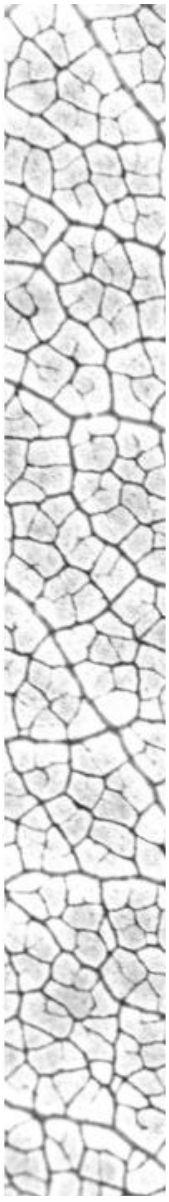

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Exploration of the relationship of vitamin B12 with some anthropometric measurements in Type2 diabetic patients

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Abstract

Background: Diabetes Mellitus (DM) is the most prevalent metabolic unrest affecting the people all over the world. Vitamin B12 (Vit B12), is a water-soluble vitamin, one of the eight B vitamins, metabolically important Vit B12 deficiency later will consequence in diabetes-related complications. current data was undertaken to exploration of the relationship of Vit B12 with some anthropometric measurements in type2 diabetic patients. **Materials and methods:** This study consisted of 60 patients with T2DM, attending Al- Ramadi teaching hospital and Al-Fallujah teaching hospital and 24 healthy individuals as controls. Serum Vit. B12 level was determined by ELISA technique while weight, height, waist, thoracic, neck, and hip circumferences carefully measured, also body mass index (BMI), waist/neck ratio (W/N), waist/thoracic ratio (W/T), waist/hip ratio (W/H) and were documented. **Results:** Vitamin B12, was found to be decreased in the patients with T2DM as compared to controls (P< 0.000l), and waist to hip ratio, waist to thoracic, and Body mass index were importantly greater in T2DM patients than in HCs with (P < 0.000l) for these parameters. Vit. B12 has important negative correlation with fasting serum glucose (FSG), weight, (P<0.001), HC, NC, BMI (p<0.05), W/H, W/T (p>0.05), while positive relationship between thoracic circumference (TC) and W/N (p= 0.05) was noticed. Studied variables presented the following descending order of area under the receiver operating characteristic (AUROC) FSG (1), BMI (0.875) Vit. B12 (0.825), W/H (0.8743), W/T (0.7837), weight (0.764), W/N (0.6715), W. C (0.7646) H. C (0.6444). **Conclusion:** Serum Vit. B12 level can be used as a novel biomarker in identification type 2 DM, also BMI, W/H and W/T may be a good biomarker in diagnosis type 2 DM.

Keywords: Type2 Diabetes Mellitus, Vitamin B12, BMI, waist circumference

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INTRODUCTION

Diabetes mellitus (DM) is know as a chronic illness distinguish by high blood sugar that occurs due to insufficient insulin production and excretion and/or reduced insulin efficacy due to insufficient skeletal muscle, liver, and adipose tissue sensitivity. (American Diabetes Association). Classification and diagnosis of diabetes: standards of medical care in diabetes-(2018). Diabetes specific microvascular disease is a main cause of blindness, nerve damage and renal failure, (Cade, 2008). T2DM is the most widespread kind of diabetes, constitutes about 90% of all diabetes. Hyperglycaemia is the result of insufficient insulin output and the body's inability to respond completely to insulin, well-defined as insulin resistance (IR) (World Health Organization 2019). Vitamin B12 (Vit B12), is a water-soluble vitamin, one of the eight B vitamins, that shows an important role in nervous system functioning and normal brain. (Miller, et al. 2005). The body can't be produced it, Therefore, it should be taken from an external source. also It involves the production of RBS and helps to make, organize DNA, the metabolism of fatty acids, amino acids and, in particular, the Metabolism which affects DNA create (Oh R, Brown D 2003). It practices its biological effects by facilitating two main enzymatic pathways, i.e., the procedure of homocysteine to methionine methylation; whose is last organized into S-adenosyl-methionine, which gives its methyl group to methyl acceptors like membrane phospholipids, neurotransmitters and myelin (Malouf, et al. 2003)., and transformation of methylmalonyl acid (MMA) coenzyme A (CoA) to succinyl-CoA, this conversion pathway decreases in the existence of Vit. B12 lack and increases in methylmalonyl acid (MMA) (Bottiglieri, et al. 2000). Metabolically severe deficiency of Vit. B12 can consequence in disturbance of the mechanism of methylation and cumulation of serum homocysteine and intracellular. Hyper homo cysteineemia, which has been demonstrated as a hazard factor for complications

