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ORIGINAL RESEARCH

Correlation of glycemic control with dyslipidemia, atherogenicity, c reactive protein and microalbuminuria in type 2 diabetes patients

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ABSTRACT

Background: Diabetes mellitus, characterized by persistent hyperglycemia due to insulin resistance or deficiency, is rapidly increasing in prevalence, with projections estimating 438 million cases by 2030. The rising incidence, especially of type 2 diabetes, is associated with obesity, sedentary lifestyles, and an aging population. This study investigates correlations between glycemic control, dyslipidemia, C-reactive protein (CRP), and microalbuminuria in patients with type 2 diabetes.

Aim: This study aims to correlate glycemic control, assessed by glycated hemoglobin (HbA1c), with dyslipidemia, atherogenicity, CRP levels, and microalbuminuria in individuals with type 2 diabetes mellitus.

Methodology: A cross-sectional study was conducted involving 200 patients with type 2 diabetes, recruited from outpatient and inpatient settings at Index Medical College, Hospital and research centre, Indore, Participants underwent comprehensive clinical examinations, with glycemic control evaluated through HbA1c measured via high-performance liquid chromatography. Lipid profiles, including triglycerides, total cholesterol, HDL, and LDL, were analyzed enzymatically. The atherogenic index of plasma (AIP) was calculated, CRP levels were assessed using latex agglutination, and urinary albumin excretion was measured to determine microalbuminuria.

Results: The analysis revealed significant differences in total cholesterol, triglycerides, LDL, HDL levels, AIP, CRP, and urinary albumin excretion between patients with HbA1c <7% and >7%. These findings highlight strong correlations with cardiovascular risk and nephropathy, suggesting that poor glycemic control is associated with adverse lipid profiles and inflammatory markers.

Conclusion: HbA1c not only serves as a vital marker for glycemic control but also as an important biomarker for evaluating atherogenic dyslipidemia, cardiovascular risk, and early nephropathy in patients with type 2 diabetes, emphasizing the need for regular monitoring and management strategies to mitigate complications.

Key words: Diabetes mellitus, glycemic control, glycated hemoglobin (HbA1c), dyslipidemia, atherogenicity, C-reactive protein (CRP), microalbuminuria, cardiovascular risk, type 2 diabetes, lipid profiles

INTRODUCTION

The metabolic illness known as diabetes mellitus is described by relentlessly high glucose levels, which might be brought about by insulin obstruction, relative insulin lack, or both. Diabetes Mellitus has had a colossal expansion in recurrence throughout recent years, going from an expected 30 million cases in 1985 to 285 million in 2010.Nearly 438 million individuals will be living with diabetes continuously 2030, according to the International Diabetic Federation's projections [1].

Increasing rates of obesity, decreased levels of physical activity as nations grow more industrialized, and an aging population are likely contributing factors to the quick expansion in the predominance of type 2 diabetes mellitus, though both types of the disease are on the rise globally. People between the ages of 45 and 64 will have the highest prevalence of diabetes in 2030, according to global estimations. When insulin

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levels are dangerously low, type 1 diabetes develops. Glucose production increases, insulin secretion is compromised, and insulin resistance varies in severity across the several illnesses that make up type 2 diabetes mellitus. Despite the fact that type 2 diabetes generally appears in middle age or later, it is progressively being identified in younger patients, especially those who are overweight or have just reached puberty [2].

Atherosclerosis in type 2 diabetes is brought about by changes in the lipid and lipoprotein profile [3]. High convergences of plasma fatty oils and low groupings of high-thickness lipoprotein cholesterol (HDL-C) are typical features of diabetic dyslipidemia, along with an abundance of tiny, thick LDL-C and a raised apolipoprotein B [4-7]. The pathogenesis of this dyslipidemia seems to revolve on the increased hepatic emission of VLDL, which is rich in big triglycerides, and decreased clearance of this lipoprotein. The Grown-up Treatment Board III plays recognized the huge parts of HDL-C and TGs, alluding to this blend as atherogenic dyslipidemia, even though much research on the link between lipids and coronary heart disease (CHD) has focused on LDL-C [8].

The atherogenic list of plasma (AIP) is a recently proposed prescient marker for plasma atherogenicity. It is characterized as the logarithm of the proportion of plasma grouping of fatty substances to high-thickness lipoprotein (HDL) cholesterol and is emphatically corresponded with the risk of cardiovascular disease [9].

The ratio of atherogenic to protective lipoproteins is reflected in AIP triglycerides and HDL-cholesterol. Molecule size of favorable to and hostile to atherogenic lipoproteins is corresponded with AIP. As indicated by clinical exploration, AIP is a risk factor for cardiovascular sickness. AIP is a practical indicator of therapy efficacy and a readily accessible cardiovascular risk marker [10, 11].

