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Characteristics of anemia in patients above 60 years of age attending a tertiary care hospital

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Abstract:

Anaemia is a common problem in the elderly population. It is a major contributor of morbidity and mortality. The common causes of anaemia in the elderly are nutritional deficiency, anaemia of inflammation and unexplained anaemia. The aim of this study was to characterize the clinical types of anaemia in elderly hospitalized patients. This was conducted as a hospital based longitudinal study undertaken among elderly patients in a tertiary care hospital. 70 patients more than 60 years admitted in the medical wards with anaemia were included in the study. History related to diet, antiplatelet use was recorded. Co morbidities were assessed using Charlson Co morbidity Index. Laboratory investigations including Haemoglobin, RBC indices, S.Ferritin, renal function tests(RFT), stool occult blood(SOB) were noted and analyzed. S.Cobalamine, Folic acid, GI endoscopy, bone marrow studies were done only in indicated patients. Of the patients included in the study 53% were male and 47% were females. Majority of patients were in the age group of 60-70 years (44.3%). All patients were taking a non-vegetarian diet. Majority of patients (95.70%) did not give a history of chronic blood loss, but 17.10% had stool occult blood positivity. The most common anaemia detected was iron deficiency anaemia(28.6%). 27.10% had anaemia of chronic disease, 21.40% had unidentified anaemia, 20% had anaemia of chronic kidney disease (CKD) and 2.90% had mixed anaemia. None of the patients had either Cobalamine or Folic acid deficiency. 20% of elderly anaemic in the study did not have any associated comorbidities. 34.3% had a Charlson Co morbidity Index(CCI) of 1-2, 28.50% had CCI of 3-4 and 17.10% had CCI of 17.10%. The most common co morbidities associated were hypertension, diabetes mellitus, CKD and myocardial infarction(MI). Thus it was concluded that iron deficiency anaemia appeared to be the commonest cause of anaemia in elderly in this study. Other common causes being anaemia of chronic disease and anaemia of CKD. The commonest co morbidity associated with elderly anaemic patients was hypertension. We will be able to prevent the morbidity and mortality related to anaemia by treating the correctable factors.

Keywords: 1 Anaemia, 2 Elderly, 3 Iron deficiency, 4 Anaemia of chronic disease, 5 Anaemia of CKD

Introduction:

Populations are growing older in countries throughout the world. The ageing population of India has increased over the last few decades. In India the life expectation at birth was 39 and 38 for males and females respectively during 1950 which rose to 63 and 65 respectively during 2003.¹Globally, the number of persons aged 80 years or over is projected to increase more than threefold between 2017 and 2050, rising from 137 million to 425 million.² In India majority of people older than 60 years are suffering from non communicable diseases and there is a significantly higher load of old age related morbidity^{3,4,5}

Anaemia of any degree is recognized as a significant independent contributor to morbidity, mortality, and frailty in elderly patients⁶ Anaemia in elderly arises in part from the cumulative effect of age-related co morbidities and physical decline as well as age-specific changes in the hematopoietic system that influence red blood cell production. Understanding of these changes could have important diagnostic and therapeutic implications for addressing this common problem. Because the number of elderly individuals is expected to reach unprecedented levels in the 21st century, anaemia represents an emerging global health problem negatively impacting quality of life in a significant proportion of the elderly population and requiring an ever-greater allocation of health care resources⁷ Several studies have shown decreased physical performance and strength in elderly anaemic patients^{8,9} Moreover anaemia has been shown to impact mortality in elderly patients with other co-morbid conditions¹⁰ Improvement in haemoglobin levels can also lead to improvements in end-organ function¹¹ Three general causes for anaemia in the elderly, nearly equal in frequency, emerged from the NHANES III study. These are 1) anaemia due to blood loss/nutritional deficiencies (34%), 2) anaemia associated with chronic illness/inflammation or chronic renal failure (32%), and 3) unexplained anaemia (34%)¹²

Using the World Health Organization (WHO) definition of anemia (< 13g Hb/dL for men and < 12 g Hb/dL for women), 11.0% of men and 10.2% of women were anemic according to the NHANES III data set in United States. In India the prevalence of anemia is much higher^{13,14}. As a significant proportion of elderly may be having an anemia which is correctable with treatment it is worthwhile to look into the causes of anemia in elderly patients so as to prevent morbidity and mortality in these elderly citizens.

