

Trainees' forum-case-based discussion
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Uncovering hidden causes of anaemia in an older person

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Introduction

- MR. S
- 70 Year old
- Married
- Father of one
- Retired Ticket checker at CGR
- From Panadura-30 km away from the National hospital Colombo

Background

- Had rheumatic fever at the age of 12
- Traditional treatments given
- Was not on penicillin prophylaxis
- Identified to be having mitral stenosis at the age of 25 years.
- Underwent valvotomy at the age of 25 years
- Re-valvotomy after 10 years due to restenosis
- Mitral valve replacement done at the age of 35 years - **27 MEDTRONIC HALL VALVE 9 (Mechanical prosthetic valve)**
- Was on warfarin ever since, started on warfarin 7mg and target INR was 2.5-3.5
- Followed up at tertiary care hospital

Background continued.....

- Recurrent hospital admissions due to on and off melaena and exertional shortness of breath and lethargy since 2022 March

2022/March

2022/April


2022/May

2022/ September 1st to 5th

2022/ September 13th to 21st

2022/ October 3rd to 22nd

2022/ November 17th to December 25th



On warfarin 6mg
In all the admissions INR
was found within the
normal therapeutic range.
Needed blood transfusions
in most of the admissions

He first presented to our ward

- History of melaeana for 3 days
- Three to four episodes per day
- No fresh bleeding
- No hematemesis
- Regurgitation over 3 days
- No dysphagia, odynophagia and no loss of appetite and loss of weight
- Bowel habits had been normal
- No history of chronic NSAID use

- He complained of exertional dyspnea (NYHA class 3)
- paroxysmal nocturnal dyspnea
- Bilateral ankle oedema
- No chest pain
- No palpitations
- Easy fatiguability
- No hematuria or dark-coloured urine
- No other features suggestive of connective tissue diseases

- Drug history-
 - Spironolactone 25mg mane
 - Losartan 50mg bd
 - Bisoprolol 5 mg bd
 - Warfarin 6mg mane
 - Pantoprazole 20mg bd
 - Furosemide 40 mg bd
- } Good drug adherence
- No family history of haemolytic anaemias/bowel malignancies

- At the time of his assessment, he was **independent on basic ADL** and he was not involved in any of the IADLs. His participation in social and family events were completely restricted.
- His vision and hearing had been normal.
- He had been taking a Sri Lankan rice-based non-vegetarian diet with adequate proteins

- He **didn't** have episodes suggestive of delirium and was oriented in T/P/P. He was able to list the days of the week in reverse order. **His cognitive domains before this event were intact** and he was functioning within his full capacity
- His **sleep was occasionally fragmented** with a history of paroxysmal nocturnal dyspnea.
- With a history of recurrent admissions, he **felt helpless and dissatisfied with life** but had no idea of suicide. (GDS 2/4)
- History of increased urinary frequency with furosemide but no history of incontinence
- He never had a fall in the preceding six months.

- He was educated up to GCE A/L and was the sole breadwinner of the family where his child was married and living separately.
- His wife was the main caregiver during this illness who had diabetes and hypertension. Their financial support during the illness was mainly from his pension.
- He lived in a single-story house where the bathroom was inside his house.
- He is a **non-smoker and non-alcohol consumer**
- His main concern was multiple recurrent admissions to the hospital, at the time of the admission he believed that warfarin was causing the current admissions, He had been searching for a solution for recurrent admissions and he requested for clear diagnosis.

On examination

- He had a normal build with a BMI of 22 kgm²
- Afebrile
- He was pale
- Mildly icteric
- No lymphadenopathy
- No other features suggestive of micronutrient deficiencies
- No peripheral stigmata of infective endocarditis
- No peripheral stigmata of chronic liver cell disease
- No skin manifestations of over coagulation
- Mild bilateral pitting ankle edema

CVS examination

- Pulse rate- 80 bpm, irregularly irregular
- BP- 110/60 mmHg no postural hypotension
- Thrusting and deviated apex
- Early diastolic murmur best heard at left lower sternal edge
- Metallic click

Respiratory system examination

- Respiratory rate – 12
- Trachea -central
- Lungs – Air entry equal bilaterally with occasional end-inspiratory fine crepts

Abdominal system examination

- Soft
- No organomegaly
- DRE- Melena

- Neurological examination
normal

- CFS-4
- GDS-2/4
- TUG test-12 secs
- Chair rise test-12 secs
- 4-point balance test-3/4
- Minicog-4/5

Cause ??????????



