Original Article

PERIPHERAL UNILATERAL/ BILATERAL LIMB EDEMA AS AN EARLY WARNING SIGN IN DIABETES MELLITUS- A PROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Objective: Lower limb edema is one of the frequently encountered pathological conditions in the clinical scenario and subjected to critical evaluation. Multiple pathologies are involved in the development of limb edema. So the present study was conducted to evaluate peripheral unilateral/ bilateral limb edema an early warning sign in diabetes mellitus.

Methods: This was an observational study conducted on 71 patients presented with edema. Using quantitative and qualitative analysis, the cause and prognostic impact of diabetes mellitus in both unilateral and bilateral leg edema as well as in other pathologies were evaluated.

Results: In this study the prevalence of edema was 91.5% with majority of the patients (83.1%) with unilateral edema. In patients with edema, diabetes was present in 73.2% of the cases. There was significant association between the presence of edema in diabetes mellitus patients ($p=0.02$). . Further, there was no significant association in the formation of edema in ulcer, cellulitis, gangrene and filariasis patients ($p>0.05$).

Conclusion: Thus, limb edema is an early warning in diabetes or local diabetic foot diseases. An evaluation and accurate treatment must be followed to prevent morbidity and mortality.

Keywords: Limb edema, unilateral, diabetes, diabetic foot ulcer, filariasis.

Introduction

Edemais a pathological entity with fluid accumulation in intercellular tissueas a result of altered expansion of interstitial fluid volume. The presence of fluid between interstitial and intravascular spaces is mediated by capillary hydrostatic and oncotic pressure gradient across the capillary. When this equilibrium is distorted by systemic or local disease, the capillary hydrostatic pressure increases followed by increased plasma volume, reduced plasma oncotic pressure (hypoalbuminemia), elevated capillary permeability, or lymphatic obstruction.[1]Peripheral edemais the most prevalent clinical sign in cardiac, renal and hepatic diseases as well as during inflammation, metabolic diseases and pregnancy.[2]Further, adverse reaction mediated by drugs is also one of the possible causes of edema. Drug-induced edema specifically occurs in the lower extremities and forms in a week after drug intake and it is dose dependant.[3–5]Usually, type 2 diabetes mellitus (T2DM) displays higher prevalence of peripheral edema as compared to healthy subjects, but some anti-hyperglycemic medicines, precisely when taken along with insulin also leads to edema.[5] In a prospective study of 314 patients with diabetic

foot ulcers, the incidence of lower extremity edema is 38%.[6]In T2DM patients, occurrence of lower extremity edema lead to poor prognosis and it is significantly associated with amputation and mortality. T2DM is one of the vital and independent risk factor for cardiac failure and one of the leading causes for renal failure. Edemais one of the early sign for marked fluid retention and leads to cardiac overload and prelude to cardiac failure. Albeit,physicians understand the need of assessing the edema, accuracy and consistency in evaluating the edema impose a significant challenge. In this backdrop, the present study was conducted to evaluate peripheral unilateral/ bilateral limb edema an early warning sign in diabetes mellitus.

MATERIALS AND METHODS

This was an observational study conducted among the inpatients presented with edema. A total of 71 cases presented between March 2016 to December 2016 at the Department of General Surgery, Meenakshi MedicalCollege hospital & research institute, presented with edema of leg were investigated. Using quantitative and qualitative analysis, the cause and prognostic impact of diabetes mellitus in both unilateral and bilateral edema leg were assessed and also various aetiopathogenesis for edema of leg are also assessed and compared.

Patients with an active wound infection, untreated osteomyelitis, wide spread malignancy, systemically immuno-compromising disease, restless leg syndrome, Parkinson's disease, or any other disease that can cause involuntary movement during microvascular assessment were excluded from the study. Patients with deep and/or large ulcers that required copious bandaging that would have prohibited the donning of study socks were also excluded from the study.

