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EFFECT OF VITAMIN D AND/OR ATORVASTATIN ON HIGH FAT DIET INDUCED HYPERLIPIDEMIC ADULTMALE ALBINO RATS

By

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ABSTRACT

Background: Atorvastatin has been used as anti-hyperlipidemic agent in the primary and secondary prevention of atherosclerotic related vascular complications with adverse effects on liver and muscles. The classical functions of vitamin D are to regulate calcium-phosphorus homeostasis, andcontrol bone metabolism. In addition, evidence has been accumulated on the pleiotropic effects of vitamin D other than on bone health.

Objective: To study the effect of treatment with vitamin D and/or atorvastatin on high fat diet induced hyperlipidemic adult male albino rats.

Materials and methods: Forty-eight adult male albino rats of a local strain were used as an animal model for this study. They were divided into 8 equal groups; group 1 (control), group 2 (treated with vitamin D), group 3 (treated with atorvastatin), group 4 (treated with vitamin D and atorvastatin), group 5 (hyperlipidemic), group 6 (hyperlipidemic treated with vitamin D), group 7 (hyperlipidemic treated with atorvastatin), and group 8 (hyperlipidemic treated with vitamin D and atorvastatin).After 4 weeks, body weight was measured and then blood samples were collected and serum was separated for the measurement of fasting blood sugar (FBS), cholesterol, LDL, HDL, TAGs, ALT, AST and CPK.

Results: There was a significant improvement of FBS in hyperlipidemic vitamin D-treated group when compared to the hyperlipidemic non treated group. ALT and AST levels showed significant improvement in hyperlipidemic vitamin D-treated group when compared to the hyperlipidemic group. When compared to atorvastatin-treated group, vitamin D and atorvastatin treated groups showed significant improvement in ALT, AST and CPK levels.

Conclusion: Vitamin D shared in controlling blood sugar, and it has a protective effect against hyperlipidemia induced liver injury and against atorvastatin induced liver and muscle injury

Key words: Vitamin D, Atorvastatin, hyperlipidemia.

INTRODUCTION

People with hyperlipidemia are at greatly higher risk of developing atherosclerotic vascular disorders as compared to those with normal lipid profile. Therefore, early detection and treatment of hyperlipidemia are imperative to reduce cardiovascular events and premature death. Statins are the mainstay treatment for hyperlipidemia. However, the limitations of statins include treatment resistance, intolerance due to adverse events, and a lack of adherence which contribute to poor outcomes. As

such, many patients require adjunct therapies to properly control hyperlipidemia *(Karr, 2017)*.

Vitamin D is a group of fat-soluble secosteroids (steroids with a broken steroid ring). The most important compounds in this group are vitamin D3 (cholecalciferol) and vitamin D2 (ergocalciferol). The major natural source of the vitamin is synthesis of cholecalciferol in the lower layers of skin epidermis through a chemical reaction that is dependent on sun exposure (specifically to UVradiation) *(Borel et al., 2015)*.

The classical functions of vitamin D are to regulate calcium-phosphorus homeostasis andcontrol bone metabolism. However, the discovery of vitamin D receptors (VDR), and confirming their presence in various tissues has opened the mechanistic link between vitamin D, and the occurrence of many diseases and disorders such asobesity, insulin resistance, metabolic syndrome,type II diabetes mellitus, cardiovascular risk, Alzheimer's disease, depression and cancer. Over the past 2 decades, interest in vitamin D has increased significantly. Requests for serum vitamin D concentration measurements increased by many folds and the number of vitamin D supplements sales has raised several times *(Dzik and Kaczor, 2019)*.

Besides role of vitamin D in the maintenance of bone tissue, as well as in the maintenance of calcium and phosphorus homeostasis, some authors have shown its relationship to different pathologies. They suggest that it is also involved in many processes such as secretion of hormones such as insulin, regulation of body weight, and role in the immune system. Some studies have shown that vitamin D acts as a potent modifier of the risk of developing cardiovascular complications *(Barbalho et al., 2018)*.

The present work aimed at studying the effect of treatment with vitamin D and/or atorvastatin on high fat diet induced hyperlipidemic adult male albino rats.

