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Spectrum of Anemia in patients of Diabetes Mellitus

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Abstract
Diabetes mellitus (dm) represents a group of metabolic disorders characterized by chronic hyperglycemia, resulting from defects in insulin secretion, insulin action, or both. The global prevalence of diabetes has been on the rise, making it a significant public health challenge. Complications of diabetes are multifaceted, affecting various organs and systems in the body. Among these complications, anemia has emerged as a condition that is both a contributor to and a consequence of diabetic pathology. The prevalence of anemia in diabetic patients is higher than in the general population, which has implications for the management and outcomes of these patients.1
Anemia in diabetes mellitus is multifactorial, involving mechanisms such as erythropoietin deficiency, the impact of hyperglycemia on red blood cell lifespan, and the role of inflammation. Additionally, certain treatments for diabetes, particularly oral hypoglycemic agents, may influence anemia's prevalence and severity. Understanding the interplay between diabetes and anemia is crucial, as anemia can exacerbate cardiovascular complications, reduce quality of life, and increase mortality risk among diabetic individuals.2
Despite the recognized association between diabetes and anemia, gaps remain in our understanding of this relationship. Specifically, the effects of different oral hypoglycemic agents on anemia in diabetic patients have not been thoroughly explored. Furthermore, while the impact of chronic kidney disease (ckd) on anemia in diabetes has been well-documented, less is known about how the duration and complications of diabetes, excluding ckd, affect anemia. Addressing these gaps is vital for developing comprehensive management strategies for diabetic patients with anemia.3
This research aims to shed light on the spectrum of anemia among patients with diabetes mellitus in a tertiary care setting. By elucidating the relationship between oral hypoglycemic agents and anemia, as well as the impact of diabetes duration and complications on anemia, this study could inform clinical practices and enhance patient care. The findings may lead to more personalized treatment approaches for managing diabetes and its complications, ultimately improving patient outcomes and quality of life.
The objectives of this thesis are threefold. First, it seeks to assess the profile of anemia in patients with diabetes mellitus in a tertiary care hospital, providing insight into its prevalence and characteristics in this population. Second, it aims to evaluate the effect of oral hypoglycemic agents on anemia in diabetic patients, exploring whether these medications influence the condition's development or severity. Third, it intends to examine the influence of the duration and complications of diabetes mellitus on anemia, with a focus on factors other than ckd. Through this research, we aspire to contribute valuable knowledge to the field of diabetes care, with implications for both clinical practice and future studies.
The escalating global prevalence of diabetes mellitus, coupled with its complex interrelation with anemia, underscores the urgent need for this study. Despite the recognized impact of anemia on the morbidity and mortality of diabetic patients, the nuances of this association—particularly the influence of various oral

hypoglycemic agents and the broader effects of diabetes duration and non-ckd complications on anemia—remain inadequately explored.4 this gap in knowledge hampers the development of targeted interventions and optimized management strategies for this patient population. By delving into the spectrum of anemia within the diabetic cohort in a tertiary care environment, this research aims to illuminate aspects that are critical for enhancing patient outcomes, guiding clinical decisions, and paving the way for future investigations. This study is poised to make a significant contribution by providing a deeper understanding of anemia's prevalence, characteristics, and determinants in the context of diabetes mellitus, thereby fulfilling a pressing need in the realm of diabetes care and management.

Research question:

How does the profile of anemia in patients with diabetes mellitus, including its prevalence, characteristics, and response to oral hypoglycemic agents, differ based on the duration and complications of diabetes in a tertiary care setting, excluding chronic kidney disease?

Aim:

- *To study the profile of anemia in patients of diabetes mellitus in a tertiary care hospital.*

Objectives:

- *To assess the effect of oral hypoglycemic agents in patients of diabetes having anemia (if any).*
- *To assess the effect of duration and complications of diabetes mellitus on anemia except ckd*

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I. Introduction

The intricate interplay between diabetes mellitus and anemia presents a significant clinical challenge, warranting a thorough exploration of its spectrum and implications within a tertiary care setting. Diabetes mellitus, a global health epidemic, is fraught with a myriad of complications, among which anemia stands out due to its capacity to exacerbate the morbidity and impair the quality of life of affected individuals.5 This thesis seeks to illuminate theprevalencecharacteristics, and nuances of anemia among patients with diabetes mellitus, scrutinizing the impact of oral hypoglycemic agents and dissecting the influence of diabetes duration and its complications, exclusive of chronic kidney disease (CKD), on this hematological condition. Through a meticulous examination of these aspects, the study aims to fill the gaps in current knowledge, offering insights that could refine diagnostic and therapeutic approaches, thereby enhancing patient care in a tertiary care environment.

II. Diabetes Mellitus And Its Global Impact6

- Diabetes Mellitus (DM) has emerged as a global health crisis, affecting millions worldwide with its prevalence continuously rising. It not only poses a substantial burden on healthcare systems due to its direct impact on individuals but also contributes to increased morbidity and mortality rates. The chronic nature of DM, coupled with its associated complications, underscores the urgent need for effective prevention, management, and treatment strategies to mitigate its global impact.

A. Epidemiology of diabetes mellitus.7

- Diabetes mellitus (DM) stands as a globally prevalent metabolic disorder characterized by chronic hyperglycemia due to insulin resistance, insufficient insulin production, or both. The epidemiological landscape of diabetes reflects a rapidly escalating health crisis, with the International Diabetes Federation (IDF) estimating approximately 463 million adults (20-79 years) were living with diabetes in 2019, a figure projected to rise to 700 million by 2045. This surge underscores not only the expanding public health challenge but also the socio-economic burden associated with diabetes management, complications, and mortality.
- Type 2 diabetes mellitus (T2DM) accounts for the majority of cases worldwide, representing about 90-95% of all diabetes instances. This form of diabetes is largely driven by obesity, sedentary lifestyles, aging populations, and genetic predispositions. In contrast, Type 1 diabetes mellitus (T1DM), although less prevalent, poses significant health implications, especially among children and young adults, requiring lifelong insulin therapy for management.
- The distribution of diabetes varies significantly across regions, with the Western Pacific, Southeast Asia, and the Middle East and North Africa witnessing the highest prevalence rates. Such disparities highlight the influence of ethnic, socio-economic, and lifestyle factors on diabetes risk. Furthermore, urbanization and economic development have been linked to increased diabetes prevalence, suggesting a shift towards higher-risk environments and behaviors.

- Diabetes-related complications further compound the disease's impact, leading to increased morbidity and mortality. These include cardiovascular diseases, renal failure, visual impairment, and diabetic neuropathy, among others. The economic implications are profound, encompassing both direct medical costs and indirect costs related to loss of productivity, disability, and premature death.
- In summary, the epidemiology of diabetes mellitus paints a picture of a widespread and growing disease burden with significant health, economic, and social implications. This underscores the urgency for effective public health strategies, including prevention, early detection, and comprehensive management approaches, to mitigate the impact of diabetes on individuals and healthcare systems globally.

B. Overview of diabetes mellitus types and their pathophysiology.8

- Diabetes Mellitus (DM) encompasses a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.
- Type 1 Diabetes Mellitus (T1DM) – T1DM is primarily caused by autoimmune destruction of the insulin-producing β-cells in the pancreas, leading to absolute insulin deficiency. This process is influenced by genetic predisposition and possibly environmental factors that are still not completely understood. Individuals with T1DM are dependent on exogenous insulin for survival. The onset of T1DM is typically in childhood or adolescence, but it can occur at any age. Pathophysiologically, the immune system mistakenly targets and destroys β-cells, resulting in a gradual decline in insulin production until the pancreas can no longer produce sufficient insulin to regulate blood glucose levels.
- Type 2 Diabetes Mellitus (T2DM) – T2DM is characterized by a combination of peripheral insulin resistance and inadequate insulin secretion by pancreatic β-cells. In the early stages of T2DM, insulin resistance leads to increased insulin production as the pancreas tries to compensate for the reduced efficacy of insulin. Over time, the β-cells become unable to maintain the high level of insulin production needed to overcome the resistance, leading to the onset of hyperglycemia. T2DM is more prevalent in adults but is increasingly being diagnosed in children and adolescents. Risk factors include obesity, physical inactivity, poor diet, advancing age, and genetic susceptibility. The pathophysiology of T2DM reflects a complex interaction between lifestyle, environmental, and genetic factors that affect both insulin sensitivity and secretion.
- Gestational Diabetes Mellitus (GDM) – GDM is a form of diabetes diagnosed during pregnancy that is not clearly overt diabetes. It is characterized by glucose intolerance of variable severity. GDM reflects the emergence of insulin resistance during pregnancy, which is thought to be due to the hormonal changes and weight gain that occur during this time. Management focuses on controlling blood glucose levels to prevent complications in both the mother and the fetus. Women with GDM are at increased risk of developing T2DM later in life.
- Other Specific Types of Diabetes – This category includes forms of diabetes that result from specific genetic conditions, surgery, drugs, malnutrition, infections, and other illnesses that affect the pancreas's ability to produce insulin, such as cystic fibrosis-related diabetes or monogenic diabetes syndromes like MODY (Maturity Onset Diabetes of the Young).
- The pathophysiology of DM involves a complex interplay of genetic, environmental, and lifestyle factors that impact insulin availability and/or action. Understanding these mechanisms is crucial for developing targeted therapeutic strategies and managing the disease effectively.

