ORIGINAL ARTICLE

# To evaluate the renal function deterioration along with other anemia predictors in patients with diabetes mellitus type 2 in Karachi, Pakistan

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**Abstract**

**Object: The aim of our study is to determine the prevalence and evaluate the renal function deterioration along with other anemia predictors in patients with diabetes mellitus type 2 in Karachi, Pakistan.**

**Method: The type of study is a cross sectional study conducted for a period of 6 months duration from March 2015 to August 2015, at a tertiary care centre in Karachi, Pakistan. The patient population consisted of all the patients with diabetes mellitus type 2 over 20 years of age, who were being treated at our institute as outpatient visits. The patients involved in the study underwent an annual evaluation including various clinical and laboratory evaluations. A well designed proforma noted the patient's data. The criterion for anemia determination was set as per WHO standards. Estimated glomerular filtration rate (eGFR) was calculated with the MDRD (Modification of diet in renal disease) study group formula. Data was analyzed using SPSS version 23.**

**Results: The patient population consisted of 640 patients of which 340 were males and 300 were females, having a mean age of 56.5±10.5 years and an age range between 20 and 80 years of age respectively. The median duration of diabetes in the patients was 4 years, and females of the study population were likely to be obese (p-value of 0.042) and have poor control of the diabetes mellitus based on their HbA1c levels (p-value of 0.046), but males of the population consumed more tobacco products (p-value of less than 0.001) The mean hemoglobin level of the study population was found to be 13.1±2.0 g/dl in the male population and 12.2±1.5 g/dl in the female population having a p-value of less than 0.001 respectively. The prevalence of anemia according to the world health organization criteria was found to be in 267 patients, of which 129 were females and 138 were males, while according to the threshold of intervention 95 patients 50 females and 45 males have anemia, while 373 patients were not anemic. The mean estimated glomerular filtration rate (eGFR) was 86.1±31.8 ml/min/1.73 m2, and we found that patients with anemia had significantly lower of eGFR (eGFR= 72.8±35.8 ml/min/1.73 m2) as compared to non anemic patients (eGFR= 89.5± 29.6 ml/min/1.73 m2) having a p-value of less than 0.001 respectively. The trend is that as renal function deteriorates anemia prevalence increases and those patients with eGFR of less than 90 ml/min/1.73 m2 are twice as likely to suffer from anemia. The patients with eGFR less than 60 ml/min/1.73 m2 that is chronic renal failure, 37% patients were anemic and required intervention as compared to the 9.7% of patients without CRF having a p-value of less than 0.001.**

**Conclusion: Our study showed, the prevalence of anemia in type 2 diabetic patients in Karachi, is high, including the patients with normal renal functioning and those with chronic kidney disease. The decline renal functioning may contribute to the lower levels of hemoglobin, and it is recommended that diabetic patients be screened for anemia on a regular basis.**

**Keywords: Ch. kidney disease, anemia, type-II diabetes, estimated glomerular filtration rate**

**Introduction**:

The prevalence of diabetes and its complications have been on a rise in the under developed countries.[1,2] And it is estimated that the long term complications of diabetes will increase with time, in these countries due to low awareness and poor control of diabetes in the patients due to the lack of resources.[1,3] Diabetic nephropathy one of the microvascular diabetes complication can present with anemia, with the progressive deterioration of kidney function, and is reported at a prevalence of 13% in the European, 23% in the Australian and 46.5% in the Caribbean population respectively.[4-7] The presence of chronic kidney disease fails to explain all the diabetic anemic patients, various other sources for this anemia might be due to the erythropoietin deficiency, decline in the renal function, nutritional deficiency, inflammation and infectious disease.[8] Hence anemias that occur in diabetic patients have an earlier onset and is more severe, even without overt nephropathy.[9] The negative effects of anemia on life of diabetic patients is not well recognized by both the patients and the physicians.[10] The contribution of anemia to cardiovascular complications in the diabetic patient contributes to mortality, and an early intervention to cure anemia has proven to delay the onset of complication and improve the quality of life.[11-13] Currently the guidelines for diabetes management don't emphasize anemia, and the data is lacking from this part of the globe, concurrent diseases like nutritional deficiencies, genetics and infectious diseases may worsen the anemia burden, hence the aim of our study is to determine the prevalence and evaluate the renal function deterioration along with other anemia predictors in patients with diabetes mellitus type 2 in Karachi, Pakistan.

