Original Research Article

A comparative study of primary cellulitis and its local complications in lower limbs in diabetics and non-diabetics through the new Amit Jain's staging system from India

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ABSTRACT

Background: The objective of the study was to validate Amit Jain's staging system for cellulitis in diabetic and non-diabetic lower limbs and to predict the outcomes associated with cellulitis and surgical procedures done in them.
Methods: We conducted a prospective study in department of surgery at Raja Rajeswari Medical College and Hospital Bengaluru, India. The study period was from December 2018 to November 2019. Statistical analysis was done using SPSS 22 and R environment ver.3.2.2.
Results: A total of 36 patients were included in this study of which 21 were diabetics and were in placed in group A and 15 were non diabetics and placed in group B. 83.3% of the patients were males. 73.3% of non-diabetics had stage 1 cellulitis and 33.3% of diabetics had stage 1 and 2 each. 47.2% of patients underwent debridement and it was significantly common in diabetics (p=0.037) and also it was common in higher stages of cellulitis (p=0.001). 8.3% had amputation in this series. All the major amputations were done in stage 4 cellulitis (p=0.002).
Conclusions: In this validation study, it can be seen that cellulitis is common in both diabetics and non-diabetics but it is severe in diabetic patients. Stage 3 was more common in diabetics compared to non-diabetics. Amit Jain's staging system of cellulitis is a simple, easy, practical, focal classification that guides therapy and predicts amputation.

Keywords: Diabetes, Cellulitis, Staging, Amputation, Debridement

INTRODUCTION

Diabetes mellitus is a global problem where the prevalence is increasing both in developing and developed countries.[1,2] It is predicted that by 2030, there will be 366 million diabetics and by 2040, it will raise to 642 million.[3,4]

The foot complications remain the most disturbing and expensive complication in diabetes and is one of the commonest causes for hospitalization.[3-6] Diabetic foot can lead to amputations, thereby increasing disability and decrease the quality of life.[7]

Amit Jain's classification for diabetic foot is the newly proposed classification for diabetic foot complications which divides diabetic foot into 3 simple types namely, type 1, type 2 and type 3 diabetic foot complications which encompasses all the lesion seen in diabetic foot universally.[8-10] Type 1 diabetic foot complications are infective complications and consist of abscess, wet gangrene, necrotizing fasciitis, etc and they are one of the commonest cause for hospitalization in countries like India.[11-14]

Cellulitis is a type 1 diabetic foot complication.[8] Infection sets in once there is breach in the skin, thereby exposing the deeper tissues for progression of infections. Cellulitis is common in diabetics and non-diabetics and is known to account for 2-3% of all hospital admissions.[15-17]

Cellulitis is known to affect the lower limbs most commonly and there is been an increase in its incidence.[15,18] We conducted a prospective study of cellulitis in lower limbs in both non-diabetics and diabetics and analyzed them through the Amit Jain's staging system for cellulitis in extremities.[19,20] This staging system divides cellulitis into 4 simple progressive stage and offers treatment guidance for these stages (Figure 1).
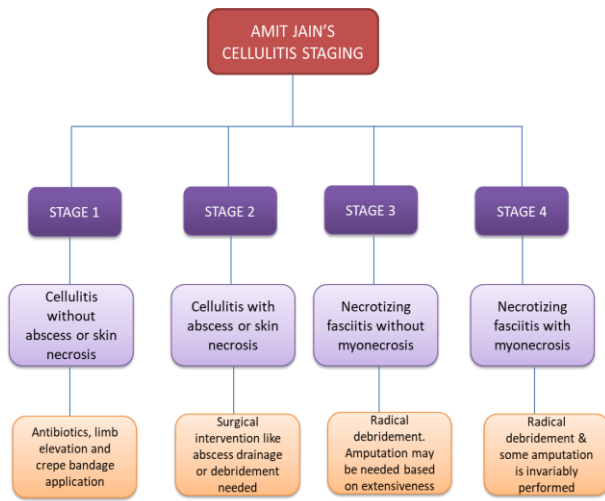

Figure 1: Amit Jain's staging for cellulitis.

METHODS

This was a prospective descriptive analysis was conducted in Department of Surgery of Raja Rajeswari Medical College, Bengaluru, India. This is a tertiary care teaching hospital which mainly caters rural patients. The study period was from December 2018 to November 2019. The following were inclusion and exclusion criteria.

