

## Association of High Density Lipoprotein Cholesterol with Renal Function in Type 2 Diabetic Subjects in a Bangladeshi Population

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### Abstract

**Background:** Abnormalities in lipid metabolism are associated with renal diseases. Association of serum lipid parameters with renal function is less studied in subjects with type 2 diabetes in Bangladeshi population. **Objective:** To assess the correlation of high density lipoprotein cholesterol with glomerular filtration rate (GFR) in type 2 diabetic subjects. **Materials and Methods:** One thousand three hundred thirty confirmed diabetic subjects advised for HbA<sub>1c</sub>, serum creatinine, serum total cholesterol, serum triglycerides, serum HDL cholesterol and LDL cholesterol were included in the study. Serum total cholesterol, HDL cholesterol, triglyceride, serum creatinine, HbA<sub>1c</sub> were measured by standard methods and serum LDL cholesterol was calculated by Friedewald's formula. GFR was calculated by MDRD4 variables prediction equation. Total subjects were grouped according to sex; both males and females were subdivided into three subgroups depending on GFR values. Results of lipid parameters were compared by one-way ANOVA among different groups and correlation of lipid parameters with GFR were expressed by Pearson r. **Results:** HDL cholesterol was significantly different among different GFR groups ( $p < 0.05$ ) and positively correlated with GFR ( $r = 0.1386$ ,  $p < 0.001$ ) in males. Total cholesterol and LDL cholesterol showed feeble positive correlation with GFR ( $r = 0.0789$ ,  $p < 0.05$  for total cholesterol and  $r = 0.0768$ ,  $p < 0.05$  for LDL cholesterol), but are not significantly different among GFR groups ( $p > 0.05$ ) in males. Total cholesterol, HDL cholesterol, LDL cholesterol, non-HDL cholesterol and LDL-C/HDL-C were significantly different among three different GFR groups ( $p < 0.01$ ) and only HDL cholesterol and LDL-C/HDL-C showed weak correlation with GFR ( $r = 0.0770$ ,  $p < 0.05$  for HDL cholesterol and  $r = -0.0803$ ,  $p < 0.05$  for LDL-C/HDL-C) in females. **Conclusion:** The study revealed that HDL cholesterol was significantly and positively correlated with glomerular filtration rate in both male and female diabetic subjects and assessment of lipid parameters might be a helpful tool to prevent or delay the progression of renal insufficiency.

**Key words:** Type 2 diabetes, Glomerular filtration rate, Serum lipid parameters

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### Introduction

Abnormalities in lipid metabolism are associated with renal diseases in both diabetic and non-diabetic subjects. There is an inverse association of serum lipids with renal function.<sup>1,2</sup> Lipid associated renal

dysfunction may be mediated by tubulointerstitial inflammation, foam cell formation and tissue injury<sup>3,4</sup>, matrix production and glomerulosclerosis due to accumulation of native and oxidized low-

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density lipoprotein (LDL) in glomerular mesangium.<sup>5-7</sup> Low plasma high-density lipoprotein (HDL) has been identified as an independent risk factor for progression of renal disease.<sup>8,9</sup> Animal studies showed that consumption of lipid-rich diet exacerbates and correction of hyperlipidemia attenuates the severity of glomerulosclerosis and tubulointerstitial fibrosis<sup>3,6,10-12</sup> and normalization of HDL metabolism without changing serum total cholesterol retards the progression of renal disease in 5/6 nephrectomized rats.<sup>13</sup> Studies on animal models of hyperlipidemia including apo-lipoprotein E knockout (apo E-KO) mice and Otsuka Long Evans Tokushima Fatty (OLETF) rats have also suggested the association of hyperlipidemia with the development of early renal lesions.<sup>14,15</sup> Moreover, HDL serves as a potent endogenous inhibitor of inflammation, platelet adhesion and LDL oxidation.<sup>16</sup> Since type 2 diabetes is recognized as an inflammatory condition associated with insulin resistance<sup>17</sup> and abnormal endothelial vascular reactivity<sup>18</sup>, HDL particles may partly play role to prevent progression of renal injury. We conducted this study to evaluate the relationship of lipid parameters, particularly HDL cholesterol with GFR in type 2 diabetic subjects in a Bangladeshi population.

