 75% to 80% of individuals. Hence a failure to evaluate anaemia in elderly may lead to delayed diagnosis and management of potentially treatable causes (5).

National programme for health care of elderly defines an elderly as a person above the age of 60 years. According to WHO, anaemia in adults is defined as hemoglobin concentration less than 12gms/dl in women and less than 13 gm/dl in men (6).

Advancing age may lead to anaemia whether due to decreased hematopoietic reserve or a consequence of some underlying disorder leading to hematopoietic stress (7). Three general causes for anaemia in the elderly, nearly equal in frequency, emerged from NHANES 3 study. These are
1. Anaemia due to blood loss or nutritional deficiencies.
2. Anaemia associated with chronic illness or inflammation or chronic renal failure.
3. Unexplained anaemias (8).

Malnutrition is a frequent, under evaluated clinical condition, including iron, folate or B12 deficiencies, and accounts for one-third of all anaemia in the elderly. The anaemia of chronic disease develops specifically in patients suffering from chronic inflammatory diseases such as autoimmune disorders, cancer or chronic infections, or in patients undergoing dialysis (3).

Materials and Methods:
Study site: department of internal medicine, KIMS hospital, Secunderabad.

Duration of the Study
12 months

Study Design
Prospective observational study.

Sample Size
For this observational study sample size was calculated based on study geriatric anaemia: an Indian perspective by varnamala Alwar et al, the prevalence of anaemia in elderly over 60 years found to be 37.88%.

Utilizing the formula:
\[ \text{sample size} = \left( \frac{Z_{1-\alpha/2}}{d} \right)^2 \frac{P(1-P)}{d^2} \]

After submitting all the values in the formula we get the required sample size as 362.

Study Population
The study will be conducted in all consecutive elderly patients admitted in the department of internal medicine, during the one year period satisfying the following inclusion and exclusion criteria.

Inclusion criteria
1. Age over or equal to 60 years
2. Patients with anaemia as per WHO criteria.

Exclusion Criteria
1. Patient's age < 60 years.
2. Patients who are not willing to participate.
3. Patients who received blood transfusion prior to admission.
4. Patients who are on hematinsics.
Statistical Analysis
In the present study we have taken informed consent from 363 patients and collected their demographical data, laboratory data. Data was transformed into Microsoft Excel spreadsheets. Statistical analysis was performed using SPSS version 25.0. Descriptive statistics including mean and standard deviation for continuous variables and frequencies with percentages were calculated for categorical variables. A p-value ≤ 0.05 is considered as significant.

Table 1: Age-wise distribution of Anaemia Patients.

| Age group       | No. of Anaemia patients (%) |
|-----------------|-----------------------------|
| 60-70 Years     | 217 (59.78%)                |
| 71-80% Years    | 102 (28.10%)                |
| >80 Years       | 44 (12.12%)                 |
| Total No. of Anaemia Patients | 363 (100%)                 |

Table 2: Severity of anaemia among different age groups.

| Age group       | Severity of Anaemia | Mild(n=52) | Moderate(n=238) | Severe(n=73) |
|-----------------|---------------------|------------|-----------------|--------------|
| 60-70 Years(n=217)| 36 (69.23%)         | 141 (59.24%) | 40 (54.79%)     |
| 70-80 Years(n=102)| 11 (21.15%)        | 69 (29.00%)  | 22 (30.14%)     |
| >80 Years (n=44) | 5 (9.62%)           | 28 (11.76%)  | 11 (15.07%)     |
| Total No. of Anaemia patients(n=363) | 52 (14.3%)        | 238 (65.6%)   | 73 (20.1%)     |
**Table 3:** Gender Distribution.

| Gender     | No. of Anaemia Patients(%) |
|------------|----------------------------|
| Male       | 197 (54.3%)                |
| Female     | 166 (45.7%)                |
| Total No. of Anaemia Patients | 363 (100%)                |

**Table 4:** Severity of Anaemia.

| Anaemia Grade    | No. of Patients(%) |
|------------------|--------------------|
| Mild Anaemia     | 52 (14.3%)         |
| Moderate Anaemia | 238 (65.6%)        |
| Severe Anaemia   | 73 (20.1%)         |
| Total No. of patients | 363 (100%)        |

**Table 5:**

| Anaemia grade             | Male (n=197)   | Female (n=166) | Chi-Square test   |
|---------------------------|----------------|----------------|------------------|
| Mild Anaemia (n=52)       | 34 (17.26%)    | 18 (10.84%)    | p-val=0.150;     |
| Moderate Anaemia (n=238)  | 128 (64.97%)   | 110 (66.26%)   | Chi-Square value : 3.788; d.f=2|
| Severe Anaemia (n=73)     | 35 (17.77%)    | 38 (22.90%)    |                 |
| Total No. of Patients (n=363) | 197 (100%)    | 166 (100%)    |                 |

