



Original Research Article

TO DETERMINE THE CLINICOPATHOLOGICAL CHARACTERISTICS OF ULCERS ON THE LOWER LIMB AND DEVELOPING EFFECTIVE MANAGEMENT STRATEGIES

Abnish Kumar Karn¹

¹Associate Professor, Department of General Surgery, Sri Narain Medical College, Saharsa, Bihar, India.

Received : 02/02/2024
Received in revised form : 03/04/2024
Accepted : 18/04/2024

Corresponding Author:

Dr. Sumit Dhruve
Associate Professor, Department of
Community Medicine, SBDMS GMC
KORBA (C.G.), India.
Email: dr.avnishkarn@yahoo.com

DOI: 10.5530/ijmedph.2024.2.91

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2024; 14 (2); 465-470

ABSTRACT

Background: Chronic ulceration of the lower leg is a common ailment that occurs often in those over the age of 60. The prevalence of ulceration is increasing because to the aging population and heightened risk factors for atherosclerotic occlusion, such as smoking, obesity, and diabetes. Ulcers are characterized as sores that penetrate through all layers of tissue and have a propensity to heal slowly. Typically, the sluggish healing process is not just determined by the depth and size of the wound, but rather by an underlying pathogenetic element that must be eliminated in order to promote recovery. The primary factors contributing to this issue include venous valve insufficiency, lower extremity vascular disease, and diabetes. Less common causes include infection, vasculitis, skin cancers, and ulcerating skin illnesses including pyoderma gangrenosum. **Aim:** To determine the clinicopathological characteristics of ulcers on the lower limb and developing effective management strategies.

Materials and Methods: A total of 100 patients with lower leg ulcers were included in this research, all of whom attended the surgery outpatient department and were subsequently admitted to the surgery ward. The research included patients who expressed their willingness to participate, patients who were experiencing any kind of lower leg ulcers, and patients aged between 18 and 65 years.

Results: Among the 12 patients in our research who had varicose veins, the ulcers were determined to have a venous origin. Out of the patients included in our research, 8 individuals had symptoms of Raynaud's phenomenon. Additionally, the ulcers seen in these patients were shown to have an arterial origin. Among the 33 patients in our research who had loss of feeling, the primary causes of ulcers were diabetes, followed by arterial and venous factors. Our investigation found that 10 individuals had a lack of peripheral pulses, with arterial reasons being the primary factor contributing to the development of ulcers, followed by venous factors. Out of the total number of patients in our research, 43 of them had hypertension. The main causes of ulcers were diabetes, followed by an equal number of ulcers caused by arterial and venous factors. Out of the 58 patients in our research, the primary cause of ulcers was diabetes, followed by venous and arterial factors. Among the 65 patients in our research, a history of smoking was present. Our research included 45 patients who had surgical debridement. In our research, 15 individuals had amputation.

Conclusion: Our clinic's pathological examination highlights the need of a comprehensive, interdisciplinary approach to diagnosing and treating lower leg ulcers, in addition to contributing to the growing body of knowledge on this topic.

Keywords: Clinicopathological, Ulcers, Lower limb.