The glycemic management, the DCCT (Diabetes Complications and management Trial) made HbA1c the benchmark. Patients with elevated HbA1c levels are more likely to have severe dyslipidemia.

An indicator of systemic inflammation, C-Reactive Protein (CRP) is now becoming recognized as a separate risk factor for cardiovascular disease [12-14].

At every stage of the metabolic disorder and the computed Framingham risk, C-reactive protein (CRP) provides additional prognostic information and it seems to be a more strong indicator of cardiovascular occasions than low-density lipoprotein (LDL) cholesterol [15]. In addition, C-reactive protein levels are greater in diabetics than in non-diabetics [16-18] together with HbA1c.

One of the risk elements of microalbuminuria (incipient nephropathy), which accelerates the progression of renal disease, is poor glycemic management, which is assessed as high HbA1C [19].

To reduce renal damage caused by diabetes mellitus, it is recommended to screen for microalbuminuria regularly and to continuously measure glycated hemoglobin (HbA1C) three times a month. At this point, the diabetic nephropathy (microalbuminuria) may be reversible if the patient maintains tight control over their blood sugar levels [20].

MATHODOLOGY

This study was carried out from "Correlation of glycemic control with dyslipidemia, atherogenicity, C reactive protein and microalbuminuria in patients with type 2 diabetes mellitus".

200 individuals with type 2 diabetes who were either outpatients at medical outdoor clinics or inpatients at Index Medical College's Department of General Medicine participated in the current cross-sectional research. All patients were informed and given the chance to pose inquiries about the review's motivation and methodology before they were enrolled. Thorough clinical examinations and pertinent investigations were conducted on all patients. In order for participants to be considered for participation in the research, all exclusion and inclusion criteria had to be satisfied.

INVESTIGATION

1. **GLYCATED HEMOGLOBIN** (HbA1c) was estimated by particle trade technique. A Superior Presentation Fluid Chromatography framework and a particle trade or liking segment were utilized to seclude HbA1c from the other hemoglobin atoms in the chromatographic test. The HbA1c content is determined by dividing the overall peak area of hemoglobin by the ratio of the HbA1c peak area.
2. **SERUM LIPID PROFILE** by enzymatic method.

Following analytes were assessed by using commercially available reagents and kits (Kit method).

- Triglycerides
- Total Cholesterol
- HDL
- LDL

a) ESTIMATION OF SERUM TRIGLYCERIDE

TEST PRINCIPLE

The quantitative estimation of triglyceride was done by the enzymatic kit (GPO-POD method).

b) ESTIMATION OF SERUM CHOLESTEROL

TEST PRINCIPLE: The quantitative assessment of complete serum cholesterol was finished by the enzymatic unit (CHOD-PAP strategy).

c) ESTIMATION OF HDL CHOLESTEROL

TEST PRINCIPLE

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The enzymatic unit (Phosphotungstic Corrosive) was utilized to gauge HDL cholesterol quantitatively.

d) SERUM LDL CHOLESTEROL ESTIMATION

Using the Friedwald and Frederickson formula, the serum LDL cholesterol was determined.

LDL cholesterol (mg/dl) = Total cholesterol-(HDL+TG/5) mg/dl

4. ATHEROGENIC INDEX OF PLASMA (AIP)

This is the consequence of taking the base-10 logarithm of the TG/HDL proportion.

5. C-REACTIVE PROTEIN (CRP)

The C-responsive protein level was evaluated using the latex agglutination technique as a binary variable, meaning it was either raised or not elevated. A C-responsive protein level (CRP) in excess of 6 mg/dl was considered to be high.

6. URINARY ALBUMIN EXCRETION (UAE)

Subjects had their urine sampled every hour for 24 hours. The sample was used to measure urinary albumin excretion (UAE), which does not include any preservative. We utilized particle trade elite execution fluid chromatography (HPLC) to get a gauge of microalbuminuria. There were three categories for urinary albumin:

a) Normal albuminuria is defined as a UAE below 30 mg/d.
b) The presence of microalbuminuria (UAE 30-300 mg/d).

Urea albuminuria (UAE 300 mg/d or above).

STATICALLY ANALYSIS

Data will be entered on SPSS in the form of master chart. This data will be classified and analyzed as per aims and objectives. Quantitative data will be expressed in the form of Mean + SD. Inference will be drawn with the use of appropriate test of significance.

