Project on

A Survey on patients with chronic kidney disease induced anemia at Saidpur in Bangladesh.

[In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy]

Submitted To

Department of Pharmacy,

Faculty of Allied Health Sciences,

Daffodil International University

Submitted By

Student ID: 191-29-1429

Faculty of Allied Health Sciences

Daffodil International University

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APPROVAL

This project paper, **"A Survey on patients with chronic kidney disease induced anemia at Saidpur in Bangladesh"** submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

BOARD OF EXAMINERS

……

Dr. Muniruddin Ahmed

Professor and Head,

Department of Pharmacy,

Faculty of Allied Health Sciences,

Daffodil International University

…… Internal Examiner 1

……. Internal Examiner 2

…… External Examiner 3

DECLARATION

I hereby declare that this project report, **"A Survey on patients with chronic kidney disease induced anemia at Saidpur in Bangladesh"**. I am declaring that this Project is my original work. I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor degree.

Supervised By

……..

Ms. Farjana Islam Aovi

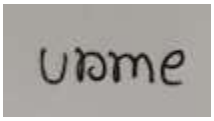
Assistant Professor

Department of Pharmacy

Faculty of Allied Health Sciences

Daffodil International University

Submitted By



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Student ID: 191-29-1429

Department of Pharmacy

Faculty of Allied Health Sciences,

Daffodil International University

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I might want to communicate my profound applause to the All-powerful Allah who has given me the capacity to finish my undertaking work and the chance to concentrate in this subject.

I would like to express my humble regards to Dr. Muniruddin Ahmed, Professor and Head, Department of Pharmacy, Daffodil International University.

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Finally, I would like to express my gratitude towards my parents and other family members for their kind cooperation and encouragement which helped me in completion of this project.

Dedication……..

My Parents

The persons who always encourage me in every sphere of my life

Abstract

Anemia of chronic kidney disease (CKD), is a form of normocytic, normochromic, hypo proliferative anemia. The objective of the study to determine which factors, contribute to the progression of CKD induced anemia & awareness of common people about this illness. Prepared number of many question about CKD-induced anemia. Then has been gone to some renown hospital at Saidpur in Bangladesh for individual patient's response collection. Permitting to the report, the majority of people (67%) have idea about chronic kidney disease, some people (33%) never any idea about CKD (Chronic kidney disease). The ordinary of participants believed low energy (35%) and decreased physical function (32%) was the chief sign of chronic kidney disease induced anemia, according to the inspection. Few respondents said fatigue (23%) is the symptoms of CKD induced anemia. According of survey, most of the people said that when your kidneys are damaged, they produce less erythropoietin (EPO) (45%) is the cause of CKD induced anemia. (25%) respondents consider that blood loss due to kidney failure is the cause of CKD induced anemia. Allowing of inspection, most of the people thought that Erythropoiesis-stimulating agent (53%) is the treatment of CKD induced anemia. The majority of participants said that they have been taken Eprex Iv (32%) and Recormon Iv (49%). On the other hand, few responders have been taken Iron intravenous (11%). 16% of persons 46-60 age range are more prone to CKD induced anemia.

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Chapter 1
Introduction

1. Introduction

Anemia is a frequent occurrence in CKD patients and has been associated with a lower quality of life. Furthermore, it accelerates the rate at which CKD progresses and increases morbidity and mortality rates [1]. Chronic inflammation is common in CKD patients. This is linked to a wide range of hidden constructions, such as an increase in infections, an increase in proinflammatory cytokines, a uremic environment, and other factors [2]. It is also linked to a rise in the incidence of arteriosclerosis. Proinflammatory cytokines including TNF- and IL-1 have prolonged serum half-lives in animals missing renal function, according to animal experiments [3]. Now, researchers are eagerly awaiting the discovery of novel therapies for the treatment of anemia in CKD patients. For some subjects, but not all, erythropoietin (EPO) therapy for anemia was linked to considerable benefits. The lackluster performance to EPO therapy is likely influenced by inflammation, according to data from clinical and scientific investigations. The therapy of people who respond poorly to EPO may benefit from anti-inflammatory medicines and drugs that could inhibit hepcidin's actions [6].

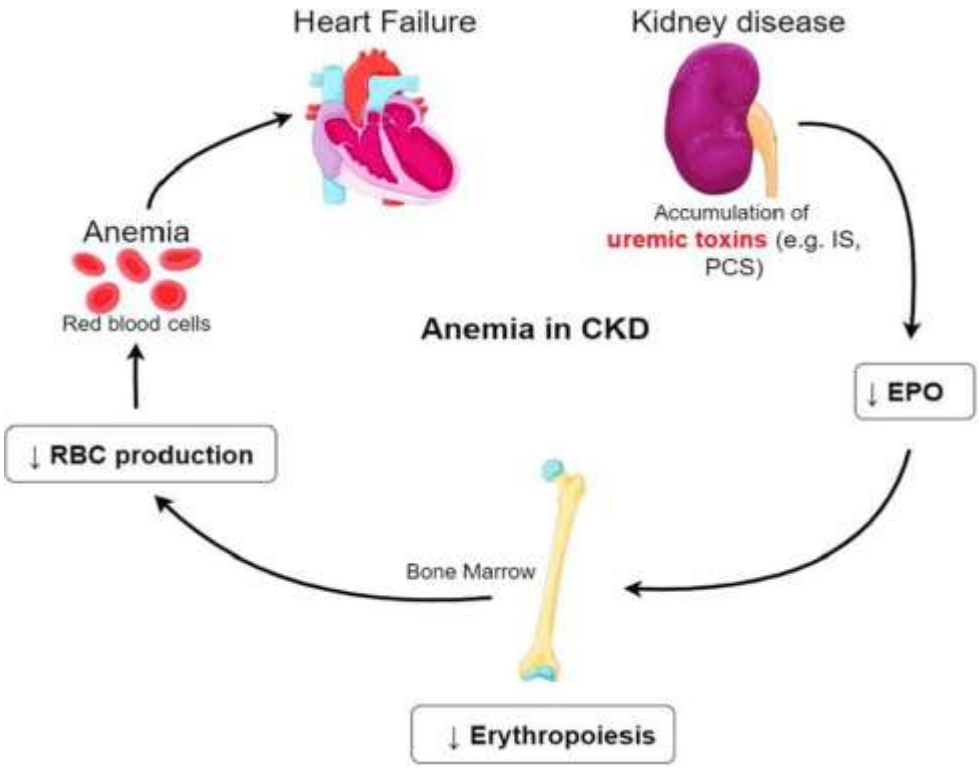

Figure 1: Figure 1: Erythropoiesis dropping process [7]

Anemia is a typical complication in CKD patients [7]. CKD usually includes normocytic, normochromic, and hypo proliferative cells [8]. According to large-scale studies, anemia (hemoglobin 12 g/dL) is less prevalent in patients with CKD stages I and II, 20%–40% in phases III, 50%–60% in phases IV, and more prevalent in individuals with end-stage renal dysfunction (stage V). Another study found that anemia might be 90% prevalent in dialysis patients [12,13]. Patients with stage 3 CKD experience anemia (hemoglobin 10 g/dL) with a frequency of 5.6%, whereas stage 5 non-dialysis CKD patients experience anemia at a prevalence of 27.2% [13,14]. These results conclusively show that impairment appears early in the development of CKD and that its recurrence increases as glomerular filtration rate decreases [11]. Thus according data from the National Health and Nutrition Examination Research study (NHANES) in 2007-2008 and 2009-2010 [12], only 20% of patients with stage 4 CKD and 42% of those with level five CKD in the United States garnered therapy, despite the fact that anemia is really quite prevalent among those with advanced CKD. In this study, anemia was determined using gender-specific thresholds (12 g/dL for female patients and 13 g/dL for male patients). Glomerular filtration rate, gender, age, race, and illnesses are suggested to be indications of CKD anemia [13]. The most important factors contributing to the development of anemia in CKD patients include chronic inflammation, erythropoietin deficit, iron metabolism abnormalities, blood loss all through hemodialysis meetings, uncontrolled hyperparathyroidism, a lack of essential nutrients like iron, folic acid, and vitamin B12, and the use of a few treatments like antihypertensive drugs and uremic toxins [14]. Understanding the underlying mechanisms of anemia in CKD is important since erythropoietin boosting agents (ESA) treatment may be ineffective or even detrimental in some patients with this illness [15]. persons undergoing dialysis who had CKD. According to research, people with CKD have poor erythropoiesis since the kidney's peritubular cells produce very less erythropoietin (EPO) [16]. Erythropoietin deficiency is associated with difficulties in red blood cell precursor formation and maturity. The development of anemia may be influenced by circulating renal tubular erythropoiesis regulators, according to the results of various studies [17]. It has been demonstrated that sera from uremic patients decrease the growth of hematopoietic progenitors [18]. Chiang et al. demonstrated that indoxyl sulfate (IS), a protein-bound uremic toxin, inhibits EPO gene transcription under hypoxia and suppresses erythropoiesis

in a hydroxylase inhibitor (HIF)-dependent manner. The way that IS stimulates the production of hepcidin via the aryl hydrocarbon receptor (AhR) and oxidative stress seems to be the cause of iron buildup and decreased iron absorption in CKD [19]. Moreover, hepcidin, an essential modulator of systemic iron absorption, has been associated to the development of anemia in CKD patients. Its amounts have been demonstrated to be affected by inflammation [20]. It is plausible that peripheral resistance to or hypo responsiveness to EPO is the true cause of anemia considering that it happens in patients with CKD despite having elevated EPO concentrations [21]. CKD patients receiving dialysis. Anemia can also result from iron loss in dialysis patients, in addition to the previously described factors. According to Besarab et al. [21], persistent bleeding caused by platelet dysfunction, frequent phlebotomies, hemolysis, and blood maintained in the extracorporeal circulation during dialysis are all associated with iron losses in hemodialysis patients that vary from 1-3 g annually. It was discovered that these alterations and the rupturing of the membrane are accelerated by the uremic environment, inflammation, and oxidative stress [22]. According to Bataille et al [23].

