

# Frequency of Anemia among the Patients of Type 2 Diabetes Attending Outpatient Clinic of Mirpurkhas, Sindh

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## ABSTRACT

**Background:** Anemia is the most common blood disorder in patients with type 2 diabetes. The hematological profile of diabetic patients is often missed clinically until to start the manifestation of clinical features of anemia. Anemia increases the hindrances and financial burden on the patient by frequent hospitalization. It increases the risk of microvascular complications, heart diseases, morbidity and death in diabetes mellitus. Therefore, it is imperative to recognize and treat anemia for the sake of patient care.

**Objectives:** To evaluate the frequency of anemia in type 2 diabetic patients attending diabetic out patients clinics of Mirpurkhas, Sindh.

**Methodology:** A case-control study has been done to compare the hemoglobin level of type 2 diabetics and non-diabetics. The data was collected over a period of three months from the patients who were visiting the diabetes clinic for their regular checkup. Data for controls were collected from the patient's attendants. Diabetics and non-diabetics were under observations throughout the period. There were 206 subjects' including 106 diabetics (52 females and 54 males) and 100 non-diabetics (50 females and 50 males). Research concerns included the duration of the disease, family history & presence of hypertension. Methods such as cyan methemoglobin were used to estimate hemoglobin & random blood glucose by glucose oxidase as recommended by the World Health Organization (WHO) and then read through Micro-lab 300 chemistry analyzer.

**Results:** The frequency of occurrence of anemia in diabetics was 33.3% in males and 48.1% in females. Whereas in controls, 16.0% males and 32.0% females were anemic. The family history of diabetes and hypertension was also found higher among diabetic individuals as compared to healthy counterparts.

**Conclusion:** The study has shown that anemia is twice common in diabetics as compared with non-diabetics. Early diagnosis of anemia in a diabetic patient, and to treat so, will improve the quality of life and delay the complications to be developed in these patients.

### Keywords

Anemia, type 2 Diabetes mellitus, Hemoglobin, Microvascular complications.

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### Article info.

Received: June 29, 2020

Accepted: December 10, 2020

**Cite this article** Muhammad K, Mohsin S, Pirzada S, Qasmi SA, Kanpurwala MA. Frequency of Anemia among the Patients of type 2 Diabetes Attending Outpatient Clinic of Mirpurkhas, Sindh. *RADS J Biol Res Appl Sci.* 2020; 11(2):89-95.

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## INTRODUCTION

According to 2019 statistics, the prevalence of diabetes in Pakistan is 26.19%. About 19.05% of cases of diabetes mellitus were reported and 7.14% new cases

were found. Baqai Institute of Diabetology and Endocrinology (BIDE), Karachi conducted a survey (National Diabetes Survey) in association with Pakistan

Health Research Council, Diabetic Association of Pakistan, Ministry of Health Services, Regulations and Coordination, Islamabad and WHO Collaborating Centre in Pakistan. According to the National Diabetes Survey (2016-2017) by BIDE, it has been revealed that the prevalence of diabetes in Pakistan is about 35 to 38 million above the age of 20 years. Consequently, 26% of the Pakistani population is suffering from type 2 diabetes and around 14.47% of the population is pre-diabetic. Moreover, previous studies showed that the number of patients with type 2 diabetes in Pakistan were around 7-8 million or between 7-8% and it will rise up to 15-20% by 2040<sup>1</sup>.

It has been estimated by the International Diabetes Federation (IDF) that the budget of total global healthcare on diabetes has increased by about 8% as compared to 2015 diabetes expenditure estimation. Likewise, global expenditure on diabetes in 2017 was about 727 billion USD. In 2017, it had been estimated that about 327 million adults (age: 20-64) were diabetics worldwide, and it is predictable that the number may rise up to 438 million by 2045. Consequently, there are more chances to develop associated risk factors such as for overweight or obesity. Findings showed that there has been a high prevalence of diabetes in lower and middle-income countries over the past decade than in higher income countries<sup>2</sup>.

In 2012, the mortality rate of diabetic patients was around 1.5 million. Amongst this, 43% of the people were expired before 70 years of age, with higher death rate in lower and middle-income countries rather than in higher income countries. Type 2 diabetes is common in adults, but now the cases have also been reported in children. It is expected to have long term complications in younger age diabetics, and this may lead to have a social and economic burden in their productive years<sup>3</sup>.

