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Prevalence of prediabetes and metabolic syndrome and their association in an Iraqi sample

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Abstract:
Background: *Prediabetes and are increasing in prevalence all over the world, they each carry risks to the future development of diabetes mellitus and cardiovascular disease. These risks will be greatly exaggerated if they occur together in the same individual. The aim of the study was to find the prevalence and the association of prediabetes and metabolic syndrome, in addition to analyzing the correlation of the risk factors that lead to their development.*
Material and Methods: *This was a cross-sectional, simple random study that included 300 Iraqi individuals, aged between 30-75 years, who accepted to take part in this study were recruited.*
Result: *Prevalence of prediabetes and metabolic syndrome was (33.66%) and (42%) respectively. Patients with prediabetes had 9.82 times the odd of having metabolic syndrome and is significantly associated (P value <0.001)*
Conclusion: *Prediabetes and metabolic syndrome are not only common but also significantly associated with each other, increasing the burden on public health care and needs to be addressed globally.*
Keywords: *Association, prediabetes, metabolic syndrome, Iraq.*

I. Introduction

The precise history of when the term "prediabetes" was first used is not very clear; Professor Sir K G ALBERTI stated "it was first used to indicate abnormalities of pregnancy (e.g., high– birth weight babies, hydramnios) or a strong family history of type 2 diabetes (T2DM)" [1].

In 1979 and 1980, both the National Diabetes Data Group [2] and the World Health Organization (WHO) [3] formally defined a post challenge state of glucose tolerance that lay between what was considered normal and diabetes, i.e. an elevated 2-hours post prandial plasma glucose (2–h PG) with a nondiabetic fasting glucose level and was termed "impaired glucose tolerance" (IGT).

20 years later in 1997 a similar category of elevated, but nondiabetic, fasting glucose levels was also officially recognized by the American Diabetes Association (ADA) and then by the WHO in1999, and so they added the term "impaired fasting glucose" and "impaired fasting glycemia" respectively to the available diagnostic categories of Diabetes Mellitus. [4-5].

Since then many differences between these two scientific bodies have surfaced, leading to discrepancies in the terms and values adopted and used in the definitions and diagnostic criteria of "prediabetes". The WHO and since 1980 to date discards the term "prediabetes", largely because many subjects with borderline glucose levels do not convert to diabetes and because many would be alarmed unnecessarily [6].

Instead in 2008 they use the term "intermediate hyperglycemia" to signify individuals with IGT and IFG, defining IGT level as fasting plasma glucose of <126mg/dl (7.0mmol/l) and 2–h PG plasma glucose ≥140mg/dl and < 200mg/dl (7.8 -11.1mmol/l) and the IFG level as fasting plasma glucose 110mg/dl - 125mg/dl (6.1 - 6.9mmol/l) and (if measured), the 2–h PG plasma glucose <140mg/dl (7.8mmol/l). Also the WHO stated that, currently the hemoglobin A1c (HbA1c) is not considered a suitable diagnostic test for diabetes or intermediate hyperglycemia [7].

On the contrary the ADA and since 2005 used the term "prediabetes" to signify individuals with IFG and/or IGT [8] and recently added borderline levels of HbA1c as another indicator in 2010[9], defining IGT level as 2-h PG plasma glucose in the 75-g OGTT 140 mg/dL to 199 mg/dL (7.8 mmol/L -11.0 mmol/L). and the IFG level as fasting plasma glucose 100 mg/dL to 125 mg/dL (5.6mmol/L - 6.9 mmol/L) and the borderline levels of HbA1c level as 5.7–6.4 %[9].

Persons with IFG and/or IGT and/or HbA1c of 5.7–6.4%, relatively have higher risk for the future development of T2DM, they alone and/or due to the future development of diabetes also have higher risk for the development of cardiovascular disease (CVD) [9, 10]. In addition, the IFG, IGT and HbA1c of 5.7–6.4%, are associated with many cardiovascular risk factors as, obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension[11]. These CVD risk factors, as they aggregates with prediabetes, makes up the metabolic syndrome (MetS), therefore it is not surprising that the prevalence of prediabetes, MetS and their synergistic effect on increasing T2DM and CVD risk overlap[12].