**Table 6:** Smear findings among anaemia patients.

| Smear Findings | No. of Anaemia patients(%) |
|----------------|-----------------------------|
| Normocytic     | 277 (76.3%)                 |
| Microcytic     | 60 (16.5%)                  |
| Macrocytic     | 9 (2.5%)                    |
| Dimorphic      | 17 (4.6%)                   |
| Total No. of Anaemia patients | 363 (100%)              |
Table 7: Anaemia grade vs MCH status.

| Anaemia Grade         | MCH status | Chi-Square test |
|-----------------------|------------|-----------------|
|                       | Normal     | Abnormal        |
| Mild Anaemia (n=52)   | 39         | 13              | p-val=0.036*; Chi-Square value: 6.649 d.f=2 |
| Moderate Anaemia (n=238) | 157       | 81              |
| Severe Anaemia (n=73) | 39         | 34              |
| Total no. of Patients (n=363) | 235   | 128             |

Table 8: Anaemia grade vs MCHC status.

| Anaemia Grade         | MCHC status | Chi-square test |
|-----------------------|-------------|-----------------|
|                       | Normal      | Abnormal        |
| Mild Anaemia (n=52)   | 42          | 10              | p-val=0.0019*; |
| Moderate Anaemia (n=238) | 193       | 45              | Chi-square value: 7.929 |
| Severe Anaemia (n=73) | 48          | 25              | D.f.=2 |
| Total no. of patients | 283         | 80              |
Table 9: PCV status in Anaemia patients.

| PCV Status | No. of Anaemia Patients(%) |
|------------|---------------------------|
| Normal     | 20(5.5%)                  |
| Abnormal   | 343(94.5%)                |
| Total No. of Anaemia Patients | 363(100%) |

Table 10: Anaemia grade vs ESR status.

| Anaemia grade          | ESR status | Chi-Square test |
|------------------------|------------|-----------------|
|                        | Normal     | Abnormal        |
| Mild Anaemia (N=52)    | 17         | 35              | p-val=0.211; Chi-Square value: 3.116; d.f.=2 |
| Moderate Anaemia (n=238)| 56         | 182             |
| Severe Anaemia (n=73)  | 14         | 59              |
| Total No. of Patients (n=363) | 87         | 276             |

Fig 11: Status of ESR in anaemia patients.

Table 12: Anaemia grade vs Sr. Ferritin status.

| Anaemia Grade          | Sr. Ferritin status | Chi-Square test |
|------------------------|---------------------|-----------------|
|                        | Normal              | Abnormal        |
| Mild Anaemia(n=52)     | 43                  | 9               | p-val=0.001*; Chi-Square value: 13.341; d.f.=2 |
| Moderate Anaemia (n=238)| 180             | 58               |
| Severe Anaemia(n=73)   | 41                  | 32               |
Figure 13: Status of Sr. Ferritin levels

Table 14: Anaemia grade vs Transferrin Saturation status:

| Anaemia Grade       | Transferrin Saturation status | Chi-Square test          |
|---------------------|-------------------------------|--------------------------|
|                     | Normal                        | Abnormal                 |                            |
| Mild Anaemia (n=52) | 37                            | 15                       | p-val<0.0001*;             |
| Moderate Anaemia (n=238) | 143                         | 95                       | Chi-Square value: 22.314; |
| Severe Anaemia (n=73) | 24                           | 49                       | d.f.=2                    |
| Total No. of patients (n=363) | 204                  | 159                     |                            |
Table 16:- Prevalence of Absolute and Functional Iron deficiency:

| Type of Iron Deficiency     | No. of Patients(%) |
|-----------------------------|--------------------|
| Absolute Iron Deficiency    | 44(12.12%)         |
| Functional Iron Deficiency  | 71(19.56%)         |

Figure 15:- Prevalence of Absolute and Functional Iron deficiency:

