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Assessment Of Neck And Wrist Circumference Measurement As An Indicator Of Insulin Resistance In Type 2 Diabetes Mellitus Patients

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Abstract

Introduction: Insulin resistance poses to several disease conditions. The methods employed are difficult to apply in clinical practice. There is a need for accurate, reproducible, and simple methods for measuring insulin resistance in vivo. Anthropometric measurements have been shown to have positive correlation with insulin resistance in healthy volunteers.

Material and methods: A total of 200 subjects (100 Diabetic and 100 healthy subjects) participated in the study. It was a prospective, cross-sectional Observational study. The height, weight, BMI, Neck Circumference (NC), Wrist Circumference (Wrc), Waist Circumference (WaC), Hip Circumference (HC), and Waist Hip Ratio (WHR) were measured. Blood was collected for Fasting blood sugar (FBS), Fasting serum insulin levels, HbA1c and lipid profile. The association between neck circumference, wrist circumference and Body Mass Index (BMI) versus insulin resistance index (HOMA - IR) in was estimated.

Results: In diabetic patients, a weak positive correlation between NC and HOMA - IR ($P < 0.001$) as well as Wrc and HOMA - IR ($P < 0.05$) was found whereas a significant positive correlation ($P < 0.0001$) was found in healthy subjects. Correlation of other anthropometric measurements - WaC, HC, and WHR with HOMA - IR was not significant in diabetic group.

Conclusions: Neck and wrist circumferences were positively correlated with HOMA-IR and BMI in both diabetics and healthy subjects. NC also correlated well with glycemic parameters - serum fasting insulin level and HbA1c, especially in diabetics.

Keywords: Insulin resistance, Anthropometric measurements, Neck Circumference, Wrist Circumference, BMI

Introduction

Diabetes Mellitus (DM) is a syndrome of impaired carbohydrate, fat, and protein metabolism either by lack of insulin secretion (Type 1 DM) or by decreasing the sensitivity of tissues to insulin (Type 2 DM) [1]. It is characterized by hyperglycemia, Insulin resistance and relative impairment of insulin secretion. The latest estimates show a global prevalence of 382 million people with diabetes in 2013, expected to rise to 592 million by 2035 [2]. In

recent times there has been dramatic increase in the prevalence of type II DM in India.

Insulin resistance is the core metabolic abnormality in type 2 diabetes and metabolic syndrome. It has high prevalence and association with Obesity, Dyslipidemia, Hypertension, hyperinsulinemia and high coronary and cerebrovascular mortality [3]. Hence several surrogate markers were developed to measure IR. They include Homeostasis Model Assessment (HOMA), which provided equations for estimating insulin resistance (HOMA-IR), Quantitative Insulin sensitivity check index (QUICKI), Glucose/insulin ratio (G/I ratio), Minimal model analysis of frequently sampled intravenous glucose tolerance test etc [4]. Validated model like HOMA - IR is suitable to quantify IR and beta cell function from basal (Fasting) glucose and insulin concentrations [5].

In the recent past, it had been showed that Neck circumference (NC) was independently associated with glycemic parameters, including fasting blood glucose (FBG), insulin levels, insulin resistance (IR), and glycosylated hemoglobin (HbA1c). However, the results were inconsistent. Lee et al. found that NC was positively associated with fasting plasma glucose [6, 7]. It was also proved in Chines elderly population [8], Japanese postmenopausal women [9], Chinese adults [10] and other population [11]. However, some studies reported that NC was not significantly associated with fasting plasma glucose, insulin or insulin resistance [12, 13, 14]. So, it is uncertain whether NC is a better predictor of type 2 diabetes compared to traditional adiposity measurement. Recently in a systematic review and meta - analysis, Namazi et al [15] showed positive associations between NC, wrist circumference (WrC), BMI, hypertension, FBG, TC, LDL - C, SBP, DBP, and HDL - C concentrations.

Therefore, NC and WrC are more practical anthropometric indicators for insulin resistance. These are simple to measure and time saving. There were many studies showing a positive correlation between neck and wrist circumferences with insulin resistance in healthy volunteers. But there were very few studies which have shown this correlation in type 2 Diabetic patients. Hence the present study was aimed to evaluate the association of neck and wrist circumferences with insulin resistance in type 2 DM patients using HOMA - IR model.