MetS without prediabetes carries an approximate 5-fold increase in diabetes risk and 2-3 fold increase in CVD risk, while prediabetes without MetS carries an approximate 5- 7 fold increase in diabetes risk and a modest increase in CVD risk. When pre-diabetes combines with MetS, these risks are markedly augmented [13].

The MetS itself also faced considerable disagreement over its name, clinical definitions and diagnostic criteria. The terms "syndrome X", "pluri-metabolic syndrome", "Reaven's syndrome", "the deadly quartet", "the awesome foursome", "the metabolic syndrome" and many other terms were used [14].

Its origins can be dated back to the 1920's when Kylin, a Swedish physician, demonstrated the association of high blood pressure, high blood glucose, and gout are associated with metabolic abnormalities [14], but the first formalized definition of the syndrome was proposed in 1998 by a consultation group on the definition of diabetes for the WHO [15].

Then other major criteria came from the National Cholesterol Education Program Adult Treatment Panel III (ATP III) in 2001 [16]. then the International Diabetes Federation (IDF)[17] and the American Heart Association /National Heart, Lung, and Blood Institute (AHA/NHLBI) in 2005[18]. Each of these organizations has its own clinical definitions and diagnostic criteria.

The most widely recognized and accepted risk factors of the MetS in these criteria were atherogenic dyslipidemia, elevated blood pressure, elevated plasma glucose, in addition to prothrombotic and a proinflammatory states.

In 2009 a meeting between several major organizations in an attempt to unify the criteria. of MetS, agreed that "there should not be an obligatory component in the diagnostic criteria, that waist measurement would continue to be a useful preliminary screening tool, three abnormal findings out of 5 would qualify a person for the metabolic syndrome. [19].

After that both the WHO and NHLBI. started reconsidering their definition of metabolic syndrome, to produce a further statement with the intention of having a worldwide single agreed-upon set of diagnostic criteria[19].

The aim of the study is to find the prevalence and the association of prediabetes and metabolic syndrome, in addition to analyzing the correlation of the risk factors that lead to their development.

II. Material And Methods

2.1 Study Design and subjects:

This was a cross-sectional, simple random study that included 300 Iraqi individuals, 160 males and 140 females, aged between 30-75 years, visiting Baghdad Teaching Hospital, who accepted to take part in this study were recruited.

2.2 History and examination:

All participants underwent a thorough baseline evaluation including a detailed review of their medical history, physical examination, and contemporary assessments of basic demographics: (age, gender, waist circumference, systolic and diastolic blood pressure). A full medical history including the history of diabetes. hypertension and their medical treatment were recorded. Participants were excluded if they were diabetics or on anti diabetic drugs.

Physical examination included measurements of waist circumference, systolic and diastolic blood pressure (Bp).

The waist circumference was measured by a non stretchable tape, the patient was positioned symmetrically in a standing position, and the measurement was taken halfway between lower rib and iliac crest at the end of a normal expiration and to the nearest 0.1 cm [20].

The Bp was measured using mercury sphygmomanometer, the centre of the cuff bladder placed over the brachial artery and the lower edge of the cuff is 2-3 cm above the point of brachial artery pulsation. Two blood pressure recordings were obtained from the right arm of patients in a sitting position, the arm and heart at the same level, after 30 minutes of rest at 5-min intervals, and their mean value was calculated [21].

2.3 Definitions:

Prediabetes was defined according to ADA criteria[9] as FPG 100 mg/dL (5.6mmol/L) to 125 mg/dL (6.9 mmol/L) (IFG) OR 2-h PG in the 75-g OGTT 140 mg/dL (7.8 mmol/L) to 199 mg/dL (11.0 mmol/L) (IGT) OR HbA1C 5.7–6.4%.

