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RESEARCH ARTICLE

CONVERSE CONTRIBUTIONS OF FASTING AND POSTPRANDIAL GLUCOSE TO HBA1C AND GLYCATED ALBUMIN.

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Abstract

Introduction:-

Diabetes mellitus (DM) comprises a group of common metabolic disorders that share phenotype of hyperglycemia, and is often accompanied by presence of glucose in urine, from which the name of condition is derived (**Gowenlock ,2002).** It is found that a 14 to 16% decrease in macro vascular complication occurs forevery 1% absolute reductions in glycated Hb **(Stratton et al ., 2000).** However, HbA1c is not used for diagnosis as it is not sufficiently sensitive **(Haslett et al., 2002).** The measurement of glycated albumin (GA), which is considered to be a marker of glycemic control over the preceding 2–3 weeks, is convenient and accurate regardless of diet **(Kouzuma et al., 2004).** A recent study showed that GAcould be a better marker for glycemic control than HbA1c in diabetic patients, especially for evaluating glycemic excursion **(Yoshiuchi et al., 2008).**

The aim:-

It was to evaluate the relative contribution of fasting and postprandial plasma glucose to both glycated heamoglobin (HbA1C) and glycated albumin(GA) in type 2 diabetic patients.

Subjects and methods:-

This cross-sectional study was conducted on 50 non acarbose non insulin receiving type 2 diabetic subjects attending the out patient endocrinology clinc at Benha University Hospitals during the period from July 2014 to July 2015 after approval of BenhaUniversity ethical committee. All the patients were subjected to full history taking with special stress on age,sex,type and duration of diabetes ,medications and complications, Complete physical examination ,fasting , postprandial and prelaunch blood glucose measurement ,serum GA and HbA1C measurement. Serum GA concentration was quantitatively measured using an Enzyme–Linked Immuno-Sorbant Assay (ELISA) kit (Quantikinehuman GA Immunoassay; R&D Systems, Minneapolis, MN, USA) according to manufacturers' instructions. Patients were classified into 3 groups according to HbA1C:Group 1 patients where HbA1C < 7.3% and

it comprises 20 patients ,Group 2 patients where HbA1C ranges from 7.3% to 8.0% and it comprises10 patients and Group3 patientswhere HbA1C >8.0% and it comprises 20 patients .

Statistical analysis:-

The collected data were tabulated and analyzed using SPSS version 16 soft ware (SpssInc, Chicago, ILL Company). Categorical data were presented as number and percentages while quantitative data were expressed as mean ± standard deviation, an and range. Fisher's exact test (FET), was used to analyze categorical variables. Quantitative data were tested for normality using KolomogrovSmirnove test, using Student "t", if normally distributed, or Man Whitney U test, Krauskal Wallis test and Spearman's correlation coefficient (rho) if not normally distributed. Statistical significance was accepted at P value <0.05 (S). A P value <0.001 was considered highly significant (HS) while a P value >0.05 was considered non-significant.

Results:-

Among the 50 studied patients 12 were males (24%) and 38 were females (76%)with their age ranged from 43-75 year with the mean age being 57.4±8.6 **(Table1)**.

Table 1:- characters of the studied sample.

Variable		No. (N=50)	% (100%)
Age	Mean ±SD	57.4±8.6	
	Range	43-75	
Sex	Male	12	24.0
	Female	38	76.0

In our study 20 patients belonged to group 1with the mean of HbA1C being 6.27± 0.42and. 10 patients belonged to group 2wih the mean of HbA1C being 7.84 ±0.08and 20 of them belonged to group 3with the mean of HbA1C being 9.11±0.47 **(Table 2).**

Table 2: Distribution of the studied patients according to the level of glycated hemoglobin.

HbA1C	n.	Mean	± SD	Range
Group I (<7.3%)	20	6.27	0.42	5.5-6.8
Group II (7.3-8.0)	10	7.84	0.08	7.8-8.0
Group III (> 8%)	20	9.11	0.47	8.7-10

The study revealed that that the mean value of FBG was significantly higher in group 3 patients compared to group 1 patients (185.6 ±43.01 and 130.8±31.75 respectively). On the other hand the mean value of PPG was significantly higher in group 1 patients compared to group 3 patients (210.6± 39.06 **and**157.0± 24.61 respectively **(Table 3).**

Table3:- Mean values of Fasting and PostPrandial and prelaunch plasma glucose glucose in the different groups.