INTRODUCTION

A chronic leg ulcer, often referred to as a chronic lower limb ulcer, is a persistent lesion on the leg that does not exhibit any signs of healing after three months of adequate therapy or remains incompletely healed after twelve months.^[1] The prevalence of ulceration is increasing because to the aging population and heightened risk factors for atherosclerotic occlusion, such as smoking, obesity, and diabetes. Ulcers are sores that have a depth that extends through all layers of tissue and have a propensity to heal slowly. Skin ulcers may lead to the full loss of the outermost layer of skin, known as the epidermis, as well as parts of the layer underneath it called the dermis, and in certain cases, even the layer of fat beneath the skin known as subcutaneous fat.^[2] Lower leg and foot ulcers are a prevalent and extensively spread affliction that may be associated with a range of medical, surgical, and dermatological problems. The patient's distress is intense and is often noticed in both surgical wards and outpatient departments. Leg ulcer problems include a wide spectrum of diseases, causes, severity, and impact on health. The main causes include diabetes, lower extremity arterial disease, and insufficient venous valve function. Less often seen issues include infections, vasculitis, skin malignancies, and ulcerative skin conditions such as pyoderma gangrenosum.^[3] Nevertheless, there are instances where unusual circumstances occur, such as the newly discovered combination of increased blood clotting and inflammation of blood vessels. Having a comprehensive understanding of the many potential causes of leg ulcers is essential in order to provide suitable treatment to patients. Leg ulcers may provide challenges for surgeons due to their anatomical placement, which can lead to problems that need ingenuity and patience to address. Ulcers are more common in the aged population and are linked to increased risk factors for atherosclerotic occlusion, such as obesity, diabetes, and smoking. Over the last three decades, significant advancements have been made in understanding the structure, function, diseases, and medical interventions related to chronic leg ulcers. However, there is still potential for further advancements in the treatment of chronic leg ulcers.^[4] The work "Venous Leg Ulcers: Pathophysiology and Classification" by B Vasudevan.^[5] comprehensively discussed the pathophysiology, classification, clinical assessment, and investigative strategy to patients with leg ulcers. Leg ulcers may result from a multitude of factors. However, the majority of chronic leg ulcers (>90%) are caused by problems with blood vessels. Specifically, chronic venous hypertension is believed to be the main cause in around 70% of cases, while a mix of venous and arterial issues contributes significantly in the remaining 15% of cases. Arterial insufficiency is responsible for 5% of instances. The other instances may be attributed to diabetes, vasculitis, cancer,

hematological issues, rheumatoid arthritis, pressure, and other traumas.^[6] The authors have extensively addressed the pathophysiology of venous ulcers, including the clinical, etiologic, anatomical, and pathophysiological (CEAP) category. This categorization is essential for clinical evaluation and treatment. A short discussion of the pathophysiology of other common ulcers is warranted. Arterial leg ulcers are caused by reduced arterial blood flow and subsequent tissue perfusion. Three pathologic mechanisms have been identified: (a) extramural strangulation, (b) mural thickening or accretion, and (c) intramural blood flow restriction. It is projected that around 15% of individuals with diabetes may experience the development of diabetic foot ulcers at some stage throughout their lifetime. Diabetic foot ulcers usually have a multifaceted cause. Peripheral neuropathy has been identified as the primary cause of foot ulcers. Ulceration may be caused by three factors: peripheral neuropathy, biomechanical distortion, and superimposed mild trauma.^[7] Neuropathy-related loss of sensation often leads to unnoticed repetitive tension and pressure, which causes the breakdown of skin and soft tissues, creating an entry point for infection.

MATERIAL AND METHODS

The present investigation an interventional investigation was undertaken in the General Surgery department. A total of 100 patients with lower leg ulcers were included in this research, all of whom attended the surgery outpatient department (OPD) and were subsequently admitted to the surgery ward. The research included patients who expressed their willingness to participate, patients who were experiencing any kind of lower leg ulcers, and patients aged between 18 and 65 years. The research excluded patients who declined to participate, patients under the age of 18 or above the age of 65, immunocompromised patients, and patients with suspected cancer.

RESULTS

Among the 12 patients in our research who had varicose veins, the ulcers were determined to have a venous origin. The numerical value assigned to the variable z is 1.13. The value of p is less than 0.001. Out of the patients included in our research, 8 individuals had symptoms of Raynaud's phenomenon. Additionally, the ulcers seen in these patients were shown to have an arterial origin. The numerical value assigned to the variable z is 0.43. The value of p is less than 0.001. Among the 33 patients in our research who had loss of feeling, the primary causes of ulcers were diabetes, followed by arterial and venous factors. Z has a value of 1.32. The value of p is less than 0.001. Our investigation found that 10 individuals had a lack of peripheral pulses, with arterial reasons being the primary factor

