



## ASSOCIATION OF HIGH DENSITY LIPOPROTEIN LEVELS WITH ADVANCING AGE IN TYPE 2 DIABETES PATIENTS IN TERTIARY HOSPITAL.

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**ABSTRACT... Background:** HDL particles have several biological functions. Low levels of HDL-cholesterol are responsible for atherosclerotic disease. Type 2 diabetes is a metabolic disease of chronic etiology and low HDL-cholesterol is frequent finding in diabetics. Levels of HDL with advancing age are inconsistent, few study show decline in HDL with increasing age while others show vice versa results. **Objectives:** Objective of this study was to establish an association between low HDL levels with advancing age in type 2 diabetic patients. **Study Design:** Cross sectional descriptive study. **Setting:** Diabetes Outpatient Department Nishtar Hospital Multan. **Period:** 6 months extending from March 2018 to August 2018. **Materials and Methods:** 145 patients with newly or previously diagnosed type 2 diabetes mellitus, age >35 years were considered for the study. Those diabetics who had family history of dyslipidemias (to rule out familial hyperlipidemias) were excluded. Study was started after acquiring permission from ethical committee. All the patients were evaluated for the HDL levels by getting a fasting lipid assay. **Results:** Out of 145 cases 78 (53.6%) were males while remaining 67 (46.4%) were female. Mean age of the patients was  $57.27 \pm 6.91$  years. Mean HDL level was  $37.82 \pm 8.42$ . It was seen that HDL is low in 116/145 (80%) patients. Those diabetic patients who were  $\leq 60$  (91 cases), HDL was noticed to be low in 67/91 (73.62%) patients. Among patients >60 years (54 cases), HDL was identified to be low in 49/54 (90.7%) patients. P-value was found out to be 0.012 **Conclusion:** Due to falling levels of HDL with advancing age in diabetic patients, there is increase in cardiovascular events in elderly diabetic patients. So the measures which tend to increase HDL level will also give protection against adverse cardiovascular event in elderly diabetics.

**Key words:** Advancing Age, Low HDL, Type 2 Diabetes Mellitus

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### INTRODUCTION

HDL particles have several biological functions, the most important is the ability of HDL to promote efflux of cholesterol from cells and help to transport cholesterol in reverse direction from lipid laden macrophages. Low levels of HDL-cholesterol are responsible for atherosclerotic disease in an indirect way by causing increased concentration of triglyceride-rich lipoproteins. Low levels of HDL-cholesterol potentially aggravates the chances of adverse coronary events in individuals already having CAD as well as among those who don't have previous CAD.<sup>1-2</sup> It also potentiates the risk of silent myocardial infarction and silent coronary artery disease in high risk T2DM patients.<sup>3</sup> Although Low-HDL levels are predictor of CHD

irrespective of sex, ethnicity and race, however, the data supporting its role in cardio protection is lacking.<sup>4-6</sup>

Type 2 diabetes is a metabolic disease of chronic etiology which occurs due to defective action and/or secretion of insulin. Low HDL-cholesterol is frequent finding in diabetes<sup>7-8</sup> every second diabetic female has low levels of HDL-cholesterol and every forth diabetic male has very low HDL-cholesterol. Initial observational studies recognized HDL-cholesterol as a potent independent factor for increasing cardiovascular (CV) hazards among those patients who are already taking optimum statin dose.<sup>9-10</sup> Park JH et al<sup>11</sup>, noticed that the HDL-C level in males tend

to fall linearly, while a more rapid decline of these levels was seen in females during their middle age period. It has been seen that the HDL-C level in the elder members of longevity family remain higher as compared to younger members of non-longevity family. HDL-C tends to remain high in healthier elderly persons when compared with younger persons with co-existing diabetes and coronary artery disease.<sup>12</sup> Various cross sectional and longitudinal studies show that HDL-cholesterol concentration is higher in healthy older subjects.<sup>13-17</sup> Numerous studies show that HDL-Cholesterol level changes with growing age is not consistent.<sup>18-23</sup> Some studies illustrated that HDL-C declines<sup>20-22</sup> with increasing age while other suggest that HDL-C does not change with advancing age.<sup>18,23</sup>

Walter noticed that plasma HDL-C levels tend to fall in men during teenage and early youth, however in old age individuals levels either remain unchanged or tend to rise.<sup>24</sup> On the other hand HDL-C levels in females remains invariably stable throughout the span of their life, however, once menopause occurs only there and then HDL-C concentration starts falling.<sup>25</sup>

All the previous work has been done to see the relationship of HDL levels with advancing age in otherwise healthy people. Little work has been done to look for this association in diabetic population who are more prone to untoward effects of low HDL. This study will provide a good baseline data to establish the relation of low HDL with increasing age in diabetic population. It would also help in taking measures to prevent fall in HDL in elderly diabetic so that adverse cardiovascular risk can be minimized.