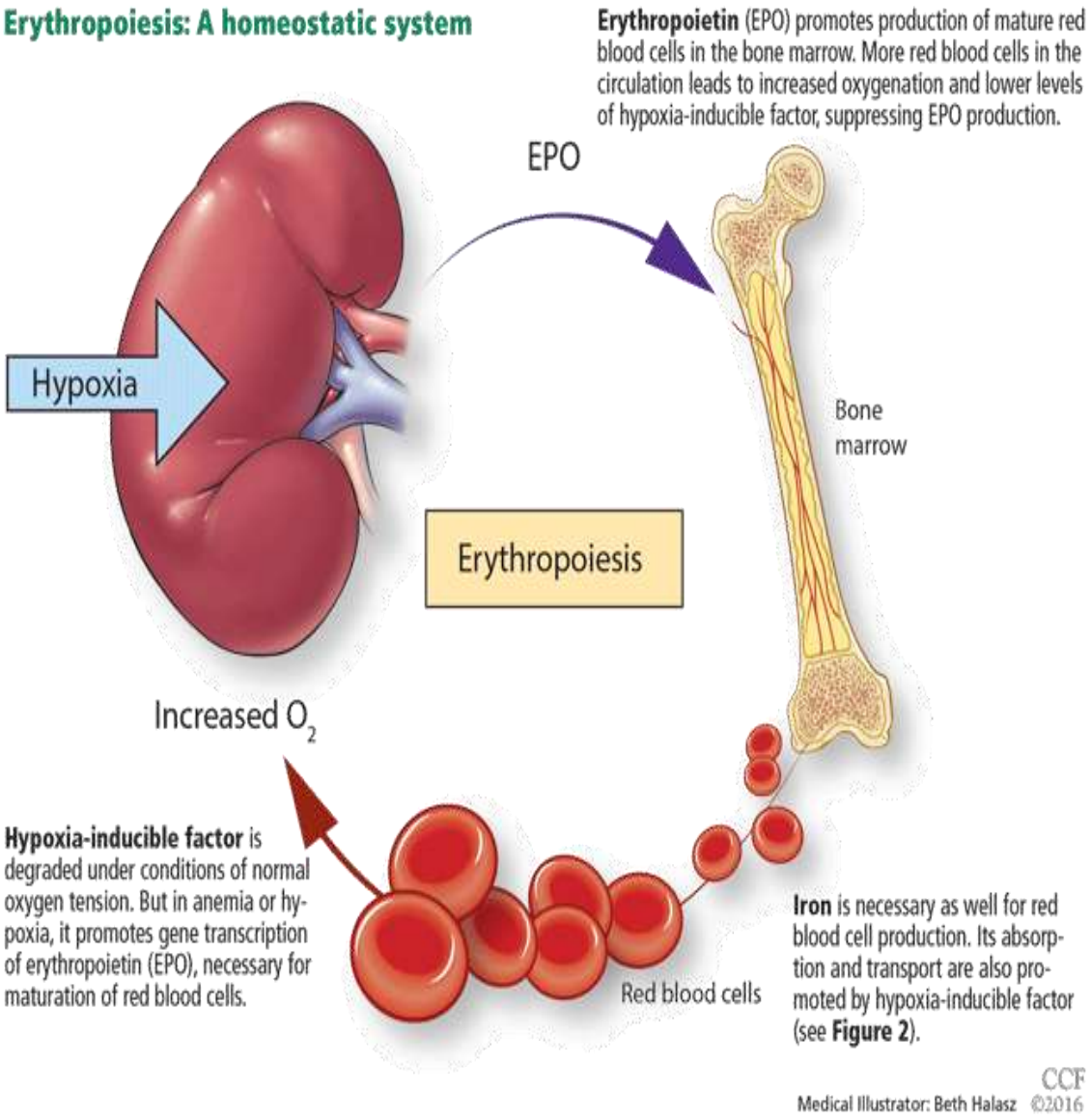

Figure 2: Anemia in CKD Patients [24]

1.1 Epidemiology of anemia of CKD

Chronic kidney disease (CKD) frequently results in anemia, which has been associated with decreased renal lifespan, increased morbidity and mortality, a reduction in quality of life, and higher costs [25]. According to a number of research studies, anemia rates among CKD patients who are not receiving dialysis (NDD) range from 20 to 60 percent. Anemia becomes more prevalent and intense when the estimated glomerular filtration rate (eGFR) decreases. Based on an analysis of the data from the National Health and Nutrition Examination Survey, anemia was twice as prevalent amongst CKD patients as in the

general population. Anemia prevalence rose from 8.4% at stages 1 to 53.4% at stage 5 as CKD progressed. Similar information was discovered in a much new analysis by the CKD Prediction Consortium [26] major cardiovascular incidents (16.4 vs. 7.2%), and mortality (10.3 vs. 6.6%), as well as quicker progression to CKD stages 4-5 [27]. Regarding the "real-world" management of anemia in CKD, the existing guidelines involve major disagreements and variability. Iron use was shockingly low, particularly in NDD patients receiving ESA medication, when compared to the regulations' recommendations, although a fifth of dialysis patients receiving ESA had hemoglobin levels above the recommended thresholds [28]. Additionally, a multicenter cross-sectional research performed at highly specialized nephrology health centers in Ireland found low rates of iron deficiency testing (only 45% of anemic patients), low medication adherence (86% of patients with confirmed iron deficiency were not undergoing care), and increased numbers of anemia (varying from 21 to 63%; p 0.001, guess it varies on the CKD Stage) [29].

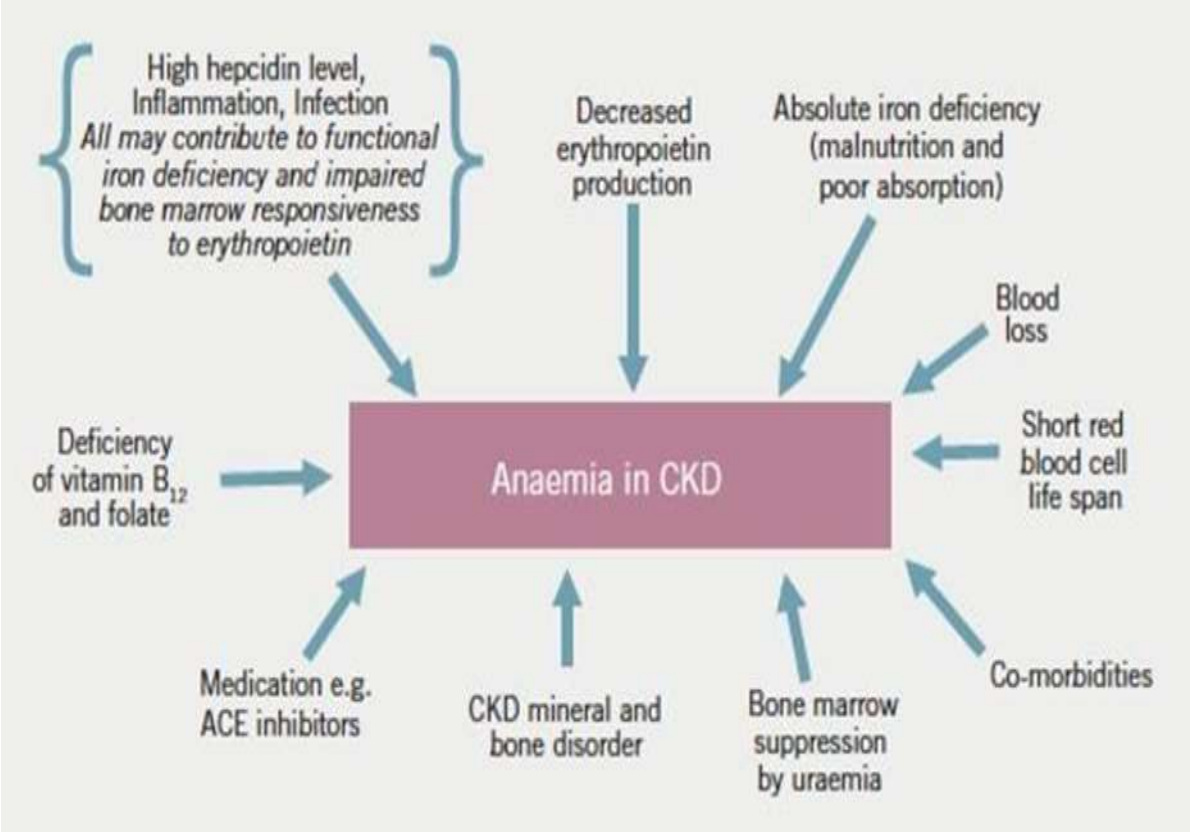

Figure 3: Causes of Anemia in CKD [26]

1.2 Pathophysiology of anemia in CKD

There are several causes of anemia in CKD. It has long been believed that intrinsic erythropoietin (EPO) levels steadily declining have a significant influence. [31] These specific factors, such as an outright iron deficiency introduced on by blood loss or poor iron absorption, an inefficient use of iron stores decided to bring on by increased hepcidin levels, system-wide inflammation decided to bring on by CKD and related comorbidities, a reduced response of the blood stream to EPO since of uremic toxins, a shortened red cell life span, or vitamin B12 or folic acid deficiencies, have also been identified as causing to anemia in CKD [32].