### Materials and Methods

This cross sectional study was carried out in the Department of Clinical Biochemistry, Bangladesh Institute of Health Sciences, Dhaka during July 2010 to August 2010. One thousand three hundred thirty specimens of confirmed diabetic subjects, both males and females, advised for HbA<sub>1c</sub>, serum creatinine, serum total cholesterol, serum triglycerides, serum HDL cholesterol and LDL cholesterol were included for the study. HbA<sub>1c</sub> was measured by HPLC based automated analyzer D-10™ (Bio-Rad, USA), serum creatinine was measured by modified Jaffe's method using Dimension RxL Max (Siemens Health Care Ltd.). Serum total cholesterol, serum triglyceride and serum HDL cholesterol concentrations were measured by kits manufactured by Siemens Health Care Ltd. using Dimension RxL Max automated analyzer. Serum LDL cholesterol was calculated by Friedewald's formula<sup>19</sup> and eGFR was calculated using the simplified MDRD4 equation.<sup>20</sup> Subjects were grouped according to sex, both males and females were subdivided into three groups depending

to eGFR (Group-I, eGFR < 60 mL/min/1.73m<sup>2</sup> for males, eGFR < 55 mL/min/1.73m<sup>2</sup> for females; Group-II, eGFR 60–89 mL/min/1.73m<sup>2</sup> for males, eGFR 55–85 mL/min/1.73m<sup>2</sup> for females and Group-III, eGFR > 89 mL/min/1.73m<sup>2</sup> for males, eGFR > 85 mL/min/1.73m<sup>2</sup> for females). Results are expressed as mean ± SD and correlation of lipid parameters with eGFR were done by Statsoft STATISTICA version 8 for windows in the total study subjects, in male and female subjects and compared by GraphPad Prism version 5.03 for windows.

### Results

The mean ± SD of age of the total study subjects was 50.12 ± 11.65 years. Of the total study subjects 653 (49%) were males and 677 (51%) were females. In the total population mean ± SD of HbA<sub>1c</sub>, serum total cholesterol, serum triglycerides, serum HDL cholesterol, serum LDL cholesterol, non-HDL cholesterol, serum creatinine and estimated GFR were 9.28 ± 2.43%, 186.93 ± 44.04 mg/dL, 200.38 ± 147.5 mg/dL, 38.48 ± 8.28 mg/dL, 110.26 ± 37.13 mg/dL, 148.24 ± 42.89 mg/dL, 0.99 ± 0.28 mg/dL and 79.5 ± 20.98 mL/min/1.73m<sup>2</sup> respectively. In the total study population eGFR significantly correlated with age ( $r = -0.5076$ ,  $p < 0.0001$ ), HDL cholesterol ( $r = 0.0669$ ,  $p < 0.05$ ) but not with HbA<sub>1c</sub> ( $r = 0.0400$ ,  $p > 0.05$ ), total cholesterol ( $r = 0.0015$ ,  $p > 0.05$ ), triglycerides ( $r = -0.0199$ ,  $p > 0.05$ ), LDL cholesterol ( $r = 0.0134$ ,  $p > 0.05$ ), non-HDL cholesterol ( $r = -0.0115$ ,  $p > 0.05$ ) and LDL-C/HDL-C ( $r = -0.0313$ ,  $p > 0.05$ ). Comparison of different variables between males and females are shown in Table I. Serum total cholesterol, serum HDL cholesterol, serum LDL cholesterol were significantly higher in females than males (Table I) and serum triglyceride, serum LDL-C/HDL-C, serum creatinine and eGFR were significantly lower in females than in males (Table I). No statistically significant difference was observed for age, HbA<sub>1c</sub> and non-HDL cholesterol between males and females.