Adobe Stock | #531908983

Diagnostic assessment

	Day 1	Day 3	Day 6	Day 10
WBC	16	17	11.88	8.7
Hb	7.3	8.6	9.4	10.6
Mcv	83			
PLT	388	300	294	394



1 pint
of RCC

1 pint
of RCC

- Blood picture- Normochromic normocytic RBC- reduced in number, Few polychromatic RBC, Few fragments and spherocytes, Mild to moderate rouleaux formation
- Conclusion – Severe anaemia could be due to bleeding or ongoing hemolysis

	Day 1	Day 3	Day 6	Day 10
PT/INR	3.4	2.5	1.63	2.6



w/H
WARFARIN



Bridged
with
enoxaparin
and started
warfarin 5
mg vesper

	DAY 1	DAY 3	DAY 6
LDH	845	774	297

- Retic count – 8%
- DAT- negative
- Serum Haptoglobin- 11.6 (30- 200)

- Serum iron- 41 mcg/dl (70 -180)
- TIBC- 348 mcg/dl (274-385)
- TSAT – 11.8 %
- Serum ferritin- 90.4 ng/ml(12-150)

Liver function tests

- AST- 52
- ALT- 20
- ALP- 56
- Gamma GT- 34
- T. Bilirubin- 5.1 (0.3- 1.2)
- D. Bilirubin- 0.8 (<0.2)
- Total Protein- 6.5
- S. Albumin— 3.8 (3.5- 5.2)

Renal function test

- Serum creatinine-1.1 mg/dl
- Serum potassium-4 meq/l
- Serum sodium-138 meq/l

- USS abdomen- Normal liver size and architecture.. No intra or extra hepatic duct dilatation
- Kidneys normal in size and echo texture

- UGIE (day 2) - no ulcers and no point of active bleeding

- ECG- AF (Rate- 80)
Evidence of LVH
No acute ischemic changes

2D- ECHO (day 3)

- LV EDD- 51 EF- 55 %
 ESD- 32
 RV- Normal
 LA- Severely Dilated (6.3*6.5 cm)
 MV- no paravalvular or perivalvular leaks
 Max PG- 22mm Hg Mean PG- 28 mm Hg
 MVA- 2.3
 AV- calcified aortic valve/no aortic stenosis/Grade 1-2 Aortic regurgitation. Max PG- 29 mm Hg
 TV- Trivial TR/ TRPG – 23/ No pulmonary hypertension

- S.Amylase - 78 (22-80)
- ESR- 21
- CRP- less than 6

- **Diagnosis- valve induced haemolysis and gastro intestinal bleeding leading to iron deficiency anaemia in patient with mechanical mitral valve with rate controlled AF**

Management

He was started on

Oral bisoprolol 5mg bd

Losartan 50 mg bd

Oral atorvastatin 40 mg nocte

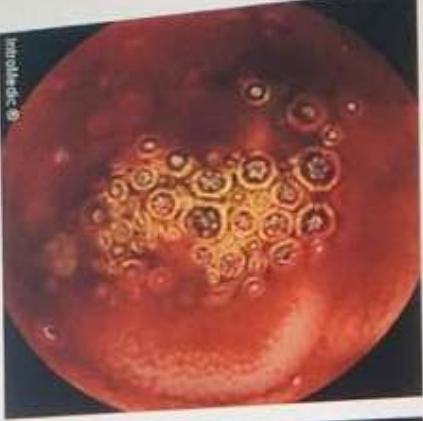
Oral frusemide 40 mg bd

Oral spironolactone 25 mane

Oral pantoprazole 40 mg bd

- He was also given a blood transfusion and iron supplementation and warfarin was withheld and restarted once the malena was settled and bridged by subcutaneous enoxaparin until the therapeutic range of PT/INR was achieved
- The patient was discharged with routine drugs and warfarin 5mg vesper dose with a plan for a LGIE.

