ORIGINAL ARTICLE

Insulin Secretory Defects and Determinants of Attending at a Tertiary Hospital in Northern Region of Bangladesh

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ABSTRACT

Background: Bangladesh has one of the largest diabetic populations in the world and its Rajshahi region has distinct geographical and cultural identity. Determinants and basic defects of the disorder which vary substantially among populations due to racial and environmental heterogeneity.

Materials & Methods: This study was conducted to characterize the new patients attending the Rajshahi Diabetic Center which gives an idea about the proportion and risk indicators of DM among people in the Rajshahi region. It was a hospital based observational analytic study with a hybrid research strategy having both cross-sectional and nested case-control designs. A multistage sampling technique was followed with 660 subjects.

Results: Out of the total subjects attending the OPD of RDC for the first time, 65% were found to suffer from T2 DM. mostly (75%) of middle age (37% within 30-40 yrs and 37% within 41-50 yrs), only 2% cases had age <30 yrs and 23% had age >51yrs. The mean $\pm$SD calorie consumption (2549 ± 637) of the diabetic subjects was higher than that in non-T2 DM subjects and it came mainly from CHO (59.3%) and fat (55.9%). 47.3% of subjects were normal weight, 36.1% over weight and 16.6% obese. Fasting serum Insulin was significantly higher in the T2 DM group as compared to non-T2DM (Serum Insulin level μIU/ml, M$\pm$SD) (13.5 ± 4.9) subjects ($p=<0.001$). HOMA%B was (37 ± 17) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects. HOMA%S was (41 ± 13) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects.

Conclusion: Both (HOMA%B) and (IR) constitute the basic defects of diabetes in Rajshahi population, but (HOMA%B) seems to be more predominant in these subjects. (HOMA%B) in Rajshahi population is associated with males and level of education and insulin resistance (IR) is associated with males and daily CHO intake.

Key Words: Diabetes mellitus, Insulin secratory defect, Rajshahi.

Introduction

Among the NCD, diabetes mellitus (particularly T2DM) and other disorders of metabolic syndrome are creating major health burden all over the world. These have produced great concern for both health care providers and recipients. It has been declared that diabetes has reached epidemic proportion and it has been predicted that most of the increase will be contributed by developing country (i.e, India, Indonesia, Japan, Pakistan, Russian Federation, Brazil, Italy and Bangladesh).[1] Thus Bangladesh is one of the most vulnerable countries as regards to the burden of T2 DM. Bangladesh, as one of the least developed

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countries is facing the burden of diabetes in a rapidly increasing trend. As per rating of diabetics among most prevalent countries, Bangladesh was in 10th position in 2000. But it is projected that, if the present trend of increase continues, in 2030 Bangladesh will rank in 6th position among the 10 countries having highest number of diabetics.[2] As estimated on the basis of present prevalence rates of T2DM (5.2%) and IGT (12.5%), more than 10 million Bangladeshi would suffer from DM by 2025.[2,3,4]

Rational management and prevention strategies for DM require an understanding on the burden, determinants and basic defects of the disorder which vary substantially among populations due to racial and environmental heterogeneity. Bangladesh has one of the largest diabetic populations in the world and its Rajshahi region has distinct geographical and cultural identity. Limited information on the prevalence, risk factors and basic defects of DM are present among Bangladeshi population in general but, so far, no study has yet been conducted on any epidemiological or pathophysiological aspects of DM in Rajshahi population. This study was conducted to characterize the new patients attending the Rajshahi Diabetic Center which gives an idea about the proportion and risk indicators of DM among people in the Rajshahi region. At the same time the study also aimed to investigate the basic defects of T2 DM in this population.

Materials & Methods

It was a hospital based observational analytic study with a hybrid research strategy having both cross-sectional and nested case-control designs. A multistage sampling technique was followed with 660 subjects in stage 1 for exploring the proportion of T2 DM and its association with clinical, socio-demographic and biochemical risk factors. In stage 2, a subgroup of subjects and non-diabetic controls, selected through a nested case-control design, were investigated for the basic defects (insulin secretory defect or insulin resistance) of DM and their association with various risk factors. Nutritional intake was assessed by food frequency questionnaire (24 hr dietary recall) method. Each subject went through OGTT following appropriate preparation and DM was diagnosed as per WHO Study Group Criteria. Blood glucose was measured by glucose oxidase method (Randox, UK) using a semi auto analyzer (300 MICROLAB). Lipids were measured by enzymatic methods. Serum insulin was measured by Chemiluminscent ELISA using mulite auto-analyzer (DPC, USA). Insulin secretory capacity (HOMA% B) and insulin sensitivity (HOMA% S) were calculated by homeostasis Model assessment method using HOMA-CIGMA software.