C. Complications associated with diabetes mellitus.9

- Diabetes mellitus (DM) is associated with a wide range of complications that can affect virtually every part of the body and significantly impact the quality of life of those diagnosed. These complications are generally categorized into microvascular and macrovascular complications, alongside other associated conditions that arise over time, particularly in the presence of persistent hyperglycemia.
- Microvascular Complications – Diabetic Retinopathy: This condition is a leading cause of blindness among working-age adults. It results from damage to the small blood vessels in the retina, leading to blurred vision, vision loss, and ultimately blindness if left untreated. Diabetic Neuropathy: High blood sugar levels can damage the nerves throughout the body, leading to symptoms such as numbness, tingling, pain, and weakness, predominantly in the hands and feet. This condition can lead to foot ulcers and, in severe cases, amputation due to loss of sensation and poor wound healing. Diabetic Nephropathy: Diabetes can also damage the kidneys' filtering system, leading to chronic kidney disease (CKD) and, eventually, kidney failure requiring dialysis or kidney transplantation. It's a leading cause of end-stage renal disease.
- Macrovascular Complications – Cardiovascular Disease: Diabetes significantly increases the risk of various cardiovascular problems, including coronary artery disease with chest pain (angina), heart attack, stroke, and atherosclerosis (narrowing of arteries). Peripheral Arterial Disease (PAD): This condition, characterized by

narrowed blood vessels outside of the heart and brain, often affects the legs and can lead to pain on walking and ulcers.

- Other Associated Conditions – Infections: Individuals with diabetes are more susceptible to infections due to changes in immune function and, sometimes, complications related to neuropathy and peripheral vascular disease. Psychological Complications: Diabetes management's chronic nature and complexity can lead to psychological issues, including diabetes distress, depression, and anxiety.
- The risk and severity of these complications can be mitigated through tight blood glucose control, healthy lifestyle choices, and regular monitoring and treatment adjustments. Early detection and intervention are crucial in preventing the progression of complications, underscoring the importance of comprehensive care in diabetes management.

III. Anemia: Definition, Types, And General Pathophysiology10

- Anemia is a condition characterized by a deficiency in the number of red blood cells (RBCs) or the amount of hemoglobin, leading to decreased oxygen transport to the body's tissues. It manifests in various forms, including iron deficiency anemia, vitamin B12 and folate deficiency anemias, and anemia of chronic disease, each with distinct pathophysiological mechanisms such as impaired RBC production, increased RBC destruction, or blood loss, contributing to the diverse clinical presentations and management strategies of this condition.

A. Types of anemia and their general causes.11

- Anemia, characterized by a decrease in the number of red blood cells (RBCs) or the amount of hemoglobin in the blood, can significantly impact the body's ability to oxygenate tissues. It manifests in various forms, each with distinct causes:
- Iron Deficiency Anemia – The most common type worldwide, iron deficiency anemia, results from a shortage of iron, crucial for producing hemoglobin. Causes include inadequate dietary intake, chronic blood loss (e.g., from heavy menstruation or gastrointestinal bleeding), increased iron needs during pregnancy or growth spurts, and malabsorption syndromes.
- Vitamin B12 and Folate Deficiency Anemias – These anemias arise from insufficient intake or absorption of vitamin B12 or folate, essential for DNA synthesis in RBC production. Contributing factors include dietary deficiencies (more common with vitamin B12 in vegetarians), pernicious anemia (an autoimmune condition affecting B12 absorption), and certain medications that interfere with folate absorption.
- Anemia of Chronic Disease – Common in individuals with chronic infections, inflammatory diseases (such as rheumatoid arthritis or lupus), and cancers, this type of anemia results from the body's inability to use stored iron properly, despite having adequate iron levels. It's associated with the chronic activation of the immune system.
- Hemolytic Anemias – These anemias occur when RBCs are destroyed faster than they can be made, due to factors such as autoimmune diseases, genetic disorders (e.g., sickle cell anemia, thalassemias), infections, and certain medications. They can lead to jaundice and an increased risk of gallstones.
- Aplastic Anemia – A rare but serious condition, aplastic anemia, results from damage to the bone marrow's stem cells, which significantly reduces RBC production. Causes include autoimmune diseases, exposure to toxic chemicals, radiation, and certain medications, as well as viral infections.
- Sickle Cell Anemia – A genetic disorder that leads to the production of abnormally shaped hemoglobin (sickle hemoglobin). The sickle-shaped cells can block blood flow, causing pain, infections, and organ damage.
- Understanding the various types of anemia and their causes is crucial for diagnosis and treatment, as the management strategies differ significantly depending on the underlying cause. Effective treatment may involve dietary supplements, changes in medication, or more advanced therapies like blood transfusions or bone marrow transplantation, tailored to address the specific type of anemia and its root cause.

B. Pathophysiological mechanisms of anemia.12

- The pathophysiological mechanisms of anemia involve complex processes that disrupt the normal production, lifespan, and function of red blood cells (RBCs) or hemoglobin, leading to inadequate oxygen delivery to the body's tissues. These mechanisms can be broadly categorized into three primary pathways: impaired RBC production, increased RBC destruction, and blood loss.
- Impaired RBC Production – Anemia due to impaired RBC production can result from deficiencies in essential nutrients, bone marrow failure, or chronic diseases. Iron deficiency, for instance, limits hemoglobin synthesis, leading to smaller, pale RBCs characteristic of iron deficiency anemia. Similarly, vitamin B12 or folate deficiencies impair DNA synthesis, resulting in the production of large, immature RBCs seen in megaloblastic anemia. Bone marrow disorders such as aplastic anemia or leukemias disrupt the marrow's

ability to produce RBCs. Chronic diseases can lead to anemia of chronic disease, where inflammatory cytokines interfere with iron metabolism and erythropoietin response, reducing RBC production.

- Increased RBC Destruction – Hemolytic anemias are caused by conditions that lead to the premature destruction of RBCs, overwhelming the bone marrow's capacity to compensate for the loss. Autoimmune disorders, genetic defects like sickle cell disease or thalassemias, infections, and exposure to certain drugs or toxins can cause hemolysis. This process can result in anemia characterized by jaundice, elevated reticulocyte counts, and, in severe cases, organ damage due to the accumulation of hemolytic products.
- Blood Loss – Acute or chronic blood loss, due to trauma, surgery, or internal bleeding (e.g., gastrointestinal ulcers, hemorrhoids, menstrual bleeding), directly reduces the volume of circulating RBCs. Chronic losses are particularly insidious as they can deplete iron stores, compounding the anemia with iron deficiency.
- Additional Mechanisms – Other factors that can contribute to anemia include altered RBC morphology and flexibility, as seen in sickle cell anemia, which can lead to vascular occlusion and further RBC destruction. Also, diseases affecting the kidney can reduce the production of erythropoietin, a hormone essential for RBC production in the bone marrow.
- Understanding these pathophysiological mechanisms is crucial for diagnosing the specific type of anemia, guiding appropriate treatment strategies to correct the underlying cause, and restoring normal RBC function and oxygen delivery to tissues.

C. Impact of anemia on overall health.13

- Anemia, characterized by reduced hemoglobin levels or a decrease in red blood cells (RBCs), significantly impacts overall health, affecting virtually every organ system and leading to a wide range of complications. The primary consequence of anemia is reduced oxygen-carrying capacity of the blood, resulting in diminished oxygen delivery to tissues and organs. This hypoxia can manifest in various symptoms and exacerbate existing health conditions.
- Cardiovascular System – The heart must work harder to compensate for the reduced oxygen availability, leading to increased cardiac output. Over time, this can cause cardiac enlargement and heart failure, particularly in individuals with pre-existing heart conditions. Symptoms such as palpitations, angina, shortness of breath, and fatigue are common.
- Respiratory System – The body's response to anemia includes increasing breathing rate to enhance oxygen uptake, which can lead to shortness of breath and, in severe cases, respiratory distress.
- Neurological Impact – Reduced oxygen delivery to the brain can impair cognitive functions, leading to symptoms such as dizziness, weakness, lethargy, and in severe cases, confusion and concentration difficulties. Chronic anemia can affect mood, causing depression or anxiety.
- Immune Function – Anemia can weaken the immune response, making the body more susceptible to infections and impairing the ability to recover from illnesses.
- Muscular System – Muscles may receive inadequate oxygen during anemia, leading to weakness and decreased endurance. This can significantly affect physical performance and daily activities.
- Gastrointestinal System – Some types of anemia, especially those caused by vitamin deficiencies, can lead to gastrointestinal symptoms such as a sore tongue, difficulty swallowing, and altered taste.
- Reproductive Health – In women, anemia can cause menstrual irregularities and, during pregnancy, increase the risk of complications for both mother and child, including preterm delivery and low birth weight.
- Growth and Development – In children, chronic anemia can impair growth and cognitive development, affecting academic performance and overall quality of life.
- Overall, the impact of anemia on health is multifaceted, highlighting the importance of early detection, proper diagnosis, and effective management to mitigate its adverse effects and improve patient outcomes.

4. Association between Diabetes Mellitus and Anemia14

- The association between Diabetes Mellitus (DM) and anemia is complex and multifaceted, characterized by a higher prevalence of anemia among individuals with diabetes compared to the general population. This relationship is underpinned by various factors, including diabetic nephropathy leading to erythropoietin deficiency, chronic inflammation affecting iron metabolism, and the impact of hyperglycemia on red blood cell lifespan. Understanding this interplay is crucial for managing both conditions effectively and improving patient outcomes.

A. Prevalence of anemia in patients with diabetes.15

- The prevalence of anemia in patients with diabetes is notably higher than in the general population, representing a significant concern given the additional complications anemia can pose to individuals already

managing the complexities of diabetes. Studies have shown varying prevalence rates, largely dependent on the study population and diagnostic criteria used, but consistently indicate an increased risk of anemia among diabetic individuals.

