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The role of vitamin D in statin treated patients complaining of myalagia

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SOUHRN

Kontext: Existuje řada důkazů dokládajících přínos užívání statinů u kardiovaskulárních onemocnění, nicméně hlavním důvodem pro vysazování léčby statiny a obecně non-adherenci je statiny indukovaná myopatie. Se svalovou slabostí a těžkou myopatií byl nezávisle spojen deficit vitaminu D, který může působit jako faktor zkreslující skutečné příčiny statiny indukovaných myopatií.
Cíle: Zjistit, zda jsou nízké koncentrace vitaminu D v séru spojeny se vznikem myalgie u pacientů léčených statiny.
Pacienti a metody: Do této průřezové studie bylo zařazeno 60 pacientů léčených statiny. Pacienti byli rozděleni do dvou skupin po 30. V první skupině byli pacienti užívající statiny a trpící myalgií, zatímco druhou skupinu tvořili pacienti také užívající statiny, avšak bez bolesti svalů.
Výsledky: Symptomatičtí pacienti trpěli myalgií již 5,03 ± 2,4 týdne. U pacientů s myalgií se skóre Statin Myalgia Clinical Index pohybovalo v rozmezí 9 až 11. Předložená studie nalezla významnou spojitost mezi nízkou koncentrací vitaminu D v séru a myalgií u pacientů léčených statiny. Pacienti se statinovou myalgií vykazovali významně nižší koncentrace vitaminu D než asymptomatičtí pacienti (29,3 ± 12,4 vs. 97,4 ± 15,1 nmol/ml; $p < 0{,}001$).
Závěr: Tato studie přinesla působivé důkazy o spojitosti mezi koncentracemi vitaminu D v plazmě a statinovou myalgií. U pacientů s myalgií indukovanou užíváním statinů byly naměřeny významně nižší koncentrace vitaminu D než u asymptomatických jedinců. Koncentrace vitaminu D mohou být užitečné v diagnostice a léčbě svalových symptomů v souvislosti s užíváním statinů.

Keywords:
Myalgia
Statins
Vitamin D

ABSTRACT

Background: There is a multitude of evidence supporting the benefit of statin use in cardiovascular disease; however, statin-induced myopathy is a major reason for statin discontinuation and non-adherence. Vitamin D deficiency has been independently associated with muscle weakness and severe myopathy, and may be a confounder for statin-induced myopathies.
Objectives: To determine whether low serum vitamin D is associated with the occurrence of myalgia in statin treated patients.
Patients and methods: This cross-sectional study enrolled 60 statin-treated patients. Patients were divided into two groups each was formed of 30 patients. Group 1 enrolled patients taking statins and suffering from myalgia, while group 2 enrolled patients on statins yet free of muscle pains.
Results: The duration of myalgia in symptomatic patients was (5.03±2.4 weeks). Statin Myalgia Clinical Index score in myalgic patients ranged between 9 to 11. The current study found a significant association between low serum vitamin D level and myalgia in statin treated patients. Patients with statin-associated myalgia had significantly lower levels of vitamin D compared to asymptomatic patients (29.3±12.4 vs. 97.4±15.1 nmol/mL, $p < 0.001$).
Conclusion: This study provided suggestive evidence that there is an association between plasma vitamin D levels and statin-associated myalgia. Patients with statin-associated myalgia had significantly lower levels of vitamin D compared to asymptomatic patients. Vitamin D levels may be useful for the diagnosis and management of statin-associated muscle symptoms.