Methods

The prevalence of anaemia is high in elderly patients. So we hypothesised that there will be a significant proportion of patients with treatable anaemia in elderly age group. Thus the aim of this study was to characterize the clinical types of anaemia in elderly hospitalized patients. It was a hospital based descriptive study done in the Department of Internal Medicine, Government T.D. Medical College, Alappuzha. Permission to conduct the study was obtained from Institutional Research committee [Protocol No.S23/2019 dated 10.4.2019] and Institutional Ethics committee [EC46/2019 dated 9.5.2019] of TDMC Alappuzha. Confidentiality of the patients was maintained during every stage of the study. Informed written consent was obtained from patient and relative. If patient is too sick to give consent, consent was obtained from immediate relative. All the expenses for the study were met by the investigator. Consecutive sampling of 70 patients older than 60 years admitted in medical wards with anaemia who satisfy the inclusion and exclusion criteria were included in the study. Patients aged 60 years or over with anaemia were included. Patients who have received blood transfusion within 3 weeks prior to hospitalization or already on oral/parenteral iron / Cobalamine/Folic acid therapy were excluded. Terminally ill patients were also not included in the study.

Defenitions used in the study:

- **Anaemia** is defined according to WHO criteria ie; Hb <12g/dl for females and <13g/dl for males. Anaemia severity is graded as severe with Hb. <8 g/dl, moderate with Hb. between 8 g/dl and 9.5 g/dl and mild with Hb.>9.5 g/dl .
- **Iron Deficiency Anaemia (IDA)** Patients with Hb levels under 12 g/dL (women) and 13 g/dL (men) and a S.Ferritin <30 microgm /dl and ESR <50mm/hr

- **Anaemia of chronic disease:** Anaemia with S.Ferritin >100 micro gm/ml with ESR >50mm/hr
- **Mixed anaemia:** Anaemia with S.Ferritin between 30 and 100 micro gm/dl and ESR>50mm/hr
- **Anaemia due to Cobalamine deficiency:** Anaemia with MCV >100fl and S.Cobalamine levels <150 pico gm /ml
- **Anaemia due to Folic acid deficiency:** Anaemia with MCV >100fl and S.Folic acid levels <2 micro gm/dl
- **Anaemia of chronic kidney disease(CKD):** Anaemia with S.Creatinine >1.2 in females and >1.5 in males
- **Unexplained anaemia:** Anaemia not included under any of these.
- **Treatable anaemia:** Iron deficiency anaemia or anaemia due to Folic acid or Cobalamine deficiency

Study was conducted in Government Medical College Hospital, Alappuzha, a 1000 bedded teaching tertiary care hospital situated in coastal Kerala catering for the major group of low and middle class socioeconomic population of central Kerala .In this study, patients who were admitted in the Medical wards of Government Medical college Hospital, Alappuzha, Kerala between 10 th May 2019 and 15 th June 2019 were included after getting informed consent from patient or a close relative if patient is too sick to sign the consent form.

A detailed history to assess the co morbidities was done using the Charlson's co morbidity index¹⁶. History of chronic blood loss and history of current anti platelet use was recorded. History regarding the type of diet: whether vegetarian or non vegetarian was documented. Blood samples were drawn from the patient and sent for the following tests which include Haemoglobin, S.Ferritin, Total iron binding capacity(TIBC), Transferrin saturation(TSat), ESR, RBC indices(MCV,MCHC,MCH) and S.Creatinine. S .Folic acid and Vitamin B12 were done only in selected patients with a MCV >100fl. Stool occult blood for 3 consecutive days was also checked for any evidence of gastrointestinal blood loss. Colonoscopy or upper gastrointestinal endoscopy was done in patients with evidence of gastrointestinal blood loss. Bone marrow examination was done only in indicated patients with unexplained anaemia.

The primary objective of this study is to determine the different etiological subtypes of anaemia in a hospitalized geriatric patient population. Descriptive statistics are attained through the calculation of arithmetical means, standard deviations, and minimum and maximum values of all data. To test the significance of all categorical variables, the Chi-squared test (Pearson) is performed. Arithmetical means are calculated with *t*-tests for dependent and independent samples, and correlations are determined using the Spearman Rho method. All outcomes with a minimum of $P < 0.05$ are considered significant. Missing values are disregarded in all statistical tests. All statistical analyses are performed using IBM SPSS Statistics 20SPSS statistical software.