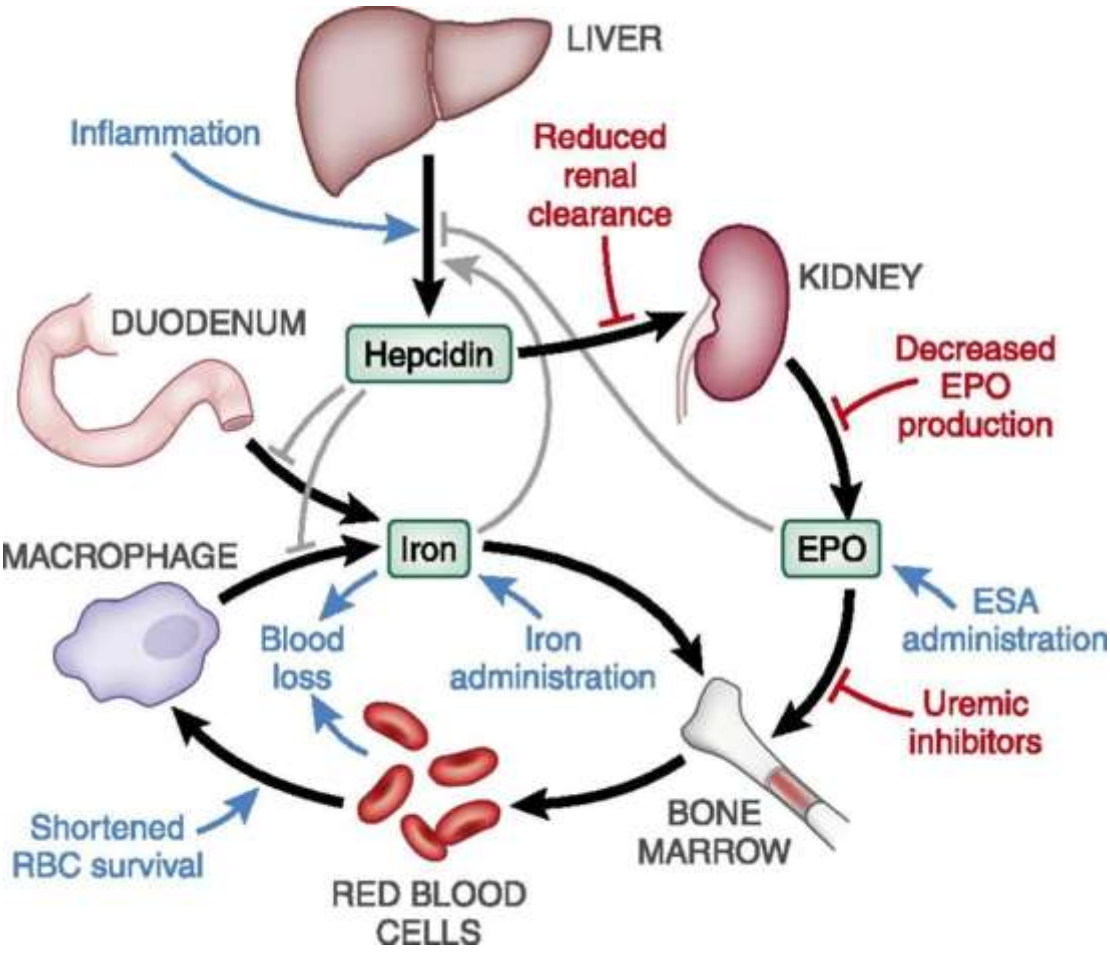

Figure 4: Pathophysiology of anemia in CKD [31]

1.3 EPO Production in CKD

EPO levels are inadequate for the degree of anemia in CKD patients. EPO deficiency manifests early in the course of CKD, although it appears that when eGFR falls below 30 ml/min per 1.73 m2, this shortfall gets exacerbated [33]. Errors in EPO detection as well as a decrease in EPO synthesis may be to blame for this comparative EPO deficit. Because of reduced blood flow, CKD is associated with a shift in how oxygen is supplied to the kidneys. [34] In order to maintain a normal tissue oxygen gradient, the renal muscle adjusts to consume less oxygen. As a consequence, PHD enzymes remain active and neither the HIF heterodimer nor the EPO gene are activated. Moreover, it has been experimentally proved that a number of inflammatory cytokines, including tumor necrosis factor-a (TNF-a), transforming growth factor-beta (TGF-beta), interleukin-la (IL-la), and IL-l beta, decrease oxygen deprivation-induced EPO production [35]. It is well known that CKD itself increases inflammatory markers and immunological activating chemicals, which would inhibit the production of EPO brought on by hypoxia [36]. Although certain CKD patients can periodically produce more endogenous EPO in their liver and kidneys, such as when undergoing maximal elevated or bleeding, this route of EPO generation seems to be modulated in some of these people rather than abolished. In cells that are producing and sensing oxygen (REPOS), it seems that boosting HIF signaling can cause the production of EPO [37]. It is characterized as an operational EPO deficiency or EPO awareness [38] when low hemoglobin (Hb) concentrations in CKD patients are combined with normal range EPO levels. This indicates that the bone marrow's response to endogenous and exogenous EPO is compromised in these patients [39]. Proinflammatory cytokines are also thought to block the EPO receptor's activator function. Furthermore, it has been found that exogenous EPO-treated CKD patients have increased resistance due to neocytolysis, a physiological homeostatic process that preferentially hemolyzes young circulating red blood cells [40]. Finding novel therapeutic alternatives for these patients is essential. In order to increase endogenous EPO synthesis and, consequently, improve the utilization of iron stores, the HIF system's elements have already been looked into as prospective novel anemia-targeted medicines. [41]

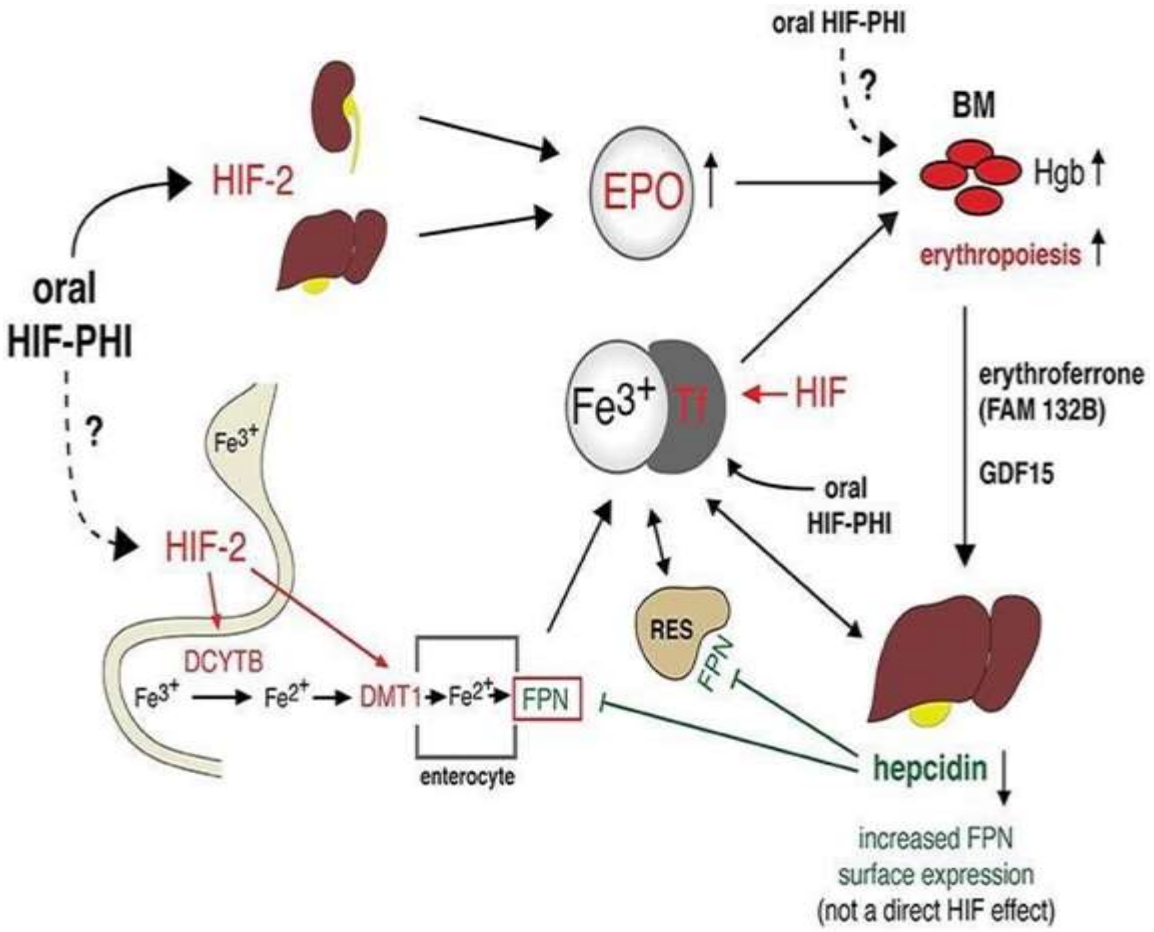

Figure 5: EPO Production in CKD [[43]