MATERIALS AND METHODS

Forty-eight adult male albino rats of a local strain were used as an animal model for this study. Their ages were 8 weeks, and their weight 110 – 140 g. They were kept in suitable cages (20x32x20 cm for every 3 rats)at room temperature with the natural light-dark cycle. They were kept for 10 days for the adaptation to the new environments before starting the experiment. The animals were divided into eight equal groups:

- **Group 1 (control)** was maintained on a standard diet of a commercial rat chow and tap water.
- **Group 2** was maintained on a standard diet of a commercial rat chow and tap water and treated with vitamin D3 (cholecalciferol from medical union pharmaceuticals company - Egypt) orally at a dose of 500 IU/kg daily *(Elbassuoni et al., 2018)*.
- **Group 3** was maintained on a standard diet of a commercial rat chow and tap water and treated with atorvastatin (from medical union pharmaceuticals company - Egypt) orally at a dose of 25 mg/kg daily *(Khan et al., 2018)*.
- Group 4 was maintained on a standard diet of a commercial rat chow and tap

water and treated with both vitamin D and atorvastatin.

- **Group 5** (hyperlipidemic) had free access to high fat diet (HFD) (Vanaspati ghee and coconut oil in a ratio of 3:2 respectively) in addition to normal diet for 4 weeks *(Mehanna et al, 2020)*.
- **Group 6** was hyperlipidemic treated with vitamin D.
- **Group 7** was hyperlipidemic treated with atorvastatin.
- **Group 8** was hyperlipidemic treated with vitamin D and atorvastatin.

After 4 weeks from the onset of the experiment, body weight was determined; andblood samples were collected from the retro-orbital venous plexus by using a heparinized capillary tube (about 0.75 – 1.0 mm internal diameter) from the medial canthus, after whole night fast. The collected blood samples were kept in graduated plastic centrifuge tubes containing EDTA. The blood was centrifuged at 5000 rotations per minute for about 15 minutes to separate the serum. Serum was sucked out into Eppendorf tubes, and stored frozen at -20oC till used for the measurement of:

- Fasting blood sugar (FBS) (mg/dl).
- Triacylglycerols (TAGs) (mg/dl).
- Total cholesterol (mg/dl).
- High density lipoproteins (HDL) (mg/dl).
- Low density lipoproteins (LDL) (mg/dl).
- Alanine transaminase (ALT) (U/L).
- Aspartate transaminase (AST) (U/L).
- Creatin phosphokinase (CPK) (U/L).

Statistical analysis: Collected Data were analyzed using SPSS version 25.One-way Analysis of variance (ANOVA) and the post hoc “Tukey” test were used to compare means. Data were expressed as means ± SD and $P \leq 0.05$ was considered significant.

RESULTS

Concerning body weight, it was135.6 ± 9.6 grams in group 1, 137.6 ± 9.1 grams in group 2, 135 ± 7.2 in group 3, 136.4 ± 6.5 grams in group 4, 161 ± 11.3 grams in group 5, 150.8 ± 7.4 grams in group 6, 157.4 ± 6.6 grams in group 7 and 151.2 ± 5 grams in group 8. As regard FBS levels, they were 77.7 ± 5.1, 82 ± 5.9, 80.1 ± 9.9, 81.3 ± 5.5, 113.4 ± 10.1, 83.5 ± 4.5, 114.2 ± 15.2 and 84.7 ± 6.5 mg/dl in order from group 1 to group 8. Comparisons between different groups are detected in **Table 1** and **Table 2**.

Table (1): Comparing different groups as regard body weight

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group1		P>0.05	P>0.05	P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group2			P>0.05	P>0.05	P≤0.05*	P>0.05	P>0.05	P>0.05
Group3				P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group4					P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group5						P>0.05	P>0.05	P>0.05
Group6							P>0.05	P>0.05
Group7								P>0.05

Table (2): Comparing different groups as regard FBS

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P>0.05	P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 2			P>0.05	P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 3				P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 4					P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 5						P≤0.05*	P > 0.05	P≤0.05*
Group 6							P≤0.05*	P>0.05
Group 7								P≤0.05*

The hyperlipidemic group 5 and the hyperlipidemic atorvastatin treated group 7 showed a statistically significant elevation ($P \leq 0.05$) in body weight and FBS when compared with the control group 1. The hyperlipidemic vitamin D-treated group 6 and the hyperlipidemic vitamin D- and atorvastatin-treated group 8 showed a reduction in body weight and FBS when compared with the hyperlipidemic group 5. The reduction in FBS was statistically significant ($P \leq 0.05$). However, the difference was not significant concerning the reduction in body weight **(Figure 1)**.