OBSERVATION

Table 1: Relationship between age and glycated hemoglobin in type 2 diabetic patients: a case distribution

Age Group (years)	Glyeated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
< 30	0		8	6.8	8	4
31-50	20	24.1	20	17.1	40	20
51-70	43	51.8	71	60.7	114	57
>70	20	24.1	18	15.4	38	19
Total	83	100	117	100	200	100
Mean	61.6		60.26			
SD	10.74		14.04			
t	0.734					
p	0.464					

The prevalence of glycated hemoglobin patients is broken down by age group in Table 1. Out of the 83 patients in the glycated hemoglobin group below 7 gm%, 20, 43, and 20 were found to be in the age groups of 31-50, 51-70, and 70 years old, respectively. In contrast, 117 patients were found to have a glycated hemoglobin level above 7, with 8, 20, 71, and 18 being in the age groups of 30, 31, 50, 51-70, and 70 years old, respectively. No statistically significant change was found ($p>0.05$) in the statistical analysis.

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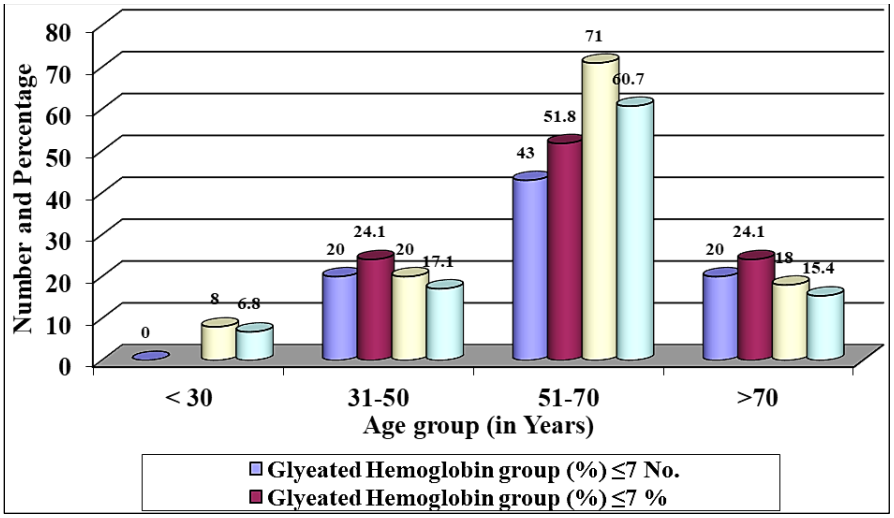
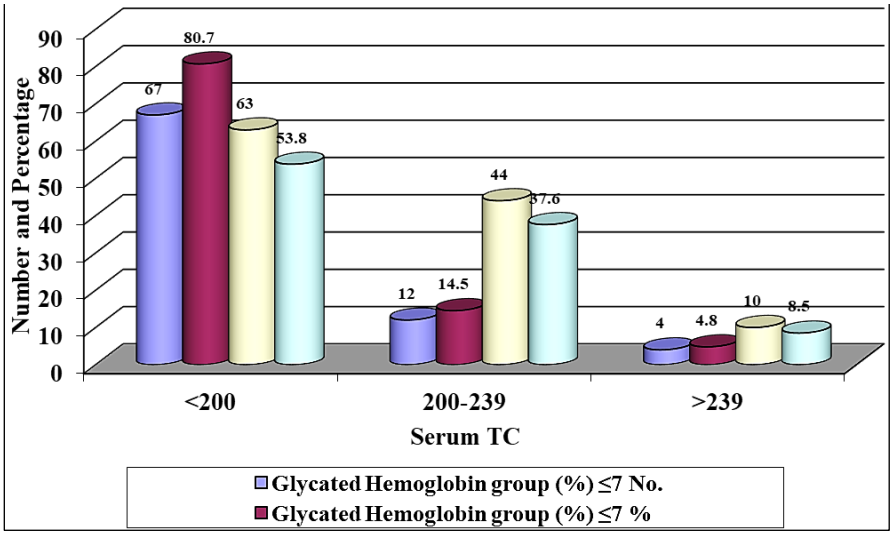


Graph 1: Relationship between age and glycated hemoglobin in type 2 diabetic patients: a case distribution

Table 2: Case distribution in type 2 diabetic patients according to blood total cholesterol and glycated hemoglobin

Serum TC	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
<200	67	80.7	63	53.8	130	65.0
200-239	12	14.5	44	37.6	56	28.0
>239	4	4.8	10	8.5	14	7.0
Total	83	100	117	100	200	100
Mean	173.50		190.62			
SD	32.55		34.99			
t	3.550					
P	<0.001					

Out of total 83 patients who had their glycated hemoglobin ≤7gm%, 67, 12 and 4 had their total cholesterol level <200, 200-239 and >239 respectively while out of total 117 patients who had their glycated hemoglobin >7, 63, 44 and 10 were from total cholesterol level <200, 200-239 and >239 respectively and this difference was also highly significant (p<0.001).



