

A Prospective Study of Factors Affecting On the Outcome in Diabetic Foot Ulcer Patients

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Abstract

Background: In diabetes mellitus patients there is a 15% increased lifetime risk of developing a foot ulcer. There have been many studies conducted to know the role of various risk factors that worsens the outcome in diabetic foot ulcers and among them important are reduced blood sugars levels, peripheral neuropathy, ischemia, joint deformity, and infection. This study was designed to evaluate various factors affecting on the outcome in diabetic patients with foot ulcers.

Methods: A prospective study was conducted on 125 diabetic patients with foot ulcers who attended Sri Venkateshwara Ramnaraian Ruiya Government General Hospital, Tirupati. Patient age, sex, rural/urban origin, type and duration of diabetes, history of trauma, duration of ulcer, previous history of ulceration, previous treatment, and site of ulcer was recorded on the first visit. Outcomes recorded as complete healing or lower extremity amputation (LEA). LEA is defined as major amputation if there is loss of any part of the lower limb above the ankle and as minor if below this joint.

Results: In the present study, the majority, 36% of the cases belong to the age group of 51 – 60 years. In patients with WBC count between 4000 – 11000 cells/cu.mm, 48.9% of cases managed conservatively, and in 11000 – 15000 cells/cu.mm, 32% of the cases had Minor amputation while in cases with WBC count >15000 cells/cu.mm, the majority (66.7%) had Major amputation. In the present study, creatinine levels >4.0 mg/dl was noted in 21.6% with mean creatinine level 2.79 ± 1.75 . Conservatively managed with serum Creatinine 1.0mg/dl (75%) and 1.1 – 2.0 mg/dl (63.4%), while conservative treatment (34.1%) and Disarticulation (29.3%) were commonly done in cases with serum creatinine 2.1– 4.0 mg/dl. In cases with serum Creatinine levels >4.0 mg/dl, 44.4% of the cases had Minor amputation, and 48.1% of cases had Major amputation, and the difference was found to be statistically significant ($p = 0.000$).

Conclusion: From this study it was concluded that age, long duration of diabetes, ischemia, high serum creatinine and WBC levels were considered as the risk factors for the poor outcome in diabetic foot ulcer patients. Patients at high risk of foot complications need more frequent monitoring including counselling, professionally fitted footwear, and early referrals to a tertiary care centre with trained professionals in foot ulcer management.

Keywords: Diabetics, Foot ulcers, Renal failure, Risk factors, Mortality, Prevention

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I. Introduction

Of all the people diagnosed with diabetes mellitus, there is a 15% increased lifetime risk of developing a foot ulcer. Limb amputation is one of the consequences of a foot ulcer, which occurs commonly in people with diabetes when compared to nondiabetics^{1,2,3}. More than one million diabetic patients lose a leg worldwide as a consequence of this disease. There have been many studies conducted to know the role of various risk factors that worsens the outcome of diabetic foot ulcers and among them important are reduced blood sugars levels, peripheral neuropathy, ischemia from peripheral arterial disease, structural damage to the foot, and infection^{4,5}.

A multidisciplinary team approach is always needed to achieve better results in patients with diabetic foot ulcers^{6,7}. At least 40% of amputations in diabetic patients can be prevented with effective wound care and management. Among all the other complications diabetic foot ulcers incidence is increasing recently at a high rate despite of all treatment options⁸. Amputation is always the last resort in patients with diabetic foot ulcers with failed conservative treatment. In the United States overall, 3% of the total population suffer from Diabetic Mellitus and, half of them lose their limbs because of foot ulceration⁹. Annually 1 to 4 % of diabetic patient develop foot ulcers and 15% once in their lifetime¹⁰. 85% of patients with intractable foot ulcers have undergone lower limb amputations¹¹.

There are various factors that alter the outcome of diabetic foot ulcers including the age of onset of diabetes, duration of diabetes, age and sex of patient, socioeconomic status, living status, haemoglobin A1C

levels (HbA1C), white blood cell count (WBC), C-reactive protein (CRP), and serum creatinine. Several studies demonstrated the role of risk factors in treatment failure in diabetic patient foot ulcers but some of them were controversial. Therefore, this study was focussed on assessing the role of various factors affecting on the outcome (Complete healing versus lower extremity amputation (LEA)) of diabetic foot ulcer patients.