- The patient got readmitted 3 weeks later, with similar complaints. His latest Hb was 8.1 g/dl, had a high LDH of 782, a high retic count of 4.53 % and an indirect bilirubinemia was noted. The PT/INR was 1.83.
- UGIE was visualized up to the proximal jejunum with no focus of bleeding and LGIE visualized up to the ileum with finding a small polyp less than 0.5cm. **Capsular endoscopy revealed jejunal bleeding and enteroscopy was normal.**

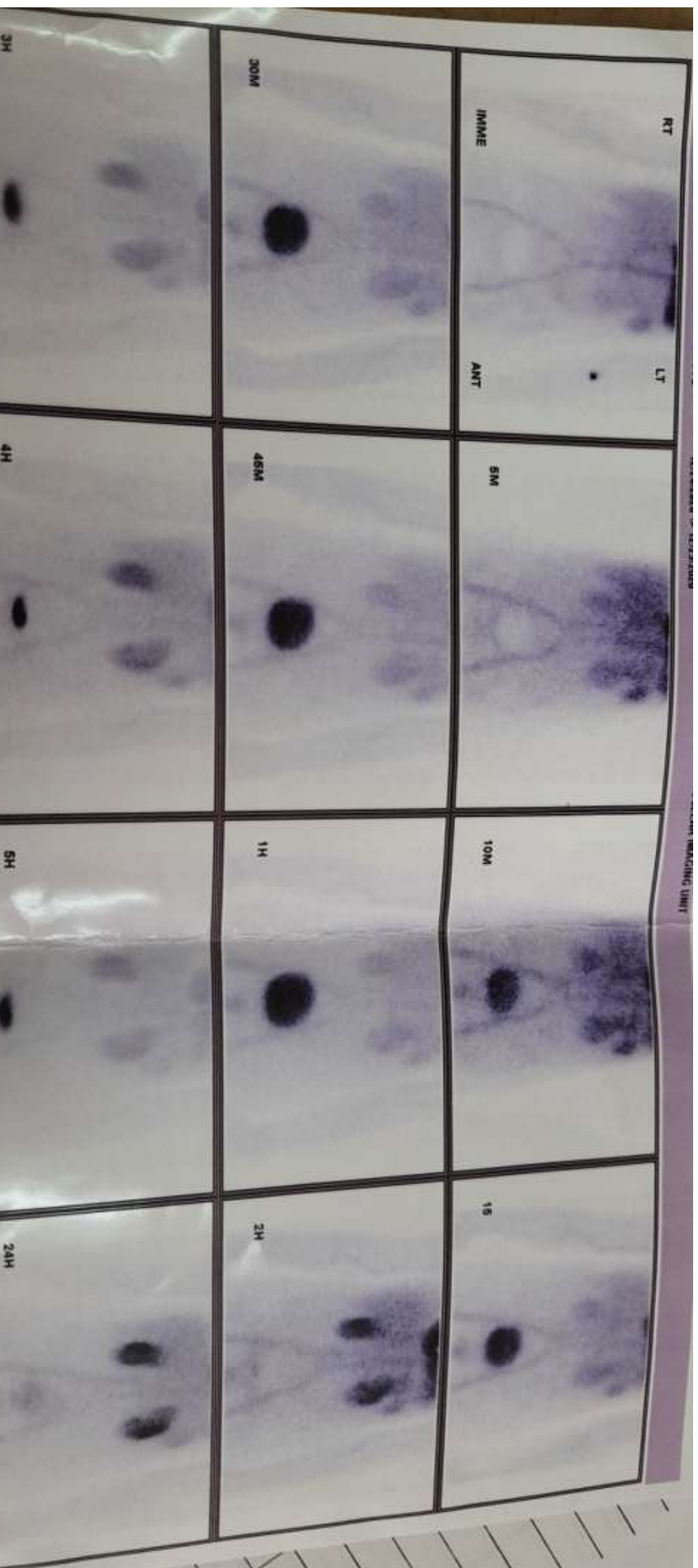


01:05:13
Active bleeding in proximal
Jejunum

01:05:13

01:05:14





Nuclear RBC scan

Transoesophageal echo

- Mitral valve-fibrous disc functioning well, paravalvular leak noted (grade 1-3), No valve dehiscence
- Aortic valve-very thickened, moderate AR, no obvious vegetation
- The conclusion was **grade 3 paravalvular leak** could be the cause of hemolysis
- No obvious evidence of vegetation.