1.4 Iron Metabolism

In anemic conditions, addressing iron deficiency allows for lower exogenous EPO dosages since iron is required for an optimal erythropoietic response to EPO. Thus, they support the idea that iron deficiency needs to be treated independently of Hb condition [43]. Iron is necessary for the protein myoglobin to carry oxygen into muscle cells. Two more oxidative activities that greatly profit from the iron present are the electron transport chain and oxidative phosphorylation. Iron is necessary for numerous DNA synthesis, degradation, and repair mechanisms. Not uncommon among other important members of the cytochrome P450 family is iron [44]. A growing body of epidemiological research has shown that deficiency is associated with worse outcomes in persons with chronic kidney disease (CKD) [45]. The preponderance of the iron requirements is satisfied by utilizing the iron present in senescent erythrocytes and discharging iron from storage facilities

(Figure 2). Much little iron is absorbed by dietary consumption. Additionally, there is no physiological mechanism in place to regulate iron expulsion [46]. It is lost by the dilatation of intestinal epithelial cells, skin cells, and blood losses; these damages are compensated for by dietary iron absorption, which is regulated by hepcidin. The sole known iron importer, ferroportin, allows macrophages to phagocytose time of life red blood cells, hepatocytes, or enterocytes (nutritional iron absorbed in the duodenum) and discharge their mineral content into the bloodstream. [47] When iron attaches to transferrin, it is subsequently transported through the bloodstream and delivered to the desired cells [48]. Transferrin receptors are modulated by cellular growth and internal iron concentration. The main controllable factor of iron metabolism is hepcidin, an acute-phase protein made by the liver. Its objective is to maintain healthy levels of systemic iron. [49]

Chapter 2
Purpose of the study

2.1 The objective of the study

- To have a better understanding of the many diagnostic techniques used to identify this illness.
- To get a complete grasp of the ailment, including its cause, manifestations, effects, and available nursing and medical treatments.
- The aim of this study was to gain a better understanding of the anemia caused by CKD in Bangladesh.
- To identify the variables that influence how CKD-induced anemia develops.
- To identify the preventive measure of this disease.

Chapter 3
Literature Review

3.1 The Influence of Inflammation on Anemia in CKD Patients

Anemia is frequently present in patients with chronic kidney disease (CKD), which is known to have a negative impact on their quality of life. Furthermore, it speeds up the progression of CKD and raises morbidity and mortality. Patients with CKD frequently experience chronic inflammation, which is frequently triggered by a variety of fundamental factors. Researchers have discovered that CKD patients frequently exhibit fluctuating Hb levels and methods to improve to erythropoietin boost the productivity (ESA), both of which may be brought on by persistent inflammation. Understanding the intricate web of interactions between the numerous factors engaged in the pathogenesis of chronic illness anemia may allow one to better understand how inflammatory cytokines influence the production of hepcidin and erythropoietin. Pharmacological treatments for ESA hypo responsiveness caused by inflammation seem to be shifting between anti-cytokine and anti-oxidative therapy techniques. Currently, there is great anticipation for the discovery of new therapeutic approaches for the treatment of anemia in CKD patients. Erythropoietin (EPO) therapy for anemia was associated with considerable benefits for some patients, but not all. [34]

3.2 Anemia in chronic kidney disease patients in predialysis and postdialysis stages

Anemia is frequently a co-morbidity of chronic kidney disease, and degrees of anemia are negatively associated with the degree of renal failure. The extent of anemia and the connection among blood creatinine levels and anemia in pre- and post-dialysis patients with chronic renal illness were investigated in this study. At the pathology and nephrology faculty of the KIST Medical College, a cross-sectional research involved 40 people with chronic kidney disease was conducted. Hemoglobin, hematocrit, red cell parameters, peripheral blood smears, and serum creatinine levels were assessed using traditional techniques. Hemoglobin and hematocrit levels in patients were substantially different between before and after dialysis (P 0.005). All 40 of the patients had anemia. Postdialysis patients exhibited a higher incidence of severe anemia (5% vs. 15%), despite the fact that both patient groups had a higher incidence of mild anemia. The most common kind of anemia was normocytic normochromic, which was detected by peripheral blood smear examinations to be 80% in predialysis patients and 77.5% in postdialysis patients. There was no clinically important correlation between the amount of anemia and serum creatinine

levels in the pre- and post-dialysis categories (P > 0.05), with r=- 0.14 and -0.17, correspondingly. As a result, the most common type of anemia in patients with chronic renal failure was fairly severe normocytic and normochromic anemia. There was no statistical significance correlation between the degree of anemia and serum creatinine levels in the pre-dialysis patient group or the post-dialysis patient subgroup. [47]

3.3 New options for the anemia of chronic kidney disease

Anemia is a common adverse consequence of chronic renal illness. Using erythropoiesis-stimulating agents (ESA) has been a crucial part of treatment throughout 1990. Huge investigations revealed that ESAs are linked to a rise in deaths, cardiovascular and thrombotic incidents, as well as serious safety concerns. Studies suggest that high pharmacological doses of ESAs rather than extremely increased hemoglobin may be more likely to cause harm. Hypoxia-inducible factor (HIF) activators boost iron bioavailability while promoting the generation of endogenous erythropoietin. Initial clinical studies indicate that these oral medications may be able to replace ESA medications and lessen the need for IV iron therapy for anemia related to chronic renal illness, along with other possible positive outcomes. Comprehensive phase 3 investigations are now being conducted on a number of HIF activators. This judgment addresses the current approaches to treating anemia, safety issues with available medications, the role of HIF in regulating erythropoiesis, and the varied effects of HIF catalysts. [49]

Chapter 4
Methodology

4.1 Setting and Participants

A randomly chosen group of individuals with a range of ages and degrees of proficiency were given access to a face to face assessment. Firstly, prepared number of many question about CKD-induced anemia. Then has been gone to some renown hospital at Saidpur in Dhaka for individual patient's response collection. Question module has been asked individual patients for their response. Finally accumulated many responder's responses.

4.2 Content of the survey

The test had 15 short-answer questions and took roughly 6-8 minutes to finish. The survey includes (1) socio-segment data (welcome, name, age, sex, instructional level, instructional foundation, and occupation status), (2) a preface, and (3) disease impacts.

4.3 Evidence collection process

The right data was gathered using a hospital patients survey. The categorization of the material was kept under the secret agreement, and members were not provided financial incentives. This study was carried out physically under the supervision of the pharmacy department of Daffodil International University.

4.4 Data analysis strategy

Data analysis is the disciplined application of statistical and/or logical tools for describing and illustrating, condensing and summarizing, and assessing data. Microsoft Excel was used to analyses the data.

Chapter 5
Results & Discussion

5.1 Age range of responders

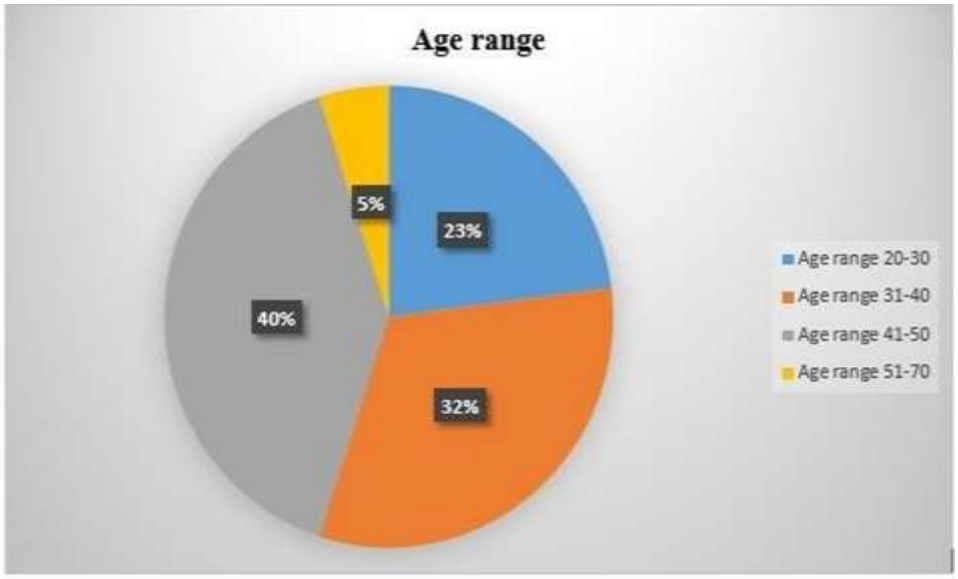

Figure 6: Age range of responders

Discussion

According to the survey, majority of the participants age range 41-50 (40%). Age range 20-30 have (23%) respondents & also 31-40 have (32%) participants.

5.2 Gender of responders

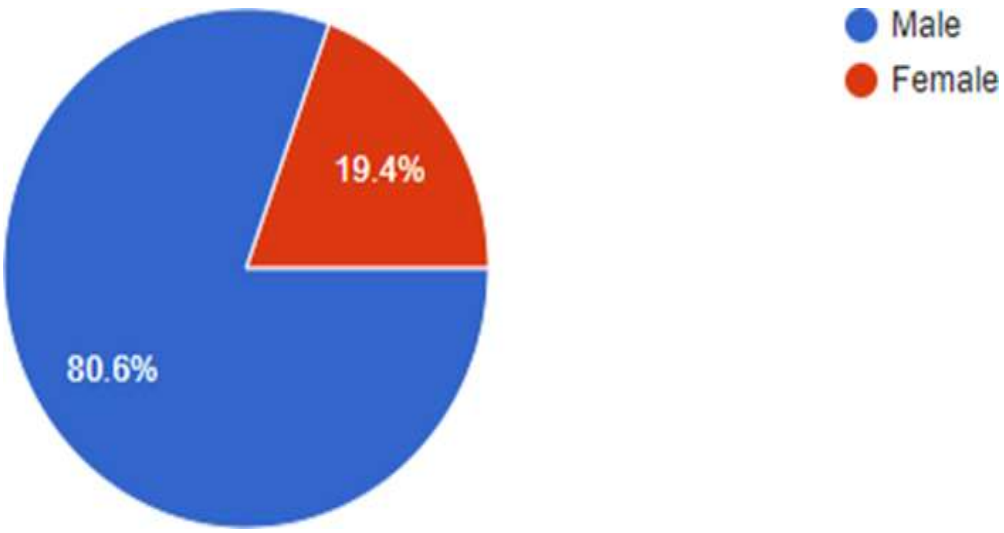

Figure 7: Gender of responders

Interpretation: Among all responders 19.4 percent of them existence female and 80.6 percent existence male.

