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Association of Risk Factors with Insulin Resistance/Sensitivity Biomarkers among Manufacturing Industry Workers

Kalahasthi Ravibabu[1], Raju N[1], Jamalpur Ravi Prakash[1], Vinay Kumar Adepu[1], Jakkam Surender[1]*

[1]Department of Biochemistry, Regional Occupational Health Centre (Southern), Indian Council of Medical Research, Devanahalli, Bengaluru-562110 (Karnataka) India

Abstract:

Background: The association of risk factors with the insulin resistance/sensitivity biomarkers were assessed in population based studies but not in industrial settings. *Aim and Objectives:* This study assessed the association of risk factors with the Insulin Resistance (IR) and Insulin Sensitivity (IS) biomarkers among industrial workers. *Material and Methods:* A cross-sectional study. IR and IS biomarkers were assessed in 137 (94 male and 43 female) industrial workers. Serum levels of glucose, Triglyceride (TG) and High Density Lipoprotein–Cholesterol (HDL-C) were measured using diagnostic kit. Serum level of insulin was quantified using ELISA method. IR and IS biomarkers were compared with gender, age, and occurrence of smoking, alcohol consumption, waist circumference, body mass index, hypertension, diabetes, elevated triglyceride, low HDL-C and metabolic syndrome among industrial workers. *Results:* The levels of IR biomarkers: Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), computerized model of IR (HOMA2-IR), β-cell function (HOMA-%B), TG/HDL-C, insulin: glucose, Metabolic Score of Insulin Resistance (METS-IR) and Triglyceride/ Glucose (TyGI) were increased and IS biomarkers: Quantitative Insulin Sensitivity Check Index (QUICKI) and HOMA-% S were decreased in workers with the exhibits of risk factors. A positive and significant association was noted between HOMA-IR and HOMA2-IR ($r=0.988$; $P<0.01$), HOMA-%B ($r=0.554$; $P<0.01$), TG/HDL-C ($r=0.362$, $P<0.01$), Insulin: Glucose ($r=0.862$; $P<0.01$), METS-IR ($r=0.457$; $P<0.01$) and TyGI ($r=0.477$; $P<0.01$). A negative and significant association was observed between HOMA-IR and QUICKI ($r=-0.976$; $P<0.01$) and HOMA-%S ($r=-0.988$; $P<0.01$). The association of risk factors with the IR and IS biomarkers was assessed by using linear multiple regression analysis. The results indicated that 86% of risk factors influenced by METS-IR and followed by 66% TyGI, 57% TG/HDL-C, 49% HOMA-IR, 37% HOMA-%S, 34% QUICKI, 30% HOMA2-IR, 16% HOMA-%B and 16% of Insulin: Glucose. *Conclusion:* The IR markers such as METS-IR, TyGI and TG/HDL-C were mainly influenced by risk factors compared to other biomarkers of IR/IS.

Keywords: Industrial Workers, Insulin Resistance, Insulin Sensitivity

Introduction:

Insulin Resistance (IR) and Insulin Sensitivity (IS) are the possible risk factors for the development of Metabolic Syndrome (MetS), Type 2 Diabetes Mellitus (T2DM) and Cardiovascular Disease (CVD) [1]. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is the tool used for the IR identification in both epidemiological and clinical studies [2-3]. HOMA2-IR represents the computerized model of IR that estimates the HOMA-%S and β-cell function (HOMA-%B) using the determination of fasting blood glucose and insulin. Quantitative Insulin Sensitivity Check Index (QUICKI) is the contrivance used for IS