Graph 2: Case distribution in type 2 diabetic patients according to blood total cholesterol and glycated hemoglobin

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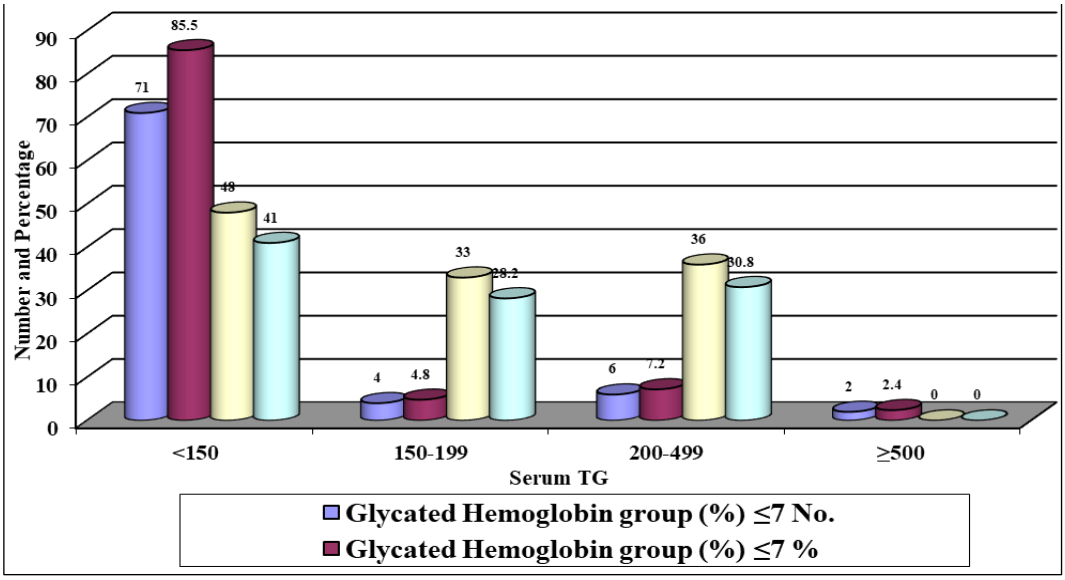
Table 3: Distribution of cases according to serum tryglyceride in relation to glycated hemoglobin in Type 2 DM patients

Serum TG	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
<150	71	85.5	48	41.0	119	59.5
150-199	4	4.8	33	28.2	37	18.5
200-499	6	7.2	36	30.8	42	21.0
≥500	2	2.4	0	-	2	1.0
Total	83	100	117	100	200	100
Mean	116.16		166.28			
SD	95.91		54.09			
t	4.700					
P	<0.001					

In serum triglyceride group <150 total 119 patients were found and out of them 71 and 48 had glycated hemoglobin ≤7 and >7. In serum triglyceride group 150-199 total 37 patients were found and out of them 4 and 33 had glycated hemoglobin ≤7 and >7 respectively. In serum triglyceride group 200-499 total 42 patients were found and out of them 6 and 36 had glycated hemoglobin ≤7 and >7 respectively. In serum triglyceride group ≥500 only 2 patients were found and they both belonged to glycated hemoglobin ≤7 group. The statistical analysis revealed a very significant difference.



Graph 3: Distribution of cases according to serum tryglyceride in relation to glycated hemoglobin in Type 2 DM patients

Table 4: Distribution of cases according LDL Cholesterol in relation to glycated hemoglobin in Type 2 DM patients

LDL Cholesterol	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
<100	30	36.1	38	32.5	68	34.0
100-129	41	49.4	31	26.5	72	36.0
130-159	9	10.8	38	32.5	47	23.5
160-189	3	3.6	7	6.0	10	5.0
≥190	0	-	3	2.6	3	1.5
Total	83	100	117	100	200	100
Mean	106.38		115.28			
SD	26.73		31.07			
t	2.113					