Comparison of lipid parameters among the three predefined eGFR groups is shown in Table II. One way ANOVA showed that only HDL cholesterol was significantly different among three eGFR groups in male diabetic subjects (Fig 1A) and total cholesterol, HDL cholesterol (Fig 1B), LDL cholesterol, non-

HDL cholesterol and LDL-C/HDL-C were significantly different among different eGFR groups in female diabetic subjects (Table II).

The correlation coefficient of age, HbA<sub>1c</sub> and lipid parameters with GFR is presented in Table III. The correlation coefficients of total cholesterol, HDL cholesterol and LDL cholesterol are statistically signi-

ficant with eGFR in male diabetic subjects and correlation coefficients of HDL cholesterol and LDL-C/HDL-C are statistically significant with eGFR in female diabetic subjects (Table III). The correlation coefficient of HDL cholesterol is statistically significant in the total study population, and also in male and female diabetic subjects.

Table I: Comparison of different variables between male and female diabetic subjects

Variables	Male (n = 653)	Female (n = 677)	t values	p values
Sex (%)	49	51		
Age (years)	50.47±11.40	49.78±11.89	1.094	0.2744
HbA <sub>1c</sub> (%)	9.33±2.46	9.23±2.40	0.7443	0.4568
Serum total cholesterol (mg/dL)	182.3±42.58	191.4±44.97	3.815	0.001
Serum triglycerides (mg/dL)	208.7±167.8	192.4±124.5	2.011	0.0446
Serum HDL cholesterol (mg/dL)	36.00±7.12	40.86±8.63	11.18	<0.0001
Serum LDL cholesterol (mg/dL)	107.1±36.14	113.3±37.84	3.062	0.0022
Serum non-HDL cholesterol (mg/dL)	146.3±41.71	150.1±43.93	1.646	0.1001
Serum LDL-C/HDL-C	3.05±1.08	2.85±1.00	3.556	0.0004
Serum creatinine (mg/dL)	1.08±0.25	0.90±0.28	12.10	<0.0001
eGFR (ml/min/1.73m <sup>2</sup> )	81.74±19.49	77.35±22.12	3.838	0.0001

Table II: Comparison of lipid parameters among different GFR groups in male and female diabetic subjects

Parameters	Sex	Group-I	Group-II	Group-III	p values
Serum total cholesterol (mg/dL)	Male	177.7±39.54	181.3±41.92	185.9±44.87	0.2686
	Female	182.7±45.61	192.8±47.24	185.3±39.47	0.0003
Serum triglycerides (mg/dL)	Male	205.9±100.4	203.9±131.7	218.5±235.9	0.6042
	Female	195.9±97.58	198.4±107.2	181.7±155.8	0.2784
Serum HDL cholesterol (mg/dL)	Male	34.13±6.42	35.80±7.04	37.15±7.37	0.0032
	Female	37.64±9.03	41.49±8.40	41.38±8.48	0.0002
Serum LDL cholesterol (mg/dL)	Male	103.9±36.38	106.7±35.47	109.1±37.31	0.5221
	Female	106.1±38.47	118.3±39.94	109.2±33.14	0.0019
Serum non-HDL cholesterol (mg/dL)	Male	143.6±39.63	145.5±41.04	148.8±43.82	0.5514
	Female	145.1±44.87	156.7±45.23	143.9±37.92	0.0009
Serum LDL-C/HDL-C	Male	3.14±1.18	3.06±1.07	3.01±1.06	0.6194
	Female	2.95±1.23	2.91±1.01	2.71±0.89	0.0298

Table III: Correlation of age, HbA1c and lipid parameters with GFR in males and females