**Materials and methods**:

The type of study is a cross sectional study conducted for a period of 6 months duration from March 2015 to August 2015, at a tertiary care centre in Karachi, Pakistan. The patient population consisted of all the patients with diabetes mellitus type 2 over 20 years of age, who were being treated at our institute as outpatient visits. The patients involved in the study underwent an annual evaluation that includes but is not limited to, clinical examination including fundoscopy, assessment of diabetes, laboratory tests such as HbA1c levels, serum creatinine, lipid profile, protein uria by dip stick and other cardiovascular risk factors. The exclusion criterion was all the patients who had a known hematologic condition, or received blood transfusion in the last four months of assessment. A well designed proforma noted the patient's data which included history and examination, modifiable and non -modifiable risk factors, height, weight, body mass index (BMI), waist to hip ratio, abdominal obesity (measure as waist circumference of greater than 80 cm for females and greater than 94 cm for males) and other factors. The criteria for anemia determination was set as per WHO standards, that is a hemoglobin level of less than 12 g/dL for females and less than 13 g/dL for males.[14] Treatment of anemia was carried out at a blood hemoglobin level of less than 11 g/dL with erythropoietin analogs in CKD (threshold for intervention).[15] The rest of the blood parameters were set for anemia as follows, mean corpuscular volume (MCV) of less than 80 fl for microcytic anemia, between 80 fl and 100 fl for normocytic anemia, and greater than 100 fl for macrocytic anemia, while mean corpuscular hemoglobin concentration (MCHC) was set as hypochromic anemia as MCHC of less than 32 g/dL, normochromic anemia for MCHC greater than or equal to 32 g/dL. Estimated glomerular filtration rate (eGFR) was calculated with the MDRD (Modification of diet in renal disease) study group formula.[14] And the chronic kidney disease was classified into five groups, with group 1 having (eGFR ≥90), group 2 having (eGFR between 60 and 89), group 3 having (eGFR between 30 and 59), group 4 having (eGFR between 15 and 29) and group 5 having (eGFR <15).[15,16] Data was analyzed using SPSS version 23, for categorical variables use chi square test and for continuous variables use student t-test, means, standard deviations, frequencies and percentages are used where applicable. Univariate associations among the continuous variables was analyzed using Pearson

*Table 1:Demographic and other variables of the patient population*

| Characteristic | Total 640 | Males 340 | Females 300 | P value |
|---|---|---|---|---|
| Age in years | 56.5 ± 10.5 | 55.5 ± 9.6 | 56.6 ± 11.0 | 0.190 |
| Use of tobacco/smoking | 87 (13.50%) | 73 (21.47%) | 14 (4.66%) | <0.001 |
| BMI in kg/m2 | 29.3±14.6 | 28.1±5.2 | 30.5±6.5 | <0.001 |
| Overweight (BMI ≥ 25 kg/m2) | 469 (73.28%) | 239 (70.29%) | 230 (76.6%) | 0.042 |
| Obese (BMI ≥ 30 kg/m2) | 226 (35.31%) | 102 (30%) | 125 (41.66%) | 0.009 |
| Hip circumference | 105.4±12.4 | 103±10.7 | 109 ±13.4 | <0.001 |
| Waist circumference | 98.1±12.8 | 98.6±13.0 | 97.2±12.5 | 0.167 |
| Abdominal Obesity | 454 (70.93%) | 200 (58.82%) | 254 (84.66%) | <0.001 |
| Systolic blood pressure in mm of Hg | 137.1±21.7 | 137.8±22.3 | 136.1±21.2 | 0.339 |
| Diastolic blood pressure in mm of Hg | 82.2±12.4 | 82.0 ± 12.7 | 82.3 ± 12.1 | 0.764 |
| Hypertension | 398 (62.18%) | 208 (61.17%) | 190 (63.33%) | 0.542 |
| **Medication use** | | | | |
| Use of antihypertensive medications | 356 (55.62%) | 186 (29.06%) | 170 (56.66%) | 0.576 |
| ACEI or ARB | 312 (48.75%) | 165 (48.52%) | 147 (49%) | 0.575 |
| Diuretics | 222 (34.68%) | 116 (34.11%) | 106 (35.33%) | 0.654 |
| Calcium channel blockers | 144 (22.5%) | 70 (20.58%) | 74 (24.66%) | 0.129 |
| Beta blockers | 17 (2.65%) | 8 (2.35%) | 9 (3%) | 0.410 |
| Metformin | 516 (80.62%) | 270 (79.41%) | 246 (82%) | 0.696 |
| Sulfonylureas | 368 (57.5%) | 194 (57.05%) | 174 (58%) | 0.585 |
| Acarbose | 18 (2.81%) | 10 (2.94%) | 8 (2.66%) | 0.335 |
| Insulin | 72 (11.25%) | 39 (11.47%) | 33 (11%) | 0.383 |
| **Laboratory Analysis** | | | | |
| HbA1c in % | 8.6±2.5 | 8.2±2.4 | 8.4±2.7 | 0.046 |
| Fasting blood gluscose | 150±62 | 140±62 | 150±62 | 0.646 |
| Serum Creatinine levels in mg/dl | 1.09±0.46 | 1.21±0.59 | 0.92±0.35 | <0.001 |
| eGFR in ml/min/1.73m2 | 86.2±31.8 | 86.2±32.2 | 86.4±30.2 | >0.999 |
| **Diabetic complications on examination** | | | | |
| Retinopathy | 139 (21.71%) | 85 (25%) | 54 (18%) | 0.080 |
| Nephropathy | 215 (33.59%) | 130 (38.23%) | 85 (28.33%) | 0.020 |
| Neuropathy | 310 (48.43%) | 167 (49.11%) | 143 (47.66%) | 0.821 |