- Anemia in diabetic patients is multifactorial, with causes including chronic kidney disease (CKD), which is a common complication of diabetes, diminished erythropoietin production due to diabetic nephropathy, nutritional deficiencies, and potential effects of diabetes medications on erythropoiesis. The prevalence of anemia tends to increase with the progression of diabetes, particularly as kidney function declines. For instance, in patients with diabetic nephropathy, the prevalence of anemia can exceed 40%, highlighting the close relationship between kidney disease and anemia in the context of diabetes.
- Moreover, the prevalence is influenced by the type of diabetes, with Type 2 Diabetes Mellitus (T2DM) patients showing higher rates of anemia compared to Type 1 Diabetes Mellitus (T1DM) patients, partly due to the higher incidence of comorbid conditions such as CKD and the older age profile of T2DM patients. The risk of anemia also escalates with the duration of diabetes, underscoring the impact of long-term metabolic disturbances on hematopoiesis.

Study area: Department of Endocrinology and Medicine, PGIMS, Rohtak
Study design: Observational study, prospective study.
Study period: 1 year

Study population –
Inclusion Criteria:

- Confirmed cases of diabetes mellitus of age >18 year.
- Patients willing to give written informed consent.

Exclusion Criteria:

- Those who refused to give consent to participate in the study.
- Pregnant females.
- Patients of age less than 18 years.
- Patients with anemia due to other causes including known chronic diseases, infection, malignancy, hemoglobinopathies, and bleeding diathesis.
- Subjects with clinical suspicion of any other endocrine system diseases other than diabetes.
- Patients who were under the treatment that might affect blood parameters, such as steroids or who had received treatment for anemia previously.
- Patients with chronic kidney disease.
- Patients with acute or chronic blood loss from the gastrointestinal tract, respiratory, genitourinary systems, and menorrhagia due to uterine pathology.
- Patients on hematinic.

Sample size and sample technique –
Sample size – 200 cases.
Sampling technique – Random selection of patient.
Justification of sample size

On the basis of the prevalence of anemia in diabetes patients was found to be 68.25 % and 36% from previous studies (average = 52.1), the minimum sample size required to achieve a confidence interval of 95% and a power of 80% will be estimated and a non-response rate of 5% will be assumed and the final sample size will be obtained.

Using this, Sample size (N) was calculated by using following formula:

$$Sample\ size = \frac{Z^2_{1-\alpha/2}\ 1(1-p)}{d^2}$$

Z21-a/2 = Is standard normal variate =1.96 (at 5% type 1 error)

P = Expected proportion in population

D = absolute error or precision

Thus n = 1.96 x 1.96 x 52.1 x 47.9 / 10 x 10 = 95.87 (96 approximately)

Considering 5% drop out the sample size will be 95.87+4.79= 100.66 (101 approx.)

However, for this study we will be using a sample size of 200.

Keeping in mind the given duration of the study and concerned patient flow in this setup, it was decided to recruit all available subjects sequentially till the sample size is reached.

IV. Methodology:

Consent – Informed, written consent was obtained from all study subjects after the study's purpose, procedures, and potential risks were explained thoroughly.

Patient Evaluation – A detailed history was taken, and general physical and systemic examinations were performed on the study subjects.

Initial Laboratory Assessment – A complete hemogram was conducted, and peripheral blood film (PBF) was examined to guide the subsequent investigations.

Further Investigations Based on PBF Findings – For Microcytic Hypochromic Anemia – Stool was tested for occult blood, Upper gastrointestinal endoscopy was performed when indicated, An iron study was conducted to assess iron status. For Normocytic Normochromic Anemia – A Coombs test was carried out to check for autoimmune hemolytic anemia. For Macrocytic Anemia – Vitamin B12 levels were measured, Serum Folic Acid levels were assessed.

Comprehensive Testing – Complete Blood Count (CBC) and Indices – RBC indices including MCV, MCH, MCHC, and RDW were evaluated. The reticulocyte count and the corrected reticulocyte count were calculated.

Diabetes Monitoring – Fasting blood glucose, postprandial blood glucose, and HbA1c levels were measured.

Iron Profile – Serum iron and transferrin saturation levels were assessed.

Additional Testing – Renal function tests were performed, An electrocardiogram (ECG) was obtained, A fundus examination and a complete urine examination were conducted, 24-hour urine protein was measured.

Further Investigations if Required – Bone marrow aspiration and biopsy were considered, Testing for IgA – Tissue transglutaminase was conducted if celiac disease was suspected.

Interpretation of Study

Objective Interpretation – Data were analyzed to study the anemia profile in diabetic patients and to investigate the impact of antidiabetic drugs, diabetes duration, and diabetes-related complications on anemia.

Statistical Analysis

Data Management – Data were recorded and input into an Excel sheet, and SPSS version 21 was utilized for analysis.

Analytical Techniques – The mean, median, and standard deviation were employed for demographic data analysis. The Chi-square test was utilized for categorical data analysis. Tests of normalcy were applied to assess homogeneity. The Wilcoxon rank sum test was used for categorical and continuous data. Karl Pearson correlation was implemented to find the correlation between anemia and diabetes parameters.

Statistical Significance – P values less than 0.05 were considered statistically significant.

A total of 200 subjects were analysed.

Table 1: Sex

		Frequency	Percent
Sex	Female	84	42.0
	Male	116.	58.0
	Total	200	100.0

In present study there were 42% females and 58% males.

Figure 1: Pie chart of Sex

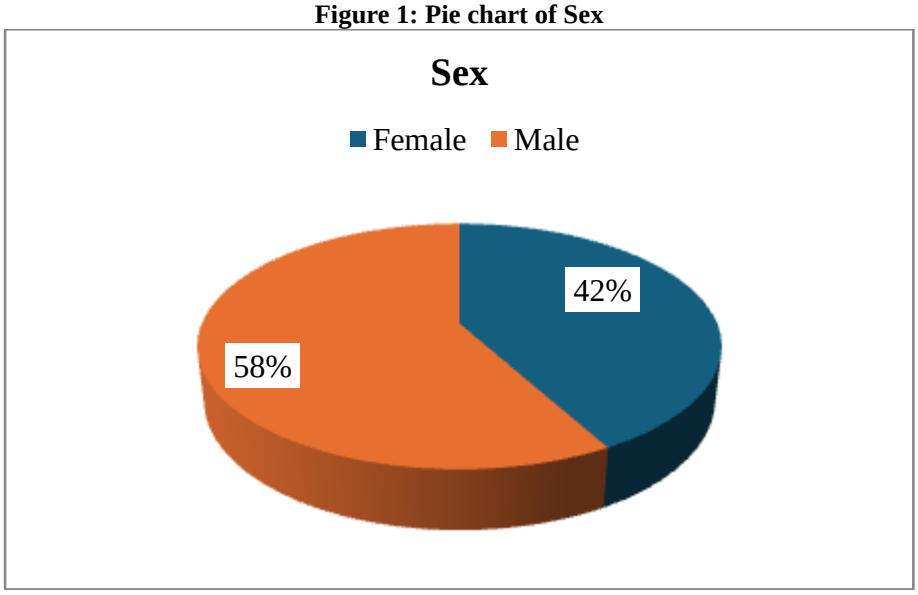

Table 2: Sex

	Frequency	Percent
Diabetes Type		
Type 1.	36	18.0
Type 2 .	164	82.0
Total	200	100.0

In present study 18% participants were having type 1 diabetes and 82% were having type 2 diabetes.

Figure 2: Pie chart of Sex

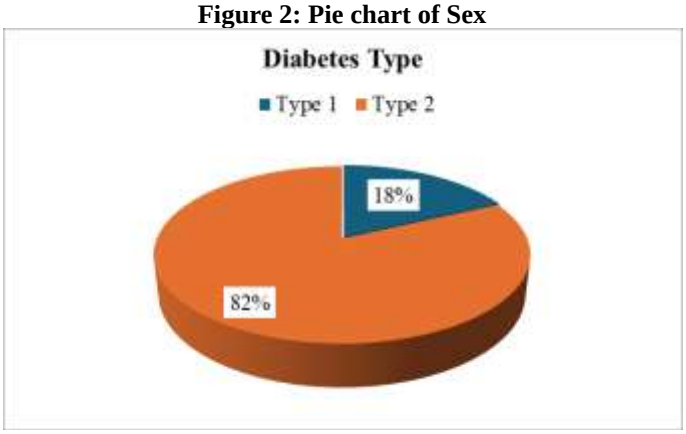

Table 3: Complications of Diabetes

	Frequency	Percent
Complications of Diabetes		
Cardiovascular Disease	52	26.0
Neuropathy	37	18.5
None	77	38.5
Retinopathy.	34	17.0
Total.	200	100.0

In present study Cardiovascular Disease was seen among 26% participants, Neuropathy was seen among 18.5% participants, Retinopathy was seen among 17% participants and no complications were seen among 38.5% participants.

Figure 3: Pie chart of Complications of Diabetes

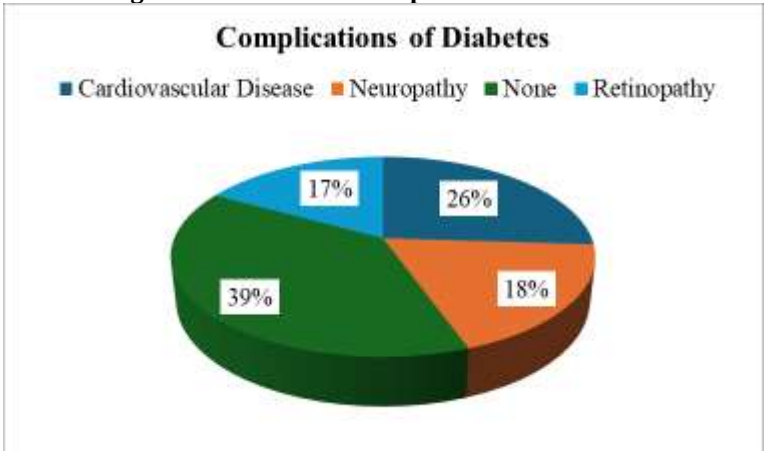

Table 4: Anemia Type

.		Frequency	Percent
Anemia Type	Macrocytic	32	16.0
	Microcytic Hypochromic	44	22.0
	Normocytic Normochromic	124	62.0
	Total	200	100.0

In present study Macrocytic anemia was seen among 16%, Microcytic Hypochromic anemia was seen among 22.0% and Normocytic Normochromic anemia was seen among 62%.