- **MDT meeting** was held to decide about future management with the participation of the **treating physician, gastroenterologist, haematologist, cardiologist and cardiothoracic surgeon**
- **Issues that need to be addressed:**
 - Recurrent gastrointestinal bleeding occurred in a patient with a mechanical mitral valve within the therapeutic range of warfarin.
 - Paravalvular leak in a prosthetic valve resulting in mild to moderate valve-induced intravascular hemolysis
 - Is severe anemia due to one cause or does it result from both?
 - Recurrent hospital admission contributes to poor quality of life, psychological stress and financial strain on the patient and family members and worsening clinical frailty

- **Possible solutions made during the MDT discussion**
 - Maintain low therapeutic INR 2-2.5
 - Replace the mechanical valve with a bioprosthetic valve. *Redo surgery carries significant risk.*
 - Early enteroscopy/direct angiography during GI bleeding trying to find the bleeding point and cauterize.
 - Labile INR – frequent INR reviews (weekly)
 - Nutrition input regarding iron-rich food and high-protein diet

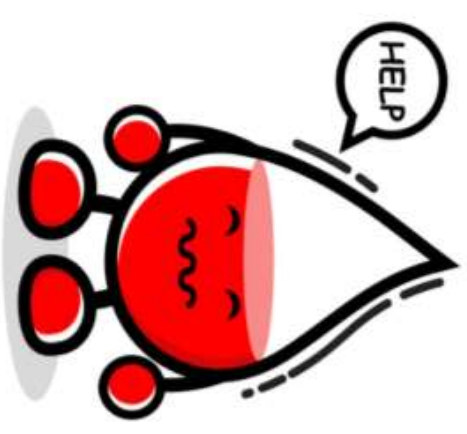
Definition of anaemia

According to the World Health Organization (WHO)

Anaemia is defined as:

<12.0 g/dL	in women
<13.0 g/dL	in men

Normal Hb distribution varies with sex, ethnicity and physiological status.



Prevalence of anaemia by age

No age-adjusted levels as it is difficult to find a healthy older cohort to define the range

WHO recommends working up older adults with anaemia in ‘**Low normal**’.