## OBJECTIVE

Purpose of carrying out this study was to establish any relation between low HDL levels and advancing age in type 2 diabetic patients.

## OPERATIONAL DEFINITIONS

### Low HDL Levels

Low HDL is defined as HDL <40mg/dl for males and <50mg/dl for females.

## Type 2 Diabetes

Patients already diagnosed as T2DM or recently diagnosed on the grounds of fasting blood sugar levels > 126 mg/dl or 2 hours after meal blood sugar level > 200mg/dl in a patient over 35 years of age.

## Setting

Diabetes Outpatient Department Nishtar Hospital Multan.

## Duration of Study

6 months extending from March 2018 to August 2018.

## Sampling Technique

Consecutive non probability

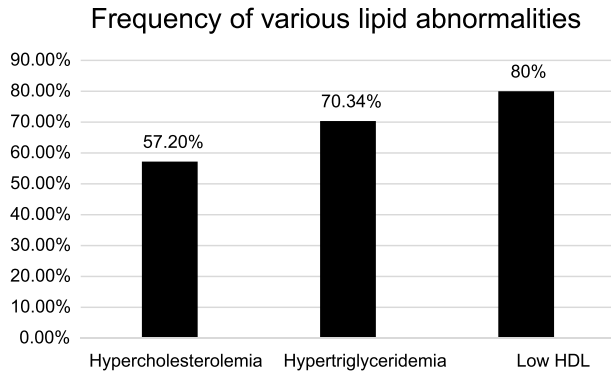
## Data Collection Procedure

145 consecutive patients diagnosed with non-insulin dependent diabetes mellitus who attended the diabetes outdoor clinic and meeting the inclusion criteria were considered for the study. Study was started after acquiring permission from ethical committee. After taking duly signed informed consent individuals having diabetes were enrolled. All the patients were evaluated for the HDL levels by getting a fasting lipid assay from Central Lab. of Nishtar Hospital. The results were entered in a specially designed proforma. All the data was analysed by using SPSS version 20. Mean and standard deviation for age, duration of diabetes and serum HDL were calculated. Frequencies were calculated for low HDL level with respect to age groups. Stratification was done for variables of age, gender, duration of diabetes. Chi-square test was applied to see the association of HDL level with advancing age. P-value < 0.05 was considered significant.

## RESULTS

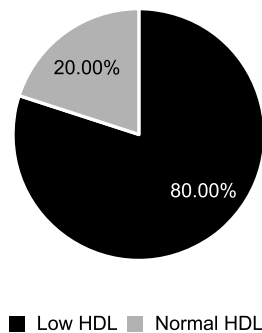
A total of 145 patients were taken as study cases. Out of these 78 (53.6%) were males while remaining 67 (46.4%) were female. Mean age of the patients was 57.27 + 6.91 years. Mean duration of diabetes mellitus was 9.22 + 4.69 years. Frequencies of various lipid abnormalities seen in study population were hypercholesterolemia (57.20%), hypertriglyceridemia (70.34%) and low

HDL (80%) Graph-1). Mean HDL level was  $37.82 + 8.42$ . It was seen that HDL is low in 116/145 (80%) patients (Graph-2). Among 78 diabetic male patients mean HDL was  $36.01 + 7.65$  and among 67 female patients mean HDL was  $42.09 + 7.89$ . So HDL levels were low in male patients as compared to female patients.



**Figure-1. Frequency of various lipid abnormalities in study population.**

**Frequency of low HDL**



**Figure-2. Frequency of low HDL in study population.**

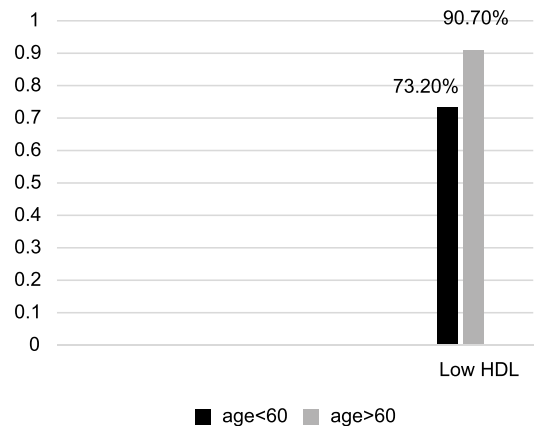
In age group < 60 years, there were 91 patients, males were 54/91(59.34%) while females were 37/91(40.65%). Mean duration of diabetes mellitus was  $8.075 + 2.105$  years, mean HDL level was  $39.07 + 8.6$  and HDL was low in 67/91(73.62%) patients. Hyperlipidaemias was present in 72/91(79.27%). Serum triglyceride was found to be high in 63/91(69.36%). LDL was found to be high in 54/91(59.45%). There were 24(16.5%) males and 30(20.65%) females.

