

B.L.D.E (DEEMED TO BE UNIVERSITY) SHRI B.M. PATIL MEDICAL COLLEGE HOSPITAL & RESEARCH CENTRE VIJAYAPURA, KARNATAKA

DISSERTATION

On

"CLINICAL PROFILE OF ANEMIA AND ITS IMPACT ON FUNCTIONAL CAPACITY AND COGNITION IN ELDERLY"

Submitted in partial fulfillment of

M.D DEGREE EXAMINATION GERIATRICS

By

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P.G. IN GERIATRICS

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ABBREVIATIONS

ACI	Anemia of Chronic Inflammation	
ADL	Activities of Daily Living	
AOCD	Anemia of Chronic Disease	
AOCKD	Anemia of Chronic Kidney Disease	
EPO	Erythropoietin	
GFR	Glomerular Filtration Rate	
Hb	Hemoglobin	
HSC	Hematopoietic Stem Cell	
IADL	Instrumental Activities of Daily Living	
IL-6	Interleukin – 6	
MCH	Mean Corpuscular Hemoglobin	
MCHC	Mean Corpuscular Hemoglobin Concentration	
MCV	Mean Corpuscular Volume	
MDS	Myelodysplastic Syndrome	
MOCA	Montreal Cognitive Assessment	
NHANES - III	National Health and Nutrition Examination Survey – III	
OR	Odd's Ratio	
PCV	Packed cell Volume	
RBC	Red blood Cell	
RDW	Red cell Distribution Width	
RI	Reticulocyte Index	
TIBC	Total Iron Binding Capacity	
UGI	Upper GI Endoscopy	
WBC	White Blood Cell	
WHAS	Women's Health and Aging Study	
WHO	World Health Organization	

ABSTRACT

This study is a case control analysis, with fifty elderly anemic cases that meet the WHO definition of anemia and fifty non-anemic controls, matched for age and sex. This comparative study aims to determine how anemia hastens the onset of cognitive decline and functional disability in the elderly. Furthermore, it assesses the comprehensive clinical profile of fifty elderly cases of anemia, which will aid in determining the prevalence of common anemia types, dietary patterns, drug history, clinical manifestations, and the most common aetiology leading to occurrence of anemia.

Standardised scales such as the Katz ADL and Lawton IADL were used to evaluate the functional capacity of the cases and controls. Cognition assessment was done using MOCA scale. Data for clinical profile was collected by thorough history taking, clinical examination and lab investigations.

Female preponderance was seen in our study and mean age of the study population was 69.8 years. Iron deficiency anemia was the most common type of anemia and the most common etiology leading to occurrence of anemia was due to poor bioavailability secondary to various causes. Katz ADL assessment among the cases and controls revealed a significant odds ratio (OR = 15.8) which implies the odds of anemic elderly getting their daily activities impaired were found sixteen fold higher than non-anemic elderly. The Lawton IADL performed on study population revealed a considerable odds ratio (OR = 10.62) which implies that the anemic elderly are eleven times more prone to get dependent on others for their instrumental activities of day to day life. MOCA assessment performed among the cases and controls reveals that odds of anemic elderly undergoing cognition decline is tenfold higher than the non-anemic elderly (OR = 9.75).

Considering this note, anemia not only impairs the older individuals physically but it also impacts their mental capacity which will make older people more dependent on caretakers to do everyday tasks. Due to their greater dependence on others, elderly people in developing nations like India, where there is a shortage of skilled caregivers, face a costly dilemma that increases their vulnerability to elder abuse in multiple ways. Therefore, the government should take action to raise awareness about the need of early diagnosis and treatment of anemia in the elderly in order to prevent functional impairment and cognitive decline and preserve their quality of life.

INTRODUCTION

Human life expectancy is rising everywhere. The number of people above 60 years of age is predicted to increase from 0.9 billion (12% of the world population) in 2015 to almost 2 billion (22% of the world population) by 2050 ⁽¹⁾. This means that the number of elderly people will have doubled worldwide. Additionally, it is anticipated that 80 percent of all elderly people would reside in low and middle income nations by 2050, making it difficult to provide them with the necessary medical care and financial resources.

Global population ageing is a concern, but it is especially significant in emerging nations like India. This means that in addition to the burden of frail elderly, there is also an ageing population inside the existing population. Prioritising health concerns that affect the elderly survival and functional capacity requires consideration in this demographic reality.

Anemia can have far more serious consequences than anemia in younger persons, making it a common worry in the geriatric population ⁽²⁾. According to current theory, anemia can arise from any one of the homeostatic dysregulations that cause ageing, including hormones, oxidative stress/antioxidant equilibrium, and immunological regulatory mechanisms.

After anemia sets in, it alters the distribution of oxygen in the body, potentially resulting in tissue hypoxia and cell death, which leaves the aged frail and disabled.

As people age, anemia becomes more common; also, anemia may be a warning indicator of serious illnesses including cancer, malabsorption, or hypothyroidism.

One of the most prevalent illnesses among the elderly that can lead to serious consequences, such as lengthy hospital stays, severe disabilities, and even death, is anemia. It is challenging to determine whether anemia is a measure of disease burden or a mediator in a causal pathway leading to negative outcomes because anemia is a complex disorder. While anemia may be common in the elderly and vary in severity, it should not be viewed as a typical aspect of ageing.

Geriatric patients may have physical, psychological and social changes resulting from aging which may lead to poor outcomes in treatment and increased rate of mortality. A thorough geriatric assessment must include the identification of anemia as a crucial component in order

to proceed with clinical detection ⁽³⁾. Diagnosing anemia at earlier stage will help to prevent unnecessary investigations and treatments, thereby reducing polypharmacy and financial burden for the elderly.

Disability is characterised as an inability to carry out daily tasks required for independent living, such as instrumental activities of daily living (IADL) and basic activities of daily living (ADL)⁽⁴⁾⁽⁵⁾. The increased rates of disability are caused by chronic sickness, injuries, and health concerns related to a variety of disorders. A person with a disability encounters numerous obstacles throughout their life worldwide. It consists of institutional, environmental, and attitude barriers that keep someone from fully engaging in all facets of life.

Normal age related cognition decline are subtle and it mostly affects the speed of thinking and attention. In abnormal aging, cognition decline symptoms are more severe and may affect thinking abilities like rapid forgetting, difficulty navigating, difficulty in solving day to day problems and some behavioural changes. This aspects would make them more dependent on others to carry out their daily activities.

OBJECTIVES OF THE STUDY

- 1. The primary objective is to find how anemia is accelerating the process of declination of cognition and functional capacity of elderly people.
- 2. To assess the cognition of cases and controls using MOCA (Montreal Cognitive Assessment) scale.
- 3. To assess the functional capacity of cases and controls using Katz ADL (Activities of Daily Living) scale and Lawton's IADL (Instrumental Activities of Daily Living) scale.
- 4. To evaluate the results obtained from the above scales of fifty anemic elderly patients (cases) with fifty age and sex matched controls and compare the cognition and functional capacity of anemic elderly (cases) and controls.
- 5. In addition, to assess the aetiology, risk factors, co-morbidities, medication history and clinical findings of the fifty elderly anemic cases.

REVIEW OF LITERATURE

EVOLUTION OF ANEMIA

A Dutch draper by the name of Antoni van Leeuwenhoek (1632–1723) gave a thorough explanation of human red blood cells in 1674. He wrote a letter dated 7 April 1764 to the Philosophical Transactions of the Royal Society mentioning that "I have diverse times endeavoured to see and to know, what parts the Blood consists of; and at length I have observed, taking some Blood out of my own hand, that it consists of small round globules driven through a crystalline humidity or water."

The 1860s and 1870s saw a rise in the comfort level of doctors seeing patients blood under a microscope. In just 8 years, from 1877 to 1885, a number of methods were developed that completely changed the discipline of haematology.

Year of Discovery	Techniques	
1877	Hemocytometer for counting red blood cells	
1878	Hemoglobin measurement	
1879	Staining of peripheral smears	
1889	Device for measuring hematocrit	

The term "anemia" was first used in English literature in 1807, when a paper titled "Concise observations on Anemia" was published. The author, Professor Halle of the School of Medicine in Paris, listed "the universal loss of colour and yellow tinge of the skin, swelling, impossibility of walking without suffocation, palpitations, and habitual sweats" as among the typical symptoms of anemia⁽⁶⁾.

DEMOGRAPHY

The number of older persons in India has been rapidly increasing; by 2025, it is expected to reach 158.7 million, and by 2050, it will climb to approximately 324 million, surpassing the number of children under the age of fourteen.

According to a WHO estimate, 164 million people worldwide suffer from anemia, with a global prevalence of 23.9% among the elderly. Anemia prevalence estimates from different research conducted worldwide varied from 8.8% in Italy to 45.5% in India.

Every fourth person over the age of 60 is anemic worldwide. Every fourth person over the age of 60 is anemic worldwide. In India the prevalence of anemia in elderly ranges between 21% and 92%. In a survey conducted among Adolescents, adults and elderly in eight states of India, Anemia prevalence was 45% in elderly women and 37% in elderly men of India.

The anemia prevalence in elderly was higher among the rural studies (71.4%) than in the studies from the urban areas (61.5%). Better standard of living, diet, income, treatment facilities, treatment feasibility may be the reasons behind such observations. Despite the urban-rural variation, the anemia prevalence was increased in both the population, which should emphasize the importance of immediate corrective action of anemia in the elderly and prompt steps has to be taken by policymakers.

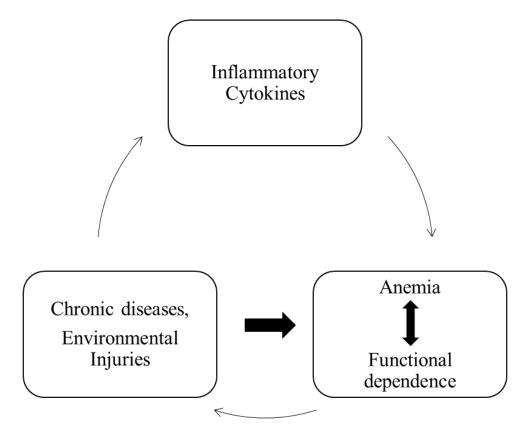
According to 2019 WHO census on Prevalence of anemia in elderly Indian population, the following table represents the age group and prevalence of anemia in each age group respectively.

Age group	Prevalence (%)	Age group	Prevalence (%)
60 - 64	51.70	80 - 84	63.35
65 – 69	57.06	85 – 89	67.24
70 – 74	62.06	90 – 94	61.12
75 – 79	69.26	≥ 95	62.68

BIOLOGY OF AGING AND ITS CLINICAL COMPLICATIONS

One definition of ageing is a decline in entropy. A reduction in the capacity of various organ systems to withstand stressful situations is indicated by a loss of entropy ⁽⁷⁾.

Prolonged and increasing inflammation resulting in entropy loss is the biological signature of ageing. The aforementioned inflammation results from the interplay of a person's genetic makeup, illnesses, and surroundings. Elevated levels of pro-inflammatory cytokines, like interleukin-6 (IL-6), have been linked to significant functional impairment and a higher death rate. High levels of inflammatory cytokines may also lead to anemia which may ultimately lead to increased functional dependence and multiple geriatric syndromes including Intellectual impairment (dementia), immobility & instability (falls) as age progresses. Hence correction of anemia may play an important role in breaking this vicious cycle and delay the complications of aging.



Anemia and aging – a vicious cycle (7)

Loss of entropy, which is a consequence of aging, is reflected in declining function of several organ systems which may ultimately lead to anemia.

A progressive decline in glomerular filtration rate (GFR) as age progresses which is universal, may be associated with reduced production of erythropoietin.

A gradual decrease in nutrient absorption and digestion brought on by a decrease in stomach motility, splanchnic circulations, absorbing surface, and gastrointestinal secretions.

Iron deficiency anemia can result from age-related increases in hepcidin, a glycoprotein produced by the liver and whose synthesis is triggered by inflammatory cytokines such as IL-6.

Older people may absorb less vitamin B12 because they have trouble breaking down food-bound cobalamin.

Progressive reduction in marrow cellularity as age progresses is associated with reduced ability to withstand haematopoietic stress ⁽⁷⁾.

PATHOGENESIS OF ANEMIA IN ELDERLY

There is still disagreement about whether the anemia that affects older people has the same underlying cause as it does other age groups or if it is only the result of marrow function declining with age.

Age-related hemopoietic alterations in the marrow reveal a rise in fat and a decrease in committed stem cells. Apart from these modifications, it has been discovered that anemia is caused by a reduced reaction to hemopoietic stressors such as iron deficiency, chronic kidney illness, malnourishment, and chronic inflammatory disease.

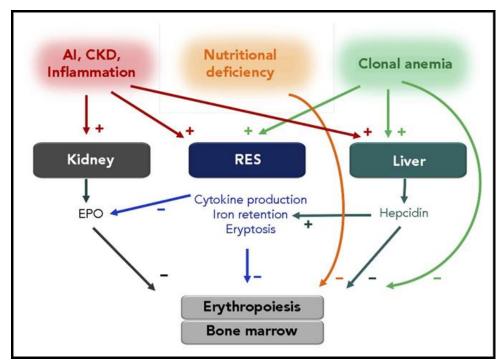
According to reports, older people in western countries do not typically have nutritional deficiencies as young people do. This is mostly due to the accumulation of iron stores in tissues over time.

The hemopoietic system's ability to respond to stress and the hemopoietic stem cells capacity for replication both decline with age.

An aged hemopoietic system is characterised by inadequate responsiveness in stimulusdriven situations and failure to maintain hemostasis. Numerous variables, including alterations in the marrow microenvironment, age-related abnormalities in marrow progenitor cells, and a decrease in the generation of regulatory growth factors, contribute to this muted response.

Higher hepcidin levels and recuded erythropoietin level are seen in elderly with anemia of inflammation than their counterparts without anemia.

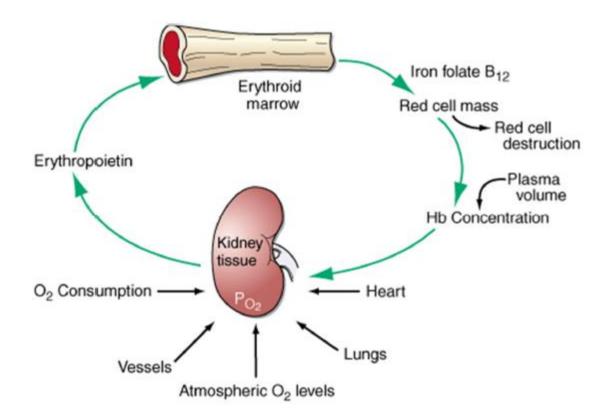
The below image shows possible mechanisms of anemia in older adults (adapted from ref.28)



BIOLOGY OF HAEMATOPOIESIS

A little pool of hematopoietic stem cells gives rise to the hematopoietic system, which either self-renews itself or develops into adult leukocytes, erythrocytes, or platelets. Precursors and committed progenitors enable HSC differentiation. Complex interactions between hematopoietic growth factors, stromal microenvironment, and HSCs regulate hematopoiesis. Therefore, self-renewal, differentiation, maturation, and cell loss require a precise equilibrium. The pronormoblast is the earliest erythroid precursor in the bone marrow that can be identified by its morphology. This cell can divide four or five times, yielding sixteen to thirty-two adult red blood cells. Increased erythrocyte counts are a result of expanded early progenitor cell numbers, which are achieved through increased EPO synthesis or pharmacological administration of EPO. O2 availability is correlated with the regulation of EPO production.

Mammals receive oxygen transportation to their tissues through the hemoglobin found in their circulating red blood cells. To successfully navigate the microcirculation, the mature red cell is an 8 micron diameter, is anucleate, discoid in form, and is remarkably pliable. The intracellular production of ATP maintains the membrane integrity of the mature red cell.



The above image shows the physiologic regulation of red cell production by tissue oxygen tension ⁽⁸⁾.

Since the average red cell has a lifespan of 100–120 days, normal red cell synthesis makes daily replacement of 0.8–1% of all circulating red cells in the body. The erythron is the organ that produces red blood cells. The erythron is a dynamic organ composed of a huge mass of mature circulating red blood cells and a pool of marrow erythroid precursor cells that proliferate rapidly. The balance between the creation and elimination of red cells is reflected in the mass of red blood cells. Understanding the physiologic underpinnings of red cell formation and death helps to explain the various pathways that might result in anemia.

CONSEQUENCES OF ANEMIA (7)

Consequences of Anemia

- 1. Increased risk of mortality
- 2. Increased risk of functional dependence
- 3. Increased risk of dementia
- 4. Increased risk of delirium
- 5. Increased risk of chemotherapy related toxicity
- 6. Increased risk of congestive heart failure and coronary death
- 7. Increased risk of falls

Anemia has been shown to be an independent risk factor for death in older people in at least seven cohort studies, with the WHAS research being the most provocative. The WHAS necessitated an adjustment to the WHO definition of anemia in older women and found an increased risk of death for hemoglobin levels <13.4 gm/dl in home-dwelling women aged 65 and above, followed for an average of 11 years.

The emergence of functional dependence is a sign that one of the primary goals of managing the elderly has not been met; research indicates that functional dependence is among the most dangerous outcomes of anemia in the elderly.