quantification and it is a product of logarithmic values of fasting glucose and insulin and predict the risks of T2DM [4], hypertension and disturbances in glucose metabolism [5]. Serum Triglyceride/ High Density Lipoprotein– Cholesterol (TG/HDL-C) ratio, Triglyceride/ Glucose (TyGI) index and Metabolic Score of Insulin Resistance (METS-IR) are the contemporary biomarkers used for the detection of IR and IS. TG/HDL-C ratio is product of fasting triglyceride and HDL-C and is used to identify the risk of IR, CVD, MetS, diabetes and dyslipidaemia [6]. TyGI is the product of fasting glucose and triglyceride and predicts the risk of IR, MetS, and diabetes and IS [7-8]. METS-IR is a product of fasting glucose, triglyceride, BMI, and HDL-C and is used to test the IS, incidents of T2DM[9], hypertension and pre-hypertension [10]. Basulaka *et al.* [11] found an increased HOMA-IR, HOMA2-IR, TG/HDL-C and decreased HOMA-%B and HOMA-%S in subjects with T2DM. Yeh *et al.* [12] have found TyGI had highest association with the risk factors in comparison with METS-IR and TG/HDL-C among general adult population. The age and gender have shown significant association with IR and IS biomarkers in the general population [13]. The prevalence of CVD, high risk of BMI, central obesity, hyperglycaemia, dyslipidemia, impaired GTT, hypertension, and low physical activity were reported in industrial workers [14-16]. The association of risk factors with the insulin resistance/sensitivity biomarkers were reported in population based studies but not in industrial settings. This study was assessed the association of risk factors with the IR and IS biomarkers among industrial workers.

Material and Methods:

A cross -sectional study was conducted among manufacturing industrial workers to observe the association between risk factors and IR/IS biomarkers. The sample size was calculated based on target population, which were 200 industry workers. The inputs of confidence levels of 95%, margin of error 5% and worst case-percentage 50 were assumed. The sample frame was calculated as 131. A total of 137 (94 male and 43 female) industrial workers were enrolled from automobile bearing components, flavours and waste management industries (Karnataka). The levels of IR and IS biomarkers were compared with gender, age, and presence of smoking, alcohol consumption, WC, BMI, hypertension, diabetes, elevated triglyceride, low HDL-C and MetS among industrial workers. This study was approved by the Institutional Ethics Committee with file no.142 dated 13-12-2018.The informed written consent was obtained from each subject before enrolment in the study. A standard questionnaire was used to collect the demographics and lifestyle factors information. The physical examination of subjects was performed. The details of height in centimetre, weight in Kg and waist circumference in centimetre were recorded. BMI was calculated by using subjective weight (Kg) and height (meter) and expressed as Kg/m^2.

Blood Collection:

Four ml whole blood was collected into vacuurate easy clot activator tubes (manufactured by M/s Labtech disposables, India) from overnight fasted (>10 hours) subjects. The serum was separated after centrifugation at 4000 Rotations per Minute (RPM) and used for the estimation of glucose, triglyceride, HDL-C and insulin. The levels of serum glucose, triglyceride and HDL-C were analysed using the diagnostic kit. The levels of

serum insulin levels were analysed using the ELISA kit.

Serum Glucose:

The levels of serum glucose were analysed by using the GOD-POD kit method. In this approach, glucose oxidase oxidizes glucose to gluconic acid and hydrogen peroxide. The formed H_2O_2 produces red colour complex in the presence of peroxidase and 4-aminoantipyrine, which can read at 505 nm. Optical Density (OD) of the samples was compared with the standards to obtain a glucose concentration in samples and results were expressed as mg/dL.

Serum Triglyceride:

Serum triglyceride was analysed using the GPO-POD kit method. In this protocol, 10µl of serum sample was added to 1ml of reagent mixture consists of lipoprotein lipase, which cleaves triglyceride into glycerol and free fatty acid. The liberated glycerol is converted into glycerol-3-Phosphate, dihydroxyacetone phosphate and H_2O_2 by a series of enzyme activity. In the last reaction, H_2O_2 reacts with 4-aminophenazone and P-chlorophenol in the presence of peroxidase to give a red-colour dye, which read at 505nm. The OD of the samples was compared with standards to obtain a triglyceride concentration in the samples and results were expressed as mg/dL.

Serum HDL-C:

LDL/VLDL cholesterol in serum was precipitated by using polyethylene glycol and the supernatant was used for cholesterol analysis. Cholesterol esters are enzymatically hydrolysed by cholesterol esterase to cholesterol and free fatty acids. Free cholesterol is then oxidized by cholesterol oxidase to cholest-4-ene-3-one and H_2O_2. It reacts with 4-aminophenazone and P-chlorophenol in the presence of peroxidase to give a red-colour dye, which read at 505 nm. The OD of the samples was compared with standards to obtain an HDL-cholesterol concentration in the samples and results were expressed as mg/dL.

Serum Insulin:

Serum insulin levels were analysed by using a direct ELISA kit method (Diametra, Italy. DK0076). The sensitivity of the method is 0.25 µIU/ml and detection range is 3-200 µIU/ml.