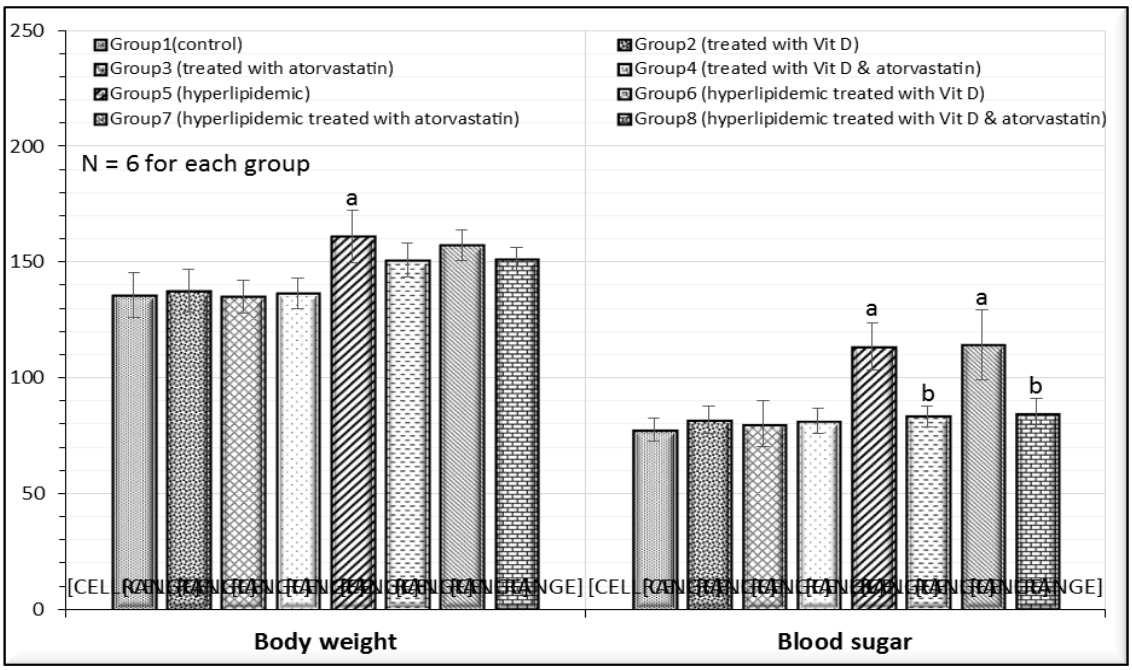

Figure (1): Body weight and FBS in different groups of the study

a = significant difference when comparing with group 1
b = significant difference when comparing with group 5

Concerning cholesterol level, it was 98.1 ± 4.1 mg/dl in group 1, 98.7 ± 7.4 mg/dl in group 2, 82.3 ± 5.9 mg/dl in group 3, 81.3 ± 5.5 mg/dl in group 4, 135.5 ± 4.8 mg/dl in group 5, 125.5 ± 5.8mg/dl in group 6, 97.1 ± 10.5mg/dl in group 7 and 85.5 ± 6.1mg/dl in group 8. As regard TAGs levels, theywere81.7 ± 5.6, 79.3 ± 5.6, 74.04 ± 2.3, 75.9 ± 2.8, 129.9 ± 4.8, 120.7 ± 5.8, 83 ± 5.7 and 86.6 ± 3.4 mg/dl in order from group 1 to group 8. LDL levels were 51.8 ± 1.8, 49.4 ± 7.14, 29.7 ± 5.4, 29.4 ± 5.7, 82.6 ± 6.4, 68.7 ± 8.3, 42.6 ± 10 and 29.6 ± 6.3 mg/dl respectively in the studied groups from group 1 to group 8. Whereas HDL level was 30.02 ± 3.5 mg/dl in group 1, 33.4 ± 2.9 mg/dl in group 2, 37.8 ± 2.2 mg/dl in group 3, 38 ± 2.8 mg/dl in group 4, 27.5 ± 2.7 mg/dl in group 5, 32.8 ± 4.5 mg/dl in group 6, 38 ± 2.8 mg/dl in group 7 and 40.9 ± 2.4 mg/dl in group 8. Comparisons between different groups are detected in tables No 3 to No 6.