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Introduction

3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGR) is the rate-controlling enzyme of the mevalonate pathway which is responsible for cholesterol and other isoprenoid biosynthesis (Fig. 1).[1]

HMG-CoA reductase inhibitors (statins) decrease mortality and morbidity in patients with coronary artery disease. They belong to the most widely worldwide used drugs. However, statins have been associated with muscle-related adverse effects, such as myalgia and creatine kinase elevation.[2,3]

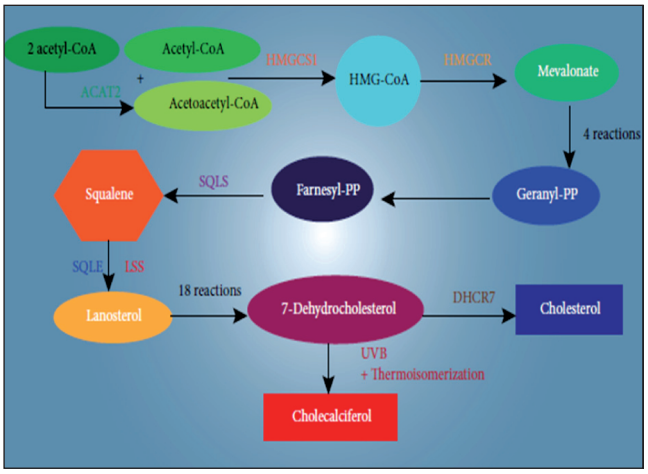

Fig. 1 – Pathway of cholesterol and cholecalciferol biosynthesis.[1] ACAT2 – acetyl-CoA acetyltransferase 2; DHCR7 – 7-dehydrocholesterol reductase; FDPS – farnesyl diphosphate synthase; HMG-CoA – 3-hydroxy-3-methylglutaryl-CoA; HMGCR – HMG-CoA reductase; HMGCS1 – HMG-CoA synthase 1; LSS – lanosterol synthase; PP – pyrophosphate; SQLE – squalene; SQLS – squalene synthase; UVB – ultraviolet B rays.

Muscle-related side effects are the most common cause for discontinuation of statin and therefore significant barrier to cardiovascular risk reduction.[4] The exact mechanism underlying this complication has not been elucidated. Potential factors were implicated, e.g. genetic predisposition, high drug dose, low body mass index, female gender, hypothyroidism, alcohol abuse, polypharmacy, low plasma vitamin D level, concomitant use of fibrates and impaired kidney and liver function.[2–6]

Statin-associated muscle symptoms

Autoimmunity may be a causative mechanism in statin induced myotoxicity.[4] Statins are transported into hepatocytes by the organic anion transporting polypeptide (OATP1B1) which is encoded by the gene *SLCO1B1*. Fluvastatin is presently the only available statin not transported through this system.[4] Studies revealed combination between *SLCO1B1* polymorphisms and myotoxicity.[7] Figure 2 illustrated other factors potentially involved in statins associated muscle injury.[8]

The cytochrome P (CYP) enzyme system is the most significant enzyme system that is responsible for phase 1 metabolism of the different statins. There are >30 known isoenzymes. Genetic variations in these isoenzymes may influence the rate of metabolism of statins.[9]

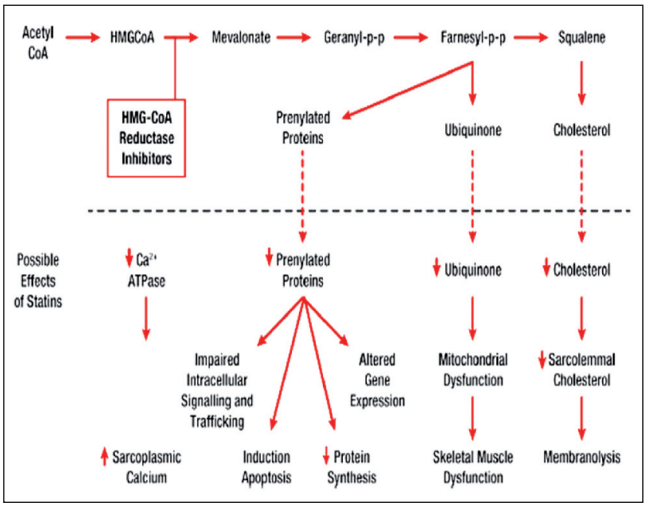

Fig. 2 – Effects potentially involved in statin-related muscle injury/symptoms.[8]

