International Journal of Pharmacy and Biological Sciences- ISSN: 2321-3272 (Print)
IJPBS | Volume 5 | Issue 4 | OCT-DEC | 2015 | 130-136
Research Article – Biological Sciences

ASSOCIATION OF BMI WITH INSULIN RESISTANCE IN TYPE 2 DIABETES MELLITUS -A STUDY IN LOCAL TELANGANA POPULATION

[1]Madhavi Kandregula, [2]Noorjahan Mohammed and [3]Priscilla Abraham Chandran

Department of Biochemistry, Nizam's Institute of Medical Sciences, Hyderabad

***Corresponding Author Email: m_noorjahan@yahoo.co.in**

ABSTRACT

Context: *Type 2 diabetes (DM), a heterogeneous disorder characterized by impaired insulin secretion and insulin resistance, is closely related to obesity. But lack of the evaluation of insulin resistance syndrome in such patients could delay the initiation of therapeutic measures.* ***Aims:*** *we investigated the associations among BMI, insulin resistance and beta-cell function in type 2 DM.* ***Settings and Design:*** *A prospective study (carried out in local Telangana people) in a tertiary care hospital.* ***Methods and Material:*** *Total 81 subjects with DM were investigated. Fasting samples were collected for the estimation of FBS, HbA1c, Insulin and C-Peptide.* ***Statistical analysis used:*** *Statistical analysis was performed using Medcalc version 15.2.1 software. Data is expressed as the mean ± SD or median and 25th& 75th percentiles. A two-tailed p value of < 0.05 was considered statistically significant.* ***Results:*** ***S****tudy subjects were divided into 2 groups. BMI < 24.9 kg/m^2 was taken as Group 1 and BMI > 25 kg/m^2 was taken as Group 2. Statistically significant difference was found when BMI [22±2 vs 29±4.3 kg/m^2; p=<0.0001] HOMA IR [5.7(3.4-12.4) vs 9.74(6-22.6) p=0.008], HOMA-ß [100.1(42-153) vs 147.8(70.4-415.2)p=0.006] were compared between Group 1 &2. A higher BMI was associated with increased HOMA-IR and HOMA-ß.* ***Conclusions:*** *A higher BMI in Diabetics is associated with insulin resistance. BMI could thus be a sensitive anthropometric marker of evaluation in obesity as well as insulin resistance in diabetics. The desirable approach would be to advocate an initiation of increasing the physical activity especially for weight reduction and if required therapeutic measures.*

KEY WORDS

BMI- Body Mass Index, HOMA - Homeostasis Model Assessment, IR Insulin Resistance, DM-Diabetes Mellitus

INTRODUCTION:

Type2 diabetes, a heterogeneous disorder characterized by impaired insulin secretion and resistance[1], is closely related to obesity. Insulin resistance (IR) is typically defined as decreased sensitivity or responsiveness to metabolic actions of insulin[2]. Several factors including BMI has complicated impact on insulin resistance and β-cell function[3]. Few studies analysed changes in insulin secretion depending on BMI using various tools used for quantifying insulin sensitivity and resistance directly and indirectly.

HOMEOSTASIS MODEL ASSESSMENT (HOMA) uses fasting blood glucose and insulin concentrations to calculate IR and beta-cell function. HOMA-IR value of 2.5 is taken as an indicator of IR in adults[4]. The frequency of IR also varies among ethnic groups.

Subjects and Methods:

This study was conducted from June 2014 to July 2015 in a tertiary care hospital. Study was approved by institutional ethics committee and all participants gave informed consent. In total, 81 patients with type 2 diabetes mellitus were investigated. Diabetes was diagnosed based on the ADA criteria.

Patient's complete history including duration of diabetes, height, weight were recorded. BMI was calculated and expressed as kg/m^2.

Sample collection: Fasting plasma and serum samples were collected for the estimation of FBS, HbA1c, Insulin and C-Peptide.