Table 17:- Anaemia Specific Clinical Features:

| Clinical Feature                   | No. of Patients |
|------------------------------------|-----------------|
| Easy Fatigability                  | 190(52.34%)     |
| Pallor                             | 91(25.06%)      |
| Anorexia                           | 54(14.87%)      |
| SOB                                | 48(13.22%)      |
| Pedal Edema(+Gen Edema)            | 23(6.34%)       |
| Bleeding(+Malena)                  | 18(4.95%)       |
| Light headedness                   | 16(4.4%)        |
| Nail changes                       | 8(2.2%)         |
| Hematemesis                        | 3(0.83%)        |
| Menorrhagia                        | 1(0.3%)         |
| Total No. of Anaemia Patients      | 363(100%)       |
### Table 18: Distribution of Chronic Conditions among Anaemia patients:

| Chronic Condition (n=180) | No. of Anaemia Patients(%) |
|---------------------------|----------------------------|
| Malignancies              | 34(19.1%)                  |
| Chronic kidney Disease    | 66(37.08%)                 |
| Liver Disease             | 15(8.43%)                  |
| Hypothyroidism            | 23(12.92%)                 |
| Rheumatoid Arthritis      | 6(3.37%)                   |
| Others(DVT,Hemorrhoids,TB,Ulcerative,Colitis) | 34(19.1%)                 |
| Total No. of Anaemia Patients | 178(100%)                |

#### Chronic Conditions

- **Others(DVT,Hemorrhoids,TB,Ulcerative,Colitis)**: 34
- **Rheumatoid Arthritis**: 6
- **Hypothyroidism**: 23
- **Liver Disease**: 15
- **Chronic kidney Disease**: 66
- **Malignancies**: 34

![Chronic Conditions Graph](image-url)
Discussion:-

Present study is conducted in people over and equal to 60 years of age diagnosed with anemia as per WHO criteria mentioned above. This age is particularly selected because of the impact anemia has on morbidity and mortality in elderly irrespective of degree of anemia. This study includes clinical profile and etiology of anemia in people aged 60 years and above.

We have included 363 patients diagnosed with anemia as per the WHO criteria, of which majority i.e., 59.78% were in 60-70 years age group, 28.10% were in 71-80 years age group, 12.12% were in more than 80 years age group, with the mean age of study population being 70.26±7.88 years (Range 60-98 yrs.).

This is comparable to the study done by Bhasin et al (9), where they included 100 elderly anemic patients with a mean age of 70.51. This is also comparable to study done by Humaney et al (10), where they included 116 elderly anemic patients with mean age of 71.51 and 59.78% in the present study.

The present study 54.3 percent are male and 45.7 percent of female with male female ratio of 1.18:1. This is comparable to study done by Humaney et al (10), in which 56.89% were males and 46.1 percent were females and male female ratio 1.3:1. And also comparable to study done by Joshi et al (6), where male female ratios were 1.49:1.

The mean hemoglobin in this study was 9.23±1.65. Moderate anemia was the most common degree of anemia seen in this study with a percentage of 65.6% followed by severe anemia 20.1% and mild anemia 14.3%. This is compared to study done by Humaney et al (10), in which moderate anemia (43.97%) is the most common degree but is followed by mild degree (41.37%) and then severe degree (14.66%) and comparable to study done by Joshi et al (6), in which moderate anemia is most common followed by severe and then mild anemia similar to our study.

In this study, there is no significant difference in frequency distribution of anemia based on gender (p=0.15) but is significant in study by Joshi et al (p=0.05).

In this study, Normocytic anemia (76.3%) was the most common morphological pattern followed by microcytic (18.1%), Dimorphic (4.6%) and then macrocytic (2.5%).

In this study, majority of patients presented with more than one symptom and they are often overlapping. The most common symptom encountered is easy fatigability, seen in almost 52.34% of total subjects followed by anorexia (14.87%), SOB (13.22%) and other constitutional symptoms and bleeding symptoms like light headedness, Malena, bleeding PR, menorrhagia etc.

The most common sign in this study is pallor seen in 25.06% subjects followed by pedal edema (6.34%) of the subjects.

The present study, Anaemia of chronic disease was found to be the most common etiology of anaemia in elderly which constitutes almost half of the study population around 49.03% followed by iron deficiency anaemia (both absolute and functional) of 31.68%, anaemia of unexplained etiology constitutes 15.97% and the rest of 3.3% (no underlying chronic condition and no iron deficiency) had other causes of anaemia like vitamin B12 and folic acid deficiency, haematological conditions including MDS, AML, aplastic anaemia, malaria, HLH etc. Multiple myeloma is the most common hematological malignancies encountered but since it is associated with other chronic issues like CKD etc, it is being considered under anaemia of chronic condition.

Most of the patients with gastrointestinal bleeding as evidenced by colonoscopy, endoscopy etc or some other bleeding manifestations like menorrhagia, bed sore bleeding, mucosal bleeding have iron deficiency anaemia.

Among the chronic conditions, chronic kidney disease was the most commonest condition encountered, seen in 37.08% followed by various underlying malignancies (19.1%) then by Hypothyroidism (12.92%), chronic liver disease (8.43%), rheumatoid arthritis (3.43%) and various other chronic conditions (19.1%) including chronic infection and inflammatory conditions like chronic DVT, Tuberculosis, Ulcerative colitis, SLE etc. Evidence of gastrointestinal bleeding seen in 10.46% of all patients. And 26.08% subjects with iron deficiency anaemia had evidence of GI bleed.
Bhasin et al study(9), also shows that anaemia of chronic disease was the most common cause followed by iron deficiency anaemia, however in this study, an upper GI lesion was found in 78.6% of the patients and the colonic lesion was found in 29.4% of the patients.