HbA1c	n.	FBG			KWT	P	Sig. pairs
		Mean	± SD	Range			
Group I (<7.3%)	20	130.8	31.75	84-177.9	7.58	0.023 (S)	Gp I ≠ Gp III
Group II (7.3-8.0)	10	172.6	22.59	135.3-204.5			
Group III (> 8%)	20	185.6	43.01	142.8-232.3			
		1h PP					
Group I (<7.3%)	20	198.6	33.97	154.7-243.8	18.6	<0.001 (HS)	Gp I ≠ Gp III
Group II (7.3-8.0)	10	174.8	26.55	139.8-210.3			
Group III (> 8%)	20	148.9	26.17	104.8-199.5			
		2h PP					
Group I (<7.3%)	20	222.5	45.23	166.5-286.3	24.7	<0.001 (HS)	Gp I ≠ Gp III Gp II ≠ Gp III
Group II (7.3-8.0)	10	183.0	20.84	156.7-217.3			
Group III (> 8%)	20	165.0	23.42	121.8-211.6			
		Mean PP					
Group I (<7.3%)	20	210.6	39.06	170.5-265.0	22.8	<0.001 (HS)	Gp I ≠ Gp III Gp II ≠ Gp III
Group II (7.3-8.0)	10	178.9	22.04	148.2-205.3			
Group III (> 8%)	20	157.0	24.61	113.3-205.5			
		Prelaunch					
Group I (<7.3%)	20	181.2	28.05	141.1-220.8	18.4	<0.001 (HS)	Gp I ≠ Gp III Gp II ≠ Gp III
Group II (7.3-8.0)	10	179.4	21.34	157.4-210.9			
Group III (> 8%)	20	242.4	44.74	158.5-294.3			

The study revealed that the relative contribution of the postprandial plasma glucose to HbA1C (rho =0.710 and p<0.001) was higher than that of fasting plasma glucose (rho=.574 and p=0.021) in group 1 patients,the relative contribution of the postprandial plasma glucose to HbA1C (rho=0.707 and p= 0.02 2) was equal to that of fasting plasma glucose (rho=0.707 and p=0.022) in group 2 patients and the relative contribution of the fasting plasma glucose to HbA1C (rho=0.679 and p=.001) was higher than that of the postprandial plasma glucose (rho =0.659 and p= 0.002) in group 3 patients**(Table 4).**

Table 4: Correlation between HbA1c and both means of Fasting and PostPrandial plasma glucose levels in the different groups.

With	HbA1c					
	Group I (<7.3%) (N=20)		Group II (7.3-8.0) (N=10)		Group III (> 8%) (N=20)	
	rho	P	rho	P	rho	P
FBG	0.574	0.021 (S)	0.707	0.022 (S)	0.679	0.001 (HS)
Mean PP	0.710	<0.001 (HS)	0.707	0.022 (S)	0.659	0.002 (S)

rho = Spearman's correlation coefficient

The study revealed that the relative contribution of the postprandial plasma glucose to glycated albumin(rho =0.515 and p< 0.001) was higher than that of fasting plasma glucose (rho=0.338 and p=0.016) **(Table 5).**

Table5 :Correlation between glycated albumin and Fasting and PostPrandial plasma glucose levels.