contributing to the development of ulcers, followed by venous factors. The numerical value of z is 1.43. The value of p is less than 0.001. Out of the total number of patients in our research, 43 of them had hypertension. The main causes of ulcers were diabetes, followed by an equal number of ulcers caused by arterial and venous factors. Z has a value of 1.76. The numerical value assigned to the variable p is 0.001. Out of the 58 patients in our research, the primary cause of ulcers was diabetes, followed by venous and arterial factors. The numerical value of z is 1.34. The numerical value assigned to the variable p is 0.001. Among the 65 patients in our research, a history of smoking was present. The primary causes of ulcers in these individuals were diabetes, followed by venous and

arterial factors. Z has a value of 1.55. The value of p is less than 0.001. Our research included 45 patients who had surgical debridement. The primary causes of ulcers in these individuals were diabetes, followed by venous and arterial etiology. The numerical value assigned to the variable z is 1.31. The numerical value assigned to the variable p is 0.001. Our investigation included four individuals who had lumbar sympathectomy. The ulcers in these patients were caused by vascular factors. Z has a value of 0.88. The value of p is less than 0.001. In our research, 15 individuals had amputation. Among them, the ulcers were mostly caused by arterial factors, followed by an equal number of cases with diabetic and venous origins. The numerical value of z is 0.76. The value of p is less than 0.001.

Table 1: Gender and age of the participants

	Number	Percentage	P value
Gender			0.16
Male	64	64	
Female	36	36	
Age			0.02
Below 20	6	6	
20-30	11	11	
30-40	31	31	
40-50	36	36	
50-60	13	13	
Above 60	3	3	
Mean Age	47.34± 5.87		

Table 2: Causes of ulcers association with All Parameters

	Causes of ulcers	Absent	Present	Grand Total	Z	P Value
Varicose veins	Arterial	15	0	15	1.13	0.001
	Diabetes	36	0	36		
	Trauma	9	0	9		
	Venous	28	12	40		
	Grand Total	88	12	100		
Raynaud's phenomena	Arterial	7	8	15	0.43	0.001
	Diabetes	36	0	36		
	Trauma	9	0	9		
	Venous	40	0	40		
	Grand Total	92	8	100		
Loss of sensation	Arterial	4	11	15	1.32	0.001
	Diabetes	23	13	36		
	Trauma	9	0	9		
	Venous	31	9	40		
	Grand Total	67	33	100		
Peripheral pulses	Arterial	8	7	15	1.43	0.001
	Diabetes	0	36	36		
	Trauma	0	9	9		
	Venous	2	38	40		
	Grand Total	10	90	100		
HTN	Arterial	3	12	15	1.76	0.001
	Diabetes	21	15	36		
	Trauma	5	4	9		
	Venous	28	12	40		
	Grand Total	57	43	100		
DM	Arterial	11	4	15	1.34	0.001
	Diabetes	0	36	36		
	Trauma	9	0	9		
	Venous	22	18	40		
	Grand Total	42	58	100		
H/O Smoking	Arterial	2	13	15	1.55	0.001
	Diabetes	8	28	36		
	Trauma	5	4	9		
	Venous	20	20	40		
	Grand Total	35	65	100		

Surgical debridement	Arterial	12	3	15		
	Diabetes	7	29	36		
	Trauma	9	0	9	1.31	0.001
	Venous	27	13	40		
	Grand Total	55	45	100		
Lumbar sympathectomy	Arterial	11	4	15		
	Diabetes	36	0	36		
	Trauma	9	0	9	0.88	0.001
	Venous	40	0	40		
	Grand Total	96	4	100		
Amputation	Arterial	4	11	15		
	Diabetes	34	2	36	0.76	0.001
	Trauma	9	0	9		
	Venous	38	2	40		
	Grand Total	85	15	100		