HOMA- IR:

It is calculated product of fasting serum glucose and insulin levels and described by Mathew *et al*. [2]. HOMA-IR: Fasting insulin (µIU/ml)* Fasting glucose (mg/dL)/405

HOMA2-IR, HOMA-% B and HOMA-% S:

The levels of HOMA2-IR, HOMA-%B and HOMA-%S were calculated values from fasting serum glucose and insulin levels with the formula released by the Diabetes Trials Unit, University of Oxford: http://www.dtu.ox.ac.uk/ homacalculator/ index.php.

QUICKI is a product of logarithmic values of fasting glucose and fasting insulin and calculated with the formula = 1/ [log (I0) +log (G0)], where I0 (µIU/ml) and G0 (mg/dl) stand for fasting insulin and glucose values respectively [17].

TG/HDL-C Ratio:

It is a product of serum triglyceride and serum HDL-C and calculated using the formula: (TG (mg/dL)/ HDL-C (mg/dL) [6].

Insulin: Glucose Ratio:

The ratio of fasting insulin to glucose was calculated using serum insulin and glucose of each subject.

METS-IR:

It is a calculated value from fasting glucose, triglyceride, HDL-C with BMI and formula of Ln ((2*G0) +TG0)*BMI)/ (Ln (HDL-C)). G0= fasting glucose, TG0= fasting triglycerides, BMI=body mass index, HDL-C: high-density lipoprotein-cholesterol [9].

TyGI:

It is a product of serum TG and serum glucose and is calculated from the formula: ln [FBS (mg/dl) × TG (mg/dl)]/2 [7].

Statistical Analysis:

Statistical Package for the Social Sciences (SPSS) version 20 was used for data analysis. The data are presented in proportion and means with standard error. Student 't' test and One-way Analysis of Variance (ANOVA) test was used to assess the association of risk factors with the IR and IS biomarkers. Spearman correlation coefficient (r) test was used to evaluate the association between HOMA-IR and other contemporary IR and IS biomarkers. Multiple linear regression analysis was used to evaluate the association between IR and IS biomarkers with independent risk factors among industrial workers. Probability <0.05 is considered as significant.

Results:

The demographic details among industrial workers are presented in Table 1.

The frequency distribution of gender was found that the maximum number of industrial workers were males (68.6%) followed by females (31.4%). The age distribution showed that maximum number of workers were in the age group of 26-33 years and the minimum was in the age group of

Table 1: Demographical Details and Risk Factors among Industrial Workers

Variables	n=137	Percentage
Gender		
Male (M)	94	68.6
Female (F)	43	31.4
Age (years)		
18-25	29	21.2
26-33	48	35.0
34-41	34	24.8
>42	26	19.0
Smoking		
Yes	18	13.1
No	119	86.9
Alcohol consumption		
Yes	32	23.4
No	105	76.6

Continued...

Variables	n=137	Percentage
BMI (Kg/m^2)		
<18.5 (underweight)	13	9.5
18.5-22.9 (Normal)	42	30.7
23-24.9 (Overweight)	30	21.9
>25 (Obese)	52	38.0
Waist circumference (risk)		
No (<90 cm M or < 80 cm:F)	72	52.6
Yes (>90 cm M or >80 cm:F)	65	47.4
Hypertension		
No (SBP<140 or DBP<90)	105	76.6
Yes (SBP>140 or DBP>90)	32	23.4
Diabetes		
No (<126 mg/dL)	127	92.7
Yes (>126 mg/dL)	10	7.3
TG (mg/dl)		
<150(Normal)	84	61.3
>150(High)	53	38.7
HDL- C (mg/dl)		
(M<40, F <50)Low	98	71.5
(M>40, F>50)Normal	39	28.5
Metabolic syndrome (IDF)		
No	102	74.5
Yes	35	25.5

>42 years. Among these industrial workers13.1% were smokers and 23.4 % were having alcohol consumption habits. The BMI of subjects was classified according to Asia-Pacific cut-off values [18]. The BMI of the workers revealed that 30.7% had normal BMI, 21.9% were overweight, 38.0% were obese and only 9.5% were underweight. WC risk evaluated using the cut-off values of Asians population recommended by National Cholesterol Educational Program-Adult Treatment Panel -III (NCEP- ATP-III) that is > 90 cm for men and > 80 cm for women [19]. WC risk was noted in 47.4% of industrial workers. Essential hypertension was assessed using the Joint National Committee-8th Report Guidelines [20]. As per these guidelines, the Systolic Blood Pressure (SBP) >140 mmHg or Diastolic Blood Pressure (DBP) >90 mmHg considered as essential hypertension. The distribution of essential hypertension among industrial workers was found to be 23.4%.