5.3 Marital status of the responders

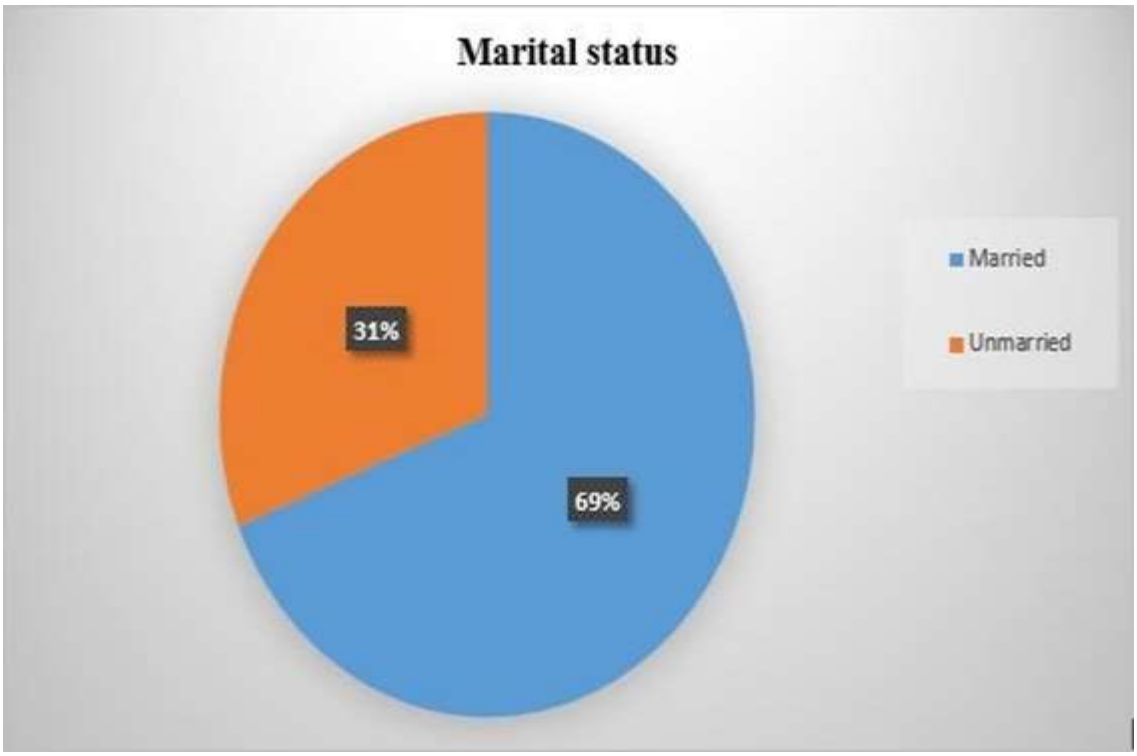

Figure 8: Marital status

Interpretation: Among all responders 69% of whom were married and 31% of whom were unmarried.

5.4 Location of the responders

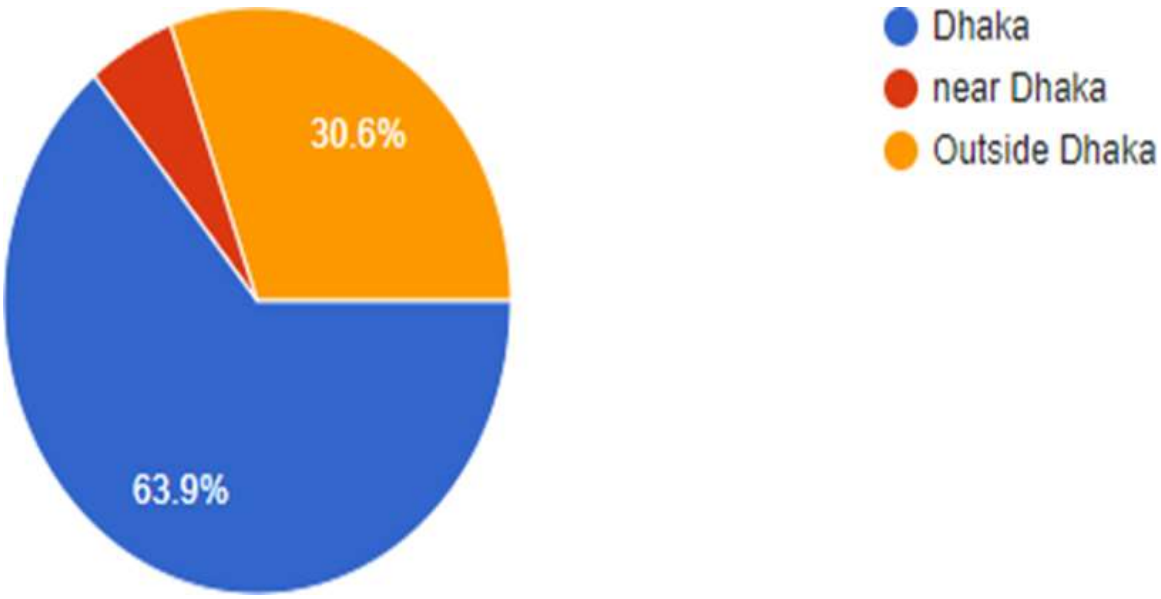

Figure 9: Location of the responders

Interpretation: The majority of respondents (63.9%) lived in urban areas, followed by rural areas (30.6%).

5.5 Idea about chronic kidney disease (CKD)

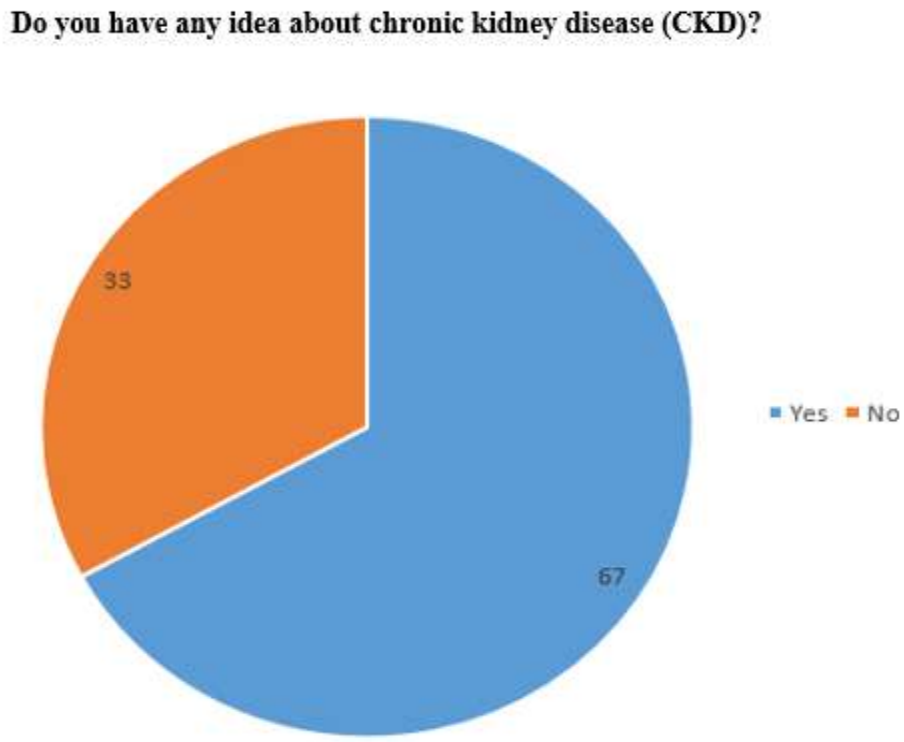

Figure 10: Idea about chronic kidney disease

Interpretation: Kidney disease causes CKD, a disorder in which they are unable to filter blood as effectively as they should. Permitting to the report, the majority of people (67%) have idea about chronic kidney disease, some people (33%) never any idea about CKD (Chronic kidney disease).