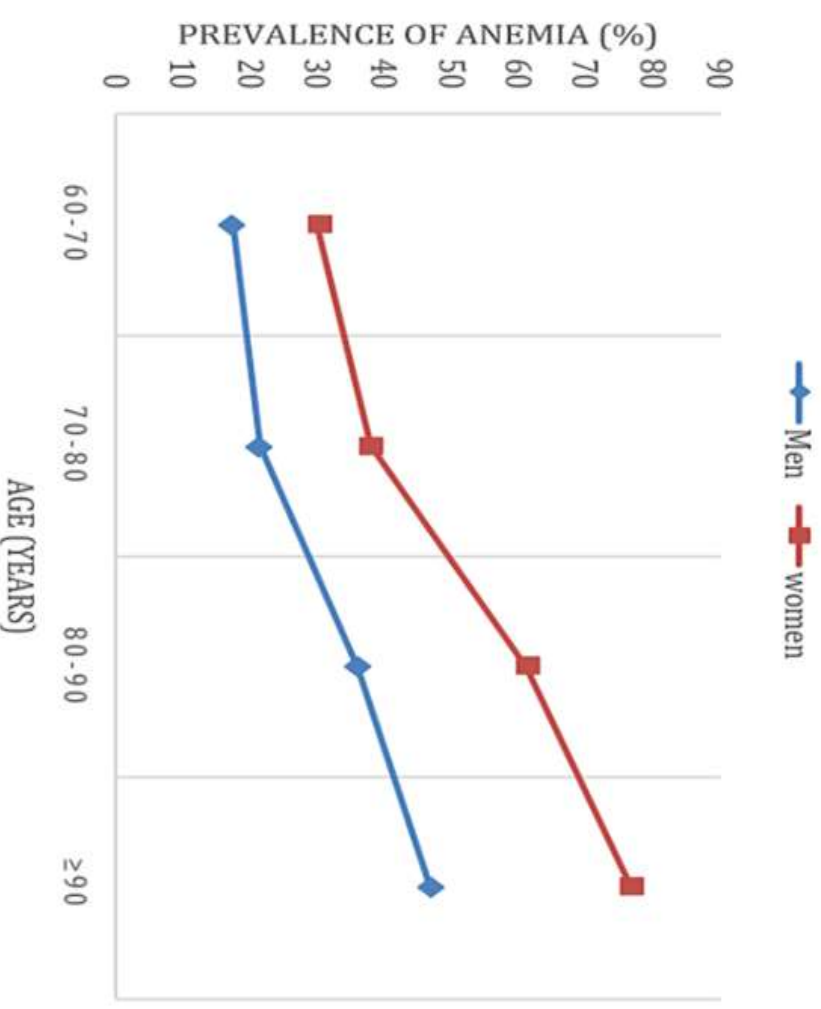


Figure 1: Increase of anemia prevalence in older adults

(Alvarez-Payares et al., 2021)

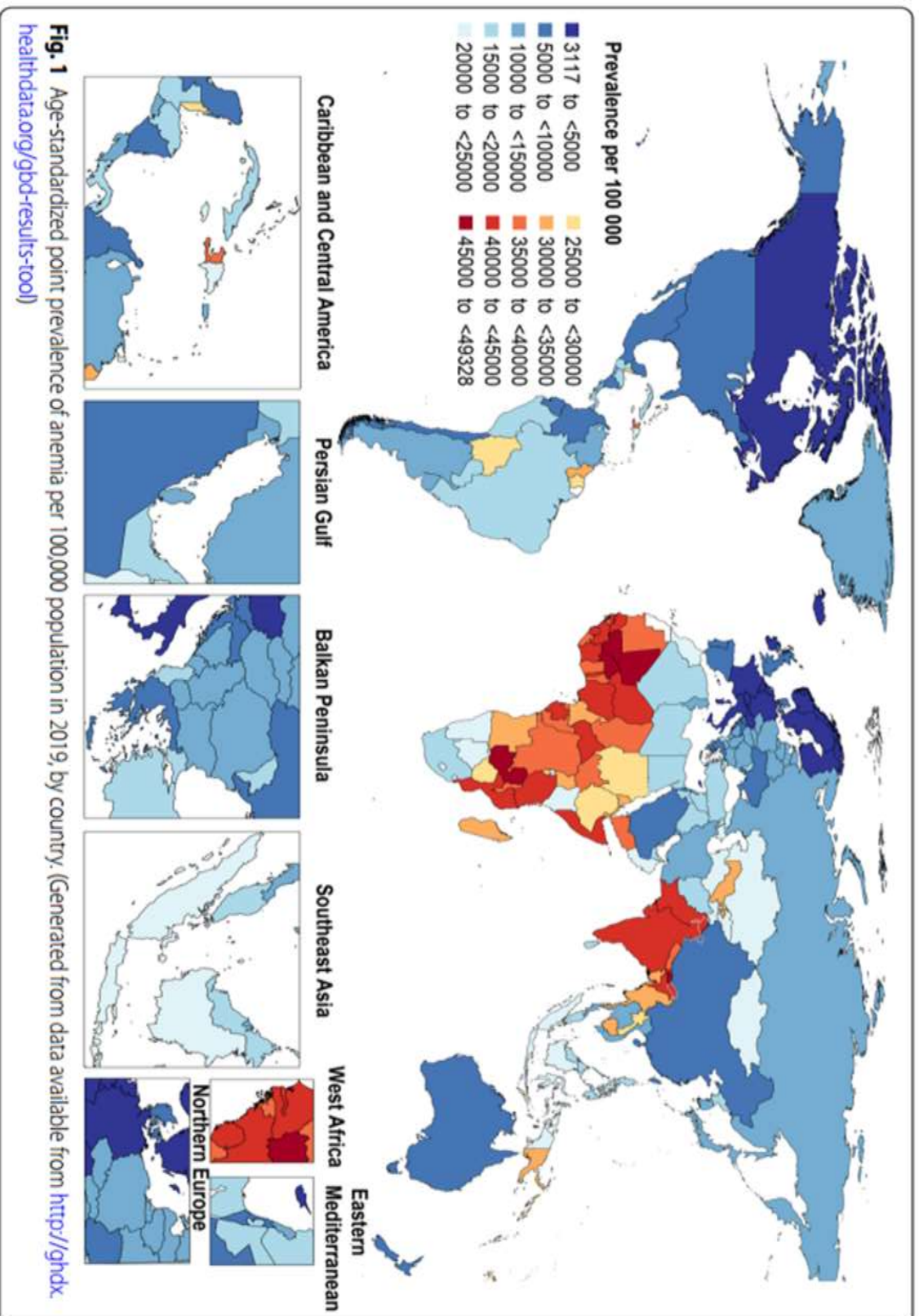
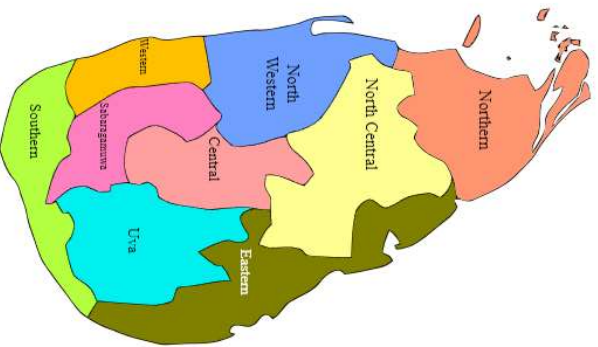