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associated with T2DM and hypertension (Malouf, et al. 2003)., earlier clinical and community based studies have shown a high prevalence of Vit. B12 deficiency in adults with T2DM (Akabwai, et al. 2016).,new report suggests that metformin use is correlated with a decline in terminal iliac absorption of Vit. B12, although other studies also confirm that long-dated utilize of metformin results in malabsorption of Vit. B12, with concomitant decrease in serum Vit. B12 levels (Chapman, et al. 2016). In 2018, Jayashri, *et al.,* studied the spread of Vit. B12 lack in urban South Indian people in persons with varying levels of glucose tolerance, and found that Vit. B12 levels fell as the tolerance to increased FSG (Jayashri, et al. 2018). Anthropometry is known as body weight and body measurements and is used in specific epidemiological studies or clinical settings. It is a simple, effective, inexpensive and widely used method for estimating body fat distribution (Han, et al. 2006). Recent longitudinal study has shown that a significant risk factor for T2DM is increased BMI, men and women are found to have a clear positive correlation between obesity and T2DM.(Almubarak, 2016). Obesity is associated to increased danger of developing T2DM and IR (Almdal, et al. 2008). Waist circumference (WC) is a simple and dependable anthropometric test used as a replace for centric obesity in epidemiological studies (Millar, et al. 2015). WC captures an assessment of both the intra-abdominal fat tissue and the subcutaneous abdominal fat tissue, though. These two compartments are significantly and metabolically active lead to metabolic disorders comprehensive T2DM resistance and insulin (Misra, et al. 2018). Previous related study has shown that WC in Asian adults could be better T2DM indicator than (BMI) (Zhang, et al. 2017). And since it does not reflect differences between the sexes in body fat loads, BMI may not be a clear measure of body fat) (Zhang, et al. 2017). The single most significant danger factor and its predisposition to T2DM for metabolic disorder is abdominal obesity (Huang, et al. 2015; Nor Afiqah, et al, 2016). The main aim of this study to evaluate and serum level of Vit. B12 in patients with T2DM and explore of the relationship of Vit. B12 with some anthropometric measurements (AMs) in Type2 Diabetic Patients.

MATERIALS AND METHODS

This data contains of sixty patients with T2DM and 24 HCs were recorded in the study, the age range within 38-65 year haphazardly chosen from Al-Anbar

Governorate those attending in Ramadi teaching hospital and Al-Fallujah teaching hospital between Augusts 2019-November 2019.

Rejection principles for T2DM patients: were empty of severe diseases or contagion at time of study also those with known illness, which are linked with disordered glucose metabolism; such as acromegaly, pancreatactomy and Cushing's disease were excluded, as well as, those with pregnant women and chronic kidney disease.

Rejection principles for HCs: were chosen Among those who were healthy control with respect to non-diabetic, no other endocrine disorders, non-hypertensive, or kidney diseases and were free of acute illness or contagion at sampling time. This study was confirmed by the ethics council of University of Anbar and our inquiry was directed consistent to the standards of the statement of Helsinki (1964). Samples of blood were taken after fasting for 8-12 hours.

The Anthropometric measurement (AMs) were performed for all participants in the study that included weight and height were measured, BMI was calculated as weight (kg) divided by height squared (m^2). Measurement Waist circumference (WC) and hip circumference (HC) and the waist and hip circumference ratio was calculated as the WC divided by the HC. FSG was measured using enzymatic methods and with commercial kits (Spain, Linear) and the level of vitamin B12 was measured by Elisa kit (Monobind Inc, USA).

STATISTICS

Statistical investigates of our results were done by GraphPad Prism 7.04 provided from (GraphPad Software, La Jolla, CA, USA). The consequences are stated as medium, standard error of mean (SEM) and standard deviation (SD).The statistical importance of the differences among the subjects with and without T2DM was verified with t-test, bivariate associations were tested through a Pearson correlation investigates with two-tailed, while the precision of the investigation was measured through the area under the curve (AUC) of the receiver operating characteristic (ROC) curve. $P < 0.05$ was measured to be statistically important.