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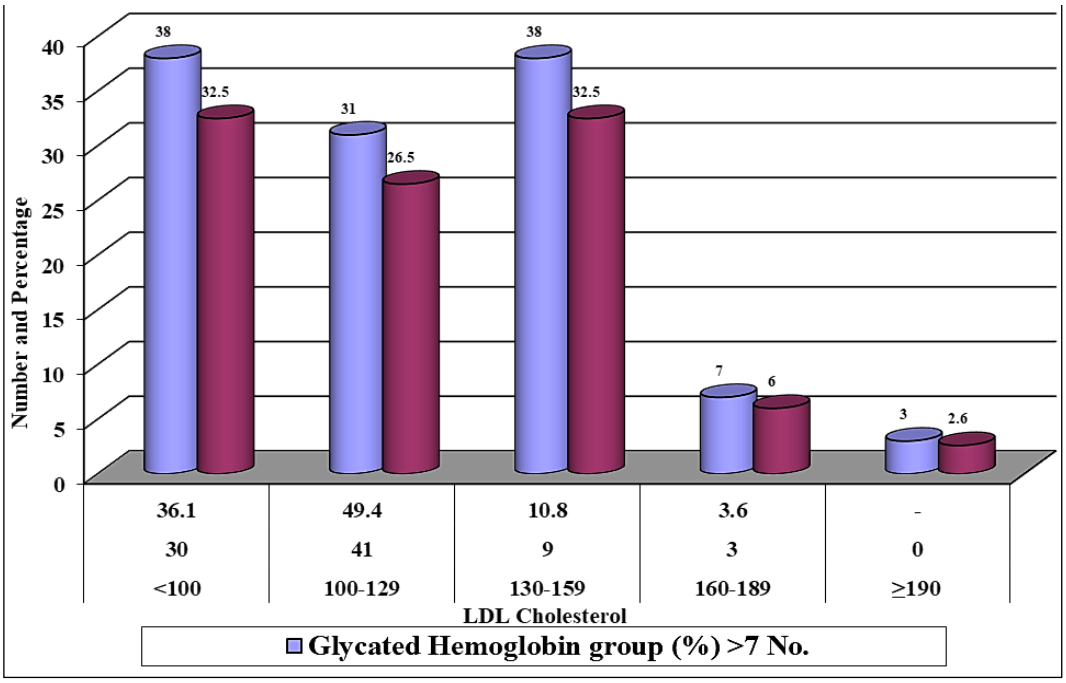
P	0.036	

In LDL cholesterol group <100 total 68 patients were found and out of them 30 and 38 had glycated hemoglobin ≤7 and >7. In LDL cholesterol group 100-129 total 72 patients were found and out of them 41 and 31 had glycated hemoglobin ≤7 and >7. In LDL cholesterol group 130-159 total 47 patients were found and out of them 9 and 38 had glycated hemoglobin ≤7 and >7. In LDL cholesterol group 160-189 total 10 patients were found and out of them 3 and 7 had glycated hemoglobin ≤7 and >7. In LDL cholesterol group ≥190 only 3 patients and they all were belonged to glycated hemoglobin group >7. We observed a significant difference ($p<0.05$) when we compared statistically.



Graph 4: Distribution of cases according LDL Cholesterol in relation to glycated hemoglobin in Type 2 DM patients

Table 5: Case distribution in type 2 diabetic patients according to HDL cholesterol and glycated hemoglobin

HDL Cholesterol	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
<50	24	28.9	26	22.2	50	25.0
≥50	1	1.2	18	15.4	19	9.5
<40	16	19.3	32	27.4	48	24.0
≥40	42	50.6	41	35.0	83	41.5
Total	83	100	117	100	200	100
Mean	43.69		42.08			
SD	6.08		7.51			
T	1.605					
P	0.110					

Out of absolute 69 females, 50 females had their HDL cholesterol level <50 while remaining 19 females had their HDL Cholesterol level ≥ 50. In HDL level <50 24 and 26 females had their glycated hemoglobin ≤7 and >7 gm% respectively while in HDL ≥50, only 1 female had her glycated hemoglobin level ≤7gm%. In HDL group <40, total 48 males were found and out of them 16 and 32 were from glycated hemoglobin level ≤7 and >7 respectively while in HDL cholesterol level ≥40, out of total 83 males, 42 and 41 were from glycated hemoglobin level ≤7 and >7 gm%.