Biochemical estimations:

All the parameters were estimated on automated analyzers. FBS was estimated using GOD-POD method, HbA1c by HPLC method, Insulin and C-Peptide were estimated by chemiluminescence immunoassay method.

Determination of Homeostasis Model Assessment (HOMA) — IR

HOMA IR and HOMA β are calculated by using the following formulas.

HOMA IR = (FBS mg/dl) X (Fasting Insulin mU/L) / 450

HOMA β % = 360 X Fasting Insulin (mU/L) / FBS (mg/dl) – 63.

Statistical analysis

Statistical analysis was performed using Medcalc version 15.2.1 software. Data is expressed as the mean ± SD unless otherwise stated. Non-normally distributed variables were expressed as median and 25^{th}& 75^{th} percentiles and log-transformed for other analysis. Independent t test was used to compare the variables between two groups. Pearson's correlation analysis was done to observe correlation between variables. A two-tailed *p* value of < 0.05 was considered statistically significant.

RESULTS:

Our study included 81 known cases of type 2 diabetes mellitus, out of which 36 were males and 45 were females. Study subjects were divided into two groups based on BMI.

Group 1 – BMI < 24.9 kg/m^2

Group 2 – BMI > 25 kg/m^2

Gender distribution of subjects in both the groups was shown in Table 1.

Table 1: Gender distribution of study subjects

	Males	Females
Group 1 (n=28)	20 (71.4%)	8(28.5%)
Group 2 (n=53)	25 (47.1%)	28 (52.8%)

Baseline characteristics of study subjects of both the groups were expressed as Mean ± SD. unpaired student t test is used to compare the difference between two groups and the results are shown in Table 2.

Table 2: Baseline characteristics of study subjects

Variable	Group 1 (n= 28)	Group 2 (n= 53)	P value
Age (yrs)	51.5 ± 9.2	52.7 ± 7.3	0.4
BMI(kg/m^2)	22 ± 2	29 ± 4.3	<0.0001
Duration of DM (yrs)	6.9 ± 7.1	8.7 ± 7.9	0.3

As shown in table 2, Mean BMI between the two groups is different and is statistically significant (22 ± 2 kg/m^2vs 29 ± 4.3 kg/m^2; p <0.0001).Mean age among the two groups is almost similar.Mean duration of DM in group 2(8.7 ± 7.9yrs) is higher when compared to group 1(6.9 ± 7.1yrs), but not statistically significant (p= 0.3).

Biochemical parameters of two groups are normally distributed and expressed as Mean ± SD and to know the significance of difference between two groups, unpaired student t test is used and the results are shown in Table 3.

Table 3: Biochemical parameters of study subjects

Parameter	Group 1 (n= 28)	Group 2 (n= 53)	P value
FBS (mg/dl)	156 ± 61.6	155 ± 73.1	0.9
HbA1c(%)	8.3 ± 2.3	8.2 ± 1.8	0.8
C-Peptide (ng/ml)	2.3 ± 1.5	3.2 ± 1.7	0.02

As shown in Table 3, mean C-Peptide levels (2.3 ± 1.5 vs 3.2 ± 1.7ng/ml; p= 0.02; Fig: 2) are significantly different between two groups.