Inclusion criteria

Inclusion criteria were all patients with cellulitis of lower limb (diabetic or non-diabetics) treated in our surgery department and patients initially treated conservatively at other hospitals and subsequently referred to our hospital for further management were included.

Exclusion criteria

Exclusion criteria were patients who refused surgery or were discharged against advice, patients operated elsewhere, ppatients with incomplete records, cellulitis occurring around ulcer or furuncle, and snake bite cellulitis.

The patients were divided into 2 groups. All diabetics were placed in group A and non-diabetics were placed in Group B. This study was approved by institutional ethics committee (RRMCH-IEC/02/2018-19).

Statistical analysis

Data was analyzed using statistical software SPSS 22.0 and R environment ver.3.2.2. Microsoft word and excel were used to generate graphs and tables. Both descriptive and inferential statistics were carried out in the study. Results on continuous measurements were presented on mean±SD (min-max) and results on categorical measurements were presented in number (%). Significance was assessed at 5% level of significance.[21-24]

The following assumption on data is made, dependent variables should be normally distributed, samples drawn from the population should be random, and cases of the samples should be independent.

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (inter group analysis) on metric parameters. Leven's test for homogeneity of variance has been performed to assess the homogeneity of variance. Chi-square/fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups, non-parametric setting for qualitative data analysis. Fisher exact test was used when samples were very small.

Significant figures

Suggestive significance (p value: <0.05), *moderately significant (p value: <0.01), and **strongly significant (p value: p≤0.01).

RESULTS

A total of 36 patients were included in this study. Males were most commonly accounting for 83.3% of the total cases (p=1.000). In group A, 81% of them were males and 19% were females and in group B, 86.7% were males and 13% were females. The average age in group A was 61.62±12.13 years (Table 1) whereas in group B, it was 56.53±14.89 years (p=0.267).

In group A, 1 patient (4.8%) had cellulitis confined below ankle, 19 patients (90.5%) had cellulitis extending below knee and in 1 patient (4.8%) had above knee extension. In group B, in 2 patients (5.6%) it was below ankle, in 31 patients (86.1%) it was below knee and in 3 patients (8.3%), it extended above knee. There was no difference in both groups (p=0.778).

Around 30.6% had history of trauma and there was no significance in both groups. 44.4% had history of blister (Table 2) and it was significant in group A (p=0.070, significant). Majority of patients in group B had stage 1

cellulitis (73.3%) as the commonest stage whereas in group A, both stage 1 and 2 accounted for 33.3% of cases each. Stage 3 was more common in group A patients with diabetics (p=0.086, significant). 16.7% had past history of cellulitis. 9.5% had past cellulitis in group A and 26.7% in group B (p=0.210). Around 5.6% had bilateral cellulitis and both occurred in group B (p=0.167). Significant number of patients under debridement or fasciotomy in group A compared to group B (p=0.037*, significant) (Table 2). 8.3% of patients (group A - 9.5%, group B - 6.7%) underwent some form of amputations and there was no difference in both groups (p=1.000). 5.6% underwent major amputation (one each in both groups) and there was no difference (p=1.000). Around 50% had co morbidities (group A - 52.4%, group B - 46.7%) and there was no difference in both groups (p=0.735). 41.7% had hypertension and 16.7% had ischemic heart disease and there was no difference in both groups (Table 2). There was no association of gender, area of lesion extension, trauma, co morbidities, acute kidney injury (AKI) with Amit Jain's stages (Table 3).

Table 1: Age distribution of patients in both groups.

Age in years	Group A N (%)	Group B N (%)	Total N (%)	P value
<40	0 (0)	1 (6.7)	1 (2.8)	
40-50	4 (19)	7 (46.7)	11 (30.6)	
51-60	7 (33.3)	0 (0)	7 (19.4)	
61-70	5 (23.8)	4 (26.7)	9 (25)	0.267
71-80	4 (19)	3 (20)	7 (19.4)	
>80	1 (4.8)	0 (0)	1 (2.8)	
Total	21 (100)	15 (100)	36 (100)	
Mean±SD	61.62±12.13	56.53±14.89	59.50±13.39	

Table 2: Variables distribution in both groups of patients.