Results

Out of the total subjects attending the OPD of RDC for the first time, 65% were found to suffer from T2 DM. The diabetic subjects were mostly (75%) of middle age (37% within 30-40 yrs and 37% within 41-50 yrs), only 2% cases had age <30 yrs and 23% had age >51yrs. There was a male preponderance in the proportion of T2 DM (56.4% female and 76.7% male). The diabetic subjects were mostly from middle (34.7%) to upper middle class (31.6%) background and by occupation females were mostly housewives (77.7%). Out of the diabetic subjects 37.7% had lower educational levels. The mean±SD calorie consumption (2549±637) of the diabetic subjects was higher than that in non-T2 DM subjects and it came mainly from CHO (59.3%) and fat (55.9%). Based on WHO criteria for BMI for Asian population, 47.3% of subjects were normal weight, 36.1% over weight and 16.6% obese. All the newly diagnosed diabetic subjects in RDC were found to have poor diabetic control when judged by their fasting blood glucose level (mmol/l, M±SD) (13.4±4.4). Also when considered by blood glucose 2 hrs postprandial values, 97.9% of the T2 DM subjects had poor control. Lipid levels were also found to be largely uncontrolled in the diabetic subjects. On multiple regression, FBG was found to be associated with age ($p=0.002$) and occupation ($p=0.026$) in females and age ($p=<0.001$) and TG level ($p=0.026$) in males T2 DM subjects. Fasting serum Insulin was significantly higher in the T2 DM group as compared to non-T2DM (Serum Insulin level μIU/ml, M±SD) (13.5±4.9) subjects ($p=<0.001$). HOMA%B was (37±17) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects. HOMA%S was (41±13) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects. On multiple regression analysis with HOMA%B was found to be significantly associated with sex (<0.001) and education ($p=0.010$). On similar analysis, with HOMA%S was found to have significant association with males ($p=0.002$) and daily CHO intake ($p=0.028$).

Table-1: Impact of sociodemographic status on the onset of diabetes (Stage 1)

Variables	Male subjects		P value	Female Subjects		P value	Total subjects		P value
	Nondiabetic n=63(23.3%)	Diabetic n=207(76.7%)		Nondiabetic n=170(43.6%)	Diabetic n=220(56.4%)		Nondiabetic n=233(35.3%)	Diabetic n=427(64.7%)	
Age	**49±10**	**46.7±9**	**0.299**	**41±9.8**	**43±8.3**	**0.087**	**43±10**	**44±8**	**0.174**
Education									
Illiterate	11(17.5%)	48(23.2%)	0.505	26(15.3%)	79(35.9%)	<0.001	37(15.9%)	127(29.7%)	<0.001
Secondary	23(36.5%)	68(32.9%)		58(34.1%)	93(42.3%)		81(34.8%)	161(37.7%)	
Higher secondary	13(20.6%)	52(25.1%)		53(31.2%)	28(12.7%)		66(28.3%)	80(18.8%)	
Graduate	16(25.4%)	39(18.8%)		33(19.4%)	20(9.1%)		49(21.0%)	59(13.8%)	
Occupation									
Officials work	43(68.2%)	130(62.8%)	0.144	72(42.4%)	28(12.7%)	<0.001	115(49.4%)	158(37.0%)	<0.001
Business	16(25.4%)	40(19.3%)		6(3.5%)	9(4.1%)		22(9.4%)	49(11.5%)	
House wife	0(0%)	0(0%)		87(51.2%)	171(77.7%)		87(37.3%)	171(40.0%)	
Teacher	2(3.2%)	14(6.8%)		5(2.9%)	7(3.2%)		7(3.0%)	21(4.9%)	
Farmer	2(3.2%)	23(11.1%)		0(0%)	5(2.3%)		2(0.9%)	28(6.6%)	
Monthly income									
Low income	9(14.3%)	26(12.6%)	0.389	18(10.6%)	32(14.5%)	0.011	27(11.6%)	58(13.6%)	0.043
Middle	15(23.8%)	64(30.9%)		44(25.9%)	84(38.2%)		59(25.3%)	148(34.7%)	
Upper middle	27(42.9%)	67(32.4%)		64(37.6%)	68(30.9%)		91(39.1%)	135(31.6%)	
Higher	12(19%)	50(24.2%)		44(25.9%)	36(16.4%)		56(24.0%)	86(20.1%)	

