HOMA-IR Mean Values in Healthy Individuals: A Population Based Study in Iranian Subjects

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Research

Keywords: Insulin resistance, HOMA-IR, Healthy individuals, Iranian population

Posted Date: September 17th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-816508/v1

Abstract

Aims

HOMA-IR considers as the valid index for estimation of insulin sensitivity (IS) and insulin resistance (IR) in different pathological conditions. Few studies have evaluated the relation of IR with a broad group of health related-outcomes in population-based human subjects. In this population-based investigation, we sought to report the mean value of HOMA-IR in different subgroups of a large population-based database in Iranian healthy subjects.

Methods

This population-based study recruited adult healthy individuals between the ages of 18 to 70 years old who referred to Massoud Medical Laboratory, Tehran, Iran. Fasting insulin was measured by using the Electro chemiluminescence method using Roche Cobas 6000 e601/602 instrument.

Results

The mean value of HOMA-IR of the entire population was 2.11 ± 0.99. It was observed that the HOMA-IR index tended to be higher in age subgroups of 18–25 (839 individuals), 40–45 (642 individuals) and 35–40 (1179 individuals), HOMA-IR values of 2.17 ± 0.98, 2.19 ± 1.01, and 2.16 ± 1.01 respectively.

Conclusion

Our findings showed the mean value of 2.11 ± 0.99 HOMA-IR in the Iranian healthy population. Considering the large sample size in our study, more clinical investigations in terms of ethnicity should be done to provide a precise standardized HOMA-IR index in the Iranian population.

Introduction

Insulin resistance (IR) is principally defined as the impaired regulation of insulin production and secretion of hepatic glucose that is recognized as hepatic IR [1]. In the liver, IR refers to impaired suppression of glucose production, whereas peripheral IR is a decreased response to insulin in skeletal muscle or adipose tissue. In the IR state, pancreatic B cells respond to insulin impairment by the production and secretion of insulin. This compensatory action can maintain glycaemia at the normal values [2]. In clinical settings, several dynamic and static methods such as HOMA-IR, QUICKI, and OGTT are proposed to measure IR. Among these indices, homeostasis model assessment-insulin resistance is developed to measure insulin compensatory response by measuring fasting glucose and circulating insulin levels [3].

It has been argued that HOMA-IR can consider as the valid index for estimation of insulin sensitivity (IS) and insulin resistance in a different type of phenotypes (background) such as healthy and lean subjects, Type 2 diabetes (T2D), obese individuals, children, adolescents and pregnant women [4–7]. In a retrospective study, Kim et al. evaluated the correlation between insulin sensitivity with obesity indices in obese youth compared to adults with impaired glucose intolerance (IGT) [8]. This study revealed that obese adolescents are more insulin resistant with lower insulin sensitivity and have higher HOMA-IR compared with adult subjects in spite of similar adiposity [8].

Moreover, previous findings have postulated the association of IR with lipid profile, inflammatory markers, hepatic function and cardiovascular dysfunction [1, 5, 6, 9]. These studies investigated metabolic syndrome outcomes in case-control studies with small a sample size [10]. In clinical practice, IR assessment through HOMA-IR is considered a vital index for early management and screening of T2DM [11]. In addition, HOMA-IR is useful to distinguish different high-risk groups as screening guidelines are introduced. It has been noted that via HOMA-IR evaluation IR subjects can distinguish from those with healthy status [12–14]. To our knowledge, there is no valid reference value for HOMA-IR in the Iranian population. Moreover, few studies have evaluated the relation of IR with a broad group of health related-outcomes in large and population based human subjects. In this population based investigation, we sought to report the mean value of HOMA-IR in different subgroups of a large population-based database in Iranian healthy subjects.