DISCUSSION

Phillips, Tania, et al. reported that the prevalence of leg ulcers is estimated to be between 0.18% and 1%.^[8] Gilliland states that leg ulcers are mostly caused by vascular issues, which account for 95% of cases. Among all chronic wounds, lower limb venous ulcers are the most common, making up to 90% of cases. Arterial problems account for 10% to 5% of instances, whereas the remaining cases are either attributable to neuropathy or a combination of both.^[11,12] Our research, among a total of 100 patients, a majority of the individuals (36%) fell between the age range of 40-50 years. This finding was determined to be statistically significant with a p-value of 0.02. In the study conducted by Mohanta PK et al,^[13] it was shown that diabetes was the leading cause of ulcers, accounting for 36.3% of cases. Venous ulcers were the second most common cause, accounting for 22.3% of cases, followed by traumatic ulcers at 15.5%, arterial ulcers at 12.4%, and (Z=2.17; p=0.01). In addition, Yound J. R,^[11] observes that the prevalence of different kinds of ulcers varies throughout studies: venous ulcers vary from 70% to 90%, arterial ulcers from 5% to 15%, and miscellaneous ulcers from 1% to 5%.

Our analysis found that ulcers caused by vascular factors accounted for only 57 (57%) of all ulcers. Among the 100 patients, 40% had Venous ulcers, 34% had Diabetes ulcers, 17% had Arterial ulcers, and 9% had Traumatic ulcers. The numerical value assigned to the variable z is 3.47. The value of p is less than 0.00001. The research was undertaken by Callam M.J.^[12] Not just the elderly, but also 22% of the subjects in his investigation were found to have ulcerations that began before the age of 40. The average age of the patients in our research was 47.34± 5.87. Mohanta PK et al.^[13] discovered that the male population constituted 84.5% of the research participants, significantly higher than the female population (15.5%) (Z=9.89; p<0.0001). Based on our study findings, the male population accounted for 64% while the female population accounted for 36%. The observed difference was statistically significant at a significance level of p<.003. In the research conducted by Mohanta PK et al,^[13] the percentage of the left leg (49.2%) was higher than that of the right leg (47.2%). However,

this difference was not found to be statistically significant (Z=0.28; p=0.77). Out of all the patients, a mere 3.6% exhibited ulcers on both of their legs. In our study, 65% of the patients (n=65) were positioned on the left side, while the remaining 35% (n=35) were positioned on the right side. The value of Z is 2.78. The value of P is 0.007. In a study conducted by Mohanta PK et al,^[13] it was shown that 79.2% of the microorganisms causing the ulcer were identified, which was significantly higher than the 20.8% where no growth was seen (Z=8.25; p<0.0001).

During our analysis, we found that 46 out of 100 patients (46%) had sterile cultures, meaning no organisms were detected. On the other hand, 54 out of 100 patients (54%) had cultures that showed growth, indicating the presence of organisms. The value of Z is 0.45. The value of P is 0.32. Mohanta PK et al,^[13] discovered that the primary source of ulcers was muscle in 35.2% of cases, followed by bone in 26.4% of cases, and subcutaneous tissue in 24.9% of cases. In 6.7% of cases, just the skeletal foundation and a tendon were found. The values are as follows: p = 0.11 and Z = 1.58. Out of the total number of patients in our investigation, 54% had bone conditions, 23% had muscle conditions, and 23% had tendon conditions. The value of Z is 4.18. The value of P is 0.004. In Mohanta PK et al.'s research,^[13] the ulcer floors were mostly composed of inadequate granulation tissue and slough (36.3%), with pale granulation tissue and slough being the second most common (22.3%). The prevalence of cases with higher abnormal granulation tissue that expanded beyond the margin was 2.1%. The statistical analysis yielded a p-value of 0.03 and a Z-score of 2.17. Out of the total number of patients in our investigation, 51% were found to have Granulation Tissue, while 49% had Slough in the Floor. The value of Z is 0.19, whereas the value of P is 0.76. In the research conducted by Mohanta PK et al,^[13] it was shown that 38.3% of ulcer margins had irregular edges, which was significantly greater (Z=2.46; p=0.0139) compared to the prevalence of thin bluish irregular edges (22.3%). 55.4% of the ulcers had shallow margins, whereas 20.7% had sloping edges (Z=5.05; p<0.001). Only 3.1% of the ulcer edge displayed regularity.