Ghatak et al. suggested two factors that may decrease the significance of the CYP p450 system in statin myopathy. The first is that the CYP system is more significant when statins are used with other drugs that used the CYP system in their metabolism. The second factor is that statins are also metabolized by glucuronidation, a separate pathway that does not include in CYP system.[10] The *CoQ2* gene is implicated in the CoQ10 synthetic pathway. Previous study found that *CoQ2* gene mutations were associated with statin induced myotoxicity.[11]

Since statin induced myotoxicity is dose-dependent, any medications that elevate the plasma concentration of statins will raise the risk of myotoxicity. Moreover, medications that affected the pharmacokinetic properties of statins can influence their potential toxicity. These pharmacokinetic properties include hepatic metabolism (oxidation by the CYP isoenzymes or glucuronidation by the uridine diphosphate glucuronosyltranferase [UGT] enzyme), the synthesis of active metabolites and use of hepatic transporters, bioavailability, protein binding and excretion (Table 1).[12,13]

Vitamin D

Vitamin D is a hydrophobic vitamin (or hormone as it is popularly called in recent years), which is mostly synthesized in human skin by way of ultraviolet sunlight (the reason for it being called hormone) or assimilated in the body in negligible amounts by ingestion of egg yolk, some kinds of fish, and mushroom. Then 25 hydroxylated in the liver and 1α-hydroxylated in the kidney to produce its biologically active form.

In association with parathormone, vitamin D provides Ca homeostasis via its major target organs, i.e., small intestine, bone, and kidney (Fig. 3).[14,15]

Muscle cells have vitamin D receptors. It was found that >30 various tissues including skeletal muscle tissue express vitamin D receptors (VDR).[16] Deficiency of vitamin D not only bone mineral density are affected but also the muscle function, an entity called osteomalacic myopathy which is characterized by diffuse muscle pain, proximal muscle weakness, difficulty in rising from a chair, and climbing up stairs.[17]