Figure 4: Pie chart of Anemia Type

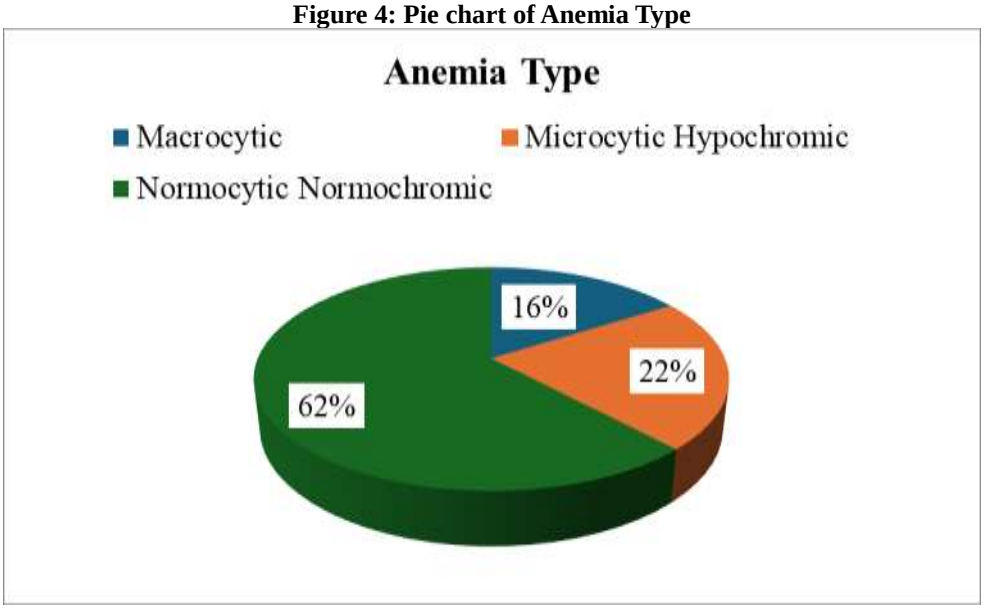

Table 5: Effect of Oral Hypoglycemic Agents on Anemia

	Frequency	Percent
Effect of Oral Hypoglycemic Agents on Anemia		

Increased risk of Macrocytic anemia due to potential Vitamin B12 deficiency	56	28.0
No direct effect, good diabetes control can mitigate anemia risk.	102	51.0
No effect from oral hypoglycemic agents	1	.5
Not applicable	41	20.5
Total	200	100.0

In present study due to oral hypoglycemic agents Increased risk of Macrocytic anemia due to potential Vitamin B12 deficiency seen among 28%, No direct effect, good diabetes control can mitigate anemia risk was seen among 51% and No effect from oral hypoglycemic agents was seen among 0.5%

Figure 5: Pie chart of Effect of Oral Hypoglycemic Agents on Anemia

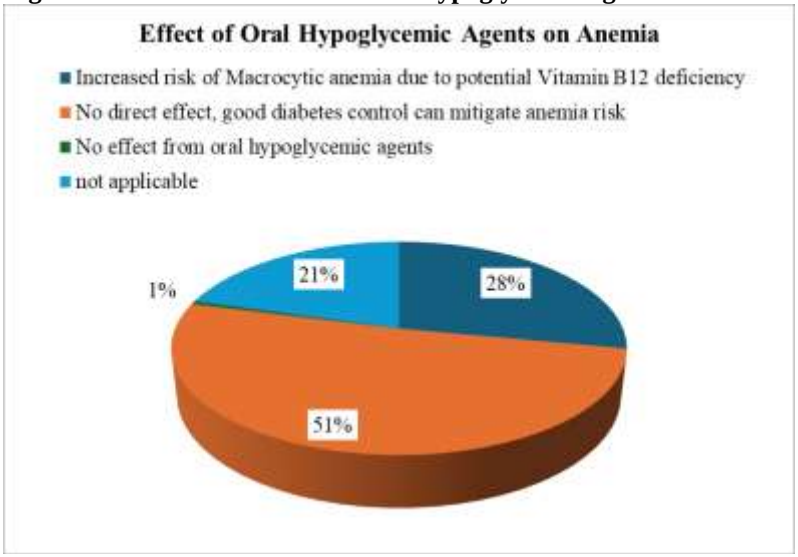

Table 6: Stool Test for Occult Blood

	Frequency	Percent
Stool Test for Occult Blood		
Negative	176	88.0
Positive	24	12.0
Total	200	100.0

In present study Stool Test for Occult Blood was seen positive among 12% participants.

Figure 6: Pie chart of Stool Test for Occult Blood

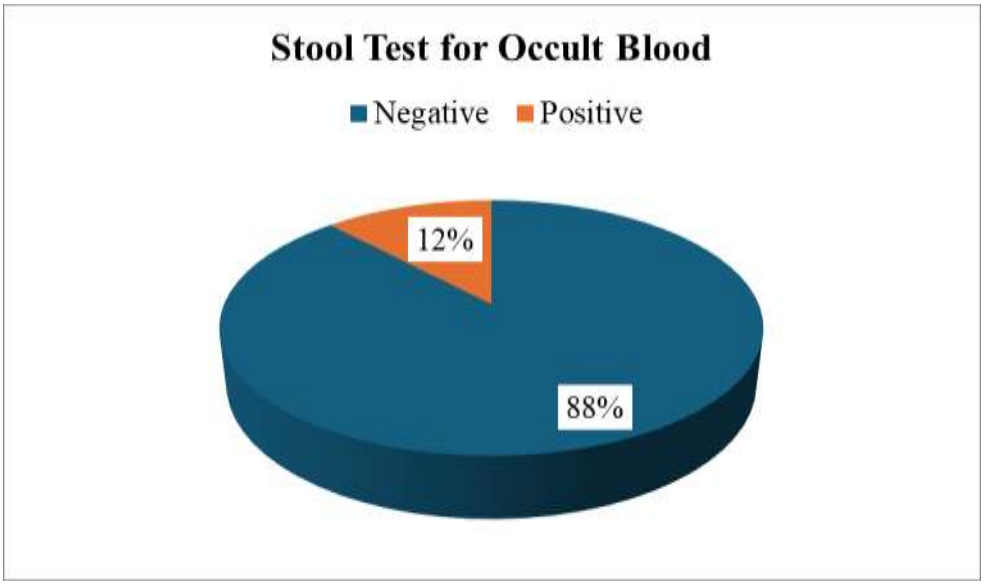

Table 7: Fundus Examination

	Frequency	Percent
Fundus Examination		
Mild NPDR	54	27.0
Moderate NPDR	32	16.0
Normal	92	46.0
Severe NPDR to PDR	22	11.0
Total	200	100.0

In present study Fundus Examination showed Mild NPDR among 27% participants, Moderate NPDR among 16% participants, Normal among 46% participants and Severe NPDR to PDR among 11% participants.

Figure 7: Pie chart of Fundus Examination

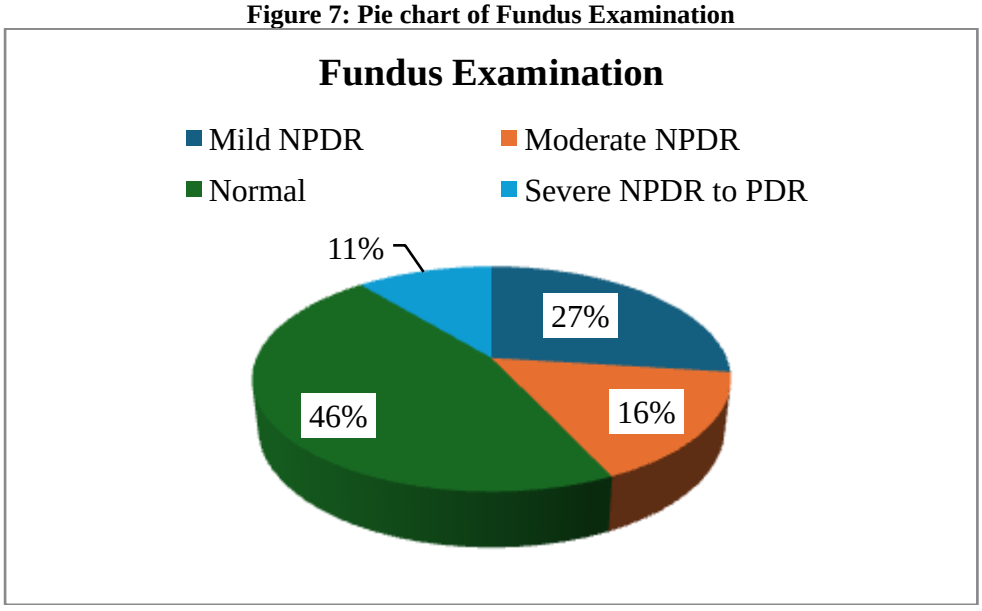

Table 8: Complete Urine Examination

	Frequency	Percent

Complete Urine Examination	Glucosuria	22	11.0
	Normal	96	48.0
	Proteinuria	52	26.0
	Signs of Infection	30	15.0
	Total	200	100.0

In present study urine examinations showed Glucosuria among 11% participants, Normal among 48% participants, Proteinuria among 26.0% participants and Signs of Infection among 15% participants.

