ISSN (Print): 2209-2870 ISSN (Online): 2209-2862



International Journal of Medical Science and Current Research (IJMSCR) Available online at: www.ijmscr.com Volume 5, Issue 1, Page No: 559-583 January-February 2022



# A Study Of Clinical Evaluation Of Anemia In Geriatric Patients

<sup>1</sup>Dr. K. Geetha Priyadarsini, <sup>2</sup>Dr. T.V.S.R.Raghu, <sup>3</sup>Dr T. Sree Dhar, <sup>4</sup>Dr. T.L.N. Geetha

MD, <sup>1,3</sup>Assistant Professor, <sup>2</sup>Designated Associate Professor, <sup>4</sup> MBBS;MD <sup>1,2,4</sup>Department of General Medicine, <sup>3</sup>Department of Pathology <sup>1,2,4</sup>Andhra Medical College, KGH, Visakhapatnam <sup>3</sup>Rangaraya Medical College, Kakinada

# \*Corresponding Author:

Dr. T.V.S.R. Raghu

MD, Designated Associate Professor, Department of General Medicine, Andhra Medical College, KGH, Visakhapatnam

Type of Publication: Original Research Paper Conflicts of Interest: Nil

# Abstract

Keywords: NIL

#### Introduction

Anemia is defined as a decrease in the quantity of hemoglobin. Anemia is prevalent in older individuals. The reported prevalence ranges from <3% in healthy persons aged 65 years and over to 61% in older patients admitted to geriatric wards.<sup>1;2</sup> These numbers not only diverge because of various definitions of anemia, but also because of significant differences in study populations concerning gender, age, race, living situation, and health status<sup>1,2</sup>.

The Third National Health and Nutrition Examination Survey (NHANES III), a nationally representative study of non-institutionalized civilian adults in the United States, the overall prevalence of anemia among adults aged 65 years and older was 11.0% in men and 10.2% in women.<sup>3</sup> For this study, anemia was defined according to World Health Organization criteria (hemoglobin concentration less than 12 g/dL (7.5 mmol/L) in women and less than 13 g/dL (8.1 mmol/L) in men<sup>4</sup>). Interestingly, the prevalence of anemia increased significantly with age, up to 26.1% in men and 20.1% in women aged 85 years and over.

In older persons, anemia is associated with impaired survival,<sup>5</sup> and also with decreased physical performance, disability in daily living, cognitive

impairment, depression, diminished quality of life, and an increased number of hospital admissions<sup>6,7</sup>.

### Aims & Objectives Of The Study

- 1. To study the clinical profile of Geriatric patients, presenting with a hemoglobin level of less than 11 gm %.
- 2. To study the etiological profile of anemia in Geriatric patients

### **Review Of Literature**

### Prevalence In The World And India

Who has classified anemia as the problem of public health significance into mild (5-19.9% prevalence of anemia), moderate (20-39.9%), and severe (>40% prevalence of anemia.) category<sup>9</sup>.

WHO global database on the worldwide prevalence of anemia has revealed that geriatric anemia is globally a public health problem of moderate category. The 3rd national health and nutrition examination survey (NHANES III)<sup>10</sup> undertook one of the comprehensive studies of geriatric anemia in the elderly USA population.

It is found that the overall prevalence of anemia in the population 65 yrs of age and older was 10.6%, with a prevalence of 11% for men and 10.2% for women. Mauro

LO

Tettamenti at al<sup>11</sup> studied 8744 elderly in Italy and found overall prevalence of anemia and mild anemia in the population to be 13.2% (14.1% in men and 12.6 % in women) and 11.1% he found that mild anemia(defined as hemoglobin concentration as 10-11.9 gm/dl in women and 10-12.9gm/dl in men ) accounted for the most of the cases (83%). The majority of these subjects were unaware of being anemic. They inferred that mild anemia in the elderly often goes unscreened and undiagnosed or is disregarded and not reported to the patient by the physician. Chronic disease anemia and renal insufficiency and thalassemia trait were the most frequent types of mild anemia. The underlying cause of mild anemia was unexplained in 26.4% of cases, almost one-third of which might be accounted for myelodysplastic syndrome. They concluded that mild anemia is common and frequently undiagnosed in the elderly.

#### **Anemia General Considerations**

#### **Definition Of Anemia**

A functional definition of anemia is a state in which the circulating red cell mass is insufficient to meet the oxygen requirements of the tissues. However, there are many compensatory mechanisms that restore the oxygen supply, and therefore in clinical practice, this definition is of limited value. A working of clinically useful definition would be that, anemia is present when hemoglobin concentration in blood is below the lower extreme of normal range, for the age and sex of the individual with often clinical findings like pallor of skin and the conjunctivae, Such a precise definition is essential because {a} the symptoms of anemia are often nonspecific and can be misinterpreted as symptoms of emotional, respiratory or cardiovascular disorder. {b} the reference values vary for different groups of the population.

### **Diagnostic Criteria For Anemia**

A normal range of hematological values are required for the diagnosis of anemia, which has been difficult to establish because of the problems encountered in the selection of the reference population. Locally prevalent values, cannot be equated to normal values. Hence the definition of anemia usually involves the adoption of certain arbitrary criteria. WHO recommends the following hemoglobin levels for diagnosis of anemia: Adult male <13g/dl, adult female <12g/dl.

#### A General Approach To Anaemias

Anemia is not a diagnosis, but merely an objective sign of the presence of a disease. Therefore an orderly approach is required to come to the etiological diagnosis of anemia, which is necessary for appropriate management. This requires consideration of

- 1. The clinical features
- 2. The type of anemia indicated by examination of blood
- 3. The results of further investigations did as required.

In the recognition and investigation of anemic patients, three fundamental questions have to be considered

1:- Is patient anemic.

2:- If yes, what is the type of anemia indicated by examination of blood.

3:- What is the cause of anemia

### IS THE PATIENT ANEMIC

The symptoms that point to the possibility of anemia are fatigue, tiredness, effort intolerance, palpitations, giddiness, etc. These symptoms are not specific for anemia and can be easily misinterpreted. Unequivocal conjunctiva pallor is not inevitably present in all the patients with anemia. The presence of anemia is established by laboratory confirmation of a subnormal hemoglobin level.

### The Type Of Anemia

.......

The type of anemia is generally indicated by the features of the red cells, leukocytes, and platelets noted in the examination of blood. Three main types of anaemias are recognized on the basis of the mean cell volume {MCV}, mean cell hemoglobin {MCH}, and mean cell hemoglobin concentration of the red cells. {MCHC}.

Red cell indices<sup>17,18,19</sup>, Mean cell volume {MCV} – normal MCV:85+/-9fl. ,Mean cell hemoglobin {MCH – normal MCH:29.5+/-2.5pg ,Mean cell

. . . . . . . . . . . .

hemoglobin concentration {MCHC} normal-33+/-2/dl<sup>20</sup>.

### Hypochromic microcytic anemia's<sup>21</sup>:-

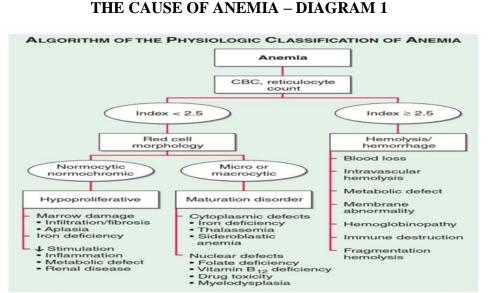
The MCV is subnormal, {<approx.80fl}, as is the MCH, {<approx.27pg} and MCHC, {< approx.30g/dl}, Such abnormal indices correspond to microcytosis and hypochromia, respectively of red cells in the blood film this type of anomaly can be viewed as the result of a defect in red cell formation in which hemoglobin synthesis is impaired to a greater extent than other cellular components. Ex: iron deficiency anemia, thalassemia.