Results

Sex ratio of patients almost equal with slight majority for males(53%). Majority of patients were in the age group of 60 – 70 years(44.3%). Only 4% gave a history of chronic blood loss.Stool occult blood positivity was seen among 17.1%.Antiplatelet use was seen among 64.3%.The mean haemoglobin was found to be 8.91(SD 2.18)(Fig 1).An ESR of >50mm/hr was seen in 44.3%. In this study anaemia of chronic disease and mixed anaemia had a raised ESR above 50 mm/hr. Based on levels of haemoglobin anaemia can be grouped as mild (Hb >9.5 g/dl, moderate Hb 8-9.5g/dl and severe (Hb <8 gm/dl). Majority of patients (55.70%) were having either a moderate anaemia or a severe anaemia(Fig 2).Majority of patients were having iron deficiency anaemia and none had anaemia due to Cobalamine or Folic acid deficiency.(Fig 3). Ferritin levels <30ng/ml suggested absolute iron deficiency.38.6% had absolute iron deficiency in our study. Least common(2.9%) was an anaemia with high MCV which may be classified as macrocytic anaemia. Charlsons Co morbidity Index(CCI) of 0 suggests no associated comorbid conditions. Score of 1-2 suggest mild comorbidities,3-4 moderate and >5 suggests severe.The CCI among patients and the distribution of co morbidities is as shown in figures 3 and 4 respectively. Hypertension, Diabetes, CKD and MI are the commonest co morbidities associated with anaemia in elderly.

Discussion:

Geriatric anaemia is considered as a serious clinical condition by many physicians. Anaemia of any degree is considered as a significant independent contributor to morbidity, mortality and frailty in elderly patients^{6,17}. The current study aims to discuss the rationale for increased awareness of anaemia, the aetiology and the increased association of co-morbid conditions linked with anaemia especially in the hospitalized elderly.

In our study 53% were males and 47% patients were females which correlates with the general Indian population sex ratio where 51.80% are males and 48.20% females (UN Population Prospects 2017). It also gives an inference that anaemia is more common in males than females which is seen in other Indian studies.^{18,19} The majority of study participants were in the age group of 60-70 years (44.30%). This also correlates with other studies^{19,20}. All patients included in the study were taking a non vegetarian diet which differs from other studies of similar type.^{20,21} which had showed more than 50% of study participants to be pure vegetarians. The difference in the dietary habits could be explained by the fact that the study was conducted in a tertiary care hospital of a coastal segment of Kerala where majority of the population consumes a diet consisting of rice and fish. In the study only 4% gave a history of chronic blood loss in the form of hematemesis or melena although stool occult blood positivity was found in 17.10% of patients. This difference could be because the elderly people may not be aware of the chronic blood loss due to their associated medical conditions like poor vision and impaired cognition. 64.3% of patients in the study group were taking anti platelets but there was no significant correlation of anti platelet use and stool occult blood positivity.

The mean haemoglobin of study subjects was 8.91+/- 2.180. (Fig1) Out of total 70 patients, 27.10% had severe anaemia with Hb <8g/dl; 28.60% had moderate anaemia with Hb between 8-9.5g/dl and 44.30% had mild anaemia with Hb > 9.5g/d. (Fig2) This is almost comparable to another Indian study¹⁹. With regard to the type of anaemia (fig 3); 28.6% had iron deficiency anaemia, 27.10% had anaemia of chronic disease, 20% had anaemia of CKD, 21.40% had anaemia of unknown aetiology /unexplained anaemia, 2.9% has mixed anaemia and none had Cobalamine or Folate deficiency. This can be compared with other similar studies (Table 1) Our study had shown that iron deficiency anaemia is the commonest cause of anaemia in elderly patients. This correlates with other Indian studies^{15,21}; whereas few western studies have shown preponderance for anaemia of chronic diseases^{12,22}. This may reflect that nutritional deficiencies, malabsorptions or chronic iron loss through the GI tract may be responsible for such a finding in the Indian sub population which may necessitate further studies. Patients with S.Ferritin levels <30 may be considered as having absolute iron deficiency. These constituted about 38.60%. These group of patients need to be treated for iron deficiency aggressively as they have very negligible iron stores.