Table (3): Comparing different groups as regard cholesterol

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P>0.05	P≤0.05*	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 2			P≤0.05*	P≤0.05*	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 3				P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 4					P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 5						P > 0.05	P≤0.05*	P≤0.05*
Group 6							P≤0.05*	P≤0.05*
Group 7								P > 0.05

Table (4): Comparing different groups as regard TAGs

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P>0.05	P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 2			P>0.05	P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 3				P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 4					P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 5						P>0.05	P≤0.05*	P≤0.05*
Group 6							P≤0.05*	P≤0.05*
Group 7								P>0.05

Table (5): Comparing different groups as regard LDL

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P≤0.05*	P≤0.05*	P≤0.05*	P≤0.05*	P>0.05	P≤0.05*
Group 2			P≤0.05*	P≤0.05*	P≤0.05*	P≤0.05*	P>0.05	P≤0.05*
Group 3				P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 4					P≤0.05*	P≤0.05*	P>0.05	P>0.05
Group 5						P > 0.05	P≤0.05*	P≤0.05*
Group 6							P≤0.05*	P≤0.05*
Group 7								P>0.05

Table (6): Comparing different groups as regard HDL

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P≤0.05*	P≤0.05*	P>0.05	P>0.05	P≤0.05*	P≤0.05*
Group 2			P>0.05	P>0.05	P>0.05	P>0.05	P>0.05	P≤0.05*
Group 3				P>0.05	P≤0.05*	P>0.05	P>0.05	P>0.05
Group 4					P≤0.05*	P>0.05	P>0.05	P>0.05
Group 5						P>0.05	P≤0.05*	P≤0.05*
Group 6							P>0.05	P≤0.05*
Group 7								P > 0.05

The hyperlipidemic group 5 showed a statistically significant elevation ($P \leq 0.05$) in cholesterol, TAGs and LDL when compared with the control group 1. These parameters showed significant reduction in hyperlipidemic atorvastatin-treated group 7, and hyperlipidemic vitamin-D & atorvastatin-treated group 8 when compared with the hyperlipidemic group 5 ($P \leq 0.05$). Also, HDL significantly elevated in hyperlipidemic atorvastatin treated group 7 and hyperlipidemic vitamin-D & atorvastatin-treated group 8 when compared with the hyperlipidemic group 5 ($P \leq 0.05$). There was no significant difference in lipid profile when comparing hyperlipidemic atorvastatin-treated group 7 with hyperlipidemic vitamin D- & atorvastatin-treated group 8 **(Figure 2)**.