#### Normocytic normochromic anemia's

The MCV, MCH, and MCHC are within the normal range, corresponding to normal size and hemoglobinization of red cells in the blood film. Ex: following the loss of substantial volumes of blood, hemolysis, impaired red cell production by the bone marrow.

# Macrocytic anemia's <sup>22</sup>

The MCV is above the upper limit of normal {>96fl}, corresponding to macrocytosis of red cells in the blood film. The red cells are usually normochromic. Ex: vitamin B 12 deficiency, folic acid deficiency



Anemia is generally regarded to result from – blood loss

Impaired red cell production

Excessively rapid red cell destruction

**Basic Etiopathophysiological Categories Of Anemia** 

# **1. IMPAIRED RBC PRODUCTION**

### i) Inadequate supply of nutrients

- a) Iron deficiency
- b) Vitamin B 12 deficiency
- c) Folic acid deficiency
- d) Protein calorie malnutrition
- ii) Depression of erythropoietic activity
- iii) Anemia associated with renal failure
- iv) Anemia associated with chronic diseases, such as

Infections, connective tissue disorder, an inflammatory disorder, disseminated malignancy, etc.

v) aplastic anemia

#### vi) Anemia due to infiltration of normal bone marrow by

- \* leukemia
- \* lymphoma
- \* myeloproliferative disorders
- \* myeloma
- \* myelodysplastic syndromes
- vii) anemia due to inherited abnormality, such as thalassemias.

### 2. EXESSIVE RED CELL DESTRUCTION:

- i) Due to intrinsic defect in RBD
- ii) Due to extrinsic effects on RBC

### **BLOOD LOSS**

### 3. ANEMIA DUE TO BLOOD LOSS and ANEMIA DUE TO ACUTE BLOOD LOSS <sup>27</sup>

# 4. ANEMIA DUE TO IMPAIRED RED CELL PRODUCTION.

# INADEQUATE SUPPLY OF NUTRIENTS ESSENTIAL FOR ERYTHROPOIESIS:

- a) IRON DEFICIENCY ANEMIA.
- b) ANEMIA DUE TO DEFICIENCY OF VITAMIN B-12<sup>34</sup>
- c) ANAEMIA DUE TO DEFICIENCY OF FOLIC ACID.
- d) ANEMIA ASSOCIATED WITH CHRONIC DISORDERS <sup>41</sup>.

### 5. APLASTIC ANEMIA.

### 6. ANEMIA DUE TO REPLACEMENT OF NORMAL BONE MARROW

Leukaemias:

- Lymphomas
- i) Hodgkin's disease
- ii) Non-Hodgkin's lymphoma

Myelodysplastic syndromes 49:

### 2.ANAEMIAS DUE TO EXCESSIVE RED CELL DESTRUCTION

### CLASSIFICATION OF HAEMOLYTIC ANAEMIAS:

### 1. Haemolytic anaemia's due to intravascular mechanisms

i. CONGENITAL:

1) Membrane defects<sup>59</sup>:

- -- hereditary Spherocytosis
- -- hereditary elliptocytosis
- -- hereditary xerocytosis and hydrocytosis.

2) Hemoglobin defects:-

-- hemoglobinopathies

- Sickle cell anemia
- Unstable hemoglobin disease
- Hb-C, Hb-E, Hb-D.
- -- thalassemias
- -- sickle beta-thalassemia

3) Enzyme defects—Non-spherocytic congenital hemolytic anemia's<sup>60</sup>

- Deficiency of pyruvate kinase

- Deficiency of G-6 PD

-- Drug-induced hemolytic anemia's

ii. ACQUIRED:

Paroxysmal nocturnal hemoglobinuria.

### 2. Hemolytic anemia due to extracorpuscular mechanisms:

- i. IMMUNE MECHANISMS:
  - 1. Autoimmune acquired hemolytic anemia
    - -- Warm antibody
    - -- Cold antibody
  - 2. Hemolytic disease of the newborn.
  - 3. Incompatible blood transfusion
  - 4. Drug-induced hemolytic anemia.

### ii. NON IMMUNE MECHANISMS:

Mechanical - cardiac, microangiopathic, etc.

- iii. MISCELLANEOUS:
- 1. Infections
- 2. Burns
- 3. Lead poisoning.

### 3. <u>HAEMOLYTIC ANEMIA DUE TO RED CELL ENZYME DEFECTS</u>:

### 1. Drug-induced hemolytic anemia's:

Is due to the deficiency of glucose-6 phosphate dehydrogenase  $(G-6PD)^{67}$ . The disorder is transmitted by a sexlinked gene of intermediate dominance, which is located on the long arm of the X – chromosome.

Drug causing hemolysis in G-6PD deficient subjects:

- 1. Antimalarials: primaquine, primaquine
- 2. Sulphones: dapsone
- 3. Sulphonamides: sulphamethoxazole, sulphasalazine, sulphapyridine.
- 4. Nitrofurantoin

- 5. Analgesics: acetanilid
- 6. Miscellaneous: Vitamin-K, methylene blue, doxorubicin, toluidine blue, furazolidone, niridazole, nalidixic acid, naphthalene, trinitrotoluene, phenazopyridine.

#### 2. Non-spherocytic congenital hemolytic anemia's:

These are due to the deficiency of enzymes in the HMP pathway. There is no spherocytosis in the peripheral film. The osmotic fragility of the red cell is not increased and splenectomy gives a little or only moderate benefit.

#### 4.<u>AUTOIMMUNE ACQUIRED HAEMOLYTIC</u> <u>ANAEMIAS</u>

The result from the development of antibodies directed against an antigen on the surface of the red cells<sup>68</sup>. The formation of the antibodies appears to be due to breakdown in the T-cell regulation of the B-cells, with the emergence of a hostile clone of immunocytes to a change in the antigen structure of the RBC surface, which is then recognized as non-self by the immune system.

Warm antibody AIHA occurs at all ages, but adults are affected more Frequently than children<sup>69.</sup>

#### 1) COLD HAEMAGGLUTININ DISEASE:

2).PAROXYSMAL COLD HAEMOGLOBINURIA:

#### 5.<u>HAEMOLYTIC ANEMIA DUE TO DRUGS</u>:

- 1. Direct toxic actions of drugs and chemical:
- 2. Drugs that cause hemolysis in subjects with G-6PD deficiency.
- 3. Drugs that cause by immune mechanisms:<sup>72</sup>
- 4. Immune: Cephalosporins, cis-platinum, erythromycin, penicillin, quinine
- 5. Rifampicin, PAS, sulfonamides, tetracycline's
- 6. Autoimmune: L-dopa, methyl dopa, procainamide, mefenamic acid.

### 6.<u>ANAEMIA OF UNKNOWN ETIOLOGY<sup>73</sup></u>

Anemia of unknown etiology is usually mild, with hemoglobin levels lower than the WHO standard. The red blood cells are typical of normal morphology, and examination of the peripheral smear reveals no abnormality. However, anemia of unknown etiology is not so much unexplained as it is multi-factorial. Several age-associated physiological changes may contribute to either a decreased red blood cell production or shortened red blood cell survival, and these in the composite are likely to be at the root of UA. Included in these physiological changes are age-related renal insufficiency, stem cell aging, androgen insufficiency.

#### 7.<u>PHYSIOLOGICAL CHANGES ASSOCIATED</u> <u>WITH AGING</u>

Insufficiency of erythropoietin- Age-associated decline in GFR and the corresponding reduction in erythropoietin response.

Inhibition of erythropoiesis by cytokines-Proinflammatory cytokines, like IL-6, is elevated in serum and tissue sections with advancing age.

