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RESEARCH ARTICLE

The association of vitamin D deficiency in hypertensive patients with other metabolic syndrome risk factors

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Abstract

BACKGROUND: Vitamin D deficiency is now recognised as a common health problem associated with various chronic diseases; however, it has not been fully elucidated among Iraqi patients.

OBJECTIVE: The aim of the study is to investigate the association between, vitamin D deficiency and other metabolic syndrome risk factors (atherogenic dyslipidemia, impaired fasting glucose/diabetes mellitus, obesity /increased waist circumference) in a group of hypertensive Iraqi patients.

PATIENT AND METHODS: Eighty Iraqi patients were recruited from a health center , mean age 56.3 year. Male were 32 and female were 48. All the patients were hypertensive and vitamin D deficient. Blood tests were performed in those patients to quantify serum levels of 25-hydroxyvitamin D (25 OH-Vit D) and different laboratory parameters associated to metabolic syndrome . The association between vitamin D deficiency and metabolic syndrome (and each of its components) was examined.

Results: Eighty Iraqi patients were studied, all the patients were vitamin D deficient and hypertensive (100%),69 patients (86.25%) have associated atherogenic dyslipidemia ($P < 0.001$), 44 patients (55%) have associated diabetes mellitus(DM)/impaired fasting blood glucose(FBG) ($P < 0.001$), 54 patients (67.50%) have associated obesity/
increased waist circumference ($P < 0.001$), 62 patients (77.5%) have 3 combined risk factor (fulfilling the definition criteria of metabolic syndrome) ($P < 0.001$).

Conclusion: vitamin D deficiency is strongly associated with metabolic syndrome risk factors, larger randomised controlled trials are needed to better define whether vitamin D repletion can modify these risk factors and reduce the consequences of metabolic syndrome.

Introduction:-

Metabolic syndrome is a constellation of CVD risk factors, i.e. abdominal obesity, atherogenic dyslipidemia (high triglycerides and reduced high density lipoprotein cholesterol [HDL-c]), disturbed carbohydrate metabolism, elevated blood pressure, along with a prothrombotic and proinflammatory profile [(1).] In recent years, there have been marked advances in our understanding of the potential role of vitamin D status and its associations with metabolic syndrome and cardiovascular disease (CVD).

Vitamin D, obtained largely from sunlight exposure and to a lesser extent from dietary and supplemental sources, increases the efficiency of intestinal calcium absorption. Hypovitaminosis D is associated with increased bone turnover, osteoporosis, osteomalacia, and an increased risk of fracture [(2-4).] More recent evidence from several lines of research has suggested non traditional roles for vitamin D in conditions which are frequently observed with

metabolic syndrome, including reduced insulin secretion and sensitivity [5,6], obesity [7], diabetes [8-11], and hypertension [12]
Systematic reviews of several randomized trials [10, 16, 19, 21] suggest a possible inverse association between Vitamin D and cardiovascular risks. In a meta-analysis by Parkera et al [22], individuals with the highest levels of serum vitamin D were associated with a 43% reduction in cardio-metabolic disorders (OR 0.57, 95% CI: 0.48-0.68).
So it is possible that by correcting this vitamin D deficient population, we can modify these cardio-metabolic disorders.

This study aims to investigate the association between vitamin D deficiency and the metabolic syndrome risk factors in a group of adult Iraqi patients.

Patients and method:-

Eighty Iraqi patients were recruited from a health center , mean age 56.3 year. Male were 32 and female were 48. All the patients were hypertensive and vitamin D deficient.

Participants were excluded if they received glucocorticoid, antivulsant within one year, had severe liver or kidney insufficiency, and had overt hyperparathyroidism.

Vitamin D adequacy was evaluated by measuring serum 25(OH)D concentration. This serum concentration of 25(OH)D is a good reflection of cumulative exposure to sunlight and dietary intake of vitamin D, and is widely regarded as a robust "gold standard" indicator of vitamin D status [24]. The biochemical test used was the Roche 25 OH Vitamin D total assay. This assay used electrochemiluminescence immunoassay (ECLIA) technology for the quantitative determination of 25(OH) D. Cut-off values for serum 25(OH)vitamin D levels in adults include: >30 ng/ml for vitamin D sufficiency, 20-30 ng/ml for insufficiency and <20 ng/ml for deficiency. This definition was based on the fact that the serum iPTH will rise significantly once the serum 25 (OH) D levels drops to less than 30 ng/ml [25]. Analyses for cholesterol, HDL-C and triglycerides were performed using commercially available enzymatic methods. Fasting plasma glucose (FPG) was measured using standard hexokinase enzymatic assays.