Figure 8: Pie chart of Complete Urine Examination

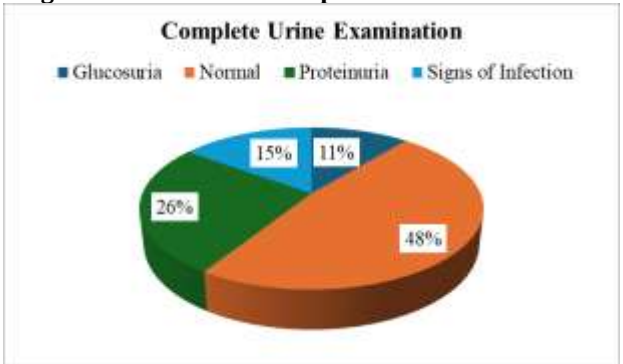

Table 9: Testing for IgA – Tissue Transglutaminase

		Frequency	Percent
Testing for IgA – Tissue Transglutaminase	Negative	196	98.0
	Positive	4	2.0
	Total	200	100.0

In present study Tissue Transglutaminase was positive among 2% participants.

Figure 9: Pie chart of Testing for IgA – Tissue Transglutaminase

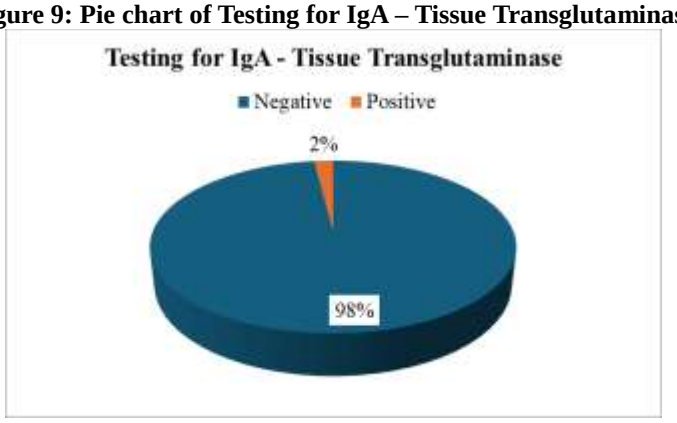

Table 10: Oral Hypoglycemic Agents Used

Oral Hypoglycemic Agents Used	Frequency	Percent
Metformin	56	28.0

Metformin + DPP-4 Inhibitors	36	18.0
Metformin + Sulfonylureas	66	33.0
None	42	21.0
Total	200	100.0

In present study, No oral hypoglycemic were given among 21.0%, 28% were given with Metformin, 18.0% were given with Metformin + DPP-4 Inhibitors and 33.0% were given with Metformin + Sulfonylureas.

Figure 10: Pie chart of Oral Hypoglycemic Agents Used

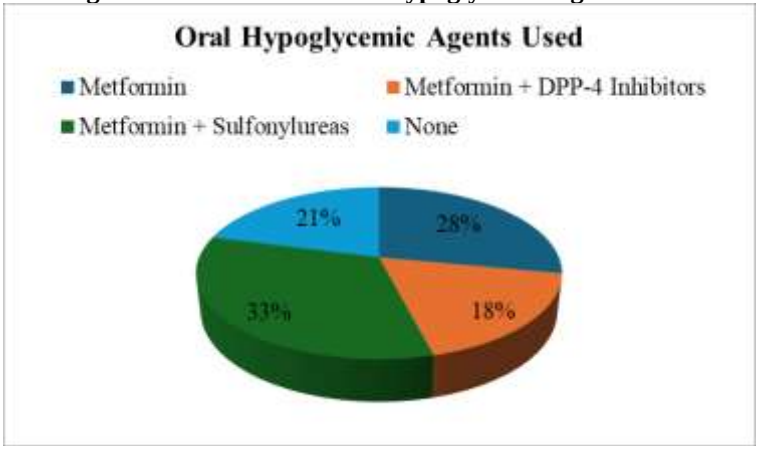

Table 11: Duration of oral hypoglycemic drugs usage (years)

Kruskal Wallis Test

	N	Mean	SD	p
Duration of oral hypoglycemic drugs usage (years)				
Metformin	562.8146			<0.001
Metformin + DPP-4 Inhibitors	36	7.611	3.6117	
Metformin + Sulfonylureas	66	6.273	3.7969	
None	42	.000	.0000	

In present study, there was statistically significant difference in mean Duration of oral hypoglycemic drugs usage (years) between different oral hypoglycemic groups (i.e., p<0.001)

Table 12: Descriptive Statistics of Age, Duration of Diabetes (years), Hemoglobin Level (g/dL), Duration of oral hypoglycemic drugs usage (years), FBG (mg/dL), PPBG (mg/dL), HbA1c (%), Vitamin B12 Level, Serum Folic Acid Level, Renal Function Test (Serum creatinine), 24-hour Urine Protein, MCV (fl), MCH (pg), MCHC (%), RDW (%), Reticulocyte Count (%), Corrected Reticulocyte Count, Serum Iron, Transferrin Saturation

Descriptive Statistics

	N	Min	Max	Mean	SD
Age	200	18.0	79.0	51.160	17.383
Duration of Diabetes (years)	200	1.0	19.0	8.420	6.146
Hemoglobin Level (g/dL)	200	8.400	11.980	10.736	0.618

Duration of oral hypoglycemic drugs usage (years)	200	0.0	18.0	5.140	4.067
FBG (mg/dL)	200	100.0	178.0	136.400	24.393
PPBG (mg/dL)	200	140.0	217.0	179.270	21.869
HbA1c (%)	200	6.069	14.870	8.579	2.410
Vitamin B12 Level	200	152.0	886.0	463.550	216.347
Serum Folic Acid Level	200	3.0	16.0	9.720	3.867
Renal Function Test (Serum creatinine)	200	0.74	1.20	0.952	0.141
24-hour Urine Protein	200	2.333	248.182	98.282	61.553
MCV (fl)	200	80.254	99.910	89.719	5.573
MCH (pg)	200	27.042	32.914	29.986	1.754
MCHC (%)	200	33.004	35.895	34.408	0.829
RDW (%)	200	11.543	14.472	12.973	0.878
Reticulocyte Count (%)	200	0.516	1.989	1.274	0.476
Corrected Reticulocyte Count	200	0.368	1.956	1.066	0.406
Serum Iron	200	30.00	168.00	93.4600	39.40651
Transferrin Saturation	200	10.00	49.00	29.9850	11.12762

Mean Age of participants was 51.160+17.383, Mean Duration of Diabetes (years) of participants was 8.420+ 6.146, Mean Hemoglobin Level (g/dL) of participants was 10.736+0.681, Mean Duration of oral hypoglycemic drugs usage (years) was 5.140+4.067years, Mean FBG (mg/dL) of participants was 136.4+24.393, Mean PPBG (mg/dL) of participants was 179.270+21.869, Mean HbA1c (%)of participants was 8.579+2.410, Mean Vitamin B12 Level of participants was 463.550+216.347, Mean Serum Folic Acid Level of participants was 9.720+3.867, Mean Renal Function Test (Serum creatinine) of participants was 0.952+0.141, Mean 24-hour Urine Protein of participants was 98.282+61.553, Mean MCV (fl) of participants was 89.719+5.573, Mean MCH (pg) of participants was 29.986+1.754, Mean MCHC (%)of participants was 34.408+0.829, Mean RDW (%)of participants was 12.973+0.878, Mean Reticulocyte Count (%)of participants was 1.274+0.476, Mean Corrected Reticulocyte Count of participants was 1.066+0.406, Mean MCV (fL) of participants was 89.403+5.934, Mean MCHC (g/dL) of participants was 34.070+1.170, Mean Serum Iron of participants was 93.46+39.46 and Mean Transferin saturation of participants was 29.985+11.127.

Table 13: Duration of diabetes correlated with various parameters (Hemoglobin, HbA1c, Vitamin B12, Serum folic acid, Serum iron, Transferrin saturation)

	Pearson Correlation	
	Duration of Diabetes (years)	interpretation
Hemoglobin Level (g/dL)	Pearson Correlation	0.146 Week -ve
	Sig. (2-tailed)	0.039 significant
	N	200
HbA1c (%)	Pearson Correlation	-0.331 Week -ve

	Sig. (2-tailed)	<0.001	significant
	N	200	
Vitamin B12 Level	Pearson Correlation	-0.034	Week -ve
	Sig. (2-tailed)	0.630	Insignificant
	N	200	
Serum Folic Acid Level	Pearson Correlation	0.076	Week +ve
	Sig. (2-tailed)	0.282	Insignificant
	N	200	
Serum Iron	Pearson Correlation	0.062	Week +ve
	Sig. (2-tailed)	0.382	Insignificant
	N	200	
Transferrin saturation	Pearson Correlation	0.076	Week +ve
	Sig. (2-tailed)	0.283	Insignificant
	N	200	

Hemoglobin Level (g/dL) and HbA1c (%) had a significant week negative correlation with duration of diabetes mellitus (p=0.039 & p<0.001), Vitamin B12 Level had a week negative correlation with duration of diabetes mellitus which is insignificant (p=0.630) and Serum Folic Acid Level, Serum Iron and Transferin saturation all had a week positive correlation with duration of diabetes mellitus which is insignificant (p=0.282, 0.382 and 0.283) respectively.

Table 14: Duration of diabetes vs oral hypoglycemic drug usage

Kruskal Wallis Test

		N	Mean	SD	p
Duration of Diabetes (years)	Metformin	56	10.393	6.5745	<0.001
	Metformin + DPP-4 Inhibitors	36	7.389	5.7881	
	Metformin + Sulfonylureas	66	9.591	5.8097	
	None	42	4.833	4.6534	

In present study, there was statistically significant difference in mean Duration of Diabetes (years) between different oral hypoglycemic groups (i.e., p<0.001).