5.6 Idea of chronic kidney disease (CKD) induced Anemia

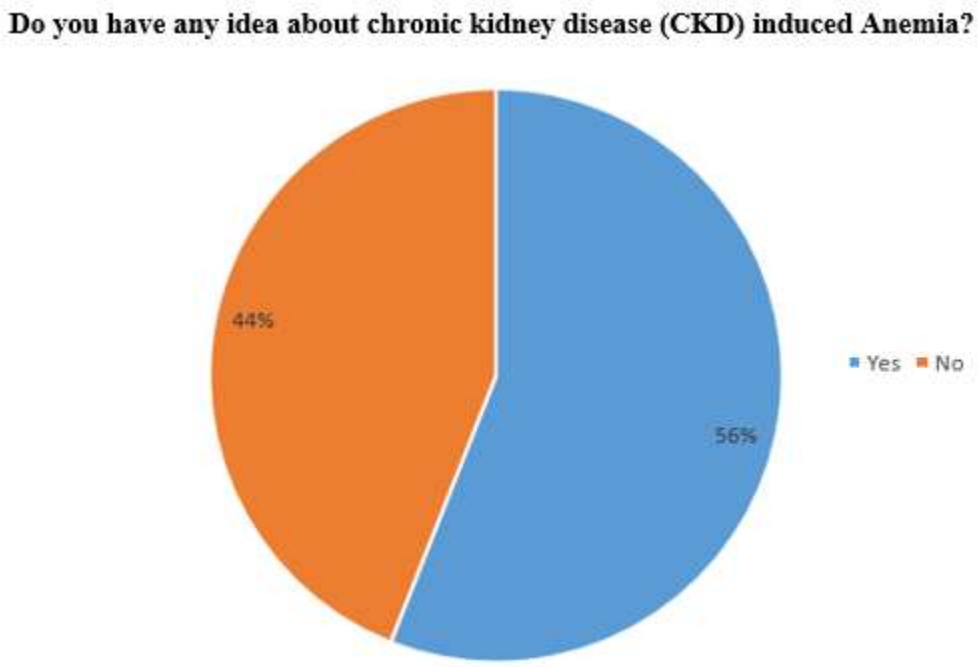

Figure 11: Idea of CKD induced Anemia

Discussion

According to the survey, the mainstream of people (56%) have idea about CKD induced anemia, some people (44%) never idea CKD (Chronic kidney disease) induced anemia.

5.7 Primary symptoms of CKD induced anemia

What are the Primary symptoms of CKD induced anemia?

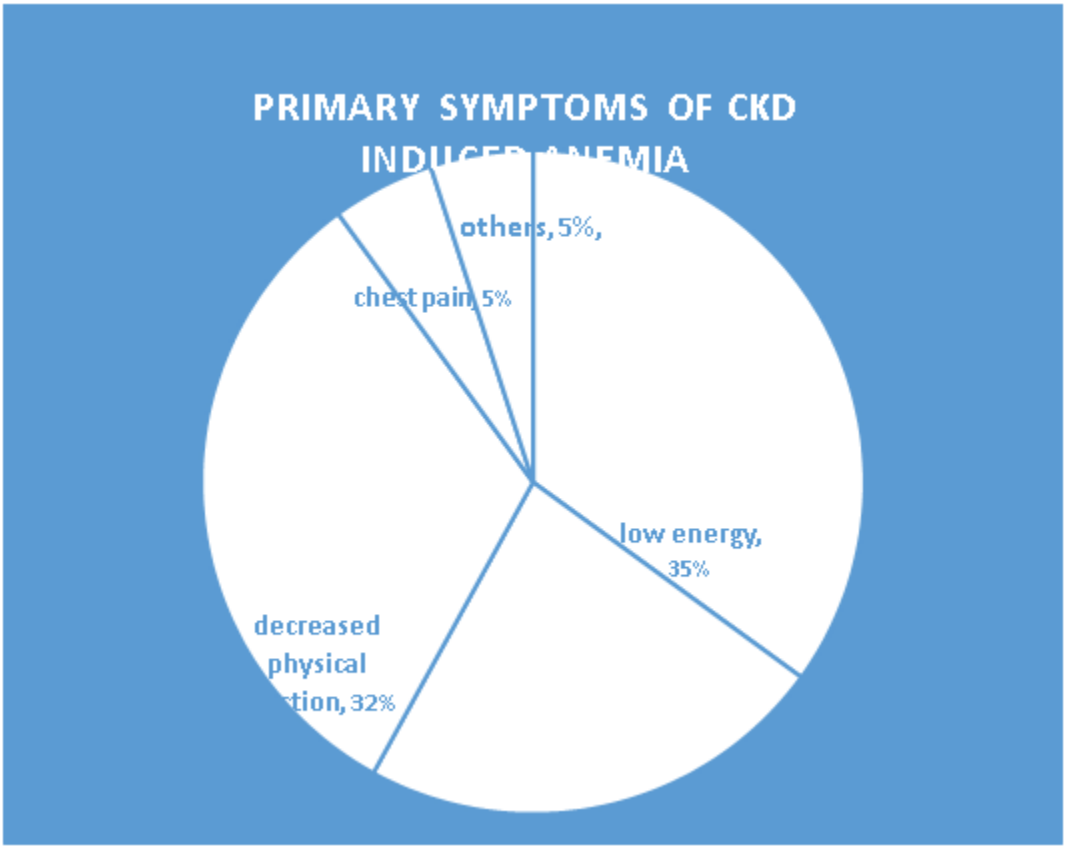

Figure 12: Primary symptoms of CKD induced anemia

Anemia caused by chronic renal disease might present as chest pain, weariness, low energy, and impaired physical performance. According to the investigation, the average participant thought reduced energy (35%) and impaired physical function (32%) was the main symptom of anemia caused by chronic renal disease. Only (23%) of respondents identified exhaustion as one of the signs of CKD-induced anemia.

5.8 Causes of anemia in CKD

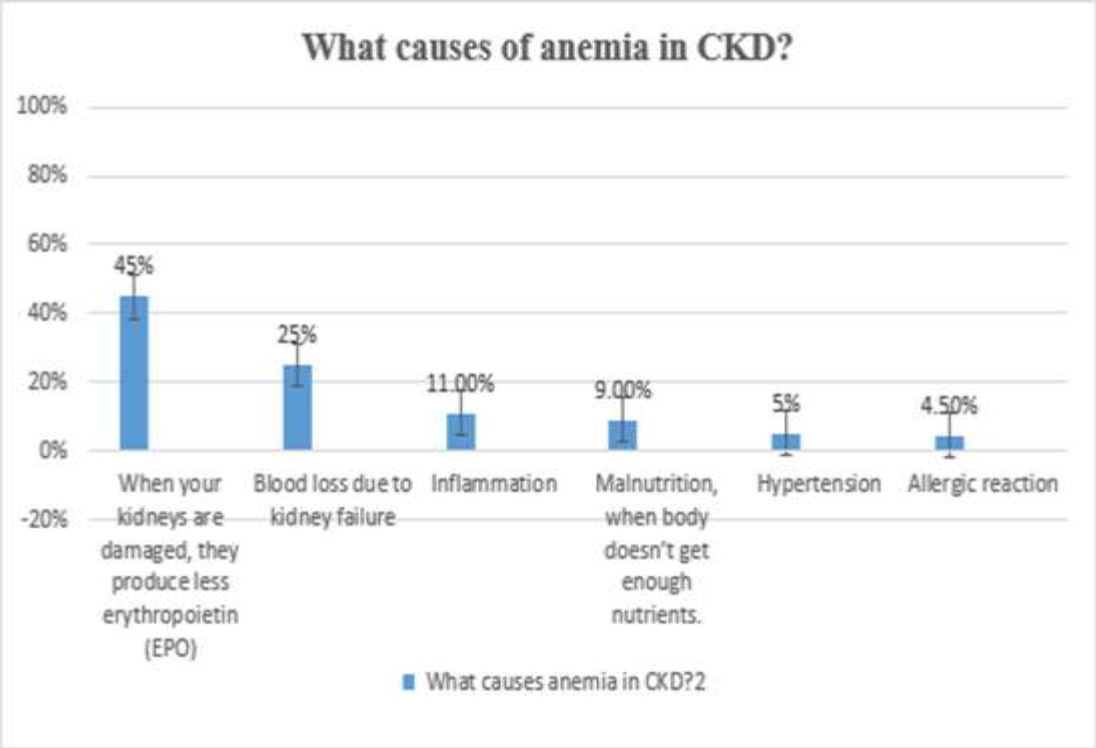

Figure 13: Causes of anemia in CKD

Discussion

According to a study, the majority of respondents claimed that erythropoietin (EPO) deficiency caused by kidney impairment (45%) is what causes CKD-induced anemia. (25%) of respondents believe that kidney failure-related blood loss is the root cause of anemia brought on by CKD. Approximately (5%) of people think that hypertension and (4.5%) think that allergic reactions are what causes CKD-induced anemia.

5.9 Treatments of CKD induced anemia

Do you know what are the treatments of CKD induced anemia?

