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Evaluation of insulin resistance and its associated risk factors: Identification of adolescents at higher risk for diabetes

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Abstract

Insulin resistance is a major risk factor for developing type 2 diabetes mellitus and metabolic diseases. It is a decrease response to the effect of the hormone, mainly by the liver, skeletal muscles and adipose tissues. Despite its widely reported prevalence among the elderly, information on its prevalence among adolescents is relatively limited. The study was aimed at assessing the prevalence of insulin resistance and its contributing risk factors among the students of a tertiary institutions in Ebonyi State, Nigeria. A total of 260 students who consented to the study were recruited, fasting blood glucose (FBG) and fasting blood insulin (FBI) levels were determined, anthropometric data were collected using meter rule, flexible tape and digital scale for calculation of body mass index (BMI) and waist/hip ratio (WHR). A structured questionnaire was used to collect demographic data and information on lifestyle. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also measured. The findings showed a 5.4% prevalence of insulin resistance with more in males than in females. Sociodemographic and anthropometric characteristics were found to positively correlate with HOMA-IR. A strong association ($p < 0.05$) was observed between HOMA-IR and lifestyle. The differences in the levels of HOMA-IR within and between the various groups of participants were not statistically significant ($p > 0.05$) except in gender. The findings of this study may have potential implications with regards to strategies for amelioration and prevention of insulin resistance amongst adolescents.

Keywords: Anthropometric; Glucose; HOMA-IR; Insulin; Metabolic-disorder

1. Introduction

Insulin resistance (IR), also referred to as diminished insulin sensitivity developed as a result of reduced responsiveness or sensitivity of peripheral tissues such as skeletal muscles, liver as well as adipose tissues to insulin signaling leading to increase secretion of insulin in other to maintain normal glucose and lipid homeostasis [1]. It is a situation where the expected biological effect of a given amount of insulin is low. Mechanisms behind the development of insulin resistance remain poorly understood, however, it could be linked to genetic or primary target cell defect, accelerated insulin degradation and autoantibodies to insulin [2]. Development of IR could be attributed to tissue-specific inflammatory responses occasioned by oxidative stress triggered by free radicals [3] which is the gateway to inflammation pathways [3,4] with interleukin-1 beta (IL-1 β), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) playing important roles [5].

Insulin resistance is a classical feature of type 2 diabetes mellitus and it also plays a pathogenic role in the development of conditions such as hypertension, cardiovascular disease, atherosclerosis and dyslipidemia [6]. A strong association has been reported between IR and obesity as well as with psychobiologic habits such as smoking, unregulated diets among others. These conditions are growing concern worldwide with a high rate of morbidity and mortality [7]. Obesity,

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which is one of the most common causes of insulin resistance due to its associated decrease in the number of receptors and the failure of post-receptor to activate tyrosine kinase [8] has been implicated in the increasing risk of cardiovascular disease [7]. Alteration of inflammatory markers production culminating in systemic chronic inflammatory response has been linked to obesity [9]. Compensatory hyperinsulinaemia has been reported in IR as a mechanism of maintaining normoglycaemia with its consequential increase reabsorption of sodium [10]. Other factors that contribute to the development of insulin resistance include diet, exercise, smoking and stress [11,12] as well as genetic factors.

Among the models developed for the assessment of IR, Homeostasis Model Assessment of IR (HOMA-IR) is widely utilised and accepted as insulin resistance index in clinical and epidemiological studies [13] in preference to euglycaemic hyperinsulinaemia clamp technique which is too cumbersome for standard clinical practice though more accurate [14], QUICK index [15] and insulin resistance index (IRI), originally described by Belfiore et al. [16]. HOMA analysis does not only assess B-cell function and insulin sensitivity, it also characterise pathophysiology in those with abnormal glucose tolerance [17]. However, there still exists variability in the threshold HOMA-IR cut-off to determine IR because the diagnosis of IR using HOMA-IR may vary depending on race and age [13,18].

