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Association Between Dyslipidaemia And Severity Of Diabetic Foot Ulcer (DFU).

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Abstract
Diabetic foot ulcers (DFUs) prove to be a severe diabetic complication because they frequently require amputation of the foot. Dyslipidaemia has been reported to be associated with the progression of DFUs; further research is needed to assess its impact. This cross-sectional study explores the relationship between lipid profile and severity of DFU in 59 patients who were classified using Wagner's grading system. Results indicated significant correlations between the severity of DFU and high-density lipoprotein, low-density lipoprotein, and triglycerides ($p < 0.05$) suggesting a relationship between lipid management and prevention of progression of DFU and early lipid testing for risk assessment.

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I. Introduction

India has a high burden of diabetes, with the second highest number of diabetic patients in the world. The number of people with diabetes in India is projected to increase to 124.9 million by 2045. [1,2]. Among the most important complications of diabetes, the diabetic foot ulcer (DFU) emerges as a growing problem for public health systems since it is a leading cause of hospitalization and amputation in patients with diabetes [3]. According to the International Working Group on the Diabetic Foot (IWGDF), a diabetic foot ulcer is a full-thickness wound penetrating through the dermis (the deep vascular and collagenous inner layer of the skin) located below the ankle in a diabetic patient.[4] Three factors are usually involved in DFU formation: diabetic neuropathy, trauma with secondary infection, and arterial occlusive disease [5].

Patients with diabetes often have an altered lipid profile, which contributes to the appearance of these factors [6]. These alterations are multifactorial; nevertheless, one of the most important alterations involves protein glycosylation, such as low-density lipoprotein (LDL). This event impedes the recognition of lipoproteins by cell receptors, and as a result, they remain in circulation for a more extended period. Thus, dyslipidaemia is a major risk factor in the development of vascular complications in diabetes, such as DFU. [7]. Some literature have also reported that there are risk factors for diabetic patients that can aggravate and are closely related to the occurrence of ulcers in the diabetic foot such as age, diabetic duration, smoking, obesity, hypertension, poor ankle-brachial index (ABI), and high neutrophil/lymphocyte ratio (NLR).[8]

Patients with diabetes have a 25% chance of developing diabetic foot ulcers in the future [9]. It is a complication with a mortality rate of approximately 16%, an amputation rate of 25%, and a 3-year mortality rate after amputation is 37%. However, this pathology is preventable through certain measures such as lifestyle modification and lipid management [10].

Additionally, it is necessary to have tools to identify diabetic patients at higher risk of developing this pathology early to prioritize surveillance. Biomarkers are valuable tools for these purposes. Dyslipidaemia is a modifiable risk factor and can be managed with therapeutic lifestyle changes and drug therapy.[11] Hence, this study was conducted to find the association of dyslipidemia with the severity of diabetic foot ulcers.

II. Objectives

• To assess and find the association of lipid profile with severity of diabetic foot ulcer

III. Methodology

This was an observational cross section study involving diabetic foot ulcer patients of both sexes, aged above 25 years. The study was conducted in a tertiary care hospital after taking prior approval from the ethics committee. The sample size estimated was 59. The willing patients were enrolled into the study after taking a valid informed consent.

Inclusion criteria are Diabetic patients of either sex diagnosed with diabetic foot ulcer.

And exclusion criteria are the patients with history of intake of lipid lowering drugs, patients with hematological disorders and patients who had undergone recent surgeries, hyperthyroidism, cancer and pregnancy.

The DFU participants were classified based on the severity of diabetic foot by Wagner's classification which is as follows:
Class 1: Foot at risk;
Class 2: Superficial ulcers;
Class 3: Deep ulcers without osteitis;
Class 4: Deep ulcers with osteitis;
Class 5: Localized gangrene;
Class 6: Extensive gangrene;
Lipid profile of all the DFU patients were estimated for finding the association.

Statistical analysis: The data collected were analysed with descriptive statistics to express demographic data and Anova test to find association between different variable. p value of less than 0.05 was considered significant.

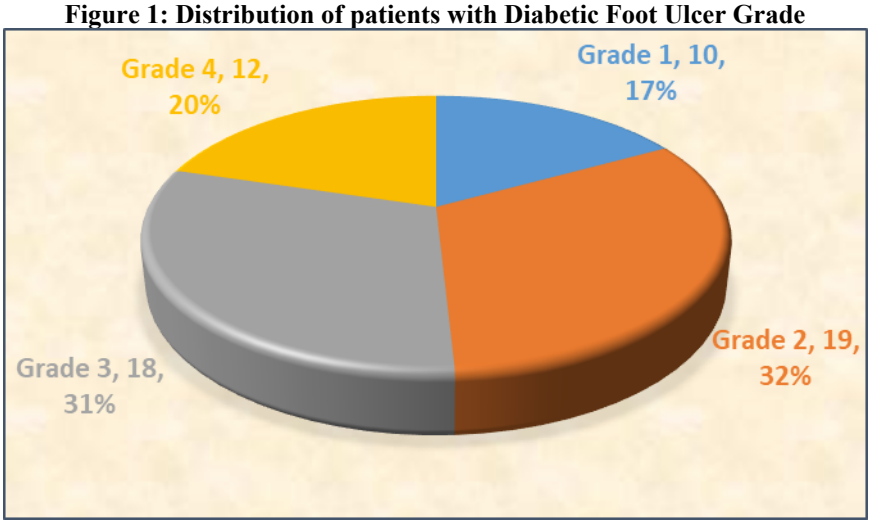
IV. Results:

A total of 59 patients with diabetic foot ulcer were enrolled into this study after taking informed consent. The participants mean age was 58 ± 12.65 with the predominant age being 51-60 years. Male preponderance was 61% as shown in table 1. The mean duration of diabetes observed was 7.44±3.17 and Hypertension (98.5%) being the only comorbid condition. The Diabetic foot ulcer subjects were classified based on the severity of diabetic foot by Wagner's classification. Majority of them were in grade 2 and 3 (32.2 and 30.5%) respectively as shown in Figure 1.

Table 1: Demographic characters of study participants

Variables	Category	Frequency	Percent
Age (Years)	<40	4	6.8
	41-50	9	15.3
	51-60	21	35.6
	61-70	14	23.7
	>70	11	18.6
Mean Age±SD		58.69±12.65	
Mean Duration of Diabetes±SD		7.44±3.17	
Sex	Male	36	61.0
	Female	23	39.0
Comorbidities	**HTN**	5	8.5

Figure 1: Distribution of patients with Diabetic Foot Ulcer Grade



It was observed that, with increase in duration of disease there are more chances of ulcer progression (grade 2: 8+/-3.89 and grade 3: 7.28+/-3.56). The mean FBS also found to be high in these grade 2 (217.68+/-86.19) and grade 3 (203.89+/- 37.08) ulcer patients. The results are not statistically significant as shown in Table-2.

Table 2: Association of age, duration of diabetes and Fasting blood sugar with diabetic foot ulcer

Parameters	Grade	N	Mean	Std. Deviation	F	P-value*
Age	Grade 1	10	55.60	10.66	1.072	0.369
	Grade 2	19	60.05	12.85		
	Grade 3	18	61.78	13.14		
	Grade 4	12	54.50	12.94		
Duration of Diabetes	Grade 1	10	6.30	1.64	0.671	0.573
	Grade 2	19	8.00	3.89		
	Grade 3	18	7.28	3.56		
	Grade 4	12	7.75	2.14		
FBS	Grade 1	10	174.30	58.81	1.077	0.367
	Grade 2	19	217.68	86.19		
	Grade 3	18	203.89	37.08		
	Grade 4	12	195.83	52.86		