Results are expressed as (Mean±SD), number and (%), n= numbers of subjects, chi-square test were done as tests of significance, according the nature and distribution of variables.

Table-2: Frequency distribution of daily dietary intake of total study subjects (n=660)

Variables	Male subjects		P value	Female Subjects		P value	Total subjects		P value
	Nondiabetic n=63	Diabetic n=207		Nondiabetic n=170	Diabetic n=220		Nondiabetic n=233	Diabetic n=427	
Daily total Calorie Intake									
<1800 k cal	44(69.8%)	24(11.6%)	<0.001	113(66.5%)	35(15.9%)	<0.001	157(67.4%)	59(13.8%)	<0.001
1800-2200 k cal	7(11.1%)	31(15%)		22(12.9%)	36(16.4%)		29(12.4%)	67(15.7%)	
>2201 k cal	12(19%)	152(73.4%)		35(20.6%)	149(67.7%)		47(20.2%)	301(70.5%)	
Daily total CHO Intake									
<269gm	53(84.1%)	45(21.7%)	<0.001	31(77.1%)	55(25.0%)	<0.001	184(79.0%)	100(23.4%)	<0.001
270-328gm	8(12.7%)	36(17.4%)		23(16.5%)	38(17.3%)		31(13.3%)	74(17.3%)	
>330gm	2(3.2%)	126(60.9%)		16(9.4%)	127(57.7%)		18(7.7%)	253(59.3%)	
Daily total Protein Intake									
<66 gm	0(0%)	0(0%)	0.695	0(0%)	1(0.5%)	0.618	0(0%)	1(0.2%)	0.605
67.5-81 gm	12(19.0%)	35(16.9%)		34(20%)	40(18.2%)		46(19.7%)	75(17.6%)	
>82 gm	51(81%)	172(83.1%)		136(80%)	179(81.4%)		187(80.3%)	351(82.2%)	
Daily total Fat Intake									
<49 gm	34(54.0%)	25(12.1%)	<0.001	105(61.8%)	24(10.9%)	<0.001	139(59.7%)	49(11.5%)	<0.001
50-60 gm	18(28.6%)	55(26.7%)		44(25.9%)	84(38.2%)		62(26.6%)	139(32.6%)	
>61.1 gm	11(17.5%)	126(61.2%)		21(12.4%)	112(50.9%)		32(13.7%)	238(55.9%)	

Results are expressed as number (%), n= number of subjects, Chi-square test were done as tests of significance, according to the nature and distribution of variables. DM=Diabetic Mellitus.

Table-3: BMI level of male, female, and total study subjects (n=660)

Variables	Male subjects		P value	Female Subjects		P value	Total subjects		P value
	Nondiabetic n=63	Diabetic n=207		Nondiabetic n=170	Diabetic n=220		Nondiabetic n=233	Diabetic n=427	
Normal BMI	24(38.1%)	91(44%)	0.582	69(40.6%)	111(50.5%)	0.012	93(39.9%)	202(47.3%)	
Over weight	28(44.4%)	89(43.0%)		75(44.1)	65(29.5%)		103(44.2%)	154(36.1%)	0.108
Obese	11(17.5%)	27(13.0%)		26(15.3)	44(20%)		37(15.9%)	71(16.6%)	

Results are expressed as number (%), n= number of subjects, Chi-square test were done as tests of significance, according to the nature and distribution of variables. DM=Diabetic Mellitus.

Table-4: Initial control status of the T2DM subjects (n=427).

