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# A CORRELATIVE STUDY OF HBA1C AND LIPOPROTEIN APO-B IN PATIENTS OF TYPE 2 DIABETES MELLITUS WITHOUT RETINOPATHY

Medicine

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| **Brijesh Kumar Chaudhary** | Assistant Professor, Dept of Medicine , Maa Vindhyavashini Autonomous State medical College Mirzapur |
| **Abhishek Kumar** | Assistant Professor, Dept of general Medicine, Dr. RML IMS Lucknow |
| **Priyanka Gupta** | Senior resident, Dept of pathology, BRD Medical College, Gorakhpur |
| **Ravi Tandon** | Ex Professor, Dept of general Medicine, IMS BHU |
| **Vikram Singh** | Additional Professor, Dept of general Medicine, Dr. RML IMS Lucknow |
| **Vinay Kumar Verma** | Senior resident, Dept of general Medicine, Dr. RML IMS Lucknow |

## ABSTRACT

**Introduction:** Diabetes is a leading cause for the cardiovascular diseases, stroke, blindness, amputations and end stage renal disease in the world. Increasing evidences in both the experimental and clinical studies suggest that oxidative stress plays a major role in the pathogenesis of diabetes mellitus. Elevated circulating levels of soluble adhesion molecules as markers of endothelial dysfunction have been related to insulin resistance and its associated metabolic abnormalities. **Aims And Objective** 1- To find the relationship between Apo-B and type 2 diabetes mellitus without retinopathy 2-To find a relationship between HbA1C and type 2 diabetes mellitus without retinopathy. 3-To study the correlation between Apo-B and HbA1C in type 2 diabetes mellitus without retinopathy. **Materials And Methods:** 45 patients of newly diagnosed type 2 diabetics without retinopathy of age between 20 to 65 years were selected. For control, 20 age and sex matched healthy non-diabetic & Normotensive individuals were selected as the controls, whose blood samples were drawn with their consent for comparison with the blood samples of the cases. **Results:** We have found statistically non significant positive correlation between HbA1C % and level of Apo "B" **Conclusion:** The study also showed statistically significant difference in HbA1c ($p<0.001$) when compared between diabetics without retinopathy and normal healthy controls. Further levels of HDL-C were significantly lower in patients of diabetes without retinopathy($p<0.001$).

## KEYWORDS

HbA1C, Lipoprotein Apo-B, Type 2 Diabetes mellitus, Retinopathy, cardiovascular disease, dyslipidaemia

## INTRODUCTION:

One of the most prevalent non-communicable diseases in the current clinical picture worldwide is diabetes mellitus (DM). About 90–95% of all instances of diabetes are type 2, which is the most prevalent kind of the disease. Globally, diabetes is the primary cause of end-stage renal disease, stroke, cardiovascular illnesses, blindness, and amputations. It has been shown that systemic inflammation negatively affects the metabolism of glucose. (1,2).

Many studies have been conducted in order to develop the relationship between various inflammatory mediators and T2DM, and have found abnormally high levels of various cytokines, plasminogen activator inhibitor, chemokines, acute phase proteins (such as CRP) in type 2 diabetic patients (1,2)including that high circulating levels of IL-1b, IL-6, and CRP can be the main predictive indicators for progression of T2DM (1,3) These high levels of numerous cytokines and CRPs may induce the activation of innate immune system in type 2 diabetic patients.

According to current estimates, the primary cause of new onset blindness in working-aged adults in developed countries is diabetic retinopathy. It was first thought that the microvascular problems would only manifest in the early stages of diabetes mellitus's natural history, based on clinical data. However, in both the UKPDS and the Hoorn Study (4), At the time of diagnosis, nearly 20% of the patients developed microvascular diabetes sequelae, such as proteinuria, neuropathy, and retinopathy. These results begged the question of whether the microvascular disease genuinely arises in the early stages of diabetes mellitus, or if diabetes had been diagnosed late in these patient cohorts.

There are several interrelated metabolic pathways that have been suggested as possible connections between hyperglycemia and diabetic retinopathy. These include hemodynamic changes, accelerated formation of advanced glycation end products (AGEs), oxidative stress, activation of the renin-angiotensin-aldosterone system (RAAS), increased flux of the polyol pathway, activation of the diacylglycerol-(DAG) PKC pathway, increased expression of growth factors such as vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1), and subclinical inflammation and leukostasis. (5) .

