Postprandial Hyperglycemia as a Significant Risk Factor for Coronary Heart Disease

*** Khalid I. Al-Lehibi** *CABM, MD* **** Mousa Q. Hussein** *MBCh B, FI C M,CS*
***** Zaidan K.Al-Hergani**, *MRCP ,FRCP I, FRCP G*

Abstract:

Background: The highest concentrations of blood glucose during the day are usually found postprandialy. Postprandial hyperglycemia (PPH) is likely to promote or aggravate fasting hyperglycemia. Evidence in recent years suggests that PPH may play an important role in functional & structural disturbances in different body organs particularly the cardiovascular system.

Objective: To evaluate the effect of (PPH) as a risk factor for coronary Heart disease in Type 2 diabetic patients.

Methods: Sixty-three type2 diabetic patients were included in this study. All have controlled fasting blood glucose, with HbA1c correlation. They were all followed for five months period (from May to October 2008). A two hour postprandial glucose (PPG) was done for all. Other risk factors were taken in consideration such as hypertension, obesity, and dyslipidemia. The study was performed on those patients after at least three months of controlled fasting blood glucose. ECG was done to all of them.

Results : Out of the 63 type 2 diabetic patients, 20 had normal PPG and HbA1c levels, one of them (5%), has ischemic changes on ECG twenty patients had normal HbA1c & High PPG with 7 (35%) of them showed ischemic changes on ECG 17 patients showed a high PPG and a high HbA1c with four of them showed ischemic changes on ECG $P<0.05$. The remaining 6 patients had normal PPG but high HbA1c & also only one of them showed ischemic changes on ECG.

Conclusion This study showed that PPH is a significant risk factor for ischemic heart disease (IHD).

Keywords: Postprandial Hyperglycemia Coronary Heart Disease Type 2 Diabetes Mellitus Glycated.

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Introduction:

The period during and following a meal is known as postprandial state [(1)], during this time the absorbed nutrients cause transient changes in plasma levels of glucose, lipids, and hormones, which induce metabolic events in many tissues. Normally the postprandial state lasts for more than half of the awaking time [(2)].

Whitehall study was one of the first studies demonstrating the relation between the increased risk of coronary disease and mortality and elevated glycemia level [(3)].

It was also noticed that high – normal physiologic increases in blood glucose after meals aggravate inflammatory processes in lean, young adults [(4)].

Postprandial glucose is the product of a balance between the increased elevation of glucose level in the blood flow and the subsequent return of these levels to a baseline concentration. This elevation is derived from 2 sources; oral glucose ingested with a meal and endogenous production by the liver. Hepatic glucose production in the postprandial state in the normal subject is reduced because of the increased insulin level and the reduction of glucagons levels. After an oral glucose load, hepatic glucose production reaches the lowest level after 45 minutes and this nadir is maintained for 90 minutes. Thereafter, hepatic glucose production rises towards fasting state. Factors that contribute to excessive PPG excursions are evident in type 2 DM, including a reduction or loss of early phase insulin secretion and disruption of physiological fluctuating pattern of insulin secretion [(3)].

In the regulatory process of glucose balance in the postprandial state, four different conditions may lead to postprandial hyperglycemia [(4, 5)]:

- An abnormally rapid gastrointestinal glucose absorption.
- A reduced hepatic glucose uptake.
- An impaired suppression of endogenous glucose release.
- An impaired peripheral glucose uptake.

It is suggested that the mechanism primarily responsible for PPH in patients with impaired glucose tolerance (GT) and type 2 DM is probably the impaired suppression of hepatic glucose production. Two possibilities might explain the phenomenon of reduced suppression of endogenous glucose release; impaired insulin secretion or impaired insulin sensitivity [5, 6].

It is said that therapy focused on lowering PPG but not lowering fasting glucose, may be superior for maintaining low HbA1c[7].

Hyperglycemia is a primary mediator of diabetic endothelial dysfunction. Impaired endothelial dependent relaxation can be induced by a short exposure (several hours) to high glucose concentration, which implies hyperglycemia dependent metabolic defect rather than irreversible endothelial damage [8].

Other factors which may play a role in the etiology of IHD in diabetic patients are increased platelets adhesion.

