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C-peptide, liver enzymes and CRP-protein related with vitamin D deficiency in obese and diabetic (type 2) women

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Abstract :

This study aims to investigate the relationship of vitamin D deficiency and some other biochemical parameters (C-peptide, Alanine transaminase ALT, Aspartate transaminase AST, Alkaline phosphatase ALP and C-reactive protein CRP) levels in obese and diabetic women. The whole sample included 60 women aged 30 – 40 years, divided to three groups (20 women / group) as control, obesity and diabetes groups (the participants in obesity and diabetes groups were diagnosed with vitamin D deficiency). Results revealed: C-peptide increased significantly ($p \leq 0.01$) in obesity group and not significantly in diabetes group in comparison with the control , ALT increased significantly ($p \leq 0.01$) in different groups in comparison with the control , AST increased not significantly in different groups in comparison with control, ALP increased significantly ($p \leq 0.01$) in diabetes group and significantly ($p \leq 0.05$) in obesity group in comparison with the control, CRP increased significantly ($p \leq 0.01$) in different groups in comparison with the control. The physiological impacts of these results be discussed according to the impact of vitamin D deficiency that associated with different metabolic and inflammatory disturbances, leading to diverse detrimental influence on the biochemical profiles of the studied groups.

Key words: Vitamin D deficiency, C-peptide, CRP, obesity, diabetes.

Introduction:

Vitamin D deficiency has become a global pandemic and a public health concern that involved billions of people and has contributed to multiple health complications, even in areas that receive adequate sunlight (Aparna *et al*., 2018; Maia *et al*., 2019).

In addition, the deficiency may be results by inadequate both sunlight exposure and nutritional vitamin intake, disorders reducing vitamin absorption, conditions that impair vitamin conversion into active metabolites, life style habits, ethnicity and genetic polymorphisms (Vierucci *et al*., 2013).

Furthermore, this deficiency has been associated with numerous disorders, such as rickets in children and osteomalacia /osteoporosis in adults, cardiovascular diseases, arterial hypertension, dyslipidemia, cancer, multiple sclerosis, depression, dementia, psychiatric diseases, diabetes type 2 (T2D), obesity and others, but the causative role of deficiency in many of these conditions remains unclear (Milic *et al*., 2015; Reid and Bolland 2014).

Obesity, is one of the most important risk factors for T2DM, which causes insulin resistance and inflammation due to the increase of fat tissue in the body (Rohm *et al*., 2022). It has been reported that vitamin D receptor (VDR) changes involved in the pathogenesis of some chronic disorders such as diabetes (Isnuwardana *et al.*, 2020), the active form of vitamin D, 1,25 (OH)2D, binds to VDR and induces genes related to glucose transport, insulin secretion (Maestro *et al*.,2003) and cellular growth in β cells (Wolden-Kirk *et al* ., 2013), in addition , vitamin D may also have a beneficial effect on the action of insulin, either directly, by stimulating the expression of insulin receptors and thereby improving insulin responsiveness to glucose transport, or indirectly, through its role in the regulation of extracellular calcium and ensuring the influx of calcium through the cell membrane (Mitri *et al.*, 2011).Vitamin D deficiency is also linked to predisposition of diabetes and may play a role in the development of diabetes (McCarthy *et al*., 2022), moreover, a strong relationship with insulin production and insulin resistance among T2DM patients (Rafiq and Jeppesen 2021).

Vitamin D deficiency associated with inflammatory biomarkers in patients suffering from metabolic syndrome such as obesity, furthermore, serum levels of IL-6, TNF-α, and CRP trend towards higher levels in subjects with vitamin D deficiency (Khademi *et al*., 2022; Pott-Junior *et al*., 2020)

The relationship between vitamin D and the liver function may be attributed to the prevalence of vitamin D receptors and local conversion of this vitamin to its active form inside the non-parenchymal liver cells (Zúñiga *et al*., 2011; Putz-Bankuti *et al*., 2012).

Vitamin D acts as an "immune-modulator" to prevent liver cirrhosis by suppressing fibroblast proliferation and collagen production (Artaza and Norris, 2008) and is considered a factor implicated in the regulation of homeostasis, inflammation, and liver fibrogenesis (Triantos *et al*., 2021).