Materials And Methods

Subjects

This is a population-based study recruited adult healthy individuals between the ages of 18 to 80 years old who referred to Massoud Medical Laboratory, Tehran, Iran between January 2015 to August 2020. Inclusion criteria were determined as follows: healthy adult subjects with fasting blood glucose between 70–100 mg/dl and fasting insulin value between 2–20 (μIU/ml), glycated hemoglobin (HbA1c) based on the National Glycohemoglobin Standardization Program (NGSP) ≥ 6.5% at baseline [15]. Exclusion criteria were individuals with FBS more than 100 and FINS higher than 20, history of Type 1 diabetes and Type 2 diabetes, subjects with chronic kidney disorder, NAFLD, and any chronic diseases such as inflammatory and autoimmune disorders, and endocrine dysfunction. Subjects with a history of insulin sensitizer usage and pregnant women were excluded from the study. This study was in accordance with the Helsinki Declaration.

Biochemical assays

Upon 8–12 hours fasting, 5 mL venous blood was taken from all participants. Then Samples were centrifuged at 4000 RPM for 10 minutes and serum separated. FBS level was detected by the Hexokinase method using Roche Cobas 6000 c501/502 auto analyzer. Fasting insulin was measured by using the Electro chemiluminescence method using Roche Cobas 6000 e601/602 instrument. Serum levels of triglycerides, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and total cholesterol (mg/dl) were examined by Roche Cobas 6000 c501/502 instrument. All analyses were performed according to the manufacturer's instructions and after verification of methods. Insulin resistance was assessed by Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) index using the following formula: Fasting insulin (μIU/ml) × fasting plasma glucose (mg/dL)/405

Statistical analysis

Statistical analyses were performed by SPSS version 23.0 (SPSS Inc, Chicago, IL) and Graph Pad Prism software version 8.01 (Graph Pad, San Diego, CA). Data presented as mean ± SD and median and interquartile range (IQR) from 0.25 through 97.5 percentile.

Results

Baseline And Clinical Characteristics Of Study Population

Demographic and biochemical parameters of subjects in the total population and different age subgroups are presented in Table 1. In total, 6637 individuals were recruited that included 57.7% (3696) women and 44.3% (2940) men. All subjects were divided into 7 age subgroups. The median ± IQR age of the total population was 37.8 ± 12.1 with

BMI 26.5 ± 3.8 kg/m2. At baseline, the mean values of TG, cholesterol, HDL-c and LDL-c in the whole population were 124.3 ± 7.2, 179.9 ± 36.7, 48.6 ± 11.9 and 108.2 ± 30.0, and respectively. The results revealed that the mean FBS levels in the whole population were 89.4 ± 5.9 and the age group between 18–25 had lowest (87.5 ± 5.8) level compared with other age subgroups. The mean value of fasting insulin was 9.5 ± 4.3 for the whole population and age subgroup of 30–35 had the lowest insulin concentration (9.1 ± 4.2). Age subgroups of 18–25 and 40–45 had the highest fasting insulin levels (9.9 ± 5.7 and 9.8 ± 4.4 respectively). Other biochemical parameters such as AST, ALT, urea, Cr, and TSH values are shown as mean ± SD.