Decreased levels of androgens in both females and males-

- 1. Androgens support erythropoiesis, and levels are decreased with advancing age.
- 2. Stem cell function- Hematopoietic stem cells decline in both proliferative and replicative capacity with age
- 3. Age-Associated Renal Insufficiency<sup>74</sup>

Renal function decreases with age, even in the absence of clinical disease. The decline may be more pronounced in persons with underlying conditions, such as diabetes mellitus or hypertension. In addition to the excretory function, the kidney is the primary source of erythropoietin, and erythropoietin production is known to be decreased in patients with renal insufficiency, accounting for the anemia associated with renal failure. Under normal circumstances, as age increases, erythropoietin levels increase. However, for subjects with a history of hypertension and diabetes mellitus, the ageassociated rise in erythropoietin is significantly less, or not existent, and hemoglobin levels for these individuals decline in later years. Erythropoietin levels are lower than expected in the larger group of the geriatric population who fulfill criteria for UA, and this occurs even in the absence of clinically evident renal insufficiency.

# Stem Cell Aging<sup>75</sup>

As age progresses, hematopoietic stem cells undergo qualitative changes, resulting in reduced regenerative

and proliferative capacity. In the absence of disease, stress, or an abnormal homeostatic demand (e.g., erythroid reconstitution after systemic chemotherapy), whether these age-related changes account for cytopenias in general or specifically anemia, remains unknown.

#### Androgen Insufficiency<sup>76</sup>

Androgens have a stimulatory effect on erythropoiesis, and hormonal treatment remains effective for some patients with hypoplastic or aplastic anemia. Patients with androgen insufficiency, such as observed after pharmacologic androgen ablation for prostate cancer or orchiectomy, typically have a drop in hemoglobin level ranges from 1 g/dL to 2.5g/dl. Thus, it is likely that an age-related decline in androgen contributes to some extent to a decline in erythroid mass and development of anemia

#### **Materials And Methods:**

#### **Inclusion Criteria**

Geriatric patients above 60 years of age, with anemia and hemoglobin of less than 11 gm% were included in the study.

**Study period-** From October 2018 to September 2019.

#### **Exclusion Criteria**

1. All female patients and male patients below 60 yrs.

- 2. Hemolytic anemias
- 3. Patients on treatment for anemia were excluded from the study

#### **Study Protocol**

100 elderly patients admitted to the medical wards with various clinical presentations were studied. All the patients were subjected to a detailed history and physical examination. Their social and dietary habits were enquired. The details were recorded in the proforma.

All the patients underwent a series of diagnostic investigations. They were haemograms, ESR, blood urea, blood sugar, serum creatinine, serum electrolytes, complete urine examination, stool for ova and cysts, stool for occult blood, and a chest Xray, iron studies, serum b12 and folate levels. Additional investigations were done as required in the case of the establishment of the diagnosis. Bone marrow aspiration cytology was performed and when needed bone marrow trephine biopsy was also done.

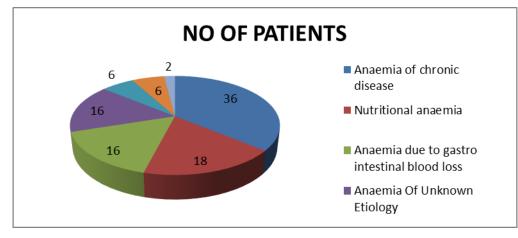
#### **Observations, Results And Data Analysis**

#### Etiology

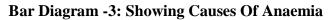
Based on the clinical history, examination, morphological characteristics are seen on peripheral smear and bone marrow, stool for ova and cysts, stool for occult blood and a chest X-ray, iron studies, serum b12, and folate levels and other relevant diagnostic modalities the following etiological recognized categories were in this study.

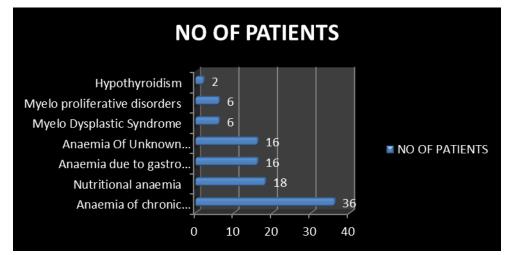
Sno	ETIOLOGY	NO OF PATIENTS	PERCENTAGE
1	Anemia of chronic	36	36%
	disease		
2	Nutritional anaemia	18	18%
3	Anemia due to gastro	16	16%
	intestinal blood loss		
4	Anaemia Of Unknown	16	16%
	Etiology		
6	Myelo Dysplastic Syndrome	6	6%
7	Myeloproliferative disorders	6	6%
8	Hypothyroidism	2	2%

#### TABLE NO 1









#### Age & Sex Distribution

There were 44 female and 56 male patients with age starting from 60 yrs and above. The distribution of 100 patients is as follows

#### TABLE NO 2

S no	AGE GROUP	MALE	FEMALE	TOTAL	PERCENTAGE
1	60-65	18	16	34	34%
2	66-74	18	12	30	30%
3	75-84	14	10	24	24%
4	85 ABOVE	6	6	12	12%
TOTAL		56	44	100	100

iage 566

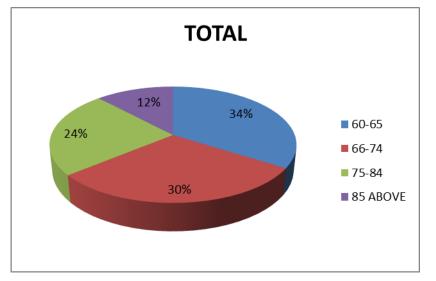
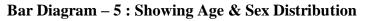


Diagram No 4- Pie Diagram Showing Age Distribution



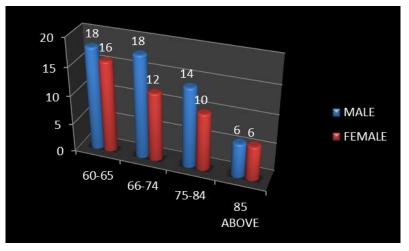


Table No 3- Etiology - Age Groups

		80 8	-	
ETIOLOGY	60-65	66-74	75-84	85 &above
1.Nutritional anaemia	4	4	6	4
2.Anaemia of chronic disease	12	16	6	2
3.Anemia due to GI blood loss	2	12	2	
4.Anemia of unknown etiology	6		4	6
6.Myeloid dysplastic syndrome		2	4	

Fage 567

7.Myeloproliferative disorders	6		
8.Hypothyroidism	2		

According to the distribution of age groups above 60 years, the etiologies including Nutritional anemia, Anaemia due to chronic disease, Anaemia due to GI blood loss, and anemia of unknown etiology are distributed equally in all age groups.

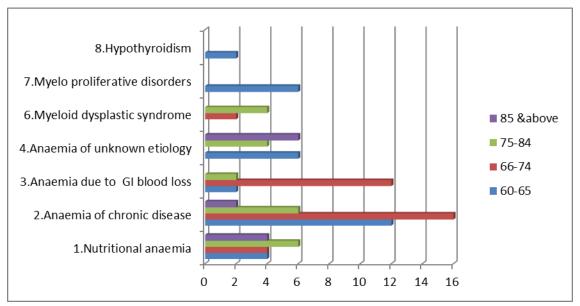


Diagram No 6 - Bar Diagram Showing Etiology –Age Groups

### **Clinical Features**

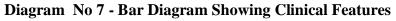
The common symptoms with which patients presented in this study are :

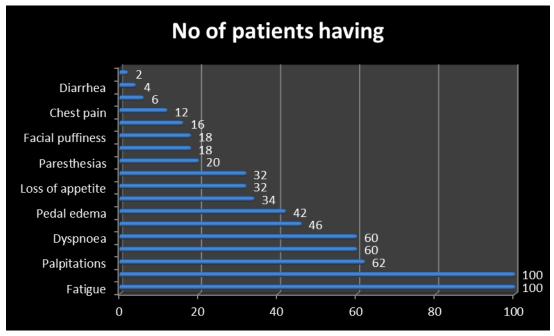
#### **TABLE NO 4**

Symptoms	No of patients having	% of the total
Fatigue	100	100
Tiredness	100	100
Palpitations	62	62
Giddiness	60	60
Dyspnoea	60	60
Wt loss	46	46
Pedal edema	42	42
Fever	34	34
Loss of appetite	32	32
Abdominal pain	32	32
Paresthesias	20	20

Oliguria	18	18
Facial puffiness	18	18
Blood in stools	16	16
Chest pain	12	12
Jaundice	6	6
Diarrhea	4	4
Focal deficit	2	2

All the patients had easy fatiguability, and tiredness.60% of them had giddiness and shortness of breath on exertion in 60% and palpitations in 62%, pedal edema in 42% of patients, and oliguria and facial puffiness in 18% of patients. Blood in stools in 16% of patients. The varied symptomatology in the study might be due to the varied etiological categories.





