



Clinical and Biochemical Features of Type 2 Diabetic Patients in Gaza Governorate, Gaza Strip

Aspects cliniques et biochimiques du diabète de type 2 dans la province de Gaza, Bande de Gaza

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ABSTRACT

BACKGROUND: Diabetes is a multifactorial disease characterized by several metabolic disorders. Its prevalence rate in Gaza Strip is alarming.

OBJECTIVE: To describe the clinical and biochemical features of patients with Type 2 diabetes in Gaza Governorate.

METHODS: Data were obtained through a questionnaire interview, patients' records and of 99 type 2 diabetes patients and 95 healthy individuals.

RESULTS: Family history and obesity were risk factors for diabetes. The mean age at diagnosis was 41.7 ± 8.1 years. Fifty five (55.6%) patients had diabetes since >5 years. Distribution of diagnosed diabetic complications was low. Micro- and macroalbuminuria in controls and patients ($8.4 \text{ v } 22.2\%$ and $9.5 \text{ v } 22.2\%$, respectively) were associated with diabetes ($\chi^2=7.06$, $P=0.007$ and $\chi^2=5.87$, $P=0.015$, respectively). HbA1c% was significantly higher in diabetics ($6.93 \pm 1.22 \text{ v } 5.36 \pm 0.57$, $p < 0.001$). Serum urea and creatinine were significantly decreased in diabetics than controls (mean = $23.5 \pm 6.9 \text{ v } 27.2 \pm 7.4$ and $0.49 \pm 0.15 \text{ v } 0.58 \pm 0.14$, % differences = 13.6 and 15.5, respectively, $p = 0.000$). Alkaline phosphatase (ALP) was increased in diabetics ($136.9 \pm 38.7 \text{ v } 117.4 \pm 23.5$, % difference = 16.6, $p = 0.001$). Cholesterol, triglycerides and low density lipoprotein cholesterol (LDLC) were significantly higher in diabetics (207.6 ± 36.5 , 184.1 ± 104.5 and 124.6 ± 32.9) than controls (181.2 ± 39.1 , 139.8 ± 76.1 and 102.2 ± 37.4) with % differences of 14.6, 31.7 and 21.9%, respectively, $p < 0.001$. In contrast, high density lipoprotein cholesterol (HDLc) was significantly lower in diabetics ($42.6 \pm 7.8 \text{ v } 48.2 \pm 5.7$, % difference = 11.6 and $p < 0.001$).

CONCLUSIONS: Diabetes was associated with family history, obesity and micro- or macroalbuminuria. HbA1c%, ALP, cholesterol, triglycerides and LDLC were higher in diabetics than controls. In contrast, urea, creatinine and HDLC were lower in diabetics. *WAJM* 2011; 30(1): 51–56.

Keywords: Clinical and Biochemical Features, Gaza Strip, Type 2 Diabetes, Lipids, albuminuria, Family history, complications.

RÉSUMÉ

CONTEXTE: Le diabète est une affection multifactorielle caractérisée par divers troubles métaboliques. Son taux de prévalence dans la bande de Gaza est préoccupante.

OBJECTIFS: Décrire les caractéristiques cliniques et biochimiques de patients atteints de diabète de type 2 dans le gouvernorat de Gaza.

METHODES: Les données ont été obtenues par un questionnaire sur les dossiers de 99 patients atteints de diabète de type 2 et 95 personnes en bonne santé.