*Table 2:Prevalence of anemia in patients according to eGFR levels*

| eGFR levels | Anemia according to WHO classification | Anemia according to threshold of intervention |
|---|---|---|
| <15 | 100% | 87.5% |
| 12 to 29 | 75% | 62.5% |
| 30 to 59 | 55.9% | 27.4% |
| 60 to 89 | 41.2% | 10.6% |
| >90 | 31.6% | 6.8% |

correlation. Odds ratio (OR) with confidence intervals (CI) was used to identify determinants of anemia and were analyzed using multivariable logistic regressions. A p-value of less than 0.05 was considered to be statistically significant.

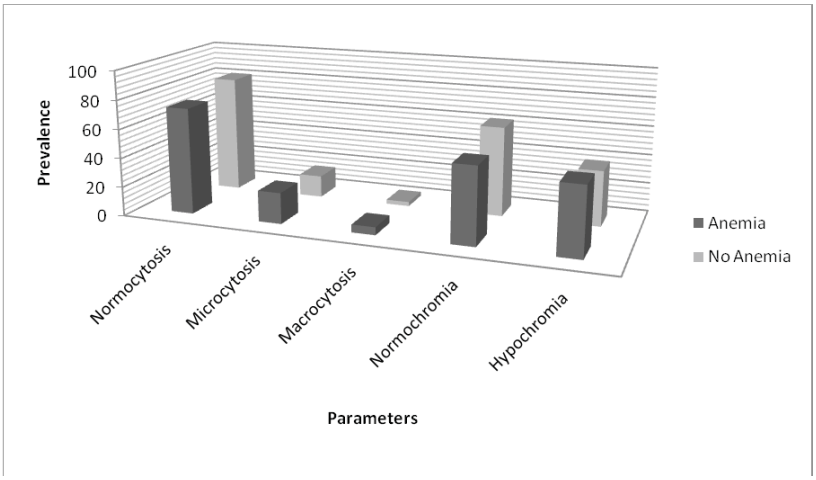
**Results**:

The patient population consisted of 640 patients of which 340 were males and 300 were females, having a mean age of 56.5±10.5 years and an age range between 20 and 80 years of age respectively. The median duration of diabetes in the patients was 4 years, and females of the study population were likely to be obese (p-value of 0.042) and have poor control of the diabetes mellitus based on their HbA1c levels (p-value of 0.046), but males of the population consumed more tobacco products (p-value of less than 0.001) For other demographic variables refer to table 1. The mean hemoglobin level of the study population was found to be 13.1±2.0 g/dl in the male population and 12.2±1.5 g/dl in the female population having a p value of less than 0.001 respectively. The prevalence of anemia according to the world health organization criteria was found to be in 267 patients, of which 129 were females and 138 were males, while according to the threshold of intervention 95 patients (females= 50, males= 45) were found to have anemia, while 373 patients were not anemic. The mean corpuscular volume (MCV) was found to be 86.2±7.6 fl, the patients with anemia and those without anemia had a statistically significant difference in the MCV having a p value of less than 0.001, with the anemic patients having microcytosis and macrocytosis respectively, refer to graph 1. The mean MCHC (mean corpuscular hemoglobin concentration) was found to be 32.3±2.6 in the patient population, with anemic patients having a low MCHC (47.19%) as compared to non anemic (38.06%) patients having a p value of 0.05. The incidence of proteinuria was found in 182 (68.16%) of anemic patients versus 214 (57.37%) of non anemic patients having a p value of 0.001. the mean estimated glomerular filtration rate (eGFR) was 86.1±31.8 ml/min/1.73 m2, and we found that patients with anemia had significantly lower values of eGFR (eGFR=72.8±35.8 ml/min/1.73 m2) as compared to non anemic patients (eGFR= 89.5±29.6 ml/min/1.73 m2) having a p value of less than 0.001 respectively. For cor-