II. Materials And Methods

Study Design: Prospective Observational Study

Study Subjects: 125 Diabetic patients with foot ulcers were included in the study.

Study Settings: Department of General Surgery, Sri Venkateshwara Ramnaraian Ruiya Government General Hospital, Tirupati.

Study Period: One Year From the approval by Ethical Committee

Inclusion Criteria:

1. Patients with Diabetic Foot Ulcers
2. Patient with recurrent Diabetic Foot Ulcers

Exclusion Criteria:

1. Patient with Foot Ulcers and Non-Diabetic
2. Patients not willing to participate in the Study

Methodology:

A prospective study was conducted on diabetic patients with foot ulcers who attended Sri Venkateshwara Ramnaraian Ruiya Government General Hospital, Tirupati. Patient age, sex, rural/urban origin, type and duration of diabetes, history of trauma, duration of ulcer, previous history of ulceration, previous treatment, and site of ulcer was recorded on the first visit. Important laboratory tests like complete blood count, fasting/ random blood sugar, blood urea, and creatinine was collected at the first visit. Clinical signs of infection, ischemia, and neuropathy were recorded at presentation. Wound depth was evaluated using a sterile blunt probe. The ability to probe to bone along with the presence of local or systemic infection and suggestive radiological features provides a clinical diagnosis of osteomyelitis. Each patient was assessed for the vascular status by manual palpation of femoral, popliteal, dorsalis pedis, and posterior tibial arteries to define patency and grade. Patients having clinical signs of ischemia were considered for non-invasive ultrasound (Doppler) vascular studies. Wound debridement was done to drain the pus and remove necrotic tissue and extensive callus. After discharge from the hospital, patients were initially seen in the OPD on a weekly basis, and later as the healing started on a monthly basis. Outcomes recorded as complete healing or lower extremity amputation (LEA). LEA is defined as major amputation if there is loss of any part of the lower limb above the ankle and as minor if below this joint.

III. Results

Table 1: Comparison of Treatment given with various socio-demographic variables – Age

Age group	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
21 – 30	1 (100%)	0	0	0	1
31 – 40	7 (77.8%)	0	1 (11.1%)	1 (11.1%)	9
41 – 50	11 (44%)	8 (32%)	3 (12%)	3 (12%)	25
51 – 60	19 (42.9%)	6 (13.3%)	10 (22.2%)	10 (22%)	45
61 – 70	9 (31%)	7 (24.1%)	5 (17.2%)	8 (27.6%)	29
71 – 80	6 (46.2%)	2 (15.4%)	2 (15.4%)	3 (23.1%)	13
81 – 90	0	1 (33.3%)	2 (66.7%)	0	3
Total	53 (42.4%)	24 (19.2%)	23 (18.4%)	25 (20%)	125(100%)

Chi square = 19.46, df = 18, p = 0.362

In our study, conservative management was the most common treatment given for the cases in the age group 21 – 30 years (100%), 31 – 40 years (77.8%), 41 – 50 years (44%) and 51 – 60 years (42.9%). In the age group of 61 - 70 years, 31% of the subjects underwent conservative management followed by, Major amputation in 27.6% of cases and Disarticulation in 24.1% cases. Minor amputation was done in 17.2% of cases. In the age group of 71 – 80 years, 46.2% of the cases underwent Conservative management followed by Major amputation in 23.1% of cases. In the age group of 81 – 90 years, 66.7% of the cases underwent Minor amputation, while 33.3% of the cases underwent Disarticulation.