A standard questionnaire was used to collect information on age, sex, smoking, alcohol drinking and self-reported diabetes, hypertension, and dyslipidemia. Resting blood pressure was measured. Anthropometric measurements such as weight, height and waist circumference were also taken. Body height was measured to the nearest 0.5 cm and body weight to the nearest 0.1 kg. The waist and hip circumferences were measured with a circumference measurement tape. The waist was defined as the point midway between the iliac crest and the costal margin (lower rib) [23]

Metabolic Syndrome was defined according to the definition of National Cholesterol Education Program ATP III 2005 update criteria [26] as the presence of any **three** of the following five traits:

- Abdominal obesity, defined as a waist circumference in men ≥102 cm (40 in) and in women ≥88 cm (35 in)
- Serum triglycerides ≥150 mg/dL (1.7 mmol/L) or drug treatment for elevated triglycerides
- Serum high-density lipoprotein (HDL) cholesterol <40 mg/dL (1 mmol/L)
  in men and <50 mg/dL (1.3 mmol/L) in women or drug treatment for low HDL cholesterol
- Blood pressure ≥130/85 mmHg or drug treatment for elevated blood pressure
- Fasting plasma glucose (FPG) ≥100 mg/dL (5.6 mmol/L) or drug treatment for elevated blood glucose

Statistical analysis:-

The data was entered and analyzed entirely using computer software program of The Statistical Package for the Social Science (SPSS) version 15.0. Standard approaches were used including frequencies, descriptive summaries, Chi-square test (X 2) with 95% confidence interval and Kolmogorov - Smirnov Z test to obtain the significant differences in the study variables. A P- value of < 0.05 has been considered to indicate the level of significance throughout the study.

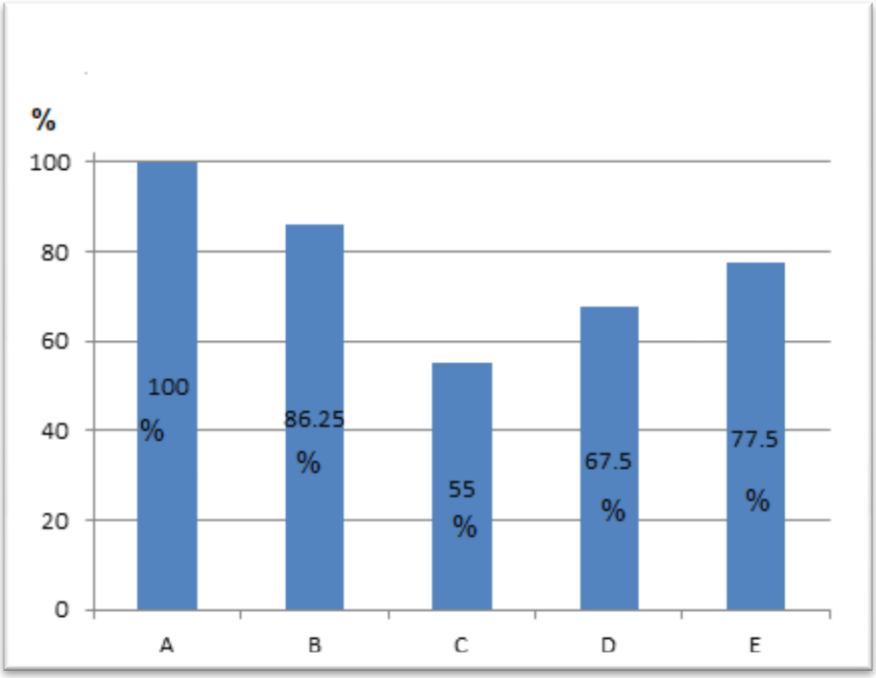
Results:-

Eighty adult patients were studied, mean age 56.3 year. Male were 32 and female were 48. All the patients were hypertensive and vitamin D deficient (100%) the mean serum 25 (OH) D levels was 15.5 ng /mL (table -1, graph-1)

(Table – 1) patients characteristics

Patients characteristics	Pat. No.	%
Male	32	
female	48	
Mean age	56.3	
Vit D deficiency	80	100
Hypertension	80	100
Obesity/Increased waist circumference	54	67.5
Diabetes mellitus	30	37.5
Impaired fasting glucose	14	17.5
Elevated triglycerides	36	45
Low HDL	33	41.2

Graph-1



A= patients with hypertension

B =patients with dyslipidemia

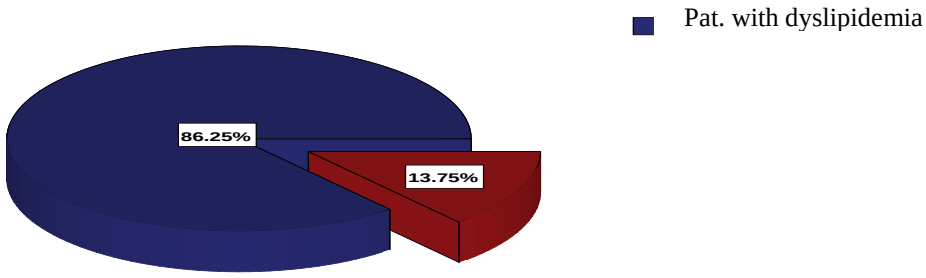
C = Patients with impaired fasting blood glucose/ DM