The stool occult blood is an important diagnostic test which can be used to screen patients with underlying GI malignancy / ulcer. In our study the stool occult blood (SOB) positivity were seen in 17.10% of patients where as in the study conducted by Bhasin & Rao¹⁵ anaemia of chronic blood loss constituted 31%. Out of the patients with SOB positivity we could do upper GI endoscopy/colonoscopy only for a minor group which revealed abnormalities like gastric erosions, ulcers, varices and haemorrhoids. It is worthwhile to repeat the SOB at a fixed intervals in elderly patients with IDA and proceeding with endoscopies in these elderly citizens as they are likely to harbour occult GI malignancies complicating anaemia. In our study on comparing the different variables which are likely to cause a positive stool occult blood only chronic liver disease was found to have a significant association with $p < 0.01$.

Anaemia of chronic disease accounted for 27.10% of patients. This corresponds with studies done by^{12,21}. Anaemia of chronic disease is usually due to cancer, chronic infections & autoimmune diseases. Another concept is the role of "inflamm ageing" which describes a low grade pro-inflammatory state associated with aging²³. In our study, patients who had a high ferritin of >100fl & and ESR >50 mm/hr were labelled as having anaemia of chronic disease. Clinical evaluation for inflammatory conditions as well as measurements of C- reactive protein, fibrinogen, IL6 & hepcidin levels (if available) may be useful in identifying this type of anemia²⁴.

21.40% of patients in our study had an unexplained anaemia. This is probably a hypo proliferating, normocytic anaemia that is not due to nutritional deficiency, CKD or an inflammatory disease¹². This may be related to a blunted erythropoietin response in the elderly which needs further research. The role of testosterone deficiency and Vitamin D deficiency in elderly anaemic patients is also currently being studied²⁵. While searching for the cause of anaemia in our study we could pick up one case of CML, one case of lymphoma and one case of multiple myeloma with a bone marrow examination.

Anaemia of CKD represented 20% of our patients. This is compatible to other studies which showed 22%¹⁵ & 19.49%²⁶ association with CKD. Anaemia attributable to CKD was seen in 8% of all cases of anaemia in elderly according to NHANES III. The cause of anaemia should be investigated in these individuals; this can range from erythropoietin deficiency due to CKD, to deficiency of vitamin B(12) and/or folate, iron deficiency, blood loss, inflammation, malignancy, and aluminium intoxication. After other causes of anaemia have been excluded, CKD is the most likely aetiology, and it should be treated with an Erythrocyte Stimulating Protein. Currently, epoetin alfa and darbepoetin alfa are the only 2 ESPs approved for use in the United States²⁷. As anaemia of CKD constituted a significant percentage of patients in our study this needs to be addressed and managed as anaemia in CKD is associated with worse cardiac outcomes and increased risk of mortality.

If we classify anaemia based on MCV; an MCV <80 fl is considered as microcytic anaemia, MCV between 80-100 fl as normocytic and >100fl as macrocytic. Microcytic anaemia constituted the majority(55.70%) of our anaemic patients. Even though only 2.9% represented macrocytic anaemia none had either Cobalamine or Folic acid deficiency. This is probably because all patients in our study group were non vegetarians. Deficiency of Cobalamine and Folic acid rarely occurs due to inadequate intake except in pure vegans.

While assessing co morbidities using the Charlson Co morbidity Index the percentage of patients with a score of 1-2 was 34.3%; a score of 3-4 was 28.50% and a score of >5 was 17.10%(Fig 4) The most common co morbidity among elderly anaemic patients was hypertension(Fig 5). There was no statistical correlation between a higher CCI and anaemia of chronic disease as expected. We had also made a comparison between different variables and the severity of anaemia. We could not find any statistical positive correlation between gender, age, sex, anti platelet use, CCI score and SOB.(Table2)

Even though this had been a properly conducted study, it had certain limitations. The study population was small, hence the statistical power of this study is less. Only hospitalised patients with multiple co morbidities and other acute illnesses were included in this study. This is likely to increase the percentage of anaemia of chronic disease. The entity called unexplained anaemia reflects an inadequately studied group in this study which needs further studies for detailed evaluation for categorization and etiological assessment. Patients with iron deficiency anemia were not thoroughly evaluated with GI endoscopy which could have picked up more lesions responsible for chronic blood loss.