Anemia raises the chance of therapeutic side effects from both surgery and medications. Research has demonstrated that anemia stands alone as a risk factor for cytotoxic chemotherapy side effects. Because red blood cells contain the majority of antineoplastic drugs, anemia increases the amount of free medication in the blood and increases the risk of toxicity. Chronic hypoxia of a normal tissue might potentially make such tissues more vulnerable to side effects from treatment. In elderly people with anemia, hypoxia of the brain tissues raises the risk of medication-induced delirium.

According to an examination of Medicare records, people 65 years of age and over who a myocardial infarction with a haematocrit of less than 30% had had a higher risk of dying if they did not receive blood transfusions ⁽⁷⁾.

Studies on patients with chronic renal failure revealed that patients whose anemia had not been treated with erythropoietin had a considerably higher probability of developing dementia, suggesting that anemia may have been the cause of the dementia.

Research has demonstrated a stronger correlation between anemia and the risk of falls, including falls that occur in both the community and institutions ⁽⁷⁾. A geriatric syndrome known as falls is linked to higher rates of morbidity and death, including hip fractures.

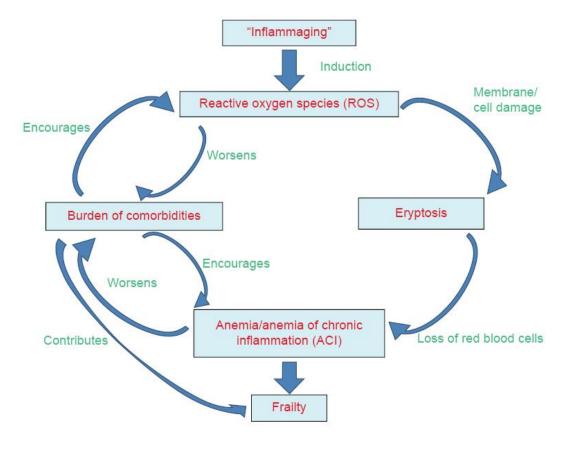
ANEMIA AND ITS RELATIONSHIP WITH FRAILTY AND INFLAMMAGING

A state of heightened susceptibility to stress is described by the term frailty. Sarcopenia, malnourishment, decreased strength and endurance, and decreased neuromuscular flexibility are the hallmarks of the syndrome known as frailty.

Anemia leads to development of functional loss and poor outcome in the elderly, hence it is main causative factor for development of frailty. Inflammaging refers to chronic low grade inflammation that characterizes the process of aging. Reactive oxygen species, which are highly reactive chemicals that damage cell membranes, DNA, enzymes, and proteins and may change genetic information, are produced as a result of inflammaging.

Eryptosis is a physiologic mechanism to remove defective erythrocytes from circulation. The reactive oxygen species leads to enhanced eryptosis which may lead to onset of anemia of chronic inflammation, which in long term may lead to development of a frail elderly.

The below image shows association between frailty, ACI and Inflammaging (adapted from ref.29)



WHO DEFINITION OF ANEMIA

A hemoglobin concentration below 7.5 mmol/L (12 g/dL) for women and below 8.1 mmol/L (13 g/dL) for men is considered anemia, according to WHO guidelines ⁽⁹⁾.

The variations in hemoglobin distribution between older men and women account for the gender variances in hemoglobin values.

In theory, anemia is a clinical condition brought on by a decrease in the mass of red blood cells in circulation.

In practical terms, anemia is defined as a lower level of the following parameters

- Hemoglobin concentration in the whole blood.
- Hematocrit (Hct)
- RBCs count in Standardized volume of whole blood

The units of measurement for hemoglobin, hematocrit, and red blood cell count are g/dl, %, and million/cu.mm, respectively.

CLASSIFCATION OF ANEMIA

MORPHOLOGICAL CLASSIFICATION OF ANEMIA

Based on MCV, MCH, and MCHC, three primary forms of anemia are identified.

- 1. Hypochromic microcytic anemia
 - a) Mean Corpuscular Volume is subnormal <80 fl
 - b) Mean Corpuscular Hemoglobin <27 pg
 - c) Mean Corpuscular Hemoglobin Concentration < 30g/dl

The two most notable instances are thalassemia, which results in a faulty globin component of hemoglobin, and iron deficiency anemia, which occurs when there is insufficient iron for the heme component of hemoglobin to form.

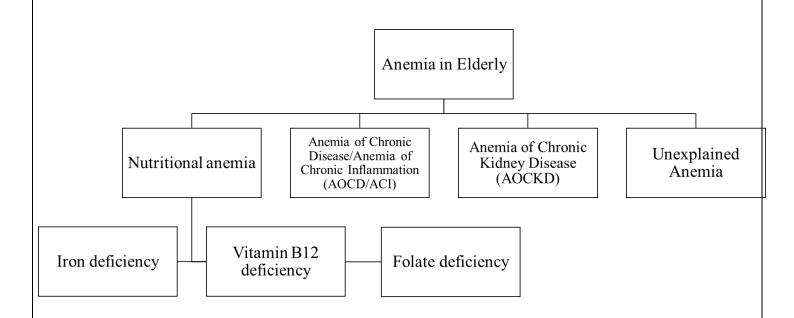
- 2. Macrocytic anemia
 - a) Mean Corpuscular Volume >100 fl
 - b) Megaloblastosis of bone marrow
 - c) Secondary to Vitamin B12 or folate deficiency
- 3. Normocytic normochromic anemia
 - a) MCV, MCH, MCHC are within normal range.
 - b) Bone marrow failure
 - c) Hemolysis
 - d) Loss of substantial amount of blood
 - e) Chronic kidney disease or chronic infection

BASIC PATHOPHYSIOLOGICAL CATEGORIES OF ANEMIA

- 1. Impaired production of red cell
- a. Decreased nutrient supply
 - Iron deficiency
 - Vitamin B12 deficiency
 - Folate deficiency
 - Protein calorie malnutrition
- b. Decreased erythropoetic activity
 - Inflammatory disorders
 - Chronic infections
 - Connective tissue disorders

- Metastasis
- Associated with kidney failure
- Aplastic anemia
- 2. Anemia due to bone marrow replacement
 - Myelodysplastic syndrome
 - Leukemias
 - Lymphomas
 - Myeloproliferative disorders
 - Myeloma

CLINICAL CLASSIFICATION OF ANEMIA IN ELDERLY



$\underline{\textbf{SEVERITY CLASSIFICATION OF ANEMIA ACCORDING TO HEMOGLOBIN}}^{(10)}$

	Hemoglobin (g/dl)			
Gender	No anemia	Mild anemia	Moderate anemia	Severe anemia
Male	≥13	11 – 12.9	8 – 10.9	<8
Female	≥12	11 – 11.9	8 – 10.9	<8

SIGNS AND SYMPTOMS OF ANEMIA

- 1. Giddiness
- 2. Easy fatigability
- 3. Generalized weakness
- 4. Loss of appetite
- 5. Dyspnea on exertion
- 6. Palpitations
- 7. Swelling of legs
- 8. Conjunctival pallor
- 9. Facial pallor
- 10. Glossitis
- 11. Koilonychia
- 12. White nails
- 13. Tachycardia
- 14. Orthostatic hypotension
- 15. Raised JVP
- 16. Hyperpigmentation over Knuckles
- 17. Splenomegaly
- 18. Hepatomegaly

TESTS DONE TO ASSESS AN ANEMIC PATIENT

Investigations such as the complete blood count, peripheral smear, and reticulocyte count are employed in the first evaluation of an anemia case.

Complete Blood Count includes parameters like hemoglobin, haematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), red blood cell count (RBC), White blood cell count, Differential count, Platelets, along with this other additional tests like serum iron, serum ferritin are done for iron deficiency anemia.

Peripheral smear gives a pictorial representation which will help us to diagnose the type of anemia. Reticulocyte will help us to differentiate between hypo and hyper-proliferative anemia.

To assess Vitamin B12 deficiency, Serum Vitamin-B12 is done, and to assess folate deficiency serum folate and RBC folate are done.

Serum creatinine and glomerular filtration rate (GFR) are evaluated to assess renal function. Serum haptoglobin concentration, serum lactate dehydrogenase concentration, and indirect bilirubin concentration are tested for the assessment of hemolysis.

Upper Gastrointestinal endoscopy is performed to assess upper gastrointestinal bleeding. Stool occult blood is done to rule out gastrointestinal malignancy. Inflammatory markers like erythrocyte sedimentation rate, serum ferritin are done to look for anemia of chronic inflammation.

Bone marrow is evaluated by bone marrow and trephine biopsy. Serum erythropoietin and pro-inflammatory markers such as Interleukin-6, C-reactive protein, and TNF-alpha are measured in addition if necessary. Hepcidin is a significant iron pathway modulator that is involved in the pathophysiology of Anemia of chronic inflammation.

INVESTIGATIONS

HEMOGLOBIN

METHODS OF ESTIMATION OF HEMOGLOBIN (11)

- 1. Sahli's method- observer error common.
- 2. Artificial neural network approach (ANN).
- 3. Drabkin method- more reliable.
- 4. Acid hematin-automated counter. Useful in estimation of Hb in large batches, in tertiary laboratory.
- 5. Portable Hb Photometer (Hemocue)
- 6. Hemoglobin estimation in auto analyzers (Sysmex)

Compared to the Hemocue or direct technique, the prevalence of anemia was greater when the indirect method was employed. Despite the technician immersing the paper in Drabkin's solution, it is possible that the blood on the filter paper only partially disintegrated, leading to this issue.

Before comparing the findings of several surveys, a methodological difference should be carefully investigated if there are greater variations in the estimated prevalence of anemia ascertained by two different methodologies.

The amount of hemoglobin measured in capillary blood was somewhat less than that measured in venous blood. This is due to the tiny capillary blood vessel and the capillary blood's red cell volume being 1-3% less than that of the venous blood.



Sysmex Hematology analyzer

RETICULOCYTE COUNT

One of the initial tests for anemia is the reticulocyte count. A measurement of immature red blood cells devoid of a cell nucleus is what it is. It accurately forecasts the activity of the bone marrow. After developing and maturing in the red bone marrow, reticulocytes circulate in the bloodstream for a day before maturing into mature red blood cells. They appear somewhat larger and bluer with greater MCV when stained with Romanowsky stain (12) (13).

- Normal range : 0.5-1.5 %
- Reticulocyte production index (RPI) is an absolute measure of marrow function.
- Reticulocyte index (RI) > 2 % adequate response
- Reticulocyte index (RI) < 2 % hypoproliferation of bone marrow

Reticulocyte production index (RPI) / Absolute reticulocyte count (ARC) is calculated by the formula:

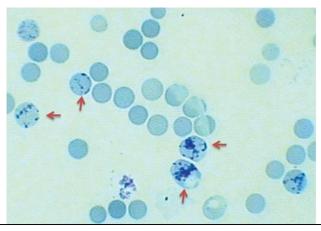
Patient haematocrit / Normal hematocrit x Reticulocyte count

High reticulocyte occur in:

- Acute / Chronic Hemorrhage
- Hemolytic anemia

Low reticulocyte occur in:

- Bone marrow malignancy
- Aplastic anemia
- Nutrition deficient anemia
- Anemia of Chronic Disease



Methylene blue staining demonstrating residual RNA in newly made red cells

PERIPHERAL SMEAR

In every instance of anemia, a peripheral smear is a necessary study. The crucial test to be performed is a peripheral smear, which is necessary once the diagnosis of anemia is confirmed using Hb levels and other indicators. A bone marrow aspiration or biopsy becomes crucial if grossly abnormal peripheral smear results are discovered ⁽¹⁴⁾.

USES:

- 1. To categorise various forms of anemia
- 2. To investigate haematological problems
- 3. To search for parasites such as Filaria or malaria

PROCEDURE

- A sterile blood drop is inserted on one end of the slide, and the blood is spread out down the slide's length using a spreader slide.
- Methanol is used to
- glue the slide once it has air dried.
- The Giemsa/ Wright/ Romanowsky staining is done. Use of Wright Giemsa stain is widespread.
- The monolayer film's cells are counted and differentiated.
- The total platelet, WBC, and RBC counts are reported.
- Red cell inclusions or abnormal red cell morphology are evaluated.
- Aberrant morphology of white blood cells and platelets is also evaluated.
- The presence of normoblasts and blast cells was observed.



Left slide shows unstained smear, Right slide shows smear stained with Wright Giemsa stain

SERUM FERRITIN

The body's overall iron stores are reflected in serum ferritin. Ferritin is a complex of 24 protein subunits that are globular in shape. It is available in a soluble, non-toxic form. Acute phase protein ferritin levels are elevated in chronic inflammatory diseases.

Normal range of ferritin levels:

- Male 20 to 300 ng/dl
- Female 15 to 150 ng/dl

IMPLICATION OF SERUM. FERRITN

- Iron deficiency anemia: Serum ferritin is less than 10 ng/dl
- Anemia of chronic diseases: Serum ferritin is more than 60 ng/dl
- Rheumatoid arthritis, malignancies, and chronic renal illnesses are examples of inflammatory disorders that cause a moderate rise in Serum ferritin.
- Serum ferritin levels rise in hepatitis and end-stage renal disease.
- Low serum ferritin are observed in Vegetarians, Celiac disease patients, Vitamin –C deficiency, hypothyroidism.
- Iron overload conditions such as hemosiderosis, hemochromatosis, etc. can also be detected using ferritin.
- Men who have high serum ferritin are at risk for myocardial infarction.
- The complexed protein ferritin is where iron is stored in cells.
- Serum ferritin and total body iron reserves have a strong correlation under normal circumstances. Therefore serum ferritin is used to estimate iron stores.
- Adult males average approximately 100 μg/dl, while females average only 30μg/dl.
- As we age, our iron stores decrease and our serum ferritin level drops to less than $15\mu g/dl$.

METHODS FOR ESTIMATION OF FERRITIN

- The ELISA approach can be used to quantify ferritin levels in serum or plasma. Sensitivity- 92.4%, specificity- 94.6%
- Radio immunoassay

BONE MARROW ASPIRATION

- A wide bore, short beveled needle with a stillete placed into the bone marrow cavity is used to aspirate the bone. A guard that can be adjusted is there to stop over penetration.
- Despite being extremely helpful, bone marrow aspiration is not performed on all anemic patients due to its invasive nature.
- When confirming the diagnosis is crucial, the test is performed in low hemoglobin quantities and when there is a possibility of hematological malignancies.
- One benefit of this process is that the created films are inspected right away.
- The iliac crest and sternum body are the most frequently used sites.

PROCEDURE

- After injecting local anaesthetic into the bone's periosteum, a needle is rotated to and fro within the bone.
- The stillette is removed upon cavity penetration, and a syringe that fits snugly is affixed.
- A powerful, quick suction is used to extract roughly 0.2 millilitres of bone marrow tissue and peripheral blood.
- Film preparation begins right away with the aspirated material being placed on a glass slide and the particles being evenly distributed.
- The aforementioned method is used to prepare about three or four slides. After air drying, the films are stained appropriately.

STAINS USED

Romanowsky stain

It provides information about the developing cells, such as megaloblastic or normoblastic. One can determine the proportion of various cell lines, such as the myeloid:erythroid ratio. It is possible to detect the presence of extramarrow cells such as secondary cancer and aberrant macrophages (storage disorders). Lastly, the marrow's cellularity is also ascertained. Leukemic cell detection is aided by it.

Iron stain

- To measure the quantity of iron in the reticulo endothelial stores like macrophages and as fine granules (sideroblastic granules) in developing erythroblasts.

BONE MARROW TREPHINE BIOPSY

Compared to bone marrow aspiration, this is preferable. This biopsy carried out to identify different kinds of neoplastic cells, to find lymphoma foci, and to aid in the stage of the lymphoma. The primary drawback is that a single biopsy could not be helpful because to the uneven distribution of neoplasia and hypoplasia foci.