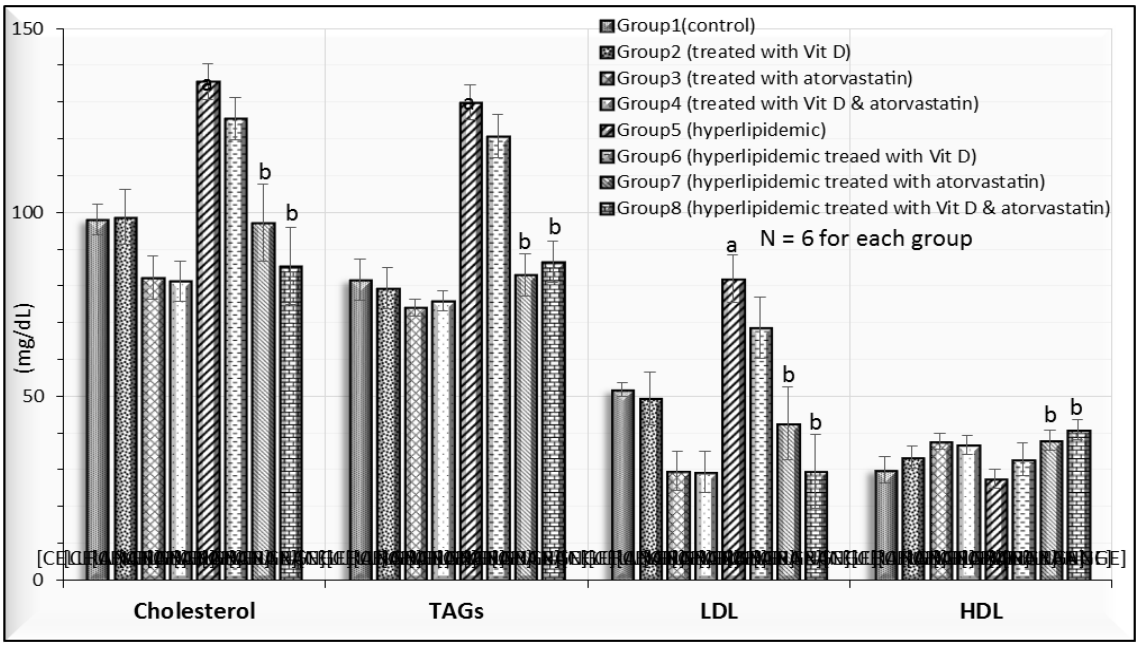

Figure (2): Lipid profile in different groups of the study

a = significant difference when comparing with group 1
b = significant difference when comparing with group 5

Concerning ALT level, it was39.9 ± 3.1U/L in group 1, 37.9±3.7U/Lin group 2, 53.1± 3.6U/L in group 3, 42.6 ± 4.6U/L in group 4, 51.9 ± 4.6U/L in group 5, 38.9 ± 3.3U/L in group 6, 57.3 ± 5.1U/L in group 7 and 40.1 ± 3.2U/L in group 8.

As regard AST level, it was 82.1 ± 5.6 U/L in group 1, 79.2 ± 5.3 U/L in group 2, 116.9 ± 6.5 U/L in group 3, 84.9 ± 4.5 U/L in group 4, 103.1 ± 6.8 U/L in group 5, 88.2 ± 3.7 U/L in group 6, 108.2 ± 7.3 U/L in group 7 and 90.5 ± 4.5 U/L in group 8.

CPK levels were 152.6 ± 7.3 U/L, 152.4 ± 7.5 U/L, 208.7 ± 14.3 U/L, 159.7 ± 9.3 U/L, 157.2 ± 7.8 U/L, 153.9 ± 8.8 U/L, 214.9 ± 10.7 U/L and 162.2 ± 4.4 U/L respectively in the studied groups from group 1 to group 8. Comparisons between different groups are detected in tables 7 and 8.

Table (7): Comparing different groups as regard ALT and AST

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 2			P≤0.05*	P>0.05	P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 3				P≤0.05*	P>0.05	P≤0.05*	P>0.05	P≤0.05*
Group 4					P≤0.05*	P>0.05	P≤0.05*	P>0.05
Group 5						P≤0.05*	P>0.05	P≤0.05*
Group 6							P≤0.05*	P>0.05
Group 7								P≤0.05*

Table (8): Comparing different groups as regard CPK

	Group 1 Control	Group 2 Vit D treated	Group 3 Atorvastatin treated	Group 4 Vit D & atorvastatin treated	Group 5 hyperlipidemic	Group 6 Hyperlipidemic Vit D treated	Group 7 Hyperlipidemic atorvastatin treated	Group 8 Hyperlipidemic Vit D & atorvastatin treated
Group 1		P>0.05	P≤0.05*	P>0.05	P>0.05	P>0.05	P≤0.05*	P>0.05
Group 2			P≤0.05*	P>0.05	P>0.05	P>0.05	P≤0.05*	P>0.05
Group 3				P≤0.05*	P≤0.05*	P≤0.05*	P>0.05	P≤0.05*
Group 4					P>0.05	P>0.05	P≤0.05*	P>0.05
Group 5						P>0.05	P≤0.05*	P>0.05
Group 6							P≤0.05*	P>0.05
Group 7								P≤0.05*

The hyperlipidemic group 5 showed a significant elevation in ALT and AST when compared to the control group 1. However, the hyperlipidemic vitamin D-treated group 6 showed a significant reduction in ALT and AST levels when compared to the hyperlipidemic non treated group 5.

The atorvastatin-treated group 3 and the hyperlipidemic atorvastatin-treated group 7 showed significant elevation in ALT, AST and CPK when compared to the control group 1. The vitamin D-& atorvastatin-treated group 4 showed a significant reduction in ALT, AST and CPK levels when compared to the atorvastatin treated group 3. Also, the hyperlipidemic vitamin D-& atorvastatin-treated group 8 showed a significant reduction in ALT, AST and CPK levels when compared to the hyperlipidemic atorvastatin-treated group 7 **(Figure 3)**.