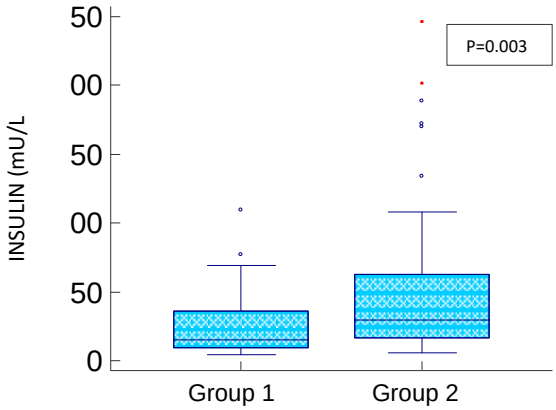

Figure 1: Comparison of Insulin between two groups

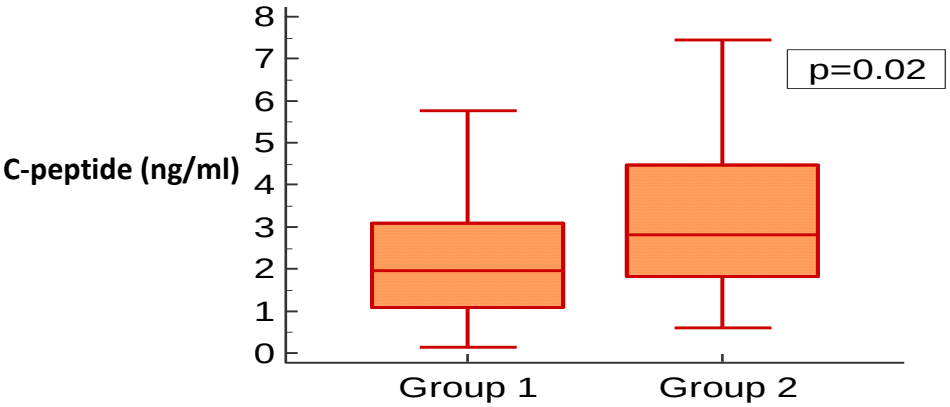

Figure 2: comparison of C-peptide between two groups

FBS and HbA1c did not show any significant difference among two groups.

Insulin, HOMA IR and HOMA β values are non-normally distributed and expressed as median and 25th& 75th percentiles. The three parameters are log transformed and then compared between the two groups by using unpaired students- t test and the results are showed in Table 4.

Table 4: comparison of HOMA IR and HOMA β between two groups

Parameter	Group 1		Group 2		P value
	Median	25th and 75th percentiles	Median	25th and 75th percentiles	
Insulin (mU/L)	15.4	9.2 & 36	29.3	16.7 & 62.4	0.003
HOMA IR	5.7	3.4 & 12.4	9.74	6 & 22.6	0.0082
HOMA β	100.1	42 & 153	147.8	70.4 & 415.2	0.006

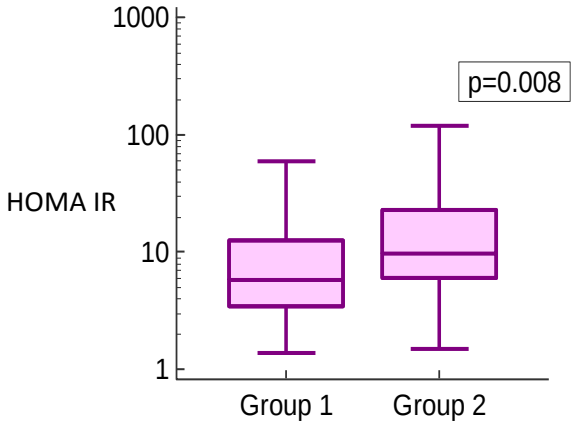

Figure 3: comparison of HOMA IR

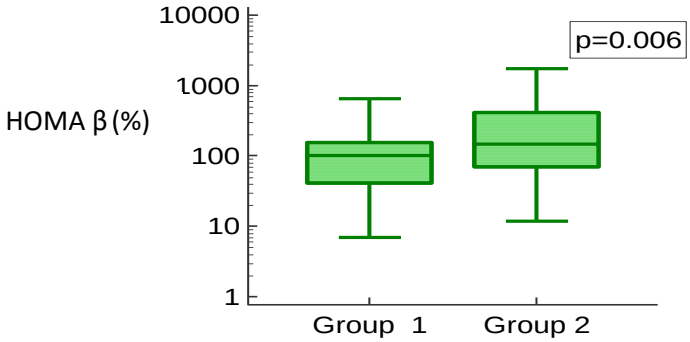

Figure 4: comparison of HOMA β between two groups

HOMA IR was compared between males and females in both the groups, but was not found to be significantly different.