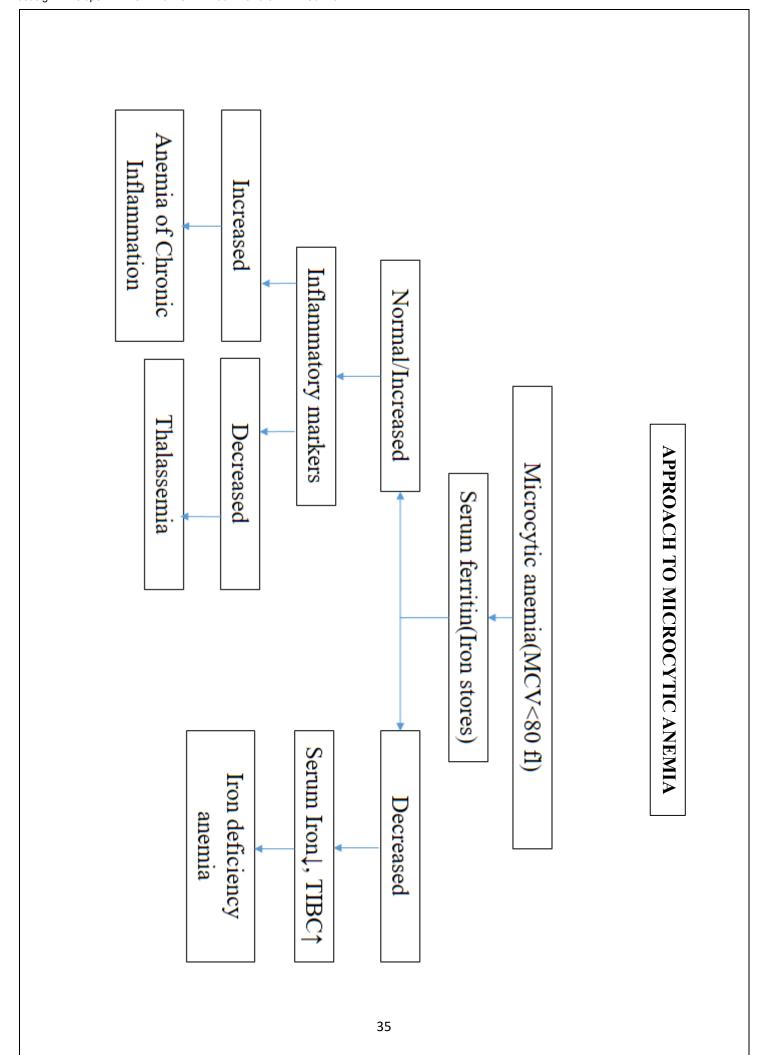
BONE MARROW BIOPSY INDICATIONS

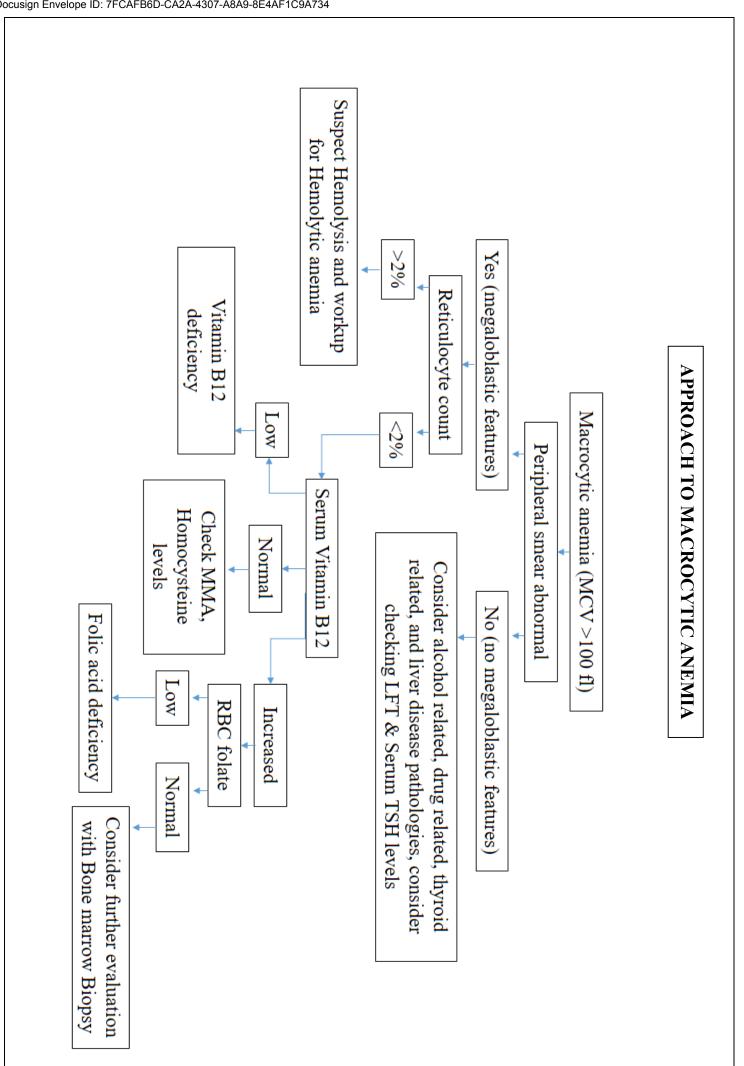
- 1. Pancytopenia
- 2. Myelodysplastic syndrome
- 3. Monoclonal gammopathy
- 4. Immature white and nucleated red cells
- 5. Indeterminate iron stores
- 6. Undiagnosed and untreated anemia

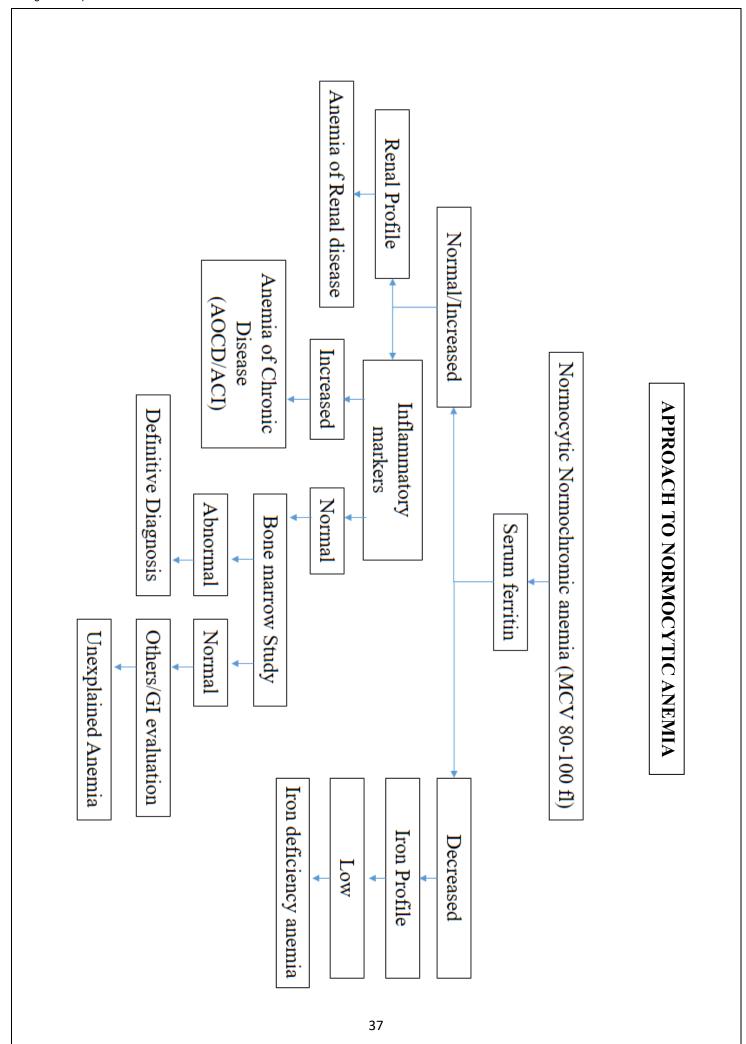


Jamshidhi needle – Bone marrow biopsy needle

The following pages will illustrate the approach for anemia and its workup ⁽⁷⁾. Hypoproliferative anemia B12 or Folate deficiency anemia Anemia of Chronic Iron deficiency Renal insufficiency Myelopthisic anemia Inflammation Cytotoxic Chemotherapy Low **ANEMIA WORKUP** Reticulocyte count Anemia Increased loss of red blood cells Acute hemorrhage Microangipathic anemia Auto-immune hemolytic anemia High







Nutritional Anemia

The primary cause of the elderly's low nutritional state is the loss of access to adequate diet for practical or economic reasons. Poor food intake and malnutrition are caused by aging-related changes, appetite loss, and diminished sensations of taste and smell. Therefore, evaluating the nutritional status of the elderly, identifying those who are at risk, and enhancing their nutritional status will help avoid illnesses related to nutrition, such as Tuberculosis and anemia.

IRON DEFICIENCY ANEMIA

It is the most common nutritional anemia seen in the elderly. It is caused about by a decrease in the amount of iron taken orally, a decrease in iron absorption, and chronic blood loss. In elderly, iron deficiency is a sign of underlying pathology. The following table shows the stages of development of iron deficiency anemia ⁽⁷⁾.

Stage	Stages in the development of Iron deficiency
1	Negative iron balance
2	Fall in iron stores (serum ferritin falls to <12-15 ng/ml)
3	Serum iron and transferrin saturation fall
4	Hypochromic reticulocytes appear in circulation
5	Hemoglobin falls
6	MCV falls

The following tables shows the causes of iron deficiency anemia in elderly (7)

Causes of Iron deficiency in elderly

Inadequate absorption

- Antacid therapy or high gastric pH
- Excess dietary bran, phytates, tannin or starch
- Competition from other metals (eg., lead or copper)
- Loss of dysfunction of absorptive enterocytes
- Bowel resection
- Celiac disease
- Inflammatory bowel disease
- Intrinsic enterocyte defects

Increased loss

Gastrointestinal blood loss

- Epistaxis
- Varices
- Gastritis
- Ulcer
- Tumor
- Meckel's diverticulum
- Parasitosis
- Vascular malformations
- · Inflammatory bowel disease
- Diverticulosis
- Hemorrhoids

Genitourinary blood loss

- Menorrhagia
- Cancer
- Chronic infection

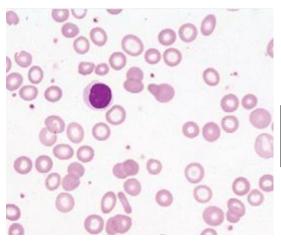
Pulmonary blood loss

- Pulmonary hemosiderosis
- Infection

Other blood loss

- Trauma
- Excessive phlebotomy
- · Large vascular malformations

LAB DIAGNOSIS OF IRON DEFICIENCY ANEMIA



Peripheral smear showing microcytic hypochromic RBCs

The following tables enumerates the screening diagnostic tests for iron deficiency anemia $^{(15)\,(16)\,(17)}$.

Laboratory Tests for Iron Deficiency Anemia		
Screening tests		
Haemoglobin	Decreased	
MCV	Decreased	
MCH	Decreased	
MCHC	Decreased	
RDW	Increased	
RBC Count	Decreased	
Di	agnostic tests	
Serum Ferritin	Decreased	
Serum Iron	Decreased	
TIBC	Increased	
Transferrin Saturation	Decreased	
S	Special tests	
Bone marrow iron stores	Reduced or absent	
Bone marrow morphology	Hypercellular initially, later subsided. Late normoblasts show "shaggy" blue cytoplasm	
FEP/ZPP	Increased	

VITAMIN B12- DEFICIENCY ANEMIA

Deficiency of vitamin B12 (cobalamin) in the elderly is probably far more frequent than it is recognised. The diminished ability of older people to breakdown food-bound cobalamin may result in decreased B12 absorption. Some common causes of Vitamin B12 deficiency in elderly are given below in table ⁽⁷⁾.

Causes of B12 deficiency in an elderly population

- 1. Food cobalamin malabsorption
- 2. Pernicious anemia
- 3. Dietary deficiency
- 4. Malabsorption
- 5. Hereditary causes

Despite glossitis, peripheral neuropathy and altered cognition, laboratory investigations play a major role in diagnosis of B12 deficiency anemia

PERIPHERAL SMEAR FINDINGS

Red Blood cells

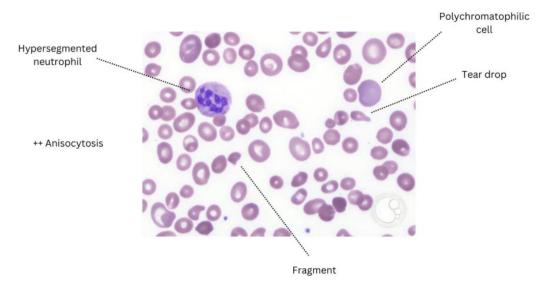
- RBC's are characteristically large and oval (Macrocytosis)
- In severe anemia along with macroovalocytes other variations in RBC's are
 - Marked Anisopoikilopoiesis
 - Basophilic stippling
 - Howell Jolly bodies
 - Cabot rings
- Late or intermediate erythroblasts may sometimes be seen in severe anemia

White blood cells

- Total leukocyte count: This value could be lower or normal.
- Severe anemia is more likely to cause leukopenia.
- Hypersegmentation of neutrophil nuclei is among the early signs

Platelets

- Thrombocytopenia is usual
- Giant platelets can be sometimes seen (15).



BONE MARROW FINDINGS

- Marrow is hyper cellular with megaloblastic features in all erythroid precursors
- Erythroid precursors
 - Megaloblasts differ from normoblasts in having increase in cell size, nuclear size and amount of cytoplasm. Nuclear chromatin is sieve like or stippled.
 Nuclear maturation falls behind the cytoplasmic maturation (Nuclear cytoplasmic asynchrony)
 - Depending upon the stage they are termed as promegaloblast, early, intermediate and late megaloblasts
 - In bone marrow early erythroid precursors with megaloblastic features are increased (promegaloblasts and early megaloblasts) when compared to more mature precursors (intermediate and late megaloblasts)
 - Mitotic activity is increased
- Myeloid series
 - Granulocytic series also show megaloblastic features.
 - Giant metamyelocytes and band forms with horse shoe shaped nuclei and finer chromatin is the characteristic feature
- Megakaryocytes are large with multiple nuclear lobes and paucity of cytoplasmic granules (17).

The screening and diagnostic tests of megaloblastic anemias like Vitamin B12 and folate deficiency anemia are shown below in table⁽¹⁵⁾⁽¹⁷⁾.

Screening tests			
Investigations	Vitamin B12 deficiency	Folate deficiency	
Complete blood count	Decrease in HGB, Haematocrit, WBCs, RBCs, Platelets. Increase in MCV & MCH	Decrease in HGB, Haematocrit, WBCs, RBCs, Platelets. Increase in MCV & MCH	
Cell morphology	Oval macrocytes Anisocytosis and Poikilocytosis RBC inclusions Hypersegmented neutrophils	Oval macrocytes Anisocytosis and Poikilocytosis RBC inclusions Hypersegmented neutrophils	
Absolute reticulocyte count	Decreased	Decreased	
Serum total & Indirect bilirubin	Increased	Increased	
Serum lactate dehydrogenase	Increased	Increased	

Diagnostic tests			
Investigations	Vitamin B12 deficiency	Folate deficiency	
Bone marrow examination	Erythroid hyperplasia and presence of megaloblasts	Erythroid hyperplasia and presence of megaloblasts	
Serum Vitamin B12	Decreased	Normal	
Serum Folate	Normal or Increased	Decreased	
RBC folate	Normal or Decreased	Decreased	
Serum methylmalonic acid	Increased	Normal	
Serum/Plasma Homocysteine	Increased	Increased	
Antibodies to intrinsic factor and gastric parietal cells	Present in pernicious anemia	Absent	
Serum gastrin	Can be markedly elevated in pernicious anemia	Normal	
Gastric analysis	Achlorhydria in pernicious anemia	Normal	
Stool analysis for parasites	Diphyllobothrium latum may be the cause of deficiency	Negative	

FOOD COBALAMIN MALABSORPTION

The most prevalent cause of vitamin B12 insufficiency in the elderly is malabsorption of food cobalamin. The inability to release cobalamin from food or intestinal transport proteins is what distinguishes it, especially when hypochlorhydria is present. The cobalamin deficit that persists in this illness even with a healthy diet is what defines it. Here are some factors that contribute to malabsorption of food cobalamin ⁽⁷⁾.

Factors that contribute to malabsorption of food cobalamin

- 1. Intestinal microbial proliferation
- 2.Long term ingestion of drugs
 - Biguanides
 - Antacids
 - H2 receptor antagonists
 - Proton pump inhibitors
- 3. Chronic alcoholism
- 4. Gastric reconstruction
- 5. Pancreatic exocrine failure
- 6. Sjogren's syndrome

Schillings's test is performed to evaluate the absorption of Vitamin B12 in the Gastrointestinal Tract.

ANEMIA OF CHRONIC INFLAMMATION/ ANEMIA OF CHRONIC DISEASE (ACI/AOCD)

One of the main causes of hypo proliferative anemia in the elderly is anemia of chronic inflammation. ACI has been linked to inflammation resulting from autoimmune disorders, infections, and other diseases. Whether or not the associations are contagious, they all show some degree of inflammation and cytokine release. When a simple tissue injury occurs, like in a cardiac infarction or during surgery, the healing process triggers an inflammatory response.

The anemia of chronic inflammation is caused by four main mechanisms (7)

Four major mechanisms that contribute to anemia of chronic inflammation (ACI/AOCD)

- 1. Impaired Erythropoietin (Epo) Production
- 2. Impaired response of erythroid progenitor cells to Epo
- 3. The effect of inflammation on iron homeostasis
- 4. Hepcidin

Common conditions associated with anemia of chronic inflammation are mentioned in the table (7)

Conditions associated with ACI/AOCD

- 1. Acute and chronic infection (viral, bacterial, protozoal)
- 2. Autoimmune disease (eg., Rheumatoid arthritis)
- 3. Tissue injury (eg., surgery, trauma, myocardial infarction, menses)
- 4. Neoplasms
- 5. Chronic renal failure
- 6. Aging

Evidence of iron deficient erythropoiesis with a serum ferritin of greater than 200ng/ml suggests anemia of chronic inflammation. Iron deficiency and anemia of chronic inflammation shares some similarities like decreased serum iron, here is table showing some similarities and differences between iron deficiency anemia and anemia of chronic inflammation ⁽⁷⁾.

