IMPORTANCE OF ASSESSING INSULIN RESISTANCE AND C-PEPTIDE IN NORMOGLYCAEMIC YOUNG ADULTS WITH RISK ANTHROPOMETRIC PARAMETERS

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Introduction

Increased fasting serum insulin (FSI), insulin resistance (IR) and fasting serum C-peptide (Cpep) indicate metabolic imbalances that may lead to the development of metabolic syndrome and non-communicable diseases such as type 2 diabetes mellitus (T2DM). Cpep is considered as a reliable marker of insulin secretion from the pancreatic β cells as it is secreted in equimolar amounts with insulin, and it is currently being utilized to monitor endogenous insulin secretion in diabetic patients. Anthropometric parameters such as Body Mass Index (BMI), Waist Circumference (WC) and Waist to Hip Ratio (WHR) have shown correlations with obesity related metabolic abnormalities such as increased insulin resistance, C-peptide, insulin, glucose and lipid levels. BMI is the most widely used risk assessment parameter, even though the reliability of this is debatable. WC is considerably a powerful measurement of health risks associated with increased fat around the waist giving rise to central obesity. Asian population has shown a higher degree of central obesity compared to European population. WHR gives an indication for the visceral fat distribution. WHR can be taken as a predictor for risk of developing metabolic abnormalities.

The aim of the current study was to assess levels of FSI, IR and Cpep in normoglycaemic young adults who were at risk and no risk of developing metabolic complications based on some anthropometric parameters (BMI, WC and WHR).

Methodology

Non-diabetic subjects (n = 100) aged 20-40 years who were confirmed with fasting serum glucose (FSG) level < 100 mg/mL involved in this study. The data collection was carried out at Family Practice Center (FPC), Faculty of Medical Sciences (FMS), University of Sri Jayewardenepura (USJP), and biochemical analysis carried out at Department of Biochemistry, FMS, USJP. Ethical approval was obtained from the Ethics review committee, FMS, USJP prior to the study. Informed written consent was obtained from all the participants prior to the study. An interviewer administered questionnaire was used to collect information about socio-demographic factors. About 4 mL of fasting (8-10 hours) venous blood samples were obtained from each subject to analyse FSG, FSI and Cpep. Glucose oxidase method was used to estimate plasma glucose concentration and solid phase Enzyme-Linked Immunosorbent Assay (ELISA) method was used for the estimation of serum insulin and serum Cpep concentrations. IR was estimated by using the equation HOMA-IR= [FSI (μU/mL) x FSG (mmol/L)]/22.5. As a measure of IR, subjects having HOMA-IR ≥ 2.6 were considered as insulin resistant. Hyperinsulinaemia was

measured as ≥ 13.63 µU/mL. Weight (kg), Height (cm), WC (cm) and Hip Circumference (HC) (cm) were measured using a non-stretchable commercial tape, and BMI and WHR calculated. The risk groups of developing metabolic complications were categorized as follows: BMI > 22.9 kgm^{-2} (Overweight/ Obese); WC ≥ 90 cm (males) and WC ≥ 80 cm (females); WHR ≥ 0.9 (males) and WHR ≥ 0.8 (Females).

Results were analysed using SPSS version 16 and Microsoft Excel 2010. Student T test was done to assess the significant differences between means and $p<0.05$ was considered as significant level.

Results and Discussion

Among 100 study subjects equal percentage of males and females were present. Mean age of the study population was 27 ± 5 years and majority was Sinhalese (97%).

IR was significantly higher in all the three risk groups compared to the corresponding non-risk groups ($p<0.05$). FSI was significantly higher only in the risk groups based on WC and WHR ($p<0.05$). Cpep was also higher in all 3 risk groups compared to non-risk groups but the difference was not significant ($p>0.05$) (Table 1). These findings suggest that IR is the strongest marker among the other biochemical parameters measured assessing the risk of developing metabolic complications. Even though the three risk groups were in the normoglycaemic range, more than 32% of the subjects in the risk group were having elevated values for both insulin (FSI ≥ 13.63 µg/mL) and IR (IR ≥ 2.6).

BMI is a measure of general obesity; WC and WHR are measures of central obesity. Obesity is thought to give rise to increased FSI, Cpep and IR. Recent research reports have mentioned that in obese subjects, high levels of free fatty acids (FFA) stimulate an increased production of insulin. Since Cpep is being co-secreted with insulin, the Cpep levels also rises. This might be the reason for the presence of higher FSI, Cpep and IR level in the risk groups compared to non-risk groups, and also this would explain the presence of high number of hyperinsulinaemic and insulin resistant individuals in the risk groups (Table 1). In non-risk groups also, there were fewer hyperinsulinaemic and insulin resistant individuals (Table 1), but except for one individual all the others belonged to one of the three risk categories (i.e. the subjects who were not in the risk group according to WC, were at risk according to BMI/WHR).

Table 1. Comparison of FSI, IR and Cpep values of risk / no risk groups based on the anthropometric parameters

Anthropometric parameter / Biochemical parameter	BMI (kgm^{-2})		WC (cm)		WHR (cm)	
	Risk n = 59	No risk n = 41	Risk n = 49	No risk n = 51	Risk n = 58	No risk n = 42
FSI (µIU/mL)	13.53 ± *8.40*	10.53 ± *5.80*	14.40 ± *8.89**	10.28 ± *5.42*	13.48 ± *8.06**	10.21 ± *6.20*
Hyperinsulinaemic subjects	20	3	18	5	19	3
IR	2.65 ± *1.72**	1.95 ± *1.07*	2.80 ± *1.94**	1.87 ± *1.01*	2.60 ± *1.94**	1.95 ± *1.15*
Insulin resistant subjects	20	3	18	5	19	3
Cpep (ng/mL)	4.65 ±	4.04 ±	4. 55 ±	4.20 ±	4.51 ±	4.19 ±

	1.50	*1.03*	*1.60*	*1.00*	*1.54*	*1.13*

Difference was significant at the level of 0.05 – comparison of means by T- test

Metabolic complications are linked with basal hyperinsulinaemia, reduced sensitivity to insulin (increased IR), and disturbances in insulin release. C-peptide is co-secreted with insulin from the pancreatic β-cells, thus is often used as a measure of the insulin secretion. Also, C-peptide possesses physiological characters such as, the negligible amount of liver extraction, constant peripheral clearance and having a half-life of 20-30 minutes which is 6-8 times longer than the half-life of insulin. Hence measurement of C-peptide is more promising in measuring the amount of secretion of insulin from pancreatic cells than FSI itself. The higher Cpep values in the risk groups compared to no risk groups may indicate an increase in insulin secretion due to the impact of obesity. There are no recorded cut off values for the range of Cpep in non-diabetic Asian population. Establishment of normal and risk values for Cpep would be of use in clinical practise.

Conclusions and Recommendations

At present, the commonly used diagnostic tests to detect metabolic complications in Sri Lanka are FSG, FSI and lipid profile. Present study validates the incorporation of IR in predicting the risk of developing metabolic complications and recommends incorporating IR values in reports of patients who have done FSG and FSI tests - even in normoglycaemic young adults. Subjects in the risk category should be made aware of the importance of early predictions of metabolic complications. Assessment of Cpep may be used as a novel marker in Sri Lanka, which will aid in determining the abnormalities of insulin secretion, not only in diabetics but also in non-diabetic young adults, with the establishment of normal and risk cut off values.

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