### **Cardiovascular Signs & Symptomatology**

**Cardinal Murmurs In Cvs** 

	No of		Hem	oglobin g	gm/dl	Pe	rcentage	
Murmurs	pts	% age						
			3-5.5	5.6-8	8.1-11	3-5.5	5.6-8	8.1-11
P ESM	58	58%	12	34	12	12%	34%	12%
A ESM	_	_	_	_	_	_	_	_

Fage 569

-								
M PSM								
	—	_	—	_	_	—	—	-

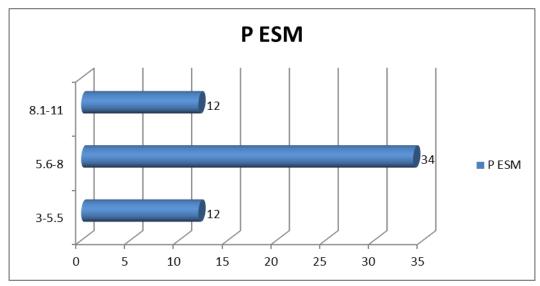
P ESM: pulmonary ejection systolic murmur

A ESM: aortic ejection systolic murmur

M PSM: Mitral pan systolic murmur

About 58 (58%) patients had a P ESM

Diagram No 8: Bar Diagram Showing Cardinal Murmurs In Cvs



**Congestive Cardiac Failure :** The presence of congestive cardiac failure was established on the major/minor Framingham criterion for the diagnosis of congestive heart failure

Age group	Number	Pts in CHF	% of pts having CHF
60-65	34	6	15.9%
66-74	30	2	6.6%
75-84	24	12	50%
85above	12	2	16.7%

#### **TABLE NO 6 - AGEWISE**

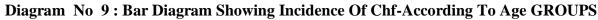
#### **TABLE NO 7- SEVERITY**

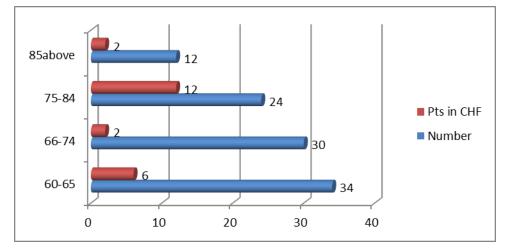
Hemoglobin %	Number of pts	Pts with CHF	% of pts in CHF
3.1-5.5	10	8	80%
5.6-8	38	10	26.5%
8.1-11	52	4	7.6%

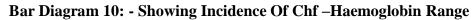
The above two tables show a high incidence of CHF in pts who are in the age group of 75-84 with 50% of patients, and about 80% of patients with hemoglobin in the range of 3.1-5.5 had CHF. Only 2 patients with

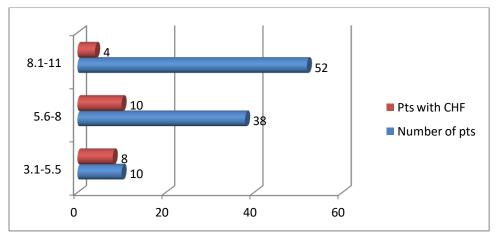
Page

hemoglobin in this range did not have CHF. And the incidence of CHF decreased as the severity of anemia decreased, being about 7.6% with hemoglobin of 8.1-11 gm%.





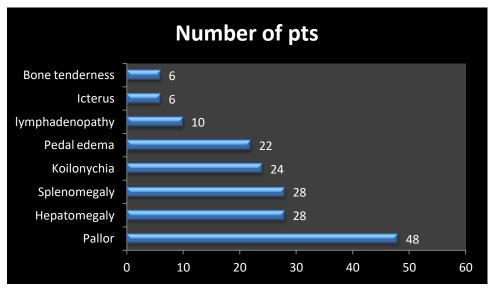




Clinical Signs In Hemopoietic System - Table No 8

Clinical sign	Number of pts	% of patients
Pallor	48	48%
Hepatomegaly	28	28%
Splenomegaly	28	28%
Koilonychia	24	24%
Pedal edema	22	22%
lymphadenopathy	10	10%
Icterus	6	6%
Bone tenderness	6	6%

Of the clinical features, pallor was the most predominant feature in about 48 % of patients, followed by Hepatomegaly and splenomegaly in about 28% of patients, koilonychia in about 24% of patients.



Bar Diagram No 11: Showing Clinical Signs In Haemopoetic System

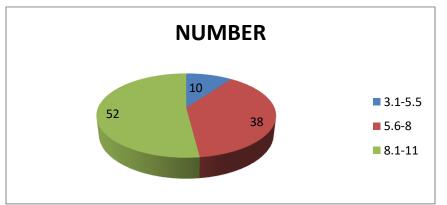
# Hematological Characteristics

### **TABLE NO 9**

Hemoglobin (gm%)	NUMBER	% OF TOTAL
3.1-5.5	10	10%
5.6-8	38	38%
8.1-11	52	52%

In this study majority of patients had hemoglobin greater than 3 gms%.

Pie Diagram 12 : Showing Haemoglobin –No Of Patients



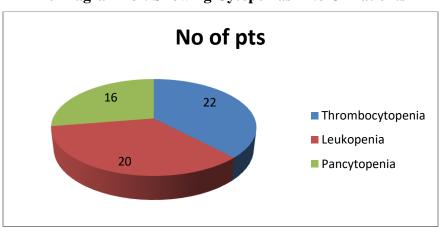
 $\dot{P}_{age}572$ 

CELL LINE	No of pts	Percentage
Thrombocytopenia	22	22%
Leukopenia	20	20%
Pancytopenia	16	16%

#### **Cytopenias Table No 10**

Of the 22 patients with thrombocytopenia 8 had nutritional anemia,6 patients had MDS,6 patients had anemia of chronic disease,2 cases had acute myeloid leukemia. Of the 20 patients with leucopenia, 6 patients had B12 deficiency anaemia,6 patients had the myelodysplastic syndrome,4 patients had anemia of chronic inflammation,2 patients had dimorphic anemia,2 patients had iron def anemia.

Of the 16 patients with pancytopenia, 4 patients had B12 deficiency anemia,4 patients had anemia of chronic inflammation, 6 patients had myelodysplastic syndrome,2 patients had dimorphic anemia.