The frequency distribution of diabetes among industrial workers were assessed using American

Diabetes Association (ADA) Guidelines [21] i.e. fasting glucose concentration ⩾ 126 mg/dL considered as diabetes. The frequency distribution showed that 7.3% workers had diabetes. The distribution of low-HDL-C level was done by using NCEP, ATP –III guidelines [19] that is ⩽ 40 mg/dL for men and ⩽ 50 mg/dL for women. 71.5% of industrial workers had low levels of HDL-C. The risk of elevated levels of serum TG was assessed using NCEP, ATP-III guidelines [19] is ⩾ 150 mg/dL. The frequency distribution of elevated serum TG was found in 38.7% of workers. The presence of MetS among industrial workers was defined by using the IDF definition [22] and 25.5% of industrial workers had MetS.

Association of risk factors with IR and IS markers among industrial workers are presented in Table 2. Student t test and ANOVA test was used to find out association of variables such as gender, age, smoking, alcohol consumption, risk of BMI, WC, hypertension, diabetes, elevated triglyceride, low HDL-C and MetS with the IR and IS markers among industrial workers. IR markers, i.e. HOMA-IR, HOMA2-IR, HOMA-%B, TG/HDL-C, METS-IR and TyGI were increased and IS markers, viz. QUICKI and HOMA-%S were decreased in male workers as compared to female workers. The markers of METS-IR and TyGI were significantly associated with increasing of age among workers. Smoking habit causes a significant decrease in HOMA-%S. Workers who had alcohol consumption habits showed a significant increase of TG/HDL-C and TyGI.

BMI was significantly associated with increased IR markers such as HOMA2-IR, TG/HDL- C, METS-IR and TyGI and decreased IS markers namely QUICKI and HOMA-%S. The presence of WC risk was associated with HOMA-%S. Subjects with essential hypertension found significant association with HOMA-IR and TG/HDL-C. Subjects with diabetes found significantly increased IR markers such as HOMA-IR and TG/HDL-C and significantly decreased IS makers namely QUICKI and HOMA-%S. Workers with elevated triglyceride risk found expressively increased IR markers viz., HOMA-IR, HOMA2-IR, HOMA-%B, TG/HDL-C, Insulin: Glucose and suggestively decreased IS marker namely HOMA-%S. Workers with low HDL-C risk found significantly increased IR markers in particular HOMA-IR, HOMA2-IR and TG/HDL-C. In workers with the presence of MetS risk found an increased IR and decreased IS markers, but it was not significantly altered.

The results of the spearman correlation coefficient (r) between HOMA-IR and contemporary IR and IS markers among industrial workers are presented in Table 3. A positive and significant correlation was noted between HOMA-IR and HOMA2-IR ($r=0.988$; $P<0.01$), HOMA-%B ($r=0.554$; $P<0.01$), TG/HDL-C ($r=0.362$, $P<0.01$), Insulin: Glucose ($r=0.862$; $P<0.01$), METS-IR ($r=0.457$; $P<0.01$) and TyGI ($r=0.477$; $P<0.01$). A negative and significant correlation was noted between HOMA-IR and QUICKI ($r=-0.976$; $P<0.01$) and HOMA-%S ($r=-0.988$; $P<0.01$).