Variables	Group A N (%)	Group B N (%)	Total (n=36) N (%)	P value
Blister	12 (57.1)	4 (26.7%)	16 (44.4%)	0.070
Trauma	6 (28.6)	5 (33.3%)	11 (30.6%)	1.000
Stage of cellulitis				
Stage 1	7 (33.3)	11 (73.3)	18 (50)	
Stage 2	7 (33.3)	2 (13.3)	9 (25)	0.086
Stage 3	6 (28.6)	1 (6.7)	7 (19.4)	
Stage 4	1 (4.8)	1 (6.7)	2 (5.6)	
Past history of cellulitis				
Yes	2 (9.5)	4 (26.7)	6 (16.7)	0.210
No	19 (90.5)	11 (73.3)	30 (83.3)	
Debridement				
Yes	13 (61.9)	4 (26.7)	17 (47.2)	0.037*
No	8 (38.1)	11 (73.3)	19 (52.8)	
Amputation				
Yes	2 (9.5)	1 (6.7)	3 (8.3)	1.000
No	19 (90.5)	14 (93.3)	33 (91.7)	
Major amputation				
Yes	1 (4.8)	1 (6.7)	2 (5.6)	1.000
No	20 (95.2)	14 (93.3)	34 (94.4)	
Comorbidities				
Yes	11 (52.4)	7 (46.7)	18 (50)	0.735
No	10 (47.6)	8 (53.3)	18 (50)	
Hypertension	11 (52.4)	4 (26.7)	15 (41.7)	0.123
IHD	3 (14.3)	3 (20)	6 (16.7)	0.677

Table 3: Association of clinical variables in relation to Amit Jain's stage of cellulitis.

Variables	Amit Jain's staging of cellulitis				Total (n=36)	P value
	Stage I (n=18)	Stage II (n=9)	Stage III (n=7)	Stage IV (n=2)		
	N (%)	N (%)	N (%)	N (%)	N (%)	
Gender						
Male	15 (83.3)	8 (88.9)	6 (85.7)	1 (50)	30 (83.3)	0.600
Female	3 (16.7)	1 (11.1)	1 (14.3)	1 (50)	6 (16.7)	
Area of extension						
Ankle	1 (5.6)	1 (11.1)	0 (0)	0 (0)	2 (5.6)	
Up to knee	16 (88.9)	8 (88.9)	6 (85.7)	1 (50)	31 (86.1)	0.375
Above knee	1 (5.6)	0 (0)	1 (14.3)	1 (50)	3 (8.3)	
Trauma						
Yes	6 (33.3)	3 (33.3)	1 (14.3)	1 (50)	11 (30.6)	0.690
No	12 (66.7)	6 (66.7)	6 (85.7)	1 (50)	25 (69.4)	
Comorbidities						
Yes	8 (44.4)	6 (66.7)	4 (57.1)	0 (0)	18 (50)	0.402
No	10 (55.6)	3 (33.3)	3 (42.9)	2 (100)	18 (50)	
Acute kidney injury						
Yes	1 (5.6)	1 (11.1)	1 (14.3)	0 (0)	3 (8.3)	0.807
No	17 (94.4)	8 (88.9)	6 (85.7)	2 (100)	33 (91.7)	

Significant association was seen between blister and staging (Figure 2). 22.2% in stage 1, 44.4% in stage 2, 85.7% in stage 3 and 100% in stage 4 had blisters. As the stage increases, the presence of blister increased and all the cases of stage 4 had presence of blisters (p=0.009*, significant).
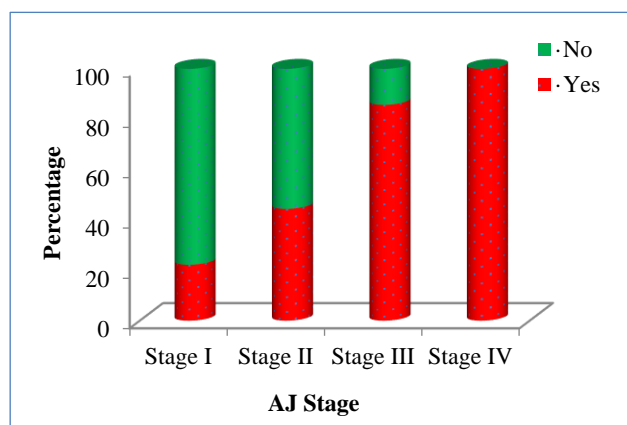

Figure 2: Relation of blisters with Amit Jain's different stages of cellulitis.