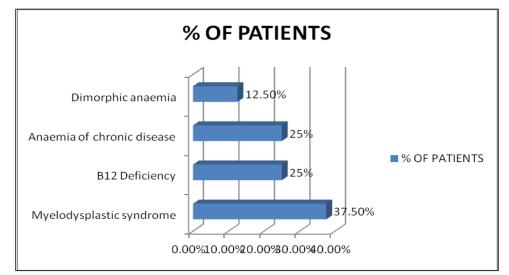


**Pie Diagram 13 : Showing Cytopenias - No Of Patients** 

### **Etiologies For Pancytopenia - Table No 11**

ETIOLOGY	NO OF PATIENTS	% OF PATIENTS
Myelodysplastic syndrome	6	37.5%
B12 Deficiency	4	25%
Anemia of chronic disease	4	25%
Dimorphic anemia	2	12.5%

Of the 16 patients with pancytopenia, 4 patients had B12 deficiency anemia,4 patients had Anaemia of chronic inflammation,6 patients had myelodysplastic syndrome,2 patients had dimorphic anemia.



### **Bar Diagram 14 - Showing Etiologies For Pancytopenia**

### Peripheral Smear - Table No 12

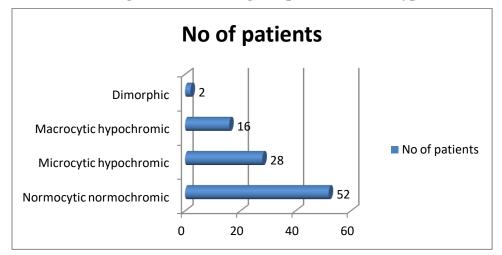
Peripheral smear	No of patients	% of patients
Normocytic normochromic	52	52%
Microcytic hypochromic	28	28%
Macrocytic hypochromic	16	16%
Dimorphic	2	2%

Of the 28 cases of microcytic hypochromic anemia 8 cases were nutritional, 16cases are due to blood loss,2 cases are due to Anaemia of chronic kidney disease, 2 cases are due to chronic inflammation.

Of the 52 cases of Normocytic normochromic anemia, 32 cases were due to anemia of chronic disease or inflammation, 16 cases were due to Anaemia of unknown etiology,4 cases were due to chronic myeloid leukemia

Of the 16 causes of macrocytic anemia, 6 cases were due to B12 def anemia,2 cases are due to folate def anemia,6 cases were due to myelodysplastic syndrome,2 cases were due to hypothyroidism.

### **Bar Diagram 15 - Showing Peripheral Smear – Types**

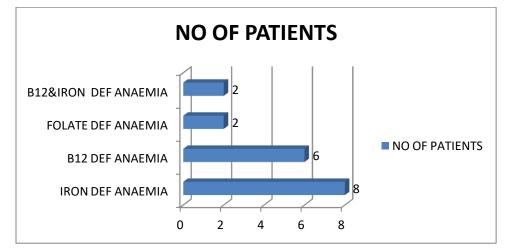


Volume 5, Issue 1; January-February 2022; Page No 559-583 © 2022 IJMSCR. All Rights Reserved

TYPE OF ANAEMIA	NO OF PATIENTS	PERCENTAGE%	
IRON DEF ANAEMIA	8	44.25%	
B12 DEF ANAEMIA	6	33.25%	
FOLATE DEF ANAEMIA	2	11.25%	
B12&IRON DEF ANAEMIA	2	11.25%	

Nutritional Anaemia Types - Table No 13

### **Bar Diagram 16- Showing Nutritional Anaemia Types**

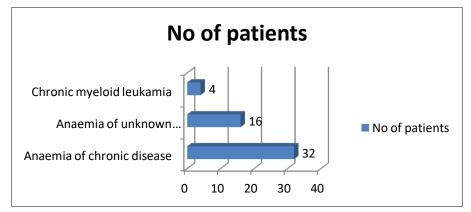


Etiologies For Normocytic Normochromic Anaemia - Table No 14

Disease type	No of patients	% of patients
Anemia of chronic disease	32	61.6%
Anemia of unknown etiology	16	29.8%
Chronic myeloid leukemia	4	7.7%

Of the 52 cases of Normocytic normochromic anemia, 22 cases were due to anemia of chronic disease or inflammation, 10 cases were due to chronic kidney disease,16 cases were due to anemia of unknown etiology,4 cases were due to chronic myeloid leukemia.



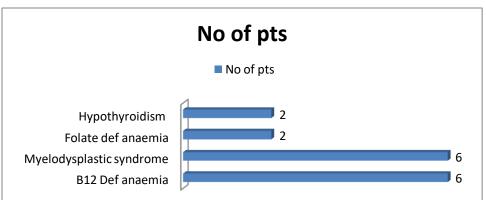


Volume 5, Issue 1; January-February 2022; Page No 559-583 © 2022 IJMSCR. All Rights Reserved

U	•	
Etiology	No of pts	% of pts
B12 Def anaemia	6	37.5%
Myelodysplastic syndrome	6	37.5%
Folate def anemia	2	12.5%
Hypothyroidism	2	12.5%

Etiologies For Macrocytic Anaemia - Table No 15

Of the 16 cases of macrocytic anemia, 6 cases were due to B12 def anemia,2 cases were due to folate def anemia,6 cases were due to myelodysplastic syndrome,2 cases were due to hypothyroidism.

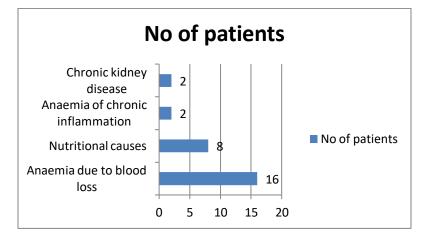


### **Bar Diagram 18 : Showing Etiologies For Macrocytic Anaemia**

<b>Etiologies For M</b>	licrocytic Hypochromic A	Anaemia - Table No 16
-------------------------	--------------------------	-----------------------

S no	Etiology	No of patients	Percentage
1	Anemia due to blood loss	16	57%
2	Nutritional causes	8	28%
3	Anemia of chronic inflammation	2	7%
4	Chronic kidney disease	2	7





Bar Diagram 19 : Showing Etiologies For Microcytic Hypochromic Anaemia

#### Discussion

The most common cause of anemia worldwide in the elderly is anemia of chronic disease. Iron deficiency is frequently seen in the elderly, typically as a result of chronic blood loss through GIT. Vitamin B12 deficiency, folate deficiency, MDS are among other causes of anemia in elderly

After evaluating 100 elderly patients with anemia and hemoglobin of less than 11 gm %, Anemia of chronic disease was found to be the most common cause (36%), Nutritional anemia accounted for the next largest group with 18% of the cases, followed by anemia due to GI blood loss & anemia of unknown etiology in 16% of patients. All the other causes were scattered in 2 or 3 patients in each. These findings were similar to the study conducted by Matthew Rong Jie Tay1, Yong Yau Ong2, Yong Loo Lin School of Medicine, National University of Singapore, Singapore.

In a study done on clinical Evaluation of Anemia in Elderly Patients A By Dr. Jyoti Vora et al<sup>77</sup> at Ahmedabad Among the causes for anemia, Iron Deficiency Anemia (IDA) was the commonest constituting 41.81% of the cases followed by Anemia of Chronic Inflammation (ACI) which constituted 31.81 % of the cases.

In patterns of geriatric anemia: A hospital-based observational study in North India by Dr Dheeraj et  $al^{78}$  showed the etiological distribution of anemia was iron deficiency in 26 patients (24.8%), chronic disease in 24 patients (22.9%), hematological disorders in 21 (20%), chronic kidney disease in 13

(12.4%), multifactorial in 8 (7.6%), vitamin B12 deficiency in 2 (1.9%), folate deficiency in 1 (0.9%), and hypothyroidism in 1 patient (0.9%). No etiology could be found in 9 patients (8.6%).

Ramachandra et al. <sup>12</sup> studied 4965 geriatric persons in the rural area situated about 30 km away from Bangalore city in the Karnataka state of south India covered by a government-run sub-center.The prevalence of geriatric anemia was estimated to be 17.7%, and the prevalence increased with age in the study.