Table 1
Clinical characteristics of total study population

	Total	18–25	25–30	30–35	35–40	40–45	45–50	> 50
Number	6637	839	1147	1574	1179	642	386	870
Female/Male (%)	57.7/44.3	66.7/33.3	51/39	68.5/41.5	54.5/45.5	51.3/48.7	56.8/43.2	52.7/47.3
Mean Age	37.8 ± 12.1	21.8 ± 2.3	28.3 ± 1.4	33.0 ± 1.4	37.8 ± 1.3	42.8 ± 1.4	52.4 ± 1.7	63.5 ± 6.9
BMI	26.5 ± 3.8	23.8 ± 4.4	25.2 ± 4.3	25.9 ± 4.1	26.3 ± 3.9	26.7 ± 3.5	27.2 ± 3.6	26.7 ± 3.6
FBS	89.4 ± 5.90	87.5 ± 5.80	88.2 ± 5.70	88.9 ± 5.92	89.6 ± 5.84	90.6 ± 5.55	90.6 ± 5.70	92.1 ± 5.85
Insulin Base	9.5 ± 4.3	9.9 ± 5.7	9.4 ± 4.32	9.1 ± 4.2	9.7 ± 4.4	9.8 ± 4.4	9.6 ± 4.3	9.2 ± 4.2
HOMA-IR Total	2.11 ± 0.99	2.17 ± 0.98	2.06 ± 0.98	2.02 ± 0.97	2.16 ± 1.01	2.19 ± 1.01	2.15 ± 1.00	2.11 ± 0.98
HOMA-IR Female	2.05 ± 0.98	2.14 ± 0.97	2.00 ± 0.97	1.95 ± 0.95	2.08 ± 1.01	2.14 ± 1.01	2.07 ± 0.98	2.06 ± 0.97
HOMA-IR Male	2.35 ± 1.00	2.37 ± 1.02	2.35 ± 1.02	2.30 ± 0.99	2.43 ± 0.98	2.35 ± 1.03	2.43 ± 1.03	2.30 ± 1.02
TG	124.3 ± 7.2	92.3 ± 50.1	114.7 ± 70.3	119.8 ± 67.2	129.2 ± 78.4	134.2 ± 74.1	133.1 ± 69.5	136.7 ± 76.6
Cholesterol	179.9 ± 36.7	164.4 ± 33.6	170.5 ± 32.8	174.7 ± 34.4	182.9 ± 35.0	188.3 ± 35.9	191.3 ± 37.6	188.4 ± 39.6
HDL-c	48.6 ± 11.9	48.3 ± 12.0	48.2 ± 11.7	47.9 ± 11.9	47.5 ± 11.3	47.4 ± 11.3	49.8 ± 11.7	51.1 ± 12.7
LDL-c	108.2 ± 30.0	97.2 ± 27.0	101.5 ± 27.3	105.5 ± 29.2	111.8 ± 28.1	115.8 ± 29.0	115.6 ± 31.7	111.3 ± 32.8
ALT	18.3 ± 7.8	16.8 ± 7.8	16.8 ± 7.9	17.7 ± 8.1	18.5 ± 8.4	19.1 ± 8.4	19.5 ± 8.5	19.6 ± 7.2
AST	17.3 ± 4.8	16.2 ± 4.5	16.4 ± 4.4	16.6 ± 4.6	16.9 ± 4.8	17.3 ± 5.1	18.0 ± 5.3	18.9 ± 4.6
Urea	26.3 ± 7.0	24.7 ± 6.2	24.6 ± 6.8	24.7 ± 6.6	25.2 ± 6.3	26.3 ± 6.9	26.8 ± 6.4	30.3 ± 7.2
Cr	0.82 ± 0.15	0.79 ± 0.14	0.80 ± 0.15	0.81 ± 0.14	0.82 ± 0.14	0.84 ± 0.15	0.86 ± 0.15	0.87 ± 0.15
TSH	2.2 ± 0.94	2.2 ± 0.88	2.2 ± 0.92	2.3 ± 0.92	2.1 ± 0.94	2.1 ± 0.93	2.2 ± 0.96	2.5 ± 1.2

BMI; body mass index, FBS; fasting blood sugar, HOMA-IR; homeostasis model assessment-insulin resistance, TG; triglycerides, HDL-c; high-density lipoprotein, LDL-c; low density lipoprotein, ALT; Alanine aminotransferase, AST; Aspartate transaminase, Cr; creatinine, TSH; thyroid stimulating hormone. * Values are presented as median ± SD.