Recent studies have proved that IR does not only affects the adult but also children and adolescents and mostly, the obese [19,20] with about 25-45% of them having decrease glucose tolerance [21]. Interest in youth-related metabolic syndrome has increased over the decade due to the rising prevalence of individual risk factors in childhood [19]. Moreover, the pathophysiologic precursors, as well as risk factors of IR including obesity, hypertension, originate earlier in life [22]. The occurrence of metabolic syndrome increases rapidly at the age of 15 to 25 [20]. Xu et al. [19] observe in their study that 18% of participants had one or more metabolic abnormalities at the age of 15 years which doubled with 5% already had metabolic syndrome at the age of 25years. In the study of Umeli [20], about 20% of the adolescents recruited in the study already had at least one metabolic abnormality and the number of metabolic syndromes rises from adolescence to adulthood. Therefore there is no gainsaying that healthy lifestyle habits should be encouraged early in life as the signs of metabolic abnormalities may already be there even the young people seem to be healthy.

The prevalence of IR among the adolescents and young adults is heterogeneous, 36.6% in Enugu, Nigeria [6], 35% in Southwestern Nigeria [23], 43.5% still in Southwest Nigeria, [12], 36.6% in Northern Nigeria [24] and 46.3% in China [25]. In all these studies, only which of Lawal et al. [24] was carried out among adolescents and young adults, others were on adults. The dearth of information on the evaluation of IR among adolescents and young adults in this part of the world necessitated this study which was aimed at determining the prevalence of IR and its associated risk factors among students of tertiary institutions in Ebonyi State, Nigeria.

2. Material and methods

2.1. Study design

The study was a cross-sectional prevalence study of 260 students who consented to the study from the three tertiary institutions in Ebonyi State. The students, made up of both genders, aged between 18 and 30 years and apparently healthy were randomly selected. Those on medications known to alter insulin sensitivity and the pregnant ones were excluded from the study. The study was carried out between February and August 2021. Laboratory analysis was carried out at Ebonyi State University Ultramodern Diagnostic and Research Laboratory

2.2. Collection of sample

Blood samples were collected from the participants at 8 am after an overnight fast for the analyses of fasting blood glucose (FBG) and fasting blood insulin (FBI). Information about lifestyle, personal and family medical history were collected using self-administered structured questionnaires.

2.3. Assessment of anthropometric data

A meter rule to the nearest 0.1cm and a digital scale to the nearest 0.1kg were used for height and body weight measurements respectively. A flexible tape rule to the nearest 0.1cm was used to measure the waist circumference at the level of the superior iliac crest at the end of normal expiration and hip circumference. Body mass index (BMI) was calculated as weight in kilogram divided by the square of height in meter. Waist-hip-circumference (WHC) was calculated as waist circumference divided by hip circumference. Based on their BMI, participants were grouped into underweight (>18.5), normal weight (18.5 – 24.9), overweight (25 – 29.9) and Obese (> 29.9) [26] and based on WHR, low (≤ 0.80), moderate (0.81-0.85) and high (≥ 0.86) for females and low (≤ 0.95), moderate (0.96 – 1.00) and high (≥ 1.00) for males [26]

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured in the right arm, in a sitting position, using a digital sphygmomanometer with appropriate cuff size, under standard conditions. Participants were group according to their BP as normal (SBP < 120, DBP < 80), prehypertension (SBP 120 -139, DBP 80 – 89), stage 1 hypertension (SBP 140 – 159, DBP 90 – 99) and stage 2 hypertension (SBP ≥ 160 DBP ≥ 100) [27].

2.4. Biochemical analysis

Fasting blood glucose level was determined by glucose oxidase enzyme colorimetric endpoint method following the instructions in the commercial test kits obtained from RANDOX Laboratories Ltd, Crumlin, Antrim, UK.