Out of the total of 100 patients in our research, 49% exhibited punched out lesions, 47% had slopped lesions, and 4% had undermined lesions. The value of Z is 4.55. The value of P is less than 0.0001. In our research, 40 individuals (40%) exhibited an irregular margin, whereas 60 patients (60%) had a normal margin. Z has a numerical value of 1.89. The numerical value assigned to the variable p is 0.03. Research undertaken by Hansson Carita,^[14] reveals that vascular insufficiency and/or diabetes are the primary factors contributing to ulcers occurring below the shoe and foot line. Insufficient blood supply to the veins is the primary cause of ulcers on the medial region of the ankle in the gaiter zone.

In our research, we observed that out of 100 patients, 43% had ulcers in the foot, 52% had ulcers in the leg, and 5% had ulcers in the thigh. The numerical value of z is 5.43. The value of p is less than 0.001. Our research found that 6% of patients had Anterior, 26% had Dorsal, 27% had Lateral, 28% had Lateral, 25% had Medial, 8% had Plantar, and 8% had Posterior. Z has a numerical value of 2.42. The numerical value of p is 0.002. The frequency of peripheral vascular diseases increases with age, with persons aged 60 and beyond seeing a 7-fold greater occurrence compared to those under 20.^[14] Our research revealed that the prevalence of arterial and venous disorders was highest among those aged 40 to 50 years. Additionally, it was observed that venous ulcers were most prevalent among those aged 40 to 50 years, whereas arterial ulcers were more often detected in individuals over the age of 60 years.

In their ongoing examination of health and sickness in a community in Michigan, Coon et al,^[15] examined the frequency and occurrence of venous thromboembolism and other venous disorders. It is estimated that over 24 million individuals in the United States have "significant" varicose veins, while 6-7 million people have irregularities in the skin of their legs due to poor blood flow. Additionally, there are now or formerly 400,000-500,000 individuals who have had varicose ulcers. The adult population has a rather high occurrence rate of second iterations. Among the 100 patients in the research, 15 (15%) had arterial ulcers. Out of them, 5 (33.33%) were in the age range of over 50 years, which showed a statistically significant association with a higher prevalence in males. According to Itin & Winkelmann,^[16] a total of 8 individuals had Raynaud's phenomenon, whereas 7 patients did not have peripheral pulses. This difference was shown to be statistically significant. The occurrence of arterial ulcers, especially in individuals with thromboangiitis obliterans (TAO), is strongly associated with a history of smoking, as stated by Mekkes et al.^[17] Out of the patients, a lumbar sympathectomy was done on 2 individuals, which accounted for 18.18% of the total. Our analysis revealed that ulcers caused by diabetes were the primary factor contributing to hypertension in 43 people. Additionally, an equal number of cases

were attributed to both venous and arterial causes. The value of Z is 1.22, whereas the value of P is 0.001. Our research found that out of 100 individuals, 33 had loss of feelings. Among these patients, 13 had diabetic ulcers, which was determined to be statistically significant. According to van Deursen,^[18] hypertension is a consequence of diabetes. Singer et al,^[19] have identified the most common co-morbidities associated with diabetes ulcers. The optimal attire is the natural covering of your body, known as the skin (Lister). It has several uses in pinch grafting or as a graft of partial thickness. It is recommended to utilize conservative therapy for large ulcers or ulcers that do not heal.^[9] Mbunda F et al,^[20] performed a descriptive prospective investigation on 300 patients with chronic lower leg ulcers, with a median age of 32 years. The male-to-female ratio was 2:1. Traumatic ulcers constituted 60.3% of all ulcer types. 33.7% of cases often included the leg, while 48.7% of cases specifically affected the right side. Among the participants in this study, a total of sixty-eight individuals (22.7%) reported a history of cigarette smoking. Out of the 300 patients, 212 of them, which is equivalent to 70.7%, showed positive development of aerobic bacteria. Out of the individuals who had surgery, 270 of them (90.0%) received debridement, which was the most common surgical therapy in 24.1% of instances. The incidence of limb amputations was 8.7%. Out of the 54 patients, which accounts for 18.0% of the total, 32 (59.3%) had diabetes mellitus, 8 (14.8%) had chronic pulmonary diseases, 6 (11.1%) had hypertension, 4 (7.4%) had peripheral vascular diseases, and 2 (3.7%) had congenital cardiac disorders and obstructive jaundice. Postoperative complication the predictor (independent) variables include age (>20 years old, p value = 0.004), female sex (p value = 0.001), pre morbid comorbidities (p value = 0.041), infective ulcers (p value = 0.001), and metabolic ulcers (p value = 0.007).