Conclusion:

Untreated anaemia in the elderly can be detrimental. It is unknown whether it is the underlying anaemia or the associated co morbidities which accounts for the adverse outcomes in elderly patients with anaemia. In elderly patients, before considering a treatment plan the primary diagnosis and accompanying disease with emphasis on treatable disorders should be properly defined. In this study we had found that iron deficiency anaemia is the most common type of anaemia, next being anaemia of chronic disease and anaemia of CKD. Iron deficiency anaemia in elderly may be due to a number of individual as well as combined factors including poor diet, reduced efficiency of iron absorption, GI blood loss, medications and chronic disease.²⁸ Iron deficiency anaemia is relevant in the elderly because patients with iron deficiency anaemia can be effectively treated with oral or intravenous iron substitution. H.Pylori infection has been implicated as a risk factor for iron deficiency-possibly a strain

related effect²⁹. As IDA is a treatable cause of anaemia more studies are needed in this regard as to the definite cause of this anaemia in elderly. Moreover there is no definite information about how ageing of GI tract affects iron absorption and this poses difficulty to calculate iron requirements in elderly. This also should be an area of research. Many of our patients had anaemia of chronic disease. This is probably related to the transient increase in cytokine levels in the setting of acute stress and co-morbidities. We need more studies as to establish an independent cause of anaemia due to inflammation associated with ageing, keeping aside the confounding factor related to co-morbid conditions. Unidentified anaemia is also another area which we should be focusing on. In our study this had constituted 21.4 % of all anaemia. Anaemia related to CKD may also be considered as a potentially treatable cause of anaemia which if treated appropriately can bring down the adverse outcome in elderly CKD patients. The co-morbidities associated with anaemia should be properly managed which may decrease the adverse outcome in these elderly patients. We need national nutrition plans including control of iron deficiency as a priority as iron deficiency is seen to be a major cause factor of elderly anaemia.

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Table 1:

	Guralnik <i>et al.</i> 2004	Bhasin <i>et al.</i> 2011	Petrosyan <i>et al.</i> 2012	Sharma D et al 2015	Our study
Anemia of chronic disease	33.6	27	62.1	22.9	
Iron deficiency anemia	16	30	30.5	24.8	28.6
Chronic kidney disease	12	21	17.8	12.4	20
Vitamin B12/folate deficiency	14.3	5	38.9	2.9	0
Hematological malignancy	NA	6	6.3	15.2	NA
Unexplained	24	2	8.4	8.6	21.40

Table 2:

VARIABLE		STOOL OCCULT BLOOD		P VALUE
		NEGATIVE	POSITIVE	
SEVERE LIVER DISEASE	NO	8	58	0.001
	YES	0	4	
MYOCARDIAL INFARCTION	NO	9	6	1.000
	YES	3	13	
CEREBRO VASCULAR ACCIDENT	NO	10	51	0.646
	YES	2	7	
ANTI PLATELET USE	NO	5	20	0.744
ANTI PLATELET USE	YES	7	38	
VARIABLE		ANEMIA OF CHRONIC DISEASE		
		NO	YES	
FERRITIN	<30	24	3	0.049
	>30	29	14	
CH SCORE	0	11	3	1.000
	≥ 1	42	14	