RÉSULTATS: Les antécédents familiaux et l'obésité sont des facteurs de risque pour le diabète. L'âge moyen au moment du diagnostic était de $41,7 \pm 8,1$ ans. Cinquante cinq patients (55,6%) avaient le diabète depuis plus de 5 ans. La survenue des complications diagnostiquées au cours du diabète était faible. La microalbuminurie et la macroalbuminurie chez les témoins et les patients diabétiques représentaient ($8,4 \text{ v } 22,2\%$ et $9,5 \text{ v } 22,2\%$, respectivement) ($\chi^2 = 7,06$, $P = 0,007$ et $\chi^2 = 5,87$, $P = 0,015$, respectivement). Le pourcentage d'HbA1c a été significativement plus élevé chez les diabétiques ($6,93 \pm 1,22 \text{ v } 5,36 \pm 0,57$, $p < 0,001$). Les résultats de l'urée et la créatinine sérique étaient significativement plus réduits chez les diabétiques que chez les témoins (moyenne = $23,5 \pm 6,9 \text{ v } 27,2 \pm 7,4$ et $0,49 \pm 0,15 \text{ v } 0,58 \pm 0,14$, les % de différence = 13,6 et 15,5, respectivement, $p = 0,000$). Les phosphatases alcalines (PAL) étaient augmentées chez les diabétiques ($136,9 \pm 38,7 \text{ v } 117,4 \pm 23,5$, % de différence = 16,6, $p = 0,001$). Le cholestérol total, les triglycérides et les lipoprotéines de basse densité (LDLC) étaient significativement plus élevés chez les diabétiques ($207,6 \pm 36,5$, $184,1 \pm 104,5$, $124,6 \pm 32,9$) que chez les témoins ($181,2 \pm 39,1$, $139,8 \pm 76,1$ et $102,2 \pm 37,4$) avec des différences de pourcentage de 14,6, 31,7 et 21,9 respectivement, $p < 0,001$. En revanche, les taux élevés des lipoprotéines de haute densité (HDLc) était significativement plus faibles chez les diabétiques ($42,6 \pm 7,8 \text{ v } 48,2 \pm 5,7$, % de différence = 11,6 et $p < 0,001$).

CONCLUSION: Le diabète est associé à des antécédents familiaux, à l'obésité et la microalbuminurie ou la macroalbuminurie. Le taux d'HbA1c, les PAL, le taux de cholestérol total, des triglycérides et des LDLC ont été plus élevés chez les diabétiques que chez les témoins. En revanche, les taux d'urée, de créatinine et des HDLC étaient plus bas chez les diabétiques. *WAJM* 2011; 30(1): 51–56.

Mots-Cles: Caractéristiques Cliniques Et Biochimiques, Bande De Gaza, Diabète De Type 2, Lipides, Albuminurie, Histoire Familiale, Complications.

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Abbreviations: AGEs, Advanced Glycosylated End-products; ALP, Alkaline Phosphatase; HbA_{1c}, Haemoglobin A_{1c}; HDL-C, High Density Lipoprotein cholesterol; LDL-C, Low Density Lipoprotein Cholesterol.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterised by hyperglycaemia.¹ Lack of or severe reduction in insulin secretion due to autoimmune destruction of β cells is responsible for Type 1 diabetes. The more prevalent form, Type 2 diabetes, accounts for more than 90% of cases and is associated with older age and obesity.² Type 2 diabetes usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. As the need for insulin rises, the pancreas gradually loses its ability to produce it.³

Lack of insulin action and/or secretion induces hepatic glucose output by inhibiting glycogen synthesis and stimulating glycogenolysis and gluconeogenesis. Increased rates of hepatic glucose production result in the development of overt hyperglycaemia, especially fasting hyperglycaemia, in patients with type 2 diabetes.⁴ In such conditions, lipolysis in adipose tissue is promoted leading to elevated circulating levels of free fatty acids.⁵ In addition, kinetics of whole-body protein metabolism are elevated, and net balance is diminished in type 2 diabetes, independently of obesity.⁶

One of the most severe complications of diabetes is the development of diabetic nephropathy (DN). The earliest clinical evidence of DN is the appearance of microalbuminuria (urinary albumin 30–300 mg/24hr). Patients with microalbuminuria are referred to as having incipient nephropathy. Without specific interventions, 20–40% of Type 2 patients with microalbuminuria progress to macroalbuminuria (urinary albumin >300 mg/24hr), but by 20 years after onset of macroalbuminuria, only ~20% will have progressed to end stage renal disease.⁷

Although diabetes mellitus is prevalent in the Gaza Strip,⁸ there is under-diagnosis and under-reporting of the disease. Biochemical data are only restricted to monitoring blood glucose level when the patient visits the clinic. Hence, we set out to assess many of the biochemical features in blood and urine of Type 2 diabetic patients in Gaza Governorate, Gaza Strip. Understanding such features could be useful in the management of the disease.