Fasting blood insulin level was determined using an insulin quantitative test kit (Insulin ELISA test, Diagnostic Automation, INC., USA) based on a solid phase enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's protocol. Briefly, the standards and test samples were added to the insulin antibody coated microtiter wells. Then anti-insulin antibody labeled with horseradish peroxidase (conjugate) was added. After 1 hour of incubation at room temperature, the wells were washed to remove unbound labeled antibodies. A solution of 3,3',5,5' tetramethyl-benzidine (TMB) was added and incubated for 20minutes, resulting in the development of a blue colour. The enzymatic reaction was stopped by the addition of sulfuric acid solution and the change in colour was measured spectrophotometrically at 450 nm.

2.5. Assessment of Insulin Resistance

The assessment of insulin resistance was based on homeostasis model assessment (HOMA-IR), calculated as the product of fasting blood glucose (IU/l) and fasting blood insulin (mmol/L) divided by 22.5 [13]. HOMA-IR ≥ 2.0 was defined as IR [28].

2.6. Data analysis

Data were presented as mean ± SD after statistical analyses using the statistical package for social science (SPSS) version 22.0 (IBM Statistics 22, Chicago, IL, USA). Student t-test and one-way analysis of variance were used for comparison of the mean difference. Also, Pearson's correlation and chi-square were used to evaluate the correlation and association respectively between variables. The differences between means were considered to be significant when $p < 0.05$.

2.7. Ethical consideration

Ethical approval for the conduct of this study was obtained from the Ethics and Research Committee of the Faculty of Health Sciences and Technology, Ebonyi State University. All ethical precepts regarding research on humans were duly followed.

3. Results

The overall and sex-related prevalence of IR is shown in table 1. Out of the 260 participants who consented to the study, 14 had HOMA-IR ≥ 2.0 making a 5.4% (14/260) prevalence of IR. The prevalence was not statistically significantly higher among the males than the females (6.2% in males vs 4.6% in females, p = 0.583).

Table 2 shows the anthropometric characteristics related levels of FBG, FBI and HOMA-IR. The females had a not statistically significantly higher level of FBG than the males ($p = 0.099$) while the males had a significantly higher level of FBI and HOMA-IR ($p = 0.006$ and $p = 0.003$ respectively). More of the participants were between the ages of 21 and 25 years. Those in the age group 31-35 years had the highest FBG level as well as HOMA-IR while the least FBI was observed among those in the age group 16-20 years. The difference within and between the groups was statistically significant for FBG ($p = 0.000$) and not significant for FBI and HOMA-IR ($p = 0.055$ and $p = 0.072$ respectively). The obese participants had the highest FBG, FBI as well as HOMA-IR when compared with other BMI groups. However, the difference in the parameter between and within the various BMI groups were not statistically significant ($p = 0.355$, $p = 0.616$ and $p = 0.401$). The prehypertensive had the highest level of FBG while those in stage 1 hypertension had the highest FBI and HOMA-IR. No significant difference was observed between and within the groups ($p = 0.839$, $p = 0.987$, $p = 0.750$). The majority of the participants had low WHR. In both genders, those with high WHR had a not statistically significantly higher HOMA-IR when compared with others (p > 0.05).

According to the lifestyle of the participants, those who never smoked had a non significantly higher level of FBG, FBI as well as HOMA-IR when compared to other types of smokers ($p = 0.599$, $p = 0.418$, $p = 0.714$). Those who ceased smoking marijuana had the highest level of FBG (4.24 ± 0.62, $p = 0.016$) while those who smoke occasionally had the highest level of FBI (6.31 ± 1.08, $p = 0.102$) and HOMA-IR (1.00 ± 0.77, $p = 0.314$). The participants who never drank

alcohol were 106, while 134 drinks occasionally and 20 drinks daily. The daily drinkers had the highest level of FBG (4.47 ± 0.51, p = 0.164) while those who never drank had the highest level of FBI as well as HOMA-IR (4.01 ± 2.41, p = 0.099; 0.79 ± 0.54, p = 0.077). In all the parameters, participants who exercise on weekly basis had the highest level of FBG, FBI as well as HOMA-IR when compared to those who never exercise, exercise occasionally, or daily. Most of the participants were occasional consumers of junk/processed foods and they had a significantly higher level of FBG (p = 0.003) while the weekly consumers had the highest level of FBI and HOMA-IR. The Daily consumers of carbonated drinks had the highest level of FBG, FBI as well as HOMA-IR when compared to the weekly or occasionally consumers. However, the difference between and within the various groups were not statically significant (p = 0.582, p = 0.480 and p = 0.234) (Table 3).