Table 2: Comparison of Treatment given with various socio-demographic variables – Gender and area of residence

Gender	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
Male	32 (42.7%)	14 (18.7%)	14 (18.7%)	15 (20%)	75
Female	21 (42%)	10 (20%)	9 (18%)	10 (20%)	50
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)
Chi square = 0.038, df = 3, p = 0.998					
Residence	Conservative	Disarticulation	Minor amputation	Major amputation	Total
Rural	43 (45.7%)	14 (14.9%)	17 (18.1%)	20 (21.3%)	94
Urban	10 (32.3%)	10 (32.3%)	6 (19.4%)	5 (16.1%)	31
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)
Chi square = 4.990, df = 3, p = 0.173					

In our study, conservative management was the most common treatment given both for males (42.7%) and females (42%) followed by Major Amputation (20%) in males and Major amputation (20%) and Disarticulation (20%) in females. While 45.7% of the cases from rural areas underwent conservative management, 32.3% of the cases from urban regions underwent conservative management, and 32.3% underwent Disarticulation.

Table 3: Comparison of Treatment given with Duration of Diabetes (in years)

Duration of Diabetes (in years)	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
0 – 1	5 (45.5%)	2 (18.2%)	3 (27.3%)	1 (9.1%)	11
2 – 5	35 (52.2%)	12 (17.9%)	9 (13.4%)	11 (16.4%)	67
6 – 10	9 (26.5%)	7 (20.6%)	6 (17.6%)	12 (35.3%)	34
11 – 15	2 (28.6%)	2 (28.6%)	3 (42.9%)	0	7
16 – 20	1 (50%)	0	0	1 (50%)	2
>20	1 (25%)	1 (25%)	2 (50%)	0	4
Total	53 (42.4%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)
Chi square = 19.44, df = 15, p = 0.194					

In our study, in cases with a duration of diabetes 0 – 1 year, 45.5% underwent conservative management, followed by 27.3% underwent Minor amputation. In cases with duration 2 – 5 years, 52.2% underwent conservative management, and in with period 6 – 10 years, 35.3% underwent Major amputation followed by conservative management in 26.5%. In cases with duration 11 – 15 years, the majority of the cases (42.9%) underwent minor amputation and in cases with duration 16 – 20 years, 50% underwent Major Amputation, and in cases with duration >20 years, the majority of the cases (50%) underwent Minor amputation.

Table 4: Comparison of Treatment given with Organism isolated in culture

Organism isolated in culture	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
Staphylococcus	17 (37.8%)	10 (22.2%)	10 (22.2%)	8 (17.8%)	45
Pseudomonas	6 (24%)	4 (16%)	9 (36%)	6 (24%)	25
Non Hemolytic Streptococcus	3 (37.5%)	1 (12.5%)	1 (12.5%)	3 (37.5%)	8
Klebsiella	8 (53.3%)	2 (13.3%)	1 (6.7%)	4 (26.7%)	15
E. coli	2 (50%)	1 (25%)	1 (25%)	0	4
Mixed	3 (27.3%)	4 (36.4%)	1 (9.1%)	3 (27.3%)	11
Negative	14 (82.4%)	2 (11.8%)	0	1 (5.9%)	17
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)
Chi square = 27.025, df = 18, p = 0.079					

In this study, conservative management was done in 37.8% of staphylococcus positive, 24% of Pseudomonas positive, 37.5% of nonhemolytic streptococcus, 53.3% of Klebsiella positive and 50% of E.coli positive cases. Disarticulation was done in 36.4% of cases with culture positive for Mixed organisms and 25% of E.coli positive cultures. Minor amputation was done in 36% of Pseudomonas positive, 25% of E.coli positive, and 22.2% of positive staphylococcus cases. Major amputation was done in 37.5% of Nonhemolytic streptococcus positive, 26.7% of Klebsiella positive, and 27.3% of mixed culture-positive cases. In cases where cultures were negative, 82.4% of them had conservative management while 20%, 19.2%, and 18.4% had Major amputation, Disarticulation, and Minor amputation, respectively.

Table 5: Comparison of Treatment given with Blood sugar level at the time of admission

Blood sugar (mg/dl)	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
<120	7 (87.5%)	0	1 (12.5%)	0	8
120 – 200	20 (57.1%)	8 (22.9%)	2 (5.7%)	5 (14.3%)	35
>200	26 (31.7%)	16 (19.5%)	20 (24.4%)	20 (24.4%)	82
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)

Chi square = 17.40, df = 6, p = 0.008

In this study, in cases with blood sugar levels <120mg/dl, majority (87.5%) of the cases received conservative treatment, while in cases with blood sugar levels >200mg/dl, 24.4% received Minor amputation and 24.4% received Major amputation, and the difference was found to be statistically significant (p = 0.008).