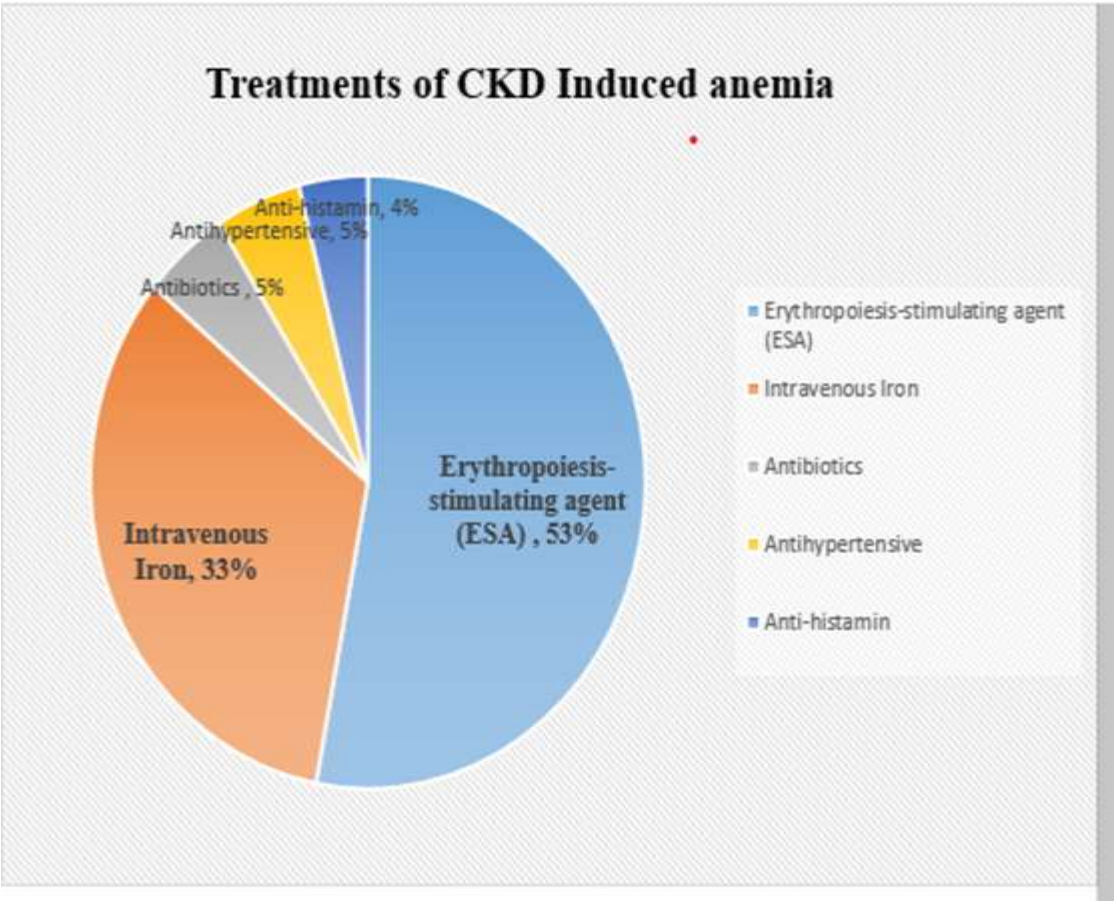

Figure 14: Treatments of CKD induced anemia

Discussion

Allowing of inspection, most of the people thought that Erythropoiesis-stimulating agent (53%) is the treatment of CKD induced anemia. (33%) respondents deliberate that Intravenous iron is the another treatment of CKD induced anemia. Some little people consider that Antibiotics (5%) & Antihypertensive (5%) is the treatment of CKD induced anemia.

5.10 Name of taken medicine

If you have been suffered CKD induced anemia. Which medicine have been taken?

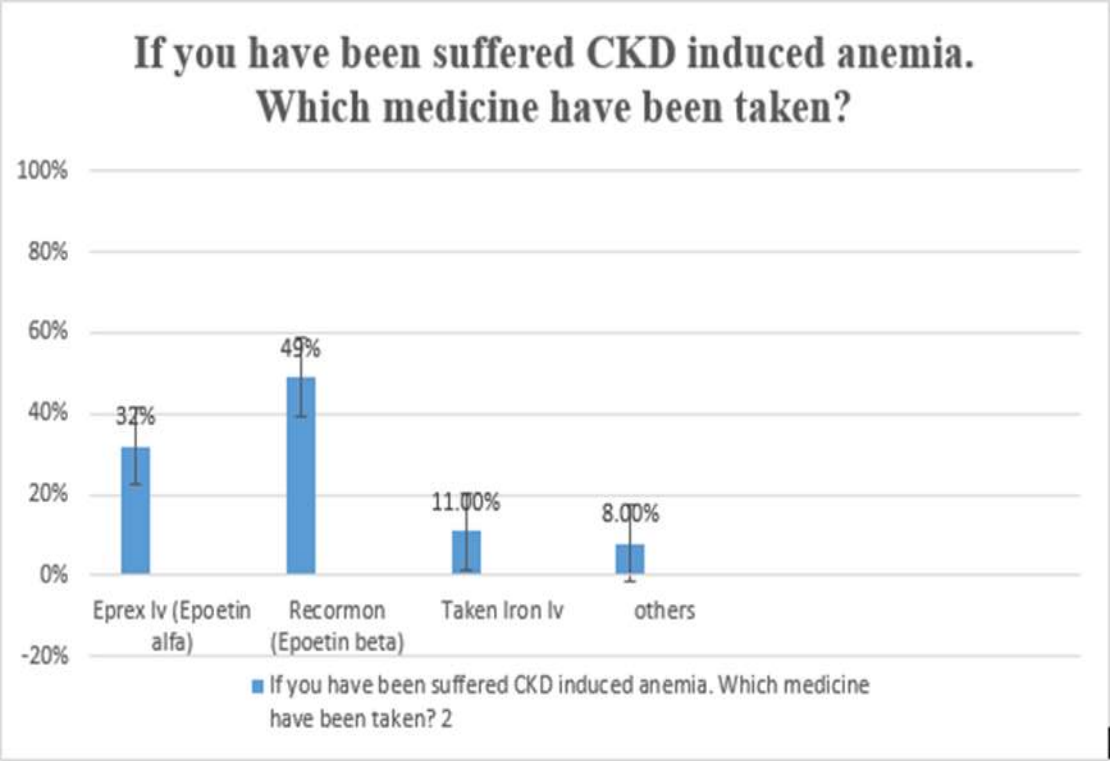

Figure 15: Name of taken medicine

Discussion

Treatments of chronic kidney disease induced anemia include Eprex (Epoetin alfa) Iv, Recormon (Epoetin beta) Iv, Iron Iv. The majority of participants said that they have been taken Eprex Iv (32%) and Recormon Iv (49%). On the other hand, few responders have been taken Iron intravenous (11%).

5.11 Doctor of CKD induced anemia patient

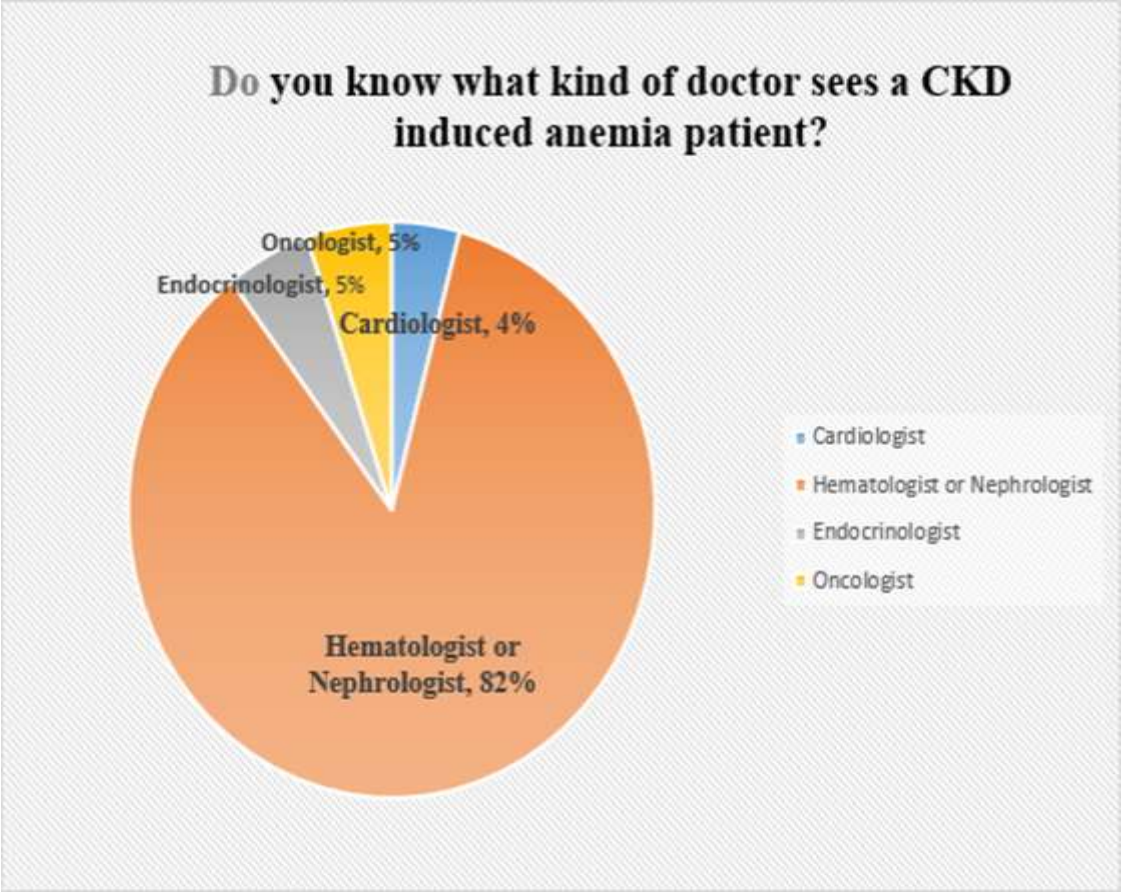

Figure 16: Doctor of CKD induced anemia patient

Discussion

According of survey, the most population is knowledgeable of the types of patients that a doctor treats. The majority of people (82%) know what types of doctors visit patients with CKD induced anemia patient. A hematologist or nephrologist evaluates CKD induced anemia patient.