A positive non-significant correlation was observed between the anthropometric characteristics of the participants including age, SBP, DBP, BMI as well as WHR and HOMA-IR (r = 0.090, r = 0.050, r = 0.113, r = 0.095, r = 0.001; p > 0.05) (Table 4).

As shown in table 5, a strong association was observed between lifestyle characteristics and HOMA-IR.

Table 1 Prevalence of IR among the students of tertiary institutions in Ebonyi State

Sex	Number of participants	HOMA-IR ≤ 2.0	HOMA-IR ≥ 2.0	p - value
Male	130	122 (93.8%)	8 (6.2%)	0.583
Female	130	124 (95.4%)	6 (4.6%)	
Total	260	246 (94.6%)	14 (5.4%)	

Table 2 Anthropometric characteristic related level of FBG, FBI and HOMA-IR

Variables	No. of participants	FBG (mmol/L)	FBI (IU/mL)	HOMA-IR
Sex				
Male	130	4.19 ± 0.62	4.39 ± 2.72	0.86 ± 0.54
Female	130	4.32 ± 0.60	3.40 ± 3.06	0.65 ± 0.57
p-value		0.099	0.006	0.003
Age				
16 – 20	24	3.97 ± 0.48	4.12 ± 2.23	0.73 ± 0.45
21 – 25	143	4.15 ± 0.59	3.92 ± 3.11	0.72 ± 0.60
26 – 30	85	4.44 ± 0.62	3.41 ± 2.70	0.66 ± 0.50
31 – 35	8	4.89 ± 0.33	4.13 ± 1.04	0.89 ± 0.57
p-value		0.000	0.055	0.072
BMI				
Underweight	4	3.86 ± 1.61	3.50 ± 1.19	0.60 ± 0.28
Normal weight	148	4.23 ± 0.61	3.76 ± 2.87	0.74 ± 0.55
Over weight	74	4.30 ± 0.59	4.21 ± 3.28	0.83 ± 0.65
Obese	34	4.38 ± 0.67	4.27 ± 1.60	0.88 ± 0.38
p-value		0.355	0.616	0.401
BP				
Normal	196	4.26 ± 0.63	3.94 ± 2.91	0.76 ± 0.55
Prehypertension	54	4.29 ± 0.62	3.96 ± 2.49	0.81 ± 0.57
Stage I	10	4.17 ± 0.91	4.09 ± 3.77	0.86 ± 0.77
p-value		0.839	0.987	0.750

WHR (Male)				
Low	62	4.41 ± 0.70	4.18 ± 1.42	0.78 ± 0.38
Moderate	28	4.04 ± 0.74	3.89 ± 1.71	0.71 ± 0.31
High	40	4.09 ± 0.49	4.64 ± 2.19	0.80 ± 0.49
p-value		0.012	0.165	0.612
WHR (Female)				
Low	68	4.10 ± 0.58	4.00 ± 2.03	0.71 ± 0.42
Moderate	42	4.32 ± 0.82	4.73 ± 1.35	0.82 ± 0.34
High	20	4.49 ± 0.53	4.46 ± 1.51	0.88 ± 0.44
p-value		0.039	0.102	0.173

Abbreviation: BMI – Body Mass Index, WHR – Waist Hip Circumference, BP – Blood Pressure