A growing body of evidence from both experimental and clinical research indicates that oxidative stress is a key player in the aetiology of diabetes mellitus. (6). The primary indicator of diabetes mellitus is hyperglycemia. Additionally, there are indicators of compromised antioxidant defence systems, including decreased endogenous antioxidant levels, decreased antioxidant enzyme activity in diabetes, (6,7). Increased levels of soluble adhesion molecules in the bloodstream, which are indicators of endothelial dysfunction, have been linked to insulin resistance and the corresponding metabolic disorders. Their relationships to microvascular problems in type 2 diabetes, however, are yet unclear. From here on, our goal was to examine HbA1C and Lipoprotein Apo-B in individuals with Type 2 Diabetes mellitus who did not have retinopathy.

## MATERIALS AND METHODS:

This study was carried out between June 2018–July 2019 at the Department of General Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, in cooperation with the Department of Biochemistry. Between the ages of 20 and 65, 45 individuals with newly diagnosed type 2 diabetes who did not have retinopathy were chosen from the Department of Medicine and Endocrinology at IMS, BHU, Varanasi. Twenty healthy individuals who were matched for age and sex and who were neither diabetic nor hypertensive were chosen as the controls. Their blood was obtained with their consent so that it could be compared to the blood samples from the patients.

Particular blood samples were taken from the antecubital vein of the participants mentioned above. About 3 millilitres of venous blood were drawn and placed in plain, dry, and clean vials without the use of an anticoagulant. A 2 millilitre EDTA vial was filled. After allowing the blood in the plain vial to clot at room temperature, it was centrifuged for ten to fifteen minutes at 2000 rpm. After being extracted, the sera were placed in a sterile, simple glass container and kept at -20°C until analysis. Once the serum had thawed, it was pipetted out for analysis.

### Sample collection method

Participants at local pathology centres underwent fasting blood collections (>8 hours) to measure serum lipids (total, high-density lipoprotein, and low-density lipoprotein cholesterol and triglycerides),

A1C, and apolipoprotein B levels. Patients will have blood and serum samples taken as soon as they are admitted, with all aseptic procedures followed. Using a single-use syringe, a venepuncture will extract around 4 millilitres of blood from a peripheral vein. In order to induce the clot to retract, the blood so collected will be left to remain at room temperature for 30 minutes in a sterile plain vial. After that, the serum will be separated by centrifuging it for ten minutes at 3000 revolutions per minute in a cool centrifuge. For examination, the serum sample will be kept frozen in a refrigerator at -20 degrees Celsius.Data analysis was performed using SPSS statistical software (version 22, SPSS, Inc., Chicago, Illinois, USA). Baseline characteristics of participants with and without diabetic retinopathy were compared using a chi squared test for proportions, t test, or Mann-Whitney U test for means. P < 0.05 was considered statistically significant, and P < 0.001 was considered highly significant.

## RESULTS

A total of 65 patients were chosen for our investigation; 41 (63.08%) were men and 24 (40.8%) were women. In cases, the male to female ratio was 30:15, while in the control group it was 11:9. In the case group, there were 66.0% men while in the control group, there were 55% men. The mean age in the sick group was 50.79±9.37, while the mean age in the healthy control group was 55.27±5.78 (p value = 0.095). Table 1

The study found that the diabetes patients without retinopathy had substantially higher fasting blood sugar (mean 216.21 ± 72.75 mg/dl) compared to the control group (mean 88.33 ± 13.69 mg/dl) with a p-value of less than 0.001 (table 2). and the diabetes patients without retinopathy had considerably higher postprandial blood sugar (mean 307.76 ± 97.04 mg/dl) than the control group (124.20 ± 9.28 mg/dl). p<0.001 (table 3)

HBA1c was significantly high in the diabetic patients without retinopathy (mean 8.01 1.83) than in the non-diabetic and non-hypertensive controls(mean 5.60 ± 0.50) p <0.001. (table 4)

There was no significant difference in the serum cholesterol between the two groups. Mean serum cholesterol level in the patient group was 191.5630.47 and the mean level in the healthy control group was 180.6712.97 .( p value > 0.05).(table 5)