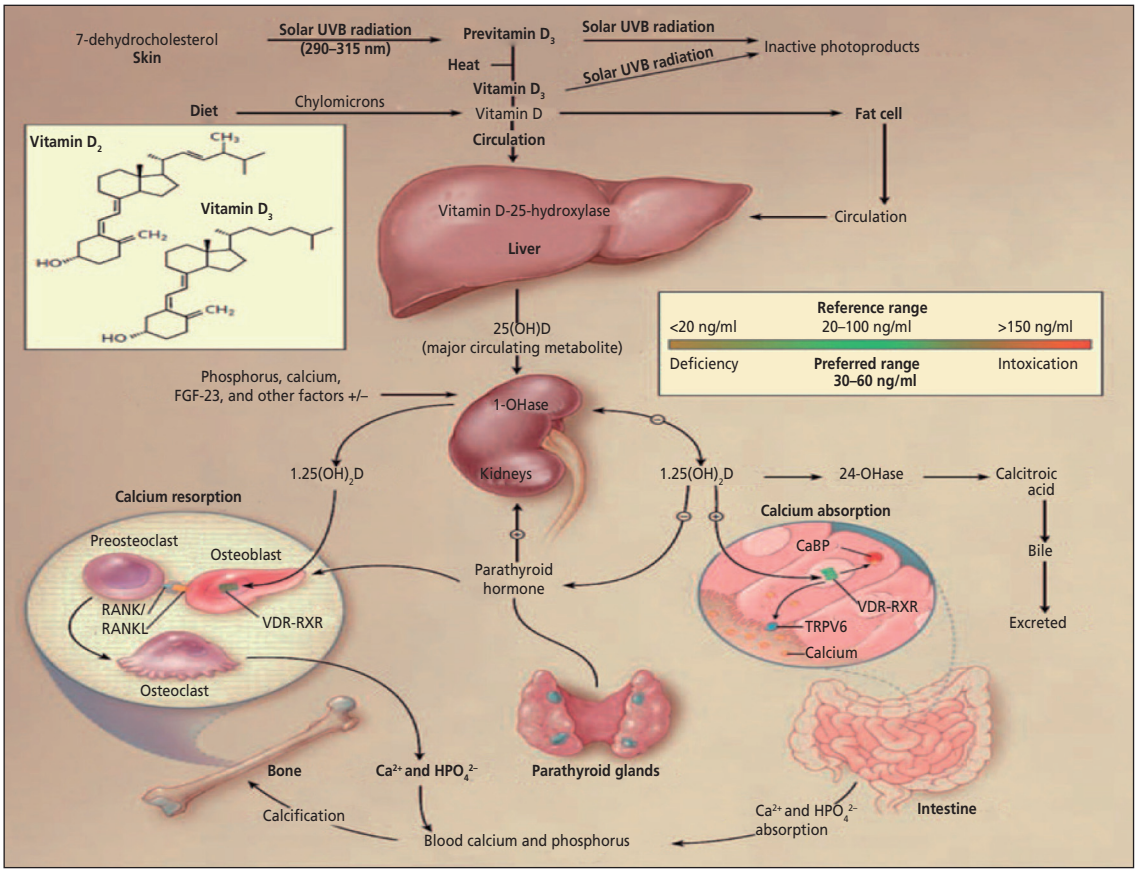

Fig. 3 – Synthesis and metabolism of vitamin D in the regulation of calcium, phosphorus, and bone metabolism.[15]

Table 1 – Risk factors for statin-associated muscle symptoms[13]

Risk factor	Description
Anthropometric	• Age >80 years (general caution advised for age >75) • Female • Low body mass index • Asian descent
Concurrent conditions	• Acute infection • Hypothyroidism (untreated or undertreated) • Impaired renal (chronic kidney disease classification 3, 4, and 5) or liver function • Obstruction in biliary tree • Organ transplant recipients • Severe trauma • Human immunodeficiency virus • Diabetes mellitus • Vitamin D deficiency
Surgery	Surgery with high metabolic demands. The American Heart Association recommends temporary cessation of statins prior to major surgery.
Related history	• History of creatine kinase elevation, especially >10× the upper limit of the normal range • History of pre-existing/unexplained muscle/joint/tendon pain • Inflammatory or inherited metabolic, neuromuscular/muscle defects (e.g. McArdle disease, carnitine palmitoyl transferase II deficiency, myoadenylate deaminase deficiency, and malignant hyperthermia) • Previous statin-induced myotoxicity • History of myopathy while receiving another lipid-lowering therapy
Genetics	Genetic factors such as polymorphisms in genes encoding cytochrome P450 isoenzymes or drug transporters
Other risk factors	• High level of physical activity • Dietary effects (excessive grapefruit or cranberry juice) • Excess alcohol • Drug abuse (cocaine, amphetamines, heroin)

Table 2 – The original Statin Myalgia Clinical Index[23]

Clinical symptoms (new or increased unexplained muscle symptoms)	Points
Regional distribution/pattern	
Symmetric hip flexors/thigh aches	3
Symmetric calf aches	2
Symmetric upper proximal aches	2
Non-specific asymetric, intermittent	1
Temporal pattern	
Symptoms onset <4 weeks	3
Symptoms onset 4–12 weeks	2
Symptoms onset >12 weeks	1
Dechallenge	
Improves upon withdrawal (<2 weeks)	2
Improves upon withdrawal (2–4 weeks)	1
Doesn't improve upon withdrawal (>4 weeks)	0
Challenge	
Same symptoms reoccur upon rechallenge <4 weeks	3
Same symptoms reoccur upon rechallenge 4–12 weeks	1
Statin Myalgia Index score	
Probable	9–11
Possible	7–8
Unlikely	<7

Statin-associated muscle symptoms (SAMS)

While consensus groups including the American Heart Association/American College of Cardiology[18] and the National Lipid Association[19] have presented definitions of SAMS based on symptoms and the magnitude of CK elevation. Indeed, a definitive diagnosis of SAMS is difficult because symptoms are subjective and there is no 'gold standard' diagnostic test.