Fig. 1 Age-standardized point prevalence of anemia per 100,000 population in 2019, by country. (Generated from data available from <http://ghdx.healthdata.org/gbd-results-tool>)

General population >65yrs of age	10-24%
Community dwelling	12%
Hospitalized	40%
Nursing home	Up to 47%

Prevalence in Sri Lanka



In hospitalized patients, the majority of them were females (63.2%; n = 129).

The mean age was 72.5 years (65 – 92 years).

Normocytic anemia was the most common type identified with the majority being of moderate degree.

Though the commonest etiological cause identified is anaemia of chronic disease, a considerable percentage had multifactorial causes.

Chathurangani, K. C., Gamaralalage, L., Darshana, T., Hewage, L., Premathilaka, R. A., Jeevani Costa, Y., Arachchige, A., Amarasekara, D. S., & Premawardhena, A. P. (2022). A descriptive study of anaemia in the elderly at a tertiary care institute in Sri Lanka. *Ceylon Medical Journal*, 67(3), 94. <https://doi.org/10.4038/CMJ.V67I3.9696>

Sujanitha, V., Sooryakumar, T., Kumarasiri, T., Rajeshkannan, N., & Tharmiga, S. (2022). Evaluation of anaemia in geriatric patients: a retrospective hospital-based study from Northern Sri Lanka. *Asian Journal of Internal Medicine*, 1(2), 21–31. <https://doi.org/10.4038/AJIM.V1I2.49>