Figure 1: Comparison of Treatment given with Blood sugar level at the time of admission

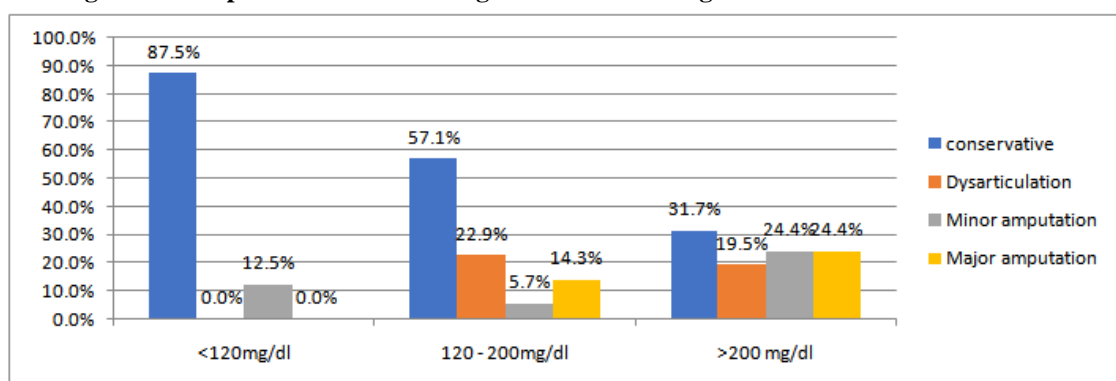


Table 6: Comparison of Treatment given with serum Creatinine levels of the cases

Se. Creatinine (mg/dl)	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
≤1.0	12 (75%)	3 (18.8%)	0	1 (6.3%)	16
1.1 – 2.0	26 (63.4%)	8 (19.5%)	3 (7.3%)	4 (9.8%)	41
2.1 – 4.0	14 (34.1%)	12 (29.3%)	8 (19.5%)	7 (17.1%)	41
>4.0	1 (3.7%)	1 (3.7%)	12 (44.4%)	13 (48.1%)	27
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)

Chi square = 54.218, df = 9, p = 0.000

In this study, conservative treatment was most commonly done in cases with serum Creatinine ≤1.0mg/dl (75%) and 1.1-2.0 mg/dl (63.4%), while conservative treatment (34.1%) and Disarticulation (29.3%) were commonly done in cases with serum creatinine 2.1-4.0 mg/dl. In cases with serum Creatinine >4.0 mg/dl, 44.4% of the cases had Minor amputation, and 48.1% of cases had Major amputation, and the difference was found to be statistically significant (p=0.000).

Figure 2: Comparison of Treatment given with serum Creatinine levels of the cases