5.12 People of age living more susceptible to CKD induced anemia

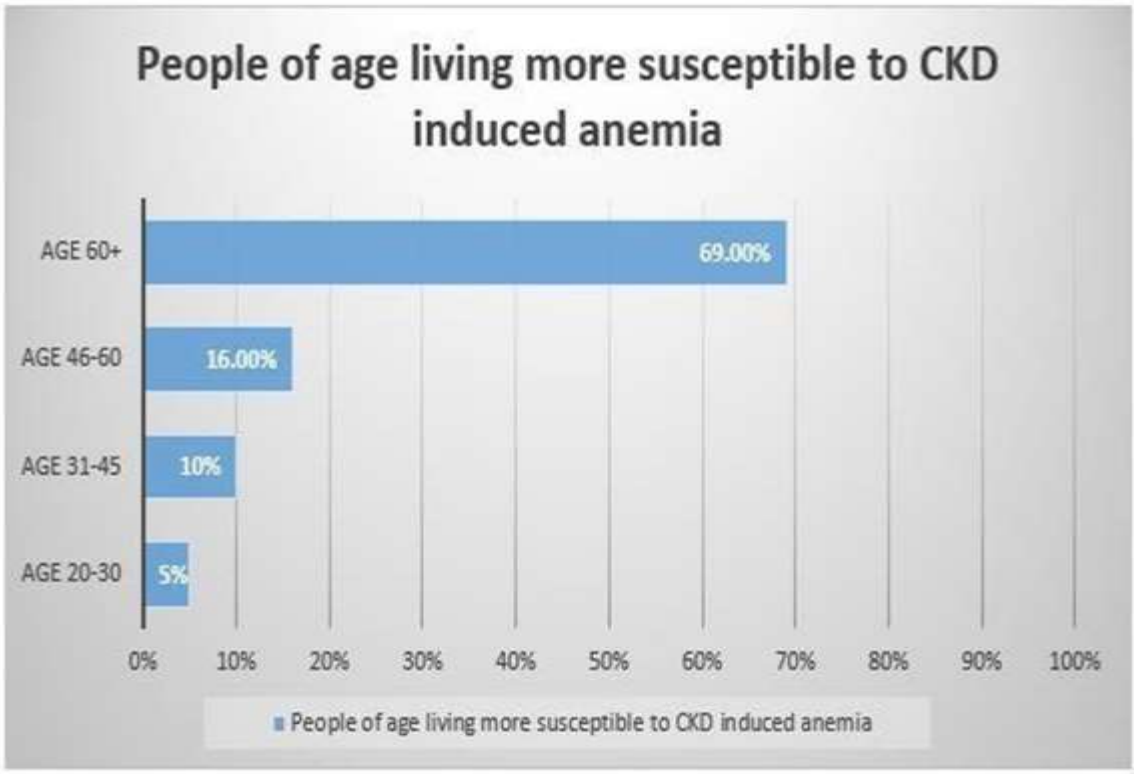

Figure 17: People of age living more susceptible to CKD induced anemia

Discussion

Most ailments have age as one of the subsidizing variables. Allowing to the inspection, 16% of persons 46-60 age range are more prone to CKD induced anemia, whereas 69% of those age range 60+ are more susceptible to CKD induced anemia.

5.13 Infected with CKD induced anemia in family member

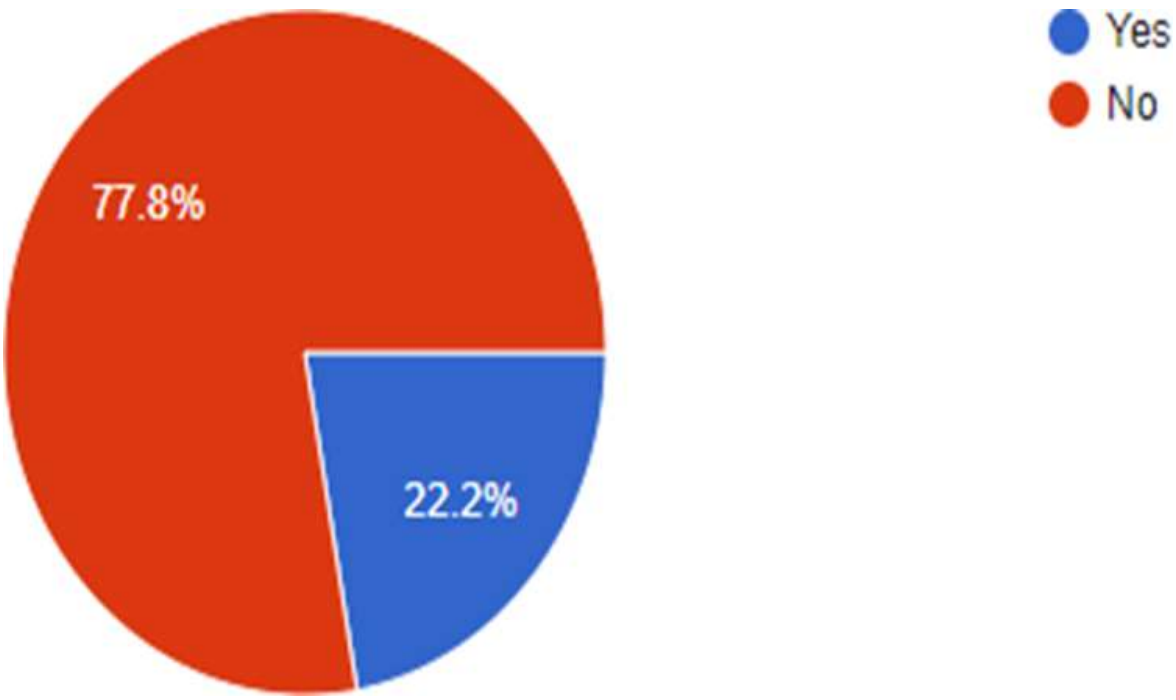

Figure 18: Infected with CKD induced anemia in family member

Discussion

Permitting to the survey, only a small percentage of respondents have family members who have CKD induced anemia (22.2%). Majority of the respondent's (77.8%) family member never infected with CKD induced anemia.

5.14 Life style modification

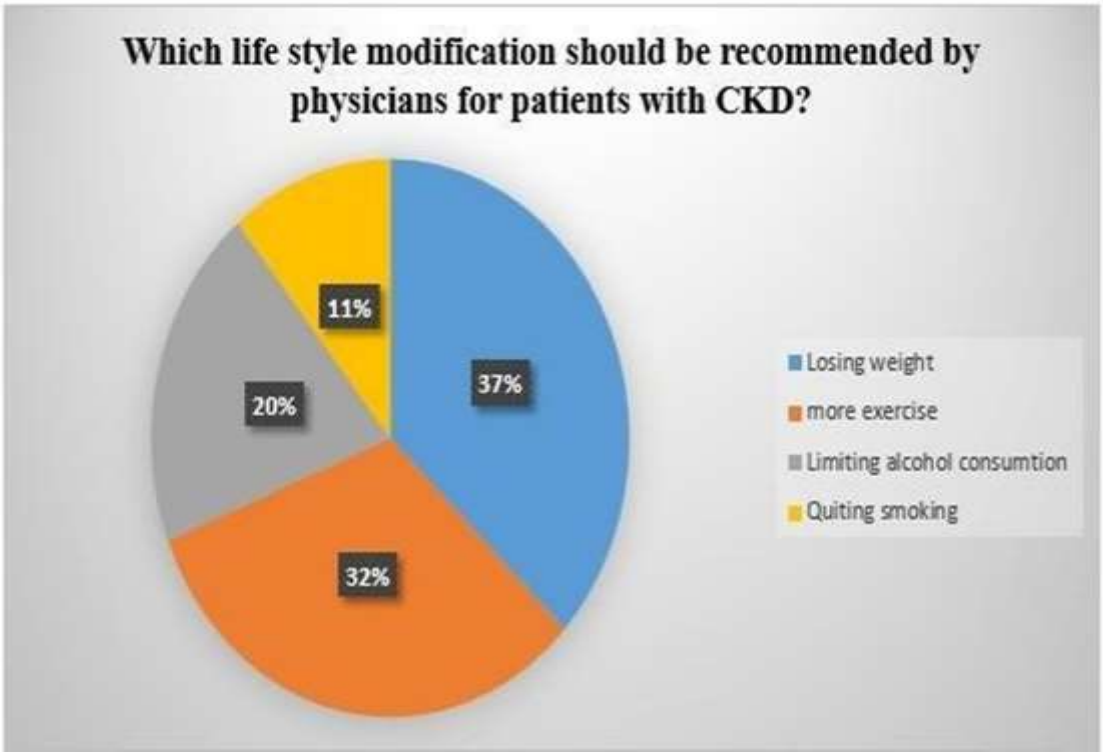

Figure 19: Life style modification

Discussion

Permitting to the assessment, (37%) participants presumed that losing weight is the recommendation by physicians for the prevention of CKD. Also (32%) participants assumed that more exercise and (20%) respondents assumed that limiting alcohol consumption is the recommendation by physicians for the prevention of CKD.

Discussion based on review of some article

Research have shown that chronic inflammation may be a factor in the Hb level fluctuation and ESA hypo responsiveness that are typically noted in CKD patients. It appears that these individuals may experience increased morbidity and death due to variability in Hb values, which are frequently below the therapeutic range [175]. The information that is now published suggests that chronic kidney disease is a condition of elevated inflammation with elevated cytokine activity, which may restrict the development of erythroid progenitor cells, leading in hypo responsiveness to ESAs and poor treatment results. Understanding how inflammatory cytokines affect erythropoietin production and hepcidin synthesis will make it possible to sort through the complex web of interactions between the various components involved in the etiology of chronic disease-related anemia. Pharmacological approaches aimed at treating inflammation-related hypo responsiveness to ESA appear to be moving toward anti-cytokine and anti-oxidative therapy modalities.

Chapter 6
Conclusion

6.1 Conclusion

This study's data adequately demonstrate the theory that anemia was brought on by chronic renal illness. to identify the contributing elements that lead to the development of anemia brought on by chronic renal disease. to better understand the many diagnostic methods used to identify this condition. It will be feasible to sort through the complicated web of interconnections between the numerous factors involved in the pathogenesis of chronic renal disease-related anemia by understanding how inflammatory cytokines regulate the production of erythropoietin and the biosynthesis of hepcidin.

Chapter 7
Reference

Reference

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