Swathi parnami et al. <sup>13</sup> studied 250 geriatric women under five zones of Baroda city and found the prevalence of anemia to be 51.6%. The sociodemographic data of elderly women subjects showed that the majority of anemia subjects were in the age group of more or equal to 70 yrs. A communitybased study of the morbidity profile among the elderly in the rural and urban areas of Chandigarh by swami et a<sup>14</sup> revealed a very high prevalence (68.2%) of anemia among the elderly. They observed that anemia was more in elderly females.

Maninder Kaur and kochar<sup>15</sup> found that 89% of the elderly rural and urban jat women in Haryana were suffering from anemia, and these high rates of anemia among elderly women reflect their social and biological vulnerability in society and the household.

A hospital-based study from Banglore <sup>16</sup> by Amith basin and MY RAO in 100 patients of geriatric anemia revealed that the mean age of the patients was 70.51 yrs with a male preponderance (52% were males, and 42% were females ). It found that the

Page

most common cause of anemia was found to be anemia of chronic disease followed by iron deficiency anemia followed by anemia of blood loss. The study highlighted that the fact that most of the anemic elderly had an underlying treatable cause for anemia.

Thus the prevalence of anemia in India varies from 17.7% to 89%. These figures communicate just half the truth. When we convert these percentages into absolute figures, When we realize that majority of elderly in India do not have health insurance and when we are confronted with the truth that elderly in our cities are being forced to lead a marooned life, the picture becomes grim and intimidating. In our study, the most common anemia was found to be AOCD, followed by Irondef anemia, followed by anemia of blood loss.

Elejalde Guerra et al<sup>79</sup>. Revealed that Iron def anemia is the most frequent, followed by hemorrhagic anemia and AOCD. Our study does not tally with the findings of this study.

A study on clinical evaluation of anemia in geriatric patients - a cross-sectional study, conducted at tertiary care hospital by Sfurti Mann<sup>80</sup> showed Among all the patients (irrespective of age groups and types of anemia), ACD was found to be most common (41.67%), followed by IDA (35%), MDS (5%), Megaloblastic anemia (3.34%), myelofibrosis and hemolytic anemia (3.34% each) and aplastic anemia (1.67%).

In this study, the age distribution was above 60 yrs. The maximum no of patients was in the 60-65 yrs age group & the minimum no of patients was represented by 85 yrs & above. Anemia of chronic disease and anemia due to gastrointestinal blood loss were the main etiologies in the age group of 66-74yrs. Nutritional anemia was distributed equally in all age groups.

It is observed in this study that nutritional anemia was still the major cause of anemia in elderly patients after the anaemia of chronic disease. The nutritional deficiency as the cause was concluded in all the cases based on the low b12 & folate levels in serum & absent iron stores in the bone marrow. All these pts were thoroughly worked up for any other explainable cause of anemia. This was similar to the study conducted by Guralnik *et al*<sup>81</sup> as Iron deficiency anemia is a common cause of anemia in the elderly

In this study, all elderly patients are presented with hemoglobin < 11 gm%, of which 10 % have hemoglobin <5.5 gm%,48% have haemoglobin < 8 gm%, and 52% of them have hemoglobin levels between 8.1-11 gm%.

In this study, all the patients had easy fatiguability &tiredness as the most common symptoms.thse were followed by the palpitations in 62% of patients giddiness and dyspnoea in 60 % of patients & weight loss in about 46% of patients pedal edema in 42 % of patients and loss of appetite in 32 % of patients.

In a study done on clinical Evaluation of Anemia in Elderly Patients A

By Dr. Jyoti Vora et al<sup>77</sup> at Ahmedabad Out Of the 110 patients, the commonest symptom was easy fatiguability (in 74.54%), followed by Abdominal Distension (22%), and the commonest sign was pallor (in 92.72%) followed by pedal edema (in 20%). 22 % of patients presented with congestive heart failure. The incidence of congestive heart failure is more in the 75-84 yrs age group. Myelodysplastic syndrome, B12 def anemia, anemia of chronic disease, and dimorphic anemia (both iron&b12 combined def) were the main causes of pancytopenia in this study. In our study, 8% had iron def anemia, 6% had a B12 deficiency, and 2% had folate deficiency.

Jack and co-workers<sup>82</sup> revealed that 16.6% of the patients had only iron deficiency, 6.4% had folate deficiency only, and 5.9% of the patients had a B12 deficiency. Hence our study corroborates with the findings of this study, iron deficiency being the most common of nutrient deficiency anemia.

In our study, normocytic anemia was the most prevalent anemia on peripheral smear which was due to anemia of chronic disease, anaemia of unknown etiology & chronic myeloid leukemia in both the sexes accounting for 52%,

This corroborates with the study done by Elis et al.<sup>83</sup> and Ania et al.<sup>84</sup> 36% of all the cases in our study were anemia of chronic disease, of which 12% of the patients in our study were found to have renal failure.

 $\infty$ 

Jack and co-workers revealed anemia due to chronic renal failure were found in 13.2% of patients.

Although there is paradoxical feedback in renal production of erythropoietin, since the levels of this hormone increase over time, it has also been reported that the erythroid marrow may become less sensitive erythropoietin stimulation, a kev to factor contributing along with possible nutritional deficits and comorbidities to the development of anemia in the elderly. Even distinguishing anemia of chronic inflammation from anemia of chronic kidney disease is somewhat challenging considering the fact that increased inflammation is seen in older adults even without chronic kidney disease, and there are coexisting morbidities in this age group.

While studies suggest that vitamin B12 (cobalamin) deficiency is the cause of anemia in 5–10% of elderly patients, the actual prevalence of vitamin B12 deficiency is likely to be much higher. Vitamin B12 deficiency is difficult to detect in the elderly. First, the symptoms and signs of vitamin B12 deficiency are not reliably present in the elderly. Only about 60% of such patients are anemic. In addition, neurologic symptoms of B12 deficiency can develop before the patient becomes anemic. Second, although this anemia is usually macrocytic and megaloblastic, it can be normocytic or even microcytic. Third, serum B12 levels do not reliably reflect tissue B12 deficiency. Up to 30% of patients with low-normal serum vitamin B12 levels have anemia and neurological disease. Like vitamin B12 deficiency, folate deficiency classically causes macrocytic anemia, although a significant proportion of elderly patients with folate deficiency have normocytic anemia .6 cases of myelodysplastic syndrome and 2 cases of hypothyroidism were represented by the macrocytic picture on peripheral smear

In our study, in patients with iron def anemia, an upper GI lesion was found in 28% of the patients, and a colonic lesion was found in 14% of the patients. A GI malignancy was detected in 7% of the patients, which is in agreement with various studies and reinforces the need for gastrointestinal tract evaluation as although some cases of iron deficiency do result from diet. blood loss through gastrointestinal including malignancies lesions contribute significantly in older adults. In our study, colonic malignancy was found in 7% of the patients with IDA.

Rockey and Cello<sup>85</sup> found that 16% of IDA had underlying colon cancer or premalignant polyps. Hence our study corroborates with this study where an underlying colonic lesion was found in a significant percentage of patients who had an iron deficiency. The diagnosis of iron deficiency in the absence of any history of hemorrhage or unexplained anemias should be taken as evidence of occult gastrointestinal bleeding, and gastrointestinal tract evaluation should be performed.

In our study, only 16% of patients had no obvious underlying cause. In our study 6% of cases had MDS. Beghe et al.<sup>86</sup> showed that 14–50% of anemic elderly had no obvious underlying cause. Jack and coworkers revealed 33.6% of the patients in his study group had unexplained anemia. Other study groups have reported that it is likely that some proportion of anemia of unknown etiology cases is caused by myelodysplastic syndrome (MDS), another common hematologic condition in older adults.