Measured variables	Good n (%)	Acceptable n (%)	Poor n (%)
BMI (male)	290(70.6)	51(12.4)	70(17)
BMI (female)	262(61.9)	41(9.7)	120(28.4)
Fasting blood glucose	-	-	427(100)
2 hr after breakfast	1(0.2)	8(1.9)	418(97.9)
Triglyceride	133(31.1)	88(20.6)	206(48.2)
Cholesterol	146(35.2)	189(45.5)	80(19.3)
HDL	217(50.8)	128(30)	82(19.2)

Result are expressed as number (%), n=number of the study subjects. The frequency as displayed by frequency cross table analysis. The good, acceptable and poor category was calculated by T2DM guideline book.

Table-5: Clinical and Biochemical status of the total study subjects (n=250)

Variables	Male subjects		P value	Female Subjects		P value
	Nondiabetic n=114	Diabetic n=73		Nondiabetic n=14	Diabetic n=49	
Age (Yrs)	40.1±9.1	42.3±9	0.637	49±10	47±10	0.129
BMI (Kg/m^2)	23.8±3.2	24.2±4.1	0.724	22.7±2.4	23±3.8	0.495
Fasting glucose level (mmol/l)	4.9±0.6	12.1±3.2	<0.001	4.8±0.6	12±3.1	<0.001
2 h after 75 g glucose admin. (mmol/l)	5.8±0.8	18.8±5	<0.001	5.7±0.7	20±5.8	<0.001
Total Cholesterol (mg/dl)	179±41	206±43	0.571	199±35	206±40	<0.001
Triglyceride (mg/dl)	137±63	191±80	0.440	177±95	196±75	<0.001
Serum LDL	114±36	131±42	0.140	121±27	109±26	0.004
Serum HDL	40±6	39±7	0.141	42±6	38±8.2	0.322

Results are expressed as Mean±SD, n= number of subjects, Independent t-test are done as tests of significance, according the nature and distribution of variables. DM-T2DM Mellitus, LDL-Low density of lipoprotein, HDL-High density of lipoprotein

Table-6: Insulinemic status of the total subjects (n=250)

Variables	Male subjects		P value	Female Subjects		P value
	Nondiabetic n=114	Diabetic n=73		Nondiabetic n=14	Diabetic n=49	
AgeSerum Insulin	9.7±2.5	14±5.4	0.005	9.4±2.4	12.6±3.8	<0.001
HOMA%B	129±36	38±20	<0.001	132±34	35±12	<0.001
HOMA%S	71±15	40±13	<0.001	74±18	43±13	<0.001
GIR	0.53±0.13	0.95±0.32	<0.001	0.53±0.13	0.98±0.25	<0.001
QUICKI	0.60±0.25	0.45±0.79	<0.001	0.61±0.92	0.46±0.95	<0.001

Results are expressed as Mean±SD, n= number of subjects; Independent t-test are done as tests of significance according the nature and distribution of variables. DM-T2DM Mellitus, HOMA%B, Insulin secretion capacity by Homeostasis Model Assessment, HOMA%S=Value of insulin sensitivity by Homeostasis Model Assessment. GIR= Glucose insulin ratio; QUICK1= Quantitative insulin sensitivity check index.

Table-7: Association of HOMA%B (dependent variable) with other baseline parameters as explored by multiple regression

Variable	β Value	P-value	(95% CI)	
Sex	0.337	<0.001	27.6	56.4
Education	0.191	0.010	2.6	19.0
Monthly income	0.010	0.878	-7.1	8.3
Exercise	0.046	0.420	-10.9	26.2
Smoking	0.001	1.000	-15.4	15.4
Daily Intake of CHO	0.024	0.685	-5.3	8.1

β *for standardized regression coefficient, DM=Diabetes Mellitus. P=Test of significance value. CI=Confidence Interval.*

Table-8: Association of HOMA%B (dependent variable) with other biochemical parameters as explored by multiple regression (Stage II).

Variable	β Value	P-value	(95% CI)	
BMI (Kg/m2)	0.002	0.956	1.1	1.2
After 75gm glucose level	0.730	<0.001	-5.6	-4.4
Total Cholesterol	0.020	0.647	-0.13	0.08
Triglyceride	0.081	0.082	-0.12	0.007

β *for standardized regression coefficient, DM=Diabetes Mellitus. P=Test of significance value. CI=Confidence Interval.*

Table-9: Association of HOMA%S (dependent variable) with other baseline parameters as explored by multiple regressions (Stage II).