*Table 3:Person correlation between variables and hemoglobin*

| Variable | P value | r (Pearson) |
|---|---|---|
| Age | 0.017 | -0.10 |
| Duration of diabetes | <0.001 | -0.18 |
| Systolic blood pressure | 0.005 | -0.11 |
| Diastolic blood pressure | 0.011 | -0.10 |
| Waist circumference | <0.001 | 0.15 |
| Hip circumference | 0.040 | 0.10 |
| eGFR | <0.001 | 0.29 |
| Fasting blood glucose level | <0.001 | 0.16 |
| HbA1c | 0.009 | 0.12 |
| Triglyceride | <0.001 | 0.15 |
| Serum Creatinine | <0.001 | -0.07 |

*Graph 1:Red Cell parameters between patients with and without anemia*




relation of anemia with eGFR refer to table 2, for Pearson correlation refer to table 3. According to the results of the eGFR values 273 (42.65%) of the patients had an eGFR of greater than 90 ml/min/1.73 m2, and among them 86 patients had anemia and 187 did not have anemia (with any other chronic kidney disease) having a p value of less than 0.001. And the trend is that as renal function deteriorates anemia prevalence increases and those patients with eGFR of less than 90 ml/min/1.73 m2 are twice as likely to suffer from anemia. The patients with eGFR less than 60 ml/min/1.73 m2 that is chronic renal failure, 37% patients were anemic and required intervention as compared to the 9.7% of patients without CRF having a p value of less than 0.001. The correlation of anemia with other variables is listed in table 3.

**Discussion**:

According to the results of our study, approximated 2 out of every 5 patients had anemia, and retinopathy and a decline in the renal functioning were deemed as independent determinants of anemia, also approximately a third of patients with normal renal functioning also were anemic, anemia decreases the patients functionality and quality of life and also affects the patients cardiovascular health and health in general.[11,17] In our study the prevalence of anemia was found to be in 41.71% of the patients which is slightly higher as compared to the study by WHO which showed a prevalence of 29.4%.[18] Our results are comparable or higher as compared to studies done in various different parts of the globe, the prevalence of anemia in the Caribbean is 46.5%, Ethiopia 17%, and 12% to 23% in the Caucasian countries.[5-7,19] These differences in the results could be due to the selection of the patient population, while Pakistan is a developing nation and co morbidities like nutritional deficiencies, poor glycaemic control, or asymptomatic hemoglobinopathies, as compared with the Caucasian nations.[20] The prevalence of chronic kidney disease in Pakistan is around 25.60%,[21] based on a study done in Karachi, and the risk factors for CKD are the same as in the Caucasian populations.[22] In our study the prevalence of anemia in patients with a normal eGFR was also high 29.21%, as compared to the 13% in the people of China.[23] Which can be explained by the nutritional and other deficiencies in our population. We found that diabetic retinopathy is a good indicator of anemia, which is in line with other studies.[24] Which is due to the fact that retinopathy is associated with nephropathy, but anemia might itself contribute to complications of diabetes,[25] We did not find a relationship between HbA1c levels and anemia, but some studies suggest that patients with normal hemoglobin levels had higher HbA1c levels.[26]

**Conclusion**:

According to our study, the prevalence of anemia in type 2 diabetic patients in Karachi, Pakistan is high, including the patients with normal renal functioning and those with chronic kidney disease. The decline renal functioning may

contribute to the lower levels of hemoglobin, and it is recommended that diabetic patients be screened for anemia on a regular basis.

**Conflict of interest**: None

**Funding source**: None

**Role and contribution of authors**:

Dr Kamal Ahmed, Assistant Professor Department of Medicine, Liaquat National Hospital Karachi did data collection, final layout and design of study

Dr Khurram Danial, Assistant Professor Nephrology, Karachi Medical and Dental College concept, study design, organizing draft, manuscript writing

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