HOMA-IR values of study population

As shown in Table 1, the mean value of HOMA-IR of the entire population was 2.11 ± 0.99. In addition, all participants were subgrouped regarding age and gender (Table 2 and Fig. 1). Analyzing HOMA-IR values in different age subgroups showed no significant relationship with age. However, it was observed that the HOMA-IR index tended to be higher in age subgroups of 40–45 (642 individuals), 18–25 (839 individuals), and 35–40 (1179 individuals) compared with other groups (HOMA-IR mean values of 2.19 ± 1.01, 2.17 ± 0.98 and 2.16 ± 1.01 respectively). The upper limit of HOMA-IR value (95th percentile) in the 18–25 age subgroup was 3.99 that slightly increased at higher ages (Table 2). Table 2 shows the HOMA-IR values based on gender in different age subgroups. In females, the 30–35 age subgroup had the lowest HOMA-IR range between 0.59–4.13 (2.5%-97.5% reference interval) while the HOMA-IR in the > 50 subgroup was greater than other age subgroups (0.62–4.35, 2.5%-97.5% reference interval). In men, the 25–30 age group had the lowest HOMA-IR range (0.73–4.32, 2.5%-97.5% reference interval) and the 35–40 age group had the highest HOMA-IR range between 0.7–4.5 (2.5%-97.5% reference interval). As depicted in Table 2, there were slight differences in HOMA-IR value between men and females but we did not find any significant differences based on gender among the mean value of HOMA-IR.

Table 2
Distribution of HOMA-IR values by sex and age in Iranian population.

Gender	Group	HOMA –IR Percentiles							
	(year)	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**Proposed Reference Interval (2.5%-97.5%)**
Total	**18–25**	0.74	0.90	1.38	2.05	2.87	3.54	3.99	**0.62–4.23**
	25–30	0.71	0.86	1.25	1.93	2.73	3.52	3.90	**0.60–4.23**
	30–35	0.72	0.88	1.25	1.83	2.65	3.47	3.87	**0.60–4.16**
	35–40	0.74	0.91	1.33	1.99	2.83	3.69	4.10	**0.57–4.32**
	40–45	0.76	0.94	1.33	2.08	2.88	3.67	4.12	**0.65–4.30**
	45–50	0.74	0.91	1.30	2.03	2.82	3.53	4.05	**0.60–4.37**
	> 50	0.77	0.91	1.32	2.02	2.74	3.52	4.04	**0.64–4.36**
Female	**18–25**	0.73	0.89	1.35	2.04	2.86	3.50	3.89	**0.60–4.21**
	25–30	0.69	0.83	1.22	1.86	2.61	3.41	3.88	**0.59–4.20**
	30–35	0.70	0.84	1.19	1.75	2.53	3.38	3.81	**0.59–4.13**
	35–40	0.70	0.88	1.25	1.87	2.78	3.60	4.06	**0.53–4.29**
	40–45	0.78	0.93	1.30	2.04	2.80	3.62	4.04	**0.65–4.27**
	45–50	0.73	0.88	1.26	1.95	2.66	3.53	3.90	**0.55–4.25**
	> 50	0.73	0.91	1.28	1.96	2.66	3.40	3.95	**0.62–4.35**
Male	**18–25**	0.83	1.02	1.63	2.23	3.04	4.02	4.27	**0.73–4.48**
	25–30	0.85	1.04	1.52	2.21	3.17	3.82	4.14	**0.73–4.32**
	30–35	0.82	1.05	1.58	2.22	3.05	3.64	3.98	**0.66–4.48**
	35–40	0.89	1.09	1.66	2.34	3.11	3.87	4.24	**0.70–4.50**
	40–45	0.74	1.02	1.49	2.28	3.08	3.82	4.25	**0.67–4.35**
	45–50	0.87	1.02	1.61	2.43	3.14	4.04	4.33	**0.70–4.44**
	> 50	0.83	0.94	1.47	2.20	3.04	3.83	4.14	**0.72–4.41**

Discussion

Insulin resistance is recognized as impaired biological insulin response with normal concentrations that correlate with a cluster of disorders such as cardiovascular disease (CVD), obesity, hypertension, type 2 diabetes [16]. Up to now, numerous methods have been suggested for the measurement of IR in clinical practice [17]. Some techniques such as a hyperinsulinemic - euglycemic clamp, as the gold standard method of IR, are difficult for use in clinical practices and population-based studies [3]. Among them, HOMA-IR index is proposed as a simple surrogate for wider use in everyday clinical practice [18, 19]. HOMA-IR is a well-established index that assesses insulin resistance status based on comparing fasting glucose and circulating insulin levels that higher HOMA-IR indicates more insulin resistance [9]. The reference value of HOMA-IR has been assessed in several human studies [13, 14, 16, 17]. To the best of our knowledge,

data regarding reference value and accurate threshold of HOMA-IR are limited in the Iranian healthy population. Therefore, this study sought to report values of the HOMA-IR index regarding age and gender in healthy Iranian individuals. In this study, the mean value of HOMA-IR was 2.11 ± 0.99 in the total population. As noted earlier, mean values of HOMA-IR were reported regarding gender and age differences. The findings of the present study showed higher mean values of HOMA-IR in the men group compared to female subjects. In addition, the HOMA-IR mean values were increased in higher ages in both female and male groups.