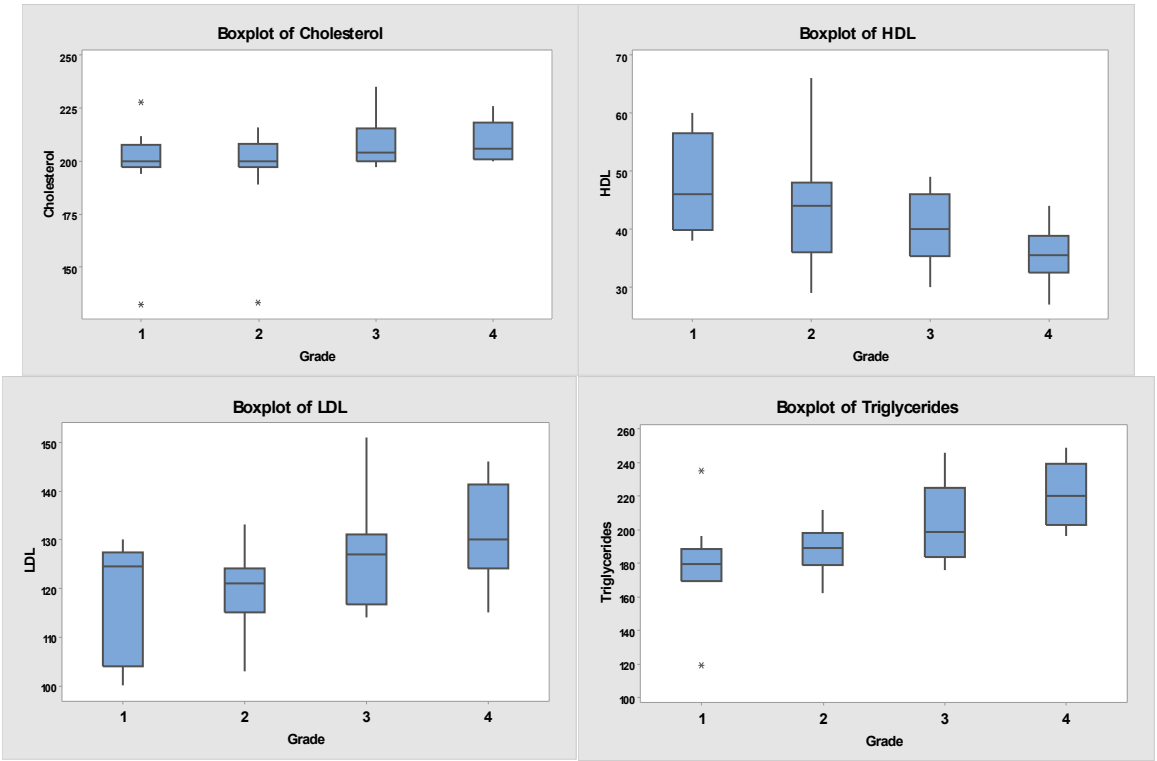
** Analysis of Variance*

The lipid profile were compared with grading of DFU and found to be strongly significant with HDL, LDL and TGs levels as shown in Table 3 and the boxplot.

Table 3: Association Lipid Profile with diabetic foot ulcer

Parameters	Grade	N	Mean	Std. Deviation	F	P-value*
CHOLESTEROL	Grade 1	10	197.20	24.85	1.951	0.131
	Grade 2	19	198.95	17.31		
	Grade 3	18	207.50	11.31		
	Grade 4	12	209.42	9.28		
HDL	Grade 1	10	47.90	8.95	5.446	0.002
	Grade 2	19	43.79	9.84		
	Grade 3	18	40.22	5.72		
	Grade 4	12	35.50	4.66		
LDL	Grade 1	10	119.00	11.53	4.498	0.007
	Grade 2	19	119.58	8.30		
	Grade 3	18	126.89	11.40		
	Grade 4	12	131.08	10.26		
TGs	Grade 1	10	178.70	28.64	10.021	<0.001
	Grade 2	19	187.37	13.96		
	Grade 3	18	203.94	22.04		
	Grade 4	12	220.33	18.32		

** Analysis of Variance*



V. Discussion

Research indicates a significant association between an abnormal lipid profile, particularly low levels of HDL cholesterol (good cholesterol), and the severity of diabetic foot ulcers (DFUs), suggesting that poor lipid management can contribute to increased risk and severity of DFU complications. Aggressive management of lipid profiles, aiming to raise HDL and lower LDL levels, could be a crucial part of preventing and managing diabetic foot ulcers. Also risk stratification by assessing lipid profiles can help identify diabetic patients at higher risk of developing DFUs, allowing for proactive monitoring and preventative measures.

The mean age of participants in this study is 58.69±12.65 with male preponderance of 61%. The maximum number of participants increased with age and duration of diabetes. There was one study which showed female preponderance.[12]

The maximum number with diabetic foot ulcer belonged to grade 2 and 3 (32.2% and 30%). The mean duration of diabetes and fasting blood sugar were high indication their association with DFU.

Our findings reinforce the role of dyslipidaemia in Diabetic Foot Ulcer (DFU) progression. The observed decline in HDL levels among patients with severe ulcers is consistent with previous research demonstrating HDL's protective role in endothelial repair and inflammation reduction.[8,13,14] Lower HDL levels are associated with impaired cholesterol efflux, increased oxidative stress, and delayed wound healing.[10]

In contrast, elevated LDL and TGs were strongly correlated with ulcer severity. High LDL levels contribute to atherosclerosis, reducing blood supply to the lower extremities and exacerbating ulcer severity.[10,13] Similarly, hypertriglyceridemia is associated with increased inflammation and endothelial dysfunction, further delaying wound healing. [10,13] But in one study it showed a paradoxical improvement.[15]

Our study also highlights the relationship between prolonged diabetes duration and higher FBS levels with ulcer severity. Poor glycaemic control promotes microvascular complications, leading to impaired immune responses and increased susceptibility to infections.[10] These findings emphasize the need for integrated metabolic management, including lipid and glucose control, to mitigate DFU progression.

Clinical Implications:

- Routine lipid profile screening can help identify diabetic patients at risk for severe DFUs.
- Early lipid-lowering interventions, including statins, omega-3 fatty acids, and lifestyle modifications, may improve ulcer healing outcomes.[11]
- A multidisciplinary approach, involving diabetologists, vascular surgeons, and nutritionists, is critical in optimizing DFU management.

Future studies should explore longitudinal interventions to establish causality and determine the effectiveness of lipid-lowering therapies in DFU prevention.

VI. Conclusion

Dyslipidaemia is significantly associated with DFU severity, highlighting the importance of lipid profile monitoring in diabetes care. Patients with lower HDL and elevated LDL and TGs exhibited more severe ulcers, reinforcing the need for early lipid interventions. Comprehensive metabolic control can play a pivotal role in reducing DFU-related complications and improving patient outcomes.

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