Materials and methods:

Subjects:

The current study was conducted in some health centers in Maysan province / Iraq, during December 2023 to February 2024. The whole sample included 60 women aged 30 – 40 years, divided to three groups (20 women / group) as following: control, obesity and diabetes groups, the samples have been checked medically by a specialist physicians and has been diagnosed with vitamin D deficiency for obesity and diabetes groups, vitamin D(less than 20.0 ng/mL), body mass index(BMI over 30 kg/m2) and glycated hemoglobinA1c (HbA1c levels more than 6.5). Women with chronic diseases, tumors and those whom treated with hormonal drug has been excluded.

Sample collection:

Eight to ten milliliters of venous blood samples were drawn at 9 - 11 am, using a disposable needle and plastic syringes for each woman. The blood was left at room temperature for 15 minutes for coagulation, centrifuged at 3000 rpm for 5 minutes, then serum and plasma separated and transferred for storage.

Data collection and laboratory tests:

C-peptide levels were accurately measured using a Cobas e-411 / Germany with C-peptide kit , CRP levels were accurately measured using a Mindray bs_200\ China CRP kit from China . ALT , AST and ALP levels were accurately measured using a Bio systems A-15/Spain kits from Spain . The range of C-peptide, CRP, ALT , AST , ALP is 1.1 – 4.4 ng/mL , 0 – 5 mg / L, Up to 45 U\L , Up to 40 U\L and Up to 105 U\L respectively. The body mass index (BMI) was calculated as the weight in kilograms divided by the height in meters squared.

Statistical Analysis:

The statistical analysis was performed by one-way Analysis Of Variance (ANOVA), followed by Duncan's new multiple range test at a ($p \leq 0.05$), ($p \leq 0.01$) significant level (Steel *et al*., 1997).

Results:

The results revealed :

C- peptide:

Results revealed that C- peptide increased significantly ($p \leq 0.01$) for obesity (5.75 ±0.65 ng/ml) in comparison with diabetes (3.05 ±0.54 ng/ml) and control (3.005 ±0.70 ng/ml) figure (1).

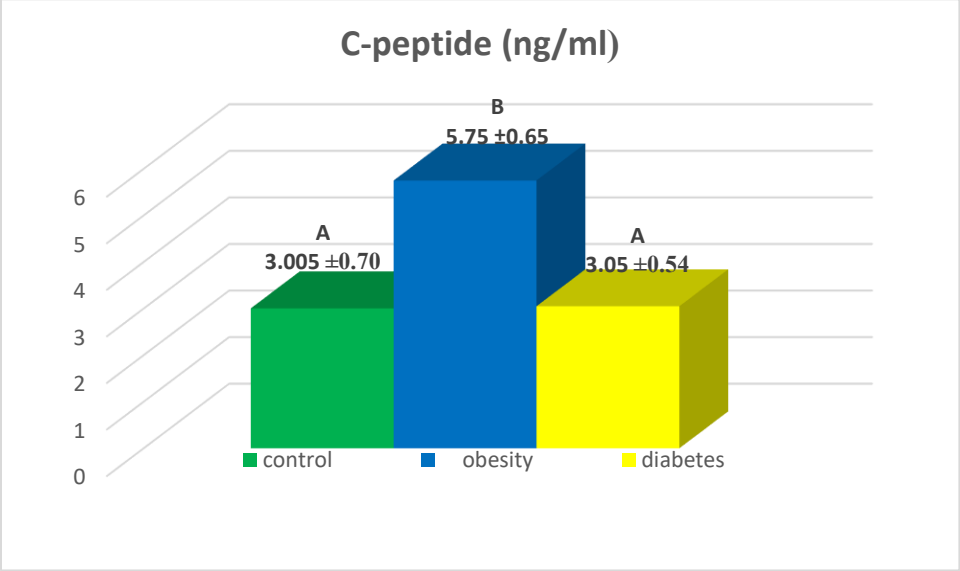

Figure (1): Changes of C-peptide levels of different study's groups.

*The values represent mean ± SD.

*Different capital letters represent significant difference between groups at $p \leq 0.01$.

*Similar capital letters represent no significant difference.

CRP

Results revealed that CRP increased significantly (p≤0.01) for obesity (6.65±0.94 mg/dl) and diabetes (4.56±0.75 mg/dl) in comparison with control (1.50±0.31 mg/dl) figure (2).

Results revealed that CRP increased significantly (p≤0.01) for obesity in comparison with diabetes figure (2).

