ASSESSMENT OF INSULIN RESISTANCE IN TYPE 2 DIABETIC SUBJETS AT A TERTIARY CARE HOSPITAL OF KARACHI-PAKISTAN

Asher Fawwad1, Rashida Qasim2, Z. I. Hydrie3, Abdul Basit4, Zahid Miyan5 and Asma Gul6

ABSTRACT

During the last few decades there has been a surge of interest in the assessment of insulin resistance. Our study aims to identify the insulin resistance in type 2 diabetic population so that we might be able to identify insulin resistance easily in daily routine clinical practice.

All type 2 diabetic subjects having age 30 years or more are selected with exclusion criteria (hepatic, renal or cardiac impairment). After taking informed consent from the patients fasting blood samples were taken. Assessment of insulin resistance was done by homeostasis model assessment HOMA. HOMA-R = Insulin (mu/ml) x glucose (mmol/l)/22.5

All statistical analyses were performed using the statistical program SPSS (version 11).

A Total of 118 subjects were recruited in the study. Mean age of subjects was 49.1±10.2 years. Mean BMI was 27.8±4.9 kg/m². Subjects comprising of 62.4% males and 37.6% females. Mean HOMA in our Type 2 diabetic subjects was 4.1 (male 4.41 and female 3.73). In our study 73.7% subjects has HOMA value of 1.77 or more, while 57% have HOMA value of 2.8 or more.

INTRODUCTION:

Type 2 diabetes, which accounts for 90-95% of those with diabetes, previously referred to as non insulin dependent diabetes, or adult-onset diabetes, encompasses individuals who have insulin resistance and usually have relative (rather than absolute) insulin deficiency at least initially, and often throughout their lifetime1. Most patients with this form of diabetes are obese, and obesity itself causes some degree of insulin resistance and are at increased risk of developing macro vascular and micro vascular complications as documented in UKPDS2,3. Although β-cell dysfunction and insulin resistance are well accepted as pathogenetic factors of type 2 diabetes, there is still controversy whether these defects have a primary genetic origin or occur secondarily due to other factors4. The concept of insulin resistance is relatively easy to understand, but determining precisely who is insulin resistant is more complicated. During the last few decades there has been a surge of interest in the assessment of insulin resistance both as an etiological factor in the pathogenesis of type 2 diabetes and as a key component of the insulin resistance syndrome. The euglycaemic-hyperinsulinaemic glucose clamp is considered the reference method for evaluating insulin sensitivity5. To avoid complex procedures or widely changing glucose levels, few mathematical formulas has been derived. HOMA was developed by Matthews et al in 19856 as a method for estimating insulin sensitivity.

So far relatively few data are available regarding the assessment of insulin resistance in type2 diabetic Pakistan subjects. Our study aims to identify the insulin resistance by simple mathematical calculation of HOMA in type2 diabetic population so that we might be able to identify insulin resistance easily in daily routine clinical practice. Identification of insulin resistance is important to target the high risk individuals with type2 diabetes and to prevent them from complications.

Research Design and Methods

All type2 diabetic subjects having age 30 years or more are selected with exclusion criteria (hepatic, renal or cardiac impairment).

Sampling and Data Collection

After taking informed consent from the patients, fasting plasma samples were collected. Fasting plasma glucose, fasting serum insulin, fasting lipid profile (cholesterol, triglyceride, HDL, LDL), were done by the standard methods using stat fax (1904 by mosquito) and ELISA (303 by sandwich technique).
Venous plasma glucose was estimated by GOD-PAP Method, serum Total Cholesterol, LDL and HDL were estimated by CHOD-PAP method and Serum Triglycerides was estimated by GPO-PAP method.

Height and weight were recorded with the help of height and weight scale. Standing height and weight were measured with subjects in light clothing and without shoes. Height was recorded to the nearest centimeter and weight to nearest 0.1 Kg. Body mass index (BMI) was calculated by: Weight (Kg) / height meter². Blood pressure was measured by a mercury sphygmomanometer.

Assessment of insulin resistance

Assessment of insulin resistance was done by homeostasis model assessment (HOMA). HOMA yields the following formula for insulin resistance:

\[ \text{HOMA-R} = \frac{\text{Insulin (mU/ml)}}{\text{glucose (mmol/l)}} \times 22.5 \]

All statistical analyses were performed using the statistical program SPSS (version 11).

Results and Discussion

A total of 118 subjects were recruited in the study. Mean age of subjects was 49.1±10.2 years. Mean BMI was 27.8±4.9 Kg/m². On average the fasting plasma glucose levels was 155.3±48.7 mg/dl. The clinical and biochemical characteristics of subjects comprising of 62.4% males and 37.6% females are shown in table 1.

Mean HOMA in our Type 2 diabetic subjects was 4.1 (male 4.41 and female 3.73) The 75th percentile value for HOMA is 5.36 as shown in table 2.

Figure 1 and 2 shows that in our study 73.7% subjects has HOMA value of 1.77 or more, while 57% have HOMA of 2.8 or more.