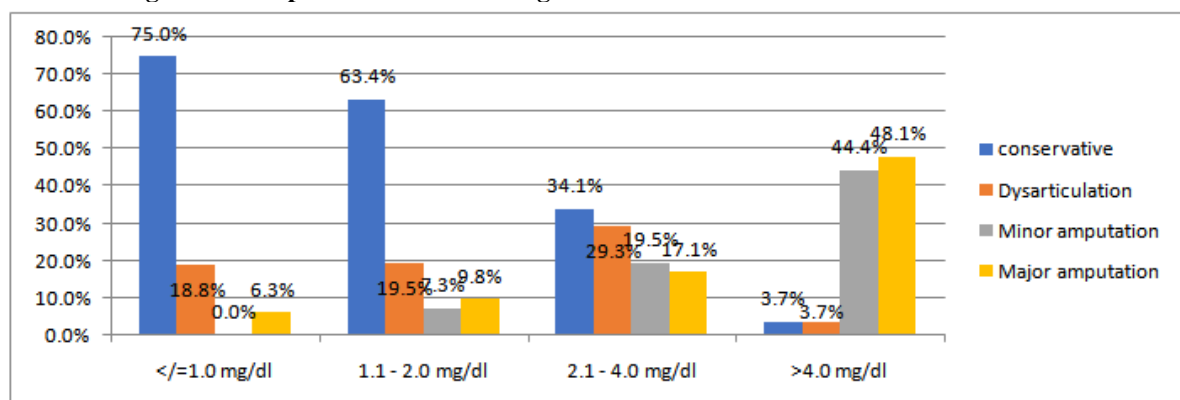


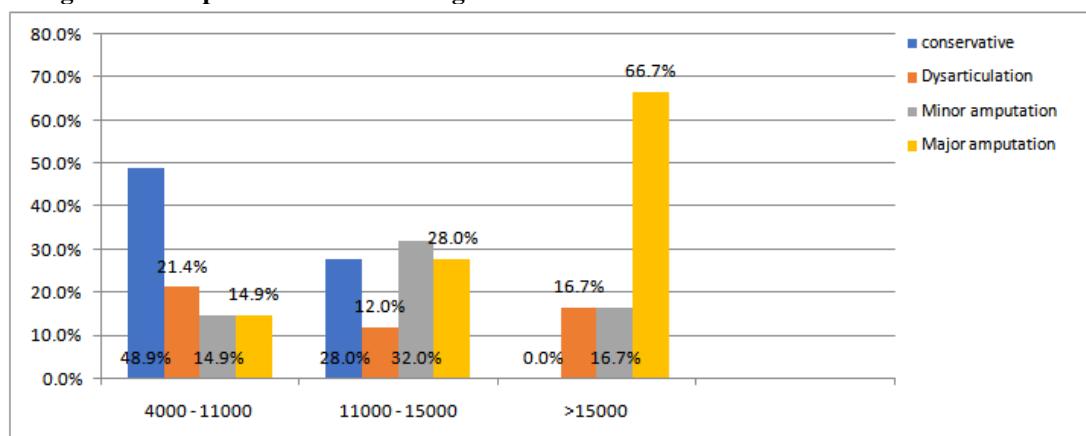
Table 7: Comparison of Treatment given with serum White Blood Cell counts of the cases

WBC count (cells/ cu.mm)	Treatment				Total
	Conservative	Disarticulation	Minor amputation	Major amputation	
4000 – 11000	46 (48.9%)	20 (21.4%)	14 (14.9%)	14 (14.9%)	94
11000 – 15000	7 (28.0%)	3 (12%)	8 (32%)	7 (28%)	25
>15000	0	1 (16.7%)	1 (16.7%)	4 (66.7%)	6
Total	53 (42.2%)	24 (19.2%)	23 (18.4%)	25 (20%)	125 (100%)

Chi square = 17.40, df = 6, p = 0.008

In our study, in cases with WBC count between 4000 – 11000 cells/cu.mm, 48.9% of cases had the conservative treatment, and in 11000 – 15000 cells/cu.mm, 32% of the cases had Minor amputation while in cases with WBC count >15000 cells/cu.mm, the majority (66.7%) had Major amputation, and the difference was found to be statistically significant (p = 0.008).

Figure 3: Comparison of Treatment given with serum White Blood Cell counts of the cases



IV. Discussion

In patients with diabetes, foot ulcers are the most crucial reason for the hospitalizations and morbidity. Many researchers studied the importance of various factors that may cause poor outcomes in diabetic foot ulcer patients. Several studies are still in progress to predict the exact cause of the foot ulcers and its poor outcome. The results differ from study to study and show that patient with similar wounds and clinical status shows the different outcome, with treatment remaining the same. In this study, various socio-demographic, clinical, and biochemical factors have been assessed to identify the reason for poor outcome in diabetic patients with foot ulcers. This help in designing new interventions and techniques to reduce the morbidity and mortality associated with diabetic foot ulcer and, further reduce the economic burden to the patients.

