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Original Article

Proinsulin/insulin ratio as a predictor of insulin resistance and B-cell dysfunction in obese Egyptians ((insulin resistance & B-cell dysfunction in obese Egyptians))

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ABSTRACT

Insulin resistance (IR) and β-cell dysfunction are key pathological features of type 2 diabetes mellitus, **the aim of this study** was to investigate the role of proinsulin level and proinsulin/insulin ratio in early prediction of beta cell dysfunction and insulin resistance in obese Egyptian adolescent.

Patients and methods: This Case control study was conducted from June 2017 to March 2018. Total of 60 patients were divided into 2 groups after exclusion of patients with diabetes:
normal body weight group and Obese group. Demographic, clinical data were collected. Laboratory investigation included fasting insulin, proinsulin, and estimation of HOMA IR and HOMA-B were done.

Results: There are highly statistically significant increase in obese group regarding insulin, proinsulin, proinsulin/insulin ratio and HOMA-IR while there is significant decrease in HOMA-B in this group. The best cutoff value of Proinsulin in prediction of beta cell function was ≥7.829 pmol/L with sensitivity 95.8, specificity 72.2. The best cutoff value of Proinsulin/insulin ratio in prediction of insulin resistance was ≥0.1545 with sensitivity 87.5, specificity 61.1.

Conclusion: both beta cell dysfunction and insulin resistance increased in obese group and so increased risk of type 2 diabetes. We found that Pro insulin/insulin ratio is a significant predictor for insulin resistance and Proinsulin is good predictor for beta cell dysfunction.

1. Introduction

Obesity is worldwide pandemic, Egypt has the highest level of age-standardized adult obesity, about one third of the Egyptian population are obese [1]. Obesity one the main parameters of metabolic syndrome and major risk factor for type 2 diabetes mellitus**.** Insulin resistance (IR) and β-cell dysfunction play the major roles in pathophysiology of type 2 diabetes mellitus [2]**.** So is essential not only to predict diabetes onset and progression but also to improve prevention and therapeutic strategies [3]..

For this reasons, The purpose of this research to study the role of proinsulin level and proinsulin/insulin ratio in early prediction of beta cell dysfunction and insulin resistance in obese adolescent Egyptians.

2. Patients and Methods

This Case control study had been conducted in internal medicine outpatient clinic and biochemistry department at Zagazig university hospitals from June 2017 to December of the same year. We started the study on 60 subjects; After exclusion of patients with diabetes mellitus type 1 or type 2 diabetes. Their ages ranged from 18 to 45 years; with mean ± SD 30.03 ± 7.59 years and 29 of them were males and the other 31 were female.

The patients divided into two groups, each of them 30 patients:

- Group I: control group with normal BMI (**normal weight group**)
- Group II: study group with BMI >30 kg/m^2**(Obese group)**

Patients were subjected to thorough history taking regarding age, sex, and body mass index, and arterial blood pressure, family history of diabetes mellitus, hypertension and obesity. Full clinical examination was done. Routine investigations were done. Specific investigations included HbA1c, 2 h post prandial blood glucose,

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Table 1
Waist circumference and biochemical parameters of the studied groups. There were highly statistically significant increase in obese group regarding **Waist circumference**, insulin, proinsulin, proinsulin/insulin ratio and HOMA-IR while there is significant decrease in HOMA-B in this group.

	NBW (N = 30)	Obese (N = 30)	Test ●	P
	Mean ± SD	Mean ± SD		
Waist circumference	81.2 ± 5.89	97.8 ± 5.4	11.379	<0.001*
FBG	80.1 ± 7.22	107.03 ± 1.79	19.84	<0.001*
2 h PG	132.3 ± 4.32	132.87 ± 4.41	0.503	0.617
Insulin	8.76 ± 22.57	13.86 ± 18.73	−3.27●●	0.001**
Proinsulin	7.81 ± 11.97	17.91 ± 8.96	−5.294●●	<0.001**
Proinsulin/Insulin ratio	0.22 ± 0.29	0.34 ± 0.35	−3.423●●	0.001**
HOMA −IR	2.2 ± 2.26	6.52 ± 4.47	−5.656●●	<0.001**
HOMA-B	113.63 ± 11.84	87 ± 6.38	−10.847●	<0.001**

**P ≤ 0.001 is highly significant.
● independent *t*-test.
● ● Mann whitney test.

fasting blood glucose, fasting insulin and proinsulin. Measurement of insulin resistance by homeostasis model assessment (HOMA IR) and HOMA-B.

2.1. Ethical

Written Informed consent was taken from the patient to participate in the study. Approval for performing the study was obtained from Internal Medicine and Medical Biochemistry Departments, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval.

2.2. Statistical analysis

Data analysis was performed using the software SPSS (Statistical Package for the Social Sciences) version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies. Kolmo gorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests. To compare means, independent sample *t*-test was used when appropriate. Nonparametric test (Mann Whitney) was used to compare means when data was not normally distributed and to compare medians in categorical data. To assess the best cutoff for study variables, ROC curve analysis was used. The level statistical significance was set at 5% (P < 0.05). highly significant difference was present if p ≤ 0.001.

3. Discussion

Pathophysiological changes usually proceed the occurrence the disease itself. so early detection of insulin resistance and b-cell dysfunction may be beneficial in early detection and may be prevention of type 2 diabetes in obese patient as high risk group. Estimation of proinsulin level and proinsulin/insulin ratio may be a good mirror for both insulin resistance and b-cell dysfunction in this group of patients [4].