In present study we tried to determine the degree of insulin resistance by using simple measurements. Our result showed that in Type 2 diabetic subjects the mean fasting serum insulin levels is 10.786±7.84mu/L. The normal range for insulin levels using RIA is 3 to 32 mu/L. However, there is no defined cut-off value indicating insulin resistance. In a population-based study Lindhal et al in 1993 examining the association between insulin levels and cardiovascular risk, they defined insulin resistance as a plasma insulin level 7.2mU/L. Chevenne D, et al. in 1999 reported that the variations in the cut off values of insulin resistance is due to the lack of established standards for insulin assay procedures, moreover the secretion of insulin vary significantly through out the day and night especially in type 2 diabetic subjects. These findings indicate that fasting plasma insulin levels are of limited value for clinical purposes, but have some utility as a research tool in population-based studies.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Female Mean ± SD (n=45)</th>
<th>Male Mean ± SD (n=73)</th>
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<tbody>
<tr>
<td>Age (Years)</td>
<td>48.7 ± 10.06</td>
<td>49.6 ± 10.4</td>
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<tr>
<td>BMI (Kg/m2)</td>
<td>28.3 ± 5.2</td>
<td>27.3 ± 4.5</td>
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<tr>
<td>Systolic BP (mmHg)</td>
<td>127.8 ± 16.2</td>
<td>129.7 ± 19.7</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
<td>79.5 ± 9.9</td>
<td>80.9 ± 10.8</td>
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<tr>
<td>FBS (mg/dl)</td>
<td>151.7 ± 42.4</td>
<td>160.1 ± 53.4</td>
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<tr>
<td>Cholesterol (mg/dl)</td>
<td>170.7 ± 23.4</td>
<td>174.5 ± 24.5</td>
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<tr>
<td>Triglyceride (mg/dl)</td>
<td>145.8 ± 57.9</td>
<td>163.8 ± 84.3</td>
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<tr>
<td>HDL (mg/dl)</td>
<td>41.4 ± 7.40</td>
<td>41.7 ± 6.65</td>
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<tr>
<td>Fasting Insulin (mIU/ml)</td>
<td>9.65 ± 7.08</td>
<td>11.47 ± 8.24</td>
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<tr>
<td>HOMA</td>
<td>4.41</td>
<td>3.73</td>
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Table 2: HOMA at different percentiles

<table>
<thead>
<tr>
<th>Percentiles</th>
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<th>P25</th>
<th>P50</th>
<th>P75</th>
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<tr>
<td>HOMA</td>
<td>0.95</td>
<td>1.73</td>
<td>3.25</td>
<td>5.36*</td>
<td>7.99</td>
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</table>

FIG 1

Insulin Resistance by HOMA
Fasting insulin level does not provide an accurate measure of insulin sensitivity in diabetic subjects; efforts have been made to incorporate fasting plasma glucose in a formula to arrive at a better estimate of insulin-sensitivity. HOMA was developed as a method for estimating insulin sensitivity from fasting serum insulin and fasting plasma glucose, low HOMA values indicate high insulin sensitivity. In the original report it was found that HOMA ranges between 1.21 and 1.45 in normal subjects and between 2.61 and 2.89 in insulin-resistant diabetic subjects, other studies performed in the general population reported higher HOMA values of 2.1, 2.7 and 3.8.

In our study 73.7% subjects have HOMA value of 1.77 or more, while 57% have HOMA value of 2.8 or more, 1.7 cut-off value was used by Kuwana B while defining reference value and cut-off value for diagnosis of insulin resistance in type 2 diabetes mellitus, while 2.8 was used as a cut-off for insulin resistance in type 2 diabetic population by Matthews DR (6).

While other researchers have suggested that HOMA correlates well with the hyperinsulinemic euglycemic clamp. Some studies suggest that the accuracy of HOMA is limited by hyperglycemia and they demonstrated good correlations between HOMA and the clamp derived insulin sensitivity in diabetic patients without significant hyperglycemia.

The coefficient of variation for calculating HOMA values is 31% (6) this high value limits its use in clinical practice and clinical research. In other studies it was suggested that if the sample size is optimized and insulin assays are standardized the coefficient of variation for calculating HOMA may range from 8 to 12%.

Most of the studies use 75th percentile of HOMA to determine insulin resistance in their population. The 75th percentile value of HOMA in our study is 5.36 which is not in agreement to other published studies data which showed a much lower value for 75th percentile, in one of the study this value is found to be 2.6 in nondiabetic subjects the reason may be that we applied HOMA to diabetic subjects only while other researchers mostly used in either nondiabetic or in impaired glucose tolerant group.

Conclusion

On the basis of the above findings it is concluded that HOMA is mostly useful for the evaluation of insulin sensitivity in euglycemic individuals and in persons with mild diabetes; however, this index appears to offer little or no advantage over the fasting insulin concentration alone. In patients with severe hyperglycemia or in lean diabetic patients with beta cell dysfunction, the HOMA IR may not be accurate; its uselessness should therefore be restricted to large population-based studies that require a simple method to assess insulin sensitivity. These conclusions are also supported by McAuley KA and Yeni-Komshian. Further studies with large number of sample size (having normal subjects, impaired glucose tolerant subjects and type 2 diabetic subjects) are needed to confirm the findings of our study. More over assessment of insulin resistance by gold standard method i.e. by clamp studies will be more accurate in order to quantify insulin resistance in type 2 diabetes. Correlation of fasting insulin resistance with clinical parameters is lost when people develop diabetes.

References