Table 2: Association of Risk Factor with IR and IS Markers among Industrial Workers

Variables	N (%)	HOMA-IR	HOMA2-IR	QUICKI	HOMA-%B	HOMA-%S	TG/HDLC	Ins:Glu	METS-IR	TyGI
Gender										
Male(M)	94(68.6)	3.4±0.4	1.76±0.2	0.99±0.3	141.8±10	107.4±8	5.3±0.5	0.15±0.02	39.7± 0.8	4.7±0.36
Female (F)	43(31.4)	2.4±0.4*	1.36±0.2	1.02±0.4	130.2±13	136.4±12	4.3±0.5	0.15±0.02	39.6 ±1.3	4.6±0.47
Age (years)										
18-25	29(21.2)	2.8±0.74	1.53±0.34	1.1 ±0.05	134.30±15	138.9±16	3.7±0.45	0.14±0.03	36.2±1.5	4.5±0.06
26-33	48(35.0)	2.6±0.40	1.42±0.20	1.05±0.04	126.16±12	124.5±11	4.9±0.49	0.13±0.02	39.3±1.1	4.7±0.05*
34-41	34(24.8)	3.7±0.66	1.90±0.30	0.95±0.05	161.70±22	97.6±13*	6.5±1.00*	0.20±0.03	42.3±1.5*	4.8±0.06*
>42	26(19.0)	3.4±0.68	1.70±0.30	0.97±0.05	133.70±18	101.2±14	4.6±0.84	0.14±0.03	41.±1.5*	4.7±0.06
ANOVA		P=0.461	P=0.464	P=0.171	P=0.440	P=0.132	P=0.056	P=0.467	P=0.020	P=0.028
Smoking										
Yes	18(13.1)	3.5±0.81	1.76±0.39	0.97±0.05	134.1±23.0	96.2±13*	5.6±1.1	0.15±0.03	38.6±1.3	4.8±0.10
No	119(86.9)	3.0±0.32	1.62±0.14	1.03±0.03	138.8±9.1	119.5±8	4.9±0.4	0.14±0.01	39.8±0.8	4.7±0.03
Alcohol										
Yes	32(23.4)	3.1±0.53	1.62±0.24	1.00±0.05	142.9±21.1	108.0±13	5.9±1.2*	0.15±0.03	38.2±1.4	4.7±0.08*
No	105(76.6)	3.0±0.35	1.64±0.16	1.02±0.03	136.7±9.0	119.1±8	4.7±0.3	0.14±0.01	40.2±0.8	4.6±0.03
BMI (Kg/m^2)										
<18.5	13(9.5)	1.3±0.46	0.8±0.30	1.3 ±0.07	95.2±18	216.0±24	2.9±0.4	0.07±0.03	27.0±0.7	4.4±0.07
18.5-22.9	42(30.7)	2.9±0.60	1.5±0.25	1.1±0.04*	128.4±16	133.7±13*	3.7±0.4	0.13±0.02	33.9±0.5*	4.6±0.05
23-27.5	30(21.9)	3.7±0.70*	1.9±0.32*	0.9±0.04*	152.6±18*	93.8±11*	7.3±1.3*	0.17±0.03*	41.3±0.9*	4.8±0.08*
>27.5	52(38.0)	3.3±0.44	1.8±0.20*	0.9±0.03*	148.4±14*	90.7±8*	5.2±0.4	0.16±0.02	46.5±0.8*	4.8±0.04*
Anova		P=0.185	P=0.097	P=0.000	P=0.256	P=0.000	P=0.001	P=0.165	P=0.000	P=0.007
WC (risk)										
No	72(52.6)	2.7±0.4	1.4±0.17	1.1±0.03	127.9±11	135.0±10	4.7±0.55	0.13±0.02	35.3±0.8	4.6±0.04
Yes	65(47.4)	3.5±0.4	1.9±0.20	0.9±0.03	150.0±12	96.4 ±8*	5.3±0.46	0.17±0.01	44.5±0.8	4.7±0.04
Hypertension										
No	105(76.6)	2.7±0.3	1.5±0.15	1.0±0.03	142.4±10	122.4±8	4.6±0.3	0.14±0.01	38.8±0.8	4.6±0.03
Yes	32(23.4)	4.4±0.7*	2.0±0.30	0.9±0.05	124.1±17	96.9 ±14	6.4±1.1*	0.15±0.02	42.8±1.4	4.9±0.07
Diabetes										
<126 mg/dl	127(92.7)	2.5±0.2	1.5±0.12	1.0±0.02	142.9±9	122.7±7	4.8±0.3	0.14±0.01	39.3±0.7	4.7±0.03
>126 mg/dl	10(7.3)	10.4±1.6*	3.7±0.66	0.7±0.05*	78.0±20	37.5±8*	7.4±2.5*	0.17±0.04	44.4±2.5	5.2±1.30
TG										
<150(normal)	84(61.3)	2.5±0.3	1.3±0.14	1.1±0.03	125.9±9	136.5±9	3.0±0.1	0.12±0.01	36.6±0.7	4.5±0.03
>150(High)	53(38.7)	4.1±0.5*	2.1±0.25*	0.9±0.03	157.6±15*	84.7 ±8*	8.2±0.7*	0.20±0.03*	44.6±1.1	5.0±0.03
HDL-C										
Low	98(71.5)	3.5±0.4*	1.8±0.2*	0.98±0.03	148.6±10	107.2±8	5.9±0.5*	0.16±0.01	41.1±0.9	4.7±0.04
Normal	39(28.5)	1.9±0.3	1.1±0.2	1.1±0.04	111.7±15	139.9±12	2.9±0.2	0.10±0.02	36.2±1.0	4.6±0.04
Mets (IDF)										
No	102(74.5)	2.9±0.3	1.6±0.2	1.0±0.03	138.5±10	124.3±8	4.3±0.40	0.14±0.01	36.6±0.6	4.6±0.03
Yes	35(25.5)	3.6±0.6	1.9±0.2	0.9±0.04	137.1±15	93.6 ±11	7.1±0.70	0.15±0.02	48.6±1.1	5.1±0.05