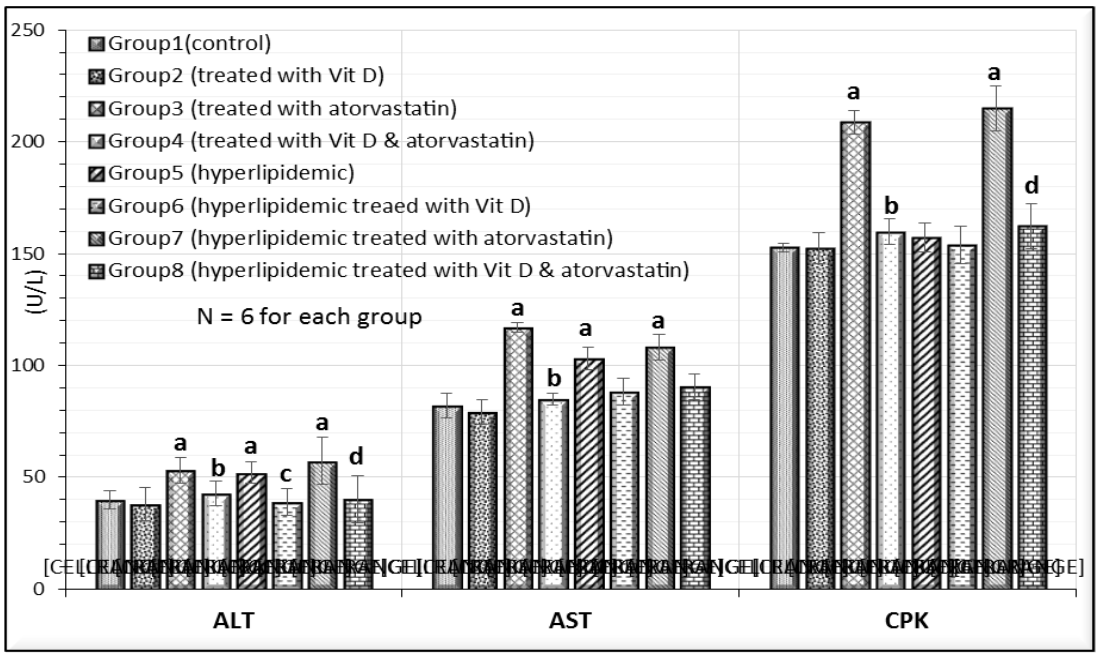

Figure (3): ALT, AST and CPK levels in different groups of the study

a = significant difference when comparing with group 1
b = significant difference when comparing with group 3
c = significant difference when comparing with group 5
d = significant difference when comparing with group 7

DISCUSSION

In this study, high fat diet (HFD) induced hyperlipidemic rats showed a significantly higher fasting blood glucose level. This finding was in agreement with *la Fleur et al. (2011)* who reported that rats fed HFD develop obesity and insulin resistance. *Zhang et al. (2020-a)* reported similar findings, and stated that the elevated concentrations of circulating lipids secondary to HFD induces insulin resistance and makes compensation of the pancreatic β-cell insufficient, resulting in glucose intolerance. These findings were also consistent with *He et al. (2012)* who stated that several mechanisms have been proposed to explain the causal role of HFD consumption in the development of insulin resistance. In the condition of nutrition over supply, mitochondrial oxidative phosphorylation metabolism would produce a larger amount ROS.

Oxidative stress results in insulin resistance and impairment of glucose disposal. *Zhang et al. (2020-b)* reported that many inflammatory cytokines are released from adipose tissue and mediates insulin resistance.

The current study showed that treatment with vitamin D significantly improved fasting blood glucose level in HFD induced hyperlipidemic rats. This was concordant with *Cordeiro et al. (2021)* who reported that vit D improves insulin sensitivity and inhibits adipogenesis via decreasing nuclear translocation of pro-adipogenic transcription factors and increasing the expression of adipogenic repressors. Also, this result was consistent with *Mostafa et al. (2016)* who stated that vitamin D supplementation ameliorated some of the abnormalities associated with metabolic syndrome, namely insulin resistance, hyperglycemia and obesity as well as dyslipidemia.