In this study one hundred twenty-five diabetic patients with foot ulcers were studied, and results are as follows. The majority of patients were male (60%) and are in the range of 50-60 years old. With the increasing incidence of diabetic foot ulcers in male patients, the individual families get affected more, which in turn affects

the community¹². Our study shows that 75.2% of patients came from rural areas and 24.8% from urban areas. While 45.7% of the cases of rural regions underwent conservative management, 32.3% of the cases from urban areas underwent conservative management, and 32.3% underwent Disarticulation. People living in rural areas have limited access to health care facilities and is the sole reason for the poor outcome.

Most of the diabetic foot ulcers are associated with type2 diabetes mellitus. In this study, 98.4% of patients have type 2 diabetes mellitus, and 65.6% of the cases presented with blood sugar levels > 200 mg/dl at the initial presentation, and 28% presented with initial blood sugars less than 200 mg/dl. In the present study, in cases with blood sugar levels <120mg/dl, majority (87.5%) of the cases received conservative treatment, while in cases with blood sugar levels >200mg/dl, 24.4% received Minor amputation and 24.4% received Major amputation, and the difference was found to be statistically significant ($p = 0.008$). Elevated blood sugars considered as an independent risk factor for lower extremity amputations in patients with a diabetic foot ulcer.

As the duration of diabetes mellitus increases, the healing of ulcers gets delayed. Nonhealing ulcers with uncontrolled blood sugars always had poor results. In the present study, 2- 5 years was the duration of diabetes in the majority (53.6%) of the cases, followed by 6-10 years in 27.2% cases. 3.2% of the cases had diabetes for more than 20 years, and the mean duration of diabetes was 5.8 ± 4.9 years.

In this study, 45.5% of patients treated conservatively followed by 27.3% with Minor amputation with recent onset of diabetes mellitus (0 – 1 year). where as in patients with 2- 5 years of duration, 52.2% treated conservatively. In patients with 6 – 10 duration of diabetes mellitus, 35.3% underwent Major amputation followed by conservative management in 26.5%. In cases with duration 11 – 15 years, majority of the cases (42.9%) underwent Minor amputation and in cases with duration 16 – 20 years, 50% underwent Major Amputation, and in cases with duration >20 years, majority of the cases (50%) underwent Minor amputation. With these results, it was estimated that as the duration of diabetes mellitus increases, the outcome becomes poor and leads to amputation (Major or Minor) of the lower extremity.

In the present study, specific baseline clinical and biochemical results were examined to predict the risk for poor outcomes and major amputations in diabetic foot ulcer patients. In particular, the potential relation between baseline laboratory results and the risk of poor outcome was studied. Baseline Acute phase reactants like CRP, WBC were closely associated with poor outcome in diabetic foot ulcer patients. A WBC count >12.0 cells/ μ L was associated with increased risk for amputation¹⁴. In the present study, WBC levels of the majority of cases (75.2%) were between 4000 – 11000 cells/cu.mm, they are followed by 11000 – 15000 cells/cu.mm in 20% of the cases. The mean WBC level in the study was 9202.4 ± 3270.6 cells/cu.mm. In cases with WBC count between 4000 – 11000 cells/cu.mm, 48.9% of cases had the conservative treatment, and in 11000 – 15000 cells/cu.mm, 32% of the cases had Minor amputation while in cases with WBC count >15000 cells/cu.mm, the majority (66.7%) had Major amputation, and the difference was found to be statistically significant ($p = 0.008$). These results suggest that diabetic foot ulcer patients with WBC count >15000 had more risk of undergoing major amputation of the lower extremity.