Table 15: Hemoglobin level vs oral hypoglycemic drug usage

Kruskal Wallis Test

		N	Mean	SD	p
Hemoglobin Level (g/dL)	Metformin	56	10.723	.653	0.309
	Metformin + DPP-4 Inhibitors	36	10.770	.642	

Metformin + Sulfonylureas	66	10.825	.577
None	42	10.586	.604

In present study, there was no statistically significant difference in mean Duration of Diabetes (years) between different oral hypoglycemic groups (i.e., p=0.309).

Table 16: FBG (mg/dL) vs oral hypoglycemic drug usage
Kruskal Wallis Test

		N	Mean	SD	p
FBG (mg/dL)	Metformin	56	135.679	25.2479	0.176
	Metformin + DPP-4 Inhibitors	36	129.333	22.2608	
	Metformin + Sulfonylureas	66	138.697	25.6227	
	None	42	139.810	22.4535	

In present study, there was no statistically significant difference in mean FBG (mg/dL) between different oral hypoglycemic groups (i.e., p=0.176)

Table 17: PPBG (mg/dL) vs oral hypoglycemic drug usage
Kruskal Wallis Test

		N	Mean	SD	p
PPBG (mg/dL)	Metformin	56	185.071	19.9817	0.106
	Metformin + DPP-4 Inhibitors	36	177.722	20.3927	
	Metformin + Sulfonylureas	66	177.242	22.8453	
	None	42	176.048	23.1969	

In present study, there was no statistically significant difference in mean PPBG (mg/dL) between different oral hypoglycemic groups (i.e., p=0.106)

Table 18: HbA1c vs oral hypoglycemic drug usage
Kruskal Wallis Test

		N	Mean	SD	p
HbA1c (%)	Metformin	56	7.219	.818	<0.001
	Metformin + DPP-4 Inhibitors	36	7.394	.957	
	Metformin + Sulfonylureas	66	7.676	.852	
	None	42	12.827	1.344	

In present study, there was statistically significant difference in mean HbA1c (%) between different oral hypoglycemic groups (i.e., p<0.001).

In this study, we delve into the intricate relationship between diabetes mellitus and anemia, a prevalent yet often overlooked complication in diabetic patients. The findings from our study shed light on the types and

prevalence of anemia within this population, emphasizing the significant impact of diabetes management, particularly the use of oral hypoglycemic agents, on anemia development. This chapter aims to contextualize these findings within the broader spectrum of existing literature, exploring how our results align with or diverge from previous studies. Additionally, we discuss the clinical implications of these findings, considering the practical aspects of managing both diabetes and its hematological complications effectively. By integrating our study results with established research, we hope to contribute to a more nuanced understanding of diabetes management strategies and their multifaceted impacts on patient health.

Gender Distribution:

In this study, the gender distribution among diabetic patients revealed a higher prevalence of diabetes among males (58%) compared to females (42%). This finding is consistent with the trends reported in the literature, such as the study by Gale EA et al., which suggests that males are more frequently diagnosed with diabetes than females.[50] This disparity may be attributed to several factors, both biological and sociocultural. Biologically, men are more prone to developing visceral fat accumulation—a risk factor for type 2 diabetes—due to differences in sex hormones and fat distribution. Men typically accumulate fat around the abdomen, which is more closely associated with insulin resistance than the subcutaneous fat more common in women.[51]

Additionally, lifestyle factors might also contribute to this difference. Men generally engage in riskier eating behaviors and have higher rates of alcohol consumption, which can predispose them to metabolic syndromes, including diabetes. Furthermore, women often participate in regular healthcare visits more frequently than men, particularly during reproductive years, which may lead to earlier detection and management of pre-diabetic conditions.

From a medical perspective, understanding these gender-based differences is crucial for developing targeted public health interventions and preventive measures. For instance, more aggressive screening and lifestyle modification programs for men might be warranted to address this imbalance and reduce the incidence of diabetes among males. Additionally, gender-specific treatment approaches could be considered to optimize diabetes management and outcomes in both sexes.

By delving deeper into the biological and lifestyle factors contributing to the gender disparity in diabetes prevalence, we can tailor interventions more effectively and potentially mitigate some of the risk associated with this chronic condition.

Type of Diabetes:

The results of this study, showing a predominance of Type 2 diabetes (82%) compared to Type 1 diabetes (18%), align with global epidemiological data indicating an increasing trend in Type 2 diabetes across various populations. This distribution is reflective of the broader epidemiological shifts noted by van Dam RM et al., where lifestyle and environmental factors play significant roles in the surge of Type 2 diabetes cases.[52]

Type 2 diabetes is largely influenced by factors such as obesity, sedentary lifestyles, and poor dietary habits, which are becoming more prevalent due to modern lifestyle changes. The increase in obesity rates worldwide, especially in urban settings, directly correlates with the rise in Type 2 diabetes incidence. Additionally, as populations age, the prevalence of Type 2 diabetes increases, given that aging is a significant risk factor for insulin resistance and beta-cell dysfunction, both key components in the pathophysiology of Type 2 diabetes.

Type 1 diabetes, being autoimmune in nature, does not exhibit the same correlation with lifestyle factors. Instead, it is influenced by genetic and possibly environmental factors that trigger the autoimmune destruction of insulin-producing beta cells in the pancreas. The lesser prevalence of Type 1 diabetes in the study reflects its overall lower incidence in the general population compared to Type 2 diabetes.

Understanding the significant predominance of Type 2 diabetes is crucial for public health planning and resource allocation. It underscores the need for targeted interventions focused on lifestyle modifications, obesity prevention, and management programs that could substantially reduce the burden of Type 2 diabetes. Furthermore, recognizing the distinct pathophysiological mechanisms behind Type 1 and Type 2 diabetes is essential for developing specific therapeutic approaches and educational programs tailored to the needs of these different patient populations.

By focusing on the distinguishing factors between Type 1 and Type 2 diabetes within different populations, healthcare providers can better design and implement preventive and management strategies that address the specific needs and risk factors of their patient cohorts.

Complications Associated with Diabetes:

The occurrence of cardiovascular diseases in 26% of the diabetic participants in this study aligns closely with broader epidemiological trends, albeit slightly lower than the 30% prevalence reported by Ma CX et al.[53] This variation could be influenced by differences in genetic backgrounds, healthcare access, and the

effectiveness of diabetes management strategies across populations. Cardiovascular disease is a well-known complication of diabetes due to the chronic hyperglycemia-associated damage to blood vessels, which accelerates atherosclerosis and increases the risk of heart attacks and strokes.

Neuropathy and retinopathy, present in lesser frequencies in this study compared to others, such as the findings by Raman R et al[54] and Pradeepa R et al[55]., might reflect variations in patient demographics, including the duration of diagnosed diabetes and the degree of glycemic control. Diabetic neuropathy, which results from sustained damage to peripheral nerves due to high blood sugar levels, and diabetic retinopathy, arising from damage to the retina's blood vessels, are both complications that typically develop progressively over time. Earlier detection and management of diabetes, possibly more prevalent in this study's setting, could contribute to lower observed rates of these complications.

Furthermore, access to healthcare plays a crucial role in the management of diabetes and its complications. Populations with better healthcare access are likely to receive more effective and timely treatments, including regular monitoring of blood sugar levels and early interventions for diabetes management, potentially reducing the incidence of severe complications such as neuropathy and retinopathy.

By understanding the factors contributing to the lower prevalence of cardiovascular diseases and other complications in certain diabetic populations, healthcare providers can tailor interventions more effectively. This could include focused strategies for early diabetes detection, aggressive management of blood glucose levels, and specific lifestyle modifications aimed at preventing the long-term complications of diabetes.

Anemia in Diabetic Patients:

The prevalence of Normocytic Normochromic anemia observed at 62% in this study underscores an important clinical consideration in the management of diabetes, as it reflects anemia commonly associated with chronic diseases, including diabetes. This form of anemia, characterized by neither abnormally large nor small red blood cells, is often indicative of underlying inflammatory processes that are typical in chronic diseases like diabetes. These findings echo those reported by Taderegew MM et al., where a similarly high prevalence highlighted the systemic impact of diabetes on red blood cell production and maintenance, potentially mediated through inflammatory cytokines and impaired renal function affecting erythropoietin production.[56]

Additionally, the notable incidences of Macrocytic and Microcytic Hypochromic anemia, at 16% and 22% respectively, suggest other underlying mechanisms at play, primarily related to nutritional deficiencies. Macrocytic anemia, often linked to deficiencies in Vitamin B12 or folate, can be particularly exacerbated by the use of diabetic medications such as Metformin, which is known to interfere with vitamin B12 absorption. Microcytic Hypochromic anemia, on the other hand, typically results from iron deficiency, which could either be due to poor dietary intake or chronic blood loss, possibly indicated in this cohort by the 12% positive rate in the stool tests for occult blood. These associations are supported by Barbieri J et al., who discussed how dietary insufficiencies and chronic inflammatory states in diabetic patients can lead to varied anemia types.[57]

Understanding these distinctions is crucial for developing targeted therapeutic approaches. For instance, addressing Macrocytic anemia in diabetic patients might require assessments of medication impacts on nutrient absorption, and interventions may include supplementation or dietary adjustments. Similarly, management strategies for Microcytic anemia should consider both iron supplementation and the investigation of potential sources of chronic blood loss.

By delving deeper into the types of anemia prevalent among diabetic patients and understanding their root causes, clinicians can better tailor their management plans to address not only the glycemic control but also the broader hematological challenges presented by diabetes. This comprehensive approach can significantly enhance the overall health and quality of life of diabetic patients, ensuring that both their primary chronic condition and its secondary complications are effectively managed.