Material and Methods:

The present study was conducted in the Dept. of Clinical Pharmacology and Therapeutics, in collaboration with Dept. of General Medicine, Nizam's Institute of Medical Sciences, Hyderabad, Telangana State, India. It was a Prospective, cross - sectional Observational study. Sample size was 200 - Diabetic patients 100 and healthy volunteers 100. Inclusion Criteria were Diabetic patients and Healthy volunteers of either gender aged between 30 - 65 years, recently diagnosed drug naive type 2 DM patients, Subjects willing to give written informed consent. Exclusion criteria were Subjects with any pathology in the neck region (Cervical lymph nodes, Deformities, Goiter, Tumors and Ulcers), Patients with impaired hepatic, renal and cardiac functions, Diabetics on any drugs or Insulin (Type 1 DM), and Patients on systemic glucocorticoids, and pregnant females.

Methodology: Study was started after approval from Institutional Ethics Committee and obtaining written informed consent. It was a prospective, cross-sectional observational study. Demographic details such as age, gender, contact details were obtained. History regarding duration of diabetes, current medication, and presence of comorbid conditions were recorded. Anthropometric measurements - height, weight, BMI, Neck Circumference (NC), Wrist Circumference (Wrc), Waist Circumference (WaC), Hip Circumference (HC), and Waist Hip Ratio (WHR) were measured. Blood was collected for analysis of Fasting blood sugar (FBS), Fasting serum insulin levels, HbA1c and lipid profile. The Insulin Resistance (IR) was estimated using Homeostasis Model Assessment (HOMA) - IR Index, from Serum insulin concentrations and FBS. The formula is

$$\text{Insulin Resistance} = \frac{\text{FBS (mg/dl) X Fasting Insulin (mU/L)}}{\text{405 or [FBS (mmol /L) X Fasting Insulin (mU/L)] / 22.5}}$$

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Body weight and BMI were recorded. Based on BMI all subjects will be divided into 3 groups. 1) BMI < 24.9 2) BMI = 25 - 29.9 3) BMI > 30 kg/m2 in both the study groups. The primary endpoints were 1. To evaluate any correlation between Neck Circumference and Wrist Circumference and Insulin resistance index (HOMA - IR). 2. To assess insulin resistance in relation to BMI. Secondary end points were 1. Any correlation of NC and WrC with other anthropometric measurements - BMI, WaC, HC, WHR. 2. Any correlation of NC and WrC with FBS, Serum Insulin and lipid profile.

Statistical Analysis: Data will be presented as mean ± SD. Unpaired t test will be used for comparisons between the study groups (Diabetics and healthy subjects). Pearson correlation test will be used to determine the relationship between anthropometric measurements and HOMA - IR, demographic parameters, FBS, and lipid profile. Comparison of insulin resistance between the groups will be done by ANOVA. P value < 0.05 will be considered statistically significant. All statistical analysis will be done using Graph Pad Prism 7 (NJ, USA). **Sample size Calculation:** with a confidence interval of 95%, power of 80% the estimated sample size of 200 (100 type 2 Diabetic patients and 100 healthy subjects) was required.

Results:

A total of 200 subjects (100 Diabetic patients and 100 healthy persons) participated in the study. In diabetic group males were 58 and females were 42. In healthy group males were 48 and females were 52 (Table - 1). A significant decrease in the heights of subjects was found in healthy group compared to diabetic group. A significant increase was found in HOMA - IR (Fig - 1), HbA1c, FBS, Neck circumference, Hip circumference and Waist Hip Ratio and serum insulin levels in diabetic patients compared to healthy subjects. Gender wise comparison of demographic characteristics between study groups were shown in table - 2.

Correlation between NC and HOMA - IR, Correlation between WrC and HOMA - IR:

We found a weak positive correlation between NC and HOMA - IR ($r = 0.32$) ($P < 0.001$) as well as Wrc and HOMA - IR ($r = 0.19$) ($P < 0.05$) in diabetic patients. Even though it was a weak correlation it was a significant correlation. In healthy subjects also we found significant positive correlation between NC and HOMA - IR ($r = 0.66$) ($P < 0.0001$) as well as Wrc and HOMA - IR ($r = 0.75$) ($P < 0.0001$) (Figs - 2 & 3).