Previous literature have evaluated HOMA-IR values in various pathological conditions with different ethnicities and clinical backgrounds [1, 4, 7, 8, 18]. One study by Esteghamati et al. investigated 1276 non-diabetic and non-hypertensive subjects in the Iranian population [17]. The authors indicated that the normal value of HOMA-IR was 1.8 ± 1.13 in the whole population and the lower limit of the top quintile of HOMA-IR distribution values in normal subjects was 1.78 (1.69 for men and 1.81 for women). In another study, Yamada et al reported mean value of 2.0 for HOMA-IR in non-obese Japanese individuals [12, 18]. Nakai et al. reported the mean value of 1.7 (90th percentile) for IR in Japanese subjects [18]. It has been noted that the optimal cut-off point for HOMA-IR was 1.77 in non-diabetic and 3.87 in diabetic Iranian subjects [20]. Gayoso et al investigated 2459 random Spanish population samples [21]. They proposed the mean value of 2 ± 1.1 in the total population and 1.9 ± 1 for women and 2.1 ± 1.2 for men. In another multicenter cross-sectional survey, Vilela et al indicated the mean value of 1.7 (1.1–2.7) for HMA-IR in 1061 non-diabetic Brazilian individuals [22].

In the present study, the mean values of HOMA-IR were higher than previous investigations. One reason for the inconsistency of our results with previous studies could be different clinical methods of insulin and glucose measurement. It has been argued that various insulin assays reflect different insulin levels and ultimately result in different HOMA-IR values [2]. Another possible explanation for this discrepancy may be population diversity in terms of ethnicity. It is noteworthy that previous studies applied different inclusion criteria for defining and measurement of insulin resistance. It has been noted that both ethnic differences and gender variations can affect the reference range of HOMA-IR in different populations [5]. In this study, the mean values of HOMA-IR in the women group were slightly lower than the male group. In accordance with these results, Isokuortti et al. reported that after adjustment for age and BMI, men had slightly higher HOMA-IRs than women [5]. Previous population-based studies including healthy individuals have not reported HOMA-IRs separately for men and women [17, 20]. Even though Individuals in the present study were non-obese with normal glucose and lipid metabolism, these differences between two genders may be related to sexual maturity and adipose tissue accumulation pattern in adolescent population. It has been argued that in Indian the adolescents HOMA-IR scores increased with sexual maturity and with progression from normal to obese and a HOMA-IR cut-off of 2.5 provided the maximum sensitivity and specificity in diagnosing [23].

In conclusion, the current results showed the mean value of 2.49 ± 1.28 for HOMA-IR in the Iranian healthy population. In addition, the finding revealed a higher HOMA-IR value in men compared to females. As noted in the current study, we reported different reference values of HOMA-IR in healthy subjects compared to previous literature. Considering the large sample size in our study, more clinical investigations in terms of ethnicity should be done to provide a precise standardized HOMA-IR index in Iranian population. Reference values for HOMA-IR, even in healthy individuals may be population-specific and every laboratory should establish its own reference value for HOMA-IR, or at least understand how its insulin assay compares with other laboratories.

Abbreviations

IR

Insulin resistance; IS:Insulin sensitivity; HOMA-IR:Homeostasis model assessment-insulin resistance; IGT:Impaired glucose intolerance; HbA1c:Glycated hemoglobin; NGSP:National Glycohemoglobin Standardization Program; FBS:Fasting blood sugar; HDL:High-density lipoprotein; LDL:Low-density lipoprotein; TG:Triglyceride.