Our study hence highlights the fact that most of the anemic elderly have an underlying treatable cause for anemia. It is essential, therefore, that the treating physician is aware of the coexistence of anemia in the elderly, although the presenting manifestation maybe for a different reason. It becomes, thus, all the more pertinent to look for severity and type of anemia, possible etiologies, and appropriate correction. As normocytic anemia is the most common blood smear diagnosis, it is important to bear in mind that normocytic blood picture in an anemic elderly should not be disregarded.

#### **Summary & Conclusions**

. . . . . . . . . . . . . . . . . . .

- 1. Anemia of chronic disease(36%) is the most common cause of elderly anemia in this study.
- 2. Easy fatiguability and tiredness are the most common symptoms in this study.
- 3. Of 80% of patients presented with hemoglobin < 5.5gm% were given with congestive heart failure.
- 4. Anemia of unknown etiology is one of the important factors observed in this study.
- 5. B12 def anemia and myelodysplastic syndrome are the important causes of pancytopenia in this study.

- 6. Normocytic normochromic type of anemia (52%) is the most predominant type on peripheral smear in this study.
- 7. Of the nutritional causes of iron deficiency, anemia is the most common occurrence in this study

#### References

- 1. Beghe C, Wilson A, Ershler WB. Prevalence and outcomes of anemia in geriatrics: a systematic review of the literature. *Am J Med.* 2004;116 Suppl 7A3S-10S.
- 2. Gaskell H, Derry S, Andrew MR, McQuay HJ. Prevalence of anemia in older persons: a systematic review. *BMC Geriatr.* 2008;8:1.
- 3. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia. *Blood.* 2004;104(8):2263-2268.
- 4. Nutritional anemias. Report of a WHO scientific group. *World Health Organ Tech Rep Ser.* 1968;4055-37.
- 5. Culleton BF, Manns BJ, Zhang J, Tonelli M, Klarenbach S, Hemmelgarn BR. Impact of anemia on hospitalization and mortality in older adults. *Blood.* 2006;107(10):3841-3846.
- 6. Chaves PH. Functional outcomes of anemia in older adults. *Semin Hematol.* 2008;45(4):255-260.
- 7. Penninx BW, Pahor M, Cesari M, et al. Anaemia is associated with disability and decreased physical performance and muscle strength in the elderly. *J Am Geriatr Soc.* 2004;52(5):719-724.
- Penninx BW, Pluijm SM, Lips P et al. Late-life anemia is associated with an increased risk of recurrent falls. J Am Geriatr Soc. 2005;53(12):2106-2111.
- Benoist BD, McLean Erin, Egli Ines, Cogswell Mary. Worldwide prevalence of anemia 1993-2005: WHO Global Database on Anaemia. Spain: WHO, 2008.
- 10. Steensma DP, Tefferi A. Anemia in the elderly: How should be define it, when does it

matter, and what can be done? Mayo Clin Proc. 2007, 82 (8): 958-966.

- 11. Tettamanti M. Lucca U, Gandini F, Recchia A, Musconi P, Apolone G et al. Prevalence, incidence, and types of mild anemia in the elderly the "Health and Anemia" populationbased study. Haematologica 2010.95 (11): 1849-1856.
- 12. Ramachandra SS, Kasthuri A. Anemia in the elderly residing in a South Indian rural community. Indian Journal for practicing doctor. 2008-09-2008-10.5 (4): 2-7.
- Parnami S, Chauhan K, Mehta P. A study on nutrition, diet and disease profile of the anemic elderly women with or without intervention through iron-folic acid supplementation. Indian Journal of Gerontology 2005.19 (2): 147-156.
- 14. Swami HM, Bhatia Vikas, Dutt Rekha, Bhatia SPS. A community-based study of the morbidity profile among the elderly in Chandigarh, India. Bahrain Med Bull, 2002,24(1): 13-16.
- 15. Kaur M. Kochar GK, Burden of Anaemia in rural and urban Jat women in Haryana state, India. Mal J Nutr. 2009, 15(2): 175-184.
- 16. Bhasin A, Rao MY. Characteristics of anemia in elderly: A hospital-based study in South India. Indian J Hematol Blood Trasnfus 2011, 27 (1): 26-32.
- 17. Bessman JD, Gilmer PR Jr, Gardener FH. Improved classification of Anemia by MCV and RDW. Am J Clin. Pathol, 1983, 80(3) 322-326.
- 18. Fisher S, Fisher SP, Mean Corpuscular volume Arch. Internal Medicine 1983;143:282-283.
- 19. Marsh WL Jr, Koenig HM. The Laboratory evaluation of microcytic red blood cells. Crit Rev Cli Lab Sci 1982; 16(3) 195-254.
- Gottfried EL, Erythrocyte indexes with the electronic counter. N. Engl J Med 1979, 300(22); 1277.
- 21. Hamilton PJ, Davidson RL. The Interrelationships and stability of Coulter-S determined blood indices-J Clin Pathol 1973; 26(9) 7 00-705.

Volume 5, Issue 1; January-February 2022; Page No 559-583 © 2022 IJMSCR. All Rights Reserved

- 22. Lindenbaum J. States of Laboratory testing in the diagnosis of megaloblastic anemia. Blood 1983, 624-627.
- 23. Pickering G, Wayne EJ. Observations on angina pectoris, and intermittent claudication in Anemia Clin Sci 1933;1:305-325.
- 24. Varat MA, Adolph RJ, Fowler No. cardiovascular effects of Anemia. Am Heart J 1972; 83(3) 415-426.
- 25. Hogen GR Jones B. The relationship of Koilonychia and Iron deficiency in infants. J Pediatric 1970, 77(6) 1054-1057.
- 26. Ebert R, Stead EA Jr, Gibson JG. The response of normal subjects to acute blood loss. Arch Intern Med 1981, 68:578-590.
- 27. Aleem Jan, MS Mir, Mubarak Muzzaffar, AS Sethi – Non-anemic Iron deficiency – diagnostic perspective. JK practioner 2003, 10(1) 47-48.
- 28. Lipschitz DA, Cook JD, Finch CA. Clinical evaluation of serum ferritin as an index of iron stores. *N Engl JMed* 1974**290**:1213–1216.
- Dallman PR Diagnosis of anemia and Iron deficiency analytic and biological variations of laboratory tests. Am J Clin Nurtr, 1984, 39(6), 937-941.
- 30. Finch LA et al., Plasma ferritin determination as a diagnostic tool. West J Med 1986, 145(5) 657-663.
- 31. Marsh WL, Nelson DP, Koenig HM free erythrocyte protoporphyrin (FEP.). The FEP test is clinically useful in classifying microcytic RBC disorders in adults. Am J Clin Pathol 1983, 79(6) 661-666.
- 32. Janella A et al., sensitivity and predictive value of serum ferritin and FEP for Iron deficiency. J Lab Clin Med 1989, 113(1) 73-78.
- Andres E, Loukili NH, Noel E, et al. Vitamin B12 (cobalamin) deficiency in elderly patients. *CMAJ*. 2004;171:251-259.
- 34. Green R, Miller JW. Vitamin B12 deficiency is the dominant nutritional cause of hyperhomocysteinemia in a folic acid-fortified

population. *Clin Chem Lab Med*.2005;43:1048-1051.