Assessment of the probability of SAMS being due to a statin take account of the nature of the muscle symptoms, the elevation in CK levels and their temporal association with statin initiation, discontinuation, and re-challenge.[20]

In absence of standardized classification of SAMS, we have to integrate all muscle-related complaints (e.g. pain, weakness, or cramps) as muscle symptoms subdivided by the presence or absence of CK elevation (Fig. 4).

A statin-associated myalgia index is proposed based on symptoms and signs notified by patients in the **STOMP study**[21] and the Prediction of Muscular Risk in Observational conditions study **(PRIMO).**[22] This score provides different weighted values based on the distribution of the muscle complaints, temporal pattern of onset, improvement after statin withdrawal and reccurrence of symptoms after rechallenge. The statin myalgia clinical index score estimate these symptoms as probable, possible or unlikely related to the statin (Table 2).[23]

Management of statin-associated muscle symptoms

For patients at low cardiovascular risk (CVD) risk, their need for a statin should be reassessed and the benefits of therapeutic lifestyle changes, such as cessation of cigarette smoking, blood pressure control, and adoption of a Mediterranean style diet, should be balanced against the risk of continuing statin therapy. Patients at high CVD risk, including those with CVD or diabetes mellitus, the benefits of ongoing statin therapy need to be weighed against the burden of muscle symptoms. Withdrawal of statin therapy followed by one or more re-challenges (after a washout) can help in determining causality. Additional approaches included the use of an alternative statin, a statin at lowest dose, intermittent (i.e. non-daily) dosing of a highly efficacious statin, or the use of other lipid lowering medications (Fig. 5).

Symptoms	Biomarker	Comment
Muscle symptoms	Normal CK	Often called 'myalgia'. May be related to statin therapy. Causality is uncertain in the view of the lack of evidence of an excess of muscle symptoms in blinded randomized trials comparing statins with placebo.
Muscle symptoms	CK >ULN <4 × ULN CK >4 <10 × ULN	Minor elevations of CK in the context of muscle symptoms are commonly due to increased exercise or physical activity, but also may be statin-related; this may indicate an increased risk of more severe, underlying muscle problems.[19]
Muscle symptoms	CK >10× ULN	Often called myositis or 'myopathy' by regulatory agencies and other groups (even in the absence of a muscle biopsy or clinically demonstrated muscle weakness). Blinded trials of statins vs placebo show an excess with usual statin doses of about 1 per 10 000 per year.[4] Pain is typically generalized and proximal and there may be muscle tenderness and weakness. May be associated with underlying muscle disease.
Muscle symptoms	CK >40× ULN	Also referred to as rhabdomyolysis when associated with renal impairment and/or myoglobinuria.
None	CK >ULN <4× ULN	Raised CK found incidentally, may be related to statin therapy. Consider checking thyroid function or may be exercise-related.
None	CK >4× ULN	Small excess of asymptomatic rises in CK have been observed in randomized blinded trials in which CK has been measured regularly. Needs repeating but if persistent, then clinical significance is unclear.

Fig. 4 – Definitions of statin-associated muscle symptoms proposed by the European Atherosclerosis Society Consensus Panel.[20]

- Ensure that there is an indication for statin use and that the patient is fully aware of the expected benefit in cardiovascular disease risk reduction that can be achieved with this treatment
- Ensure that there are no contraindications to statin use
- Counsel patients regarding the risk of 'side effects' and the high probability that these can be dealt with successfully
- Emphasize dietary and other lifestyle measures
- Use statin-based strategies preferentially notwithstanding the presence of statin-attributed muscle-related symptoms
- If re-challenge does not work; use a low or intermittent dosing preferably of a different (potent or efficacious) statin
- Use non-statin therapies as adjuncts as needed to achieve low-density lipoprotein cholesterol goal
- Do not recommend supplements to alleviate muscle symptoms as there is no good evidence to support their use

Fig. 5 – Management of statin-associated muscle symptoms.[13]

Aim of the study

Some studies suggest that vitamin D deficiency may be associated with elevated risk of statin-related muscle complaints. The current study aimed to examine whether low serum vitamin D is associated with the occurrence of myalgia in statin treated patients.