Declarations

Ethics approval and consent to participate

All participants signed an informed consent letter. We obtained ethical approval from the Massoud Medical Laboratory (ML-99-1969).

Consent for publication

All authors support submission to this journal.

Availability of data and materials

The data and materials that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

Research work concerning the outputs presented in the manuscript and the Massoud Medical Laboratory supported the manuscript creation, Confirmed proposal number: ML-99-1969-99109.

Authors' contributions

Planning of the study was performed with M.KH, M.M. and M.A. Conducting of the study was performed with M.KH, M.M. and M.A. Collecting of the data was carried out by M.KH and M.M, S.M and A.O Interpretation of data was carried out by M.KH and M.M, S.M and A.O. Drafting the manuscript was performed with M.KH, M.M. and M.A. All authors have approved the final draft and agreed to submit manuscript to this journal

Acknowledgments

The authors wish to thank laboratory staff of Massoud Medical Laboratory and all participants for their helpful enrollments.

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Figures

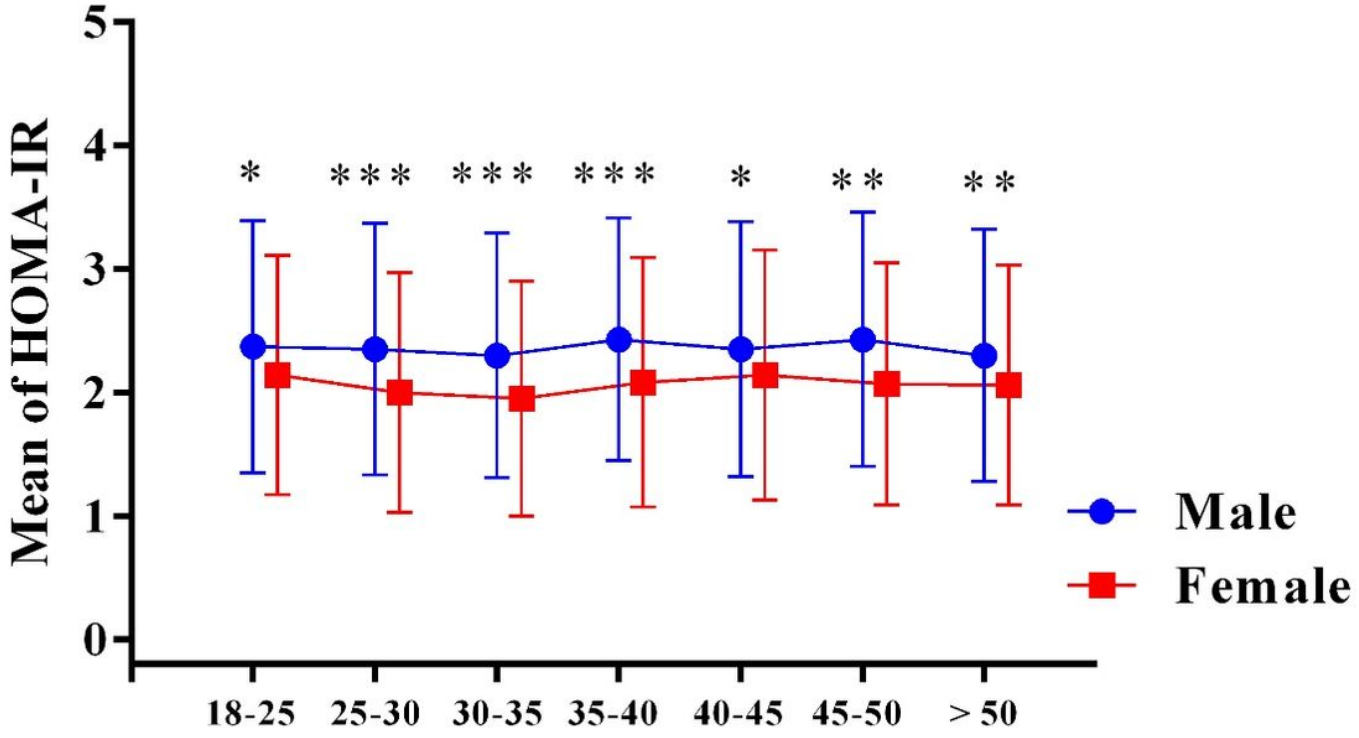

Figure 1

Mean HOMA-IR in different subgroups of Iranian population.