SUBJECTS, MATERIALS, AND METHODS

Study Design and Study Population

The present study was a cross sectional study. The study population was 99 type 2 diabetes patients (44 males and 55 females) selected randomly from Al Remal Diabetic Clinic which is the representative clinic for diabetic patients in Gaza Governorate. A total of 95 healthy individuals (52 males and 43 females) with no personal history of diabetes were selected randomly from general population and served as a control sample. The inclusion criteria were that patients and controls were 30–60 years old and normotensive. For ethical consideration, the necessary approval to conduct the study was obtained from Helsinki Committee in the Gaza Strip in 2007.

Questionnaire Interview

A meeting interview was used for filling in the questionnaire. All interviews were conducted face to face by one investigator who had a Bachelor degree of Medical Technology. The questionnaire was based on diabetic clinic questions of Al Rimal Medical Center with some modifications.⁹ Most questions were the yes/no type, which offer a dichotomous choice. A questionnaire was piloted with 10 patients not included in the population sample, and modified as necessary. The questionnaire included questions related to age, sex, smoking, and family history of diabetes.

Patients' Records

Clinical data including age at diagnosis, duration of diabetes, and diagnosed diabetic complications were obtained from the patients' records.

Body Mass Index (BMI) was calculated as Kg body weight/height in meter squared. People with BMI=18.5–24.9 were considered to have normal weight, people with BMI=25.0–29.9 were classified overweight, people with BMI=30.0–34.9 were considered obese of type I and those with BMI=35.0–39.9 were obese of type II, and people with BMI \geq 40 were classified as extremely obese.¹⁰

Blood and Urine Testing

Fasting overnight venous blood samples (about 8 ml each) were collected into vacutainer tubes from 99 Type 2 diabetic patients and 95 controls by a well trained medical technologist. About 2 ml blood was placed into EDTA vacutainer tube to perform glycohaemoglobin (HbA_{1c}) for diabetic patients. The remainder quantity of blood was left for a while without anticoagulant to allow blood to clot. Then, serum samples were obtained by centrifugation (Rotina 46 Hettich Centrifuge, Japan) at 4000 rpm/10 minutes to be used for analysis. Random urine samples were also collected from the same patients and controls. The samples were then centrifuged by the same way as serum to precipitate all the debris and then used for analysis.

Urine Analyses: Microalbuminuria (urinary albumin 30–300 mg/24hr) and macroalbuminuria (urinary albumin >300 mg/24hr) were determined by immunoturbidometry-latex method¹¹ and pyrogallol red method,¹² respectively using BioSystems kits, Spain.

Biochemical Analysis

Serum Glucose was determined by glucose oxidase (GOD)/glucose peroxidase (POD) method¹³ using Labkit Kits, Spain.

HbA_{1c} in whole blood was measured by the colorimetric determination of glycohemoglobin in whole blood¹⁴ using Stanbio Kit, Texas-USA.

Serum urea and creatinine were determined by urease-glutamate dehydrogenase (GDH)/UV method¹⁵ and by Alkaline Picrate method,¹⁶ respectively using BioSystems kit, Spain.

Alkaline phosphatase and α -amylase: Serum alkaline phosphatase was measured by 2-amino-2-methyl-1-propanol (AMP) International Federation of Clinical Chemistry (IFCC) method¹⁷ using BioSystems kit, Spain and serum \pm -amylase was determined by 4, 6-ethylidene-(G7)-1-4-nitrophenyl-(G1)- \pm -D-maltoheptaoside (EPS-G7) method¹⁸ using Diasys kit, Germany.

Lipid Profile: Serum total cholesterol was estimated by cholesterol oxidase (COD)/POD method¹⁹ using BioSystems kit, Spain. High density lipoproteins (HDL-C) was determined by precipitating method²⁰ using Labkit kit, Spain and low density lipoproteins (LDL-C) was calculated using the empirical relationship of Friedewald.²¹ Serum triglycerides were measured by Glycerol phosphate oxidase/peroxidase method²² using BioSystems kit, Spain.