**P<0.05*

Table 3: Correlation Coefficient (r) between HOMA-IR and Contemporary Markers of IR and IS among Industrial Workers

Variables	HOMA-IR	HOMA2-IR	QUICKI	HOMA-%B	HOMA-%S	TG/HDL-C	Ins:Glu	METS-IR	TyGI
HOMA-IR	1.000	-	-	-	-	-	-	-	-
HOMA2-IR	0.988**	1.000	-	-	-	-	-		-
QUICKI	-0.976**	-0.997**	1.000	-	-	-	-	-	-
HOMA-%B	0.554**	0.661**	-0.708**	1.000	-	-	-	-	-
HOMA-%S	-0.988**	-1.000**	0.997**	-0.661**	1.000	-	-	-	-
TG/HDL-C	0.362**	0.360**	-0.352**	0.165**	-0.362**	1.000	-	-	-
Ins:Glu	0.862**	0.922**	-0.945**	0.881**	-0.921**	0.288**	1.000	-	-
METS-IR	0.457**	0.463**	-0.458**	0.263**	-0.463**	0.630**	0.418**	1.000	-
TyGI	0.477**	0.423**	-0.390**	-0.650**	-0.424**	0.815**	0.220**	0.528**	1.000

**Correlation is significant at the 0.01 level (2-tailed)*

Linear multiple regression analysis of variables that affect IR and IS markers among industrial workers were presented in Table 4. In this model, each measure of IR and IS markers (HOMA-IR, HOMA2-IR, QUICKI, HOMA-%B, HOMA-%S, TG/HDL-C, Insulin: Glucose, METS-IR and TyGI) were used as the dependent variable and gender (M and F), age, BMI categories, smoking (yes=1 and no=0), alcohol consumption (yes=1 and no=0), hypertension (yes=1 and no=0), waist circumference risk (yes=1 and no=0), diabetes (Yes=1 and no=0), high triglyceride (yes=1 and no=0), low HDL-C risk (Yes=1 and no=0) and MetS (yes=1 and no=0) were used as independent variables. The results of linear regression showed that the highest percentage of independent variables were influenced by 86% in METS-IR followed by 66% in TyGI, 57% in TG/HDL-C, 49% in HOMA-IR, 37% in HOMA-%S, 34% in QUICKI, 30% in HOMA2-IR, 16% in HOMA-%B and 16% in Insulin: Glucose. In the present study, we assessed the model fit assumption using standardized β co-efficient with R square and ANOVA (F, DF and P) findings. Collinearity test parameters like tolerance, Variance Inflation Factor (VIF), and Durbin-Watson score was used to check the model diagnostics. This score indicate that below 2 is positive autocorrelation and above 2 negative autocorrelation. Collinearity test express the multicollinearity between dependent and independent variables, if the value for the tolerance is less than 10 and value of the VIF is close to 1 is no cause of concern. In our study, we observed the tolerance values range from 0.33 to 0.89 and VIF from 1.12 to 3.00. The model diagnostics indicates multicollinearity with probably cause of concern.