Anemia can be defined as an inadequate RBC mass, to deliver oxygen sufficiently to tissues, peripherally<sup>4</sup>. Anemia is often unrecognized in diabetes mellitus, but previous studies showed that it is twice common in diabetics as compared with non-diabetics, which is a cause of increase in morbidity and mortality<sup>5</sup>. Diabetic patients are more prone to become anemic if associated with chronic kidney disease. Hematological features like leukocytosis and platelet abnormalities are also common in patients of type 2 diabetic mellitus<sup>6</sup>.

Anemia has an effect on the quality of life. Renal problem or anemia is the main clinical feature to examine the hematology of diabetes patients, but usually, it left unidentified due to the lack of diagnostics or poor financial condition of patients. The possibility to develop anemia is higher with age. If diabetics have a low level of hemoglobin, it may cause a higher risk of cardiovascular diseases, microvascular complications, and mortality. Furthermore, anemia is an extra burden for diabetics who have poor wound healing or less exertional ability. Diabetics can have a better quality of life and performance without anemic condition<sup>7</sup>.

Renal impairment is the problem associated with the anemic condition in diabetics. Therefore, it has been observed that there is a manifold risk of developing anemia or renal function problems in diabetic patients compared to those without diabetes. The condition is a self-sufficient predictor of undesirable results, such as pathetic quality of life, reduced physical function, weakens cognition, higher rate of infections, and mortality rate. It has also been observed that anemia is linked with impaired activity of daily life, increased disability, and hospitalization<sup>8</sup>.

To recognize and treat anemia properly is the fundamental aspect of patient care. Adults with diabetes are more prone to develop underlying complications as a result of dietetic deficiencies, inflammation, declined renal function, and bone marrow suppression<sup>9</sup>. Findings showed that the diabetics with anemia have increased risk of hypertension, ischemic heart diseases, stroke and chronic kidney diseases as compared to the patients have a normal level of hemoglobin<sup>10</sup>.

Pallor, fatigue and lassitude are common presenting symptoms in all anemic patients. The basic symptom of anemia is fatigue. But the pathogenesis of the condition regarding fatigue is still not clear. Some studies showed that abnormal energy metabolism leads to induce the condition of fatigue. Clinically, it has been proved that there is a direct relationship between anemia and fatigue. Consequently, fatigue occurs caused by lower hemoglobin levels<sup>11</sup>.

In patients with severe anemia; dyspnea, tachycardia, and dizziness or faintness are the prominent symptoms. In chronic anemia, only moderate dyspnea or palpitation may occur but, in some patients, congestive heart failure or

angina pectoris can be the main signs. The higher healthcare expenditure and mortality rate, along with poor clinical results are linked with low levels of hemoglobin and hematocrit in patients of Chronic Obstructive Pulmonary Disease (COPD)<sup>12</sup>. Peripheral neuropathy is the common complication of diabetes; severe anemia enhances the neuromuscular symptoms, headache, vertigo, tinnitus, lack of mental concentration, drowsiness, restlessness, and muscular weakness in many folds. The condition known as paraesthesia allied with other symptoms such as vitamin B<sub>12</sub> deficiency and peripheral neuropathy<sup>13</sup>. Metformin is the drug commonly used nowadays as a hypoglycemic agent, but the long term use of the drug may cause deficiency of vitamin B<sub>12</sub><sup>13</sup>. Therefore, it is important to recognize the important aspect by physicians to monitor for decreased levels of vitamin B<sub>12</sub> in diabetic patients while on metformin therapy<sup>14</sup>

Cognition is defined as "the intellectual action to acquire knowledge and understanding via thoughts, practice, and senses". Outcomes of anemic condition via cerebral hypoxia may causes deterioration in cognition and neurological role<sup>15</sup>. CNS functions are proper if the level of hemoglobin is normal. Development of cognition mainly depends on the levels of hemoglobin<sup>16</sup>. Anemia; as studies suggested, can promote and worsen the complications. Early detection and correction of anemia may improve and delay the complications. Anemic patients are prone to develop a variety of ophthalmologic problems. Diabetic retinopathy is the most common cause of macular degeneration which results in blindness. About 20% of patients have hard exudates, flame-shaped hemorrhages, cottonwood spots, or venous tortuousness affecting the retina. The hemorrhages arise even in the nonexistence of thrombocytopenia. Papilledema is related to anemia, it clears when the anemia disappears. Iron deficiency anemia reduces the thickness of the Retinal Nerve Fiber Layer (RNFL), especially in older age women. There were considerable relationships between hemoglobin and inferior quadrant RNFL thickness, serum iron, and nasal quadrant RNFL thickness, and ferritin concentrations and Total Iron-Binding Capacity (TIBC), as

well. Reduced RNFL may lead to the condition called glaucoma<sup>17</sup>.