The patient group's mean serum triglyceride level was 210.7917.38 in the current investigation. The mean triglyceride level in the healthy control group was 135.338.43. The difference was significant with p=value < 0.001. (table 6)

In the present study , the mean serum VLDL level was 41.094.47 in the patient group and 21.934.38 in the healthy control group . The difference was significant . (0.001) (table 7)

In our study, the mean serum LDL cholesterol level was 101.9719.79 in the patient group and 92.2710.72 in the healthy control group. The difference was insignificant (p value > 0.05).(table 8)

In the present study, the mean serum HDL cholesterol level was 33.687.16 in the patient group and 43.805.28 in the healthy control group . The difference was highly significant. (p value<0.001) (table 9) In the present study, the mean concentration of Apo “B” ng/ml was 175.79±81.89 in the patients groups and 131.63±39.33 ng/ml in the healthy control group. The difference was highly significant ( p value<0.05) (table 10)

We have found statistically non significant positive correlation between HbA1C % and level of Apo “B” (Pearson correlation = 0.487, p value >0.05) (figure 1)

## DISCUSSION

Patients with diabetes mellitus were split into two groups for this study: cases, or those with type 2 diabetes mellitus without retinopathy, and controls, or normal healthy participants. Twenty controls and 45 cases were collected. A total of 65 patients were chosen for our investigation; 41 (63.08%) were men and 24 (40.8%) were women. In cases, the male to female ratio was 30:15, while in the control group it was 11:9. To reduce confounding, patients with hypertension and those receiving medication that may alter lipid metabolism were eliminated. 50.79 years was the mean age of cases, and 55.27 years was the mean age of controls.

Additionally, we found that the diabetic patients without retinopathy had significantly higher fasting blood sugar (mean 216.21 ± 72.75 mg/dl) than the control group (mean 88.33 ± 13.69 mg/dl), p <0.001. and the diabetic patients without retinopathy had considerably higher postprandial blood sugar (mean 307.76 ± 97.04 mg/dl) than the control group (124.20 ± 9.28 mg/dl, p <0.001). Compared to the controls (mean 5.60 ± 0.50), the diabetic patients without retinopathy had a substantially higher HBA1c (mean 8.01 ± 1.83), p <0.001.

Bhasker Mukherjee et al (8) study also found that the HbA1c was higher in diabetics without retinopathy (7.02%) as compared to controls (5.58%), (p<0.05) and the highest value was seen in the mild NPDR group (8.82%).

Similarly Rathnakumar Krishnamoorthy et al (9)study found that HbA1c was raised in diabetics without retinopathy(7.9% ) as compare to controls(5.6%)and highest was seen in diabetics with progressive retinopathy(13.8%), p<0.001 which was statistically highly significant.

Between the two groups, there was no discernible variation in serum cholesterol levels. The patient group's mean serum cholesterol level was 191.56 30.47, while the healthy control group's mean level was 180.67 12.97 (p value > 0.05). In the patient group, the mean serum triglyceride level was 210.79 17.38. The mean triglyceride level in the healthy control group was 135.33 8.43. With a p value of less than 0.001, the difference was extremely significant. Additionally, the patient group's mean serum VLDL level was 41.09 4.47, while the healthy control group's mean level was 21.93 4.38. There was a noticeable difference.

In our study, the mean serum LDL cholesterol level was 101.97 19.79 in the patient group and 92.27 10.72 in the healthy control group. The difference was insignificant (p value > 0.05). the mean serum HDL cholesterol level was 33.68 7.16 in the patient group and 43.80 5.28 in the healthy control group. The difference was highly significant. (p value<0.001). Also, the mean concentration of Apo “B” was 175.79 81.89 ng/ml in the patients groups and 131.63 39.33ng/ml in the healthy control group. The difference was statistically significant ( p value<0.05).

Bhaskar Mukharjee et al (8) study also shows that lipoprotein Apo B was raised in patients of diabetes without retinopathy(mean value 89mg/dl) and significant raised in diabetes with retinopathy than normal healthy control(mean value 63mg/dl) and highly raised in severe NPDR(mean value114 mg/dl), which was statistically highly significant(p valve,0.001).