Table 4: Linear Multiple Regression Analysis of Variables That Effect on IR and IS Markers among Industrial Workers

Independent Variable	HOMA-IR (β)	HOMA2-IR (β)	QUICKI (β)	HOMA-%B (β)	HOMA-%S (β)	TG/HDLC (β)	Ins:Glu (β)	METS-IR (β)	TyGI (β)
Gender	-0.146	-0.167	0.191*	-0.105	0.189*	0.081	-0.152	-0.064	-0.052
Age(years)	-0.026	-0.017	-0.014	0.020	-0.021	0.029	0.008	0.051	0.050
Smoking	-0.047	0.048	-0.015	0.042	0.012	0.073	0.053	0.105*	0.058
Alcohol	0.022	0.015	0.021	-0.070	0.029	-0.154	-0.025	0.029	0.017
BMI (Kg/m^2)	-0.083	-0.056	-0.252	0.049	-0.339**	-0.097	-0.029	0.535**	-0.078
Waist-C	0.391**	0.424**	-0.298*	0.271	-0.254*	0.109	0.383**	0.098	0.157
hypertension	0.094	0.055	0.001	-0.011	0.049	0.215**	-0.011	0.065	0.194**
Glucose	0.597**	0.375**	-0.280**	-0.172	-0.277**	0.068	0.049	0.079*	0.326**
Triglyceride	0.330**	0.347**	-0.337**	0.223*	-0.335**	0.607**	0.317**	0.228**	0.726**
HDL-C	-0.118	-0.149	0.098	-0.225*	0.061	-0.469**	-0.189*	-0.321**	-0.105
MetS	-0.337**	-0.357**	0.353**	-0.318*	0.357**	-0.154	-0.352**	0.105*	-0.132
R^2	0.49	0.30	0.34	0.16	0.37	0.57	0.16	0.86	0.66
ANOVA **F** ***P***	 10.8 <0.001	 4.8 <0.001	 5.7 <0.001	 2.1 <0.05	 6.6 <0.001	 15.2 <0.001	 2.1 <0.05	 71.5 <0.001	 22.5 <0.001
Durbin-Watson	2.05	1.99	1.72	1.64	1.70	2.05	1.84	1.90	1.98

*Dependent variables: HOMA- IR, HOMA2- IR, QUICKI, HOMA-%B, HOMA-%S, TG/HDL-C, Insulin: Glucose, METS-IR and TyGI. Predictors: Gender, age, smoking, alcohol consumption, BMI, waist Circumference, blood pressure, fasting glucose, Triglyceride, HDL-C and MetS. Collinearity parameters: Tolerance: 0.33 to 0.89 and Variance Inflation Factor (VIF): 1.12 to 3.00 β= Standardized coefficient with *P<0.05 and **P<0.01.*

Discussion:

The present study assessed the association between risk factors and IR and IS biomarkers among industrial workers. The risk factors incorporated as gender, age, smoking, alcohol consumption, BMI, WC, elevated triglyceride, hypertension, low HDL-C, diabetes and MetS. Most of the studies reported an increased IR markers, i.e. HOMA-IR, HOMA2-IR, HOMA-%B and decreased IS markers viz. QUICKI and HOMA-%S in general population of males compared to the females [23-

24]. In the current study, we noted similar findings in the comparison between male and female workers with respect to IR and IS biomarkers. This may have been due to the presence of high risk factors such as increased age, smoking, alcohol consumption, diabetes, hypertension, elevated triglycerides and low HDL-C. Another reason for increased IR and decreased IS markers in men could have been due to the high visceral& hepatic adipose tissue and worse lifestyle habits [25].

Refaie *et al.* [26] reported high levels of HOMA-IR, HOMA-%B and low levels of QUICKI in elderly subjects. In this study, we found an increased IR markers and decreased IS markers with increase of age. The age variable was significantly associated with TG/HDL-C, METS-IR and TyGI. Smokers found an increased HOMA-IR and decreased HOMA-%S, QUICKI and HOMA-%B [27]. In the present study, it was observed significant association between smoking and HOMA-%S ($P<0.05$).