Data Analysis

Data were analyzed using Statistical Package for Social Sciences Inc, Chicago, Illinois (SPSS) computer program version 13.0 for windows. Simple distribution of the study variables and the cross tabulation were applied. Statistical relationships between various variables and diabetes mellitus were assessed using Chi-square (χ^2) test and pooled T-test. Means were compared by independent-samples t-test. Probability values (P) were obtained from the student's table of "t" and significance was at $P < 0.05$.

RESULTS

General Characteristics of the Study Population

Table 1 provides the description of the study population. The mean age of controls was 41.8 ± 8.3 years whereas that of diabetics was 45.1 ± 7.4 years. Fifty-two (54.7%) of controls were males and 43 (45.3%) were females. Diabetic males and females were 44 (44.4%) and 55 (55.6%), respectively. Twenty-three (24.2%) controls and 17 (17.2%) diabetics were smokers. Twenty-nine (30.5%) controls and 45 (45.5%) patients had a family history of diabetes. There was no statistically significant relationship between diabetes and gender or smoking ($\chi^2 = 2.05$, $P = 0.151$ and $\chi^2 = 1.47$, $P = 0.225$, respectively). However, diabetes was found to be associated with family history ($\chi^2 = 4.58$, $P = 0.032$).

Duration of the Diabetes and Diabetic Complications

The mean age of diabetic patients at diagnosis was 41.7 ± 8.1 years. Table 2 shows that diabetic patients since ≤ 5 years were 55 (55.6%), whereas those with diabetic duration of 6–10 years were 29

Table 1: General Characteristics of the Study Population

Characteristic	Controls 95	Diabetics 99	P-value
Mean age (Year)	41.8±8.3	45.1±7.4	0.073
Gender			
Male	52 (54.7)	44 (44.4)	0.151
Female	43 (45.3)	55 (55.6)	
Smoking			
Yes	23 (24.2)	17 (17.2)	0.225
No	72 (75.8)	82 (82.8)	
Family History			
Yes	29 (30.5)	45 (45.5)	0.032
No	66 (69.5)	54 (54.5)	

Values are N(%) except age

Table 2: Distribution of Diabetic Patients by the Duration of the Disease

Duration of Diabetes (Year)	Number (%)
≤ 5	55 (55.6)
6–10	29 (29.3)
11–15	11 (11.1)
16–20	3 (3.0)
>20	1 (1.0)

(29.3%). The rest of the population was distributed over the intervals 11 to >20 years. In addition, diagnosed complications among diabetic patients were neuropathy 7 (7.1%), cardiovascular diseases 3 (3.0%), retinopathy 2 (2.0%) and oral cavity lesions 2 (2.0%).

Diabetes and Body Mass Index

Table 3 shows significant associations between different classes of body mass index and diabetes. Normal weight and overweight status were more common among the controls than the

diabetics ($\chi^2 = 10.54$, $P = 0.001$ and $\chi^2 = 5.33$, $P = 0.020$, respectively) whereas obesity either grade I or grade II and extremely obese was more common among the diabetics ($\chi^2 = 5.53$, $P = 0.018$, $\chi^2 = 7.16$, $P = 0.007$ and $\chi^2 = 5.94$, $P = 0.014$, respectively).

Proteinuria and Glycaemia

Urine analysis revealed that microalbuminuric controls and diabetics were 8 (8.4%) and 22 (22.2%) and macroalbuminurics were 9 (9.5%) and 22 (22.2%), respectively. Significant association was found between micro- and macroalbuminuria with diabetes ($\chi^2 = 7.06$, $P = 0.007$ and $\chi^2 = 5.87$, $P = 0.015$, respectively). Diabetic patients had higher serum glucose and HbA1c% than controls (186.0 ± 80.2 v 83.8 ± 16.1 mg/dl and 6.93 ± 1.22 v $5.36 \pm 0.57\%$, respectively, $p < 0.01$).

Serum Urea and Creatinine

As illustrated in Table 4 the mean serum urea and creatinine concentrations were significantly decreased in diabetics compared to controls showing percentage decrease of 13.6 and 15.5% (23.5 ± 6.9 v 27.2 ± 7.4 and 0.49 ± 0.15 v 0.58 ± 0.14 with $t = 3.60$, $p < 0.01$) and $t = 4.23$, $p = 0.000$, respectively).