Correlation of HOMA - IR with other anthropometric measurements- Waist circumference, Hip circumference, and waist hip ratio was not significant in diabetic group. In healthy subjects significant positive correlation was found between HOMA - IR and Waist circumference, Hip circumference, and waist hip ratio (Table - 3).

Correlation of insulin resistance (HOMA - IR) in relation to Body Mass Index (BMI):

There was significant increase in HOMA - IR as BMI increased, in both the study groups

(Table - 4). We found very weak but significant ($P < 0.05$) positive correlation ($r = 0.21$) between HOMA - IR and BMI in type 2 diabetic patients and a significant ($P < 0.0001$) positive correlation ($r = 0.79$) in healthy subjects.

Correlation of NC, WrC versus WaC, HC, WHR:

The NC and WrC showed significant positive correlation with WaC, HC in Diabetic group (Table - 5) and with WaC and WHR in healthy group.

Correlation of anthropometric measurements with other insulin resistance factors - FBS, Serum Insulin levels and Lipid Profile:

In diabetic group, NC, WrC and BMI showed significant ($P < 0.05$) positive correlation with serum insulin levels (NC vs S. insulin, Wrc vs S. insulin and BMI vs S. insulin). NC also showed a significant ($P < 0.05$) positive correlation with HbA1c in this group. We did not find any correlation between NC and WrC versus FBS and Lipid profile (Table - 6).

In healthy group, NC, WrC, WaC, HC, WHR and BMI showed highly significant ($P < 0.0001$) positive correlation with serum insulin levels, FBS and lipid profile.

Discussion:

Anthropometric measurements are practical tools applied in the clinical nutrition area. Body mass index (BMI) remains as the most widely used indicator by health care practitioners. A large number of reports over the last two decades have pointed out

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that body fat is a major factor for the development of chronic diseases [16]. During the last decade, neck circumference (NC) and wrist circumference (WrC) have been proposed as practical and inexpensive tools with the capacity to indicate elevated central adiposity and insulin resistance in healthy people. Several studies suggested that NC might have a role in prevalence of chronic diseases including cardiovascular diseases, metabolic syndrome, and diabetes. Increase in NC might result in dyslipidemia and elevated risk of cardiovascular diseases [17 - 20]. They showed that NC was positively correlated with glycemic parameters including FBG, serum fasting insulin level, HOMA-IR, and HbA1c. But most of these studies are in healthy subjects. In this study we investigated that whether NC and WrC correlated with insulin resistance in diabetics also, like in healthy subjects.

In our study, we found significant positive correlation between NC and HOMA - IR in healthy subjects ($r = 0.66$, $p < 0.0001$) as well as in diabetic patients ($r = 0.32$, $p < 0.001$). Our results were consistent with the results of previous studies. There are very few studies which showed correlation between NC and HOMA - IR in diabetics. Ashwathappa et al [18] had shown similar results in a cross - sectional study done in 700 subjects (350 diabetics and 350 non diabetics). In Brazilian metabolic syndrome (BRAMS) study [21] done in 388 healthy adolescents of both genders, it was shown that NC correlated well with insulin resistance as measured by HOMA - IR method. Another study conducted by Satomi et al [22] showed significant positive correlation between NC and HOMA-IR in post-menopausal women. Other studies [23, 24] conducted in healthy subjects showed similar results as ours. A recent meta-analysis which included 21 studies (44,031 participants) also showed positive correlation between NC and HOMA - IR, which was correlating with our results [5].

We found that the NC in males was higher compared to females in both the study groups, which were consistent with the previous studies [11, 18, 21, 23, 25].

There was significant positive correlation between WrC and HOMA - IR in healthy subjects ($r = 0.75$, $p < 0.0001$) as well as in diabetic patients ($r = 0.19$, $p < 0.05$) in our study. Our observations were in line with previous studies. Mitrea et al [26] compared correlation of WrC with HOMA - IR in diabetic and non-diabetic subjects. They found significant association between WrC and HOMA - IR. In other studies, also a positive correlation was detected between Wr C and HOMA - IR [23, 27].