D = patients with increased waist circumference/obesity

E = patients with three risk factors (metabolic syndrome)

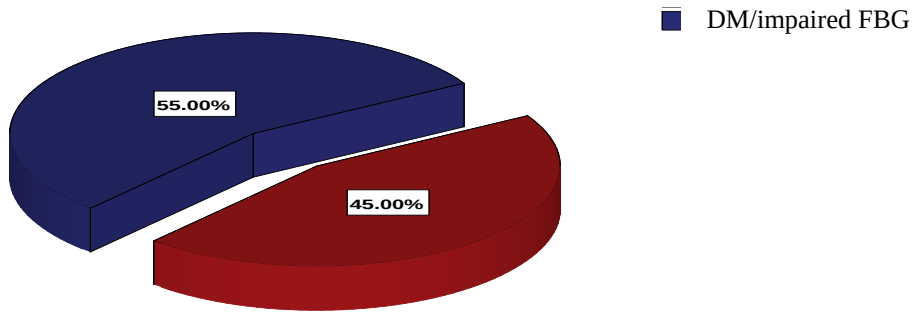
The majority of the study population, 69 patients (86.25%), were suffered from atherogenic dyslipidemia . 36 patients (45%) have elevated triglyceride level, while 33 patients (41.2%) have low HDL level. The obtained value of test **Z** Kolmogorov - Smirnov was 4.622 allowed confirming this differences (**P**<0.001) (Graph 2).

Graph-2



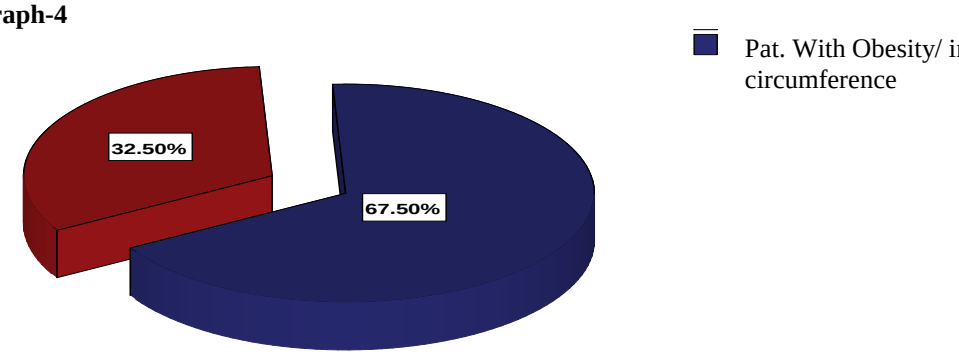
More than half of hypertensive patients with vit.D deficiency, 44 patients (55%) ,have associated diabetes mellitus(DM)/impaired fasting blood glucose(FBG) , 30 patients (37.5%) have impaired FBG., while 14 patients (17.5%) have DM. The obtained value of test **Z** Kolmogorov - Smirnov was 3.270 allowed confirming this differences (**P**<0.001) (Graph 3).

Graph-3



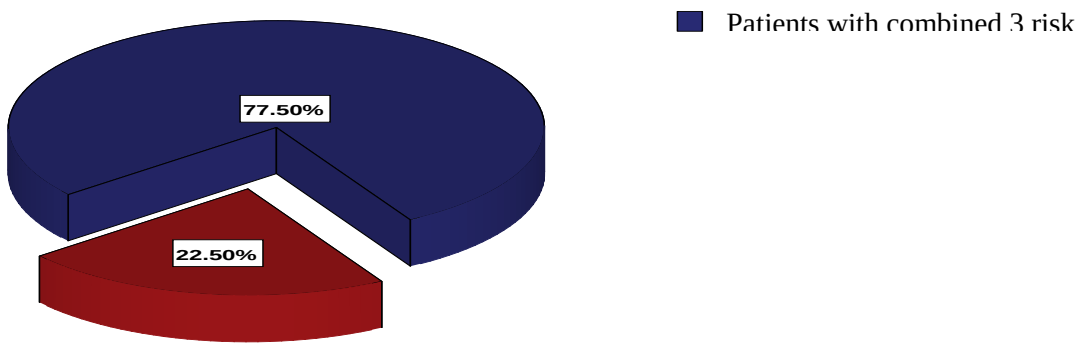
There were higher proportions, 54 patients (67.50%), of hypertensive patients with vit. D deficiency have increased waist circumference or/ and obesity.
The obtained value of test **Z** Kolmogorov - Smirnov was 3.844 allowed confirming this differences (**P**<0.001) (Graph 4).