Hyperglycemia is reported to enhance the secretion of endothelin-1 in vitro and decreases nitric oxide production in the aorta of diabetic rat and coronary micro-vessels in human. Endothelin-1 is a powerful vasoconstrictor, while nitric oxide is a powerful vasodilator and decrease platelets aggregation.

Another mechanism of potential pathogenic importance in atherosclerosis of coronary vessels is glycation of protein which forms cross linked protein termed advanced glycation end products (AGE), this substance induces synthesis and release of cytokines, vasoadhesion molecule, endothelin-1 & tissue factor. The later plays a prominent role in the initiation of coagulation. The AGE also destroys endothelium derived nitric oxide. Experimentally, AGE production may be impaired by Immunoguanidin [9].

Methods:

Sixty-three type 2 DM patients (40 males and 23 females) aged 40-68 years were recruited in this cross sectional study. They were cooperative, and followed for a period of 5 months (from May to October. 2008) in the Specialized Center for Endocrinology and Diabetes (SCED), Baghdad.

Full history taking, physical examination and ECG were done to each patient. ECG findings of ischemia during the follow-up period regarded to be a positive case of coronary heart disease, included the presence of pathological Q-wave, ST-T changes and left bundle branch block.

All the patients were either on diet control or on oral hypoglycemic agents which include either glibenclamide, metformin or both. They had a controlled FBG concentration for at least 3 months before they had been investigated for HbA1c and PPG level. The controlled FBG did not exceed 110 mg/ml (< or = 6.1 mmol/l). HbA1c level of < or = 7% was considered as target for good control and above 7% was considered as high[10,11].

The 2 hour PPG level accepted as normal as it was less than 140 mg/ml (7.8 mmol/l), and any reading above this figure was considered high level [11].

Other risk factors for coronary heart disease were also taken in consideration such as hypertension, overweight (BMI>25 Kg/M), and dyslipidemia. Blood pressure (BP) readings; any systolic BP > 140 mm Hg and diastolic BP > 90 mm Hg was considered to be elevated. Serum cholesterol level > 200 mg/ml (>5.1 mmol/L), serum triglyceride level > 180 mg/ml (2.4 mmol/L) were considered to be high, and serum high density lipoprotein (HDL)- cholesterol in male < 35 mg/ml (< 0.9 mmol/L) and in female < 40 mg/ml (< 1.1 mmol/L) were considered to be low[4,5,9].

Statistical analysis was done using descriptive analysis (frequencies and percentages) and inferential analysis using Chi-square test. P value less than 0.05 considered statistically significant.

Results:

The patients were divided into 4 groups(table 1, 2, and 3)

Group-1: Out of the 63 type 2 DM patients, 20 had normal PPG and HbA1c levels. One patient (5%) only had evidence of ischemic heart disease (IHD) .

Group-2: Out of 20 patients who had normal HbA1c but high PPG, 7 patients (35%) showed evidence of IHD (P-value < 0.05).

Group-3: Out of 17 patients who had high HbA1c and high PPG, 4 patients (23.5%) found to have IHD (P-value < 0.05)

Group-4: The remaining 6 patients (16.7%) had normal PPG but high HbA1c, only one patient fulfills criteria of IHD.

Table 1- the 4 groups of patients with their PPG, HbA1c & the related Number of cases with IHD (* P-value < 0.05 ** P-value <0.05)

Group no.	HbA1c	PPG	No.of patients	ECG
1	N	N	20	1(5%)
2	N	Increased	20	7(35%)*
3	Increased	Increased	17	4(23.5%)**
4	Increased	N	6	1(16.7%)
Total			63	13(20.6%)

Table 2 – The risk factors in the different patient groups

Risk factors	Group1 n =20	Group 2 n =20	Group 3 n =17	Group 4 n = 6	P-value
Sex					
Male	14	13	11	2	0.43
Female	6	7	6	4	
Disease					
Duration	14	7	9	2	
< 1 year	6	13	8	4	0.13
> 1 year					
Family Hx of IHD					
Positive	7	9	5	3	0.71
Negative	13	11	12	3	
BMI					
< 25 Kg/M2	13	2	7	3	
> 25 Kg/M2	7	18	10	3	0.005
BP.					
Normotensive	18	13	10	5	
Hypertensive	2	7	7	1	0.13
Lipid profile :					
High triglyc.	2	3	2	4	0.01
High chol.	5	3	5	5	0.02
Low HDL	2	3	7	1	0.12

