Original Research Article

Study of prognostic outcome of cellulitis patients with diabetes mellitus

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ABSTRACT

Background: Cellulitis is a non-suppurative, invasive infection of tissues, which is usually related to point of injury. It is a spreading inflammation. It is an acute bacterial infection causing inflammation of the deep dermis and surrounding subcutaneous tissue. To reduce morbidity and mortality early diagnosis and management with identification of co morbidities and treating them down is necessary. To make a full assessment of the cause, all patients require a detailed history, examination and investigations.
Methods: This is a cross sectional comparative study of 50 patients having symptoms of cellulitis to be divided into two groups of 25 patients each where one group is having diabetes mellitus and other group without diabetes mellitus.
Results: Diabetes mellitus patients have more morbidity and mortality in term of more days of hospital stay, rate of amputations and number of debridement. Early diagnosis, broad spectrum antibiotics and early aggressive debridement is the mainstay of management. Aggressive surgical debridement at initial stages of presentation can halt the clinical process and patient can have better prognosis. In neglected diabetic patients' debridement alone is not sufficient and amputation may be required in some cases.
Conclusions: Early diagnosis, broad spectrum antibiotics and early aggressive debridement in cellulitis patients results in better outcomes.

Keywords: Cellulitis, Broad spectrum antibiotics, Diabetes mellitus, Debridements

INTRODUCTION

Cellulitis is a skin and soft tissue infection. It is mostly caused by gram stain positive cocci, most common are *Streptococcus pyogenes* and *Staphylococcus aureus*.[1-5] Infectious cellulitis is a common disease seen by physicians in both outpatient department (OPD) and emergency.[6,7] If not treated appropriately some patients with cellulitis require multiple hospital admissions because of the recurrent nature of this infection.[8,9]

Clinical features of cellulitis presents as a poorly demarcated, warm, erythematous area with associated oedema and tenderness to palpation. The acute bacterial infection also causes inflammation of the deep dermis and surrounding subcutaneous tissue. The infection is without an abscess or purulent discharge. Beta-haemolytic streptococci typically cause cellulitis, generally group A streptococcus, followed by methicillin-sensitive *Staphylococcus aureus*. Cellulitis infects mostly to patients who are immunocompromised, colonized with methicillin-resistant *Staphylococcus aureus*, bitten by animals, or have comorbidities such as diabetes mellitus. These patients are more prone to another bacterial infections also.[10] The number of people with diabetes are increasing worldwide. It was 131 million in 2000 and it is likely to increase to 366 million by 2030.[11] Infective complications are more prevalent in diabetic lower limbs and it is estimated that about 15% of people with diabetes will develop foot ulcers during their lifetime.[12]

Amit Jain's classification of diabetic foot complications proposed in 2012 was a holistic approach to understanding diabetic foot. It includes all the lesions seen in a diabetic foot and categorizes them into 3 broad groups (infective, non-infective and mixed).[13]

Amit Jain's principles and practises in diabetic foot, also, had tried to address sub types with further classifications. One such attempt is the new staging system for cellulitis in diabetic lower limbs proposed in 2014 (Table 1).[14]

Table 1: Amit Jain's staging of cellulitis in diabetic lower limbs.

Stages	Staging of cellulitis
Stage 1	Cellulitis without abscess or skin necrosis
Stage 2	Cellulitis with either localized abscess or skin necrosis
Stage 3	Necrotizing fasciitis without myonecrosis
Stage 4	Necrotizing fasciitis with myonecrosis

In diabetic patients there is sustained hyperglycemia, pro-inflammatory environment and peripheral neuropathy. These factors lead to altered immune cell function, ineffective inflammatory response, endothelial cell dysfunction and impaired neovascularization. These all responses lead to abnormal wound healing. This is the reason for morbidity and mortality in diabetic patients.

Objective is to study the prognostic outcome of cellulitis patients with diabetes mellitus in terms of duration of hospital stay and need for surgery in terms of amputation and debridement.

