High-density lipoprotein level may be a risk factor for major cardiac events and lower extremity amputation in patients with a diabetic foot ulcer

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To evaluate that high-density lipoprotein cholesterol level is a predictive risk factor for major cardiac events and lower extremity amputation in diabetic patients with foot ulcers.

Keywords:
diabetic foot ulcers, high-density lipoprotein, lower extremity amputations, major cardiac adverse effects

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Introduction

Diabetes mellitus (DM) is a widely recognized dangerous ailment acknowledged for its multifaceted difficulties, counting heart diseases and diabetic foot ulcers (DFUs), which regularly bring about removal extremities as one of the most exceedingly terrible results of its effect.

In the future, lower extremity amputations (LEAs) related to diabetes will stay a wellspring of morbidity and mortality, considering the fast developing diabetes in population widely and high frequency of DFUs among them [1].

Every 30 s, a LEA is done because of diabetes. Of all extremity removals in patients with diabetes, 85% are presented with foot ulcers, which accordingly breaks down to a serious infection or gangrene [2].

There are two main causes for a high-frequency removal of extremities in patients with diabetes: contamination, which could go on swiftly main to extra tissue annihilation and severe peripheral arterial disease.

This review discusses the effect of high-density lipoprotein (HDL) level in patients who have DFUs on LEA as well as its relation with major adverse cardiac events (MACEs).

The prevalence rate of diabetic foot is increasing because of the enhancing pervasiveness of diabetes and increasing life time of diabetic patients. In developed nations, the yearly frequency of event of foot ulceration among people with diabetes is already 2%, being the greatest broadly recognized reason of nontraumatic amputation, and ~1% of patients with diabetes go through lower-limb amputation. In developing and poor-level countries, DFUs and extremity removal are becoming more common [3,4].

There is strong relationship between dyslipidemia and silent coronary artery disease in type 2 diabetes mellitus. It is likewise fitting to have a screening ECG for silent coronary artery diseases at the hour of determination or during the subsequent time in type 2 diabetes [5].

Pathogenesis of diabetic foot ulceration

A recent study has shown that high lipoprotein (a) and homocysteine levels are related with the advancement of vascular diabetic foot, as lipoprotein (a) has a role in the development of certain complexities of diabetes, like coronary vascular disease and peripheral arterial disease, and high homocysteine level is associated with those components which make basic changes in vascular endothelial cells [6].

Moreover, a recent study illustrated that patients with diabetes with numerous evaluations of DFU demonstrated a higher interleukin-6, high-sensitivity C-reactive protein, and tumor necrosis factor-α and lower adiponectin plasma levels in correlation with

diabetics without foot ulcer, independent of the accompanying infections, because proinflammatory and antiinflammatory processes are significant in the various periods of wound healing [7].

Relationship between high-density lipoprotein, lower extremity amputation , and major adverse cardiac event

Later on, LEA caused by diabetes will continue to be a wellspring of huge morbidity and furthermore mortality, estimating the hastily developing diabetes populace internationally and the higher frequency DFU [1].

Approximately 82% of LEAs are done on diabetic patients, a significant of which follows foot ulceration.

The pathway to ulceration and finally LEA may include essential contribution from underlying diabetes-related pathophysiology (neuropathy, foot disfigurement, and restricted joint mobility), starting situations (trauma), and consequent infections. LEA is carried out for different signs, including serious delicate tissue contamination, peripheral vessel occlusions, and gangrene.

Aside from its causes, all endeavors ought to be made to stay away from removal once DFU has created or introduces itself in the hospitals [2,3].

The diabetic foot follows a typical pathway that starts with a small ulcer. Most of DFUs (60–80%) will mend, whereas 10–15% of them will stay dynamic, and up to 24% of them will finally lead to LEA [2].

In spite of the fact that foot ulcers and amputation are normal difficulties of DM, foot ulceration and removal do not need to be normal results of diabetes. Improving glucose control and instructing patients in the standard consideration of their feet can diminish the problems of diabetic foot inconveniences [8].

Diabetic foot ulcers and lower extremity removal

DM grows hazards for LEA from 2 to 16% dependent upon look at structure and the populace contemplated [9]. Rates of LEA between patients with DM can be as much as 15 times of various events more likely than their non-diabetics [10].