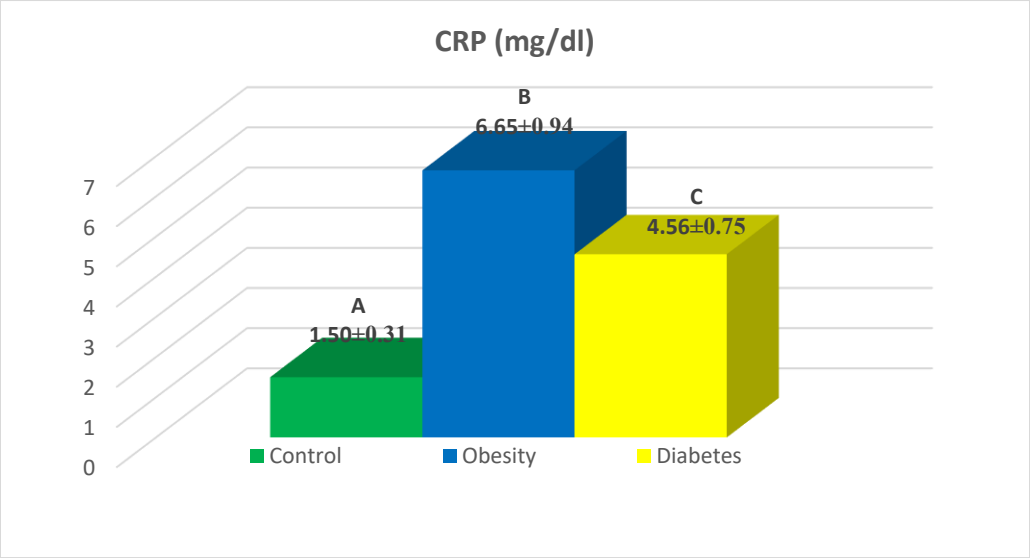

Figure (2): Changes of CRP levels of different study's groups.

*The values represent mean ± SD.

*Different capital letters represent significant difference between groups at p ≤ 0.01.

*Similar capital letters represent no significant difference.

ALT

Results revealed that ALT increased significantly (p≤0.01) for diabetes (20.95±2.24 U/L) and obesity (16.75±2.04 U/L) in comparison with control (12±1.44 U/L) figure (3).

Results revealed that ALT increased significantly (p≤0.01) for diabetes in comparison with obesity figure (3).

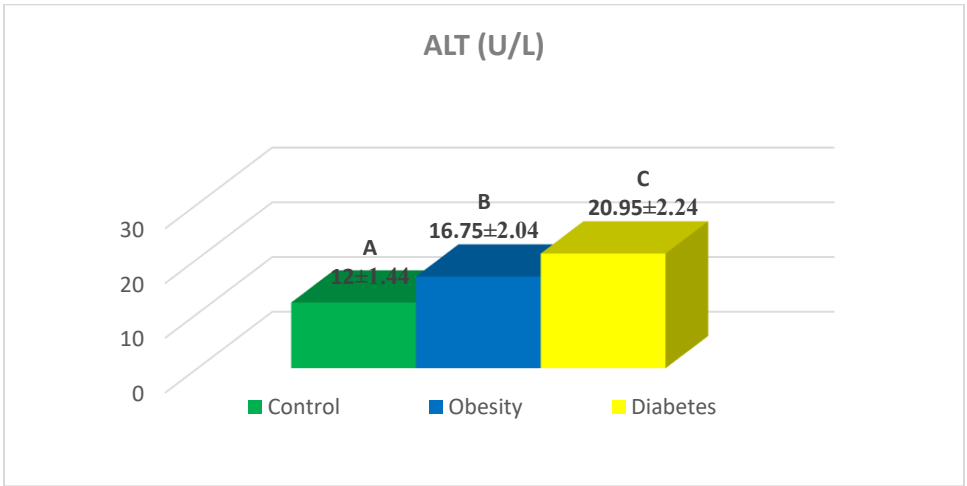

Figure (3): Changes of ALT levels of different study's groups.

*The values represent mean ± SD.
*Different capital letters represent significant difference between groups at p ≤ 0.01.
*Similar capital letters represent no significant difference.

AST

Results revealed that AST increased not significantly for obesity (16.10±2.40 U/L) d and diabetes (15.65±1.49 U/L) in comparison with control (15.05±1.93 U/L) figure (4).