Vitamin D receptors are prominently expressed in both pancreatic beta-cells that secrete insulin, and in peripheral target tissues that respond to insulin such as skeletal muscle and adipose tissue. Animals with vitamin Dreceptor mutations have impaired insulin secretion and poorer glucose tolerance than those with normal vitamin D receptors. Vitamin D can preserve insulin release and insulin-mediated processes in insulin-responsive tissues by modulating the extracellular and intracellular calcium pools *(Sergeev, 2016). Sadek and Shaheen (2014)* pointed out that vitamin D, by decreasing the number of pro-inflammatory cytokines, improve insulin sensitivity and hence blood glucose level.

In the present study, HFD induced hyperlipidemic rats showed significant elevation of ALT and AST levels. This was in agreement with *Ma et al. (2017), Xia et al, (2019)* and *Esmail et al, (2021)*. They concluded that HFD induces steatohepatitis. The affected hepatocytes release large amount of their enzymatic content namely ALT and AST into the plasma.

In the current study, HFD induced hyperlipidemic rats treated with vitamin D showed a significant improvement in ALT and AST levels compared to the non-treated rats. This was in concordance with *Yin et al, (2012)* who stated that several mechanisms are involved in the preventing effects of vitamin D on hepatic steatosis. Vitamin D improves insulin sensitivity. Therefore, it enhances anti-lipolytic effect of insulin and suppresses lipid release from adipose tissue and its eventual uptake in the liver. In addition, a direct inhibitory effect of vitamin D on lipolysis has been reported in adipocytes. Similar findings were reported by *Zhu et al. (2017)* who stated that vitamin D protects against HFD-induced liver injury by attenuating oxidative stress and up-regulating the expression of genes encoding antioxidant enzymes. *Zhang et al. (2021)* stated that many mechanisms have been included in the protecting effect of vitamin D against HFD induced liver injury. Beside its antioxidant effect and enhancing insulin sensitivity, vitamin D alsoinhibits p53 pathway which induce apoptosis. Vitamin D, by inducing autophagy, maintains normal cellular homeostasis. Vitamin D also inhibitspyroptosis (a highly inflammatory form of programmed cell death).

The current study showed that groups treated with atorvastatin alone showed significant elevation in ALT, AST and CPK whereas these enzymes were not elevated in groups treated with both atorvastatin and Vitamin D. Statins may adversely affect liver and muscles. The pattern of liver injury varies from mild cholestatic injury to marked hepatocellular injury. Documented statins adverse effects on muscles ranges from asymptomatic elevation of CPK, myalgias, and up to rhabdomyolysis *(Stroes et al., 2015)*. Statin-induced injury is due to impaired mitochondrial function, oxidative stress, induction of apoptosis, and reduction in the expression of chloride channel, in addition to the alteration of Ca2+ homeostasis *(Ghalwash et al, 2018)*. *Chogtu et al. (2020)* reported that myalgia, myopathy, rhabdomyolysis and hepatotoxicity, are encountered side effects of statins, and vitamin D can prevent statin-induced liver and muscle injury.

Inadequate vitamin D status may complicate the adverse effect risk of statins. Vitamin D is a potent antioxidant that facilitates balanced mitochondrial activities, preventing oxidative stress-related protein oxidation, lipid peroxidation, and DNA damage, thus protecting against statin induced liver and muscle injury *(Ahmed et al., 2019)*.

CONCLUSION

Vitamin D shared in controlling blood sugar in conditions of hyperlipidemia. Also, vitamin D showed a protective effect against liver injury induced by high fat diet and against liver and muscle injury induced by atorvastatin as indicated by the recovery in liver and muscle enzymes in groups treated by vitamin D compared to the non-treated groups.

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تأثير فيتامين د مع/أو أتورفاستاتين علي ذكور الجرذان البيضاء البالغة المصابة بإرتفاع دهون الدم المحدث بالغذاء عالي الدهن

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خلفيـــة البحـــث: يســـتخدم الأتورفاســـتاتين كمخفـــض لنســـب الـــدهون المرتفعـــة بالـــدم فـــي الوقايـــة الأوليـــة والثانويـــة مـــن أمـــراض الأوعيـــة الدمويـــة المرتبطـــة بتصـــلب الشـــرايين لكـــن مصـــحوبا بأثـــار ســـلبية علـــي الكبـــد والعضـــلات. والوظيفـــة الأساســـية لفيتـــامين د هـــي تنظـــيم إتـــزان الكالســـيوم والفوســـفور بالـــدم والـــتحكم فـــي الأيـــض الغـــذائي فـــي العظـــام و إضـــافة لهـــذه التـــأثيراتففي العقـــدين الأخـــرين تراكمـــت أدلـــة علـــي أن فيتـــامين د لـــه تأثيرات متنوعة أخري بخلاف تأثيره علي صحة العظام.