Vilegas *et al*. reported that the alcohol consumption had an inverse association with IS and U shaped association with IR [28]. A recent study reported decreased IS and β-cell function with accompanying of high cholesterol and triglycerides among alcoholics [29]. In the present research, it was demonstrated that the alcohol consumption showed increased IR markers (HOMA-IR, HOMA2-IR, TG/HDL-C and TYGI) and reduced IS markers (QUICKI & HOMA-%S) and β-cell function (HOMA-%B).

Diabetes develops with normal BMI through IS, whereas high BMI through IR [30]. BMI ⩾ 23 (Kg/m2) is a risk factor for IR [31]. During the study, it was perceived that the workers with BMI>23 (Kg/m2) shown significantly increased IR markers, i.e. HOMA-IR, HOMA2-IR, HOMA-%B, TG/HDL-C, Insulin: Glucose, METS-IR, TyGI and significantly decreased IS markers: QUICKI and HOMA-%S. Bhattacharya reported an increased HOMA-IR and decreased QUICKI with BMI [32]. In this research, we noted positive association between BMI and IR markers and negative association with IS markers.

Wahreberg *et al.* reported that the WC >100 cm is a good predictor for IS in both sexes [33]. In the present investigations, we noted an increased IR markers (HOMA-IR-HOMA2-IR, HOMA-%B, TG/HDL-C, Insulin: Glucose, METS-IR and TYGI) and decreased IS markers (QUICKI) in workers with WC risk. A recent study reported high HOMA-IR and low QUICKI in subjects with hypertension [34]. In this study, the levels of HOMA-IR and TG/HDL-C were significantly associated with hypertension. During the present study, a significant association was noted between diabetes and HOMA-IR, HOMA2-IR, QUICKI, HOMA-%B and TG/HDL-C. Bello-Chavolla *et al*. reported high level of METS-IR with diabetes [9]. HOMA-IR is index for IR and β-cell dysfunction, which were associated with pre-diabetes and overt diabetes [35].

Dyslipidaemia was associated with higher levels of total cholesterol, triglycerides and insufficient levels of HDL-C [36]. People with dyslipidaemia were associated with increased IR [37]. Hoffman et al reported a positive link between triglycerides and IR and negative with IS [38]. During the present study, the elevated triglycerides was significantly associated with HOMA-IR, HOMA2-IR, HOMA-%B, TG/HDL-C, Insulin: Glucose and HOMA-%S. In this study, it was noted that the workers with low HDL-C was associated with increased IR and

decreased IS markers. Studies reported positive association between IR and MetS [39]. Present study, we noted an increased IR marker and decreased IS markers among workers with MetS.

In this report, we evaluated the association between HOMA-IR and contemporary markers of IR and IS by using a Spearman correlation coefficient test. A positive and significant association was noted between HOMA-IR and HOMA2-IR, HOMA-%B, TG/HDL-C, Insulin: Glucose METS-IR and TyGI. A negative and significant association was noted between HOMA-IR and QUICKI and HOMA-%S.

In this study, we assessed the association of risk factors with the IR and IS markers among industrial workers using linear multiple regression analysis. The results of linear regression showed that the 86% of predictors were associated with METS-IR, followed by 66% in TyGI, 57% in TG/HDL-C, 49 % in HOMA-IR, 37% in HOMA-%S, 34% in QUICKI, 30% in HOMA2-IR, 16% in HOMA-%B and 16% in Insulin: Glucose. The IR markers such as METS-IR, TyGI and TG/HDL-C were mainly influenced by independent variables when compared to other IR and IS markers. Our results correlate with Yeh *et al*. findings that TyGI had highest association followed by TG/HDL-C and METS-IR in population based studies [12].

Conclusions:

The results of the study showed that the highest percentage of risk factors were associated with METS-IR and then followed by TyGI, TG/HDL-C, HOMA-IR, HOMA-%S, QUICKI, HOMA2-IR, HOMA-%B and Ins: glu. The IR markers such as METS-IR, TyGI and TG/HDL-C were principally influenced by the risk factors.

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Author for Correspondence:

Dr. Kalahasthi Ravibabu, Regional Occupational Health Centre (Southern),Indian Council of Medical Research, ICMR Complex, Kannamangala Post, Poojanahalli Road, Devanahalli Taluk, Bengaluru-562110, Karnataka, India Email: kalahasthi20012002@yahoo.co.in Phone: +91-080-22172500.

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