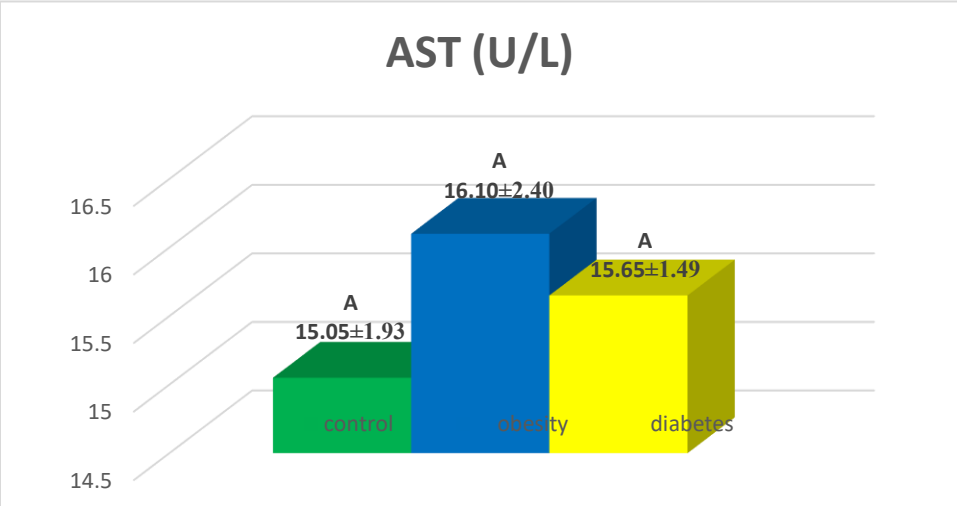

Figure (4): Changes of AST levels of different study's groups.

*The values represent mean ± SD.
*Different capital letters represent significant difference between groups at p ≤ 0.01.
*Similar capital letters represent no significant difference.

ALP

Results revealed that ALP increased significantly (p≤0.01) for diabetes (129.9±9.00U\L) in comparison with obesity (88±3.34 U\Land control (83.2±8.20 U\L) figure (5).

Results revealed that ALP increased significantly (p≤0.05) for obesity in comparison with control figure (5).

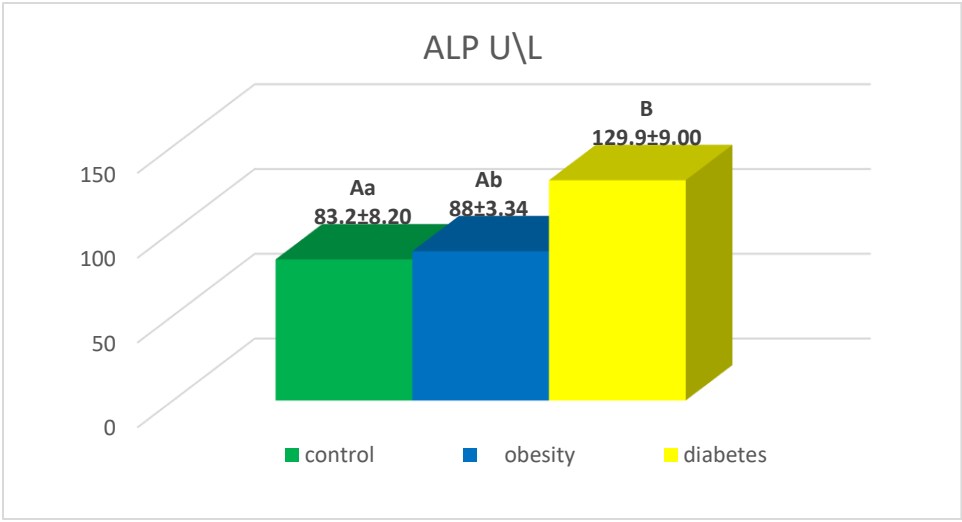

Figure (5): Changes of ALP enzyme levels of different study groups

*The values represent mean ± SD.
*Different capital letters represent significant difference between groups at $p \leq 0.01$.
*Similar capital letters represent no significant difference.
*Different small letters represent significant difference between groups at $p \leq 0.05$.
*Similar small letters represent no significant difference.

Discussion:

The deficiency of vitamin D might be behind high C-peptide levels due to the role of vitamin D in regulation of beta cells function and insulin secretion, moreover, the metabolic and inflammatory dysregulation of the studied groups might be contributed to elevated C-peptide levels, which affect β-cell function and subsequently higher insulin secretion and insulin resistance, furthermore, high C- peptide levels might be a marker for liver dysfunction due to high current levels of liver enzyme.