No association was seen between past history of cellulitis, bilateral limb involvement, antibiotic escalation and mortality with stages of cellulitis (Table 4). Significant association of Amit Jain's stages was seen with debridement (p=0.001**), re-surgeries (p=0.057), antibiotics used (p=0.089), amputations (p=0.002**). Debridement was done 100% cases of stage 2 and stage 3 cellulitis. Re-surgeries were done most commonly in stage 3 (42.9%) followed by stage 1 (5.6%). 55.6% of patients in stage 1 received amoxycillin-clavulanic acid as commonest antibiotic whereas pipercillin-tazobactum was

used more in stage 3 (85.7%) and stage 4 (50%). Antibiotic escalation was done in 44.4%. Amputation was most common in stage 4 (100%) followed by 11.1% being done in stage 2.

Two patients underwent major amputations (Figure 3) and both were done in Amit Jain's stage 4 (p=0.002**, significant).
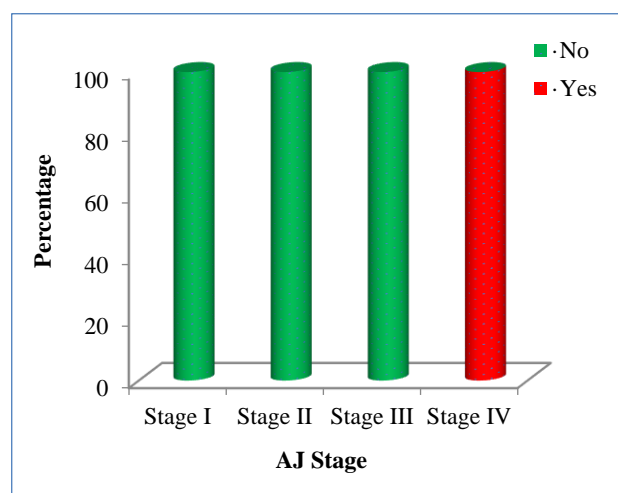
Figure 3: Major amputation being done in different stage of cellulitis.

Pipercillin-tazobactum was most commonly (52.9%) used antibiotic (p=0.062, significant) in patients who underwent debridement (Table 5).

There was one mortality in this series (2.8%) and it occurred in stage 3 cellulitis.

Table 4: Association of clinical variables in relation to Amit Jain's stages of cellulitis.

Variables	Amit Jain's staging of cellulitis				Total (n=36)	P value
	Stage I (n=18)	Stage II (n=9)	Stage III (n=7)	Stage IV (n=2)		
	N (%)	N (%)	N (%)	N (%)	N (%)	
Debridement						
Yes	1 (5.6)	9 (100)	7 (100)	0 (0)	17 (47.2)	<0.001**
No	17 (94.4)	0 (0)	0 (0)	2 (100)	19 (52.8)	
Re-surgeries						
Yes	1 (5.6)	0	3 (42.9)	0	4 (11.1)	0.057
No	17 (94.4)	9 (100.0)	4 (57.1)	2 (100.0)	32 (88.9)	
Bilateral limb involvement						
Yes	2 (11.1)	0 (0)	0 (0)	0 (0)	2 (5.6)	0.743
No	16 (88.9)	9 (100)	7 (100)	2 (100)	34 (94.4)	
Mortality						
Yes	0 (0)	0 (0)	1 (14.3)	0 (0)	1 (2.8)	0.250
No	18 (100)	9 (100)	6 (85.7)	2 (100)	35 (97.2)	
Past history of cellulitis						
Yes	4 (22.2)	2 (22.2)	0 (0)	0 (0)	6 (16.7)	0.657
No	14 (77.8)	7 (77.8)	7 (100)	2 (100)	30 (83.3)	
Antibiotics						
Amoxycillin-clavulanic acid	10 (55.6)	3 (33.3)	0 (0)	0 (0)	13 (36.1)	
Pipercillin-tazobactum	3 (16.7)	2 (22.2)	6 (85.7)	1 (50)	12 (33.3)	
Cefaperazone	4 (22.2)	2 (22.2)	0 (0)	1 (50)	7 (19.4)	
Cephalexin	1 (5.6)	0 (0)	0 (0)	0 (0)	1 (2.8)	0.089
Cefotaxim	0 (0)	1 (11.1)	0 (0)	0 (0)	1 (2.8)	
Meropenem	0 (0)	0 (0)	1 (14.3)	0 (0)	1 (2.8)	
Ceftriaxone	0 (0)	1 (11.1)	0 (0)	0 (0)	1 (2.8)	
Antibiotic escalation						
Yes	8 (44.4)	6 (66.7)	2 (28.6)	0 (0)	16 (44.4)	0.276
No	10 (55.6)	3 (33.3)	5 (71.4)	2 (100)	20 (55.6)	
Amputation						
Yes	0 (0)	1 (11.1)	0 (0)	2 (100)	3 (8.3)	0.002**
No	18 (100)	8 (88.9)	7 (100)	0 (0)	33 (91.7)	