MetS was defined according to the revised IDF criteria in 2009 for the Middle East [9] that states the presence of any 3 of the following 5 risk factors constitutes a diagnosis of metabolic syndrome.

1- Elevated waist circumference to ≥94 cm (male), ≥80 cm (female).

2- Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator) to ≥150 mg/dL.

3- Reduced HDL-C (drug treatment for reduced HDL-C is an alternate indicator) to < 40 mg/dL (1.03 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women.

4- Elevated blood pressure (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator) to systolic Bp ≥130 or diastolic ≥85 mmHg.

5- Elevated fasting glucose (drug treatment of elevated glucose is an alternate indicator) to ≥100 mg/dL.

2/4 **Laboratory tests:**

Serum Lipid profile (including serum (S) triglycerides and S HDL levels) and fasting blood glucose was obtained after 12 hours overnight fasting.

2.5 Statistical analysis:

SPSS version 20 software package and Mintab version 17 software package used in the analysis of the data when appropriate. Median and interquartile range were used to present variables that did not follow normal distribution (non-parametric) and Mann Whitney non-parametrics were used to show the statistical significance. Binary logistic regression analysis was done to assess the association between various variables with both metabolic syndrome and prediabetes. Multivariate binary logistic regression was used to find which variable is dependent and which is independently correlated (associated) with either metabolic syndrome or prediabetes. Chi square analysis was done to assess the association between prediabetes and metabolic syndrome. Level of significant (p value) chosen for this study was 0.05

III. Results

A total of 300 Iraqi's participated in the study,160 (53.33%) participant were males and 140 (46.67%) were females. Table (1).

Table 1: Gender distribution of participants

Gender	Number	Percentage	Total
Male	160	53.33%	300
Female	140	46.67%	

The mean age was (54.07) (range 30-75) years and the demographic, clinical and metabolic characteristics are summarized in table (2).

Table 2: Basic characteristic of participants

Variable	Median	IQR
Age (years)*	54.077	10.60
Waist (cm)*	97.380	12.09
SBP	125	120 – 145
DBP	80	75 – 95
FBS	94	84 – 111
TG	143.5	123 – 156
HDL	52	41 – 60

*For variables follow normal distribution we use mean and standard deviation

126 participant had metabolic syndrome with a prevalence of (42%), 60 (20%) were males and 66 (22%) were females, while 101 participant had prediabetes with a prevalence of (33.66%), 60 (20%) were males and 41 (13.66%) were females. Table (3).

Table 3: Prevalence of MetS and Prediabetes according to gender

Condition	Total Number	Gender	Number according to gender	Percentage according to gender	Total Percentage
Metabolic syndrome	126	Male	60	20%	42%
		Female	66	22%	
Prediabetes	101	Male	60	20%	33.66%
		Female	41	13.66%	

The association between various variables with both metabolic syndrome and prediabetes were assessed, Also these variables were analysed to find which of them is dependently and which is independently correlated (associated) with either metabolic syndrome or prediabetes.

Univariate Association analysis for metabolic syndrome, the age did not correlate with the metabolic syndrome, while the rest of the variable correlate well with metabolic syndrome in which the order from highest to lowest correlation were: diastolic blood pressure (DBP), FBS, systolic blood pressure (SBP), triglycerides (TG) and waist circumference, these correlate positively with metabolic syndrome; while high density lipoprotein (HDL) correlate negatively (inversely) with metabolic syndrome. Table (4).

Table 4:Univariate Association between different continuous variable and metabolic syndrome

Variable	OR	95%CI	P value
Age (years)	0.9903	0.9690 – 1.0121	0.378 [NS]
waist (cm)	1.0303	1.0101 – 1.0509	0.003 [SD]
SBP	1.0475	1.0312 – 1.0640	<0.001 [SD]
DBP	1.0722	1.0448 – 1.1004	<0.001 [SD]
FBS (mg/dl)	1.0644	1.0449 – 1.0843	<0.001 [SD]
Triglycerides(mg/dL)	1.0323	1.0208 – 1.0440	<0.001 [SD]
HDL(mg/dL)	0.8907	0.8649 – 0.9173	<0.001 [SD]

In multivariate association analysis for metabolic syndrome, All of the variables were independently associated with metabolic syndrome, when accounting for the effect of each variable together low HDL effect become the most prominent followed by FBS, then TG, SBP, waist circumference, and DBP. The module fit well (R^2= 56.45%) and explain well the variability. Table (5).