Many studies agreed with the present results, many studies showed that vitamin D deficiency associated with the changes of C-peptide levels (Liu *et al*., 2024; Xiang *et al*., 2024; Monapati *et al*., 2023), moreover, Al-Qahtani and his team 2024 demonstrated that vitamin D deficiency is associated with low levels of fasting C peptide for the diabetic women due the beta cells unresponsive, furthermore, in diabetic patents sufficient levels of vitamin D act synergically with high levels C peptide to controlled the diabetes status possibly due to impact of vitamin D on glucose metabolism through the function of β-cells and insulin sensitivity

High levels of C-peptide associated with high levels of CRP, this association suggests that these biomarkers may be useful in individuals identifying of developing type 2 diabetes (Lee *et al*., 2024; Gedebjerg *et al*., 2023)

Furthermore Akter and his team 2022 showed that high C-peptide levels associated positively with the metabolic syndrome, they mention that the high BMI was the most significant factor that influencing C-peptide levels for the development of these metabolic syndrome, moreover, elevated C-peptide levels are associated with high insulin resistance in obese women, suggesting that this elevation may be considered as a risk factor for type 2 diabetes (Can *et al*., 2023; Gilsa *et al*., 2024)

Elevated C-peptide levels associated with high AST and ALT levels in women with NAFLD and this elevation may be useful for screening or monitoring insulin resistance in NAFLD which reflecting impaired liver function (Huang *et al*., 2023; Fang *et al*., 2024).

Vitamin D deficiency might be explained this increase in CRP levels due to the anti-inflammatory role of this vitamin, in addition, these groups considered as a low-grade inflammation which might be contributed of this increase, the findings of Murugiah and his colleagues 2024 are in consistence with the presents results, they found that vitamin D deficiency showed a negative association with inflammatory markers (including CRP) in diabetic women, furthermore, Different studies demonstrated that vitamin D deficiency associated negatively with CRP levels (Holmannova *et al*., 2025; AbdElneam *et al*., 2024),moreover, the production of pro-inflammatory cytokines decreased after vitamin binding to its receptors in monocytes, thus, vitamin D helps in reducing the concentrations of CRP and other inflammatory markers (Colin *et al*., 2010).

Different studies pointed that diabetic and progression of associated with several inflammatory biomarkers including CRP (Okdahl *et al*., 2022; Ellulu and Samouda, 2022; Tang *et al*., 2022) in addition, long-term exposure to high levels of glucose significantly enhanced the increase production of pro-inflammatory cytokines, including tumor necrosis-α, interleukin (IL)-1β, and IL-6(Suzuki *et al*., 2021),furthermore, high levels of CRP might be indicated for the association between pro-inflammatory cytokines and etiology of type 2 diabetes (Bahgat and Ibrahim, 2020).

Numerous studies demonstrated that vitamin D deficiency associated with high levels of ALT, AST and ALP in obese and diabetic women (Cordeiro *et al*., 2017 ; Matar *et al*., 2024; Fang *et al*., 2024) due to the adverse effects of vitamin D deficiency on human liver function (He *et al*., 2020; Skaaby *et al*., 2014).

Furthermore, vitamin D deficiency considered as an independent risk factor for the liver enzyme's increase and the occurrence of liver diseases in nonobese , obese and diabetic women (Hashim *et al*., 2023; Ciardullo *et al*., 2023 ; Rajab, 2022) , in addition , vitamin D deficiency might be potentiated the adverse effects of obesity and diabetes on liver functions via its impairment of the lipid clearance by the liver , worsening the insulin resistance impact and increasing the inflammatory cytokines mediators … that affected all together the liver functions thereby the elevation of these enzymes (Yu-Lei *et al*., 2024;Bima *et al*., 2021).

The association between both the high levels of liver enzymes and CRP in women with metabolic syndrome (including obesity and diabetes) represents a strong predictor of metabolic syndrome (Ghani *et al*., 2023; Islam *et al*., 2020; Seo *et al*.,2019), furthermore, the overproduction of pro-inflammatory cytokines might played an important role in the liver's damage progression thereby liver enzymes elevation (Poniachik *et al*., 2006).

In conclusion these present changes might be to vitamin D deficiency that exacerbates the imbalance of glucose metabolism and inflammatory state in obese and diabetic women, moreover, vitamin D deficiency synergistic with the metabolic group’s disorders targeted the liver which is the hepatic metabolic center as evidenced by high levels of liver enzyme, thereby decline the liver abilities.

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Declaration of Competing Interest:

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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