Figure 1: Mean Hb

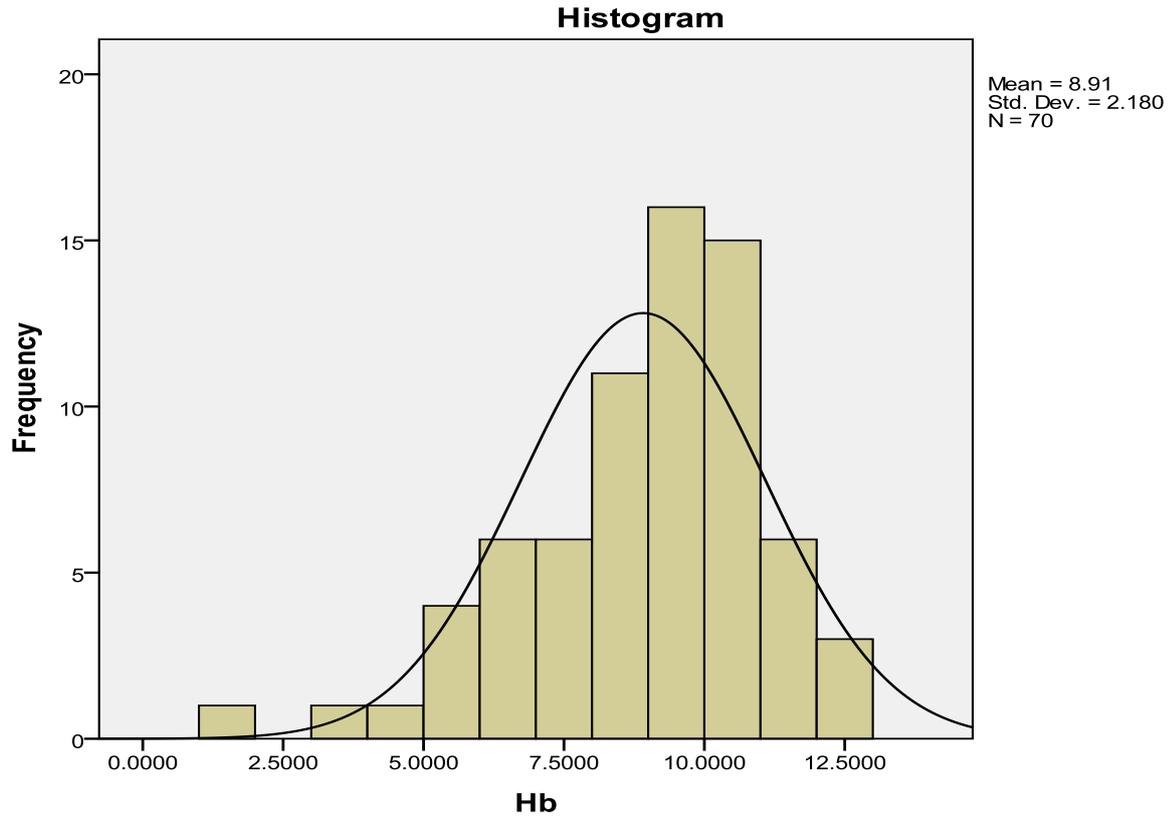


Figure 2: Levels of Haemoglobin.