Why anaemia matters



Impaired executive functions and physical performance

Decrease lower extremity strength with higher Falls and fracture risk

Cognitive impairment

Insomnia and mood disorders-Depression

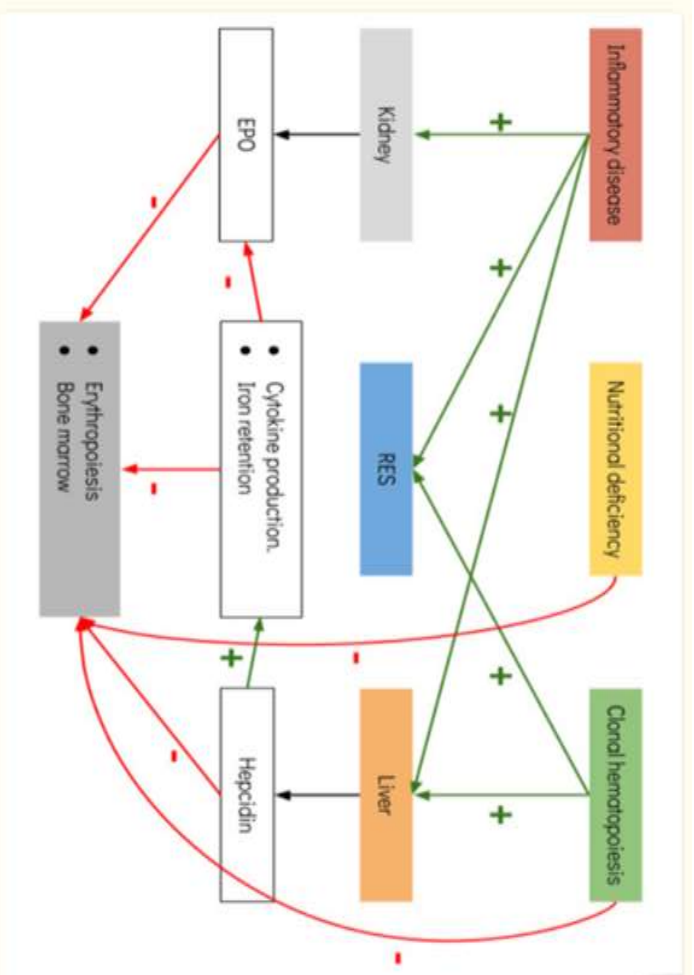
Risk of Heart failure & cardiovascular mortality