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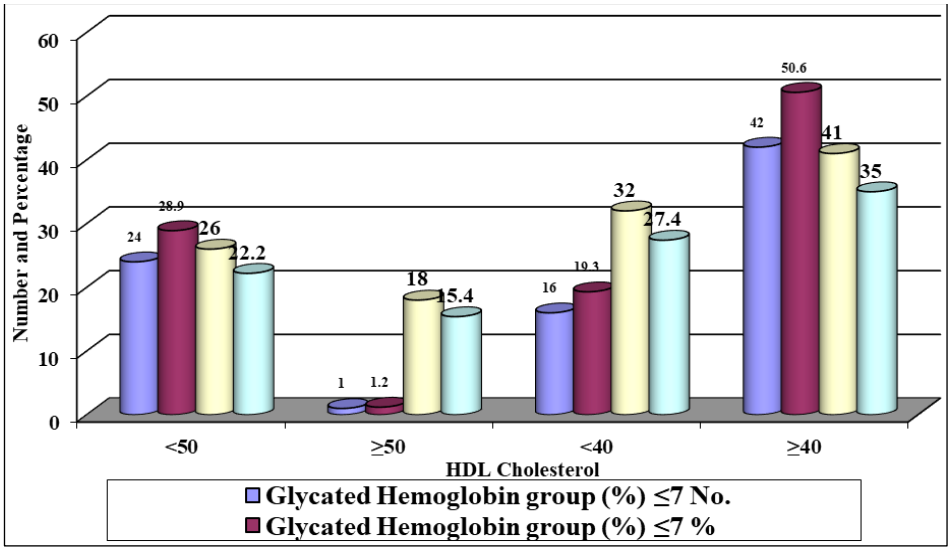
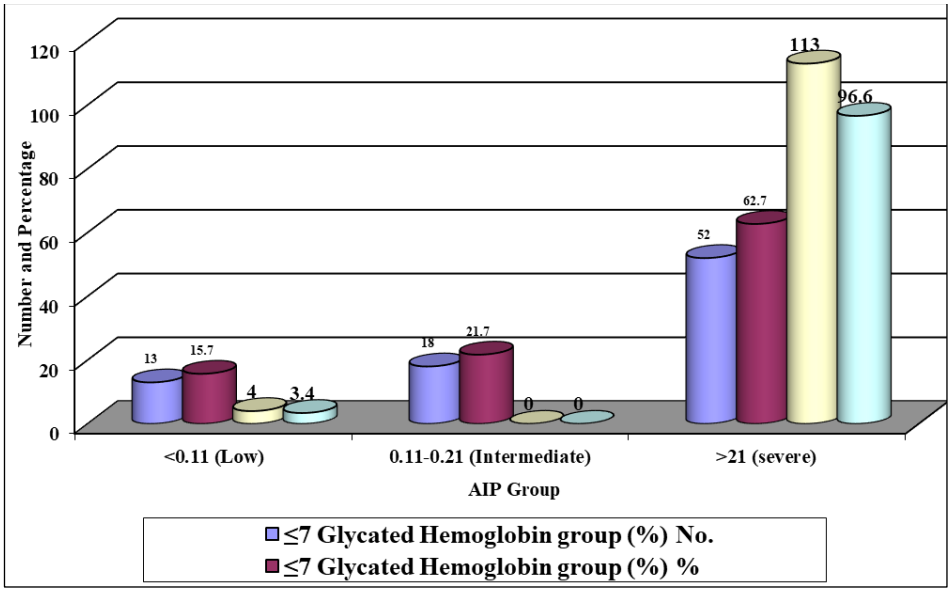


Graph 5: Case distribution in type 2 diabetic patients according to HDL cholesterol and glycated hemoglobin

Table 6: Case distribution in type 2 diabetic patients according to AIP and glycated hemoglobin

AIP Group	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
<0.11 (Low)	13	15.7	4	3.4	17	8.5
0.11-0.21 (Intermediate)	18	21.7	0	-	18	9.0
>21 (severe)	52	62.7	113	96.6	165	82.5
Total	83	100	117	100	200	100
Mean	0.36		0.58			
SD	0.24		0.18			
t	7.598					
p	<0.001					

According to above table, AIP was divided in to three groups i.e. low, intermediate and severe. In low AIP group total 17 patients were found and out of them 13 had their glycated hemoglobin level ≤7%. In intermediate AIP group total 18 patients were found and all of them belonged to HbA_{1c} <7% group while in severe AIP group total 165 patients were found and out of them only 52 had their glycated hemoglobin level ≤7%. A very significant difference (p<0.001) was found upon statistical analysis.



Graph 6: Case distribution in type 2 diabetic patients according to AIP and glycated hemoglobin

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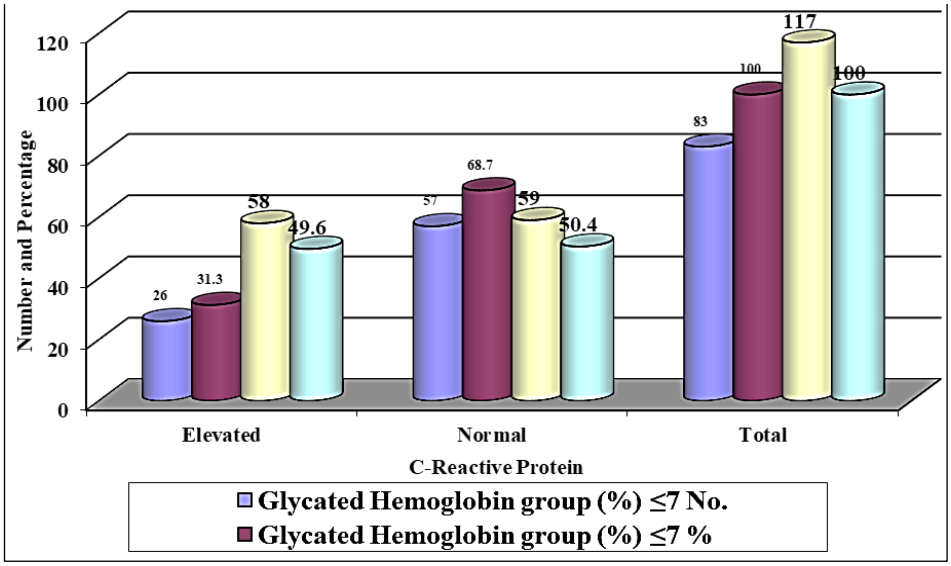
Table 7: Case distribution in type 2 diabetic patients according to C-reactive protein and glycated hemoglobin