Patients and methods

This prospective observational and cross-sectional study was conducted on 60 subjects divided into 2 groups. Group 1 patients who were taking statins and complained of myalgia diagnosed clinically as generalized muscle pain more prominent at the proximal sites of the extremities and exaggerated with exercise. It became obvious minimally one week after initiating statin therapy and can be accompanied by fatigue, nocturnal cramps, and tendon pain.

Group 2 included patients on statins yet not complaining of myalgia. Patients were enrolled from Cardiovascular Department at Cairo University Hospital. Informed consent was taken from all subjects.

Exclusion criteria

Patients who refuse to participate in this study, on exogenous vitamin D reinforcement, having other factors affecting statin metabolism (hypothyroidism, alcoholism, known muscle disease) or complaining of other clinical conditions that might cause musculoskeletal pain were excluded from the study.

Full history taking included other comorbidities (smoking, diabetes, hypertension, coronary artery disease, rheumatologic diseases [osteoarthritis, rheumatoid arthritis, fibromyalgia and chronic pain syndrome], psychiatric diseases [depression, anxiety, and post-traumatic stress disorder], medication history [anti-diabetic medications, anti-hypertensive medications, and lipid-lowering drugs] and the duration of myalgia).

All patients were subjected to clinical examination with special emphasis on demographic characteristics and risk factors. Body mass index (BMI) was calculated according to the following formula: BMI = body weight (kg) / height (m^2). Obesity was defined as BMI $\geq$ 30 kg/m^2.[24]

Statin Myalgia Index score to diagnose statin induced myalgia

The scheme of Statin Myalgia Index score was translated to the Arabic edition after that it was applied on the patients who complained of myalgia. Statin myalgia clinical index score in myalgic patients ranged between 9 to 11.

Laboratory work up

Plasma cholesterol, triglycerides, HDL (high-density lipoprotein), LDL (low-density lipoprotein), CK (creatine kinase), alanine aminotransferase (ALT), aspartate transaminase (AST), blood glucose, glycated hemoglobin, thyroid stimulating hormone (TSH) and complete blood count were done for all patients.

Serum 25(OH) vitamin D level

A 5 ml blood sample was drawn from patients and stored at 2–8 °C. Serum 25(OH) D was analyzed using the ARCHITECT 25-OH Vitamin D assay. The assay is reported to demonstrate 105% cross-reactivity with $25(OH)D_3$, 82% cross-reactivity with $25(OH)D_2$, 12.6% cross-reactivity with $1,25(OH)_2D_3$, 112% cross-reactivity with $24,25(OH)_2D_3$, minimal cross-reactivity with 3-epi-$25(OH)D_3$ (2.7%), and a measuring interval of 32.5–240.0 nmol/L (13.1–96.2 ng/mL).[25]

Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25. Data was summarized using mean, standard deviation, median, minimum and maximum for quantitative data. Frequency (count) and relative frequency (percentage) for categorical data. For comparing categorical data, Chi square (c^2) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlations between quantitative variables were done using Spearman correlation coefficient. ROC curve was constructed with area under curve analysis performed to detect best cutoff value of vitamin D for detection of myalgia. *P*-values less than 0.05 were considered as statistically significant.

Results

Sixty statin-treated patients were included in the study. Thirty patients with myalgia (group 1) and 30 asymptomatic patients (group2). The mean age of the patients was 53.1 years. There were 19 women and 41 men. Table 3 represents the comparison of risk factors and clinical data between the two study groups.

The standard deviation (SD) of duration of statin intake (months) was lower in group 1 compared to group 2 (4.6±1.7 vs 25.6±13.0, respectively, *p*-value <0.001).