Table 3 Lifestyle related level of FBG, FBI and HOMA-IR

Variables	No. of participants	FBG (mmol/L)	FBI (IU/ml)	HOMA-IR
Cigarette smoking				
Never	238	4.25 ± 0.68	4.37 ± 1.79	0.80 ± 0.41
Occasionally	10	4.17 ± 0.68	4.35 ± 1.84	0.75 ± 0.34
Ceased smoking	12	4.05 ± 0.55	3.65 ± 1.59	0.70 ± 0.34
p - value		0.599	0.418	0.714
Marijuana smoking				
Never	242	4.24 ± 0.62	3.92 ± 2.88	0.76 ± 0.55
Occasionally	4	3.69 ± 0.23	6.31 ± 1.08	1.00 ± 0.77
Ceased smoking	14	4.61 ± 0.36	2.83 ± 2.87	0.56 ± 0.57
p - value		0.016	0.102	0.314
Alcohol consumption				
Never	106	4.28 ± 0.64	4.01 ± 2.41	0.79 ± 0.54
Occasionally	134	4.20 ± 0.60	4.00 ± 3.36	0.77 ± 0.59
Daily	20	4.47 ± 0.51	2.54 ± 1.95	2.54 ± 1.94
p - value		0.164	0.099	0.077
Exercise				
Never	44	4.20 ± 0.54	3.34 ± 1.52	0.67 ± 0.29
Occasionally	159	4.24 ± 0.64	3.89 ± 3.09	0.74 ± 0.59
Daily	33	4.32 ± 0.64	4.15 ± 3.65	0.84 ± 0.69
Weekly	24	4.33 ± 0.49	4.62 ± 2.67	0.88 ± 0.53
p - value		0.763	0.352	0.364
Consumption of junks/processed foods				
Occasionally	182	4.32 ± 0.60	3.76 ± 2.85	0.73 ± 0.56
Weekly	32	3.92 ± 0.70	4.58 ± 4.30	0.84 ± 0.74
Daily	46	4.23 ± 0.54	3.95 ± 1.93	0.80 ± 0.41
p-value		0.003	0.343	0.471
Consumption of carbonated drinks				
Occasionally	172	4.26 ± 0.62	3.77 ± 2.89	0.71 ± 0.56
Weekly	64	4.13 ± 0.49	3.76 ± 2.75	0.64 ± 0.52
Daily	24	4.27 ± 0.61	4.28 ± 3.13	0.82 ± 0.55
p-value		0.582	0.480	0.234

Table 4 Bivariate Correlation between Anthropometric characteristics and HOMA-IR

Variables	r- value	p-value
Age	0.090	0.147
SBP	0.050	0.421
DBP	0.113	0.068
BMI	0.095	0.125
WHR	0.001	0.986

Abbreviation: SBP – Systolic Blood Pressure, DBP – Diastolic Blood Pressure, BMI – Body Mass Index, WHR – Waist Hip Circumference

Table 5 Pearson's Chi-square between lifestyle characteristics and HOMA-IR

variables	x^2-value	*p* - value
Cigarette smoking	408.917	0.000
Marijuana smoking	352.128	0.000
Alcohol consumption	365.805	0.000
Exercise	540.365	0.000
Consumption of junks/processed foods	357.807	0.000
Consumption of carbonated drinks	313.247	0.000

4. Discussion

The findings of the present study reported a prevalence of 5.4% among students of tertiary institutions in Ebonyi State. This is in agreement with the report of Bakari and Onyemelukwe [29] who reported a prevalence of 3.3% in the South-south, Nigeria. Other reports within the country were 35% and 43.5% in Southwest [12,23], 45.3% in Enugu [6], 36.6% in the North [24] and 46.3% in China [25]. The low prevalence observed in this study could be adduced to the fact that the population of the study was made up of individuals who are knowledgeable about healthy living. In the present study, males were observed to be at greater risk of developing IR than the female. However, the females had a higher level of FBG than the males. Contributing factors to this difference in FBG level include hormones, visceral adiposity and muscle mass which have been reported to regulate glucose metabolism [30]. Though there was no association between sex and prevalence of IR the difference in HOMA-IR between males and females was statistically significant. The higher HOMA-IR in males than females was consistent with the findings of earlier studies [31].

Bivariate correlation between age and HOMA-IR was linearly positive. Younger participants had lower HOMA-IR levels than the older ones. It has been reported that fasting glucose levels are generally known to increase with increasing age, though this may vary across ethnic and regional groups [31]. The increasing level of FBG with age as observed in this study is consistent with previous studies [30,32]. This peak at adolescence and early adulthood due to increase secretion of growth hormones, adrenocortical and gonadal hormones during puberty usually cause an increase in insulin resistance and this could explain the peaks in FBG of young adults.