Variable	β Value	P-value	(95% CI)
Sex of the patients	0.191	0.002	3.37 – 15.3
Education level	0.100	0.200	-1.1 – 5.6
Monthly income	0.098	0.159	-5.5 – 0.9
Habit of Exercise	0.006	0.918	-8.1 – 7.3
Habit of Smoking	0.060	0.332	-3.2 – 9.6
Daily Intake of CHO	0.138	0.028	0.3 – 6.0

β *for standardized regression coefficient, DM=Diabetes Mellitus. P=Test of significance value. CI=Confidence Interval.*

Table-10: Association of HOMA%S (dependent variable) with other biochemical parameters as explored by multiple regressions

Variable	β Value	P-value	(95% CI)
BMI (Kg/m^2)	-0.106	0.029	-1.179 – -0.065
After 75 gm glucose level	-0.639	0.000	-2.016 – -1.470
Total Cholesterol	-0.041	0.426	-0.070 – 0.030
Triglyceride	-0.046	0.385	-0.041 – 0.016

β *for standardized regression coefficient, DM=Diabetes Mellitus. P=Test of significance value. CI=Confidence Interval*

Discussion

Genesis of T2 DM has genetic as well as environmental factors which influence insulin sensitivity and insulin secretion. The risk factors of T2 DM include age, gender, physical activity, dietary habits, smoking, family history, educational status, ethnicity and occupation. Environmental factors associated with genesis of diabetes vary in different places and in different settings. The present study was carried out in RDC which is situated in the northern region of Bangladesh and the region has its own history, culture, geophysical characteristics and heritage. The objective of the study was to explore the proportion and characteristics of T2DM subjects attending RDC for the first time and to investigate the basic defects of diabetes (insulin secretory defect and/or insulin resistance) in this population. A multistage hybrid research design was followed in which the first stage constituted a descriptive observational study and the second stage constituted an analytic observational study with comparison between the diabetic and non-diabetic groups. This was a hospital based study on newly diagnosed subjects. Out of 660 subjects attending the OPD of RDC for the first time, in total 427 (65%) were diagnosed with diabetes. From clinical and biochemical criteria, all were diagnosed as T2DM subjects. From the age distribution of the subjects, it was found that approximately 2% of the T2DM subjects were of less than 30 yrs, 38% were within 30-40 yrs, 37% were within 41-50 yrs and 23 were above 51 yrs age range. These age distributions, in general conform to the clinical experience in BIRDEM which has the largest OPD in the world (>420000 registered by the end of 2009).

The level of general education is crucial for creating awareness about diabetes. From the educational data, it is evident that people with secondary education and upwards have the highest number of presence in RDC. It is thus important to take more organized effort to educate the illiterates/semi illiterates through special educational tools developed for themselves. It is generally thought by lay persons that diabetes is a disease of the affluents and it occurs mostly in people with middle to upper middle socio-economic status (SES). There are a number of reports challenging this view. The study done by Connolly *et al*[5] and Gikas *et al*[6] showed that prevalence of T2DM diabetes was inversely associated with SES. Among SES indicators, it has been manifested that income is more strongly associated with diabetes prevalence especially among women. Data from the present study show that only about 13% of patients from the low income group attend RDC and, in parallel to this proportion, only about 14% of the newly diagnosed cases belong to the low income group. This indicates that poorer people are largely left out from the services of RDC which emphasizes the need for strengthening the social welfare services in this center. Huxley et al, showed that Asians have lower rates of overweight and obesity than their western counterparts using conventional definitions (BMI>23 for overweight and >27 for obesity).[7] In the present study, using these criteria, 43.3% male subjects are found to be over weight and 14.1% are found to be obese. The corresponding values in female counterparts are 53.9% and 17.9% respectively. In the current study, percent body fat is found to be associated with an increased proportion of diabetes. The present study shows that the amount of total calorie intake has significant positive association with DM [(70.5%) (p=<0.001)]. This study also shows that most of subjects consume high carbohydrate and high fat (55.9%, 59.3% respectively) which may be associated with DM. The study by Julie et al (2008) showed that high fat and low carbohydrate diets were associated with onset of non-insulin dependent diabetes mellitus in humans.[8]

Regarding educational status of the respondents, it is found that the percentage of DM is higher among illiterate (29.71%) and up to secondary education (37.7%) groups in comparison to higher education group (18.8% & 13.8%) which is statistically significant (p<0.001). In line with the published reports [Gikas et al (2004)[6] and Chaturvedi et al (2008)[9]] education has been found to be a major confounder in the proportion of DM.