Longer Hospitalization

worse quality of life

Increase All cause mortality

Etiologies of anaemia

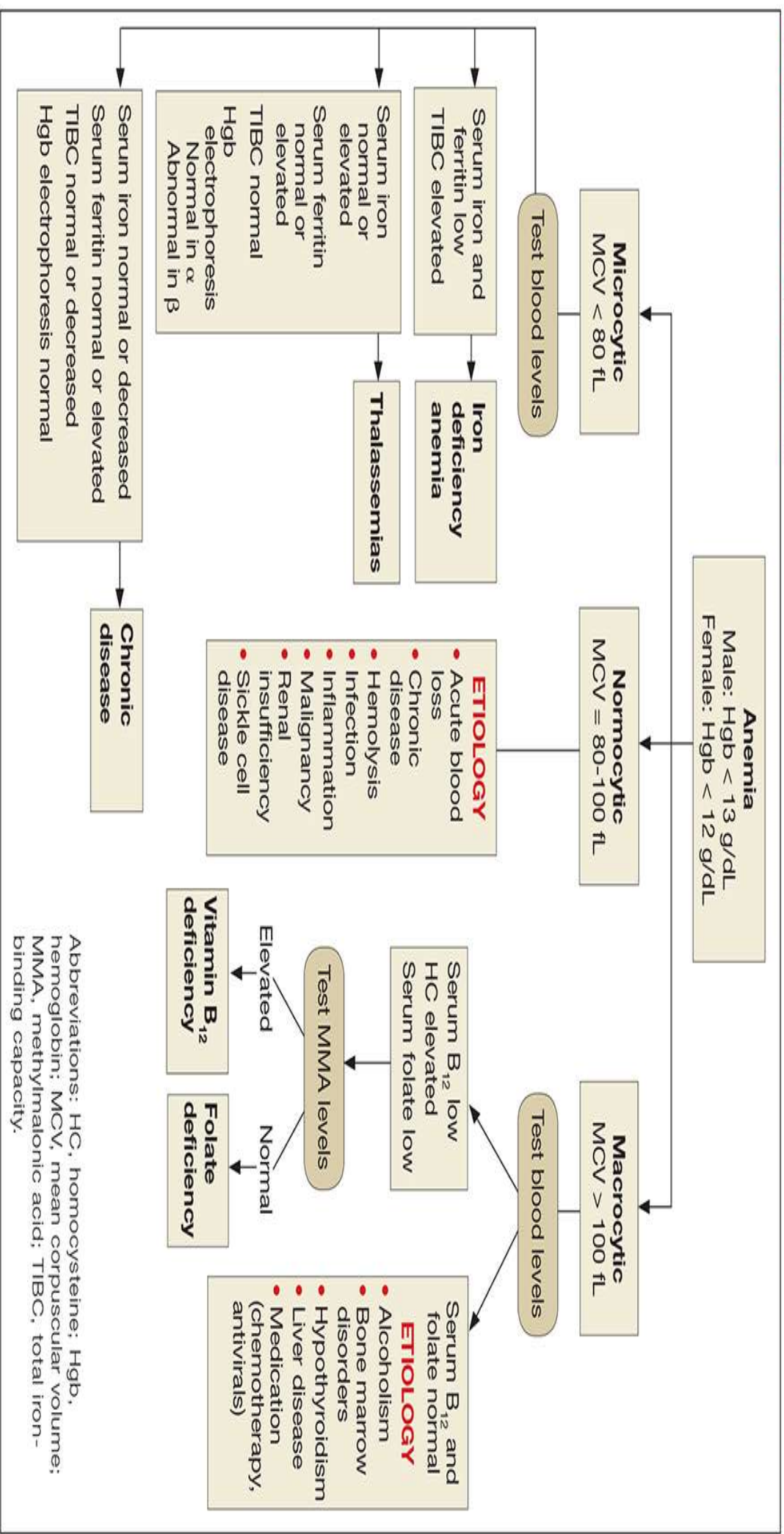


Possible mechanisms of anemia in elderly adults

(Modified from Shlush [19])

Nutritional deficiencies	1/3
Anemia of chronic disease	1/3
Unexplained anemia	1/3
30-40% of cases are multifactorial	

FIGURE
Classification of Anemia



Abbreviations: HC, homocysteine; Hgb, hemoglobin; MCV, mean corpuscular volume; MMA, methylmalonic acid; TIBC, total iron-binding capacity.

Valve induced hemolysis

- Hemolytic anaemia one of the serious complications of prosthetic valves occurs in up to **15% of cases**
- The main mechanism of hemolysis after surgical valve replacement is a **paravalvular leak** which is due to suture dehiscence due to heavy annular calcifications, endocarditis, chronic steroids or suboptimal surgical techniques
- Hemolysis also complicates a small percentage of **mitral valve repair <1%**
- Older generation valve models were associated with a high rate of hemolysis incidents with structural deterioration, and it is uncommon in **new valve models, the most common cause is a paravalvular leak in new models.**
- If a patient presents with typical symptoms in valve-induced hemolytic anaemia diagnosis is not difficult. however, valve hemolysis patients present with atypical presentations, so a systematic approach is important in diagnosing atypical presentations

- **Take home message**
 - Hidden anaemia can manifest with atypical presentations.
 - The underlying aetiology is often multifactorial.
 - Managing it may require a multidisciplinary approach.
 - Early diagnosis and intervention can significantly improve both mortality and morbidity.

- **References**

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- 2. (No date a) *Cardiac prostheses-related hemolytic anemia - wiley online library*. Available at: <https://onlinelibrary.wiley.com/doi/10.1002/clc.23191> (Accessed: 18 June 2023).
- 3. 2020 ACC/AHA heart valve disease guideline: Key perspectives, part 3 (no date) *American College of Cardiology*. Available at: <https://www.acc.org/Latest-in-Cardiology/ten-points-to-remember/2020/12/16/22/01/2020-ACC-AHA-VHD-GL-Pt-3-GL-VHD> (Accessed: 19 June 2023).
- 4. Cardiology, F. the D. of (no date) *Hemolysis associated with Prosthetic Heart Valves: A review : Cardiology in Review, LWW*. Available at: https://journals.lww.com/cardiologyinreview/Abstract/2009/06000/Hemolysis_Associated_With_Prosthetic_Heart_Valves_.4.aspx (Accessed: 19 June 2023).

- Thank you.....