Table 5 Multivariate association between different continuous variable and metabolic syndrome

Variable	^{2}	C R	95%CI	P value
waist (cm)	.18	1.0442	1.0109 – 1.0785	0.007
SBP	3.34	1.0634	1.0269 – 1.1011	< 0.001
DBP	.80	1.0737	1.0168 – 1.1338	0.009
FBS (mg/dl)	0.84	1.1062	1.0729 – 1.1404	< 0.001
Triglycerides(mg/dL)	3.11	1.0340	1.0174 – 1.0510	< 0.001
HDL(mg/dL)	3.38	0.8329	0.7902 – 0.8778	< 0.001
R^2= 56.45%, p value of the module = <0.001				

Univariate Association analysis for prediabetes, only waist circumference and TG were associated with prediabetes significantly and positively, the rest of the variables did not associate with prediabetes when analyzing them independent of the effect of each other. Table (6).

Table 6: Univariate Association between different continuous variable and prediabetes

Variable	OR	95%CI	P value
Age (years)	1.0127	0.9899 – 1.0360	0.276
waist (cm)	1.0278	1.0069 – 1.0490	0.008 [SD]
SBP	1.0103	0.9961 – 1.0248	0.157
DBP	1.0136	0.9896 – 1.0381	0.270
Triglycerides(mg/dL)	1.0081	1.0011 – 1.0151	0.015 [SD]
HDL(mg/dL)	0.9885	0.9658 – 1.0116	0.327

Multivariate Association analysis for prediabetes, Waist circumference and TG remain the only variables associated with prediabetes and also was independently correlated. Table (7) Fig (1).

Table 7: Multivariate association between different continuous variable and metabolic syndrome

Variable	^{2}	OR	95%CI	P value
Age	.44	1.0192	0.9950 – 1.0439	0.118
waist (cm)	.54	1.0273	1.0060 – 1.0492	0.011 [SD]
SBP	.10	1.0115	0.9900 – 1.0335	0.295
DBP	.06	1.0046	0.9689 – 1.0418	0.802
Triglycerides(mg/dL)	.87	1.0078	1.0004 – 1.0152	0.027 [SD]
HDL(mg/dL)	.04	0.9975	0.9732 – 1.0224	0.843
R^2= 4.44%, p value of the module = 0.009				

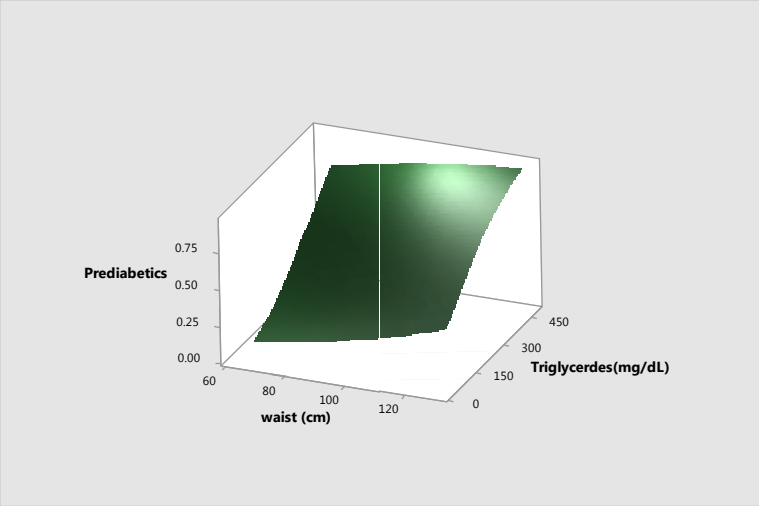

fig 1: Surface plot of waist circumference and TG and the probability of having prediabetes.