Variables	Male	Female
Age	-0.4769***	-0.5443***
HbA1c	0.0672 <sup>NS</sup>	0.0127 <sup>NS</sup>
Serum total cholesterol	0.0789*	-0.0410 <sup>NS</sup>
Serum triglycerides	-0.0019 <sup>NS</sup>	-0.0542 <sup>NS</sup>
Serum HDL cholesterol	0.1386***	0.0770*
Serum LDL cholesterol	0.0768*	-0.0217 <sup>NS</sup>
Serum non-HDL cholesterol	0.0569 <sup>NS</sup>	-0.0580 <sup>NS</sup>
Serum LDL-C/HDL-C	0.0001 <sup>NS</sup>	-0.0803*

\*, p<0.05; \*\*, p<0.01; \*\*\*, p<0.001; NS, Not significant

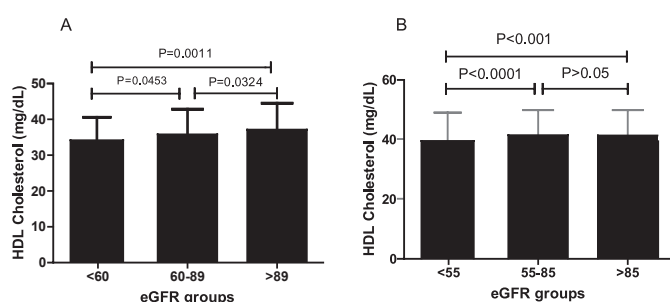


Fig 1. Comparison of HDL cholesterol among different GFR groups in males (A) and in females (B) [eGFR is expressed in mL/min/1.73m<sup>2</sup>]

### Discussion

In this study on diabetic subjects we observed significant differences of all lipid parameters except non-HDL cholesterol between males and females. Serum creatinine and eGFR were also significantly different between males and females. So we analyzed the association of lipid parameters with eGFR in male and female diabetic subjects separately.

In male diabetic subjects only serum HDL cholesterol was significantly different among different eGFR groups and showed positive association with eGFR. Though serum total cholesterol and LDL cholesterol showed weak but statistically significant positive association with eGFR, these were not significantly different among different eGFR groups. Moreover, non-HDL cholesterol was neither significantly different in different eGFR groups nor significantly associated with eGFR. No statistically significant association was observed for serum triglycerides and LDL-C/HDL-C with eGFR.

In female diabetic subjects, the correlation coefficients of serum total cholesterol, serum triglycerides, serum LDL cholesterol and serum non-HDL cholesterol with eGFR were not statistically significant, but serum HDL cholesterol and serum LDL-C/HDL-C showed statistically significant positive association with eGFR. Though serum total cholesterol, serum LDL cholesterol, non-HDL cholesterol and LDL-C/HDL-C were significantly different among different eGFR groups, these were not significantly different between subjects with eGFR >85 mL/min/1.73m<sup>2</sup> and subjects with eGFR <55 mL/min/1.73m<sup>2</sup> (Table II). Only HDL cholesterol was significantly lower in subjects with eGFR <55 mL/min/1.73m<sup>2</sup> than HDL cholesterol in subjects with eGFR 55–84 mL/min/1.73m<sup>2</sup> and eGFR >85 mL/min/1.73m<sup>2</sup>.

In different studies lipid parameters revealed different association with GFR. Krikken et al<sup>21</sup> showed that an inverse weak association exists between HDL cholesterol and GFR in non-diabetic subjects without kidney disease and Lin et al<sup>22</sup> found no association between lipid parameters and eGFR in female diabetic subjects. Kim et al<sup>23</sup> and Lin et al<sup>24</sup> showed that total cholesterol, triglycerides, LDL cholesterol and non-HDL cholesterol were inversely associated with eGFR. Lin et al<sup>24</sup> also showed that serum HDL cholesterol was positively associated with eGFR in male diabetic subjects. Our results are partly consistent with the study of Lin et al<sup>24</sup> and we found that positive association of serum HDL cholesterol with GFR is stronger in males than in females. From our study we can conclude, though traditional lipid parameters are not sufficient to explore the association of lipid parameters with GFR<sup>25</sup>, still their measurement and assessment may be helpful to prevent the progression of renal insufficiency.

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