STATISTICAL ANALYSIS

The continuous variables were displayed in frequencies. The association between categorical variables and the occurrence of edema was done cross tabs followed by Pearson's chi square test. The analysis was done using SPSS version 24.

RESULTS

Patients demographics and clinical characteristics

This was a prospective cross sectional study conducted among the 71 patients presented with edema including both unilateral and bilateral. Among the 71 patients, 43 (60.6%) were males and 28 (39.4%) were females. In this study, out of 71 analysed cases, edema was present in 65% of the patients (91.5%). Regarding the type of edema, majority of the cases 59 (83.1%) was presented with the unilateral edema. Further, the edema in majority of the patients 51 (71.8%) were due to the chronic conditions. The edema was painful in 42 (59.2%) of the patients. Among the 71 patients, foot ulceration was present in 37 (52.1%), cellulitis was observed in 30 (42.3%), gangrene was present in 9 (12.7%), filariasis was present in 6(8.5%) and varicoseveins / lymphedema was present in 19 (26.8%) of the patients. In our study, the prevalence of diabetes mellitus was higher, 52 (73.2%) among the patients presented with edema. The prevalence of edema was higher in males as compared to females but not significant (Pearson's Chi square p= 0.749).

Table 1: Association between diabetes mellitus and edema

Variables	**Edema**		**Total**	**Pearson's Chi square P value**
	No	Yes		

Diabetes Mellitus	No	4	15	19	0.02*
	Yes	2	50	52	
Total		6	65	71	

p value <0.05 was considered as statistically significant

Association between peripheral limb edema and etiological factors

In this study there was no significant association in the formation of edema in ulcer patients (Pearson's Chi square p= 0.336), edema in cellulitis patients (Pearson's Chi square p= 0.185), edema in gangrene (Pearson's Chi square p=0.339), edema in filariasis patients (Pearson's Chi square p=0.437) and varicoseveins or lymphedema (Pearson's Chi square p= 0. 179). However, in this study there was significant association between the presence of edema in diabetes mellitus patients (Pearson's Chi square p= 0.02). The results were shown in table1.

Association between diabetes and other comorbidities in the formation of edema

Further, in this study the development of leg ulcer was significantly (Pearson's Chi square P=0.009) associated with the presence of diabetes mellitus. The results were shown in table 2.

Table 2: Association between diabetes mellitus and leg ulcer

Variables		**Diabetes Mellitus**		**Total**	**Pearson's Chi square P value**
		No	Yes		
Ulcer	No	14	20	34	0.009*
	Yes	5	32	37	
Total		19	52	71	

p value <0.05 was considered as statistically significant

Meanwhile, there was no significant association in the formation of gangrene (Pearson's Chi square P=0.25) and cellulitis (Pearson's Chi square P=0.28) and the presence of the diabetes mellitus among the edema patients. Among the edema patients, there was a significant (Pearson's Chi square p=0.000) association between the presence of varicoseveins or lymphedema and diabetes mellitus. The results were shown in table 3.Among the edema patients, there was a significant (Pearson's Chi square P=0.02) association between the presence of filariasis and diabetes mellitus.

Table 3: Association between diabetes mellitus and varicose vein or lymphedema

Variables		**Diabetes Mellitus**		**Total**	**Pearson's Chi square P value**
		No	Yes		
Varicose veins or lymphedema	No	8	44	34	

	Yes	11	8	37	0.000*
Total		19	52	71	

p value <0.05 was considered as statistically significant

Risk factors for the development of edema

In the present study, based on the univariate analysis, multivariate logistic regression with the forward stepwise procedure, BMI (OR 1.8, 95% CI 1.0–2,4, P = 0.002), HDL-C (OR 3.2, 95% CI 1.2–7.8, P = 0.001), and microalbuminuria (OR8.1, 95% CI 2.1–2.6, P = 0.004) were independent risk factors for the progression of lower limb edema.