Based on WHO criteria for BMI for Asian population, 47.3% of subjects were normal weight, 36.1% over weight and 16.6% obese. All the newly diagnosed diabetic subjects in RDC were found to have poor diabetic control when judged by their fasting blood glucose level (mmol/l, M±SD) (13.4±4.4). Also when considered by blood glucose 2 hrs postprandial values, 97.9% of the T2 DM subjects had poor control and 1.9% had acceptable level. Lipid levels were also found to be largely uncontrolled in the diabetic subjects. The study done by Lindstrom et al (2006) observed that dietary fat and fiber intake were significant predictors of sustained weight reduction and progression to T2DM. Findings of both studies conform to the findings of the present study.[10]

On multiple regression, FBG was found to be associated with age (p=0.002) and occupation (p=0.026) in females T2 DM subjects and age (p=<0.001) and TG level (p=0.026) in males T2 DM subjects. Fasting serum Insulin was significantly higher in the T2 DM group as compared to non-T2DM (Serum Insulin level μIU/ml, M±SD) (13.5±4.9) subjects (p=<0.001). HOMA%B was (37±17) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects. HOMA%S was (41±13) significantly lower in the T2 DM subjects as compared to non-T2 DM subjects. On multiple regression analysis with HOMA%B as dependent variables and socioeconomic status and biochemical parameters as independent variables, the insulin secretory capacity was found to be significantly associated with sex (<0.001) and education (p=0.010). On similar analysis, with HOMA%S as dependent and other as independent variables, males (p=0.002) and daily CHO intake (p=0.028) was found to have significant association with insulin resistance.

Roy *et al.* (2007)[11], in a study on Bangladeshi T2 DM subjects, observed that both insulin secretory dysfunction and insulin resistance were present in Bangladeshi T2 DM subjects, but -cell dysfunction seemed to the predominant defect. BMI, plasma glucose and insulin were the major determinants of insulin secretory capacity and generalized, as well as central obesity, plasma glucose, total cholesterol, triglycerides and insulin were among the major determinants of insulin sensitivity among Bangladeshi population. The findings were very similar with the findings of the present study. A study was done by Wilding et al (2003)[12] on Caucasian Western population, where impaired insulin action was thought to be the predominant defect in T2 DM. The observation is not consistent with the present study. Ethnic variation seems to be the most important reason for this difference. In the present study, the group difference of HOMA% B and HOMA %S are further analyzed by logistic regression analysis. HOMA% B is associated with sex, education and blood glucose 2 hr after 75g glucose loads (β=0.337, p=<0.001; β 0.191, p=0.010 and β=0.730, p=<0.001) respectively and HOMA% S is associated with sex, daily intake of CHO and blood glucose 2 hr after 75g glucose loads (β=0.191, p=0.002; β=0.138, p=0.028 and β=-0.639, p=0.001). The findings of the predominant basic defect(s) of the diabetic subjects have great practical implications. Although the genes for these defects can not be manipulated, there phenotypic impacts can be modulated by dietary and lifestyle (particularly physical activity) factors. The present data indicates that coordinated program needs to be taken to counter the basic defects of T2 DM in Rajshahi population.

Conclusions

It may be concluded that both (HOMA%B) and (IR) constitute the basic defects of diabetes in Rajshahi population, but (HOMA%B) seems to be more predominant in these subjects. (HOMA%B) in Rajshahi population is associated with males and level of education and insulin resistance (IR) is associated with males and daily CHO intake. Lower level of general education, inadequate physical activity and consumption of disproportionate amount of calorie from carbohydrate and fat sources seem to have association with T2 DM in Rajshahi population. Both insulin secretory dysfunction and insulin resistance constitute the basic defects of diabetes in Rajshahi population, but insulin secretory defect seems to be more predominant in these subjects.

Conflict of interest: We have no conflict of interest.

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