John A. and others,^[21] The Italian Association for Cutaneous Ulcers (AIUC) funded a two-year observational study called "Studio Ulcere Vascolari" to monitor the occurrence and healing patterns of leg ulcers, as well as the most commonly used treatments for lower limb ulcers. This study was conducted across multiple centers and focused specifically on vascular ulcers of the lower limbs. The experiment included 59 diverse sites throughout 14 distinct regions in Italy, with a total of 1333 patients participating. Out of these patients, 1163 completed thorough assessment and were closely observed for a duration of nine months. An abundance of females (62%) was noted, with an average age of 70 years and a significant incidence of hypertension (62%), diabetes (38%), and obesity (29%). The most prevalent kind of ulcer was venous ulcer, accounting for 55% of cases, followed by mixed ulcers at 25% and diabetic ulcers at 8.3%. The frequency of these comorbidities varied depending on the type of ulcer, with significant

differences seen for hypertension and diabetes ($P < 0.001$, χ^2 test) and obesity ($P < 0.01$, χ^2 test). The level of granulation tissue was rather minimal, with a frequency ranging from around 17% to 23%. The exudate was seen in all of the ulcers, mostly of moderate severity, with a frequency ranging from 41.9% (arterial ulcers) to 47.9% (mixed ulcers). A study has shown that patients who received medications in combination with local treatment (LT) exhibited a statistically significant improvement ($P = 0.001$). The presence of blood hypertension in venous ulcers was shown to have a substantial negative impact on the healing process, with an odds ratio (OR) of 1.45 (95% confidence interval [CI]: 1.07-2.06; $P < 0.02$). Similarly, obesity was also found to have a negative impact, with an odds ratio of 1.46 (95% CI: 1.04-2.04; $P = 0.03$). Obesity was shown to be a harmful factor for the healing of mixed ulcers, with an odds ratio (OR) of 1.73 (95% confidence interval [CI]: 1.01-2.97; $P < 0.05$). The study done by Dhakal P et al,^[22] focused on patients who had varicose veins in the vast saphenous system. It was a retrospective observational investigation. The pigmentation and ulceration of varicose veins are affected by factors such as age, gender, duration of the condition, and symptoms. The total number of patients was 223. The male-to-female ratio was 1.47, suggesting a higher number of male patients. The mean age was 43.7 years with a standard deviation of 13.4. For males, the mean age was 41.8 years with a standard deviation of 14.3, while for women, the mean age was 46.4 years with a standard deviation of 11.9. Four variables substantially predicted the occurrence of ulceration in varicose veins. There were strong indicators for pain ($\beta = 0.366$, $P < 0.01$), itching ($\beta = 0.355$, $P < 0.01$), illness duration ($\beta = 0.204$, $P < 0.01$), and being male ($\beta = 0.196$, $P < 0.01$). Age, meanwhile, did not have a substantial impact on the likelihood of ulceration.

CONCLUSION

Our clinic's pathological examination highlights the need of a comprehensive, interdisciplinary approach to diagnosing and treating lower leg ulcers, in addition to contributing to the growing body of knowledge on this topic.