Frequency of all LEAs is four to seven times more in diabetic individuals (people) than in people without DM [9].

A large portion of LEAs in view of DM were toe removals followed by beneath knee amputation and afterward above-knee removal and foot removal, with rates of 2.6, 1.6, and 0.8 per 1000 people, respectively [11].

A few research studies in the United States and Western Europe as of late have revealed the diminishing frequency of LEAs in DM populaces, especially in light of execution of improved diabetes foot care [12,13].

In the one-year longitudinal research by Canavan *et al.* [13], recurrence pace of LEA individuals with DM decreased from 310.5 per 100 000 people to 75.9 per 100 000. Practically sensational 62% decrease in the frequency of LEAs and progressively unobtrusive 40.3% decrease in all LEAs more than 11 years were reported [12].

Major cardiac events and lower extremity amputation

MACEs may be stated as cardiac death, unexpected beginning of pulmonary edema, and abrupt heart arrest [14]. Cardiac arrest is defined as discontinuance cardiac mechanical activity affirmed with the aid of using the inadequacy of indications of dissemination [15].

Major amputation has been declared as an above-foot amputation with signs of (a) failed wound recuperation following right contamination control and wound debridement or (b) related extreme foundational comorbidities or septicemia that hindered treatments or septicemia [16].

Besides, diabetic patients with foot ulcers demonstrate existing peripheral arterial illness and diffuse atherosclerosis [17]. During DFU treatment, patients experience the ill effects of intense physiological (because of wound agony, serious infection, extreme inflammation, and inflammatory cytokines) and mental (uneasiness with strain related with appendage loss) stress, which could incite serious ischemia. Along these lines, it is sensible that we considered MACEs as a critical explanation behind mortality and morbidity during the treatment of appendage-compromising DFUs [18].

MACE becomes fulminant in nature, or potentially that determination becomes postponed in light of the fact that runs of the mill adverse effects were veiled among such patients. It is expected that patients with a serious atherosclerosis who endured huge degrees of the strain created fulminant introductions of MACEs. By and by, the cardiac chest ache ought to without a good deal of a stretch be covered by a diabetic neuropathy and the wound pain [19].

Table 1: High density lipoprotein (HDL) level may be a risk factor for major cardiac events (MACE) and lower extremities amputation (LEA)