METHODS

The cross-sectional comparative study was conducted in the department of general surgery of Sri Guru Ram Das Institute of Medical Sciences and Research Vallah, Sri Amritsar from May 2019 to May 2021.

Fifty cases of Necrotizing fasciitis were divided into two groups: group A (n=25) includes cellulitis patients with diabetes mellitus, and group B (n=25) is a comparative group which includes cellulitis patients without diabetes mellitus.

Inclusion criteria

Both groups were having men and women in age group of 20-60 years with the signs and symptoms of cellulitis and willing to participate in the study.

Exclusion criteria

Patients below 20 years of age and above 60 years of age, who are not willing to participate in the study, patients treated in other specialty department were excluded from the study.

Ethical consideration

After taking informed consent patients were included in the study. Data was collected as per proforma sheet.

Study procedure

Signs and symptoms of cellulitis includes intense pain and tenderness over the involved skin and underlying muscle. It is associated with fever, malaise and myalgias. Other findings include edema extending beyond the areas of erythema and skin vesicles.

Of those patients admitted with cellulitis, 50 patients were selected for the study. Their clinical findings were recorded as per proforma case sheet. Necessary investigations done and analyzed. Depending on clinical findings and routine investigations patients were divided into two groups, Group A includes cellulitis patients with diabetes mellitus and group B includes patients without diabetes mellitus. Medical management was done according to wound swab culture sensitivity report and other routine investigations.

Investigations includes

Routine blood investigations include: hemoglobin, total leucocyte count, differential count, erythrocyte sedimentation rate (ESR), fasting blood sugar (FBS), glycated hemoglobin (HbA1c) and corresponding urine sugar on regular basis. Routine urinalysis include: albumin, sugars, ketones and microscopy. Other investigations include: blood urea and serum creatinine; wound discharge for culture and sensitivity; and arterial and venous Doppler study (optional).

Statistical analysis

The data from the present study was systematically collected, compiled and statistically analysed with statistical package for the social sciences (SPSS) statistics-26 version to draw relevant conclusions. The observations were tabulated in the form of frequency, percentage and mean±standard deviation (SD). In parametric data, student's 't' test. Categorical variables were correlated using chi square test. The level of significance was determined as its 'p' value with $p>0.05$ as insignificant, $p<0.05$ as significant and $p<0.001$ as highly significant.

RESULTS

The present study of 50 patients in age group of 20-60 years having signs and symptoms of cellulitis were observed after taking informed consent. Patients were divided into two groups of 25 each.

Group A (n=25) included cellulitis patients with diabetes mellitus. Group B (n=25) included cellulitis patients without diabetes mellitus.

These patients were admitted in the department of surgery at Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Amritsar for various surgical procedures. The following observations were made in this study.

Out of 25 patients in group A, upper extremity was involved in one patient (4%), lower extremities were involved in 21 (84%) patients. Scrotum was involved in 2 (8%) patients, back was involved in one (4%) patient. Out of 25 patients in group B, upper extremity was involved in one (4%) patient, lower extremities were involved in 23 (92%), scrotum was involved in one (4%) patient. From this observation most common site involved in both the groups is lower extremity and data is statistically insignificant as p>0.05 (Table 2).

Table 2: Distribution of subjects on the basis of site involved in both the study groups.

Site	Group A		Group B	
	N	%	N	%
Upper extremity	1	4.00	2	8.00
Lower extremity	21	84.00	22	88.00
Scrotum	2	8.00	1	4.00
Back	1	4.00	0	0.00
Total	25	100.00	25	100.00

X^2 (df: 3, n=50) =1.690, p=0.639

Out of 25 patients in group A, electrocution was the etiological factor in one (4%) patient, insect bite was the etiological factor in 2 (8%) patients, intramuscular injection was the etiological factor in one (4%) patient, trauma was the etiological factor in 12 (48%) patients and no etiological factor was found in 9 (36%) patients. Out of 25 patients in group B, insect bite was etiological agent in one (4%) patient, thorn prick was etiological agent in one (4%), trauma was etiological agent in 11 (44%) patients, no etiological agent was identified in 12 (48%) patients. From the above observation most, common etiological agent identified in group A was trauma and in group B was idiopathic and data is statistically insignificant as p>0.05 (Table 3).