Blood pressure was observed to positively correlate with insulin resistance (HOMA-IR) which is similar to the findings of Bonora *et al*. [33] and also with the finding of Akande *et al*. [3] who like our findings reported the presence of insulin resistance among the normotensive individual. Studies have shown that insulin resistance is associated with hypertension and a pathogenetic role in the development of hypertension has been suggested. How hypertension influences the development of IR is still being debated. However, several mechanisms have been put forward: insulin resistance is implicated in the development of hyperinsulinemia culminating in increased arterial pressure and consequential essential hypertension [34]. Another explanation is that insulin resistance and the resultant hyperinsulinemia can lead to renin-angiotensin system activation and intracellular calcium accumulation in vascular smooth muscle thus leading to elevated blood pressures [36].

A positive correlation was observed between BMI and HOMA-IR as well as WHR and HOMA-IR. Although the majority of the participants (55.0%) were of normal weight. This finding is in consonance with the cause-effect relationship between BMI and insulin resistance as reported by Lawal *et al*. [24]. Studies have shown that increasing WHR and BMI are associated with increased insulin resistance, hyperinsulinemia and glucose intolerance [24,34]. Research has also shown that racial and genetic factors, as well as psychobiological and psychosocial habits, have a role to play in the development of insulin resistance [37]. WHR has been reported as a better determinant of obesity and its consequential insulin resistance than BMI mostly among women since it takes into account the abdominal fat which may be missed by BMI [29].

When examining insulin resistance-associated risk factors, a strong association was observed between HOMA–IR and cigarette and marijuana smoking. However, those who never smoked cigarettes had a higher HMOA-IR than those who occasionally or ceased smoking. Alcohol consumption was observed to have an obscuring effect on the development of insulin resistance in the study population. A strong association was observed between alcohol consumption and HOMA-IR, (x^2 = 365.805, p < 0.05), the daily consumers had a higher value of HOMA-IR, FBG and FBI than those who never or occasionally drinks. This finding is in harmony with the earlier report of Bendsen *et al*. [38] who reported that daily consumption of alcohol (>500mL/day) encourages the development of abdominal obesity which culminates in the development of insulin resistance. The low FBI associated with a daily intake of alcohol reported in this study agrees with the physiopathology of alcohol intake. Ethanol intake reduces the sensitivity of islet cells through interference with muscarinic signaling and insulin signaling, resulting in a decrease in the rate of basal insulin secretion [11].

The exercise-based intervention has been reported as an indispensable tool in the management of diabetes and the lack of exercise is a contributory factor of insulin resistance [39]. In the present study, we observed a strong association between exercise and HOMA-IR (x^2 = 540.363, p < 0.05) Regular exercise may improve blood glucose, body weight, prevent or delay diabetes development. It also has considerable benefits for people with insulin resistance [39]. The current study also reported a strong association between HOMA-IR with consumption of junk/processed foods and carbonated drinks and the difference in the levels of the parameter within and between the different groups of consumption frequency were not statistically significant (p > 0.05). Our findings confirm the report of [40] who reported that high consumption of sugar-sweetened beverages, processed red meat, refined grains and alcohol, as well as diets low in fruits, vegetables, fiber and wholegrain foods are linked to higher insulin resistance risk. Consuming excess sugars and fats found in junk and processed foods can contribute to weight gain. This excess weight is associated with insulin resistance.

5. Conclusion

It has been shown that the prevalence of insulin resistance among the students of tertiary institutions in Ebonyi State is 5.4%. Our findings may also have potential implications with regards to strategies for amelioration and prevention of insulin resistance amongst the students in the study area as well as students in other tertiary institutions. It is important to acknowledge certain limitations of this work, this includes our inability to verify the claims of the students regarding fasting overnight, and the information provided by the students in the questionnaire may have been prejudiced.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declared no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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