References	Study sample/ assessment time	Aim of the study	Study design	Findings and conclusion
Musa *et al*. [20]	A total of 82 patients were enlisted, comprising 55 men, between January 2015 and December 2016	Decide risk elements related with lower foot removal among patients with DFUs	A prospective study. Its information was gathered by utilizing a normalized pretested poll that involved demographic data (age, sex, conjugal status, habitation, and education level) History of smoking, history of liquor utilization, and term of diabetes The end result of the DFU (no matter whether or not the affected person became reduce off or not)	Study contemplated that albeit different elements had been depicted to complicate diabetic ulcers through numerous scientists, none of these elements have been diagnosed on this have a look at remote from more settled age and excessive WBC
Hung *et al*. [19]	From 2009 to 2011, 1130 continuous sufferers who have been admitted to the Diabetic Foot Care Center in Chang Gung Medical Center	Treatment for DFUs complicated by major cardiac events	Paces of in-emergency clinic mortality or occasions that result in flow to emergency unit for different serious entanglements have been reflectively analyzed	While treating sufferers with DFUs, clinical group of workers ought to know about MACEs and nosocomial contaminations. The presence of MACEs is generally fulminant and perhaps conceal by the disorder entity. Most MACEs had been cited at some point of first 10 days
Moon *et al*. [21]	1792 diabetic patients had been admitted to the diabetic wound center for managing DFUs. From those patients, 1032 diabetic patients with forefoot ulcers had been remembered for examination	The reason for this research was to explore hazard factors for significant limb removal in patients hospitalized with diabetic forefoot ulcers	Hospitalized patients determined to have DFUs whose basic situation became so terrible to the point that outpatient center primarily based totally remedies have been unrealistic, patients with critically inflamed ulcers requiring careful debridement with foundational antibiotics	Hazard elements for significant removal in patients who were hospitalized with diabetic forefoot ulcers incorporate male sex, increased magnesium, and increased platelet levels
Rodrigues *et al*. [22]	Included 129 patients, comprising 81 men and 48 females	Predominance and danger factors for diabetic lower appendage removal: Clinic-Based Case-Control Study	Using nonparametric analysis, for the following parameters (risk factors): acute myocardial Infarction, neuropathy, and dyslipidemia as major hazard elements for limb amputations	Lower appendage removal is a typical result that is associated with identity and neurovascular diabetic difficulties among patients with DFU
Rizk and Ameen [23]	80 continuous attended outpatient Egyptian patients with diabetic foot ailment with inside the National Institute of Diabetes and Endocrinology	Their research had done to identify the relationship between understanding comorbidities, chronic complications and special diabetic foot sorts for the early acknowledgment and the board of those conditions	Cross-sectional study. The patients were isolated into three groups according to the type of foot ulcer, namely, neuropathic, neuroischemic, and ischemic ulcer	Special consideration ought to be paid in the direction of recognizable proof of patients who are in danger of foot ulceration to help forestall foot issues. Comorbid situations ought to furthermore be perceived early and overseen forcefully
Pei *et al*. [24]	Review article from other four studies by using standardized mean differences	Diminished HDL cholesterol had a critical relationship with diabetic foot helplessness in fixed-influences, but no noteworthy affiliations had been located among diabetic foot	Through meta-analysis	Their outcomes proposed that diminished HDL cholesterol turned into associated with diabetic foot, should incorporate focusing on increments in HDL cholesterol
Assaad-Khalil *et al*. [25]	Between July 2008 and December 2009, 1000 female and 1000 male back to back grown-up patients with diabetes	The commonness of diabetic foot issues and associated hazard elements in Egypt	Cross-sectional study to evaluate the commonness of diabetic foot complexities among attendants of DFSC in Alexandria	Screening and identification of early neuropathy, inconsequential skin injuries ought to pull in healthcare provider's consideration and consideration and engage patients to stick to their foot care follow-up applications earlier than movement into continuously genuine stages

Contd...

References	Study sample/ assessment time	Aim of the study	Study design	Findings and conclusion
Alvarsson *et al.*, [26]	Included 150 diabetic and 191 nondiabetic patients who had been amputated in lower extremities at KS among 2000 and 2006	Explored adjustments with-inside removal rate in patients with DM at the Karolinska University Hospital following the advent of accord rules for treatment and counteraction of diabetic foot intricacies and to distinguish hazard gatherings of lower extremities amputations	Case-control study to analyze were affirmed via looking the recorded patients' case for the occasion of removal went earlier	Diabetic patients who had been amputated had a higher commonness of regular comorbidities, inclusive of foot infections and kidney issues, contrasted with amputated nondiabetic patients. The amputation charge is probably similarly reduced if all patients in danger of LEA have been alluded to the foot team on the way to get expert treatment
Ikura *et al.* [27]	163 Japanese ambulatory patients with DFUs, comprising 45 females and 118 males	HDL cholesterol levels an indicator for a frequency of LEA and wound-associated death in patients with DFUs	A single-center, observational, longitudinal chronicled partner study	HDL levels of cholesterol are probably a singular clinical pointer for the incidence of LEA and wound-associated mortality in patients with DFUs

Conclusion

In this review, we presented the reported data of different studies that have used HDL as an indicator for LEA and major cardiac events in patients with diabetic foot and providing valuable information about prognosis of DFU recovery. These reported data are promising to conduct future studies that should address many questions, including (a) when to assess lipid profile periodically for diabetic foot patients and take in considerations HDL cholesterol levels as a risk factor and predictor for lower extremities amputations for those patients and following them up for other complications such as MACE and (b) when to pay special attention toward distinguishing proof of patients at danger for foot ulceration to offer assistance to forestall foot issues. Special attention should be paid to assessment of any vascular compromise of lower limbs in diabetics with CAD, so follow-up with ECG and any history of cardiac symptoms for diabetic foot or foot infected patients (stress conditions) should be done to manage early any MACE.

Discussion

The following table (1) showing High density lipoprotein (HDL) level may be a risk factor for major cardiac events (MACE) and lower extremities amputation (LEA) in different studies

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Conflicts of interest

There are no conflicts of interest.

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