Table 3: Distribution of subjects on the basis of etiological factors in both the study groups.

Etiological factors	Group A		Group B	
	N	%	N	%
Electrocution	1	4.00	0	0.00
Insect bite	2	8.00	1	4.00
Intramuscular injection	1	4.00	0	0.00
Thorn pick	-	0.00	1	4.00
Trauma	12	48.00	11	44.00
No	9	36.00	12	48.00
Total	25	100.00	25	100.00

X^2 (df: 5, sn=50) =3.805, p=0.578

The mean HbA1c in group A was 8.34±1.12 and in group B was 5.28±0.22. Difference in mean HbA1c in both the groups are highly significant (p<0.001) (Table 4).

Table 4: Mean HbA1c in both the study groups.

Parameter	Group A (n=25)	Group B (n=25)	P value
HbA1c	8.34±1.12	5.28±0.22	0.000

Out of 25 patients in group A, 22(88%) undergone split skin grafting surgery, 2 (8%) undergone flap cover surgery and primary closure was done in 1(4%) patient. Out of 25 patients in group B, 19 (76%) patients undergone split skin grafting, 2 (8%) patients undergone flap cover surgery and 4(16%) patients undergone primary closure. In both the groups split skin surgery was the most common definitive surgery performed and data is statistically insignificant p>0.05 (Table 5).

Table 5: Distribution of subjects on the basis of definitive surgery in both the study groups.

Definitive surgery	Group A		Group B	
	N	%	N	%
SSG	22	88.00	19	76.00
Flap cover	2	8.00	2	8.00
Primary closure	1	4.00	4	16.00
Total	25	100.00	25	100.00

X^2 (df: 2, n=50) =2.020, p=0.364

Out of 25 patients in group A, amputation was performed in 3 (12%) patients and amputation was not required in 22 (88%) patients. Out of 25 patients in group B, amputation was performed in 1 (4%) patient and amputation was not required in 24 (96%) patients. From this observation, a greater number of amputations were performed in group A as compared to group B. The comparison of both the groups is statistically insignificant (p>0.05) (Table 6).

Table 6: Distribution of subjects on the basis of requirement of amputation in both the study groups.

Amputation	Group A		Group B	
	N	%	N	%
No	22	88.00	24	96.00
Yes	3	12.00	1	4.00
Total	25	100.00	25	100.00

X^2 (df: 1, n=50) =1.087, p=0.297

From Table 7, the mean hospital stay in days in group A was 26.24±11.79 and mean hospital stay in days in group B was 18.68±8. The mean hospital stays in days found to be higher in group A as compared to group B. Comparison of both the groups was found to be statistically significant (p<0.05).

From Table 8, out of 25 patients in group A, 17 (68%) patients underwent 1 debridement, 7 (28%) patients

underwent 2 debridements and 1 (4%) patient underwent 3 debridements. Out of 25 patients in group B, 20 (80%) patients underwent 1 debridement, 5 (20%) patients underwent 2 debridement's. The number of debridements required was more in group A as compared to group B. Comparison of both the groups was found to be statistically significant (p<0.05).

Table 7: Mean days of the hospital stay in both the study groups.

Parameter	Group A (n=25)	Group B (n=25)	P value
Hospital stays in days	26.24±11.79	18.68±8	0.011

Table 8: Distribution of subjects on the basis of debridement in both the study groups.

Number of debridement	Group A		Group B	
	N	%	N	%
1	17	68.00	20	80.00
2	7	28.00	5	20.00
3	1	4.00	-	-
Mean±SD	1.36±0.57		1.08±0.28	
P value	0.032			

Table 9: Distribution of subjects on the basis of swab culture in both the study groups.