Table 4 illustrates the comparison of demographic, anthropometric measures of the study groups. Patients with the long duration of statin intake tend to have less myalgia symptoms. On the other hand patients with long duration of hypertension are more myalgic. The other parameters were not statistically significant.

Table 3 – Risk factors and clinical data of the study groups

Variables		Group 1		Group 2		*p*-value
		Count	Percent	Count	Percent	
Smoking	Yes	12	40.0	11	36.7	0.791
DM	Yes	13	43.3	8	26.7	0.176
CAD	Yes	18	60.0	15	50.0	0.436
HTN	Yes	30	100.0	27	90.0	0.237

CAD – coronary artery disease; DM – diabetes mellitus; HTN – systemic hypertension; *p*-values <0.05 were considered as statistically significant.

Discussion

Statin therapy significantly reduces cardiovascular diseases morbidity and mortality in both primary and secondary prevention trials. However, statins have been associated with muscle-related adverse effects, such as myalgia and creatine kinase elevation.[26]

Muscle-related adverse effects are the most common reason for statin discontinuation and therefore an important barrier to cardiovascular risk reduction.

Myopathy is differentiated into three categories: myalgia (muscle aches/weakness without CK elevation, myositis (muscle symptoms with CK elevation) and rhabdomyolysis (muscle symptoms associated with marked CK elevations >10 times the upper limit of normal).[27] Low vitamin D serum concentration is a growing public health concern, even in regions with higher sun exposure. Vitamin D serum concentrations can be defined as sufficient (≥30 ng/mL), insufficient (21–29 ng/mL), or deficient (≤20 ng/mL).[28]

Table 4 – Demographic, anthropometric measures, and risk factors among the study groups

Variable	Group 1		Group 2		*p*-value
	Mean±SD	Median	Mean±SD	Median	
Age (years)	53.07±5.5	55.0	53.1±7.1	54.0	0.965
Duration of statin intake (months)	4.6±1.7	4.0	25.6±13.0	24.0	**<0.001**
DM duration (years)	1.9±2.6	0.00	0.8±1.5	0.00	0.124
HTN duration (years)	4.4±1.9	5.5	3.1±1.9	2.00	**0.004**
Weight (kg)	90.5±19.8	87.7	84.4±18.7	85.0	0.264
Height (cm)	167.9±8.1	167.5	166.9±6.9	169.0	0.941
BMI (kg/m^2)	32.1±6.9	32.5	30.3±6.2	29.5	0.370

BMI – body mass index; DM – diabetes mellitus; HTN – systemic hypertension; *p*-values <0.05 were considered as statistically significant.

Table 5 – Laboratory data of the study groups

Variables	Group 1		Group 2		*p*-value
	Mean±SD	Median	Mean±SD	Median	
Plasma cholesterol (mg/dl)	172.4±49.5	177.5	162.9±36.1	165.5	0.429
TG (mg/dl)	150.1±93.6	136.5	123.7±55.1	108.5	0.297
HDL (mg/dl)	40.4±12.91	39.0	39.7±9.3	40.0	0.865
LDL (mg/dl)	99.4±38.8	90.0	95.6±26.9	90.5	0.941
Creatinine (mg/dl)	0.87±0.16	0.8	0.83±0.20	0.76	0.127
HBA_{1c}	6.24±1.08	5.95	6.06±1.08	5.9	0.598
SGOT (µ/l)	23.4±4.2	23.0	23.13±4.03	22.5	0.738
SGPT (µ/l)	34.1±11.19	34.5	33.6±7.04	34.0	0.813
CK (µ/l)	119.7±57.3	111.0	105.3±37.4	110.00	0.191
Serum 25(OH) vitamin D (nmol/L)	**29.34±12.47**	**27.05**	**97.46±15.11**	**93.50**	**<0.001**

CK – creatine kinase; HBA_{1c} – glycosylated hemoglobin; HDL – high-density lipoprotein; LDL – low-density lipoprotein; SGOT – aspartate aminotransferase; SGPT – alanine aminotransferase; TG – triglycerides.