Serum Amylase and Alkaline Phosphatase (ALP) Activities

Table 4 reveals no significant difference in serum amylase activity between diabetics and controls (mean = 35.8 ± 16.0 v 36.2 ± 16.5 , % difference = 1.1, $t = 0.19$, $p = 0.846$). On the other hand, the activity of serum ALP was significantly increased in diabetics compared to controls (mean = 136.9 ± 38.7 v 117.4 ± 23.5 , % difference = 16.6, $t = 4.16$, $p = 0.001$).

Table 3: Weight Classifications* by Body Mass Index of Controls and Diabetics

BMI Group	BMI	Number (%)		P-value
		Controls 95	Diabetics 99	
Normal Weight	18.5 – 24.9	27 (28.4)	10 (10.1)	0.001
Overweight	25.0 – 29.9	42 (44.2)	28 (28.3)	0.020
Obese I	30.0 – 34.9	20 (21.1)	36 (36.4)	0.018
Obese II	35.6 – 39.9	6 (6.3)	19 (19.2)	0.007
Extreme Obesity	≥ 40	0 (0.0)	6 (6.1)	0.014

Table 4: Serum Chemistry of Controls and Diabetics

Variable	Mean \pm SD (min – max)		% Difference	P-value
	Controls (N = 95)	Diabetics (N = 99)		
Urea (mg/dl)	27.2 \pm 7.4 (14–47)	23.5 \pm 6.9 (12–43)	–13.6	<0.01
Creatinine (mg/dl)	0.58 \pm 0.14 (0.33–1.18)	0.49 \pm 0.15 (0.27–0.95)	–15.5	<0.01
Enzyme				
Amylase (μ l)	36.2 \pm 16.5 (9–93)	35.8 \pm 16.0 (10–96)	–1.1	0.846
ALP (μ l)	117.4 \pm 23.5 (69–206)	136.9 \pm 38.7 (70–249)	16.6	<0.01
Lipid Profile				
Cholesterol (mg/dl)	181.2 \pm 39.1 (106–301)	207.6 \pm 36.5 (133–314)	14.6	<0.01
Triglycerides (mg/dl)	139.8 \pm 76.1 (43–374)	184.1 \pm 104.5 (55–488)	31.7	<0.01
HDL-C (mg/dl)	48.2 \pm 5.7 (33–69)	42.6 \pm 7.8 (28–63)	–11.6	<0.01
LDL-C (mg/dl)	102.2 \pm 37.4 (36–199)	124.6 \pm 32.9 (53–210)	21.9	<0.01

Lipid Profile of Controls and Diabetics

As depicted in Table 4, the average levels of serum cholesterol, triglycerides and low density lipoprotein cholesterol were significantly higher in diabetics (mean=207.6 \pm 36.5, 184.1 \pm 104.5 and 124.6 \pm 32.9) compared to controls (181.2 \pm 39.1, 139.8 \pm 76.1 and 102.2 \pm 37.4) with percentage differences of 14.6, 31.7 and 21.9% (t=4.73, p < 0.01, t=3.71, p < 0.01 and t=4.46, p < 0.01, respectively). In contrast, high density lipoprotein cholesterol was significantly lower in diabetics than in controls (42.6 \pm 7.8 v 48.2 \pm 5.7, % difference=11.6 and t=5.85, p < 0.01 p < 0.01).

DISCUSSION

In the Gaza Strip, data on diabetes mellitus have been limited to annual reports produced by the Palestinian Ministry of Health. Biochemical tests of the disease were restricted to monitoring blood glucose level when the patient visited the clinic. This necessitated further assessment of other biochemical features not only in blood but also in urine to get a clearer picture on the patient condition, and to help in the disease management.

