

## ORIGINAL ARTICLES

## FREQUENCY OF MICROALBUMINURIA IN ABNORMAL LIPID METABOLISM AND SUFFERING FROM TYPE II DIABETES MELLITUS

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## ABSTRACT

**Objective:** To determine the frequency of dyslipidaemia in type-2 diabetic patients and to compare the frequency of dyslipidaemia in patients with and without microalbuminuria in type-2 diabetes.

**Study Design:** cross-sectional study.

**Place and Duration of Study:** Department of General Medicine, Combined Military Hospital Quetta Pakistan, from Dec 2018 to Jun 2019.

**Methodology:** All patients who fulfilled the inclusion criteria and visited General Medicine department of Combined Military Hospital Quetta with type II diabetes mellitus were included in the study. Blood sample following an 8-12 hours fasting over the last night and 24 hour urine sample for microalbuminuria was collected to assess the outcome i.e. frequency of dyslipidaemia and also its frequency with and without microalbuminuria.

**Result:** A total of 165 patients with type 2 diabetes mellitus were included. Ninety nine (60%) were males and 66 (40%) were females with the mean age of  $48.08 \pm 7.63$  years. Overall, dyslipidaemia was found in 48 (29.1%) patients, dyslipidaemia was noted in 29 (17.6%) with microalbuminuria and 19 (11.5%) without microalbuminuria. Chi-square test revealed that dyslipidaemia was significantly more in patients of diabetes mellitus having microalbuminuria than those not having it ( $p$ -value= 0.01).

**Conclusion:** Abnormal lipid metabolism was present in significantly more in patients with microalbuminuria as compared to those without microalbuminuria suffering from type II diabetes mellitus.

**Keywords:** Albuminuria, Diabetes mellitus, Dyslipidemia, Nephropathy.

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## INTRODUCTION

Diabetes and diabetes related conditions are a major cause of mortality and morbidity across the globe<sup>1</sup>. Cardiac problems may be associated with this multisystem disorder and affect the whole homeostasis of the body in one way or another. Atherosclerotic phenomenon is found more in patients suffering from diabetes as compared to those who have not been suffering from this illness. Majority of the patients with diabetes and atherosclerosis suffer from any macrovascular complication raising the mortality due to this disease<sup>2</sup>. Cardiovascular risk increase manifold in the patients having atherosclerosis secondary to diabetic changes. Quantitative lipoprotein abnormalities is one aspect of diabetic hyperlipidemias but qualitative and kinetic abnormalities result in a more atherogenic lipid profile among these patients<sup>3</sup>. Around 80% of patients with diabetes has risk of developing cardiovascular problems<sup>4</sup>. Raised low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C) levels, or elevated triglyceride (TG) levels

have been more commonly found abnormalities among patients suffering from DM. Decreased HDL-C and elevated LDL-C predict more cardiovascular disease among patients of diabetes according to a large recent study published in United kingdom<sup>5</sup>. There is no solution other than aggressive management of diabetes and hyperlipidaemias among these patients<sup>6</sup>.

Microalbuminuria has been a reliable indicator of subsequent proteinuria and chronic renal failure in all types of diabetes, but in type-2 DM it becomes more related to cardiovascular problems and mortality linked to these problems<sup>7</sup>. A good number of patients with this problem were also diagnosed with hypertension<sup>8</sup>. Microalbuminuria is important predictor of mortality and morbidity in number of medical conditions including Diabetes Mellitus, Hypertension, Chronic renal disease and peripheral vascular disease, therefore emphasis should be given on timely detection followed by a management plan<sup>8</sup>.

Ahmad *et al*<sup>8</sup>, showed in a study that frequency of dyslipidaemia was 59.6% in patients with type II diabetes. Alam *et al*<sup>9</sup>, has showed in a study that frequency of hypertriglyceridemia was 82.1% with microalbuminuria as compare to 60.41% without microalbu-

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minuria, Increased LDL-C was 91.14% versus 63.18% and decreased HDL-C 84.8% versus 72.24% in patients with type-II diabetes.

Primary prevention has always been the key strategy for managing any illness specially in our part of the world where cost effectiveness matters a lot. Therefore we planned to determine the frequency of dyslipidaemia and compare it in type 2 diabetic patients with and without microalbuminuria.

## METHODOLOGY

This cross sectional study was conducted at the department of General Medicine, Combined Military Hospital Quetta, from Dec 2017 to Jun 2018.