RESULTS

In **Table 1**, shows the standard experimental features of the subjects are described, with a mean age of 50.21years in HCs and 52.15 years in T2DM patients (P = 0.442), T2DM patients had importantly lower serum Vit. B12 levels (pg/mL) than in HCs (204.6 *vs* 313.8) with p value less than 0.001, FSG T2DM patients had importantly greater FSG, W/H, W/T and BMI than in HCs with P < 0.000l for all parameters while W/N has P = 0.0081, and Weight has p= 0.0001 also H.C, W.C has (p=0.0298, p=0.0044) respectively, as shown in **Table 1** and **Figs. 1**-**9,** respectively.

Important negative correlation was detected among Vit. B12 with FSG and weight (r=-0.360, P<0.001), (r=–0.446, P<0.001), (**Figs. 10** and **11**), also negative correlation of Vit. B12 with HC (cm), WC (cm), NC (cm), W/H, W/T and BMI (r=-0.016, p>0.05), (r=-0.248p=0.023), (r=-0.154p>0.05), (r=-0.241,P=0.027), (r=-0.296, P=0.006) and (r=-0.199, P>0.05) respectively,

Table 1. Distribution of Studied Biomarkers in HCs and T2DM Patients Group

Parameter	Healthy controls			Patients			p-value
	Mean	SD	SEM	Mean	SD	SEM	
Age (years)	50.21	7.541	1.539	52.15	6.722	0.8678	0.2515
Weight (kg)	70.58	8.915	1.82	82.13	12.96	1.673	0.0001
Height (cm)	166.9	10.5	2.142	165.7	11.77	1.519	0.6474
H. C (cm)	111.8	8.654	1.766	107.3	8.163	1.054	0.0298
W. C (cm)	103.7	7.726	1.577	111	11.1	1.433	0.0044
T. C (cm)	110.5	7.241	1.478	107.7	9.295	1.2	0.1911
N.C (cm)	46.71	3.828	0.7813	47.3	3.475	0.4487	0.4954
W/H	0.9298	0.0569	0.01162	1.035	0.07945	0.01026	<0.0001
W/T	0.9412	0.0772	0.01576	1.032	0.07794	0.01006	<0.0001
W/N	2.401	0.207	0.04225	2.276	0.1858	0.02398	0.0081
FSG mg/dL	93.92	7.12	1.453	198.7	44.98	5.807	<0.0001
BMI kg/m²	25.29	1.659	0.3386	30.15	0.7282	5.64	<0.0001
Vit. B12 pg/mL	313.8	81.64	16.66	204.6	84.76	10.94	<0.0001