Similarities and differences between Iron deficiency and Anemia of Chronic Disease		
Iron deficiency anemia	Anemia of Chronic disease (AOCD/ACI)	
Low serum iron	Low serum iron	
Low serum ferritin	Normal to elevated serum ferritin	
High TIBC	Normal to Low TIBC	
Low % Transferrin saturation	Low % Transferrin saturation	
Elevated red cell protoporphyrin	Elevated red cell protoporphyrin	
Red cell microcytosis	Normocytic to microcytic red cells	
Absent marrow iron stores; no sideroblasts	Marrow iron stores normal to increased; reduced sideroblasts	
sTrR/log ferritin <1	sTrR/log ferritin <2	

TREATMENT

- It's critical to treat the chronic diseases causing the anemia. However, this isn't always feasible.
- When the hemoglobin level is less than 8 mg/dl, transfusion is taken into consideration.
- Since ACD patients always have enough stocks of iron, iron supplements should not be administered in these instances.
- When chronic inflammation is present, iron treatment is detrimental.
- The main vascular and endothelial dysfunction in ACD is found to be treated with erythropoietic medications.
- Erythropoietin use improves responsiveness, particularly in patients with chronic diseases and connective tissue disorders.

DISADVANTAGES OF ERYTHROPOETIC DRUGS

- 1. Higher deaths with cardio vascular events
- 2. Progression or recurrence of certain types of cancers
- 3. Increased risk of venous thromboembolism

ANEMIA OF CHRONIC KIDNEY DISEASE

As kidney function deteriorates, anemia—a well-known consequence of chronic kidney disease (CKD)—develops. The glomerular filtration rate, or GFR, gradually decreases in the majority of CKD patients, and as it does, anemia becomes more common and severe.

To calculate Glomerular Filtration Rate, MDRD equation is used

MDRD equation for GFR =
$$175 \times \text{Serum Cr}^{-1.154} \times \text{age}^{-0.203} \times 1.212$$
 (if patient is black*) × 0.742 (if female)

Chronic kidney disease is defined as a GFR <60ml/min/1.73m for 3 or more months, or the existence of kidney anomalies, either structural or functional (pathologic anomalies, aberrant findings on blood, urine, or imaging examinations), with or without a decline in GFR, for a minimum of three months.

The kidney's peritubular capillary lining cells produce erythropoietin. Reduced oxygen availability in the kidneys forms the basis for production of erythropoetin. Heart failure, anemia, renal arteriosclerosis, and decreased renal blood flow can all lead to reduced oxygen supply. Anemia and a decreased erythropoietin response might result from an age-related loss in renal function.

The goal of treatment is to keep the Hemoglobin level between 10 and 12 gm/dl. The quality of life and physical function are improved with erythropoietin treatment. Depending on the severity of the illness, the reaction time varies.

MYELODYSPLASTIC SYNDROME (MDS)

People over 65 are more likely to have primary hematopoiesis disorders, particularly MDS with median age of 7th decade of life. Since MDS can manifest as either normocytic or macrocytic anemia, especially when only the erythroid lineage is affected, it is a common cause of unexplained anemia in the elderly. MDS is a diverse collection of bone marrow disorders that are marked by a higher risk of leukemic evolution and inefficient hemopoiesis. It remains a morphological and clinical diagnosis, and sufficient risk assessment necessitates meticulous examination.

The yearly incidence of MDS is 4.5 per 100,000. Risk factors include male patients with a first-degree relative afflicted by haematological cancer, smoking, radiation exposure, and exposure to organic solvents, patients presenting with unexplained anemia, infection, and bleeding. Most bone marrow is hyper- or normocellular, with a small percentage being hypocellular.

PATHOGENESIS OF MDS

MDS is seen as a clonal illness affecting stem cells or early hematopoietic progenitors. The hallmark of MDS is increased apoptosis in the hematopoietic progenitor, which results in peripheral cytopenia.

A tiny proportion of MDS patients also have paroxysmal noctural hemoglobinemia, aplastic anemia, and MDS on the diagnostic border.

As of right now, research has not demonstrated that a single genetic lesion is necessary for the disease to manifest. Histone deacetylation and promoter hypermethylation changes are epileptic changes that contribute to pathogenesis.

MOST COMMON ETILOGICAL FACTORS FOR OCCURRENCE OF MDS

- 1. Exposure to benzene
- 2. Chemotherapeutic agents
- 3. Topoisomerase inhibitors
- 4. Radiation
- 5. Genetic diseases like Fanconi's anemia

(ADL)

The best tool to evaluate functional status as an index of the client's capacity to carry out activities of daily living on their own is the Katz Index of Independence in Activities of Daily Living, or Katz ADL ⁽¹⁸⁾. At Cleveland, Ohio's Benjamin Rose Hospital, Sidney Katz and his colleagues first created the idea of ADL in the 1950s.

According to a study by Ciesla JR, et al., the Katz index has demonstrated strong dependability, as proven by reliability coefficients ranging from 0.87 to 0.94.

The tool is usually used by clinicians to identify issues with carrying out activities of daily living and to plan care accordingly.

The Index rates performance adequacy in each of the six categories of

1. Bathing	2. Dressing	3. Toileting
4. Transferring	5. Continence	6. Feeding

Clients are scored on basis of yes/no for independence in each of the six activities. 'Yes' corresponds to Score of 1, and 'No' corresponds to 0.

The score interpretation is given below,

Scoring out of 6	Interpretation
6	full function
4	moderate impairment
2 or less	severe functional impairment

Patient Nam	e:	Date:	
Patient ID #_			
	Katz Index of Independ	ence in Activities of	Daily 1

Katz Index of Independence in Activities of Daily Living			
Activities Points (1 or 0)	Independence (1 Point)	Dependence (0 Points)	
	NO supervision, direction or personal assistance.	WITH supervision, direction, personal assistance or total care.	
BATHING Points:	(1 POINT) Bathes self completely or needs help in bathing only a single part of the body such as the back, genital area or disabled extremity.	(0 POINTS) Need help with bathing more than one part of the body, getting in or out of the tub or shower. Requires total bathing	
DRESSING Points:	(1 POINT) Get clothes from closets and drawers and puts on clothes and outer garments complete with fasteners. May have help tying shoes.	(0 POINTS) Needs help with dressing self or needs to be completely dressed.	
TOILETING Points:	(1 POINT) Goes to toilet, gets on and off, arranges clothes, cleans genital area without help.	(0 POINTS) Needs help transferring to the toilet, cleaning self or uses bedpan or commode.	
TRANSFERRING Points:	(1 POINT) Moves in and out of bed or chair unassisted. Mechanical transfer aids are acceptable	(0 POINTS) Needs help in moving from bed to chair or requires a complete transfer.	
CONTINENCE Points:	(1 POINT) Exercises complete self control over urination and defecation.	(0 POINTS) Is partially or totally incontinent of bowel or bladder	
FEEDING Points:	(1 POINT) Gets food from plate into mouth without help. Preparation of food may be done by another person.	(0 POINTS) Needs partial or total help with feeding or requires parenteral feeding.	
TOTAL POINTS:	SCORING: 6 = High (patient independe	nt) 0 = Low (patient very dependent	

Source: try this: Best Practices in Nursing Care to Older Adults, The Hartford Institute for Geriatric Nursing, New York University, College of Nursing, www.hartfordign.org.

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THE LAWTON INSTRUMENTAL ACTIVITIES OF DAILY LIVING (IADL) SCALE

For evaluating independent living skills, the Lawton Instrumental Activities of Daily Living Scale (IADL) is a suitable tool (Lawton & Brody, 1969). Based on the Katz Index of ADLs, these skills are deemed more difficult than the fundamental activities of daily life ⁽¹⁹⁾.

This assessment tool is simple to use and offers self-reported data on the functional skills required to live in a community.

The tool is most helpful in determining a person's current functional level and detecting any changes or declines over time.

The sensitivity and specificity of scale were 94% and 71% respectively as demonstrated by P Barberger-Gateau et al in their study.

The Lawton IADL scale measures eight domains of function, which consist of:

1. Ability to use telephone	5. Laundry
2. Shopping	6. Mode of transportation
3. Food preparation	7. Responsibility of own medications
4. Housekeeping	8. Ability to handle finances

Traditionally, the categories of food preparation, housekeeping, and laundry have not been included in the scoring system for men. Women are assessed on all 8 areas of function. Based on their greatest level of functioning within that category, clients are assessed.

A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women, and 0 through 5 for men to avoid potential gender bias.

Patient Name:	Date:	
Patient ID #		

LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)

Scoring: For each category, circle the item description that most closely resembles the client's highest functional level (either 0 or 1).

A. Ability to Use Telephone		E. Laundry	
1. Operates telephone on own initiative-looks	1	Does personal laundry completely	1
up and dials numbers, etc.		Launders small items-rinses stockings, etc.	1
2. Dials a few well-known numbers	1	3. All laundry must be done by others	0
3. Answers telephone but does not dial	1		
4. Does not use telephone at all	0		
B. Shopping		F. Mode of Transportation	
Takes care of all shopping needs independently	1	Travels independently on public transportation or drives own car	1
2. Shops independently for small purchases	0	2. Arranges own travel via taxi, but does not	1
3. Needs to be accompanied on any shopping	0	otherwise use public transportation	
trip		3. Travels on public transportation when	1
4. Completely unable to shop	0	accompanied by another	
. , .		4. Travel limited to taxi or automobile with	0
		assistance of another	
		5. Does not travel at all	0
C. Food Preparation		G. Responsibility for Own Medications	
Plans, prepares and serves adequate meals	1	1. Is responsible for taking medication in correct	1
independently		dosages at correct time	
2. Prepares adequate meals if supplied with	0	2. Takes responsibility if medication is prepared in	0
ingredients		advance in separate dosage	
3. Heats, serves and prepares meals, or	0	3. Is not capable of dispensing own medication	0
prepares meals, or prepares meals but does			
not maintain adequate diet			
4. Needs to have meals prepared and served	0		
D. Housekeeping		H. Ability to Handle Finances	
1. Maintains house alone or with occasional	1	Manages financial matters independently	1
assistance (e.g. "heavy work domestic help")		(budgets, writes checks, pays rent, bills, goes to	
2. Performs light daily tasks such as dish	1	bank), collects and keeps track of income	
washing, bed making		2. Manages day-to-day purchases, but needs help	1
3. Performs light daily tasks but cannot	1	with banking, major purchases, etc.	
maintain acceptable level of cleanliness		3. Incapable of handling money	0
4. Needs help with all home maintenance	1		
tasks			
Does not participate in any housekeeping	0		
tasks			
Score		Score	
Score		Total score	
		Total score	1

Source: *try this:* Best Practices in Nursing Care to Older Adults, The Hartford Institute for Geriatric Nursing, New York University, College of Nursing, www.hartfordign.org.

and 0 through 5 for men to avoid potential gender bias.

A summary score ranges from 0 (low function, dependent) to 8 (high function, independent) for women

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MONTREAL COGNITIVE ASSESSMENT (MOCA)

- MOCA was developed in the year 1996 by Dr. Ziad Nasreddine MD⁽²⁰⁾
- It was developed in Montreal, Quebec, hence named after it.
- It is available in almost 100 languages (multiple versions). It has been validated in 2005 to identify mild cognitive impairment with 90% accuracy
- The sensitivity and specificity of detecting mild cognitive impairment using MOCA was 90% and 87% respectively as described by R Mahendran et al in their assessment.
- Tests 8 cognitive domains:

1. Visuospatial/executive	5. Language
2. Naming	6. Abstraction
3. Memory	7. Delayed recall
4. Attention	8. Orientation

- It comes in three additional versions in addition to the standard MOCA.
 - 1. Blind/telephone
 - 2. Hearing impaired
 - 3. Illiterate / <5 years of education
- The MOCA score interpretation is given below,

MoCA scoring out of 30	Interpretation
26 and above	Normal
18 - 25	Mild cognitive impairment
10-17	Moderate cognitive impairment
Less than 10	Severe cognitive impairment
Add 1 point if ≤ 12 yr education	

MONTREAL CO	OGNITIVE ASSES	SMEN	IT (MOCA)	Ed	NAME: ucation:		Date of birth:	
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MATERIALS AND METHODOLOGY

SETTING:

Elderly patients above 60 years old attending outpatient clinics of Department of Geriatrics and patients who are admitted in Geriatrics ward of Shri B M Patil Medical College Hospital & Research Centre.

ETHICAL COMMITTEE APPROVAL: Ethical committee clearance was obtained from the Institutional Ethical committee of Shri B M Patil Medical College Hospital & Research Centre as per the meeting held on August 2022.

STUDY DESIGN

Prospective Case-control study

STUDY PERIOD

18 months

CONSENT

Consent was taken from all patients, who participated in the study.

FINANCIAL SUPPORT

Nil

STUDY POPULATION

50 elderly who satisfied the WHO criteria for anemia were included as cases. 50 age and sex matched non anemic elderly were considered as controls.

INCLUSION CRITERIA

- Age above 60 years
- Patient with Hemoglobin levels of <12g/dl in women and <13g/dl in men

EXCLUSION CRITERIA

- Critically ill bed ridden patients
- Dementia diagnosed patients

DETAILS OF THE STUDY

A total of 50 cases that met the WHO definition of anemia (men's hemoglobin <13g/dl and women's hemoglobin <12g/dl) were enrolled as cases and 50 age and sex matched controls who were non-anemic were included in the study group.

The cases and controls were subjected to Katz Index of Independence in Activities of Daily Living (ADL), Lawton – Brody Instrumental Activities of Daily Living scale (I.A.D.L.), Montreal Cognitive Assessment (MOCA), scores were obtained and inference was done.

The anemic elderly (cases) were subjected to detailed history taking and thorough clinical examination.

The following pertinent examinations were carried out after 10 ml of venous blood was obtained from patients with their consent using a dry syringe and aseptic measures.

The cases underwent following investigations like complete blood count which includes hemoglobin concentration, haematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, red cell distribution width, red blood cell count, total count, differential count and the platelets.

Peripheral smear analysis was performed on each participant, and this was a crucial factor in the anemia classification. Patients were categorised as macrocytic, normocytic, or microcytic based on the peripheral smear image.

Serum ferritin and Serum Iron was done in patients with microcytic and normocytic picture in peripheral smear to differentiate between anemia of chronic inflammation and iron deficiency anemia. Additional investigations like inflammatory markers which includes Erythrocyte sedimentation rate and C-reactive protein was done.

Serum Vitamin B12 was done in patients with macrocytic anemia and pancytopenia. Pancytopenia patients were subjected to reticulocyte count to determine bone marrow status whether it is hypo or hyperproliferative.

In patients with abnormal renal profile GFR was calculated using MDRD equation to assess the appropriate renal function.

Patients with peripheral smears exhibiting immature white cells and nucleated red cells, as well as those with severe anemia, unexplained anemia, and suspicion of haematological malignancy such as myelodysplastic syndrome, had been subjected to bone marrow aspiration.

Patients with iron deficiency anemia, those with stool occult blood positive, and those whose underlying cause was not determined was subjected to upper gastrointestinal endoscopy procedure.

Stool occult positive patients with normal upper GI endoscopy were subjected to Colonoscopy.

Further tests were performed to determine the underlying cause, including X-rays of the chest, USGs of the abdomen and pelvis, stool examinations for parasites, serum lactate dehydrogenase, serum TSH, and liver function tests.

RESULTS

A cohort of patients 60 years of age and older, encompassing either sex, participated in this case control study. Patients who fulfill the WHO criteria for anemia was considered as cases, and controls were age and sex matched individuals who were not anemic.

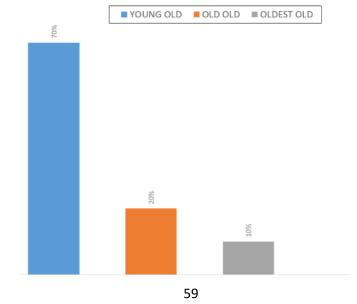
AGE DISTRIBUTION

Age distribution	n=100	Cases (n=50)	Control (n=50)
60-69	40	20	20
70-79	40	20	20
80-89	18	9	9
90-99	2	1	1
100 & above	0	0	0

The study population between the age group 60-69 years and 70-79 years had the same percentage, and population decreases as age progresses, there were no centenarians involved in our study.

According to the chronological age classification the study population comprises of 70% of the patients belonging to young old(60-74 years), 20% belonged to old old (75-84 years) and 10% belonged to oldest old (≥85 years)group. The age distribution in this study started from age of 60 to 92 years old and the median among the study population was 69.8 years.

AGE GROUP DISTRIBUTION

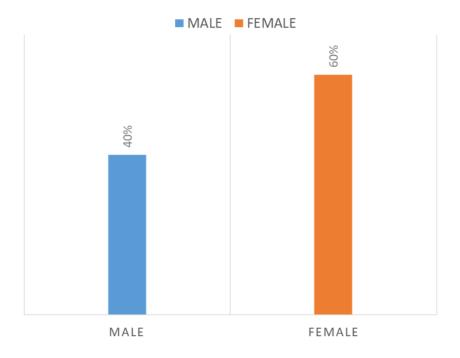


SEX DISTRIBUTION

As it was a age and sex matched case control study, gender distribution was taken equal among cases and controls. In our study the female population was more prevalent than the male population.

Sex	n = 100	Cases (n=50)	Cases (n=20)
Male	40	20	20
Female	60	30	30

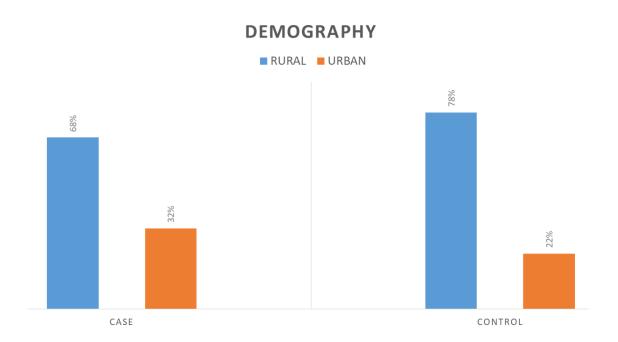
GENDER DISTRIBUTION



DEMOGRAPHY

Among the cases, 68% of patients were from rural region and 32% of population were residing in urban areas, whereas in controls, 78% belonged to rural region and 22% were from urban region. This implies that in our study population, rural populations seems to be in highest percentage.