REFERENCES

- Kuntoji SB, Guduru PK. Clinical and aetiological study of chronic lower limb ulcers. *Int Surg J* 2021; 8:1839-43.
- Rodrigues J, Salelkar R, Rodrigues FCS. A clinicopathological study on management of diabetic foot ulcer in tertiary care centre. *Foot (Edinb)*. 2023 Mar; 54:101971. doi: 10.1016/j.foot.2023.101971. Epub 2023 Feb 5. PMID: 36773396.
- Kumar AS, Binitha MP, Sarita S. A clinical and aetiological study of chronic leg ulcers. *Int J Contemporary Med Res*. 2016;3(12):3438-40.
- Gajjam Shrinivas A, AmolW. Study of the pathogenesis and diagnosis of ulcer of lower extremity under various conditions. *Int J Res Med Sci* 2016;4:621-7.
- Vasudevan B. Venous leg ulcers: Pathophysiology and classification. *Indian Dermatol Online J*. 2014; 5:366-70.
- Ghuri AS, Nyamekye I, Grabs AJ, Farndon JR, Poskitt KR. Improving the diagnosis of chronic leg ulcers: A one-stop vascular assessment clinic in a community service. *Phlebologie*. 1998; 13:148-52.
- Reiber GE, Vileikyte L, Boyko EJ, del Aguila M, Smith DG, Lavery LA, et al. Causal pathways for incident lower-extremity ulcers in patients with diabetes from two settings. *Diabetes Care*. 1999; 22:157-62.
- Phillips Tania et al. A Study of the Impact of Leg Ulcers on Quality of Life – Financial, Social and Psychological Implications, *J Am Acad Dermatol*, 1994; 31: 49-53.
- Gilliland E. L., John H. N. et al. ABC of vascular diseases: Leg ulcers. *Br Med J* 303: 776-779.
- Burton CS, Treatment of Leg Ulcers, *Dermatol Clin*, 1993; 11: 315-23
- Yound JR, 1983, Differential Diagnosis of Leg Ulcers, *Card Vaso Clin*, 13: 171-93.
- Callam MJ, et al, Chronic Ulcers of the Leg: Clinical History, *Br Med J*, 1987; 294: 1389-91.
- Mohanta PK, Mallik C, Chatterjee SK. A comprehensive study of clinical features and management of ulcers of the lower limb. *International Surgery Journal*. 2019 Oct 24;6(11):4024-31.
- Hansson Carita, Studies on Leg and Foot Ulcers, Stockholm, *Acta Derm Venereol*, 1988; 45.
- Coon, W. W., Willis, P. W., & Keller, J. B. (1973). Venous thromboembolism and other venous disease in the Tecumseh community health study. *Circulation*, 48(4).
- Itin, P. H., & Winkelmann, R. K. (1991). Cutaneous manifestations in patients with essential thrombocythemia. *Journal of the American Academy of Dermatology*, 24(1).
- Mekkes, J. R., Loots, M. A. M., van der Wal, A. C., & Bos, J. D. (2003). Causes, investigation and treatment of leg ulceration. *The British Journal of Dermatology*, 148(3), 388-401.
- van Deursen, R. (2004). Mechanical loading and off-loading of the plantar surface of the diabetic foot. *Clinical Infectious Diseases*, 39(SUPPL. 2).
- Singer, A. J., Tassiopoulos, A., & Kirsner, R. S. (2017). Evaluation and Management of Lower- Extremity Ulcers. *New England Journal of Medicine*, 377(16).
- Mbunda F, Mchembe MD, Chalya PL, Rambau P, Mshana SE, Kidenya BR, Gilyoma JM. Experiences with Surgical treatment of chronic lower limb ulcers at a Tertiary hospital in northwestern Tanzania: A prospective review of 300 cases. *BMC dermatology*. 2012 Dec;12(1):1-0.
- Apollonio A, Antignani PL, Di Salvo M, Failla G, Guarnera G, Mosti G, Ricci E, SUV Study Group. A large Italian observational multicentre study on vascular ulcers of the lower limbs (Studio Ulcere Vascolari). *International Wound Journal*. 2016 Feb;13(1):27-34.
- Dhakal P, Karmacharya RM, Vaidya S, Singh AK, Thapa P, Dahal S, Bhandari N, Bade S, Shrestha P. Influence of age, gender, duration of illness, and symptoms on pigmentation/ulceration in varicose veins of the great saphenous system. Combination therapy in the treatment of varices. 2020;27(3):106- 12.