Table 3 – The significance of the risk factors in patients with IHD

Risk factors	Non IHD patients No.	%	IHD patients No.	%	P-value
Sex					
• Male	40	63.49	7	17.5	0.42
• Female	23	36.51	6	16.4	
Duration					
> 1 year	31	49.20	8	25.80	0.32
Family Hx					
Positive	24	38.10	3	12.50	0.21
BMI					
> 25 Kg/M	38	60.31	11	28.94	0.04
BP					
Hypertensive	17	26.98	8	47.05	0.002
Lipid profile					
• High TG	11	17.46	3	27.27	0.55
• High Chol.	18	28.57	5	27.77	0.38
• Low HDL	13	20.63	6	46.15	0.01
PPG					
• High	37	58.73	11	29.72	0.03
High HbA1c	26	41.27	2	07.69	0.03

Discussion:

The effect of type 2 DM and fasting hyperglycemia on cardiovascular (CV) system especially coronary heart disease had been well studied [10,11] In the last few years there had been much focusing on the risk of PPH on the CHD [1, 12].

In this study we found that the PPH is a significant risk factor for CHD & this is clearly evident on both group 2 & 3 (group of patients with high PPH irrespective to HbA1c) compared to group 1 & 4 (group of patients with normal PPG) (P – value < 0.05) (table 1) & this is in consistent with Kuusisto &Laakso study in 1999 which found that the increased PPG level is an independent risk factor for cardiovascular disease [13].

This subject had been revised by Groeneveld & colleagues who noted that in 24 studies in which an association between glucose concentration & mortality from CV complications, the direction was in favor of hyperglycemia [14]. The same observation was found in another study which emphasized that minor increase in glucose intolerance was associated with increased cardiovascular risk [15, 16].

In Diabetes Intervention Study (DIS), they found a good correlation between statistically significant PPH and increase risk of myocardial infarction (MI) and death [17]. Similarly in Paris Prospective Study (PPS), they found that the risk from CV death in diabetic patients is around twice for PPH as compared with the fasting hyperglycemia [18].

In comparing the risk factors in the 4 studied groups (table 2) only the overweight and the dyslipidemia found to be statistically significant in patients with impaired PPG and those with impaired HbA1c, and this is similar to the study which had been done by Hanifield M, Fissure S , Julius U , et al in 1996 who stated that dyslipidemia and obesity remain the major modifiable risk factors among most risk factors in patients with impaired glucose tolerance(IGT) [19].

In studying the different risk factors in the 13 patients with IHD (table 3) it was found that hypertension and overweight were

associated with high risk compared to normotensive & normal weight patients (P-value = 0.002 & 0.04 respectively) & this is compatible with other studies elsewhere [19, 20]. Regarding dyslipidemia only the low HDL found to be statistically significant risk factor in this study (0.01) & this significant finding is similar to that found in other studies [21]. while the hypercholesterolemia & the high triglyceride level found to be statistically insignificant & this does not match the well known effect of total cholesterol & triglyceride on the IHD & this may be due to the small number of total cases & also to the relative small number of positive cases [19, 22].

It was also found that PPH is as significant as the high HbA1c (P- value = 0.03) as a risk factor for IHD & this is similar to other studies [23].

Conclusions

The PPH is a significant risk factor for IHD and may be as important as or more important than fasting hyperglycemia and high and HbA1c.

It is the every doctor's duty, especially the endocrinologist to focus their effort not only on normalizing FBG and the HbA1c, but also to manage the PPH in order to reduce its devastating cardiovascular risks. This needs a good understanding from both the patients & the doctor's side.

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****From the Department of Endocrinology, Baghdad Consultant physician Specialized Center for Endocrinology and Diabetes, Baghdad.***
Corespondence Address to :Dr. Khalid I. Al-Lehibi
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