With	GA	
	rho	P
FBG	0.338	0.016 (S)
Mean PP	0.515	<0.001 (HS)

rho = Spearman's correlation coefficient

Discussion:-

Day time suppression of post-meal excursion is lost first, followed by nocturnal deterioration of fasting sugars with worsening diabetes **(Leahy ,2005).**As HbA1c levels increases with duration of type 2 diabetes in patients not treated with insulin, diurnal glycaemic control is lost in progressive steps – first during post-prandial periods then in the morning period (during the 'dawn phenomenon' of rising blood glucose), and then in the nocturnal fasting period (**Monnier et al., 2007).** As glycaemic control improves with basal-insulin treatment,PPBG coverage is needed to achieve or to keep HbA1C at < 7%. In addition to being a marker for the onset of type 2 diabetes, elevated PPBG is an independent risk factor for the development of micro- and macrovascular complications and affects the morbidity and mortality associated with long-term hyperglycaemia **(Torffvit ,2003).T**he current study revealed that the relative contribution of the postprandial plasma glucose to HbA1C was higher than that of fasting plasma glucose in fairly controlled patients(HbA1C <7.3%) whereas the contribution of fasting hyperglycemia increases gradually with diabetes worsening (HbA1C>8 %).This was in agreement with **Monneir et al., (2003)** who conducted a study on 290 non–insulin- and non acarbose using patients with type 2 diabetes, plasma glucose (PG) concentrations were determined at fasting (8:00 A.M.) and during postprandial and post-absorptive periods (at 11:00 A.M., 2:00 P.M.,and 5:00 P.M.). They evaluated the relative contributions of postprandial and fasting PG increments to the overall diurnal hyperglycemia. The data were compared over quintiles of HbA1c.They found that the relative contribution of postprandial glucose excursions is predominant in fairly controlled patients whereas the contribution of fasting hyperglycemia increases gradually with diabetes worsening .Similar results were reached by **Woerle et al., (2004)** who found that in response to an OGTT the change in 2-h postprandial glucose concentrations was much greater than that in FPG levels for every unit increase in HbA1c, in individuals with HbA1c < 7.0% indicating that postprandial glucose contributes more than fasting glucose to HbA1c in this cohort of diabetic subjects.Regarding that the role of fasting hyperglycemia was major as soon as the HbA1c level was above 8%. This finding result was in agreement with the result of **Peter et al., (2006)** who conducted a study on T2DM subjects (n= 262) consumed a standard MTT in the morning after a 10-h overnight fast. Frequent samples for plasma glucose (PG) were collected over the 4-h test period. The relationship between HbA1c and other glycaemic indices derived from the MTT were explored. The participants were divided into three subgroups according to HbA1c (Group 1 equal or□ < 7.0%; Group 2 7.1–9.0%; Group 3 □ 9.0%) and the relative contribution calculated of the postprandial glucose and fasting hyperglycaemia were calculated.They found that the contribution of fasting hyperglycaemia to excess hyperglycaemia increases as glycaemic control deteriorates. The level of GA is approximately three times higher than that of HbA1c. Since the half-life of albumin is shorter than that of RBC, GA reflects a shorter duration, two to three weeks, of glycemic control, than that of HbA1c **(Koga et al., 2011).** when compared with HbA1c values, GA values have more correlation with postprandial glucose levels and glucose excursions**(Hirsch and Brownlee, 2010).** Our study revealed that the relative contribution of the postprandial plasma glucose to glycated albumin was higher than that of fasting plasma glucose .This was in agreement with **Sumitani et al., (2014)** who conducted a study by starting Metformin and lifestyle interventions in 18 patients with newly diagnosed type 2 diabetes.Metformin was titrated to 1500 mg/day or maximum-tolerated dose. HbA1c and GA were measured every four weeks up to 24 weeks.They concluded that Metformin decreased the GA/HbA1c ratio in patients with newly diagnosed type 2 diabetes. This suggests that metformin improves postprandial hyper-glycaemia in patients with newly diagnosed type 2 diabetes.This is indirect proof that GA correlates better with PPG.

In conclusion, both fasting blood glucose and postprandial blood glucose correlated significantly with HbA1c and GA. The relative contribution of postprandial plasma glucose was high in patients with fairly good control of diabetes (HbA1C<7.3%) and decreased progressivelywith worsening diabetes (HbA1c >8%). IN contrast the contribution of fasting plasma glucose showed a gradual increase with increasing level of HbA1c. For patientswith A1c between 7.4 percent and 8 percent, post prandial &fasting make equal contributions to overall hyperglycemia.

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