Demography	Cases (n=50)	Controls (n=50)
Rural	34	39
Urban	16	11



OCCUPATION

Occupation	Cases (n=50)	Controls (n=50)
Employed	4	14
Unemployed	32	14
Homemaker	14	22

In our study 28% of non-anemic elderly controls were doing their daily occupation, whereas it was seen only in 8% of anemic cases and most of them belong to farming occupation.

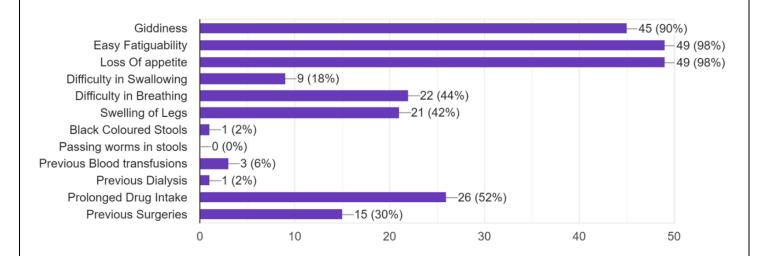
Elderly women who were still taking care of home were found more in controls (44%) than the cases (28%)

The unemployment prevailed more in the cases (64%) than the controls, which implies that the anemia impacts their quality of life which prevents them from carrying out their daily occupations and increase their dependence on others, which make them more prone for elder abuse.



Now taking cases into considerations, thorough history and clinical examinations was performed on 50 elderly anemic cases and the results are shown in the following pages,

PRESENTING HISTORY



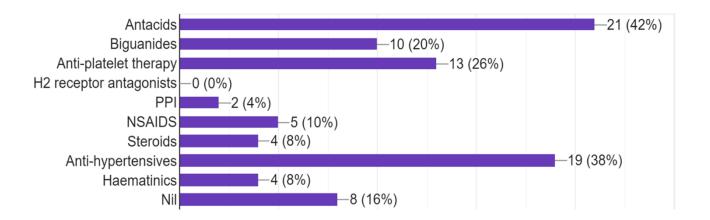
Atypical presentations like giddiness, easy fatigability and decrease in appetite were the complaints found in highest percentage than what we expect of typical complaints in anemia like breathlessness, palpitations and lower limb swelling.

This implies that while asking history to the elderly, it is always important to ask about the quality of appetite, quality of sleep, any new symptom recently developed, giddiness while getting up from bed, any bleeding manifestations especially hemorrhoids, regularity of bowel and bladder, any gastrointestinal discomfort like gastritis in additional to asking about the typical symptoms of anemia. Prolonged drug intake was seen in 52% of the case population.

Typical anemia symptoms like difficulty in breathing was seen in forty four percent of study population followed by swelling of legs which was seen in 42% of the anemic cases.

Patients who already underwent surgeries accounted for 30% of study population. Six percent of patients had blood transfusions in the past and only one patient in our study had history of dialysis in the past.

DRUG HISTORY



In our study population, antacid consumption (42%) secondary to GERD like symptoms were found most common followed by consumption of antihypertensive medications(38%) and anti-platelet therapy, which 13 out of 50 cases were taking, among them aspirin was consumed by 10 cases.

Aspirin as an anti-platelet drug, though beneficial, chronic administration of low dose aspirin 75-100mg/day may cause iron deficiency anemia in absence of major gastric bleeding.

The Biguanides especially metformin was consumed by the diabetic population which accounts for 20% of the cases.

Four percent of case population were already taking hematinic supplements. Proton pump inhibitors, NSAID's, steroids were consumed in lower proportion. Among our case population 8% of the population were not on any drugs and few were on the verge of polypharmacy.

Polypharmacy is defined as regular use of five or more medications at the same time. The brown bag concept which involves advising patients to bring all the medicine during medical review helps in detecting polypharmacy. Unnecessary and harmful drugs can be stopped and alternative drugs can be given by applying STOPP (Screening Tool of Older Persons' Prescriptions) and START (Screening Tool to Alert to Right Treatment)

DIET HISTORY



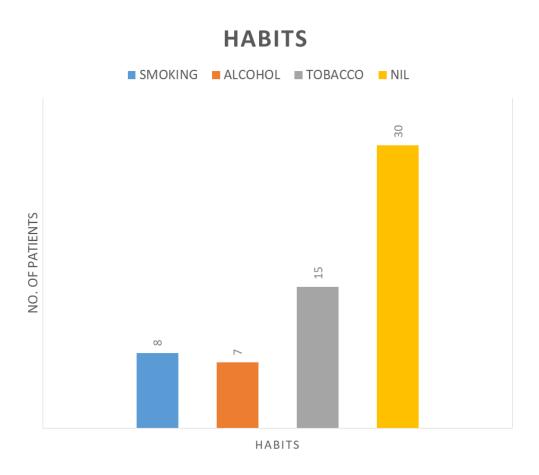
Among the 50 anemic elderly cases taken in our study, 34 people had the habit of following vegetarian diet, only 16 people had the habit of consuming mixed diet.

Studies have shown that elderly are more prone to develop nutritional anemia secondary to low bioavailability of iron and Vitamin B12 and decreased absorption in the intestine⁽⁷⁾.

Therefore we should consider starting hematinic such as iron and B12 supplements at the earliest for the elderly to avoid the onset of anemia despite the kind of diet they are following and create awareness among them to consume nutritious foods rich in iron and vitamin B12.

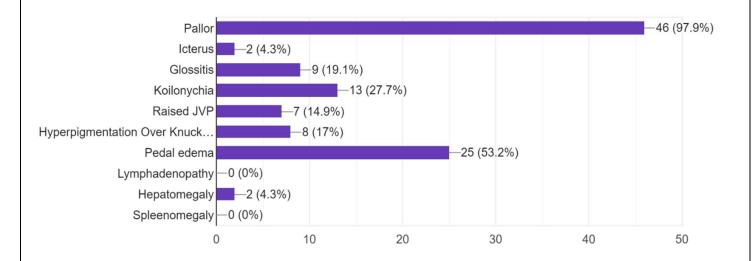
HABITS

Analyzing the habits of 50 cases, consumption of tobacco was found common accounting for 30% of the cases followed by habit of smoking and alcohol consumption. Tobacco chewing were prevalent among both males and females of the case population, tobacco chewing leads to poor dental hygiene, which results in reduction in consumption food which ultimately may lead to nutritional anemia. Thirty out of fifty patients did not have any habits injurious to health.



Alcohol consumption was seen in seven patients out of which five patients were suffering from Vitamin B12 deficiency anemia, as alcohol has a tendency to damage the lining of stomach and intestines, thereby reducing the absorption of B12 vitamin leading to its deficiency. Two patients consuming alcohol whose upper gastrointestinal endoscopy showed active bleeding leading to blood loss, ultimately lead to iron deficiency anemia.

CLINICAL PRESENTATION



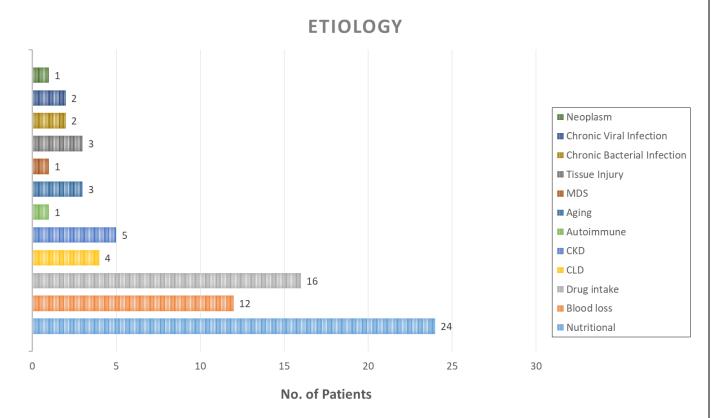
Pallor was the most common clinical sign found in almost ninety eight percent of the case population, similar to previous studies⁽³⁾ which has shown pallor is considered to have increased sensitivity and specificity to diagnose anemia.

In our study conjunctival pallor has been taken into account, whereas studies have shown that pallor at each site is associated with significantly lower hemoglobin concentration.

Followed by pallor most elderly cases in our study population had sign of pedal edema and koilonychias. Studies have shown that low hemoglobin concentration in patients with anemia causes decreased inhibition of basal endothelium derived relaxing factor activity leading to generalized vasodilatation. This may lead to low blood pressure which activates the renin-angiotensin pathway resulting in salt and water retention

Glossitis and hyperpigmentation over knuckles was found in cases with Vitamin B12 deficiency anemia.

ETIOLOGY



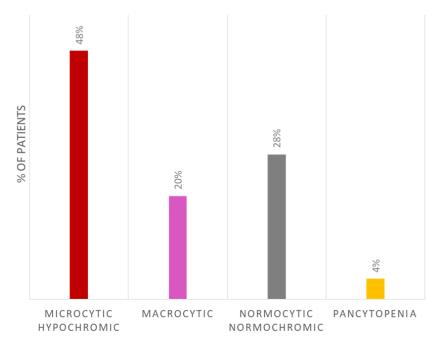
Analyzing the etiology of anemia in a broader aspect, nutritional deficit was the most common etiology found among the case population, which implies the importance of finding malnutrition in elderly at early stage and preventing the onset of anemia. Malnutrition in elderly can be picked up at early stage by doing mini nutritional assessment during outpatient visit of the elderly and can be referred to a dietician if necessary.

Followed by nutritional deficit, the next common etiology for anemia in our case population is prolonged drug intake, which involves mostly antacids, NSAID's, proton pump inhibitors along with the drugs they are taking for their co-morbidities. Therefore it is necessary to apply the concepts like brown bag and polypharmacy, which helps in reviewing the drugs that elderly are taking, and put our efforts to reduce the unnecessary drugs, and drugs that impair the absorption of nutrition, therefore preventing anemia.

The third most common cause of anemia in our case population is secondary to blood loss of different disorders which includes duodenal ulcers, antral ulcers, esophageal varices, and hemorrhoids which highlights the need for evaluation of gastrointestinal system in patients presenting with anemia.

PERIPHERAL SMEAR STUDY

Peripheral Smear (Inference)	No. of cases (n=50)
Microcytic Hypochromic anemia	24
Macrocytic anemia	10
Normocytic Normochromic anemia	14
Pancytopenia	2

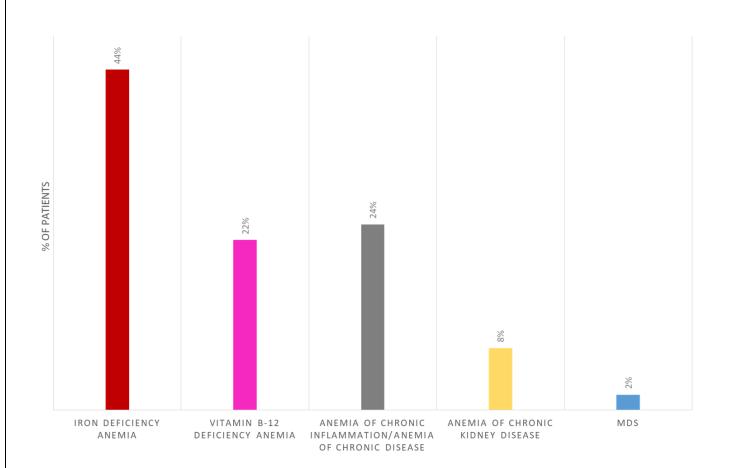


Microcytic hypochromic anemia was the most common type of anemia in our study constituting about 48% of the case population, while a study by Saurabh Srivastava et al. on patterns of anemia in Geriatric population had highest proportion of normocytic normochromic anemia. Normocytic normochromic anemia had the second highest prevalence constituting to about 28% of case population. Many different disorders produce anemia of microcytic and hypochromic pattern, to differentiate whether it is due to iron deficiency or anemia of chronic inflammation, serum iron and serum ferritin was done in all microcytic hypochromic smear pattern cases.

Normocytic normochromic type can develop after a substantial volume of blood loss, hemolysis or in bone marrow failure to identify which all patients with normocytic normochromic smear pattern was subjected to reticulocyte count. The least prevalence was the pancytopenia picture (4%) found in patients of myelodysplastic syndrome and severe Vitamin B12 deficiency.

TYPES OF ANEMIA IN THE ELDERLY

Types of Anemia	Cases (n=50)
Iron deficiency anemia	22
Vitamin B-12 deficiency anemia	11
Anemia of Chronic inflammation/Anemia of Chronic Disease (ACI/AOCD)	12
Anemia of Chronic Kidney Disease (AOCKD)	4
Myelodysplastic syndrome	1



IRON DEFICIENCY ANEMIA

According to a recently conducted study among the elderly in eight states of India ⁽²⁷⁾, Iron deficiency anemia accounted for almost 41% of the total study population, which correlates with our study in which iron deficiency anemia accounts for 44% of the total case population. This shows the burden of iron deficiency anemia in a developing country like India.

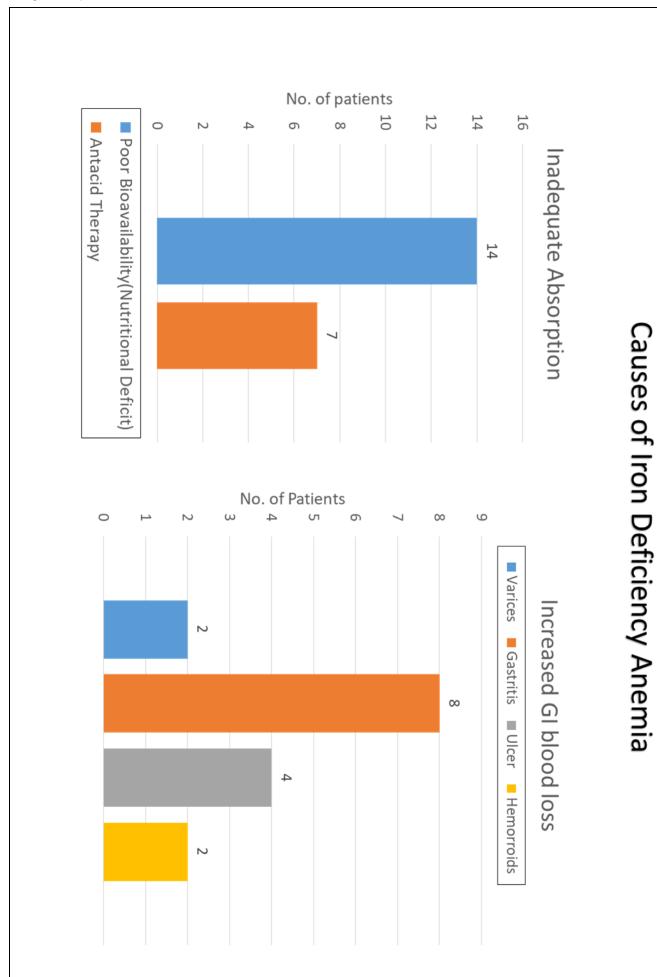
Poor oral hygiene secondary to chronic tobacco consumption, multiple child births in past, chronic antacid consumption secondary to gastro esophageal reflux disorder were the most common etiology prevalent among the elderly females in our study population. Chronic antacid consumption lead to alteration in stomach acid balance which lead to reduced absorption of iron. Poor oral hygiene and poor dentures were factors leading to decreased oral intake of food, which ultimately lead to poor bioavailability.

Next to inadequate absorption, the cause of iron deficiency anemia was gastrointestinal blood loss which were equally prevalent among both the sexes. Upper GI endoscopy done in iron deficiency anemia cases revealed significant findings.

Antral gastritis was seen in most of the cases followed by duodenal ulcers. Duodenal part of intestine is the place where more iron absorption happens.

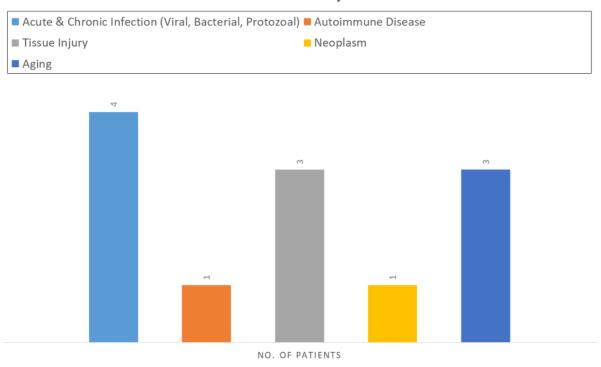
Few other patients had active bleeding through hemorrhoids. Therefore an elderly anemic patient with normal UGI scopy should be questioned for hemorrhoids, if needed can be subjected to colonoscopy after seeing the results of stool occult.

Antiplatelet drugs specifically aspirin was consumed by 26% of case population, aspirin have tendency to induce gastritis by which the patient may ultimately land up in iron deficiency anemia. Hence aspirin usage must be avoided in the elderly by considering risk versus benefit ratio and should be supplemented with other antiplatelet like clopidogrel, which studies have shown to be safe in elderly.