Correlation of BMI with other variables:
Pearsons' correlation analysis was done to know the correlation of BMI with other variables and the results were shown in Table 5.

Table 5: Correlation of BMI with other variables

Variable	r value	p value
Age	0.04	0.6
Duration of DM	0.05	0.6
FBS	-0.09	0.4
HbA1c	-0.10	0.3
Insulin	0.23	0.03
C-Peptide	0.3	0.01
HOMA IR	0.3	0.02
HOMA β	0.22	0.04

As shown in table 5, significant positive correlation was observed between BMI with insulin (r=0.23, p=0.03), C-Peptide (r= 0.3; p=0.01), HOMA IR (r=0.3; p= 0.02) (fig: 5), HOMA β (r= 0.22;p=0.04),(fig : 6).

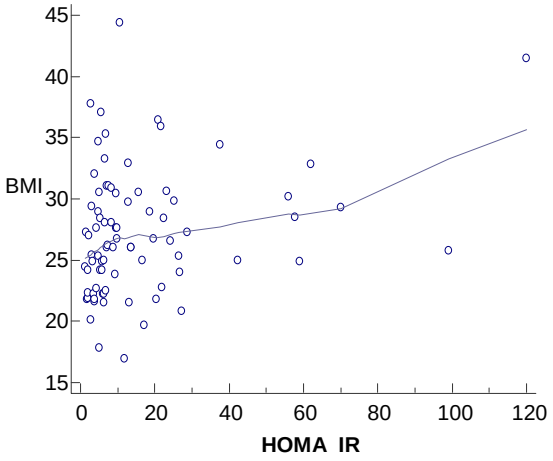

Figure 5: correlation of BMI with HOMA IR

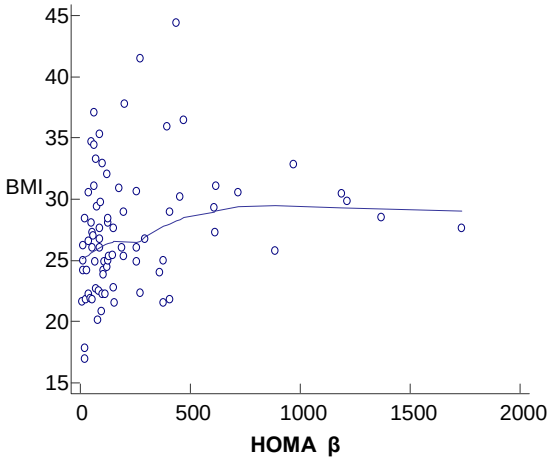

Figure 6: correlation of BMI with HOMA β

DISCUSSION:

With changes to modern lifestyles in recent years, the prevalence of type 2diabetes has increased in India[5,6]. An increasing BMI is known to be a contributing factor for the development of type 2 diabetes mellitus in India as well as in other countries[7,8].In the present study, we investigated the associations among BMI, duration of diabetes, insulin resistance, and beta-cell function in patients with type 2 diabetes.

This study has shown high prevalence of insulin resistance in women than in men. Gender difference was not significant in India[9] though non-significant higher prevalence of DM was found among women in another investigation in India[10].