Swab C/S	Group A		Group B	
	N	%	N	%
Acinobacter baumanii	-	-	1	4.00
E. coli	6	24.00	3	12.00
Klebsiella pneumoniae	5	20.00	5	20.00
Pseudomonas aeruginosa	5	20.00	6	24.00
Staph aureus	7	28.00	3	12.00
Burkhoederia cepacia	1	4.00	-	-
No growth	1	4.00	7	28.00
Total	25	100.00	25	100.00

X^2 (df: 6, n=50) =9.190, p=0.163

Out of 25 patients in group A, swab culture sensitivity report of 6 (24%) patients had *E. coli* growth, 5 (20%) had *Klebsiella pneumonia* growth, 5 (20%) patients had *Pseudomonas aeruginosa* growth, 7 (28%) patients had *Staph aureus* growth, 1 (4%) patients had *Burkhoederia cepacia* growth and 1 (4%) patients had no growth. Out of 25 patients in group B, swab culture sensitivity of 1 (4%) patient had *Acinobacter baumanii* growth, 3 (12%) had *E. coli* growth, 5 (20%) patients had *Klebsiella pneumonia* growth, 6 (24%) patients had *Pseudomonas aeruginosa* growth, 3 (12%) patients had *Staph aureus* growth and 7 (28%) patients had no growth. From this observation, most common organism isolated in group A is *Staph aureus* and most common organism isolated in group B is *Pseudomonas aeruginosa*. The data is statistically insignificant as p>0.05 (Table 9).

Out of 25 patients in group A, 2 (8%) patient was alcoholic, 1 (4%) had cirrhosis, 2 (8%) patients were hypertensive and 20 (80%) patients had no another associated risk factor. Out of 25 patients in group B, 4 (16%) patients were alcoholic, 1 (4%) patient had cirrhosis, 2 (8%) patients were hypertensive, 1 (4%) was smoker and no another risk factor was present in 17 (68%) of patients. The data is not statistically significant as p>0.05 (Table 10).

Table 10: Associated risk factors in both the study groups.

Associated risk factors	Group A		Group B	
	N	%	N	%
No	20	80.00	17	68.00
Alcoholic	2	8.00	4	16.00
Cirrhosis	1	4.00	1	4.00
Hypertensive	2	8.00	2	8.00
Smoker	-	-	1	4.00
Total	25	100.00	25	100.00

X^2 (df: 4, n=50) =1.910, p=0.752

DISCUSSION

The cross-sectional comparative study was conducted in the department of general surgery of Sri Guru Ram Das Institute of Medical Sciences and Research Vallah, Sri Amritsar. Fifty cases of cellulitis were divided into two groups: group A included cases of cellulitis patients with diabetes mellitus, and group B included the comparative group of cellulitis patients without diabetes mellitus.

Males are more commonly involved with cellulitis. The reason could be males are more commonly involved in outdoor activities and work place hazards. Trauma is more common at work place. In a study of evaluation and management of cellulitis and its local complications in diabetic lower limb using the New Amit Jain's Staging System for cellulitis which is a retrospective study conducted by Jain et al concluded that out of 26 patients, there were 20 males (76.92%) and 6 females (23.08%).[14] Similarly in our study disease is more prevalent in males, 76% in group A and 88% in group B.

Cellulitis can occur at any age group, but the most common age group involved is middle age to old age. This might be due to occurrence of risk factors in these age groups. In a study conducted by Mzabi et al: cellulitis in aged person: a neglected infection in the literature.[16] They concluded that out of 150 patients included in the study, the disease was most prevalent in aged population. The mean age was of of 73 years old (range: 65 to 94 years old).[14] Another study conducted by Gopal et al concluded that majority of the patients in the study were above 40 years of age with mean age in the study was 56 years.[15] In our study cellulitis is more prevalent in patients >50 years of age in group A, while in group B most patients affected are <30 years of

age. The median age in group A is 56.6±13.15 and in group B is 51.56±15.07.