But in present study only 26.08% of subjects with iron deficiency had evidence of GI bleed and this points that even though GI loss is the most common cause of iron deficiency anaemia, there are other causes like nutritional factors, absorption defects particularly at very old age, redistribution due to erythropoietin stimulating agents etc. some patients have more than one etiology which are often overlapping.

All patients with macrocytic picture (around 9 patients) has vitamin B12 and folate deficiency and 2 patients out of 9 had pancytopenia. But this could not be the total prevalence of vitamin B12 deficiency in the given study population because serum vitamin B12 levels were sent only on the basis of macrocytic smear picture and although this anaemia is usually macrocytic and megaloblastic, it can be normocytic or even microcytic.

Since the prevalence of iron deficiency anaemia is significantly high, Iron profile is done for all the subjects irrespective of the smear picture. Iron deficiency is diagnosed based on serum ferritin and transferritin saturation levels.

In the present study, it was found that 71 out of 115 patients have functional iron deficiency and 44 out of 115 have absolute iron deficiency.

It was also found that 12.12 percent of the total 16.5% of microcytic anaemia have iron deficiency and 9.37% out of 12.12% have absolute iron deficiency and the rest 2.75% have functional iron deficiency.

**Conclusions:-**

Anemia in elderly is a challenge and has to be approached in an organized manner for appropriate diagnosis and evaluation to look into its cause and plan management to improve the quality of life of the elderly persons. Non-specific symptoms like fatigue and weakness should not be overlooked in the geriatric population as they could be important indicators towards presence of anaemia in these patients. In our study normocytic anaemia is the commonest cause of anaemia in elderly, which indicates that underlying causes (like CKD) has to be identified with proper investigations. To identify Iron deficiency anaemia, the need for upper GI endoscopy and colonoscopy are again validated in this study. An effort should always be made to reach etiological diagnosis before instituting specific therapy.

**Limitations:**

The significance of any study increases as the sample size increases. in the present study sample size is 363. in view of ever growing elderly population and high prevalence of anaemia, this number is small to extrapolate the findings to overall population. along with sample size, duration of the study is also important. the present study was done over one year. in this time period, we could collect 363 cases which have fulfilled the inclusion criteria.

A multicenter study is always beneficial. This is a single-center study done in a multispecialty hospital situated in a metropolitan city.

**References:-**

1. Vanasse GJ, Berliner N. Anemia in elderly patients: An emerging problem for the 21st century. Hematology Am Soc Hematol Educ Program. 2010;2010(1):271–5.
2. Shavelle RM, MacKenzie R, Paculdo DR. Anemia and mortality in older persons: does the type of anemia affect survival? Int J Hematol. 2012;95(3):248–56.
3. Balducci L, Ershler WB, Krantz S. Anemia in the elderly-clinical findings and impact on health. Crit Rev Oncol Hematol. 2006;58(2):156–65.
4. Bianchi VE. Anemia in the elderly population. Journal of Hematology. 2015 Jan 3;3(4):95-106.
5. Makipour S, Kanapuru B, Ershler WB. Unexplained anaemia in the elderly. Semin Hematol. 2008;45(4):250–4.
6. Prakash KG, Devendrappa KR, Madhukumar MH, Priyashree R, Avinash BH. Clinical profile of anaemia in elderly: a cross sectional study from a tertiary care centre. Scholars Journal of Applied Medical Sciences. 2015;3(3C).
7. Joshi I, Thakur S, Bhawani R, Kaushal V, Mahajan A. Clinical profile and etiology of anaemia in elderly: A hospital based study at a tertiary care in the sub-Himalayan region. J Indian AcadGeriatr [Internet]. 2017; Available from: http://dx.doi.org/10.35262/jiag.v13i1.18-22.
8. Guralnik JM, Ershler WB, Schrier SL, Picozzi VJ. Anemia in the elderly: A public health crisis in Hematology. Hematology Am Soc Hematol Educ Program. 2005;2005(1):528–32.
9. Bhasin A, Rao MY. Characteristics of anemia in elderly: a hospital based study in South India. Indian J Hematol Blood Transfus. 2011;27(1):26–32.
10. Humaney NR, Ahmed DZ, Mundle DR. Clinicohematological Profile of Anemia in Hospitalized Elderly Patients. Journal of Medical Science and Clinical Research. 2014;2(8).