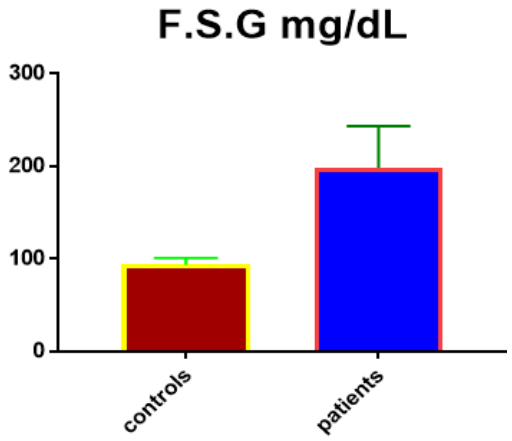

Fig. 1. mean+ S.D for FSG (mg/dL) in control and cases

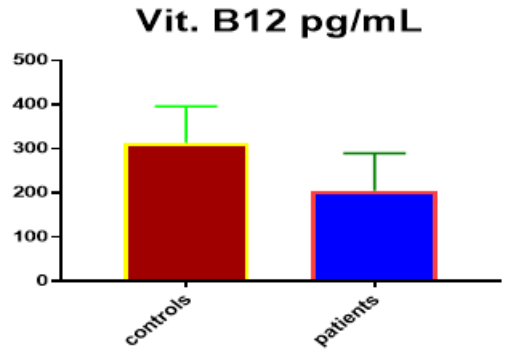

Fig. 2. mean+ S.D for Vit. B12 (pg/dL) in control and cases

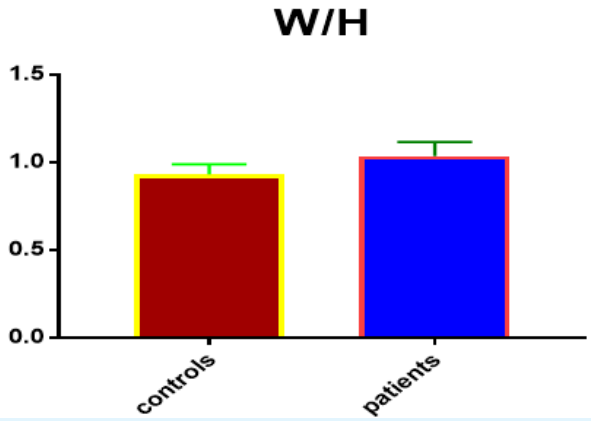

Fig. 3. mean+ S.D for W/H in control and cases

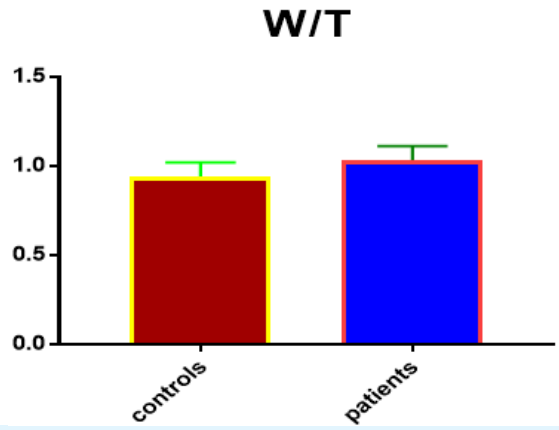

Fig. 4. mean+ S.D for W/T in control and cases

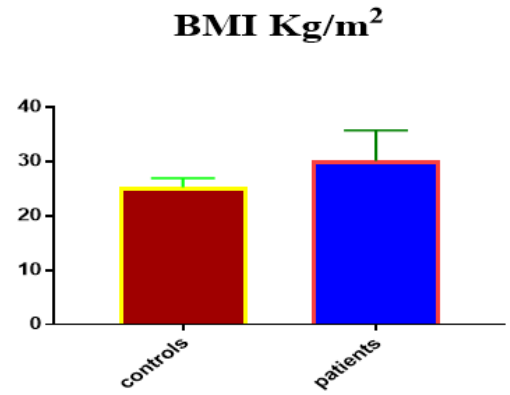

Fig. 5. mean+ S.D for BMI (Kg/m2) in control and cases

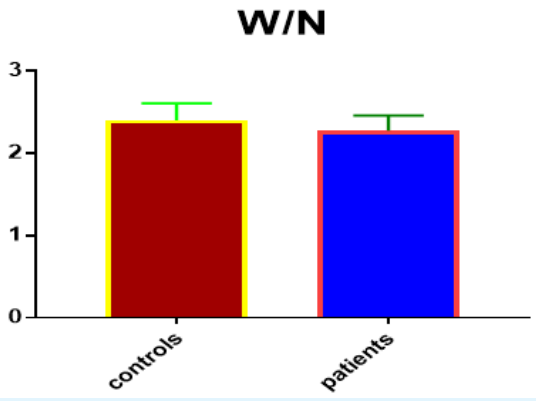

Fig. 6. mean+ S.D for W/N in control and cases

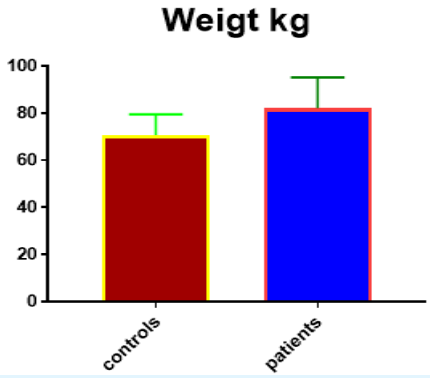

Fig. 7. mean+ S.D for Wt. (Kg) in control and cases

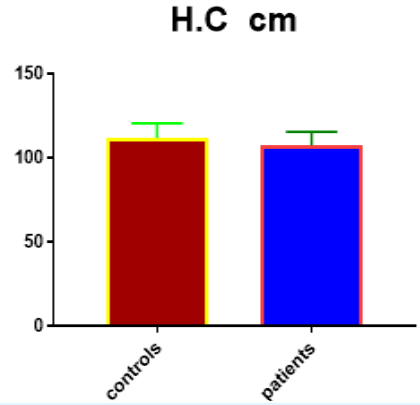

Fig. 8. mean+ S.D for H.C (cm) in control and cases

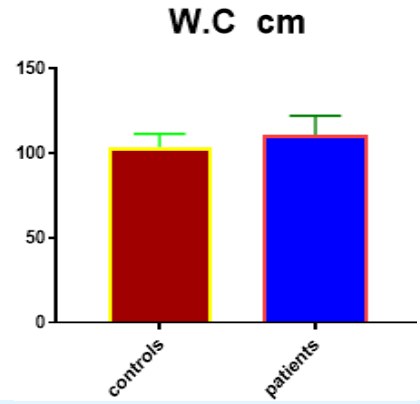

Fig. 9. mean+ S.D for W.C (cm) in control and cases

while positive relationship between TC (cm) and W/N with Vit. B12 (p= >0.05, r= 0.0367) and (p=> 0.05, r=0.123) respectively was detected as shown in **Table 2.**