Previous studies demonstrated that the frequency of anemia is higher in diabetics as compared to non-diabetics. Patients with diabetes for >10 years are more anemic. Anemia was graded as Mild, Moderate and Severe based on the WHO guidelines. Hence, it is important to diagnose anemia early in diabetics to avoid further complications which can help to increase the quality of life.

## MATERIAL AND METHODS

A study was done to compare the hemoglobin level of type 2 diabetic patients visiting a single diabetic clinic for routine follow up, and non-diabetics from same age group were taken as controls. According to the WHO criteria, patients are known as anemic when Hb is <13g/dl for males and <12g/dl for females. Samples were collected in BD Vacutainer blood collection tubes, (2 cc of blood in each tube) for hemoglobin in a tube containing potassium ethylenediaminetetra acetic acid (K<sub>2</sub>-EDTA) and for blood sugar random sample tube containing sodium fluoride as a glycolysis inhibitor.

Hemoglobin was estimated by using the cyanmethemoglobin method and reaction was read spectrophotometrically. Hemoglobin reagent was supplied by Merck diagnostic (merckotest 1.03317). Random blood glucose was estimated by Glucoseoxidase (GOD) enzymatic colorimetric method (reagent supplied by Disease diagnostics). Microlab 300 semi-automated chemistry analyzer by Merck diagnostic was used for reading the final reaction for all three tests.

The study was conducted on known diabetic subjects visiting Dr. Khan Diabetic Clinic at Mirpurkhas Sindh. The inclusion criteria include type 2 diabetic male and female age >45years, having diabetes for 5 years or more, with hypertension or without hypertension. The population study consists of every patient record who attended the clinic throughout a consecutive period of three months. The exclusion criteria included type 2 patients with renal, hematological or chronic liver disease. A sample size of 210 has been calculated using OpenEpi software as shown in Table 1.

**Table 1. Sample Size for Frequency in a Population.**

Population size (for finite population correction factor or fpc) (N):	1000000
Hypothesized % frequency of outcome factor in the population (p):	26.19% ± 5
Confidence limits as % of 100 (absolute ± %) (d):	5%
Design effect (for cluster surveys-DEFF):	1
Sample Size(n) for Various Confidence Levels	
Confidence Level (%)	Sample Size
90%	210

The data was analyzed through SPSS version 20.0. The descriptive data was presented in the form of frequency and percentage, while for the comparison of the case and control group the chi-square test was applied. To compare the mean value paired t-test was applied. The level of significance was considered as P<0.05. Statistical tests have been used at a 95% confidence interval. If the significance level is about 0.05 then the confidence level will be 95%. If the p-value is less than the level of significance, the hypothesis is statistically significant. If the confidence interval does not have any value for the null hypothesis, the results will be significant, statistically.

## RESULTS

The total sample size for the study was 210, but data of 4 individuals was discarded due to incomplete information. Out of 206, 106 were diabetics and 100 were controls (non-diabetics). Total number of males was 104 (54 diabetics

and 50 controls) which were in majority, whereas, females were 102 (52 diabetics and 50 controls). In overall cases, 43 (40.6%) were anemic, 33 (31.1%) had hypertensive history and 25 (23.6%) showed the family history of diabetes with the p-value <0.05. Whereas in controls, less number of anemic 24 (24.0%), hypertensive history 15 (1.0%) and diabetic family history 11 (11.0%) have been observed.

Family history of diabetes mellitus was found to be 13 (24.1%) in male diabetics and 5 (10.0%) in non-diabetic males. Family history of diabetes mellitus was found to be 12 (23.1%) in female diabetics and 6 (12.0%) in non-diabetic females. Hypertension was present in 16 (29.6%) male, 17 (32.7%) female cases. Out of 50 controls, 5 (10.0%) males and 10 (20.0%) females were hypertensive. Whereas, anemia was present in 18 (33.3%) male and 25 (48.1%) female cases (Table 2).