Table 5 represents the laboratory data of the study groups. Patients with myalgia had higher cholesterol, triglycerides, LDL, and CK in spite of the fact that it was statistically insignificant. Serum level of 25(OH) vitamin D was significantly lower in patients with myalgia (p <0.001). Moreover, it was found that the more the duration of statin intake, myalgia, and hypertension, the less the level of serum 25(OH) vitamin D, (r = 0.680, r = –0.825, r = –0.832, respectively and all p <0.005).

In this study the association between low serum vitamin D level and myalgia in statin treated patients were examined. This observational cross-sectional study that enrolled 60 statin-treated patients concluded that there was an association between plasma vitamin D levels and statin-associated myalgia.

Patients with statin-associated myalgia had significantly lower levels of vitamin D compared to asymptomatic patients. These findings are concordant with Ahmed's et al.[29] cross sectional study that was done on 621 patients and found that 128 patients who treated with statins with myalgia had significantly lower mean serum vitamin D level than 493 asymptomatic patients (28.6 ± 13.2 vs. 34.2 ± 13.8 ng/mL). The study reported that vitamin D was lower in 64% patients with myalgia vs 43% of asymptomatic patients.

Minissian et al.[30] conducted a retrospective clinical chart review on 20 female patients from a tertiary chest pain center in 2008–2013. All women were indicated for statin therapy and developed statin-induced myalgias. None of the women had a prior history of muscle related myalgias prior to statin therapy. The study findings supported earlier suggestions of a positive association between vitamin D deficiency and statin induced myalgias.

A retrospective chart review was conducted at the University of Mississippi Medical Center's ambulatory cardiometabolic clinic from December 2006 to April 2008 on 105 patients in a cardiometabolic clinic. The study reported that patients with statin-induced myopathy had significantly lower vitamin D concentrations and the majority of these myopathies were observed in patients with a vitamin D <32 ng/mL.[28]

In the current study we found a significant association between low serum vitamin D level and myalgia in statin treated patients. Patients with statin-associated myalgia had significantly lower levels of vitamin D compared to asymptomatic patients. Mean ± standard deviation (SD) of serum vitamin D was lower in patients with myalgia than in the asymptomatic patients (29.3±12.4 vs 97.4±15.1 nmol/mL, p <0.001). Discordant with our findings, other studies did not support an association between low vitamin D status and statin-induced myalgia.[31]

Vitamin D supplementation

Previous study concluded that vitamin D exerts a clear pro-myogenic effect on satellite cells in charge of muscle reconstitution after muscle injury or muscle waste. Moreover, the same study provided justification for vitamin D replenishment in muscle waste conditions characterized by loss of muscle mass and also in vitamin D deficient elderly adults who have an age-related loss of muscle mass and strength.[32] Kang et al.[33] concluded that replenishing low vitamin D in patients with statin-induced myopathy appeared to be an effective strategy in improving medication adherence. Other studies found that statin intolerance because of myalgia, myositis, myopathy, or myonecrosis associated with low serum vitamin D can be safely resolved by vitamin D supplementation (50,000–100,000 units/week) in most cases (88–95%).[34]

Conclusion and recommendations

Patients with statin-associated myalgia had significantly lower levels of vitamin D compared to asymptomatic patients. Vitamin D levels may be useful for the diagnosis and management of statin-associated muscle symptoms (SAMS). The current study highlighted the need for further research into the pathophysiology of statin-associated muscle symptoms. Other studies evaluating vitamin D supplementation in patients with statin-induced myalgia are needed.

Limitation of the study

Although the topic has been dealt with repeatedly it is important in a clinical and practical point of view .The sample size was relatively small. A bigger sample size would allow better analysis of the subgroups. Also the effect of vitamin D supplementation on the statin-induced myopathy was not studied.

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Conflict of interest

None declared.

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