ANEMIA OF CHRONIC INFLAMMATION (ACI)/ANEMIA OF CHRONIC DISEASE (AOCD)

CAUSES OF ACI/AOCD

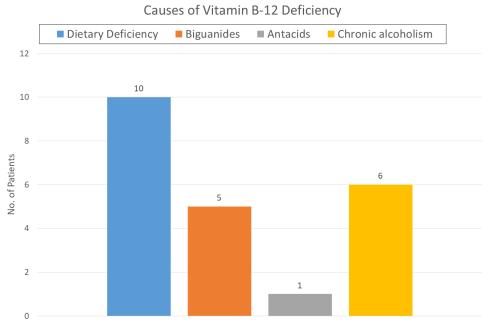


Anemia of chronic inflammation/disease was found among 24% of our case population which was comparatively lower than other studies (3) (21) (22) where its incidence was relatively high in elderly. The majority of patients with anemia of chronic disease in our study had long-term infections. The chronic disease conditions includes two cases of pulmonary tuberculosis, one case of human immunodeficiency virus infection and other hepatitis B infection. The patient with autoimmune disorder in our study was suffering from rheumatoid arthritis. Other common causes were malignancy and tissue injury like myocardial infarction.

A theory suggests that cytokines such as IL-1, IL-6, and TNF-α, which destroy RBC precursors and reduce the amount of erythropoietin receptors on progenitor cells, are the cause of anemia brought on by chronic disease.

VITAMIN B12 DEFICIENCY ANEMIA

Twenty two percent of the case population were suffering from Vitamin B12 deficiency anemia. In elderly, as age progresses the absorption of B12 decreases due to their inability to digest food bound cobalamin ⁽⁷⁾.



Poor bioavailability was the most common cause of Vitamin B12 deficiency in elderly. Vitamin B12 is readily absorbed in the last part of small intestine, ileum. Alcohol consumption damages the lining of stomach and intestines which leads to reduced absorption of Vitamin B12.

Oral hypoglycemic drugs, especially Biguanides, metformin was the commonest drug consumed by all diabetic patients in our case population (23%). Metformin reduces the absorption of intrinsic factor complex through the enteral cubilin receptor in the terminal ileum, which has the potential to result in a B12 shortage which may ultimately lead to peripheral neuropathy, autonomic neuropathy, neuropsychiatric symptoms and hematological disorders. Again stomach acid base imbalance created by antacids, proton pump inhibitors and H2 receptor antagonists will lead to impaired absorption of Vitamin B12 leading to its deficiency.

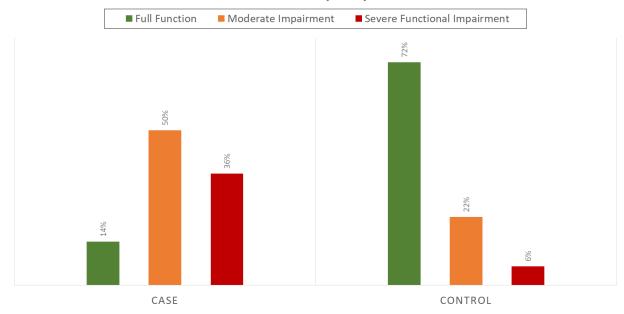
Anemia of chronic kidney disease and myelodysplastic syndrome were found in 8% and 2% of the case population respectively.

KATZ INDEX OF INDEPENDENCE IN ACTIVITIES OF DAILY LIVING (ADL)

ADL	Cases	Controls	Odd's ratio
Impaired	43	14	15.8
Intact	7	36	(OR > 1)

ADL	Total no. of patients (n=100)	Cases (n=50)	Controls (n=50)
Full function	43	7	36
Moderate impairment	36	25	11
Severe functional impairment	21	18	3

KATZ INDEX OF INDEPENDENCE IN ACTIVITIES OF DAILY LIVING (ADL)



ADL performed among the elderly anemic cases and non-anemic controls reveals that 72% of controls had full function whereas only 14% of cases had full function. Whereas severe functional impairment was seen in 36% of cases and it was found only in 6% of controls.

AGE GROUP (Cases) (n=50)	FULL FUNCTION (n=7)	MODERATE IMPAIRMENT (n=25)	SEVERE FUNCTIONAL IMPAIRMENT (n=18)
YOUNG OLD (n=29)	5	14	10
OLD OLD (n=14)	2	9	3
OLDEST OLD (n=7)	0	2	5

AGE GROUP (Controls) (n=50)	FULL FUNCTION (n=36)	MODERATE IMPAIRMENT (n=11)	SEVERE FUNCTIONAL IMPAIRMENT (n=3)
YOUNG OLD (n=29)	28	1	0
OLD OLD (n=14)	7	5	2
OLDEST OLD (n=7)	1	5	1

The Katz ADL evaluation results showed a significant odd's ratio between our cases and controls, suggesting that patients with anemia have almost 16 times greater probability of functional impairment.

Among the chronological age group distribution of cases and controls, 97% of Young-Old controls had full function whereas only 17% of Young-Old cases had full function. Moderate impairment was seen in Old-Old cases than controls. Severe functional impairment was started to be seen in Young-Old cases whereas in controls it started from age group of Old-old and Oldest-old category and comparatively very less in percentage when compared with cases of the same category.

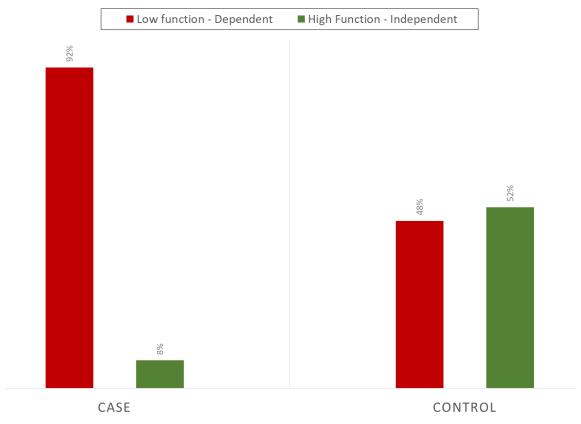
This implies that anemia plays a major role in affecting the activities of daily life, as age progresses it becomes even worse. Activities of daily living are the basic necessities for an elderly to survive independently without need of a caretaker. When anemia sets in, it slowly impacts their activities of daily living, which increases their dependence on others for their daily day to day activities, which make them prone for elder abuse kind of situations.

In a developing country like India where care takers are found in scarce amount, correcting anemia at the earliest and restoring their activities of daily life and preserving their independence is a necessity.

LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)

IADL	Total no. of patients (n=100)	Cases (n=50)	Controls (n=50)	Odd's ratio
Low function	72	46	26	10.62
High function	28	4	24	(OR > 1)

LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)



A substantial odd's ratio was found in the Lawton IADL assessment of the cases and controls, suggesting that the chances of impairment in instrumental activities of daily living are elevenfold greater in anemic cases than in non-anemic aged individuals.

IADL assessment done on the case and controls reveal that 92% of cases had low function and high dependence, whereas it was seen only in 48% of the controls.

High function and independence in instrumental activities of daily living was found in higher percentage in controls (52%) than cases (8%).

AGE GROUP (Cases) (n=50)	High function – Independent (n=4)	Low function – Dependent (n=46)
YOUNG OLD (n=29)	4	25
OLD OLD (n=14)	0	14
OLDEST OLD (n=7)	0	7

AGE GROUP (Controls) (n=50)	High function – Independent (n=24)	Low function – Dependent (n=26)
YOUNG OLD (n=29)	22	7
OLD OLD (n=14)	2	12
OLDEST OLD (n=7)	0	7

Among the chronological age group distribution of cases and controls, 76% Young-Old controls had high function, whereas it was found only in 14% of Young-Old Cases.

Fourteen percent of Old-Old controls had high function, whereas it was found in none in that specific age group cases. Oldest Old cases as well as controls had low function and high dependence for their instrumental activities of daily living like shopping, housekeeping, transportation, ability to handle finances and responsibility of their medications.

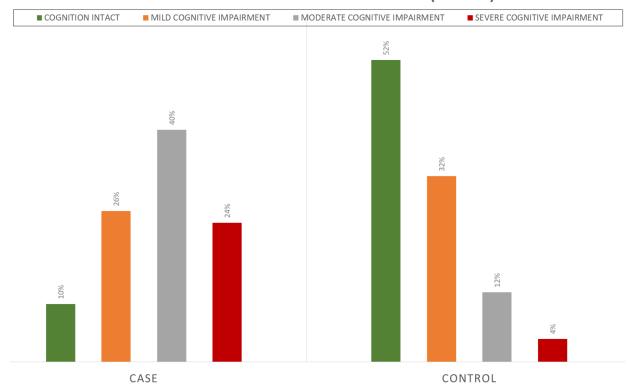
This implies that as age progresses instrumental activities of daily living declines and their dependence on others increases and anemia just fastens the process of decline.

MONTREAL COGNITIVE ASSESSMENT (MOCA)

Cognition	Cases	Controls	Odd's ratio
Impaired	45	24	9.75
Intact	5	26	(OR >1)

MOCA	Total no. of patients (n=100)	Cases (n=50)	Controls (n=50)
Cognition Intact	31	5	26
Mild Cognitive Impairment	29	13	16
Moderate Cognitive Impairment	26	20	6
Severe Cognitive Impairment	14	12	2

MONTREAL COGNITIVE ASSESSMENT (MOCA)



A significant odds ratio from the MOCA evaluation of our study population indicates that elderly individuals with anemia are ten times more likely to experience cognitive impairment than elderly individuals who don't have anemia.

According to the MOCA assessment on cases and controls, 52% of controls had their cognition intact, whereas it was found only in 10% of the cases. Severe cognitive impairment was found only in 4% of controls whereas it is found in larger proportion in controls (24%).

AGE GROUP (Cases) (n=50)	Cognition Intact (n=5)	Mild Cognitive Impairment (n=13)	Moderate Cognitive Impairment (n=20)	Severe Cognitive Impairment (n=12)
YOUNG OLD (n=29)	4	12	12	1
OLD OLD (n=14)	1	1	8	4
OLDEST OLD (n=7)	0	0	0	7

AGE GROUP (Controls) (n=50)	Cognition Intact (n=26)	Mild Cognitive Impairment (n=16)	Moderate Cognitive Impairment (n=6)	Severe Cognitive Impairment (n=2)
YOUNG OLD (n=29)	24	4	1	0
OLD OLD (n=14)	2	11	1	0
OLDEST OLD (n=7)	0	1	4	2

Among the chronological age group distribution of cases and controls, 83% of Young-Old controls had their cognition intact, whereas it was found only in 14% of Young-Old cases. In Old-Old age category controls had mild cognitive impairment more than the cases, whereas moderate cognitive impairment is seen vice versa. In Oldest-Old age category, all anemic cases had severe cognitive impairment whereas it was seen only in twenty eight percent of Oldest-Old controls.

Cognition plays an important role as age progresses to maintain stability in day to day life. These above results implies that as age progresses, anemia hastens the process of cognition decline and make the patient more prone to develop cognitive disorders like dementia, delirium. Hence MOCA should be administered in all anemic elderly and their level of cognition should be assessed to prevent its decline. In addition diagnosing and correcting anemia should be made as a routine workup for the elderly to give a good quality of life.

DISCUSSION

AGE DISTRIBUTION

Study	Age range(years)	Study	Median age group
Amit bhasin and Medha rao et al	60 – 87	Amit bhasin and Medha rao et al	70.5 years
Our study	60 - 92	Our study	69.8 years

In our study the age range started from 60 and the oldest patient in our study was ninety two years old and the median age of all patients in our study was 69.8 years which almost similar to a study done by Amit Bhasin et al.,

Age group (years)	Saurabh Srivatsva et al.	Our study
60 – 69	58.9 %	40 %
70 – 79	30.7 %	40 %
> 80	10.4 %	20 %

The patients between the age group of 60 - 69 years was found in highest percentage in Saurabh Srivatsva et al than our study, whereas the percentage of patients above 70 years were found in higher percentage in our study.

GENDER DISTRIBUTION

Gender	Saurabh Srivatsva et al.	Amit bhasin and Medha rao et al	Our study
Male	60%	52%	40%
Female	40%	42%	60%

Female preponderance was seen in our study, whereas earlier studies done in India had male prevalence in higher percentage.

PERIPHERAL SMEAR PATTERN DISTRIBUTION

Peripheral smear pattern	Amit bhasin and Medha rao et al (in %)	Saurabh Srivatsava et al (in %)	Our study (in %)
Microcytic	30	12	48
Normocytic	62	78	28
Macrocytic	6	6	20
Pancytopenia	2	-	4

Studies done by Amit bhasin et al and Saurabh Srivatsva et al had normocytic smear pattern in higher percentage, whereas results in our study was contradictory.

In our study Microcytic smear pattern was found in highest percentage which was second most common pattern of prevalence in other studies. The macrocytic smear pattern was seen lowest in all the three studies and the results correlated.

NORMOCYTIC ANEMIA

Study	Percentage of Normocytic Anemia in Peripheral smear
Amit bhasin and Medha rao et al	62%
Saurabh Srivatsva et al	78%
Elis et al	60%
Amiasal et al	62%
Our study	28%

Studies done in Western countries (21) and Indian studies (2) (3) have normocytic anemia as the commonest pattern in peripheral smear, though results in our study did not correlate, normocytic blood picture should not be disregarded as a normal peripheral smear picture, it should be subjected to further evaluation as it was one of the commonest peripheral smear seen in anemia of chronic inflammation and anemia of chronic kidney disease.

COMPARATIVE STUDIES OF ETIOLOGIES OF ANEMIA IN ELDERLY

Etiologies	Andrew et al (in %)	Joosten et al (in %)	NHANES III (in %)	Our study (in %)
Iron deficiency	15 - 23	5 – 30	20	44
Vitamin B12 deficiency	0 – 15	5 – 10	14	22
Chronic inflammation/disease	15 – 35	30 – 45	20	24
Chronic kidney disease	8	-	8	8
Myelodysplastic syndrome	0 – 5	5	-	2

In contrast to our study, the incidence of iron deficiency was lower in western studies (22)(23)(24). The high incidence in our study is a result of the high prevalence of nutritional deficiencies, especially iron deficiency among the elderly population. Hence iron deficiency anemia in elderly has to be highlighted and its prevention should be taken care in future health schemes formulated by the government.

The prevalence of Vitamin B12 deficiency is higher in our study compared to the other studies. This implies that in elderly individuals diagnosing Vitamin B12 deficiency anemia is as important as diagnosing iron deficiency anemia. It does not stop at diagnosing, finding out the etiology which is leading to deficiency is important, so that it can be corrected and which will ultimately prevent the deleterious effects such as peripheral neuropathy, autonomic neuropathy, neuropsychiatric disorders

The results of anemia of chronic inflammation/disease, anemia of chronic kidney disease was correlated with the western statistics. The myelodysplastic syndrome was less prevalent in our study when compared with the results of western studies.

NUTRITIONAL DEFICIENCY ANEMIA

Nutritional anemia	Jack & Co workers et al	Amit bhasin and Medha rao et al	Our study
Iron deficiency	16.6%	30%	44%
Vitamin B12 deficiency	5.9%	3%	22%

The highest incidence of iron deficiency anemia was found in our study, which may be related to these factors that are frequently observed in our community. Insufficient dietary intake

- 1. Dietary insufficiency
- 2. Gastric disorders
- 3. Malabsorption in elderly
- 4. Chronic bleeding
- 5. Worm infestations

Thus, iron deficiency is the most common cause of nutrition-deficient anemia, and our research supports the findings of prior studies.

The incidence of B12 deficiency is seen in comparatively higher percentage than western studies, as India being the diabetic capital of world, consumption of biguanides is seen in higher percentage, which prevents B12 absorption leading to its deficiency, hence all the patients on biguanides should be supplemented with Vitamin B12 and role played by antacids and alcohol in prevention of B12 absorption has to be kept in mind.

All the elderly individuals coming to the outpatient with multi-morbidity and polypharmacy, frail individuals should be subjected to mini nutritional assessment (MNA) and according to the inference, the clinicians should decide on referring to dietitian and provide a diet plan to the elderly, thereby preventing the onset of anemia.

ANEMIA OF CHRONIC DISEASE

Study	Results
Amit bhasin and Medha rao et al	48 %
NHANES III	30 %
Our study	24 %

The above table shows that anemia of chronic disease/inflammation was seen in lower percentage when compared with NHANES-III, Amit Bhasin et al studies. Iron deficiency anemia is more common than other kinds of anemia in the Elejalde Guerra et al study, although Amit Bhasin et al. investigation found that the prevalence of ACD is higher. Our research and that of Elejalde Guerra et al. correlated.

ANEMIA OF CHRONIC KIDNEY DISEASE

Study	Results
Amit bhasin and Medha rao et al	22 %
Jack and Co worker et al	13.2 %
Our study	8 %

Poor control of comorbidities like diabetes and hypertension leads to chronic kidney disease. In a previous Indian study done on 2011 by Amit Bhasin et al, showed higher percentage of anemia of chronic kidney disease, whereas our study showed very less percentage which implies that good control of hypertension and diabetes among the Indian population secondary to establishment of many non-communicable disease clinics by the Indian government.

MYELODYSPLASTIC SYNDROME

The incidence of MDS increases markedly with age. According to the ICMR's SEER-Medicare database, up to 75 out of 100,000 individuals aged 65 and older may have MDS. In our study the prevalence of MDS accounted for 2% of case population.