General Characteristics of Patients, Duration of Diabetes and Diagnosed Diabetic Complications

The study population was 99 Type 2 diabetic patients from Al Remal diabetic clinic which is the representative clinic for diabetic patients in Gaza Governorate. Their mean age was 45.1 \pm 7.4 years whereas that of controls it was 41.8 \pm 8.3 years. It was reported that Type 2 diabetes mellitus usually develops after age 40 years.²³ This was confirmed by considering the mean age at diagnosis which was 41.7 \pm 8.1 years. A similar study showed that the mean age at diagnosis of Type 2 diabetics was 40 years.²⁴ The family history as a risk factor for diabetes is in agreement with other studies.²⁵ The finding that more than half of the patients (55.6%) had diabetes for 5 years or less does confirm the idea that Type 2 diabetes has a long asymptomatic pre-clinical phase which frequently goes undetected. At the time of diagnosis, the patient could have one or more diabetes complications.²⁶ However, occurrence of diagnosed diabetic complications among our diabetic patients was low. This needs further investigation.

Diabetes and Body Mass Index

Body mass index provides a reliable indicator of body fatness for most people and is used to screen for weight categories that may lead to health problems. In our study this index was significantly associated with diabetes, where most of the diabetic patients were obese and extremely obese compared to controls. Similar results were obtained for diabetic patients from Saudi Arabia.²⁷

Albuminuria, and HbA1c% in Controls and Diabetics

Micro- and macroalbuminuria were found to be associated with diabetes as reflected by the higher rates of such conditions in diabetics compared to controls. This implies that many of our patients might have developed micro-albuminuria before their actual diagnosis of their diabetics. The higher HbA1c% in diabetic patients compared to controls is in line with this trend. Similar results have been reported in Type 2 diabetic patients with diabetic nephropathy.²⁸

In diabetes, prolonged hyperglycaemia superdrives nonenzymatic protein glycation, which forms reversible Schiff bases and Amadori compounds. A series of further complex molecular rearrangements then yield irreversible advanced glycosylated end-products (AGEs). AGEs accumulate in the circulating blood and in various tissues. The role of AGEs in diabetic nephropathy has been established.²⁹ Therefore, it is important to screen diabetic patients for microalbuminuria to reduce and/or slow the progression of nephropathy by optimizing control of glucose and blood pressure.³⁰

Serum Urea, Creatinine, and Enzymes

As indicated in the data serum urea and creatinine concentrations of diabetics were significantly decreased compared to that of controls. Urea is formed by the liver as an end product of protein breakdown and is one marker of the kidney function.³¹ Decrease in serum urea observed here may be due to impairment in its synthesis as a result of impaired hepatic function and/or due to disturbance in protein metabolism. Creatinine is a waste product that is normally filtered from the blood and

excreted in the urine. Lower creatinine levels in diabetic patients is rather difficult to explain, except if there is hyperfiltration in the diabetics. It is difficult to determine the onset of such changes and this may lead to controversial results.^{28,32} Therefore, we must watch the creatinine levels carefully to determine how much function the kidneys have and this does vary slightly.

Serum amylase enzyme seems not to play a major role in diabetes. However, ALP was significantly increased in diabetics compared to controls. ALP was reported to be associated with prevalence of type 2 diabetes.³³

Plasma Lipid Profile of Controls and Diabetics

Plasma Lipid profile showed significant increase in total cholesterol, triglycerides and LDL-C in diabetics when compared to controls. In contrast there was significant decrease in HDL-C in diabetics. It is worth mentioning that about two thirds of our diabetic subjects had disturbance in their lipid metabolism. It is known that cholesterol, triglycerides and LDL-C are elevated in diabetic patients.³⁴ The abnormal high concentrations of serum lipids in diabetics is due, mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase. Excess fatty acids in serum of diabetics are converted into phospholipids and cholesterol in liver. These two substances along with excess triglycerides formed at the same time in liver may be discharged into blood in the form of lipoproteins.³⁵

Conclusion

In this study, diabetes was associated with family history. The mean age at diagnosis was 41.7±8.1 years. More than half of patients had diabetics since ≤5 years. Occurrence of diagnosed diabetic complications was low. Diabetes was associated with different classes of BMI, micro- or macroalbuminuria. HbA1c%, ALP, cholesterol, triglycerides and LDL-C were higher in diabetics than controls. In contrast, urea, creatinine and HDL-C were lower in diabetics.

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