C-Reactive Protein	Glycated Hemoglobin group (%)				Total	
	≤7		>7			
	No.	%	No.	%	No.	%
Elevated	26	31.3	58	49.6	84	42.0
Normal	57	68.7	59	50.4	116	58.00
Total	83	100	117	100	200	100
χ^2	6.637					
p	0.001					

Out of total 200 patients, 84 patients had their C-reactive protein elevated and out of these 84 patients 26 had their glycated hemoglobin level ≤7 gm%. The measurable examination uncovered a massive distinction (p<0.05) while looking at the two.



Graph 7: Case distribution in type 2 diabetic patients according to C-reactive protein and glycated hemoglobin

Table 8: Case distribution in type 2 diabetic patients as measured by urine albumin in relation to glycated hemoglobin

Urine Albumin Examination		Glycated Hemoglobin Group (%)				χ^2	p
		≤7		>7			
		No.	%	No.	%		
Normoalbuminuria	Yes	70	84.3	53	45.3	31.252	<0.001
	No	13	54.7	64	54.7		
Microalbuminuria	Yes	9	49.6	58	49.6	32.692	<0.001
	No	74	50.4	59	50.4		

According to urine albumin examination, normal finding were found in total 123 patients and out of them 70 had their glycated hemoglobin level ≤7gm% while microalbuminuria was found in 67 patients and out of them only 9 patients had their glycated hemoglobin level ≤7gm%. There was a significantly significant difference between normoalbuminuria and microalbuminuria when comparing statistically (p<0.001).

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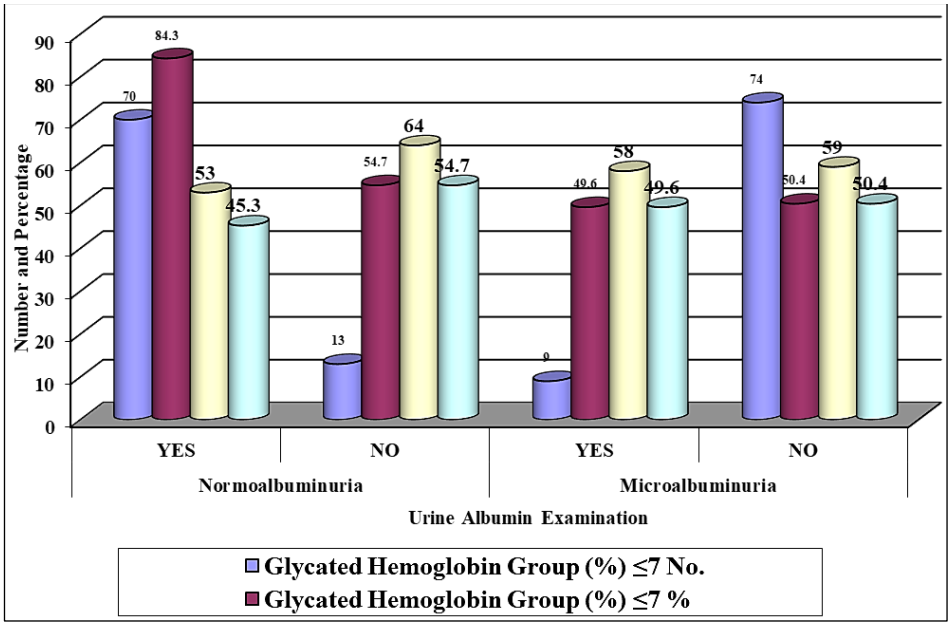

Graph 8: Case distribution in type 2 diabetic patients as measured by urine albumin in relation to glycated hemoglobin

Result and Discussion

Distribution of type 2 DM patients across various age groups (Table 1), showed that, greatest number of patients were in the age pack 51-70 yrs, wherein 43 patients out of 83 patients comprising 51.8% in the GGC group (HbA1c <7) and 71 out of 117 patients comprising 60.7% in the PGC group (HbA1c>7). Distribution of cases across all age groups including 51 to 70yrs had no significant correlation with glycemic control.