In our study; there were highly statistically significant increase in fasting blood glucose (107.03 ± 1.79) and waist circumference (97.8 ± 5.4) in the obese group which is in agreement with (Hong et al., 2009) who studied the relationship between BMI, Waist circumference and fasting blood glucose and found a significant increase in fasting blood glucose and waist circumference with increased BMI [5] (see Table 1).

In our study fasting insulin, proinsulin, proinsulin/insulin ratio and HOMA-IR are significantly increased in the obese group while HOMA-B increased in group with normal body weight which is in agreement with (von Berghes et al., 2011) who stated that insulin, proinsulin and F.B.G have positive linear relationship with BMI which would lead to increase of proinsulin/insulin ratio and HOMA-IR in obese patients [6] (see Table 1).

And also in agreement with (Shashaj et al., 2014) who stated that Overweight/obese individuals had higher HOMA-IR levels compared with normal-weight (p < 0.0001) at any age [7].

The best cutoff value of Proinsulin in prediction of beta cell function was ≥7.829 pmol/L with sensitivity 95.8, specificity 72.2, positive predictive value (PPV) 69.7%, negative predictive value (NPV) 96.3, +LR 3.45, -LR 0.058, accuracy 81.67% (p < 0.05). Which means that the positive predictive value reaches statistical significance to prove fasting PI to be a predictive value for beta cell function. It seems to be good screening test for both beta-cell dysfunction and insulin resistance but not a diagnostic one (see Figs. 1 and 2).

Which is in contrary with Andreas; who said that fasting proinsulin values are good tool not only for diagnosis but also for staging of beta-cell dysfunction and selection of appropriate therapy and monitoring of treatment [8]. He also stated that Elevated intact proinsulin is an indicator of both advanced B-cell exhaustion and is a highly specific marker for insulin resistance [9].

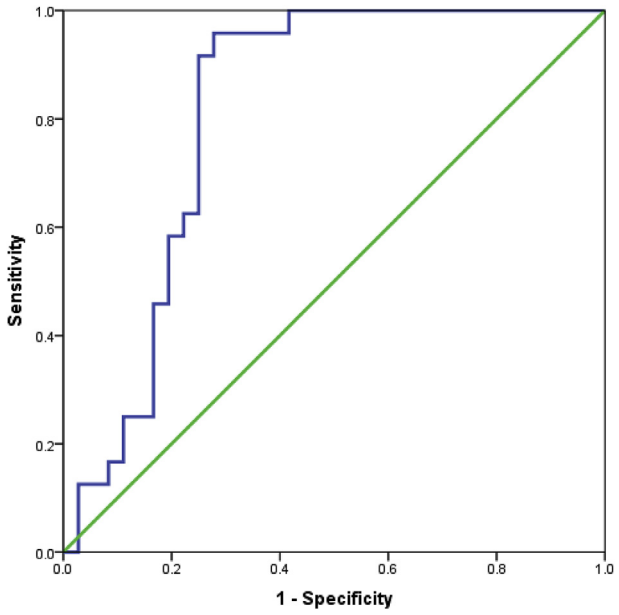

Fig. 1. ROC curve of Proinsulin in prediction of beta cell function. The best cutoff value of Proinsulin in prediction of beta cell function was ≥7.829 pmol/L with sensitivity 95.8, specificity 72.2, positive predictive value (PPV) 69.7%, negative predictive value (NPV) 96.3, +LR 3.45, -LR 0.058, accuracy 81.67% (p < 0.05).

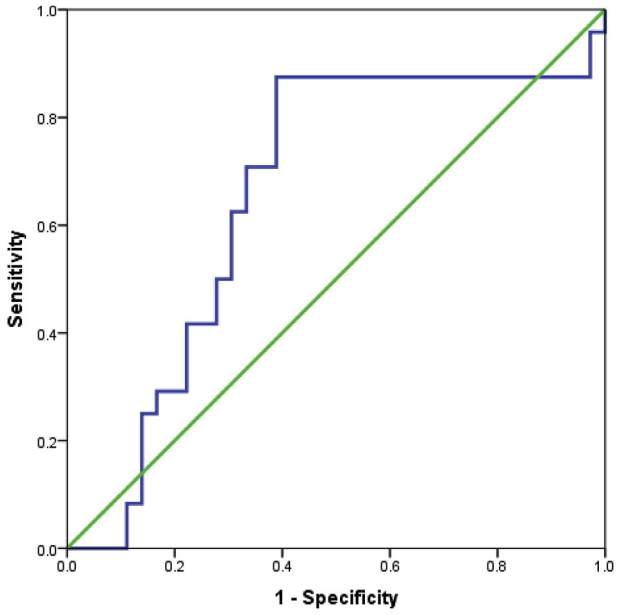

Fig. 2. ROC curve of Proinsulin/Insulin ratio in prediction of insulin resistance. The best cutoff value of Proinsulin/insulin ratio in prediction of insulin resistance was ≥0.1545 with sensitivity 87.5, specificity 61.1, PPV 60, PNV 88, +LR 2.25, -LR 0.2, accuracy 71.67% ($p < 0.05$).

We can conclude that, both beta cell dysfunction and insulin resistance increased in obese patients and so increased risk of type 2 diabetes. We found that Pro insulin/insulin ratio is a significant predictor for insulin resistance and Proinsulin is good predictor for beta cell dysfunction.

Conflicts of interest

The authors declare that they have no competing interests.

FBG, fasting blood glucose; 2 h PG, Postprandial blood glucose; HOMA-IR, homeostasis model assessment for insulin resistance; HOMA-B, homeostasis model assessment for B-cell function.

There are highly statistically significant increase in obese group regarding **Waist circumference**, insulin, proinsulin, proinsulin/insulin ratio and HOMA-IR while there is significant decrease in HOMA-B in this group.

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