Most common site involved in cellulitis is lower limb. This might be due to lower limbs being commonly injured by trauma. Jain et al in their study states that cellulitis in the lower limb is potentially serious infection that commonly occurs and recurs in diabetics. In their study 29% of the patients are known to develop recurrent lower limb cellulitis.[13] In their study, 4 patients (15.38%) had prior history of cellulitis affecting lower limb. Similarly in our study, most common site involved is lower extremity in both the groups (84% in group A and 92% in group B). Other sites involved are scrotum (8% in group A and 4% in group B), upper extremity (4% in both the groups) and back (4% in group A).

Swab culture is important for the management of cellulitis. On the basis of swab culture sensitivity report patient can be managed by appropriate antibiotics. On swab culture sensitivity of patients with necrotizing fasciitis growth can be monomicrobial or polymicrobial. A study conducted by Carratala et al factors associated with complications and mortality in adult patients hospitalized for infectious cellulitis. The infection was microbiologically documented in 128 of 332 cases (39%); by means of blood cultures in 47 of 251 cases, by needle aspiration culture in 82 of 173 cases, and by culture of the surgical sample in 32 of 48 cases. The organisms isolated most frequently were *Staphylococcus aureus* (n=46 cases), *Streptococcus pyogenes* (n=22), viridans-group streptococci (n=17), groups B, C, and G streptococci (n=15), *Pseudomonas aeruginosa* (n=13), and *Escherichia coli* (n=9). All *Staphylococcus aureus* isolates were susceptible to methicillin. Similarly in our study, most common organism isolated on swab culture sensitivity is staph aureus (28%). In group B, most common organism isolated on swab culture is *Pseudomonas aeruginosa*.

In a study of cellulitis in chronic oedema of the lower leg by Burian et al concluded that various risk factors are responsible for development of cellulitis.[18] Wounds, obesity, male sex, diabetes, midline swelling and particularly advanced stages of chronic oedema were independent risk factors for cellulitis, while control of swelling was associated with a lower risk. Similarly, in our study most common etiological factors in both the groups is trauma (48% in group A and 44% in group B). Other etiological factors are insect bite, intramuscular injection, thorn prick and electrocution.

In a study conducted by Gopal et al concluded that debridement was the most common surgical procedure performed among the patients who underwent surgery as the initial treatment (61.5%).[15] The study also showed that, a patient with higher stage of cellulitis had more chances of undergoing multiple surgical procedures (repeat debridements, fasciotomy followed by debridement etc) compared to a patient with a lower stage of cellulitis. Similarly in our study, in group A, 17 (68%) patients

underwent 1 debridement, 7 (28%) patients underwent 2 debridements and 1 (4%) patient underwent 3 debridements. In group B, 20 (80%) patients underwent 1 debridement, 5 (20%) patients underwent 2 debridements. The number of debridements required was more in group A as compared to group B.

Intravenous antibiotics according to culture sensitivity report or broad-spectrum antibiotics until culture sensitivity report is awaited in initial and most important step in the management of cellulitis. In advanced stages of cellulitis surgical debridement is a mandatory life saving step and should be performed as soon as possible. The most important determinants of mortality are the timing and adequacy of debridement. Repeated debridement may be necessary (as dictated by the state of the wound) until the infections is adequately controlled.

Limitations

Due to COVID pandemic sample size was small.

CONCLUSION

Cellulitis is a skin and soft tissue infection. Diabetes mellitus patients have more morbidity and mortality in term of more days of hospital stay, rate of amputations and number of debridements.

Early diagnosis and early broad-spectrum antibiotics and aggressive debridement is the mainstay of management.

Aggressive surgical debridement at initial stages of presentation can halt the clinical process and patient can have better prognosis.

In neglected diabetic patients debridement alone is not sufficient and amputation may be required in some cases.

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