77 participants had both MetS and Prediabetes. 49 participants had only MetS without prediabetes, 24 participants had only prediabetes without MetS. Patients with prediabetes had 9.82 times the odds of having metabolic syndrome (significant association P value <0.001). Table (8).

Table 8: Association between metabolic syndrome and prediabetes status

Variable			Metabolic syndrome		Total	R	value
			Negative	Positive			
prediabetes	Negative	Count	150	49	199	.82	0.001
		% within prediabetes	75.4%	24.6%	100.0%		
	Positive	Count	24	77	101		
		% within prediabetes	23.8%	76.2%	100.0%		

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IV. Discussion

Both the prevalence of prediabetes and MetS are rapidly rising worldwide, due to increasing rates of overweight and obesity, physical inactivity and sedentary life style, unhealthy diet, higher socioeconomic status, smoking and poor blood pressure control.

In 2007 it was estimated that 309 million individuals have prediabetes worldwide, and there is a prediction that there will be 419 million by 2025[13].

Generally the prevalence of MetS ranged from <10% to as much as 84% worldwide, the IDF estimates that one-quarter of the world's adult population has the MetS, depending on the region, urban or rural environment, composition (sex, age, race, and ethnicity) of the population studied, and the definition or criteria of the MetS used[14].

This high global prevalence of prediabetes and MetS and the tendency of future development of DM and CVD have a great impact on the public health arena. These two health problems and their burden on the public health , are both preventable and/or treatable, by simple and cheap measures, mandating the identification of the individuals with prediabetes and MetS or those having high risk of their development, and to increase general knowledge of the population on the importance of lifestyle changes, reduction of overweight and obesity, healthy diet and physical activity, in addition to addressing other risk factors as hypertension, smoking cessation, extra[19].

In Iraq, there is still uncertainty about the prevalence of prediabetes and MetS in the Iraqi population. Our study found that the prevalence of prediabetes and MetS were 33.67% and 42% respectively in the studied sample.

The prevalence of prediabetes (33.67%) was similarly high as in a study by Mansour.A.A et al [22] done in Basrah, Iraq where they estimated the prevalence of prediabetes as 29.1%.

Also the results of a study in Tehran [23] was quite similar to our study in which they estimated that one third of the adult population have prediabetes, while a study in Jordan [24] found that the age-standardized prevalence of prediabetes was found to be 7.8%, which was quite different from our results, this difference can be explained by the socioeconomic differences and the eating habits between the two countries.

The MetS prevalence in our study (42%) was within the general global range of MetS prevalence of (<10% to as much as 84%), but slightly higher than the IDF estimates of 25% of the world's adult population [22]. These similarities and differences can be explained by the differences and similarities of the region, composition (sex, age, race, and ethnicity) of the population studied, and the definition of the syndrome used.

Metabolic syndrome and prediabetes often occur together. In our study 77 participants from the total of 126 having MetS also have prediabetes, while the other 49 have only MetS. While 77 participants with prediabetes from the total of 101 have MetS also, and the other 24 have only prediabetes.. The Participants with prediabetes had 9.82 times the odd of having MetS, association was significant (<0.001), to our knowledge there was no similar study in our region that studied the association between prediabetes and MetS, but many scientific reviews and articles concluded the association and the overlap between these two conditions[12,13].

Our study also analysed the most commonly associated risk for the development of prediabetes and MetS, most of them as waist circumference, low HDL, high triglycerides are usually due to bad eating habits, lack of exercise and sedentary life style which all are common in Iraq, especially for females. Because of the traditions, it is not usual to see a female or even a male jogging early in the morning, or visiting a gymnasium (gym) even once in his life time. Also we are used to serve high calorie, high fat diets on a daily bases, although it is quite tasty but I think it is time to change.

V. Conclusions:

Prediabetes and MetS are not only common but also significantly associated with each other, increasing the burden on public health care and needs to be addressed globally.

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