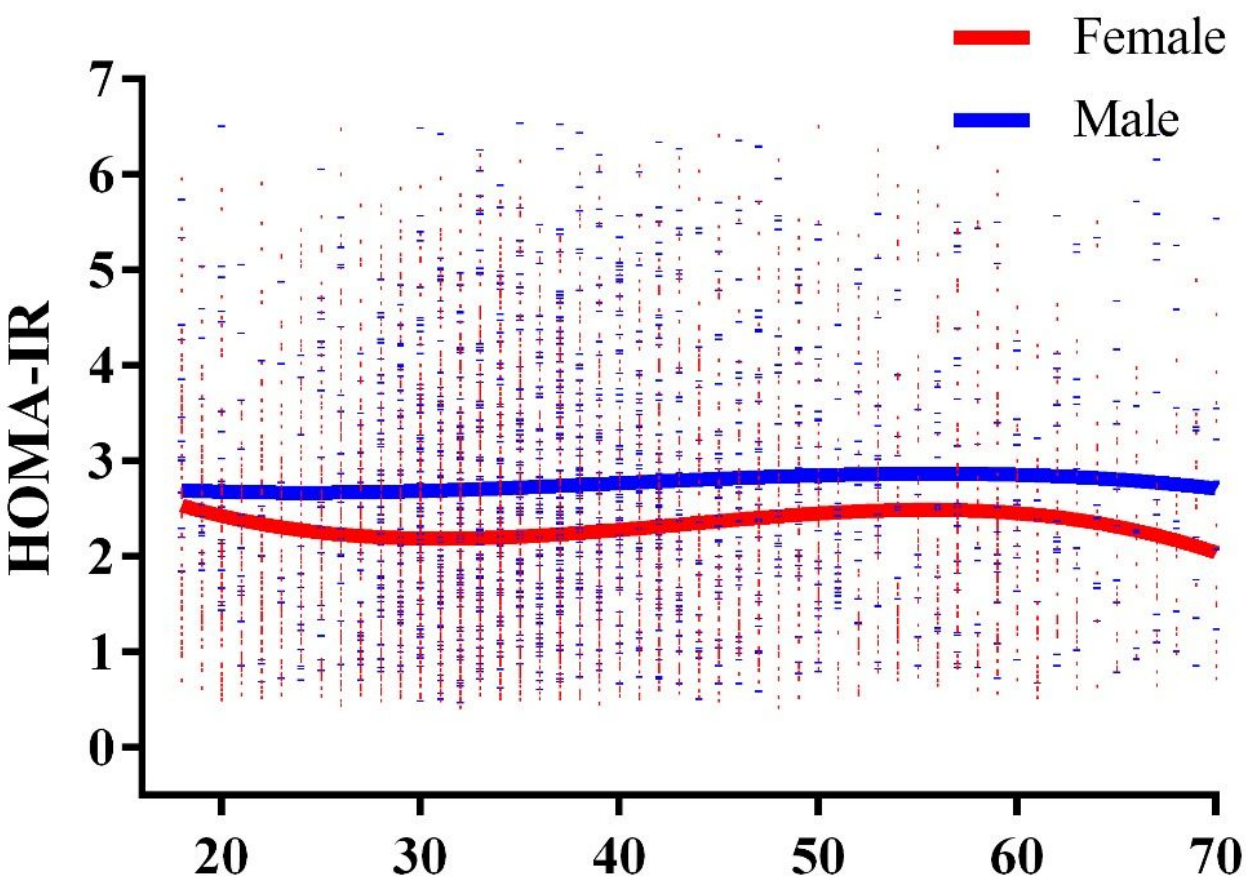

Figure 2

Regression analysis for HOMA-IR between female and male subjects.