Sample size was calculated where expected proportion (dyslipidaemia)=59.6%<sup>8</sup>. Non-probability, consecutive sampling was used to recruit the sample population. Patients of both genders with age 35-60 years diagnosed as type II diabetes mellitus by the consultant physician were included in the study. Patients with macroalbuminuria (Urinary albumin excretion >300 mg/day) or history of any malignancy or liver or cardiac disease on medical record were excluded from the study. Patients who were having active urinary tract infection or those who were pregnant were also excluded from the study.

One hundred and sixty five patients fulfilling the inclusion criteria from outdoor department of general Medicine, CMH Quetta was included in the study after permission from ethical committee (IREB Itr no: CMH QTA-IRB/020) and research department of CPSP. Informed consent was taken from all the potential participants. Basic demographics like age, gender, weight, duration of diabetes were noted for all the patients included in the study.

Five ml of venous blood was drawn from the antecubital vein from all the subjects following an overnight fast of 8-12 hours after proper aseptic precautions, into sterile and disposable plastic syringes. After removing the needle, the blood was left in the syringe, covered with foil and transported to the laboratory. Data was collected for dyslipidemia and microalbuminuria as per operational definition by researcher himself on especially designed proforma.

Diabetes mellitus was defined as fasting blood glucose level of  $\geq 126$  mg/dl at two different occasions (two days apart) by laboratory test or patient is on chronic use of antihyperglycemic drugs on medical record<sup>1</sup>. Microalbuminuria was defined as excretion of 30-300mg of albumin per 24 hours (or 20-200 mcg/

min or 30-300 mcg/mg creatinine) in urine collections by laboratory test.

Dyslipidemia was labelled as: HDL-c: (<40 mg/dL), LDL-c: (>100 mg/dL) and triglyceride (Tg) level: (>150mg/dL). Data was analysed with statistical analysis program (IBM-SPSS-22). Frequency and percentage were computed for qualitative variables like gender, dyslipidemia and microalbuminuria. Mean  $\pm$  SD was presented for quantitative variables like age, duration of diabetes, weight, height and BMI. Chi square test was applied to compare dyslipidemia in patients with microalbuminuria and without microalbuminuria. The *p*-value  $\leq 0.05$  was considered statistically significant.

## RESULT

A total of 165 patients with type 2 diabetes mellitus (DM) were selected for this study. The mean age was  $48.08 \pm 7.63$  years. Ninety nine (60%) patients were males and 66 (40%) patients were females. The mean duration of diabetes mellitus was  $3.98 \pm 1.47$  years.

The mean height was  $1.69 \pm 0.21$  meters. The mean weight was  $67.76 \pm 15.06$  kg. The mean BMI was  $25.12 \pm 3.99$  kg/m<sup>2</sup>. In this study microalbuminuria was noted in 68 (41.2%) patients. Dyslipidemia was noted in 48 (29.1%) patients. The frequencies of age groups, gender, duration of DM, BMI and microalbuminuria were calculated according to Dyslipidemia (table-I). Dyslipidemia was noted in 29 (17.6%) patients

**Table-I: Characteristics of study participants.**

Factors	n (%)
<b>Age (years)</b>	
Mean $\pm$ SD	48.08 $\pm$ 7.631
Range (min-max)	30-59 years
<b>Gender</b>	
Male	99 (60)
Female	66 (40)
Duration of Diabetes mellitus	3.98 $\pm$ 1.47 years. 12 months-15 years
Mean Body Mass Index	25.12 $\pm$ 3.99 kg/m <sup>2</sup>
<b>Dyslipidemia</b>	
No	117 (70.9)
Yes	48 (29.1)

**Table-II: Dyslipidaemia in diabetes mellitus according to microalbuminuria (n=165).**

Type 2 Diabetes Mellitus patients	Dyslipidaemia, n(%)		<i>p</i> -value
	Yes	No	
With microalbuminuria	29 (17.6)	39 (23.6)	0.001
Without microalbuminuria	19 (11.5)	78 (47.3)	

with microalbuminuria and 19 (11.5%) without microalbuminuria and there was a statistically significant relationship between dyslipidemia and microalbuminuria ( $p$ -value  $<0.05$ ) as shown in table-II.