Similarly Rathnakumar Krishnamoorthy et al (9) found that lipoprotein Apo B was raised in diabetics without retinopathy(mean valve 120mg/dl) in comparison to normal healthy control(mean valve 102mg/dl) and highly raised in diabetics with sever NPDR(mean value 174 mg/dl), which was statistically highly significant.

Additionally, the current investigation demonstrates a statistically non-significant positive connection (P>0.05) between HbA1C and Apo-B level. From this point forward, it suggests that an increase in Apo B levels over time contributes significantly to the development of retinopathy.

## CONCLUSION

In comparison to normal healthy controls, the current study has shown a statistically significant rise in the serum levels of Apolipoprotein 'B' (p<0.05) in type II diabetes patients without retinopathy. The study also revealed a statistically significant difference in HbA1c (p<0.001) between normal healthy controls and diabetics without retinopathy. Patients with diabetes who did not have retinopathy had significantly lower HDL-C values (p<0.001). When compared to healthy controls, there was no statistically significant difference in the levels of blood cholesterol and LDL (p>0.05). In the future, larger cohort studies will be required to validate our findings.

**Tables and figures:**

**Table 1: Clinical characteristics of study Population**

| Parameter | Diabetics without retinopathy (n=45) | Healthy Controls (n=20) |
|---|---|---|
| Age (in years) | 50.799.37 | 55.27±5.78 |
| Male / Female | 30 : 15 | 11 : 9 |

**Table 2 : Fasting Blood Sugar in the study population**

| Group | FBS (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 216.21 72.75 | t=6.717 | p< 0.001(HS) |
| Healthy Controls (n=20) | 88.33 ± 13.69 | | |

**Table 3 : Post Prandial Blood sugar in the study population**

| Group | PPBS (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 307.76 97.04 | t=7.269 | p< 0.001(HS) |
| Healthy Controls (n=20) | 124.20 ± 9.28 | | |

**Table 4 : HbA1C % in the study population**

| Group | HbA1c (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 8.01 1.83 | t=6.976 | p< 0.001(HS) |
| Healthy Controls (n=20) | 5.60 ± 0.50 | | |

**Table 5: Serum Total Cholesterol level in the study population**

| Group | Cholesterol (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 191.5630.47 | t=1.326 | P< 0.05(Ns) |
| Healthy Controls (n=20) | 180.6712.97 | | |

**Table 6 : Serum Triglyceride level in the study population**

| Group | Triglyceride (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 210.7917.38 | t=16.150 | p< 0.001(HS) |
| Healthy Controls (n=20) | 135.338.43 | | |

**Table 7 : Serum VLDL Cholesterol in the study population**

| Group | VLDL (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 41.094.47 | t=13.895 | p< 0.001(HS) |
| Healthy Controls (n=20) | 21.934.38 | | |

**Table 8: Serum LDL Cholesterol in the study population**

| Group | LDL (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 101.9719.79 | t=1.780 | P< 0.05(s) |
| Healthy Controls (n=20) | 92.2710.72 | | |

**Table 9 Serum HDL Cholesterol level in the study population**

| Group | HDL (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 33.687.16 | t=-4.905 | p< 0.001(HS) |
| Healthy Controls (n=20) | 43.805.28 | | |

**Table 10 Apo "B" in the study population**

| Group | Apo "B" (ng/ml) (MeanSD | t-value | p-value |
|---|---|---|---|
| Diabetics without retinopathy (n=45) | 175.79±81.89 | t=2.290 | P< 0.05(s) |
| Healthy Controls (n=20) | 131.63±39.33 | | |

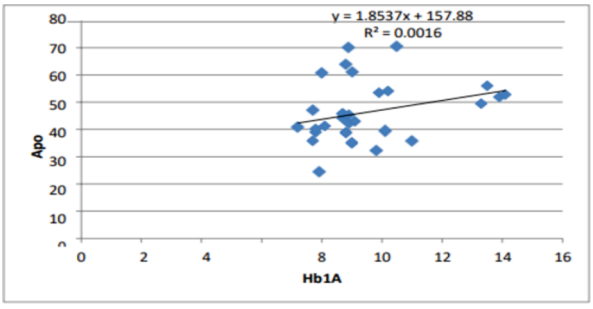


**Figure 1 : Correlation between Hb1AC vs Apo "B"**

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