In the present study, we found significant correlation between BMI and HOMA - IR in both the study groups. Our results were similar as in previous studies. Helena study conducted by Kondaki et al [28] in 1097 healthy adolescents compared several anthropometric measurements with HOMA - IR. They demonstrated statistically significant relation between BMI and HOMA - IR. Other studies also denoted similar results [23, 29, 30].

We also found significant positive correlation between NC, Wr C, BMI versus WaC, WHR in both diabetic patients and healthy subjects. Our findings were consistent with previous studies. Ashwathappa et al [18] had shown that NC was well correlated with Wac and WHR. Other studies also showed similar results as ours [25, 31, 32].

Neck and wrist circumferences and BMI showed significant positive correlation with serum insulin levels and HbA1c in diabetic group and highly significant positive correlation with serum insulin levels, FBS, HbA1c and lipid profile in healthy group. Similar results were found in a recent meta-analysis [5]. This meta-analysis of observational studies showed that NC was positively correlated with FBG, serum fasting insulin level, HOMA-IR, and HbA1c. The findings were not varied by gender, race, adjustments, correlation type, health status, and sampling method. Furthermore, meta-regression analysis showed that NC were marginally associated with FBG in a linear manner. These findings suggested that NC, as a simple and appropriate tool, could be used in clinical screening of glycemic parameters and prediction of type 2 diabetes.

In conclusion, this cross-sectional study showed that neck and wrist circumferences were positively correlated with HOMA-IR and BMI in both diabetics and healthy subjects. NC also correlated well with glycemic parameters including serum fasting insulin level and HbA1c especially in diabetics. Hence measurement of NC and WrC can be useful in clinical screening for patients at enhanced risk for insulin resistance. However, further prospective

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studies with larger sample size are required, to confirm these findings.

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Table - 1 Demographic characteristics of study groups

S No	Variable	Type 2 DM group (n = 100)	Healthy group (n = 100)	P value
1	Age (yrs)	51.4 ± 8.2	49.4 ± 7.7	0.08
2	Height (cm)	1.63 ± 0.1	1.60 ± 0.1	0.03 #
3	Weight (kgs)	72.4 ± 9.4	71.8 ± 10.4	0.66
4	BMI (kg/m2)	27.1 ± 3.2	27.2 ± 3.2	0.82
5	FBS (mg/dl)	136.4 ± 24	86.7 ± 9.7	0.0001*
6	S. Insulin level (mU/L)	20.9 ± 10.6	16.9 ± 6.4	0.001*

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7	HOMA - IR	7.1 ± 4.3	3.6 ± 1.3	0.0001*
8	Total Cholesterol (mg/dl)	183.5 ± 27.1	181.3 ± 19.1	0.5
9.	LDL - Chol (mg/dl)	123.3 ± 22.4	123.9 ± 19.5	0.84
10	HDL - Chol (mg/dl)	40.9 ± 5.7	41.2 ± 6.2	0.72
11	TG (mg/dl)	134.5 ± 22.9	132 ± 25.1	0.46
12	HbA1c	7.5 ± 0.8	5.3 ± 0.4	0.0001*
13	Neck Circumference (cm)	37.3 ± 2.4	35.7 ± 1.9	0.0001**
14	Wrist Circumference (cm)	17.4 ± 0.8	17.5 ± 0.9	0.4
15	Waist Circumference (cm)	96.3 ± 9.8	96.8 ± 6.4	0.66
16	Hip Circumference (cm)	109 ± 5.0	100.3 ± 8.7	0.0001**
17	Waist Hip Ratio	1.0 ± 0.1	0.9 ± 0.1	0.0001**