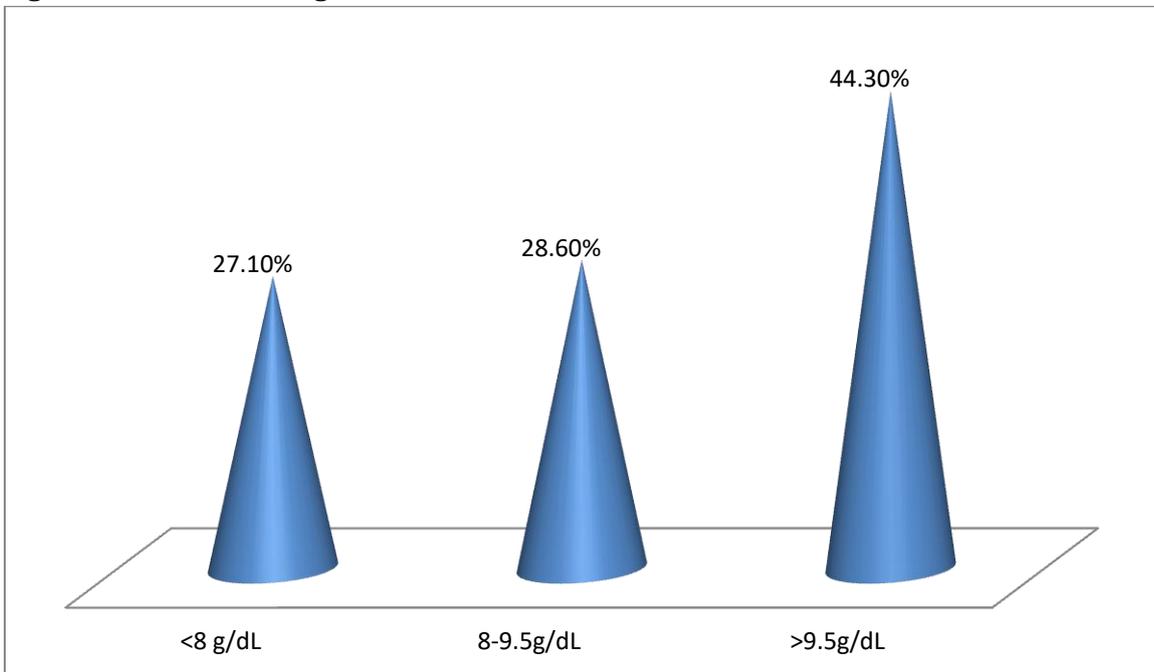


Figure 3: Types of Anaemia

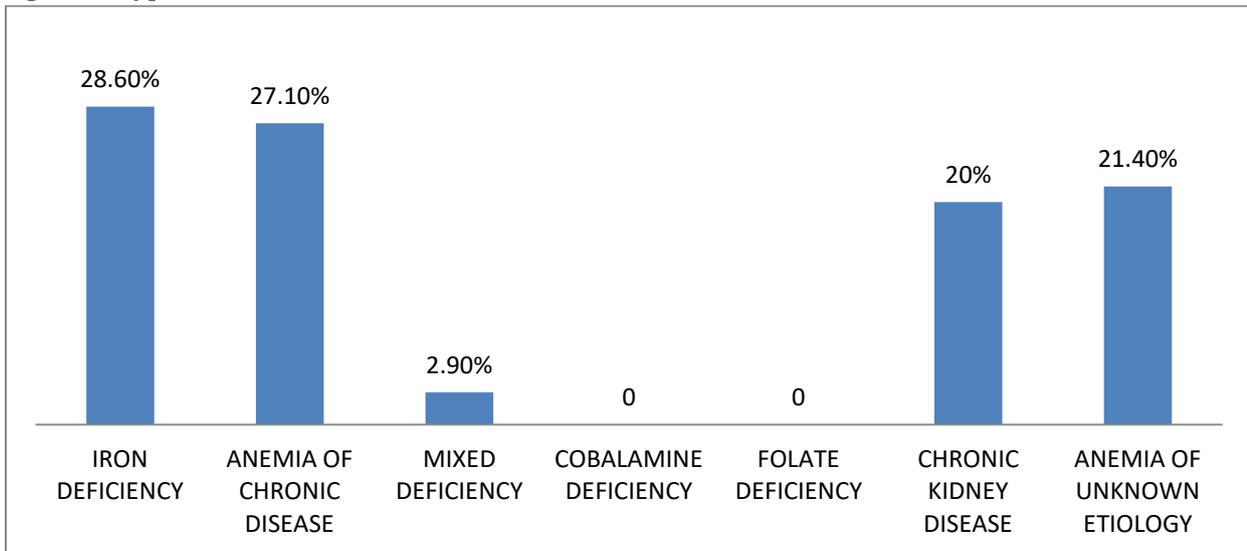


Figure 4: Charlson's comorbidity index among patients

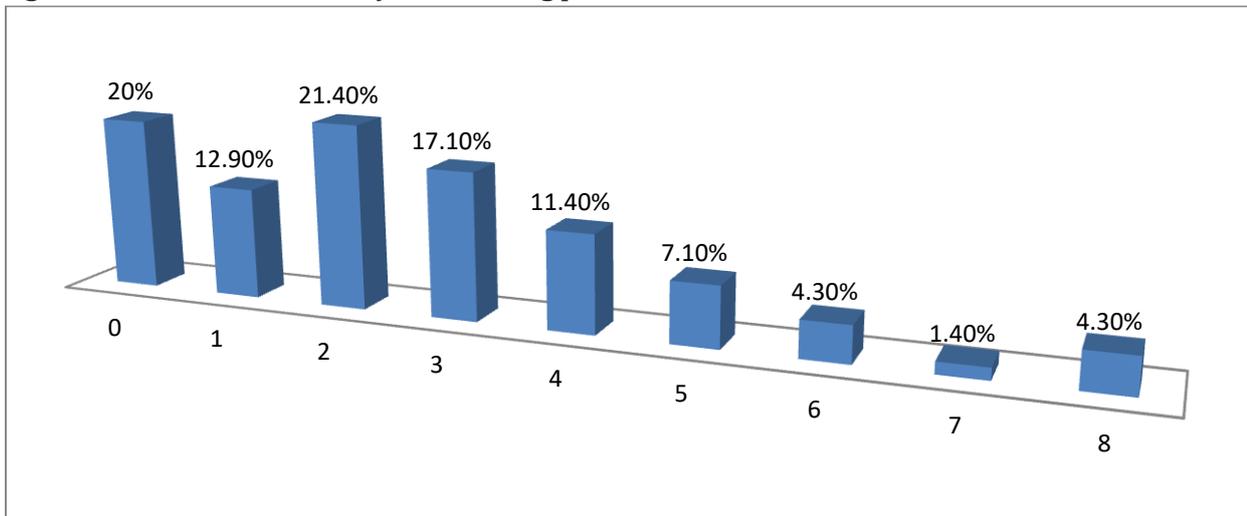


Figure 5: Distribution of comorbidities among patients