Correlation of HbA1c with total cholesterol (table 2) showed that about 70 patients had raised complete cholesterol levels over 200 mg/dl wherein 16 patients (22.85%) belonged to the GGC group whereas the remaining 54 patients (77.15%) with elevated cholesterol levels belonged to the PGC group. The mean total cholesterol levels were 173.30 with a SD of 32.55 and 190.62 in mg/dl with a SD of 34.99 in the good and poor glycemic group respectively, with the observations showing statistically significant correlations between HbA1c and total cholesterol levels signifying association of dyslipidemia with impaired glycemic control.

Correlation of HbA1c with serum triglycerides (table 3) found that, a total of 81 patients had raised TG levels (>150mg/dl) with 69 patients (85.18%) belonged to the PGC group. Patients with elevated TG levels comprised about 59% patients in the PGC bunch and 14.4% in the GGC bunch with mean TCH levels being 166.28 with SD 54.09 and 116.16 in mg/dl with SD 95.91 respectively with the elevated TG levels showing statistically significant correlation with Hba1c >7% with a p value of <0.001, thus establishing correlation of serum TG levels with glycated hemoglobin.

Correlation of HbA1c with serum LDL (table 4) showed that in LDL cholesterol group <100, total 68 patients were found and out of them 30 and 38 had glycated 41 and 31 had glycated hemoglobin <7 and >7. LDL cholesterol was found elevated in a total of 132 patients (66%). In LDL cholesterol group 100-129 total 72 patients (54.54%) were found and out of them 31(43.05%) had glycated hemoglobin 7. In LDL cholesterol group 130-159 total 47 patients (55.6%) were found and out of them 38(80.85%) had glycated hemoglobin <7 and >7. In LDL cholesterol group 160-189 total 10 patients (7.5%) were found and out of them 7 (70%) had glycated hemoglobin >7. In LDL cholesterol group >190 only 3 patients (2.2%) and they all were belonged to glycated hemoglobin group >7. Thus as the HbA1c increased there is a corresponding increase in LDL levels. When compared statistically, the thing that matters was seen as critical (p<0.05).

Correlation of HbA1c with serum HDL (table 5) showed that out of absolute 69 females, 50 females (72.4%) had their HDL cholesterol level <50 with 26 females (52%) having glycated hemoglobin >7% (while in HDL >50, only I female had her glycated hemoglobin level <7%, thus showing no huge distinction in the degree of HDL between GGC and PGC group.

In HDL group <40, total 48 males were found 32 (66.66%) were from glycated hemoglobin level >7 while in HDL cholesterol level >40, out of total 83 males, 41 (49.39%) were from glycated hemoglobin level >7%. When comparing the GGC and PGC groups, no statistically significant 'p' values were discovered (p value = 110).

Correlation of HbA1c with AIP (table 6) showed that in the patient group with low AIP risk, total 17 patients (8.5%) were found and out of them 13(76.4%) had their glycated hemoglobin level <7%. In the patient group with intermediate AIP risk, total 18 patients (9%) were found and out of them, all 18 of them (100%) had their glycated hemoglobin level < 7

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while in the group with severe AIP risk group, total 165 patients (82.5%) were found and out of them only 52(31.5%) had their glycated hemoglobin level <7gm%. Thus 113 patients (68.4%) belonged to the PGC group with HbA1c levels >7. A very significant difference ($p<0.001$) was found upon statistical analysis.

Correlation of HbA1c with CRP levels (table 7) showed that out of total 200 patients, 84 patients (42%) had their C-reactive protein elevated and out of these 84 patients 26 (30.95%) had their glycated hemoglobin level <7 gm% and the remaining 58 patients (69.05%) had their glycated hemoglobin >7. The statistical analysis revealed a significant difference ($p<0.05$) when comparing the two.

Correlation of HbA1c with urine albumin excretion (table 8) showed that normoalbuminuria was found in total 123 patients (61.5%) and out of them 70(56.91%) had their glycated hemoglobin level <7%, while microalbuminuria was found in 67 patients (54.4%) with about 58 patients (86.5%) having glycated hemoglobin level >7% demonstrating that maximum number of microalbuminuria patients have elevated glycated hemoglobin levels with the difference being statistically significant ($p<0.001$).

Conclusion

In addition to its principal function in monitoring long-term glycemic management, our results show that HbA1c may provide useful supplemental information on the degree of atherogenic dyslipidemia, the Atherogenic Index of Plasma, C-reactive protein levels and microalbuminuria. Consequently, in clinical care, obtaining good glycemic control may assist avoid problems, and frequent screening for HbA1c estimate can contribute to this. So, hemoglobin A1c may be a useful biomarker for spotting those at risk for cardiovascular disease and those whose type 2 diabetes is just beginning to cause nephropathy.

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