## DISCUSSION

Diabetes has been one of the commonest metabolic disorders in all parts of the world including our country. This multisystem and multidimensional disorder has a lot of physiological, psychological, metabolic, endocrine and neurological complications. We tried to focus on one or two metabolic aspects of this illness. It was observed that from our study participants 31.56% had microalbuminuria which is very similar to the results of a study done in United kingdom few years ago and in that study 30.8% showed this abnormality<sup>10</sup>. This number was around 14.2% in a study performed on patients of Iran and raised to 36.3% in a study done in India<sup>11</sup>. A very interesting MAP study showed that Korean patients have highest prevalence of microalbuminuria (24.2%) while patients of DM in Pakistan have lowest prevalence (5.5%) regarding albuminuria<sup>12</sup>.

Forty eight (29.1%) patients in our study had abnormal lipid profile where as Rosario<sup>13</sup>, reported that among patients of diabetes the number may go really high as lipid metabolism get grossly affected in diabetes mellitus. Multiple factors may be responsible for altered lipid metabolism among diabetes patients. Insulin resistance and defective insulin action on lipoprotein metabolism may be related to this finding. Thus, there is increased lipolysis with consecutively increased VLDL-C synthesis, TG rich LDL synthesis, increased Tg's and quick breakdown of HDL-C<sup>14</sup>. Renal impairment is also one of the serious consequences of altered lipid metabolism among the patients suffering from diabetes mellitus<sup>15,16</sup>. Proteinuria among these patients may be predictor of renal and cardiovascular mortality and must be taken seriously even if an incidental finding. Ravid *et al*<sup>17</sup>, found that albuminuria has a strong relationship with dyslipidaemia among the patients with type II DM. Similarly, Gall *et al*<sup>18</sup>, also documented similar association that albumin urinary excretion was linked with abnormal lipid profile among the diabetes patients. In Al-Jameil *et al*<sup>19</sup>, studied increased TC and LDL-C differ significantly between the their study groups and positively associated with ACR when correlated for all ranges of albuminuria at  $p < 0.05$  and  $p < 0.01$ <sup>20</sup>. A review concluded that if abnormal lipid profile has been managed effectively, it may control the progression of cardiovascular

events among the patients having diabetes as well as renal complication. Multiple factors may be linked with lipid lowering therapy but researches have widely documented that this therapy protect the individual from cardiac and vascular problems<sup>21,22</sup>. With the raised levels of TC, LDL-C, the levels of Tg, VLDL and TC/HDL-C ratio were also increased while HDL-C level was decreased among all the groups. TG, VLDL and TC/HDL-C ratio and HDL-C did not differ significantly between microalbuminuria and overt proteinuria; but DM with normo-albuminuria group. In our study dyslipidemia was noted in 29 (17.6%) patients with microalbuminuria and 19 (11.5%) without microalbuminuria. Ahmad *et al*<sup>22</sup>, studied this association in our setup and concluded that triglyceride levels have the strongest relationship with presence of albuminuria as compared to other lipid parameters. LDL and HDL levels had very weak or no association in this regard in the study of Ahmad *et al*<sup>22</sup>. Inference could be drawn from the above mentioned studies that poor control of diabetes creates a lot of biochemical problems leading to both dyslipidaemias and proteinurias.

Studies of Al-Jameil *et al*<sup>19</sup>, Rosario<sup>13</sup>, have similar findings but Shoji *et al*<sup>21</sup>, had different results in this regard and they reported that all the lipid parameters had no significant relationship with presence or absence of microalbuminuria among the patients suffering from type II DM. Study Kim *et al*<sup>22</sup>, is important in this regard as they also highlighted that triglyceride levels have a strong relationship with presence of microalbuminuria among diabetes patients. TC/HDL ratio has also been an area of interest for clinicians in type 2 diabetic patients and it has been well documented that it had a correlation microalbuminuria<sup>21</sup>.

## LIMITATION OF STUDY

This study had some limitations as well. Cross sectional study design and small sample size make the results non generalizable for local population. Only military hospital patients were included instead of a community or a multicentre study. This also adds to lack of generalizability of the results. Future researchers may plan community base or multicentric studies with better study design to generate more reliable, valid and accurate results.

## CONCLUSION

Abnormal lipid metabolism was present in significantly more in patients with microalbuminuria as compared to those without microalbuminuria suffering from type II diabetes mellitus.

**CONFLICT OF INTEREST**

This study has no conflict of interest to be declared by any author.