We found that a higher BMI was associated with higher values of HOMA-IR in patients with type 2 diabetes. Sung et al.[11] reported that obesity is a risk factor for type 2 DM and that the relative risks for DM in subjects with a BMI of > 27 kg/m2 were significantly higher than those with a BMI of < 23 kg/m^2. Chang et al.[12] also reported that BMI was the most important determinant of insulin resistance even in non-obese patients with type 2 diabetes mellitus. In the present study, a higher BMI was associated with decreased insulin sensitivity, which supports the positive relationship between BMI and insulin resistance in type 2 diabetes mellitus. As insulin resistance increases, β-cells compensate by increasing insulin secretion, resulting in

compensatory hyperinsulinemia and the maintenance of normal glucose tolerance[1]. In an autopsy-based study of individuals with normal glucose tolerance, a greater β -cell volume was found in obese individuals[13]. BMI was also positively correlated with relative β –cell volume in Korean patients with type 2 diabetes. These results suggest that increased BMI may be related to increased β -cell mass, but the impact of BMI on β -cell function is not fully understood in patients with type 2diabetes. Several previous studies have suggested that the contribution of insulin resistance and insulin secretory dysfunction might differ in nonobese and obese subjects. Arner et al.[14] found the insulin response to an IV glucose infusion was impaired in both lean and obese diabetic patients, but during insulin infusion, glucose utilization was impaired only in obese volunteers. Park et al.[15] reported that non-obese Korean patients with type 2 diabetes had lower levels of fasting serum C-peptide compared to obese subjects similar to this study.

IR greatly reduces the sensitivity of cell walls to insulin. So the vital process whereby glucose passes through the cell wall via insulin to be converted into energy gets greatly impaired.

As a result, excess glucose remains in the blood stream, causing elevated levels of blood sugar, which are sent to the liver[16]. Once it reaches there, the sugar gets converted into fat and carried via the blood stream throughout the body. This process can lead to weight gain and obesity. Evidences have revealed that normal function of Adipose tissue is disturbed during obesity and adipose tissue dysfunction plays a prominent role in the development and/or progression of insulin resistance[17].

EFFECT OF BMI ON HOMA BETA: Chang et al.[12] also reported that insulin-sensitive patients with diabetes were associated with low HOMA β. In the present study, patients with type 2 diabetes who had higher BMI also had increased values of HOMA β. In addition, BMI had a positive association for HOMA β, similar to previous studies[18,19,20,21]. Thus, our findings may suggest that increasing BMI possibly contributes to further deterioration of β -cell function with associated increasing insulin resistance.

CONCLUSION:

A higher BMI in Diabetics is associated with insulin resistance. BMI could thus be a sensitive anthropometric marker of evaluation in obesity as well as insulin resistance in diabetics. The desirable approach would be to advocate an initiation of increasing the physical activity especially for weight reduction and if required therapeutic measures. Insulin resistance as per HOMA-IR could thus be included as a mandatory biochemical parameter, as it would forewarn the obese individuals about the impending Insulin Resistance (IR) and complications which are associated with IR.

REFERENCES:

1. Ferrannini E. Insulin resistance versus insulin deficiency in non-insulin-dependent diabetes mellitus: problems and pros- pects. Endocr Rev 1998; 19:477-490.
2. Singh Y, Garg M, Tandon N, Marwaha RK. A Study of Insulin Resistance by HOMA-IR and its Cut-off Value to Identify Metabolic Syndrome in Urban Indian Adolescents. *Journal of Clinical Research in Pediatric Endocrinology*. 2013; 5(4):245-251. doi:10.4274/Jcrpe.1127.
3. Chung JO, Cho DH, Chung DJ, Chung MY. Associations among Body Mass Index, Insulin Resistance, and Pancreatic β-Cell Function in Korean Patients with New-Onset Type 2 Diabetes. *The Korean Journal of Internal Medicine*. 2012; 27(1):66-71. doi:10.3904/kjim.2012.27.1.66.
4. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance in vivo: advantages, limitations, and appropriate usage. Am J Physiol Endocrinol Metab. 2008; 294:15–26.
5. Kim SM, Lee JS, Lee J, et al. Prevalence of diabetes and impaired fasting glucose in Korea: Korean National Health and Nutrition Survey 2001. Diabetes Care. 2006; 29:226–231.
6. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index? Eur J Clin Nutr. 2010; 64:30–34.
7. Kim SM, Lee JS, Lee J, et al. Prevalence of diabetes and impaired fasting glucose in Korea: Korean National Health and Nutrition Survey 2001. Diabetes Care. 2006; 29:226–231.
8. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index? Eur J Clin Nutr. 2010; 64:30–34.
9. Rising prevalence of NIDDM in an urban population in India.
10. *Ramachandran A, Snehalatha C, Latha E, Vijay V, Viswanathan M Diabetologia. 1997 Feb; 40(2):232-7.*
11. Impacts of urbanisation on the lifestyle and on the prevalence of diabetes in native Asian Indian population. Ramachandran A, Snehalatha C, Latha E, Manoharan M, Vijay V Diabetes Res ClinPract. 1999 Jun; 44(3):207-13.
12. Sung et al. [19] reported that obesity is a risk factor for type 2 DM and that the relative risks for DM in