STUDY ON IRON STORES

Study on iron stores	Serum Ferritin less than 20ng/dl
Milman & Schultz – Larsen	5.9 %
Amit bhasin and Medha rao et al	11 %
Our study	28 %

The body's overall iron stores are reflected in serum ferritin. These findings suggest that the Indian population has extremely little iron reserves than western population as seen in their study ⁽²⁵⁾. As a result, as individuals grow older, they become more susceptible to anemia symptoms.

DISCUSSION ON KATZ ADL AND LAWTON IADL

A study by Chauhan et al. evaluated prevalence of disability among indian elderly, where they did not adapt Katz index with all six indicators, they omitted 'continence' because of lack of availability of data and in Lawton IADL which comes with eight indicators, 'Laundry was neglected because of lack of data existence.

In our study all the Indicators of Katz ADL and Lawton IADL was taken into account and evaluated on the patient, assessed scores and inference was made according to the instructions given in the respective scales.

Among the six indicators of Katz ADL index, bathing was the activity affected first in patients followed by toileting was affected which goes in accordance with a study performed by Jaggor et al ⁽²⁷⁾. The last activity to get affected in Katz ADL index was continence among our study population.

Lawton IADL consisted of eight instrumental activities, where only five activities was applicable for the male gender. The categories of meal preparation, housekeeping, and laundry were not scored for men. In female gender, the first instrumental activity to decline in our study was food preparation, whereas in male gender the first instrumental activity to decline in our study was transportation.

DISCUSSION ON MOCA

Many Western and Indian studies evaluated cognition assessment in elderly using Mini Mental State Examination by Folstein et al. Only few study data are available using MOCA to assess cognition in elderly.

Study	Abnormal MOCA score
Puustinen et al	92%
Our study	69%

A study by Puustein et al where MOCA was performed on elderly individual undergoing arthroplasty showed higher percentage of abnormal score ⁽²⁶⁾ when compared with our study where MOCA was performed on elderly anemic cases and non-anemic controls.

MOCA consisted of eight components, among our study population, the first component which got affected in the elderly was delayed recall was the component most patients scored less followed by executive functions, and more patients scored well in the naming.

Thus MOCA is been seen in higher percentage in both the studies which implies all elderly should be subjected to MOCA assessment despite their illness to assess their cognition status and steps has to be taken to prevent further decline in cognition.

ANALYTICAL REPORT

- > Our study population has female preponderance.
- ➤ The study population's mean age was 69.8 years, with the maximum number of patients belonging to the Young-old group.
- The majority of patients in our study come from rural backgrounds.
- ➤ Compared to non-anemic controls, elderly anemic subjects had a higher rate of unemployment.
- ➤ The most frequent complaints from elderly anemic cases were easy fatiguability and appetite loss.
- ➤ The most often consumed drug among the study population was antacids and a greater proportion of patients took biguanides and anti-platelet medications.
- ➤ The research population exhibited a preponderance of vegetarians.
- The greatest proportion of patients had no habits, such as alcohol, tobacco, or smoking.
- ➤ The most frequently observed clinical sign was pallor, while the most frequent symptom that patients reported having was leg swelling.
- ➤ The most common etiology of anemia was nutritional deficiency among the participants in our study
- The majority of the cases had a microcytic hypochromic smear pattern followed by normocytic pattern.
- ➤ Iron deficiency anemia was the most common anemia type prevalent in the patients followed by anemia of chronic disease.
- ➤ The majority of iron deficient anemia patients had gastritis and nutritional deficit (poor bioavailability).
- > Chronic infections were the commonest cause of anemia in chronic disease.
- > 27% of Vitamin B12 deficient anemia patients were chronic alcoholics.
- Anemia of chronic kidney disease and myelodysplastic syndrome was found in scarce number.
- ➤ Katz ADL index found disability in 57 patients and full function in 43 patients and the odd's ratio was significant. Full function was seen mostly in Young-Old controls, whereas severe impairment were found maximum in Oldest-Old cases.
- ➤ The first activity to decline in Katz ADL was bathing and last to decline was incontinence.

- ➤ Lawton IADL revealed low function, high level of dependence in 72 patients. High function and independence in instrumental activities of daily living was found in higher percentage in controls (52%) than cases (8%).
- ➤ The first activity to decline in Lawton IADL was cooking in females and transportation in males.
- MOCA assessment identified 14 cases with severe cognitive impairment in which 12 were cases and 2 were controls.
- ➤ MOCA performed on cases and controls reveals that the odds of an anemic elderly getting their cognition impaired is ten times higher than the non-anemic elderly.
- ➤ Delayed recall was the component in MOCA which most patients scored less. Naming was the component in which most patients scored well.
- A Significant odds ratio obtained on ADL, IADL, MOCA assessment on our Cases and controls reveals than anemia accelerates the onset of functional impairment and cognitive impairment in the elderly.

CONCLUSION

Our research shows that the majority of older individuals with anemia have an underlying reason for their condition. A physician needs to be aware that anemia might coexist with other illnesses and also should understand the role of anemia in aggravating the severity of ailments which may lead to fatal outcomes. It is therefore pertinent to find out the etiology of anemia, identify the type and assess the severity of anemia. Normocytic anemia should not be neglected as normal picture, it should be subjected to further evaluation.

Delays in assessing elderly individuals for anemia may cause a delay in the identification of potentially treatable conditions. Atypical symptoms like fatigueness and loss of appetite should not be ignored, as these symptoms may be an indication for anemia. Protocol should always be followed to arrive at the diagnosis of type of anemia before giving specific treatment.

Expertise in the first workup of anemia in older patients is a must for all clinicians. Multiple illnesses frequently necessitates referral to a specialist. Maintaining a strong working connection with haematologists and gastroenterologists is crucial, and consulting a nephrologist can be beneficial when interacting with patients who have chronic kidney disease.

Nutritional anemia which includes iron deficiency and Vitamin B12 deficiency anemia was found in optimum numbers in our study, which highlights the importance of nutrition among the geriatric population. All geriatric population should be subjected to Mini Nutritional assessment and should be referred to a dietitian to correct the nutritional status.

Polypharmacy and Brown Bag concept should be applied on day to day basis and STOPP-START criteria should be applied to remove unnecessary drugs, replace the detrimental drugs with a safer alternative.

All the anemic elderly patients should be subjected to functional assessment using Katz ADL index and Lawton IADL Index which helps the clinician to assess their level of disability and their level of dependence on care takers for their day to day activities. In our study the controls had very less percentage of disability and they were highly independent, even takin care of their own income by continuing their occupation, which implies anemia correction at the early stages, improve their quality of life and increase their level of independence, thereby leaving a meagre chance for elder abuse to happen.

Anemia may lead to pedal edema in elderly which affects their mobility, once mobility is affected, there is increased tendency of the person to experience fall in futures, hence symptomatic management and anemia correction is mandatory in such individuals.

Anemia may lead to increased oxygen demand which may make way for occurrence of coronary syndromes, and severe anemia may exacerbate the congestive heart failure, which increases the risk of mortality, hence priority should be given for correction of anemia in such patients.

Montreal cognitive assessment which helps to assess the cognition status should be administered in all elderly as it is easy to administer and gives us very valuable resource to take further steps to prevent cognition decline. Anemia which is low concentrations of hemoglobin can lead to brain hypoxia which makes the elderly more prone to undergo cognitive decline states like dementia and delirium. Hence MOCA should be made mandatory to administer in all anemic elderly to assess and prevent further cognitive decline.

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<u>ANNEXURE – I</u>

CLINICAL PROFILE OF ANEMIA AND ITS IMPACT ON FUNCTIONAL CAPACITY AND COGNITION IN ELDERLY" – Case Proforma

Patient no:

Name:	Age:	Sex:	IP NO:
Occupation:	Residence:		

Chief complaints:

History of

Giddiness	Passing worms in stool
Easy fatiguability	Previous blood transfusions
Loss of appetite	Previous dialysis
Difficulty in swallowing	Type of food intake: Veg/non veg
Difficulty in breathing	Prolonged drug intake
Swelling of legs	Previous surgeries
Black colored stools	

Past history

Hypertension	Tuberculosis
Diabetes	Hypothyroidism
CAD	CKD
Others:	

Personal history:

\mathbf{r}	history
Irna	nictory

General physical examination

Vitals:

Clinical signs:

Pallor	Hyperpigmentation over Knuckles
Icterus	Pedal edema
Glossitis	Lymphadenopathy
Koilonychia	Splenomegaly/hepatomegaly
Raised JVP	Hepatospleenomegaly

Systemic examination:

CVS

RS

ABDOMEN

CNS

Investigations

Hb	ESR
PCV	PERIPHERAL
	SMEAR
MCV	Vit B12
MCH	Reti count
MCHC	Sr LDH
RDW	Stool Occult
RBC	Stool culture
TC	Sr creatinine
Platelet count	B.urea
Sr Ferritin	LFT
Sr Iron	TSH
Sr Transferrin	Others:
TIBC	

Specific investigations for selected patients

Bone marrow study		
Upper GI endoscopy		
ECG	X-RAY	USG A+P

KATZ INDEX OF INDEPENDENCE IN ACTIVITIES OF DAILY LIVING (ADL)

SCORE: __/6

KATZ ADL INFERENCE:

	Full function	
	Moderate impairmen	ent
ĺ	Severe functional in	npairment

LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)

IADL SCORING: __ (score ranges from 0 (low function, dependent) to 8 (high function, independent) for women and 0 through 5 for men to avoid potential gender bias.)

INFERENCE:

Low function, Dependent
High function, Independent

MONTREAL COGNITIVE ASSESSMENT

SCORE: $_/30$ (Normal $\ge 26 / 30$, Add 1 point if ≤ 12 year education)

MOCA INFERENCE

Cognition Intact
Mild cognitive impairment
Moderate cognitive impairment
Severe Cognitive impairment

"CLINICAL PROFILE OF ANEMIA AND ITS IMPACT ON FUNCTIONAL CAPACITY AND COGNITION IN ELDERLY" -Control Proforma

Patient no:

Name:	Age:	Sex:	IP NO:
Residence:	Occupation:		Hb:g/dl

KATZ INDEX OF INDEPENDENCE IN ACTIVITIES OF DAILY LIVING (ADL) SCORE: /6

KATZ ADL INFERENCE:

Full function
Moderate impairment
Severe functional impairment

LAWTON - BRODY INSTRUMENTAL ACTIVITIES OF DAILY LIVING SCALE (I.A.D.L.)

IADL SCORING: __ (score ranges from 0 (low function, dependent) to 8 (high function, independent) for women and 0 through 5 for men to avoid potential gender bias.)

INFERENCE:

Low function, Dependent
High function, Independent

MONTREAL COGNITIVE ASSESSMENT

SCORE: /30 (Normal $\geq 26 / 30$, Add 1 point if ≤ 12 year education)

MOCA INFERENCE

Cognition Intact
Mild cognitive impairment
Moderate cognitive impairment
Severe Cognitive impairment

<u>ANNEXURE – II</u>

CONSENT FORM

BLDEDU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA- 586103

TITLE OF THE PROJECT - "Clinical profile of Anemia and its impact on functional capacity and Cognition in elderly"

PRINCIPAL INVESTIGATOR - Dr. S.VIGNESHWARAN

P.G IN GERIATRICS

P.G.GUIDE NAME - Dr. ANIRUDDHA UMARJI

ASSOCIATE PROFESSOR

DEPARTMENT OF GERIATRICS

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked a series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment to help the investigator in this study.

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment.

4) BENEFITS:

I understand that my participation in this study will help patient's survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location. If the data are used for publication in the medical literature or teaching purposes, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time. Dr.S.VIGNESHWARAN is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the study, which might influence my continued participation. If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. I will be given a copy of this consent form for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr.S.VIGNESHWARAN may terminate my participation in the study after he has explained the reasons for doing so and has helped arrange for my continued care by my physician or physical therapist if this is appropriate.

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights. I have

explained the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in the patient's language.

I, **DR. VIGNESHWARAN.S** (Investigator) have explained to the patient in detail about the study in their own language and the written copy of the same will be given to participant.

INVESTIGATOR'S NAME AND ADDRESS

DR. VIGNESHWARAN.S

POSTGRADUATE

DEPARTMENT OF GERIATRICS

SHRI B M PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE,

B.L.D.E. (DU)

VIJAYAPURA-586103

INVESTIGATOR'S SIGNATURE DATE:

STUDY SUBJECT CONSENT STATEMENT:

I confirm that DR S.VIGNESHWARAN has explained to me the purpose of the research, the study procedures that I will undergo, and the possible risks and discomforts as well as benefits that I may experience in my language. I have read and understand this consent form. Therefore, I agree to give consent to participate as a subject in this research project.

Torin. Therefore, Tagree to give consent to participate as a sao	jeet in tins research project.
PARTICIPANT / GUARDIAN SIGNATURE	DATE:
WITNESS TO SIGNATURE	DATE:

<u>ANNEXURE – III</u>

ETHICAL COMMITTEE APPROVAL FORM





BLDE

(DEEMED TO BE UNIVERSITY)

Declared as Deemed to be University u/s 3 of UGC Act, 1956 Accredited with 'A' Grade by NAAC (Cycle-2) The Constituent College

SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA BLDE (DU)/IEC/ 691/2022-23 30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "CLINICAL PROFILE OF ANEMIA AND ITS IMPACT ON FUNCTIONAL CAPACITY AND COGNITION IN ELDERLY".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: DR. S.VIGNESHWARAN.S

NAME OF THE GUIDE: DR. ANIRUDDHA UMARJI, ASSOCIATE PROFESSOR DEPARTMENT OF GERIATRIC MEDICINE

Dr. Santoshkumar Jeevangi Chairperson IEC, BLDE (DU), VIJAYAPURA,

Institutional Ethical Committee, BLDE (Deemed to be University)

MEMBER SECRETARY Institutional Ethics Committee

Dr.Akram A. Waikwadi

Member Secretary

VIJAYARURA

IEC, BLDE (DU),

E (Deemed to be University Vijayapura
Following documents were placed before Ethical Committee for Scrutinization. Ucemed to be University
Following documents were placed before Ethical Committee for Scrutinization. BLDE (Deemed to be University)

- · Copy of Synopsis/Research Projects
- · Copy of inform consent form
- · Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India. BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