Impact of Oral Hypoglycemic Agents on Anemia:

The findings of this study shed significant light on the impact of oral hypoglycemic agents, particularly Metformin, on the development of anemia in diabetic patients. The observed 28% increase in the risk of Macrocytic anemia among Metformin users can be medically attributed to the drug's interference with vitamin B12 absorption in the ileum. Metformin, a first-line treatment for Type 2 diabetes, has been documented to reduce the absorption of vitamin B12, leading to deficiencies that result in Macrocytic anemia, where red blood cells are larger than normal due to inadequate vitamin B12 or folate. These findings are in line with those reported by Chapman LE et al[58] and Kim J et al[59]., which indicated a 25% prevalence of vitamin B12 deficiency among Metformin users.

This phenomenon occurs because vitamin B12 is essential for DNA synthesis in red blood cell production. A deficiency in vitamin B12 disrupts proper red blood cell formation, leading to anemia characterized by fewer but larger cells. The deficiency impacts the DNA replication process during erythropoiesis (red blood cell formation), causing ineffective erythropoiesis and the release of immature, large,

oval cells called macrocytes. Clinically, this results in symptoms of anemia such as fatigue, weakness, and, in severe cases, neurological damage if left untreated.

Given the high prevalence of Metformin use among diabetic populations, these findings underscore the importance of regular monitoring of vitamin B12 levels in patients undergoing long-term Metformin therapy. Proactive management strategies, including periodic screening and vitamin B12 supplementation, could prevent the onset of Macrocytic anemia and improve overall patient outcomes. This approach not only addresses the hematological effects of diabetes treatment but also enhances the efficacy of diabetes management by reducing one of its potential complications.

By understanding and addressing the side effects associated with common diabetic medications, healthcare providers can offer more comprehensive care that optimizes treatment efficacy while minimizing adverse effects. This ensures that diabetes management is both effective and sustainable, improving long-term patient health and quality of life.

Stool Test for Occult Blood:

The finding of a 12% positivity rate in stool tests for occult blood among diabetic patients in this study highlights a significant health concern that warrants further attention. Occult gastrointestinal bleeding (OGIB) is not uncommon in diabetic patients, and its presence can often go unnoticed due to the absence of visible symptoms. The blood loss, although typically minimal and not immediately life-threatening, can lead to iron deficiency anemia over time, complicating the patient's overall health status.

The pathophysiological basis for increased OGIB in diabetics is multifactorial. Diabetes is associated with various gastrointestinal complications such as gastroparesis, enteropathy, and an increased risk of colorectal cancer, all of which can contribute to occult bleeding. Furthermore, the use of medications such as antiplatelet drugs, which are commonly prescribed for cardiovascular protection in diabetes, can exacerbate this risk.

Enck P et al. highlighted similar findings, noting that the prevalence of OGIB in diabetic patients is a critical issue, with implications for both the diagnosis and management of diabetes.[60] They suggest routine screening for OGIB in diabetic patients, especially those with anemia or a significant history of gastrointestinal symptoms, as a preventive measure to detect and manage potential sources of bleeding early.

In clinical terms, the 12% positivity rate found in this study suggests that healthcare providers should consider regular non-invasive testing for occult blood as part of the standard care for diabetic patients. This is particularly important because the early detection of OGIB allows for timely intervention, potentially preventing the progression to more severe conditions like anemia or critical gastrointestinal disorders. Furthermore, identifying the cause of OGIB can help tailor more specific treatments, such as adjusting medication that might increase bleeding risk or addressing any underlying gastrointestinal pathologies.

Overall, incorporating screening for occult blood in the routine evaluation of diabetic patients can significantly contribute to more comprehensive diabetes management, improving outcomes by addressing one of the often-overlooked complications of the disease.

Fundus Examination Outcomes:

The fundus examination outcomes from this study provide valuable insights into the ocular health of diabetic patients, showcasing the various stages of diabetic retinopathy. Diabetic retinopathy is a diabetes complication that affects the eyes and is caused by damage to the blood vessels of the light-sensitive tissue at the back of the eye (retina). Specifically, 27% of participants showing mild non-proliferative diabetic retinopathy (NPDR) and 16% with moderate NPDR indicate early to moderate stages of this condition where microaneurysms, dot hemorrhages, or exudates are present but not severe enough to impair vision significantly.

The progression to 11% with severe NPDR to proliferative diabetic retinopathy (PDR) marks a critical transition where neovascularization (new blood vessel growth) occurs. These new vessels are fragile and susceptible to bleeding, potentially leading to severe visual impairment or blindness if not managed effectively. The presence of 46% of participants with normal fundus findings highlights the variability in the progression of diabetic retinopathy, which can be significantly influenced by the management of blood sugar levels, blood pressure, and lipid levels.

The progression and severity of diabetic retinopathy are closely tied to the duration of diabetes and the quality of metabolic control. Poor glycemic control exacerbates the risk of all diabetic complications, particularly retinopathy, by promoting hyperglycemia-induced damage to the vascular endothelium. This damage increases vascular permeability, leading to retinal edema and progressive retinal damage.

Regular, comprehensive eye screenings, as evidenced by the findings and the recommendations in the literature by Melo GB et al., are crucial for early detection and management of diabetic retinopathy.[61] Early stages, such as mild or moderate NPDR, may not require treatment beyond optimizing diabetes management, but they do require regular monitoring to prevent progression. In contrast, severe NPDR and PDR often require

active interventions, such as laser photocoagulation, anti-VEGF (Vascular Endothelial Growth Factor) injections, or vitrectomy to prevent vision loss.

In conclusion, the variability in fundus examination outcomes within this diabetic cohort underscores the importance of integrating regular ophthalmological assessments into diabetes care protocols. These assessments not only aid in the early detection and staging of diabetic retinopathy but also serve as a crucial feedback mechanism to assess the effectiveness of the current diabetes management strategies, tailoring interventions to individual patient needs to mitigate the risk of severe ocular complications.

Urine Examinations:

The results from the urine examinations in this study reveal significant renal complications associated with diabetes, with 11% of participants showing glucosuria, 26% displaying proteinuria, 15% exhibiting signs of infection, and 48% presenting normal findings. These indicators are crucial for understanding the renal implications of diabetes and its management.

Glucosuria, the presence of glucose in urine, typically occurs when blood glucose levels exceed the renal threshold for glucose reabsorption. This condition is common in diabetic patients, especially those with poor glycemic control. Glucosuria is a clear signal that diabetes management needs to be optimized to prevent further renal burden and other complications associated with hyperglycemia.

Proteinuria, found in 26% of the cohort, is particularly alarming as it suggests the onset or presence of diabetic nephropathy. Diabetic nephropathy is one of the most significant microvascular complications of diabetes, marked by damage to the kidneys' filtering units, the glomeruli, leading to protein leakage into urine. The presence of proteinuria is often a precursor to more severe kidney damage and can advance to chronic kidney disease (CKD), highlighting the critical need for early detection and intervention. The findings are consistent with those by Chiarelli F et al., who underscore the importance of routine screening for microalbuminuria as an early indicator of nephropathy in diabetic patients. Early detection allows for timely interventions, such as optimizing blood pressure and blood sugar control, which are essential in slowing the progression of kidney disease.[62]

Signs of urinary infection in 15% of participants also underscore the vulnerability of diabetic patients to infections due to alterations in immune function and other diabetes-related changes in the urinary tract. Managing these infections promptly and effectively is crucial to prevent their escalation into more severe complications, such as pyelonephritis or sepsis.

Considering these findings, regular urine tests for glucosuria, proteinuria, and signs of infection should be integral components of diabetes management. These screenings not only provide direct indicators of renal function and its impairment but also serve as critical checkpoints to assess the overall effectiveness of the current diabetes management strategies. Addressing abnormalities identified through urine examinations can significantly impact the overall prognosis and quality of life for diabetic patients by preventing the progression of renal disease and reducing the risk of severe infections.

This detailed examination and understanding of urine test results play a vital role in the holistic management of diabetes, emphasizing the need for multidisciplinary approaches to care that encompass regular monitoring and tailored interventions to address specific complications as they develop.

Tissue Transglutaminase Positivity:

The detection of tissue transglutaminase (tTG) antibodies in 2% of the participants in this study is clinically significant, especially considering the strong association between celiac disease and Type 1 diabetes. Both conditions are autoimmune disorders, and the presence of tTG antibodies is a key marker used to diagnose celiac disease. The linkage between these two autoimmune diseases is well-documented, with studies like the one conducted by Arora S et al., showing that individuals with Type 1 diabetes have a heightened risk of developing celiac disease compared to the general population.[63]

Celiac disease affects the small intestine's ability to absorb nutrients effectively due to an immune reaction to ingested gluten, which leads to inflammation and villous atrophy in the intestine. For diabetic patients, particularly those with Type 1 diabetes, the presence of celiac disease can complicate the management of diabetes. This is because malabsorption resulting from celiac disease can lead to significant variations in nutrient intake, impacting glycemic control. For instance, malabsorption can unpredictably alter the absorption of carbohydrates and fats, complicating insulin dosing and potentially leading to both hypo- and hyperglycemia.

Moreover, undiagnosed celiac disease in diabetic patients can lead to various nutritional deficiencies (such as iron-deficiency anemia, osteoporosis, and vitamin deficiencies), further exacerbating the patient's overall health and complicating the management of diabetes. Given these implications, it is recommended that diabetic patients, particularly those with Type 1 diabetes, undergo regular screening for tTG antibodies when symptoms suggestive of malabsorption, such as chronic diarrhea, anemia, or unexplained weight loss, are present.

The management of patients who are both diabetic and have celiac disease includes a strict, lifelong gluten-free diet, which can help restore intestinal integrity and improve nutrient absorption. This dietary management is crucial not only for controlling symptoms and preventing the complications associated with celiac disease but also for stabilizing and optimizing diabetes management.