In age group >60 years, there were 54 patients in total, male were 24(16.5%) and female were 30(20.65%). Mean duration of diabetes mellitus

was  $11.59 + 2.59$  years, mean HDL level was  $38.85 + 7.83$ . HDL was found to be low in 49/54(90.7%) patients. P-value for association of low HDL and advancing age was found out to be 0.012 (Table-I, Figure-3).

	Age ≤ 60 N = 111	Age > 60 N = 34	P-Value
Males	54/91 (59.34%)	24/54 (44.45%)	0.043
Females	37/91 (40.65%)	30/34 (55.56%)	
Mean duration of DM	8.075 ± 2.105	11.59 ± 2.59	< 0.001
Low HDL	67/91 (73.62%)	49/54 (90.7%)	0.012

**Table-I. Association of gender, duration of diabetes and low HDL with advancing age.**



**Figure-3. Association of age and low levels HDL in diabetic population.**

**DISCUSSION**

The purpose of this study was to identify any relation between HDL levels and advancing age in diabetic population. The main findings were that HDL-C concentration decreases with increase in age in diabetic people. This study strongly endorses the notion that other measures like physical activity and drugs like fibrates may be recommended to increase HDL-C in elderly diabetics.

Diabetes mellitus (DM) is a cluster of several metabolic derangements. Classical derangements in lipid metabolism in type 2 diabetics include high triglycerides (Tg) levels, low levels of high density lipoprotein cholesterol (HDL-c) levels, and increased concentration of LDL. US National

Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III [ATP III]) declared in their 3rd report those diabetics who have low levels of high-density lipoprotein cholesterol (HDL-C) have profound risk factor for ischemic heart disease.<sup>26</sup>

In our study, we noticed that HDL was low in 116 (80%) patients and it was the most frequently occurring dyslipidaemia in our patients with T2DM. Harris SB et al<sup>27</sup>, discussed the common patterns of diabetic dyslipidaemias which showed that high-density lipoprotein-cholesterol (HDL) levels below normal is the commonest finding. It is also in coherence with another study<sup>28</sup> conducted in department of medicine Nepalgunj medical college and Teaching Hospital, Banke, Nepal, which showed abnormally low levels of HDL as the largest abnormality (62%) then there was hypertriglyceridemia (56.5%), then hypercholesterolemia (53.7%) and the least was high LDL in (44.4%). Weerarathna TP et al.<sup>29</sup> found prevalence of low HDL as 17.6%.

In a Pakistani research carried out by Ahmad N, et al.<sup>30</sup> 100 patients with T2DM were studied and not a single patients had a low HDL-Cholesterol. It is a very unusual finding in type 2 diabetics. It may be attributed to very small size of the sample or some laboratory related error.

In our study we see that male diabetic patients had lower levels of HDL as compared to females. In a study conducted by Gilani SY et al<sup>31</sup>, low HDL was found to be more common in females than males ( $p < 0.05$ ). This difference may be because of inequality of male and female sample in our study.

An interesting aspect of our study is that we have tried to see relation between HDL levels and increase in age in diabetic patients. Previously, a very little work has been so far done to establish an association between the two. In order to see this association we divided type 2 diabetic people in two groups. Those diabetic patient who were less than 60 years age had 73.62% frequency of low HDL levels. Patients above 60 years age

had 90.7% frequency of low HDL levels. P-value was found to be 0.012 which shows a significant relation between low HDL levels with advancing age in type 2 diabetic people. Windler E et al<sup>32</sup> and Saleheen D et al<sup>33</sup> noticed that level of HDL tend to rise with increasing age. Wilson PW et al.<sup>34</sup> had also similar findings. These are quite in accordance with our study. However, all these studies observed trends of low HDL in otherwise healthy population. Contrary to that Weerarathna TP et al<sup>29</sup> found that in diabetic patients low HDL had more strong relation with younger age in Sri Lankan population.

## CONCLUSION

In contrary to previous data which suggests that changes in HDL cholesterol with advancing age are nonlinear, our study shows that patients with non-insulin dependent DM have a linear association between HDL cholesterol and increase in age. Due to falling levels of HDL with advancing age in diabetic patients, there is increase in cardiovascular events in elderly diabetic patients. So the measures which tend to increase HDL level will also give protection against adverse cardiovascular event in elderly diabetics.

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### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Shahzad Alam Khan	Conception of idea, Planning, Data analysis.	
2	Iqra Imtiaz	Data collection.	