ANNEXURE -IV

ANTI – PLAGIARISM REPORT



Similarity Report ID: oid:3618:62726910

PAPER NAME AUTHOR

21BMGRE02-Vigneshwaran S -12.07.202 Vigneshwaran S

4.docx-EVOLUTION OF ANEMIA

WORD COUNT CHARACTER COUNT 11214 Words 62208 Characters

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Summary

ANNEXURE -V

MASTER CHART

9.6	RHONCH PRESENT	Anti-nyperter Pallor, Kollonychia, PETACHYCARDIA	Anti-nyperier Pallor, Kollonychia, PeraCHYCARUIA	Steroids, Anti-nyperter	Hypertension, Tubercu Smoking, Tobacco	Glodiness, Easy Fatig Vegetarian	Young Old	ed Hural	Unemployed	O Male	49 BASANNA
	חוסווסוו חחדפהות	TACLACADDIA	Tallor Kailonyahia Da		Lipotonion Tiboroi Omolina Toboro	Olddings Entire Vogetring	Comp of the		l loopologo	70 Mala	AO DAO ANINA
	WNL	WNL		Antacids, Anti-hyperte F	Hypertension, HYPER Tobacco		Young Old		Homemaker	65 Female	48 SUBAWWA
	P B/L WHEEZE+	BRADYCARDIA, HYP B/L WHEEZE+	s, Anti-hyperPallor, Pedal edema E	Biguanides, Anti-hyperF	Hypertension, Diabete Nil	Giddiness, Easy Fatig Mixed	Young Old	Rural	Employed	65 Female	47 CHANDBI
	WNL	WNL	Pallor, Glossitis, Hype WNL	Nii P	Nil Alcohol, Tobacco	Giddiness, Easy Fatig Vegetarian	Young Old	ed Urban	Unemployed	60 Male	46 SIDANNA
	WNL	WNL	Pallor, Pedal edema WNL	Z.	Nii	Giddiness, Easy Fatig Vegetarian	Young Old	ed Urban	Unemployed	72 Male	45 CHANDRASEKHAR
	WNL	WNL	Anti-platelet Pallor, Pedal edema \	Antacids, Anti-platelet F	Hypertension, Coronar Nil	Giddiness, Easy Fatig Vegetarian	Old Old	ed Urban	Unemployed	75 Male	44 SIDARAMMAPA MAS
	WNL	WNL		Biguanides, THYROXII Pallor	Diabetes Mellitus, Hyr Nil	Giddiness, Easy Fatig Vegetarian	Young Old	er Urban	Homemaker	60 Female	43 TYAMMA
	WNL	HYPERTENSION	Pallor, Glossitis, Hype HYPERTENSION	Biguanides F	Diabetes Mellitus Nil	Giddiness, Easy Fatig Vegetarian	Young Old	er Rural	Homemaker	65 Female	42 KAMALABAI
	WNL	TACHYCARDIA	Pallor, Pedal edema	Anti-platelet therapy, NPallor, Pedal edema TACHYCARDIA	Hypertension Nil	Giddiness, Easy Fatig Mixed	Old Old	er Urban	Homemaker	75 Female	41 TARABAI
	WNL	TACHYCARDIA	Pedal edema	Antacids, NSAIDS F	CA LEFT BREAST NII	Easy Fatiguability, Lo: Mixed	Young Old	ed Rural	Unemployed	62 Female	40 RAMANNA
	WNL	HYPERTENSION	ychia, Pe		nar	Giddiness, Easy Fatig Vegetarian	Young Old		Homemaker	68 Female	39 GAURAMMA
	HEMIC MURMUR	TACHYCARDIA	Pallor, Kollonychia, RaTACHYCARDIA	Z.	N.	Giddiness, Easy Fatig Vegetarian	Old Old	er Rural	Homemaker	75 Female	38 VINODAMMA GOUDA
	WNL	TACHYCARDIA	Pallor	Anti-hypertensives, AN Pallor	Hypertension, PARKIN Nil	Giddiness, Easy Fatig Vegetarian	Old Old	er Urban	Homemaker	80 Female	37 MANKAWWA RUNAV
	WNL	WNL	Pallor, Glossitis, Hype\	Biguanides, Anti-hyper Pallor, Glossitis, Hype WNL	Hypertension, Diabete Nil	Giddiness, Loss Of ap Mixed	Young Old	ed Urban	Unemployed	72 Male	36 SURESH
	WNL	WNL	Pallor	Antacids	Nii	Giddiness, Easy Fatig Vegetarian	Oldest Old	ed Rural	Unemployed	85 Female	35 AMBAWWA
	WNL	TACHYCARDIA		Antacids, NSAIDS, Steroids	Nii	Giddiness, Easy Fatig Vegetarian	Young Old	er Rural	Homemaker	70 Female	34 SHIVAMMA
	WNL	TACHYCARDIA	Pallor, Icterus, Glossit TACHYCARDIA	Nii	Chronic liver Disease Smoking, Alcohol	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	62 Male	33 NANAGOUDA
	WNL	WNL	Pallor, Pedal edema \	Biguanides, Anti-hype Pallor, Pedal edema WNL	Hypertension, Diabete Nil	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	60 Female	32 CHANDRAWWA
	WNL	WNL	Haematinics Pallor, Koilonychia, R. WNL	Antacids, Haematinics F	Congestive Cardiac Fa Nil	Giddiness, Easy Fatig Vegetarian	Young Old	er Rural	Homemaker	74 Female	31 SHANTABAI
	WNL	WNL	Anti-platelet Pallor, Raised JVP, P(WNL	Antacids, Anti-platelet F	Hypertension, Coronar Nil	Giddiness, Easy Fatig Vegetarian	Old Old	er Rural	Homemaker	79 Female	30 SAYABAVVA
	WNL	WNL	Pallor, Hyperpigmenta WNL	Ni P	Nii	Giddiness, Easy Fatig Vegetarian	Young Old	ed Urban	Unemployed	65 Male	29 BAMMALINGAPPA PI
	WNL	WNL	Biguanides, Pallor, Koilonychia, PtWNL	Antacids, Biguanides, F	Hypertension, Diabete Tobacco	Giddiness, Easy Fatig Vegetarian	Old Old	er Rural	Homemaker	75 Female	28 KONTEWWA
	WNL	WNL		Antacids, Anti-platelet Pallor	Hypertension, MVP Tobacco	Giddiness, Easy Fatig Mixed	Young Old	Rural	Employed	60 Female	27 MALKAWWA MADAR
	WNL	WNL	PPI, Anti-hy Pallor, Hyperpigmenta WNL	Antacids, PPI, Anti-hy F	Hypertension Nil	Giddiness, Easy Fatig Mixed	Old Old	er Rural	Homemaker	72 Female	26 MAHADEVAMMA
	WNL	HYPERTENSION	Biguanides, Pallor, Raised JVP, P HYPERTENSION	Tot Antacids, Biguanides, F	Hypertension, Diabete Smoking, Alcohol, To	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	67 Male	25 RAGHUNATH KALLAF
	WNL	TACHYCARDIA	Pallor, Glossitis, Hype TACHY CARDIA	Biguanides F	Diabetes Mellitus, CAI Nil	Giddiness, Easy Fatig Vegetarian	Young Old	ed Rural	Unemployed	60 Male	24 CHANDRASEKHAR S
	WNL	WNL	Pallor, Koilonychia \	АП	Tuberculosis Nil	Giddiness, Easy Fatig Vegetarian	Old Old	ed Urban	Unemployed	84 Male	23 B.M.PATIL
	WNL	WNL	Pallor, Koilonychia \	Nii P	Nii	Giddiness, Easy Fatig Vegetarian	Old Old	ed Urban	Unemployed	75 Female	22 DRAKSHAYANI
	WWL	WNL	Pallor, Glossitis \		Nil Smoking, Alcohol, Tot Nil	Giddiness, Easy Fatig Vegetarian	Young Old	Rural	Employed	60 Male	21 SHARANAPPA
	WNL	WNL			Hypertension, HEPATINII	Giddiness, Easy Fatig Vegetarian	Old Old	ed Rural	Unemployed	76 Female	20 SIDAWWA MUTTAGI
	WNL	WNL	Pallor, Raised JVP \		Hypertension, HOCM Tobacco	Giddiness, Easy Fatig Mixed	Old Old	ed Rural	Unemployed	70 Female	19 IRAVVA
	WNL	WNL	Pallor	Anti-platelet therapy, F	Hypertension Tobacco	Giddiness, Easy Fatig Vegetarian	Oldest Old	ed Rural	Unemployed	85 Female	18 LAYAWWA
	WNL	WNL		Biguanides, Anti-hyperPallor	Hypertension, Diabete Tobacco	Giddiness, Easy Fatig Vegetarian	Old Old	ed Rural	Unemployed	81 Female	17 CHANDIBAI
	WNL	WNL	Pallor, Pedal edema \	ANTICOAGULANTS, (Pallor, Pedal edema	Chronic kidney Diease Nil	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	60 Female	16 PREMABAI SEVURA
	WNL	TACHYCARDIA	Anti-hypertensives, THYROXINE S/TACHYCARDIA	Antacids, Anti-hyperten	Hypertension, Hypothy Tobacco	Giddiness, Easy Fatig Vegetarian	Oldest Old	ed Urban	Unemployed	89 Male	15 RAJARAM
	WNL	WNL	Isives	Antacids, Anti-hypertensives	Hypertension Tobacco	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	70 Female	14 SURATABAI
	WNL	TACHYCARDIA	Pallor, Glossitis, Hype TACHYCARDIA	Nii P	Nil Smoking, Alcohol	Giddiness, Easy Fatig Vegetarian	Young Old	ed Rural	Unemployed	69 Male	13 CHANDRAMAPPA KA
	WNL	WNL	Pallor, Pedal edema \	Anti-platelet therapy, & Pallor, Pedal edema WNL	Hypertension, Diabete Nil	Giddiness, Easy Fatig Vegetarian	Young Old	ed Urban	Unemployed	70 Female	12 SHANTA
	WNL	TACHYCARDIA	Pallor, Koilonychia, P(TACHYCARDIA	Antacids F	Nii	Giddiness, Easy Fatig Vegetarian	Oldest Old	ed Rural	Unemployed	88 Female	11 SHVALINGAMMA
	WNL	TACHYCARDIA		Anti-hypertensives, Ha Pallor, Pedal edema	Hypertension Nil	Easy Fatiguability, Lo Mixed	Young Old	ed Urban	Unemployed	65 Male	10 ABDUL JABBAR
	WNL	WNL	Pallor	OHA-DPP4 F	Diabetes Mellitus, Chr Nil	Giddiness, Easy Fatig Vegetarian	Young Old	er Urban	Homemaker	61 Female	9 NIRMAL BETAGERI
	INFRASCAPULAR CR	TACHYCARDIA		Anti-platelet therapy, EPallor	Coronary Artery Disea Smoking	Giddiness, Easy Fatig Vegetarian	Old Old	ed Rural	Unemployed	78 Male	8 DUNDAPPA
	HEPATOMEGALY	WNL	Pallor, Icterus, Glossit WNL	Antacids, NSAIDS F	Nil Smoking, Alcohol	Easy Fatiguability, Lo: Mixed	Young Old	ed Rural	Unemployed	60 Male	7 BABU CHAUHAN
	WNL	WNL	Pallor, Pedal edema \	Anti-platelet therapy, [Pallor, Pedal edema WNL	Coronary Artery Disea Nil	Giddiness, Easy Fatig Mixed	Young Old	ed Rural	Unemployed	60 Female	6 GODABAI
	WNL	WNL	NSAIDS, St Pallor, Koilonychia, RaWNL	Antacids, NSAIDS, St F	Hypertension, Coronar Tobacco	Giddiness, Easy Fatig Vegetarian	Oldest Old	ed Urban	Unemployed	85 Female	5 SHANKERAWWA
	WNL	WNL	Pallor, Koilonychia \	Antacids F	Nii Tobacco	Easy Fatiguability, Los Vegetarian	Oldest Old	ed Rural	Unemployed	91 Male	4 LAKSHMAN
	WNL	WNL	Anti-platelet Pallor, Glossitis, Koilo WNL	Antacids, Anti-platelet F	Hypertension, Cerebrovascular Accident	Giddiness, Easy Fatig Vegetarian	Old Old	er Urban	Homemaker	77 Female	3 SHANKAREMMA
	WNL	WNL	Pallor	Steroids F	Nil Smoking, Alcohol	Easy Fatiguability, Lo: Mixed	Young Old	ed Rural	Unemployed	71 Male	2 GURUBALAPPA
	WNL	WNL	Pallor, Pedal edema \	Antacids F	Zii	Giddiness, Easy Fatig Vegetarian	Young Old	Rural	Employed	74 Male	1 SHANKARAPPA
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3.52	3.49	3.2	1.85	2.87	4.35	272-	2.09	3.66	3.68	3.06	214	2.64	ω <u>:</u>	2 - 04	3.2	4.24	3.22		3.62	'	'	3.02	3.46		0.00	4.03	3.31	3.71		3.94 -	3.92	1 47	3.21	4.09	3.6		2.09	3.68 -	4 46 -	3 25 -	200	į
16.8	16.3	13.8	25.5	18.4	14.8	14	16	13.2	15.6	18.8	14.4	14.2	17.1	3 0	16.2	14.9	18	19.6 -	18.3	13.2	16 -	16.6	14.8	16.5		13.1	16.3	14.5	11.7	13.1	14.1	14.3	16.1	25.6	13.6	29.9 -	14.1	14.9	14.2	16.5	16.2	
31.2	34.5	30.6	32.8	30.8	33.6	26.2	28.8	34	31.8	31.2	35.7	36.1	30	2//	31	32	31.2	35.4	33.3	34 7	29	34.2	36.6	32.6	35	34.1	31.3	34.3	31.5	38.7	25.4	33.0	30	34	32.1	31.4	29.9	31	30.8	33 00	32.6	
23.2	25.5	29.4	35.7	28	22.5	31.8	31.6	28.7	24.7	20.6	32.7	37.2	25.2	0 C 1 C	26.1	23.8	24.7	39	23.2	29.5	32	35.4	33.8	22.7	30	27.0	26.6	30.2	28.4	28.7	29.6	44.2	26.1	22.2	27	29.6	30.6	27.7	25.4	28.3	29.00	3
72.1	78.9	95.9	108.9	90.7	67.1	110.2	100.6	84.4	77.7	66	91.6	104	76.4	97.0	72.1	74.5	68.2	110.2	69.6	84.8	102	103.6	92.5	69.6	2.10	01.0	80.9	88.1	90.6	76.1	80.7	130.6	69.5	65.5	83.1	74.4	102.4	80.4	80 4	70.4	91.5	2
24.3	25.8	30.7	20.2	26.1	29.2	23.1	22.9	30.9	28.6	20.2	19.6	23	33 -	3 =	32.7	31.6	21.2	19.5	25.2	8 6	28	31.3	32	34.4	30.4	2 22	28.1	32.7	32.9	8	32.8	10 2	30.6	26.8	30.5	16.9	21.4	32.9	36.7	27.6	32.2	3

Patient(Controls) no. Name 1 JAYAPPA 2 VENKATESH	Age Hb (g/dl) 62 63	13.4 Male 13.6 Male	Age group Young old	Residence Rural Urban	Occupation Unemployed Employed	ADL Full function Full function	ADL High function - Indeper Cognition Intact High function - Indeper Cognition Intact
2 VENKATESH	76	13.6 Male	Young old	Urban	Employed	Full function	High function - Indeper Cognition Intact
4 IRANNA	65	13.5 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
5 SHANTABAI	73	12.8 Female	Young old	Rural	Homemaker	Full function	Low function - Depend Mild cognitive impairm
6 YALLAWA	60	12.2 Female	Young old	Rural	Homemaker	Full function	High function - Indeper Cognition Intact
7 IMAMSAB	61	13 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
8 KALLAPA	70	13.2 Male	Young old	Urban	Unemployed	Full function	Low function - Depend Mild cognitive impairm
9 IRANNA	65	14.5 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
	60	14 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
11 BOURAMMA	70	12.3 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairm
12 PARVATAWWA	80	12.4 Female	Old old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Moderate cognitive imp
13 GUNDAVVA	61	12.8 Female	Young old	Rural	Homemaker	Full function	Low function - Depend Mild cognitive impairme
14 SAHUBAI	61	12.6 Female	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
15 DUNDABI	78	14.7 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Moderate cognitive imp
16 SOMALABAI	76	13.5 Female	Old old	Rural	Homemaker	Full function	Low function - Depend Mild cognitive impairme
17 ANSUBAI	70	13.4 Female	Young old	Rural	Homemaker	Full function	Low function - Depend Cognition Intact
18 SHIVBAI	70	12 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Moderate cognitive imp
19 DUNDAWWA	65	12.9 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairme
20 MADUKAR	65	14.3 Male	Young old	Rural	Unemployed	Full function	High function - Indeper Cognition Intact
21 SONABAI	70	13 Female	Young old	Rural	Homemaker	Full function	Low function - Depend Mild cognitive impairme
22 RAJARAM	60	13.2 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
23 HANAMANTRAY	64	14.2 Male	Young old	Urban	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairme
24 NANGOUDA	68	13.2 Male	Young old	Rural	Unemployed	Full function	High function - Indeper Cognition Intact
25 ANASUYA	69	12 Female	Young old	Rural	Homemaker	Full function	Low function - Depend Cognition Intact
26 SHARDA	65	12.6 Female	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
27 NEELAVA	70	12.2 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairm
28 SHARANAVVA	95	12.3 Female	Oldest old	Rural	Unemployed	Severe Functional Imp	Severe Functional Imp Low function - Depend Severe Cognitive impai
29 MAKTUMBEE	62	14 Female	Young old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairm
30 CHANDSAB	64	13 Male	Young old	Urban	Employed	Full function	High function - Indeper Cognition Intact
31 SHIVALINGAMMA	80	12 Female	Old old	Rural	Unemployed	Severe Functional Imp	Severe Functional Imp Low function - Depend Moderate cognitive imp
32 BASANGOUDA	80	13.4 Female	Old old	Rural	Employed	Full function	Low function - Depend Mild cognitive impairme
33 SANGAPPA	85	13.8 Male	Oldest old	Rural	Unemployed	Severe Functional Imp	Severe Functional Imp Low function - Depend Moderate cognitive imp
34 LAXMIBAI	84	12.6 Female	Old old	Rural	Homemaker	Moderate Functional	Moderate Functional Ir Low function - Depend Moderate cognitive imp
35 DUNDESHI	78	13.2 Male	Old old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Mild cognitive impairme
36 CHANDAVVA	92	12.8 Female	Oldest old	Rural	Unemployed	Moderate Functional	Moderate Functional Ir Low function - Depend Severe Cognitive impai
37 BASAMMA	86	12.6 Female	Oldest old	Rural	Unemployed	Full function	Low function - Depend Mild cognitive impairme
38 AMEENSAB	70	14.2 Male	Young old	Urban	Employed	Full function	High function - Indeper Cognition Intact
39 SHANKERAMMA	80	13 Female	Old old	Rural	Unemployed	Full function	Low function - Depend Mild cognitive impairme
40 NINGAMMA	86	14 Female	Oldest old	Rural	Unemployed	Full function	Low function - Depend Mild cognitive impairm
41 RUKMABAI	72	13.8 Female	Young old	Rural	Homemaker	Full function	High function - Indeper Cognition Intact
42 MAHADEVAMMA	72	13.8 Female	Old old	Rural	Homemaker	Full function	High function - Indeper Cognition Intact
43 BASAMMA	73	13.8 Female	Young old	Urban	Homemaker	Full function	High function - Indeper Cognition Intact
44 NEELA	76	14 Female	Old old	Urban	Homemaker	Full function	High function - Indeper Cognition Intact
45 SHARANAPPA	72	14.2 Male	Young old	Urban	Employed	Full function	High function - Indeper Cognition Intact
46 DUNDESHWARI	72	13.8 Female	Young old	Urban	Homemaker	Full function	High function - Indeper Cognition Intact
47 IRAMMA	70	13.5 Female	Young old	Urban	Homemaker	Full function	High function - Indeper Cognition Intact
48 GODABAI	72	13.2 Female	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
49 TIMANNA	74	13.6 Male	Young old	Urban	Unemployed	Full function	High function - Indeper Cognition Intact
50 BHIMANGOUDA	68	13.6 Male	Young old	Rural	Employed	Full function	High function - Indeper Cognition Intact
Z JIMANG CIJA	ō	13.6 Male	Y oung old	Kurai	Employed	- ull function	High function - Independen