ROC curve checking offered that the best biomarkers were fit to distinguish patients with T2DM from HCs is FSG [AUC = 1; P < 0.0001; 95% Confidence Interval (CI): 1 to 1and SE: 0] as shown in **Table 3** (**Fig. 12**), while BMI was found to be a better predicator for T2DM [AUC = 0.875; P = <0.0001; 0.8026 to 0.9474and SE: 0.03695] as shown in **Table 3** (**Fig. 13**) and Vit. B12 [AUC = 0.825; P = <0.0001; 95% CI: 0.7371 to 0.9129 and SE: 0.04483] as shown in **Table 3** (**Fig. 14**). also, the other anthropometric measurements offered in descending arrange (W/H,W/T, Weight, W/N, W.C, H. C)

Table 2.

Vit. B12 pg/mL	r	p-value
FSG (mg/dL)	-0.360	<0.001
Age (years)	-0.040	>0.05
Wt (kg)	-0.446	<0.001
Height (cm)	-0.193	0.078
HC (cm)	-0.016	>0.05
WC (cm)	-0.248	0.023
TC (cm)	0.0367	>0.05
NC (cm)	-0.154	>0.05
W/H	-0.241	0.027
W/T	-0.296	0.006
W/N	0.123	>0.05
BMI (kg/m^2)	-0.199	>0.05

Table 3. Diagnostic standard of the ROC Curves for Tested Variables in T2DM Patients

Parameter	AUC	Std. Error	95% confidence interval	P-value
FSG mg/dL	1	0	1 to 1	<0.0001
BMI (kg/m2)	0.875	0.03695	0.8026 to 0.9474	<0.0001
Vit. B12 pg/dL	0.825	0.04483	0.7371 to 0.9129	0.0001<
W/H	0.8743	0.04199	0.792 to 0.9566	<0.0001
W/T	0.7837	0.05873	0.6686 to 0.8988	<0.0001
Weight (kg)	0.7646	0.05626	0.6543 to 0.8749	0.0002
W/N	0.6715	0.06044	0.5531 to 0.79	0.0145
W. C (cm)	0.6719	0.05972	0.5548 to 0.7889	0.0143
H. C (cm)	0.6444	0.06869	0.5098 to 0.7791	0.0394

with the following values for each variable [AUC =0.8743; P<0.0001; 95% CI: 0.792 to 0.9566 and SE: 0.04199], [AUC =0.7837; P<0.0001; 95% CI: 0.6686 to 0.8988 and SE: 0.05873], [AUC =0.7646; P=0.0002; 95% CI: 0.6543 to 0.8749 and SE: 0.05626], [AUC =0.6715; P0.0145; 95% CI: 0.5531 to 0.79and SE: 0.06044], [AUC =0.7646; P0.0002; 95% CI: 0.6543 to 0.8749and SE: 0.05626], [AUC = 0.6444; P 0.0394; 95% CI:0.5098 to 0.7791and SE: 0.06869] respectively, as shown in **Table 3** (**Figs. 15**, **16**, **17**, **18**, **19** and **20**) respectively.

DISCUSSION

Diabetes mellitus, a common endocrine disorder and the complications arising from the disease are the third leading cause of death worldwide, it is a disorder in which the body's cells cannot effectively metabolize sugar due to a complete or partial lack of insulin , the body instead fracture down its own proteins, glycogen, and fats, resulting in elevated blood glucose levels (hyperglycemia), because glucose is limited without cell absorption and use of insulin (Nair, 2007). Chronic diabetes hyperglycemia is linked with long-term injury, impairment, and failure of various organs, including nerves, kidneys, blood vessels, and heart, DM is a major contributor to morbidity and mortality in society due to lack of proper management and treatment of accompanying complications (Ekpenyong, et al. 2012). In the context of our research, excess body weight has been identified as a problem for T2DM in patients with diabetes mellitus (Ganz, et al. 2014).