- 35. Antony AC vegetarianism and vit B12 deficiency. Am J Clin Nutr 2003,78,3-6
- 36. Roja Joseph, Shuba Sheshadri study of clinical profile of megaloblastic anemia in tertiary care hospital (Kasturba hospital, Manipal)
- 37. Nath BJ, Lindendaum J persistence of neutrophil hypersegmentation during recovery from megaloblastic granulo poiesis. Ann Intern Med 1979, 90(5) 757-760.
- Antony AC prevalence cobalamin and folate deficiency in India. Am J Clin Nutr 2001, 74, 157-159.
- 39. Hoffbrand AV, Neucombe FA, Mollin DL method of assay of red cell folate activity, and the value of assay as a test for folate deficiency. J Clin Pathol 1986, 19(1) 17-28.
- 40. Weiss G, Goodnough LT. Anemia of chronic disease. N Eng J Med. 2005; 352:1011-23.
- 41. Yip R, Dallman PR, the role of inflammation and iron deficiency as causes of anemia. Am J Clin Nutr 1988, 48(5) 1295-1300.
- 42. Cart wright GE. The anemia of chronic disorders. Semin Haematol 1986, 3(4) 351-375.
- 43. Broksky RA, Jones RJ. Aplastic anemia. Lancet 2005;365:1647-1656.
- 44. Young NS acquired aplastic anemia. Ann Intern Med 2002, 136(7) 539-546.
- 45. Young N Haematologic and Hematopoietic consequences of B 19 parvovirus infection. Semin Haematol 1988, 25(2) 159-172.
- 46. AK Chowdary, R Mohanty, SM Das, PK Das. Pancytopenia clinical and etiological profile. SCB Medical College, Cuttack, Orissa. Jour Assoc. Physician of India, 2005, 60(4) 213-218
- 47. Menon S, Sharck S, Nizamani MI etiological spectrum of pancytopenia based on bone marrow examination in children. J Coll Physician Surg Pak 2008 March 18(3) 163-167.

Volume 5, Issue 1; January-February 2022; Page No 559-583 © 2022 IJMSCR. All Rights Reserved

- 48. Page 730, chapter 98, Harrisons principles of internal medicine 20 th edition.
- 49. Table 98-5, page 730, World Health Organization (WHO) Classification of Myelodysplastic Syndromes/Neoplasms, chapter 98, Harrison's principle of internal medicine 20 th edition.
- 50. Office of Rare Diseases Research, National Institute of Health. Myelofibrosis page. Available at www.rarediseases.info.nih.gov/GARD/ Condition/8618/ Myelofibrosis. aspx. Accessed, 2019.
- 51. Mayo Clinic, Myelofibrosis. www.mayoclinic.com/health/myelofibrosis/ DS00886. Accessed, 2019.
- 52. Tabarra IA Haemolytic anemia diagnosis and management. Med Clin. North Am May 1992, 76(3) 649-668.
- 53. Wallerstein R, Aggeler PM, Acute Haemolytic anemia. Am J Med 1984, 37, 92-104.
- 54. Finch LA et al-Ferro kinetics in man. Medicine (Baltimore) 1970, 49(1) 17-53.
- 55. Crosby W Dameshek W the significance of Haemoglobinemia and Associated Haemosidernuria with particular reference 2 various types of hemolytic anemia. J Lab Clin Med 1981, 38, 824-841.
- 56. Ham T Haemoglobinuria. Am J Med 1955, 18, 990-1006.
- 57. Rosen H, Sears DA, Meisenzahi D spectral properties of hemotoxin haem. The schumm test. J Lab Clin Med 1969, 74(6) 941-945.
- 58. Palek S Jarolin P red cell membrane disorders. Hoffman Haematology 1995, 667-709.
- 59. Stamey C, Diamond L, Congenital hemolytic anemia in newborns relationship to kernicterus. Am J Dis Child 1987, 94, 616-624.
- 60. Trotman B et al pigment gallstone disease. Semin Liver Dis 1983, 3(2) 112-119.
- 61. Ostrow JD the etiology of pigment gallstones. Hepatology 1984, 4(suppl 5) 2155-2225.

- 62. Al Saquladi, Delpishah A, Bin Gaddem, the clinical profile of sickle cell disease in Yemeni children. Ann Trop Paed 2007 (Dec) 27(4) 253-259.
- 63. Wolfort FG, Krizek TJ skin ulceration in sickle cell anemia. Plast Reconstr Surg 1969, 43(1) 71-77.
- 64. Gendel B chronic leg ulcers in diseases of the blood. Blood 1998, 3, 1283-1289.
- 65. Wasi P, Disthasougchan P the effect of Iron deficiency on level of hemoglobins A2 and E. J Lab Clin Med. 1968, 71(1) 85-91.
- 66. Beutler E G6PD population-genetics and clinical manifestation. Blood Rev 1996, 10(1) 45-52.
- 67. Shah A acquired haemolytic anemia. Indian J Med Sci Dec. 2004, 58(12) 533-536.
- Packman CH Haemolytic anemia due to warm autoantibodies. Blood Rev Jan 2008, 22(1) 17-31.
- 69. Hashimoto C autoimmune hemolytic anemia. Clin Rev Allergy Immunol 1998, 16(3) 285-295.
- Sharma A, Khanduri V, Kumar P hematologymorphology forum paroxysmal nocturnal hemoglobinuria. Hematology Aug 2004, 9(4) 315-316.
- Packman, Leedy GP drug-related immune hemolytic anemia. Williams Haematology 5<sup>th</sup> edition, 1995, 667-684.
- 72. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodman RC. Prevalence of anemia in persons 65 years and older in the United States: Evidence for a high rate of unexplained anemia.Blood. 2004;104:2263– 2268
- 73. Balducci L, Saba HI et al. Haemalogic disease and disorders. Geriatrics review syllabus, a core curriculum in Geriatric medicine. 3rd Ed. NewYork. N.Y. American Geriatric Society. 1996: 314-8.
- 74. Rossi DJ, Bryder D, Weissman IL. Hematopoietic stem cell aging: mechanism and consequence. Exp Gerontol.2007;42:385–390

 $\infty$ 

- 75. Vora, Jyoti, et al. "Clinical Evaluation of Anemia in Elderly Patients-A Hospital-based Observational Study." *Global Journal of Medical Research* (2019).14
- 76. Sharma, Dheeraj, et al. "Patterns of geriatric anemia: A hospital-based observational study in North India." *Journal of Family Medicine and Primary Care* 8.3 (2019): 976.
- 77. Elejalde Guerra JI, Alonso Martínez JL, *et al.* (1999). [Etiological study and diagnosis of anemia in adults over 60 years of age]. Sangre (Barc) 44 (6): 418-23
- 78. Mann, Sfurti, et al. "Clinical evaluation of anemia in a geriatric patients-a cross-sectional study. conducted at tertiary care hospital." *National Journal of Community Medicine* 5.3 (2014): 316-320.
- 79. Prevalence of anemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anemia by Jack M. Guralnik, Richard S. Eisenstaedt, Luigi Ferrucci, Harvey G. Klein, and Richard C. Woodman

- 80. Chaves PHM, Ashar B, Guralnik JM, Fried LP. Looking at the relationship between hemoglobin concentration and prevalent mobility difficulty in older women. J Am Geriatr Soc.2002;50(7):1257–1264. doi: 10.1046/j.1532-5415.2002.50313.x.
- Elis A, Ravid M, Manor Y, Bental T, Lishner M. A clinical approach to idiopathic normocytic–normochromic anemia. J Am Geriatr Soc. 1996;44:832–834
- 82. Ania BJ, Suman VJ, Fairbanks VF. Incidence of anemia in older people: an epidemiologic study in a well-defined population.J Am Geriatr Soc. 1997;45:825–831
- 83. Rockey DC, Cello JP. Evaluation of gastrointestinal tract in patients with iron deficiency anemia. N Engl J Med.1999;329:1691–1695. doi: 10.1056/NEJM199312023292303.
- 84. Beghe C, Wilson A, Ershler WB. Prevalence and outcome of anemia in geriatrics: a systematic review of the literature. Am J Med. 2004;116(7):3–10. doi: 10.1016/j.amjmed.2003.12.009