Table - 2 Demographic characteristics - Gender Wise Comparison

S No	Variable	Type 2 DM patients (n = 100)		P value	Healthy volunteers (n = 100)		P value
		Males (n = 58)	Females (n = 42)		Males (n = 48)	Females (n = 52)	
1	Age (yrs)	50.6 ± 8.2	52.5 ± 8.2	0.25	49.5 ± 7.6	49.5 ± 7.9	0.85
2	Height (cm)	1.68 ± 0.1	1.57 ± 0.1	< 0.0001*	1.7 ± 0.1	1.6 ± 0.1	< 0.0001*
3	Weight (kgs)	74.7 ± 8.8	69.3 ± 9.3	0.003 #	76.0 ± 10.8	71.8 ± 10.4	0.05
4	BMI (kg/m2)	26.4 ± 2.9	28.1 ± 3.4	0.008 #	26.4 ± 3.1	27.2 ± 3.2	0.20
5	FBS (mg/dl)	137.2 ± 25.9	135.3 ± 21.4	0.68	88.3 ± 8.4	86.7 ± 9.7	0.38
6	S. Insulin level (mU/L)	20.76 ± 12.3	21.05 ± 7.7	0.89	15.9 ± 6.7	17.9 ± 6.0	0.11
7	HOMA - IR	7.1 ± 5.4	6.6 ± 2.3	0.57	3.4 ± 1.3	3.7 ± 1.3	0.48
8	Total Cholesterol (mg/dl)	180.7 ± 28.5	187.3 ± 25	0.23	180.8 ± 20.9	181.3 ± 19.1	0.9
9	LDL - Chol	120.7 ±	126.8 ±	0.18	123.2 ±	123.9 ±	0.9

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	(mg/dl)	23.6	20.4		19.4	19.5	
10	HDL - Chol (mg/dl)	38.9 ± 5.7	43.5 ± 4.5	< 0.0001*	38.3 ± 5.8	43.9 ± 5.1	< 0.0001*
11	TG (mg/dl)	133.8 ± 23.9	135.5 ± 21.8	0.71	135.9 ± 25.2	132 ± 25.1	0.44
12	HbA1c	7.5 ± 0.8	7.4 ± 0.9	0.6	5.4 ± 0.4	5.3 ± 0.4	0.21
13	Neck Circumference (cm)	38.1 ± 2.2	36.3 ± 2.3	< 0.0001*	36.1 ± 1.9	35.7 ± 1.9	0.29
14	Wrist Circumference (cm)	17.4 ± 0.8	17.4 ± 1.0	1.0	17.6 ± 0.8	17.5 ± 0.9	1.0
15	Waist Circumference (cm)	98.1 ± 9.3	93.8 ± 10.1	0.03 #	98 ± 5.3	96.8 ± 6.4	0.31
16	Hip Circumference (cm)	100.2 ± 7.8	100.5 ± 9.8	0.86	107. 1 ± 5.4	109 ± 5.0	0.07
17	Waist /Hip Ratio	1.0 ± 0.1	1.0 ± 0.1	< 0.0001*	0.9 ± 0.1	0.9	1.0

# P < 0.05 * P < 0.0001

Table - 3 Correlation between HOMA - IR with other anthropometric Measurements in both study groups

S No	Group	Comparator	WaC	HC	WHR
1	Type 2 DM (n = 100)	HOMA - IR	r = 0.14 P = NS	r = 0.10 P = NS	r = 0.10 P = NS
2	Healthy Subjects (n = 100)	HOMA - IR	r = 0.52 P < 0.0001	r = 0.26 P < 0.0001	r = 0.43 P < 0.0001

Table - 4 Comparison of insulin resistance in relation to BMI in the study groups

S No	BMI (Kg/m2)	HOMA - IR in Type 2 DM (n = 100)	HOMA - IR in Healthy Subjects (n = 100)
1	< 24.9	3.6 ± 1.2	2.0 ± 0.6 *
2	25 - 29.9	6.5 ± 3.4	3.32 ± 1.0 *
3	> 30	9.1 ± 2.2	5.47 ± 0.4 *

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* P < 0.0001

Table - 5 Correlation between NC, WrC and WaC, HC, WHR

S No	Parameter	Type 2 DM (n = 100)			Healthy Subjects (n = 100)		
		WaC	HC	WHR	WaC	HC	WHR
1	NC	r = 0.42 P < 0.0001	r = 0.34 P < 0 .0001	r = 0.20 P = NS	r = 0.68 P < 0.0001	r = 0.16 P = NS	r = 0.76 P < 0.0001
2	WrC	r = 0.49 P < 0.0001	r = 0.45 P < 0 .0001	r = 0.03 P = NS	r = 0.76 P < 0.0001	r = 0.21 P = NS	r = 0.66 P < 0.0001