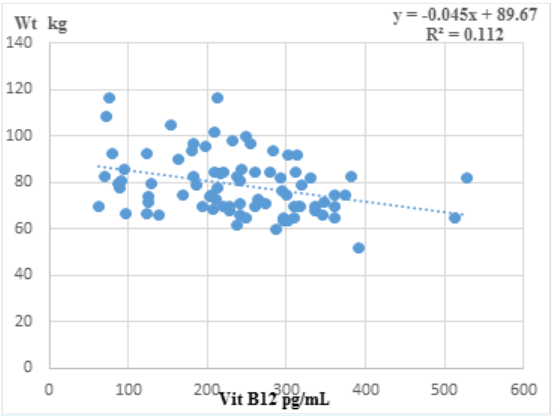

Fig. 10. Relationship between Vit.B12 with FSG

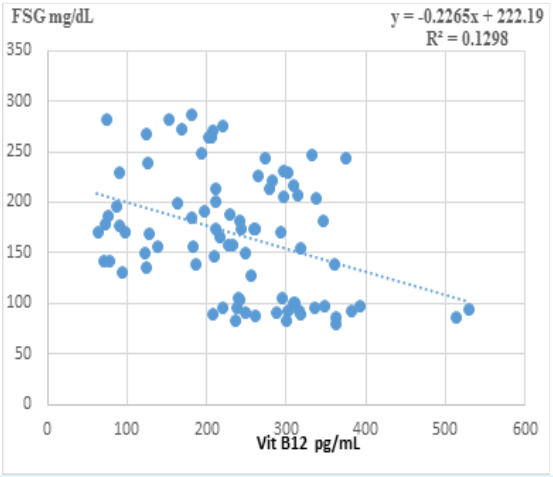

Fig. 11. Relationship between Vit.B12 with Wt

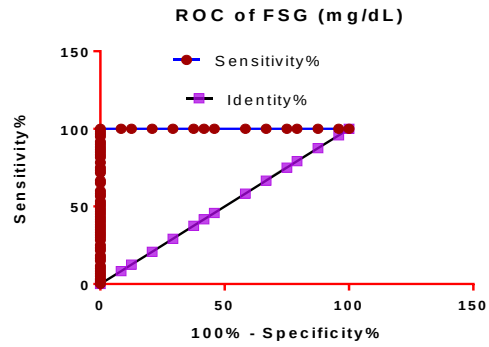

Fig. 12. AUC of ROC for FSG in T2DM patients

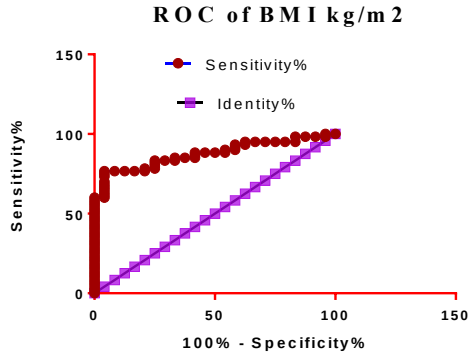

Fig. 13. AUC of ROC for BMI in T2DM patients

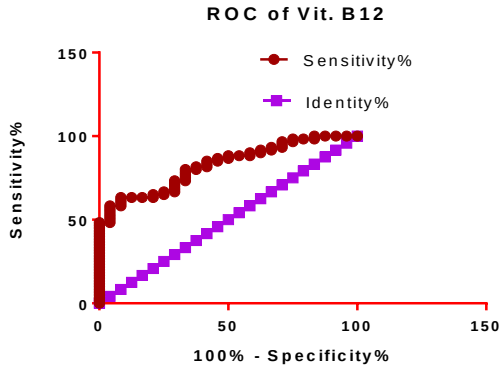

Fig. 14. AUC of ROC for Vit. B12 in T2DM patients

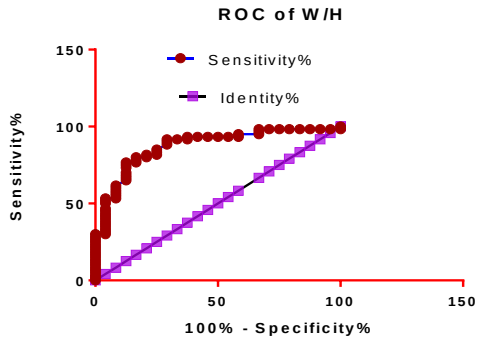

Fig. 15. AUC of ROC for W/H in T2DM patients

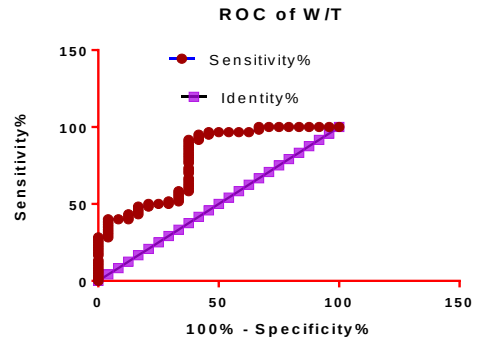

Fig. 16. AUC of ROC for W/T in T2DM patients

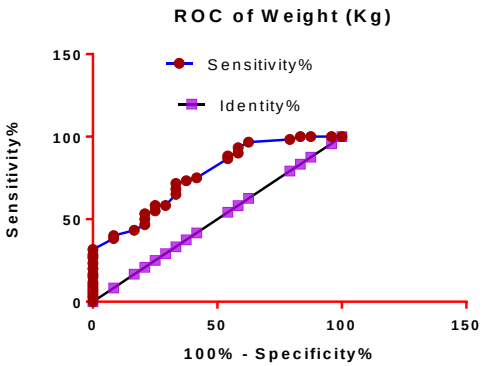

Fig. 17. AUC of ROC for Wt. in T2DM patients

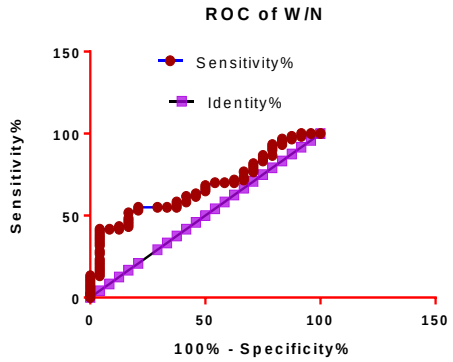

Fig. 18. AUC of ROC for W/N in T2DM patients

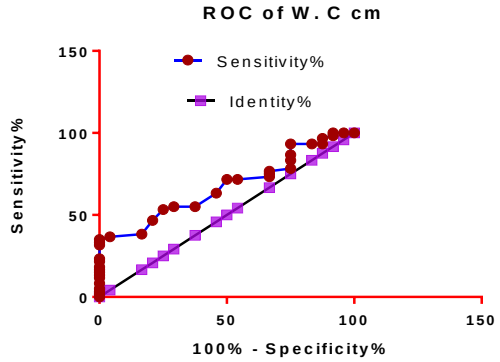

Fig. 19. AUC of ROC for W.C in T2DM patients

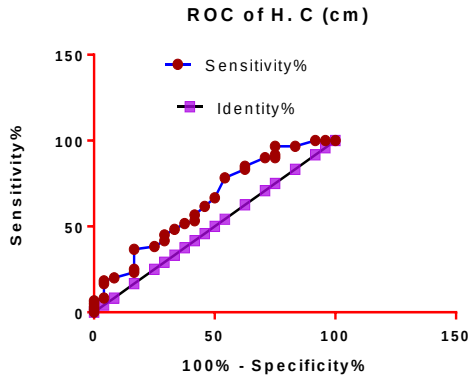

Fig. 20. AUC of ROC for H.C in T2DM patients

Obesity is an important danger factor for T2DM and 80% is obese or overweight for people with T2DM (National Institutes of Health, National Institute of Diabetes, & Digestive and Kidney Disease (2004). The Bea et al in 2016 study was found that persons in the T2DM collection were more probable to be categorized as normal weights (average BMI 18.5and b25) whereas T2DM was more probable to be categorized as obese I, II ,III; these results are consistent with our findings (Bae, et al. 2016). In recent years there has been a substantial rise in obesity in the Arab world due to many factors, such as the change in food consumption (Alzaman, & Ali, 2016). DM with central obesity is strong compared with general obesity (Kamath, et al. 2011). Acquired obesity is associated with increased coagulation and fibrinogen marker function, which is strongly associated with inflammation and IR, resulting in increased risk for events of thrombosis and cardiovascular events (Kaye, et al. 2012).

Although many epidemiological studies have examined the relationship between HC or height and risk of T2DM, the role of HC and height as danger factors for T2DM is still unknown, and reports of hazard of T2DM and HC or rising in most of them have yielded conflicting results (Bozorgmanesh, et al. 2011) but not all of the studies, (Parker, et al. 2009)HC tends to be inversely correlated with T2DM and some studies found only females to be linked (Snijder, et al. 2004) A big HC has been consistently associated with decrease glucose levels and a reduce danger of developing T2DM, independent of WC, even after amendment of BMI and age (Huebner, 2019).