Table 4: Risk factors for the development of lower limb edema

Parameters	**B**	**S.E**	**Wals**	**df**	**Sig.**	**OR (95%CI)**
BMI	−19.564	0.54	1774.34	1	0.002*	1.8 (1.0–2.4)
Microalbuminuria	17.987	0.38	1654.76	1	0.004*	8.1 (2.1–2.6)
HDL-C	16.187	0.76	586.54	1	0.001*	3.2 (1.2–7.8)

* denotes significant p<0.05

The results were shown in table 4.

Advances in Knowledge

Peripheral limb edema is one of the frequently encountered clinical scenarios with significant mortality and morbidity

- The cause of peripheral edema involves multiple pathologies and hampers the diagnosis and management.
- Peripheral limb edema is one of complication of type 2 diabetes mellitus leading to amputation and mortality.
- However, peripheral limb edema as one of the early warning in type 2 diabetes mellitus is not well reported.
- So in the present study we have analysed the peripheral limb edema as one of the early warning sign in type 2 diabetes patients.

Application to patient care

- Routine diagnosis of diabetes mellitus must be performed for all the patients presenting peripheral limb edema.
- Proper management and observation must be carried out in the prevention of edema and strict glycemic control should be advised patients with regular follow ups.

DISCUSSION

Lower limb edema is a widely encountered clinical condition and it imposes a significant diagnostic challenge. Leg swelling occurs due to elevation in interstitial fluid, when it surpasses the competence of physiologic lymphatic drainage. In majority of the cases, fluid gathers in subcutaneous tissues and lead to volume expansion, albeit the other causes such as congenital pathologies and lipedema are involved in the fluid accumulation at lower extremities. Mounting pathologies such as infra-inguinal superficial and deep venous reflux supra and infra inguinal deep vein obstruction and primary and secondary lymphatic diseases are involved in the fluid accumulation. In most of the patients with age more than 50 years , the predominant cause of unilateral lower limb edema is venous disease with multiple etiological factors.[7]Previous study has shown that the chronic edema displays significant negative impact which affects the physical and mental health of the individuals and also reduces the quality of the life.[8]

In the present study the incidence of edema was higher in males as compared to females. Similar to the present study, previous study conducted in UAE reports that the prevalence of lower limb complication among the diabetics was higher in males as compared to females.[9]

In our study, there was no significant association between lower limb edema and lower leg cellulitis. However, in contrast in a study done by Cox,[10] among the 171 leg cellulitis patients, 49 patients displayed chronic edema and it has significant correlation with the development of leg cellulitis. In addition, we have not found any significant association between gangrene and lower limb edema. However, contrast reports exist in the case of wet gangrene where the bacterial infection of the necrotic tissue and secondary sepsis accompanies a poor prognosis and the affected part becomes markedly edematous, soft, rotten, and dark. [11]

In the present study, there was significant association between lower limb edema and diabetes mellitus. Lower extremity edema is often an early sign of significant fluid retention that could result in cardiac overload and conditions such as heart failure and is a common clinical finding in persons with diabetes.[12] Persons with type 2 diabetes mellitus especially, have a higher prevalence of peripheral edema than healthy subjects.[13] In a prospective study of 314 patients with diabetic foot ulcers, 38% presented with lower extremity edema.[6] The presence of lower extremity edema was an indicator of poorer prognosis as peripheral edema presented more commonly in patients who required amputation (58%) or died (55%).

Conclusion

But on the whole edema is found to be a significant early present sign in almost 90% of the cases thus making it a highly valuable sign which would require a detailed evaluation to know about the cause inducing and optimising the management therapy. Thus the prevalence of edema as a early warning sign in most of the conditions make us believe edema is the first sign of diabetes mellitus or local diabetic foot diseases which would require the necessary assessment and prophylactic management to reduce the advanced complications of the disease and optimising the delivery of care and reducing the emergence of advanced disease stage presentation among the population group.

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Conflict of Interest: Nil

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