**Table 2. Comparison of Anemia, History of Hypertension and Family History of Diabetes in Cases and Control.**

Variables	Cases (n=106)	Control (n=100)	P-value
<b>Overall</b>			
Anemia	43 (40.6%)	24 (24.0%)	<0.011
History of Hypertension	33 (31.1%)	15 (15.0%)	<0.006
Family History of Diabetes	25 (23.6%)	11 (11.0%)	<0.017
<b>Male</b>	(n=54)	(n=50)	
Anemia	18 (33.3%)	8 (16.0%)	<0.041
History of Hypertension	16 (29.6%)	5 (10.0%)	<0.013
Family History of Diabetes	13 (24.1%)	5 (10.0%)	<0.058
<b>Female</b>	(n=52)	(n=50)	
Anemia	25 (48.1%)	16 (32.0%)	<0.098
History of Hypertension	17 (32.7%)	10 (20.0%)	<0.146
Family History of Diabetes	12 (23.1%)	6 (12.0%)	<0.142

**Table 3. Comparison of Age, Hemoglobin, Random Blood Sugar in Cases and Control.**

Variables	Cases	Control	P-value
<b>Overall</b>	(n=106)	(n=100)	
Age in years	56.2 ± 8.01	54.3 ± 8.22	<0.087
Hb. (g/dl)	12.0 ± 1.82	13.2 ± 1.61	<0.001
RBS (g/dl)	252 ± 65.7	106 ± 20.8	<0.001
<b>Male</b>	(n=54)	(n=50)	
Age in years	57.6 ± 8.18	55.2 ± 8.37	<0.131
Hb. (g/dl)	12.8 ± 1.62	14.3 ± 1.33	<0.001
RBS (g/dl)	253 ± 55.6	110 ± 21.5	<0.001
<b>Female</b>	(n=52)	(n=50)	
Age in years	54.7 ± 7.63	53.4 ± 8.06	<0.380
Hb. (g/dl)	11.1 ± 1.56	12.2 ± 1.09	<0.001
RBS (g/dl)	252 ± 71.8	110 ± 19.5	<0.001

The females were more anemic may be due to additional nutritional deficiencies and menstrual losses. According to the age distribution, the overall average age of the cases was 56.2 ± 8.01 and 54.3 ± 8.22 years of controls. The overall hemoglobin for diabetic cases were 12.0 ± 1.82 and for controls 13.2 ± 1.61 g/dl. Overall RBS (g/dl) of diabetic Cases 252 ± 65.7 and 110 ± 21.5 of controls were identified. Overall average (mean ± S.D) Hb. g/dl 12.0 ± 1.82 was less and RBS (g/dl) 252 ± 65.7 was higher in cases (diabetes) as compared to control 13.2 ± 1.61 and 106 ± 20.8 (p-value <0.01) (Table 3).

Results demonstrated that 85% of males cases were mild anemic and 15% has a moderate level anemia. Out of 52 diabetics females, 70% were mildly anemic, 30% were moderately anemic and no one from both groups was severely anemic. Thus frequency and severity of anemia is less in male diabetic cases than female diabetic cases.

## DISCUSSION

Diabetics are the patients with lower exertional capability and co-morbid vascular diseases, additionally, anemia causes more functional problems. If the person is anemic but not diabetic, he may have multiple risks such as heart diseases, microvascular complications, and mortality. However, treatment of anemia is the solution to improve performance and quality of life in diabetics<sup>18</sup>.

Studies showed that the family history of diabetes mellitus is vital for public health and it is the essential aspect to recognize patients of type 2 diabetes mellitus. In the USA, according to the survey of 2009-2014, it has been observed that about 10.1 million diagnosed diabetics were attributed with the family history<sup>19</sup>. Our findings also showed that

family history is the serious burden which contributes in the development of type 2 diabetes. The ratio is more in males rather than females.

According to some studies, there is a relationship between hypertension and diabetes mellitus. The prevalence of the disease increases with age, gender, glycemic index, type and duration of diabetes and other multiple factors. It has been identified that the mortality rate has been decreased with the proper management of blood pressure in patients with type 2 diabetes<sup>20</sup>. Our results also showed that there is a strong association between hypertension and diabetes mellitus. Hypertension was present in 16 (29.6%) male and 17 (32.7%) female cases.