An excess of this abdominal visceral adipose tissue can cause several complications, including hyperinsulinemia, glucose sensitivity, IR and T2DM (Volaco et al. 2017). Therefore, WC could be stated as a good indication of the risk of diabetes disease in patients with high measurements, since excess quantities of total abdominal adipose tissue can be seen as highly statistical of higher risk for T2DM (Yamada, 2013). NC can play a clear role in T2DM foretelling .(Al-Maskari, et al. 2012) Accumulating evidence over the past decades has shown that NC has been independently correlated with blood sugar parameters, including: IR, FSG, HbA1c, and fasting serum insulin (FSI), the findings, however, are contradictory, previous study found that NC has been positively connected with FSG in the Framingham heart study (Lee, 2017).

Vitamin B12, also known as cobalamin, is a water-soluble vitamin that contributes to the maximum processing of the neurocognitive, hemopoetic and vascular systems, it involved in the synthesis of DNA, metabolism of fatty acids, and energy production (Yamada, 2013). T2DM is a stress-oxidant disorder; Vit.B12 and folic acid lack have been shown to be linked with oxidative stress in relationship to hyperhomocysteinemia, as a consequence of this relationship, a deficiency in Vit. B12 can be considered a danger factor for diabetic complexity; one of the most widespread complications of T2DM is peripheral neuropathy (Al-Maskari, et al. 2012).

Vitamin B12 is an enzyme co-factor that plays a important part in the renewal of homocysteine methionine in the cytoplasm, and intermediate the transformation of methyl malonic acid-coenzyme A (CoA) to succinyl-coenzyme A in the mitochondria, Both reactions help the synthesis of DNA and the lipid metabolism, and also detoxify homocysteine and low-serum Vit substrates.T2DM has been correlated with levels B12 (Al-Maskari, et al. 2012). A Ko et al analysis

had found the Vit.B12 was autonomously connected to T2DM (Ko, et al. 2014).

Pflipsen M.C. et al. showed 22% of diabetic patient as having Vit. B12 deficiency, considering Vit. B12 level<100 pg/ml as deficiency, 100-350pg/ml as borderline and>350 pg/mL as normal (Pflipsen, et al. 2009). In their study, they too found the impairment more in longer-term patients in their study. This may be due to increased IR and long-term metformin use (Baltaci, et al. 2012).

The correlation of Vit. B12 with FSG may be demonstrating by the dominant role of Vit. B12 in the usage of carbohydrates, the hypothesis that Vit. B12 is significant for fat metabolism or carbohydrate is confirming by various empirical facts (Baltaci, et al. 2012). It is found that the erythrocytes of Vit. B12 deficient persons have less glutathione or enzyme activity required to degrade the glucose to ribose.(Ling, & Chow1954). Deficiency of vitamin B12 causes an rise of the content of coenzyme A in the liver, a remarkable, lowering in the decrease shape of Di Nitro Phenol (DPN) with the concomitant increase of the oxidized form in the liver(Chang, et al. 1957). Despite the role of glutathione coenzyme A and Di Nitro Phenol systems in many metabolic pathways, Vit.B12 lack can hinder the keeping of healthy enzyme systems which are necessary for carbohydrate use and fat transformation (Mahalle, et al. 2014).

A previous study of 976 people with varying degrees of obesity stated that Vit.B12 deficiency was substantially higher in people with obesity (40.1 %) and overweight (37.7%) compared to control individuals (17.1 %) (Baltaci, et al. 2013) the research found that the Vit. B12 deficiency may be an independent retinopathic diabetes risk factor (Fotiou, et al. 2014). Thus, early disclosure of Vit. B12 shortage is necessary to preserve normal neural functions; also former research has shown that vegetarians are more procumbent to evolve Vit. B12 deficiency comparative to non-vegetarians (Huang, et al. 2003). Another West India research stated that vegetarians had four-fold chance of evolve Vit.B12 Lack (Huang, et al. 2003). The most common exegesis for weak Vit. B12 case is a poor dietary intake of vitamin malabsorption and (i.e., low consumption of products of animal origin) (Allen, 2008).

In conclusion Current study found that the patients with T2DM have low levels of serum Vit. B12, which may be the cause of their various complications during the disease course, and this may be used as possible biomarkers and predicator of T2DM, also they may be used in manufacture of new treatments for T2DM disease. As well as this research supports the use of W/H and W/T preoperatively to identify the likelihood of developing T2DM as they provide an easy and reliable assessment method.

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