Graph-4



More than two third, 62 patients (77.5%), of the study population have combination of three metabolic risk factors mentioned above, i.e have metabolic syndrome by definition. The obtained value of test **Z** Kolmogorov - Smirnov was 4.283 allowed confirming this differences (**P**<0.001) (Graph 5).

Graph-5



Discussion:-

This study investigates the possibility of an association between serum vitamin D levels and the metabolic syndrome and its components in a sample of Iraqi patients.

Although our sample size was small, the prevalence of metabolic syndrome found in the current study (77.5%) was higher than. Soares LP *et al* (66.1%) [15] and much higher than Yin X, Sun Q, Zhang X, et al (44%) [14]

Over 40 studies show inverse correlations of vitamin D status with metabolic syndrome risk or with the incidence or severity of its components[33]. Also The large NHANES III and NHANES 2003-2004 have shown a significant inverse association between serum 25(OH)Vit D concentration and metabolic syndrome [3132].

Our results are in accordance with these studies showing that 25(OH) D concentration was inversely associated with metabolic syndrome risk.

Ilaria Barchetta, *etal* in his recent study found a powerful association exists between hypovitaminosis D and metabolic syndrome in obese patients, and his Multivariate model confirmed that low 25(OH)D3 levels were associated with the diagnosis of metabolic syndrome in obese patients independently from gender, age, serum PTH and body fat mass.[13]

In the present study, there were significantly higher proportions, 54 patients (67.50%) , of hypertensive patients with vit. D deficiency with increased waist circumference and / or obesity.

Obesity is known to be associated with decreased bioavailability of vitamin D, which is sequestered in body fat [17].

Infact, Forouhi et al. [18] reported a significant interaction between 25(OH)D and BMI on the risk for a 10-year increase in

HOMA-IR. In addition, the release of free fatty acids from adipose tissue can induce insulin resistance, whereas 1,25- dihydroxyvitamin D has been shown to counteract the free fatty acid–induced insulin resistance [20]. The stronger association of vitamin D with insulin resistance among the overweight and obese participants suggests that adequate vitamin D status is more important for the prevention of insulin resistance and metabolic syndrome in these individuals.

The major source of vitamin D is through synthesis by the skin from sunlight exposure. Vitamin D can also be obtained from a few dietary sources such as oily fish and fortified foods. Insufficient sunlight exposure may partially explain the low level of vitamin D in our population due to their clothing style (wearing long sleeves, long skirts and veil) which is culturally or religiously related.

A lower 25(OH) D concentration was associated with increased risk of having metabolic syndrome and its individual components. The inverse association between 25(OH) D and metabolic syndrome found in our study is consistent with that from three previous cross-sectional reports in American [27, 28] and British adults [29]. These three studies were also performed in the general population with large sample sizes; two American studies [27, 28] included subjects aged 20 years and the other one [29] comprised participants aged 45 years. In these studies [27, 28, 29], 25(OH)D concentrations were relatively higher than in our study.

A cohort study by Forouhi et al. [18] showed that the baseline concentration of 25(OH) D was inversely associated with an increased metabolic syndrome risk z score.

Although data on sun exposure and vitamin D supplementation were not available, we used a direct measure of vitamin D status, which reflects cumulative sun exposure and dietary vitamin D intake. In addition, because we did not measure serum calcium and parathyroid hormone, we could not determine whether the association of 25(OH) D with metabolic syndrome was partly mediated by calcium or secondary hyperparathyroidism. However, data from NHANES 2003–2004 [32] and the Medical Research Council Ely Prospective Study [30] suggested that the associations between 25(OH) D and insulin resistance and metabolic syndrome were independent of calcium and parathyroid hormone.

The present study has some limitations, the sample size was small and it was just observational study with no life style data. We also did not measure the parathyroid hormone and additional markers of islet β cell function or inflammation markers, further prospective, randomized placebo controlled trials are quite important to provide more information of metabolic syndrome.

Conclusion:-

In the present study our findings suggested that reduced 25(OH) D is associated with an increased risk of having metabolic syndrome and adverse values for metabolic syndrome components.

Our results may have important public health implications. Increased sun exposure and use of vitamin D supplements or fortified foods are simple and inexpensive means to prevent vitamin D deficiency and related health problems.

Nevertheless, the benefits of vitamin D on metabolic syndrome and related diseases such as type 2 diabetes need to be confirmed in future prospective studies and clinical trials.

Disclosure of conflict of interest:-

None.

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