Table - 6 Correlation of anthropometric measurements with other insulin resistance factors and lipid profile

S No	Parameters compared	Diabetics (n = 100)	Healthy subjects (n = 100)
1	NC vs Serum Insulin levels	r = 0. 35 P = 0.003*	r = 0. 47 P < 0.0001
2	NC vs FBS	r = 0. 12 p = NS	r = 0. 63 p < 0.0001
3	NC vs HbA1c	r = 0. 20 P = 0.03*	r = 0. 73 p < 0.0001
4	Wr C vs Serum Insulin levels	r = 0. 22 p = 0.02 *	r = 0. 50 p < 0.0001
5	Wr C vs FBS	r = 0. 14 p = NS	r = 0. 61 p < 0.0001
6	Wr C vs HbA1c	r = 0. 11 p = NS	r = 0. 75 p < 0.0001
7	NC vs Lipid profile	p = NS	p = NS
8	Wr C vs Lipid profile	p = NS	p < 0.0001

* p < 0.05

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Figure - 1 HOMA - IR values in both study groups

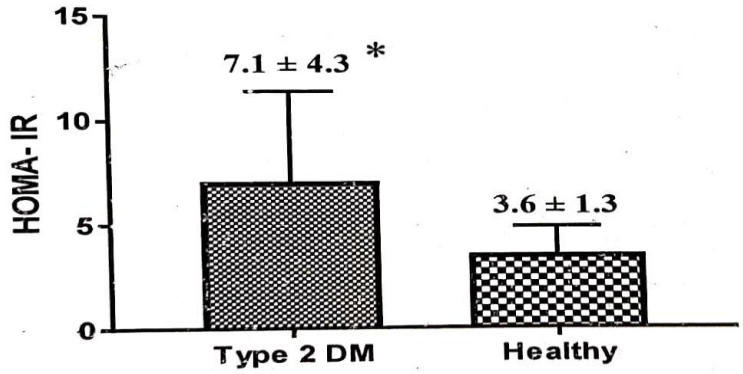


Figure - 2 Correlation between NC and HOMA - IR in Type 2 DM patients

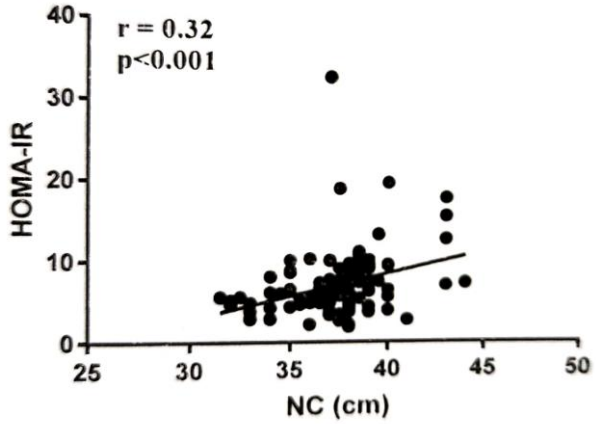
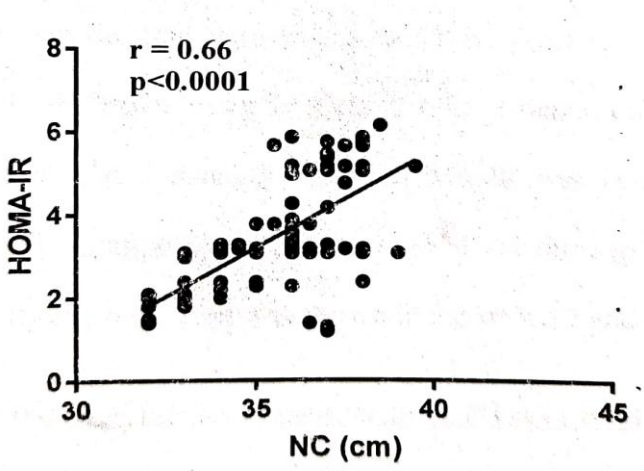


Figure - 3 Correlation between NC and HOMA - IR in Healthy subjects



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