الهـــدف مـــن البحـــث: دراســـة تـــأثير العـــلاج بفيتـــامين د مـــع أو بـــدون الأتورفاســـتاتين علـــي ذكـــور الجـــرذان البيضـــاء البالغـــة المصـــابة بإرتفـــاع دهـــون الـــدم المحـــدث بالغـــذاء عـــالي الدهون.

مـــواد وطـــرق البحـــث: ثمانيـــة وأربعـــون جـــرذا أبيضـــا ذكـــرا مـــن ســـلالة محليـــة تـــم إســـتخدامهم كنمـــاذج لهـــذه الدراســـة وتـــم تقســـيمهم الـــي ثمانيـــة مجموعـــات متســـاوية؛ مجموعـــة 1 (ضـــابطة)، مجموعـــة 2 (يـــتم علاجهـــا بفيتـــامين د)، مجموعـــة 3 (يـــتم علاجهـــا بالأتورفاســـتاتين)، مجموعـــة 4 (يـــتم علاجهـــا بفيتـــامين د والأتورفاســـتاتين)، مجموعـــة 5 (مصـــابة بإرتفـــاع الـــدهون فـــي الـــدم)، مجموعـــة 6(مصـــابة بإرتفـــاع الـــدهون فـــي الـــدم و يـــتم علاجهـــا بفيتـــامين د)، مجموعـــة 7 (مصـــابة بإرتفـــاع الـــدهون فـــي الـــدم و يـــتم علاجهـــا بالأتورفاســـتاتين)، مجموعـــة 8 (مصـــابة بإرتفـــاع الـــدهون فـــي الـــدم و يـــتم علاجهـــا بفيتـــامين د والأتورفاســـتاتين). بعـــد أربعـــة أســـابيع تـــم قيـــاس وزن الجســـم ثـــم أخـــذ عينـــات الـــدم و فصـــل مصـــل الـــدم لقيـــاس الســـكر الصـــائم والكوليســـتيرول والـــدهون الثلاثيـــة والبـــروتين الـــدهني مـــنخفض الكثافـــة والبـــروتين الـــدهني عـــالي الكثافـــة وألانـــين ترانس أميناز وأسبرتات ترانس أميناز والكرياتين فوسفوكيناز.

نتـائج البحـث: كـان هنـاك تحسـناً ذا دلالـة إحصـائية فـي مسـتوي سـكر الـدم الصـائم فـي المجموعـة المصـابة بإرتفـاع الـدهون فـي الـدم والتـي تـم علاجهـا بفيتـامين د مقارنـة بالمجموعـة المصـابة بإرتفـاع الـدهون فـي الـدم و تحسـنت مسـتويات ألانـين تـرانس أمينـاز وأسـبرتات تـرانس أمينـاز تحسـناً ذا دلالـة إحصـائية فـي المجموعـة المصـابة بإرتفـاع الـدهون فـي الـدم و التـي تـم علاجهـا بفيتـامين د مقارنـة بالمجموعـة المصـابة بإرتفـاع الـدهون فـي الـدم و عنـدما قورنـت بالمجموعـات التـي تعـالج بالأتورفاسـتاتين أظهـرت المجموعـات التـي تعـالج بالأتورفاسـتاتين وفيتـامين د تحسـنا ذا دلالـة إحصـائية فـي مسـتويات ألانـين تـرانس أمينـاز وأسـبرتات تـرانس أمينـاز والكريـاتين فوسفوكيناز.

الإسـتنتاج: يمكـن أن يسـاعد فيتـامين د علـي تحسـن مسـتويات السـكر بالـدم كمـا أن لـه تـأثيراً وقائيـاً ضـد الإعـتلال الـذي قـد يصـيب الكبـد مـن إرتفـاع الـدهون بالـدم والإعـتلال الذي قد يصيب الكبد والعضلات بسبب الأتورفاستاتين.

الكلمات الدالة: فيتامين د، أتورفاستاتين، إرتفاع الدهون بالدم.