**REFERENCES**

1. Huang I, Lim MA, Pranata R. Diabetes mellitus is associated with increased mortality and severity of disease in COVID-19 pneumonia-A systematic review, meta-analysis, and meta-regression. *Diabetes Metab Syndr* 2020; 14(4): 395-403.
2. Vrablik M, Tumova E. Cholesterol metabolism in patient with type 2 diabetes. *Vnitr Lek* 2016; 62(3): 189-94.
3. Verges B. Pathophysiology of diabetic dyslipidemia: where are we?. *Diabetol* 2015; 58(5): 886-99.
4. Olvera Lopez E, Ballard BD, Jan A. Cardiovascular Disease. [Updated 2020 May 29]. In: Stat Pearls. Treasure Island (FL): Stat Pearls Publishing; 2020. [Internet] Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535419/>
5. Warraich HJ, Wong ND, Rana JS. Role of combination therapy in diabetic dyslipidemia. *Curr Cardiol Rep* 2015; 17(5): 32-36.
6. Corsino L, Dhatariya K, Umpierrez G. Management of Diabetes and Hyperglycemia in Hospitalized Patients. [Updated 2017 Oct 1]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2000. [Internet] Available from: <https://www.ncbi.nlm.nih.gov/books/NBK279093/>
7. Hadjadj S, Cariou B, Fumeron F, Gand E, Charpentier G, Roussel R, et al. Death, end-stage renal disease and renal function decline in patients with diabetic nephropathy in French cohorts of type-1 and type-2 diabetes. *Diabetol* 2016; 59(1): 208-16.
8. Ahmad T, Ulhaq I, Mawani M, Islam N. Microalbuminuria in type-2 diabetes mellitus; the tip of iceberg of diabetic complications. *Pak J Med Sci* 2017; 33(3): 519-23.
9. Alam MM, Parvez MA, Murtaza M. Microalbuminemia; frequency of microalbuminuria in type 2 diabetic patients. *Professional Med J* 2017; 24(3): 478-81.
10. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type-2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64) *Kidney Int* 2003; 63(1): 225-32.
11. Alrawahi AH, Rizvi S, Al-Riyami D, Al-Anqoodi Z. Prevalence and risk factors of diabetic nephropathy in omani type-2 diabetics in Al-dakhiliyah region. *Oman Med J* 2012; 27(3): 212-16.
12. Wu A, Kong N, De Leon F, Pan C, Tai T, Yeung V, et al. An alarmingly high prevalence of diabetic nephropathy in Asian type-2 diabetic patients: the microalbuminuria prevalence (MAP) Study. *Diabetol* 2005; 48(1): 17-26.
13. Rosario RF. Lipids and diabetic nephropathy. *Current Diabetes Reports* 2006; 6(1): 455-62.
14. Trovati M, Cavalot F. Optimization of hypolipidemic and antiplatelet treatment in the diabetic patients with renal disease. *J Am Soc Nephrol* 2004; 15(2): 12-20.
15. Gæde P, Vedel P, Larsen N, Jensen GVH, Parving H, Pedersen O. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med* 2003; 348(1): 383-93.
16. Sowers JR, Epstein M. Diabetes mellitus and associated hypertension, vascular disease, and nephropathy: an update. *Hypertension* 1995; 26(1): 869-79.
17. Ravid M, Neumann L, Lishner M. Plasma lipids and the progression of nephropathy in diabetes mellitus type 2: effect of ACE inhibitors. *Kidney Int* 1995; 47(3): 907-10.
18. Gall MA, Hougaard P, Borch-Johnsen K. Risk factors for development of incipient and overt diabetic nephropathy in patients with noninsulin-dependent diabetes mellitus: prospective observational study. *Br Med J* 1997; 314(1): 783-88.
19. Danesh FR, Kanwar YS. Modulatory effects of HMG-CoA reductase inhibitors in diabetic microangiopathy. *FASEB J* 2004; 18(1): 805-15.
20. Al-Jameil N, Khan FA, Arjum S, Khan MF, Tabassum H. Dyslipidemia and its correlation with type 2 diabetic patients at different stages of proteinuria. *Biomedical Res* 2014; 25(3): 227-31.
21. Rosenson RS. Treatment of hyperlipidemia and beyond. *Expert Rev Cardiovascular Therap* 2008; 6(13): 19-30.
22. Shoji T, Emoto M, Kawagishi T. Atherogenic lipo-protein changes in diabetic nephropathy. *Atherosclerosis* 2011; 156(2): 425-33.
23. Ahmad T, Ulhaq I, Mawani M, Islam N. Microalbuminuria in type-2 diabetes mellitus; the tip of iceberg of diabetic complications. *Pak J Med Sci* 2017; 33(3): 519-22.