Elevated serum creatinine levels reflect renal function, and WBC levels reflect the presence and level of infection. Some studies reported that patients who had lower extremity amputation were incapable of combating infection and had a high serum creatinine level. In a study done by Sun et al.¹⁵, renal function was not considered as a significant risk factor, whereas Margolis et al.¹⁶, Yang et al.¹⁷, and Akha et al.¹⁸ did. In our opinion, the authors followed different methodologies and selection criteria. According to a study done by Lee KM et al.¹⁹, serum creatinine levels show no change between initial and late stages in both treatment success and failure group, but in the treatment success group with low serum creatinine levels at initial presentation shows a significant decrease in the WBC levels. Whereas in the treatment failure group with high serum creatinine levels show no change and is insignificant. With these results, the authors' assumed that patients with low serum creatinine at initial visit show decreased WBC levels and severity of infection, but with high serum creatinine levels, the infection cannot be controlled. This leads to a poor outcome or loss of a lower extremity. Some studies demonstrated that neutrophil glycolysis is disturbed in diabetic patients with altered renal function²⁰. This, in turn, cause phagocytic dysfunction by an accumulation of uremic toxins in the body²¹. The patients with high serum creatinine levels at the initial presentation had poor prognosis and outcome. Thus, this study focused more on the association between the elevated serum creatinine levels and the poor outcome of diabetic foot ulcer-like lower limb amputation. Multifactorial events cause amputation in diabetic patients, and we believe that the unification of other conditions is essential.

The diabetic foot infection requires a multi-professional approach with attention to local and systemic factors²². Aerobic Gram-positive cocci, especially Staphylococcus aureus, are the most common cause of diabetic foot infection. Individuals with chronic foot ulcers and previous antibiotic therapy often have infections with both Gram-positive and gram-negative organisms. Gangrenous and severely ischemic ulcers are commonly co-infected with anaerobic pathogens²³. The diagnosis of infection is clinical by identifying associated symptoms and signs such as redness, edema, increased temperature, and pain. In the present study, the most common organism isolated in culture was Staphylococcus in 36% of the cases followed by Pseudomonas and

Klebsiella in 20% and 12% of the cases, respectively. In the present study, conservative management was done in 37.8% of Staphylococcus positive, 24% of Pseudomonas positive, 37.5% of Non-haemolytic streptococcus, 53.3% of Klebsiella positive and 50% of E.coli positive cases. Dysarticulation was done in 36.4% of cases with culture positive for mixed organisms and 25% of E.coli positive cultures. Minor amputation was done in 36% of Pseudomonas positive, 25% of E.coli positive, and 22.2% of positive staphylococcus cases. Major amputation was done in 37.5% of non-haemolytic streptococcus positive, 26.7% of Klebsiella positive, and 27.3% of mixed culture-positive cases. In cases where cultures were negative, 82.4% of them had conservative management while 20%, 19.2%, and 18.4% had Major amputation, Disarticulation, and Minor amputation, respectively.

V. Summary

From this study it was noted that age, uncontrolled diabetes, ischemia, previous history of ulcers, high serum creatinine and WBC levels were considered as the risk factors for the poor outcome in diabetic foot ulcer patients. The results obtained from this study are statistically significant. The outcome is more severe if the patient presents with multiple factors than the individual factor. In foot ulcer patients with diabetes foot examination by healthcare providers should be an integral component of diabetes management to identify patients at risk of ulceration and lower-extremity amputation, and this should be performed at least annually. Patients at high risk of foot complications need more frequent monitoring as well as foot care education (including counselling to avoid foot trauma), professionally fitted footwear, and early referrals to a tertiary care centre with trained professionals in foot ulcer management. A multidisciplinary healthcare team can help prevent recurrent foot ulcers and amputation in these patients.

VI. Conclusion

This study comprised of 125 cases of diabetic foot ulcers with emphasis on the study of role of risk factors on the affect of outcome and its complications.

After analysis of the data the following are the conclusions.

- Of all the total cases 60% were males and 40% of the cases were females. The highest number of patients was seen in the age group of 51-60 years (36%).
- Duration of diabetes varied from 1 year to more than 20 years. Most of the Diabetic foot ulcer patients with long duration presents to hospital with severe disease and treated with major or minor amputation.
- In 39.2 % of the cases some sort of trauma is noted as an initiating factor for the occurrence of foot ulcers. 33.6% of the patients had a history of foot ulcers in the past and were treated conservatively.
- Peripheral vascular disease is noted in 10.4% cases and is considered as an independent risk factor for amputation. In this study patients with ischemia and uncontrolled blood sugars were treated with major or minor amputation.
- In younger patients, diabetic foot ulcers were treated conservatively and old age patients underwent major or minor amputation. So age is considered as an independent risk factor for poor outcome.

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