subjects with a BMI of > 27 kg/m2 were significantly higher than those with a BMI of < 23 kg/m^2

13. Body mass index is the most important determining factor for the degree of insulin resistance in non-obese type 2 diabetic patients in Korea. Chang SA, Kim HS, Yoon KH, Ko SH, Kwon HS, Kim SR, Lee WC, Yoo SJ, Son HS, Cha BY, Lee KW, Son HY, Kang SK Metabolism. 2004 Feb; 53(2):142-6.
14. Beta-cell deficit and increased beta-cell apoptosis in humans with type 2 diabetes. Butler AE, Janson J, Bonner-Weir S, Ritzel R, Rizza RA, Butler PC Diabetes. 2003 Jan; 52(1):102-10.
15. Different aetiologies of type 2 (non-insulin-dependent) diabetes mellitus in obese and non-obese subjects. Arner P, Pollare T, LithellH Diabetologia. 1991 Jul; 34(7):483-7.
16. Past and current obesity in Koreans with non-insulin-dependent diabetes mellitus. Park JY, Lee KU, Kim CH, Kim HK, Hong SK, Park KS, Lee HK, Min HK Diabetes Res Clin Pract. 1997 Feb; 35(1):49-56.
17. Niraj, A, Pradahan, J, Fakhry, H, Veeranna, V, & Afonso, L. Severity of coronary artery disease in obese patients undergoing coronary angiography: "obesity paradox"revisited. Clin Cardiol (2007). , 30, 391-6.
18. Goossens, G. H. The role of adipose tissue dysfunction in the pathogenesis of obesity-related insulin resistance. Physiol Behav. (2008)
19. Analysis of factors influencing pancreatic beta-cell function in Japanese patients with type 2 diabetes: association with body mass index and duration of diabetic exposure. Funakoshi S, Fujimoto S, Hamasaki A, Fujiwara H, Fujita Y, Ikeda K, Hamamoto Y, Hosokawa M, Seino Y, Inagaki N Diabetes Res Clin Pract. 2008 Dec; 82(3):353-8.
20. C-peptide response to glucagon in patients with non-insulin-dependent diabetes mellitus. Juang JH, Huang HS, Huang MJ J Formos Med Assoc. 1992 May; 91(5):491-6.
21. Selective beta-cell loss and alpha-cell expansion in patients with type 2 diabetes mellitus in Korea. Yoon KH, Ko SH, Cho JH, Lee JM, Ahn YB, Song KH, Yoo SJ, Kang MI, Cha BY, Lee KW, Son HY, Kang SK, Kim HS, Lee IK, Bonner-Weir S J Clin Endocrinol Metab. 2003 May; 88(5):2300-8.
22. Determinants of insulin secretion and sensitivity in bangladeshi type 2 diabetic subjects. Roy MN, Biswas KB, Siddiqua N, Arslan MI, Ali L Metab Syndr Relat Disord. 2007 Sep; 5(3):275-81.

***Corresponding Author:**
Noorjahan Mohammed*
Email: m_noorjahan@yahoo.co.in