This overlap of autoimmune conditions highlights the importance of a comprehensive approach in the clinical evaluation of diabetic patients. By incorporating routine screenings for celiac disease and other potential autoimmune disorders, healthcare providers can offer more personalized and effective management strategies, ensuring better overall outcomes for these patients.

Detailed Lab Values:

The laboratory values obtained in this study provide critical insights into the metabolic status and health complications of diabetic patients. The Mean Hemoglobin Level at 10.736 g/dL suggests a tendency towards anemia among participants, which is a common complication in chronic diabetes due to factors like nutrient deficiencies and chronic inflammation. Such a level of hemoglobin is concerning as it indicates that many patients are not just dealing with diabetes but also with the secondary effects that anemia can have on their overall health and energy levels.

The Mean Fasting Blood Glucose (FBG) of 136.4 mg/dL and Mean Postprandial Blood Glucose (PPBG) of 179.270 mg/dL further reflect the challenges in achieving optimal glycemic control within the cohort. These values are above the recommended thresholds for well-managed diabetes, indicating that many individuals in the study are at an elevated risk for developing complications associated with chronic hyperglycemia, such as neuropathy, nephropathy, and retinopathy.

Moreover, the Mean HbA1c of 8.579% is particularly telling. The HbA1c test measures the average blood glucose control over the last two to three months and levels above 7% are typically considered indicative of poor glycemic control according to diabetes management guidelines. An HbA1c of 8.579% signals that a significant portion of the cohort is managing their condition suboptimally, correlating with an increased risk for both microvascular and macrovascular complications. This aligns with findings from Sherwani SI et al., which highlighted the direct correlation between elevated HbA1c levels and the heightened risk of developing long-term diabetic complications.[64]

The laboratory values for Mean Serum Iron and Mean Transferrin Saturation, along with vitamin levels such as Mean Vitamin B12 and Mean Serum Folic Acid, offer additional dimensions to the metabolic challenges faced by these patients. For instance, while the Mean Vitamin B12 Level at 463.550 seems adequate, the distribution might be skewed by a few patients with high levels, potentially masking those suffering from deficiency due to factors like Metformin usage.

In essence, these detailed lab values not only underscore the multifaceted nature of diabetes management but also highlight the critical need for a tailored therapeutic approach. Optimizing treatment plans based on comprehensive lab assessments can help mitigate the risk of complications and enhance the overall quality of life for diabetic patients. Healthcare providers must consider these values in conjunction with clinical findings to adjust medical therapies, dietary recommendations, and other management strategies effectively.

By understanding and addressing these complex lab results, medical professionals can better navigate the intricate landscape of diabetes care, ensuring that management strategies are both comprehensive and individualized.

In conclusion, the findings from our study contribute valuable insights into the complex interplay between diabetes mellitus and anemia, highlighting the crucial need for comprehensive screening and proactive management of anemia in diabetic patients. The significant associations found between specific types of anemia and the use of oral hypoglycemic agents, particularly Metformin, underline the importance of vigilant monitoring and potential dietary supplementation to mitigate these risks. As we compare our results with those of existing literature, it becomes evident that while some findings align, others present new challenges and opportunities for enhancing diabetic care. Moving forward, it is imperative that these insights inform both clinical practices and future research, aiming to optimize the management of diabetes and improve the quality of life for affected individuals. This study not only advances our understanding but also calls for a continued, dynamic approach to addressing the nuances of diabetic health complications.

V. Key Findings:

1. High Prevalence of Anemia: A substantial proportion of the diabetic population, specifically 62%, was found to have Normocytic Normochromic anemia, indicating a high prevalence of anemia associated with chronic disease states common in diabetes.
2. Significant Association with Oral Hypoglycemic Agents: The study highlighted a significant relationship between the use of oral hypoglycemic agents, particularly Metformin, and an increased risk of Macrocytic anemia. This was attributed to vitamin B12 deficiency, a known side effect of long-term Metformin use.

3. Impact of Diabetes Duration and Complications: The findings showed that the duration of diabetes and the presence of complications such as cardiovascular disease, neuropathy, and retinopathy influence the prevalence and type of anemia observed in patients, reflecting the complex interplay between diabetes management and anemia.
4. Necessity for Routine Anemia Screening: The results underscore the need for routine screening for anemia within diabetic care, especially for those on Metformin, to allow for early detection and management of potential vitamin deficiencies and other types of anemia.
5. Holistic Approach to Diabetes Management: The study supports the importance of a comprehensive approach to managing diabetes that goes beyond glycemic control to include monitoring for and managing conditions such as anemia, which can significantly impact the overall health outcomes of diabetic patients.

VI. Strengths:

1. Comprehensive Scope: The study provides a detailed examination of anemia types among diabetic patients, offering insights into Normocytic Normochromic, Macrocytic, and Microcytic Hypochromic anemia. This comprehensive approach allows for a better understanding of the prevalence and characteristics of anemia within this population.
2. Focused Analysis on Medication Impact: The research specifically investigates the impact of oral hypoglycemic agents on anemia, with a particular focus on Metformin and its association with Macrocytic anemia due to vitamin B12 deficiency. This targeted analysis is crucial given the widespread use of Metformin in managing Type 2 diabetes.
3. Inclusion of Diverse Health Parameters: The study not only looks at anemia but also incorporates additional health parameters like stool tests for occult blood, fundus examinations, and urine tests. These parameters enrich the study's data set, providing a holistic view of the health status of diabetic patients.
4. Statistical Rigor: Utilizing robust statistical methods to analyze the collected data ensures that the findings are both valid and reliable. This statistical rigor supports the study's conclusions and enhances its credibility in the academic community.
5. Relevance to Clinical Practice: By highlighting the need for routine anemia screening and the potential side effects of commonly used diabetes medications, the study directly contributes to improving clinical practices. It provides evidence-based recommendations that can enhance patient care and management strategies.
6. Foundation for Future Research: The findings set the stage for future investigations, identifying areas where further research is needed, such as the long-term impact of diabetes management strategies on anemia and the effectiveness of interventions to mitigate medication side effects.
7. Interdisciplinary Insights: The study's interdisciplinary approach, incorporating elements from endocrinology, hematology, and primary care, fosters a more integrated understanding of diabetic care. This approach is critical for addressing the multifactorial nature of diabetes and its complications.

VII. Limitations:

1. Sample Size and Generalizability: Although comprehensive, the sample size may be limited in its ability to fully represent the diverse diabetic population. This could impact the generalizability of the findings to broader diabetic demographics, especially across different geographic and ethnic backgrounds.
2. Single-Center Study: Being conducted at a single tertiary care center, the findings may reflect the specific patient management and demographic characteristics of that particular institution, which might not be applicable to other settings or regions.
3. Cross-Sectional Design: The cross-sectional nature of the study limits its ability to determine causality between diabetes management and the development of anemia. Longitudinal studies would be more effective in assessing the temporal sequence and causative relationships.
4. Potential for Selection Bias: The study may suffer from selection bias if the participants who volunteered or were selected have different characteristics from those who did not participate, which can influence the results and their applicability.
5. Recall and Reporting Bias: If data collection relied on participant recall for diabetes duration, medication history, or lifestyle factors, there could be inaccuracies due to recall bias. Similarly, self-reported data are susceptible to reporting bias.
6. Lack of Control Group: Without a non-diabetic control group for comparison, it's difficult to definitively attribute the findings of anemia prevalence and type solely to diabetes and its management, rather than other potential confounding factors.
7. Confounding Variables: There could be other confounding variables not controlled for or measured in the study, such as dietary patterns, socioeconomic status, or other medical conditions, which might affect the results.

8. Dependence on Specific Laboratory Tests: The study's conclusions are also dependent on the specific laboratory tests used to measure anemia and other health parameters. Variations in test sensitivity and specificity across different labs could affect the accuracy of the results.

VIII. Recommendations:

1. Routine Screening for Anemia: Clinicians should incorporate regular screening for different types of anemia as part of comprehensive diabetes management, especially for patients using Metformin, to early detect and address potential vitamin B12 deficiency and other anemia-related complications.
2. Monitoring and Supplementation: Given the significant association between Metformin use and Macrocytic anemia, it is recommended to routinely monitor vitamin B12 levels in patients on long-term Metformin therapy. Vitamin B12 supplementation should be considered if deficiencies are detected to prevent the development of Macrocytic anemia.
3. Holistic Diabetes Management: Healthcare providers should adopt a holistic approach in managing diabetes that not only focuses on glycemic control but also monitors and manages potential complications, including anemia. This should involve nutritional counseling, management of cardiovascular risk factors, and regular monitoring of renal function.
4. Educational Programs for Patients and Healthcare Providers: Develop and implement educational programs that highlight the importance of regular monitoring for anemia and the potential side effects of common diabetic medications on hematological parameters. These programs should also train healthcare providers to recognize and manage these complications effectively.
5. Further Research on Anemia Management in Diabetics: Future studies should explore the long-term outcomes of different anemia management strategies in diabetic patients. These studies could investigate the efficacy of various supplements or alternative medications that might mitigate the side effects of traditional diabetic treatments.
6. Multi-Center Longitudinal Studies: To overcome the limitations of generalizability and causality, future research should be conducted in multiple centers over a longer duration. These studies should aim to track the development of anemia over time in a diverse diabetic population to better understand the dynamics and causal relationships.
7. Inclusion of a Control Group: Future studies should include a non-diabetic control group to help determine the specific impacts of diabetes on the development of anemia, distinct from those observed in the general population.
8. Comprehensive Data Collection: To minimize recall and reporting biases, future studies should employ more rigorous data collection methods, potentially including electronic health records and real-time data tracking, to enhance the accuracy of the information collected.

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