It has been observed that about 14-23% of the type 2 diabetic patients are anemic. If diabetics don't consider anemia to be resolved, it turns into a serious issues such as severe fatigue and breathlessness. The risk of anemia also investigated according to the gender and level of the glycemic index. Type 2 diabetes is the disease which leads to a higher rate of mortality due to multiple complications such as micro or macrovascular. Findings also show that according to the gender-based investigations, anemia rate is higher in female diabetics rather than males, 31.57% and 10.44%, respectively. The ratio is generally considered especially for the patients who have higher HbA1c. The poor glycemic index also leads to a higher risk of the anemic condition in type 2 diabetic patients<sup>21</sup>. According to our results, the prevalence of anemia was considerably higher in diabetic patients than non-diabetes persons. Like previous studies, our results also showed that the prevalence rate was higher in females than males, while results were observed on gender basis. The females were

more anemic may be due to nutritional deficiencies and menstrual losses.

Findings of our study identified that overall anemia was 40.6%, hypertensive 31.1%, family history of diabetes 23.6% which illustrates that it is significantly higher in cases (diabetics) as compared to controls i.e. 24.0%, 1.0%, 11.0% with p-value <0.05. In males, anemia was 33.3% and a history of hypertension was 29.6% were significantly higher in diabetics as compared to the controls i.e. 16.0% and 10.0%, respectively with p-value <0.05. The correlation between the duration of diabetes and hemoglobin levels indicate a severe anemic condition with an increased diabetes duration. Patients with diabetes for >10 years have a severe anemic condition.

Observations were done which demonstrated that 85% of male diabetics were mild anemic and 15% were moderate anemic. Out of 52 female diabetics, 70% have mild anemia, whereas 30% have moderate anemia, while there were no severe anemic cases. Therefore, the frequency and severity of anemia was less in male diabetics than female diabetics group. Findings of some studies have been proved that there is a high prevalence rate of anemia in diabetic patients with renal malfunction. Specifically, the condition gets worst if not controlled properly. There is a need to understand the association of anemia with type 2 diabetes in order to optimize more treatments to reduce the chances of a serious type of diabetic complications<sup>22</sup>.

Though, anemia can misdiagnose hyperglycemia as it causes to identify the lower levels of HbA1c. Moreover, studies also show that diabetics with anemia are at risk to develop cardiovascular diseases which lead to heart failure. Recent findings show that anemia is the key risk factor to develop the End-Stage Renal Disease (ESRD) in diabetics or non-diabetics with Chronic Kidney Disease (CKD). Furthermore, detailed research is required to reveal the molecular and physiological mechanisms in order to understand the association of anemia with type 2 diabetes<sup>23</sup>.

## CONCLUSION

It has been concluded from our study that the occurrence of anemia is 50% more in patients with type 2 diabetes than non-diabetics of same age and gender. It also has been observed the frequency of anemia in diabetics, and the

anemia severity is correlated with the duration of diabetes (>10 years). The hematological profile should be included as a routine screening investigation to diagnose the anemia in a diabetic patient and treat accordingly. Whatever the type or pathophysiology of anemia therapeutic intervention; treatment of anemia in type 2 diabetic patient recovers the better quality of life by minimizing the chances of diabetes complications.

## RECOMMENDATION

We emphasize the early diagnosis of anemia and quick recommendation by specialist for standard treatment, and it is recommended that hematological profile should be included as a routine screening investigation in diabetic patients at least after 5 years of diabetes. Early treatment of anemia slows the progress of complications in diabetes, thus reducing hospitalization cost and mortality due to type 2 diabetes can be reduced considerably.

## LIMITATIONS OF THE STUDY

There were three months to complete the study, less number of cases and controls were analyzed. Larger sample size would not only be helpful in generalizing the results but we may understand other associated factors too.

## CONFLICTS OF INTEREST

None.

## FUNDING SOURCE

None.

## ACKNOWLEDGMENTS

None.

## LIST OF ABBREVIATIONS

COPD	Chronic Obstructive Pulmonary Disease
CKD	Chronic Kidney Disease
ESRD	End-Stage Renal Disease
GOD	Glucoseoxidase
Hb	Hemoglobin
IDF	International Diabetes Federation
K <sub>2</sub> -EDTA	Potassium Ethylenediaminetetra Acetic Acid
RNFL	Retinal Nerve Fiber Layer
TIBC	Total Iron-Binding Capacity

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