Table 5: Association of antibiotics with debridement done.

Antibiotics	Debridement		Total (n=36)	P value
	Yes (n=17)	No (n=19)		
	N (%)	N (%)	N (%)	
Amoxycillin-clavulanic acid	3 (17.6)	10 (52.6)	13 (36.1)	
Pipercillin-tazobactum	9 (52.9)	3 (15.8)	12 (33.3)	
Cefaperazone	2 (11.8)	5 (26.3)	7 (19.4)	
Cephalexin	0 (0)	1 (5.3)	1 (2.8)	0.062, significant
Cefotaxim	1 (5.9)	0 (0)	1 (2.8)	
Meropenem	1 (5.9)	0 (0)	1 (2.8)	
Ceftriaxone	1 (5.9)	0 (0)	1 (2.8)	

DISCUSSION

Cellulitis is an acute bacterial infection of skin which can affect any part of the body although lower extremities are most frequently affected.[16,18] In fact, lower limb is involved in more than 70% of the cases.[25,26] Cellulitis, which is often caused by gram positive bacteria, results in prolonged hospital stay and can have considerable morbidity and mortality if complications ensues.[27] The local complications are abscess and necrotizing fasciitis whereas the systemic complication is septic shock.[20,27] Often, primary cellulitis can result from trauma which could be recognizable or unrecognizable. In Nassaji et al series, 38.2% of patients had history of trauma. In Adimoolam et al series, 27% had trauma whereas in Jain

et al series, 23.07% had trauma. In our series, 30.6% had trauma history.[17,26,28]

Though age is not a risk factor for cellulitis, few studies have shown it to occur over 45 years of age.[25] In Gopal et al series, mean age for cellulitis in diabetic patients was 56 years.[20] In this series, it was 59.5 years.

Bilateral cellulitis is uncommon in clinical practice. In Jain et al series, 3.85% had bilateral cellulitis whereas in our series, it was 5.6%. In Jain et al series, 26.92% of patients with cellulitis had blister whereas in this series, 44.4% had blisters and it was significant in diabetics compared to non-diabetics and also it was more common in higher stages of cellulitis.[26]

In Jain et al series, stage 2 cellulitis was the commonest stage (42.31%) followed by stage 1 (38.5%).[26] In Gopal et al series, stage 2 cellulitis (41%) was the most stage seen followed by stage 1 (33%) in diabetic patients.[20] In this series, stage 1 cellulitis (Figure 4) was commonest (50%) followed by stage 2. Stage 1 cellulitis was more common in non-diabetics (73.3%) whereas stage 1 and 2 (33.3%) occurred equally in diabetic patients in this series. In Jain et al series, 15.39% had stage 3 cellulitis whereas in Gopal et al series, 5.1% had stage 3 cellulitis as per Amit Jain's staging system.[26,20] In this series, 28.6% of patients with diabetics had stage 3 where there was necrotizing fasciitis (Figure 5) and it was significantly higher compared to non-diabetics.

Figure 4: Cellulitis over foot, this is stage 1 as per Amit Jain's staging system.

In Adimoolam et al series, 76% of patients with cellulitis required debridement.[17] In Jain et al series, 65.38% required debridement.[26] In Gopal et al series, 61.5% of patients required debridement.[20] In our series, debridement was done 47.2% and it was done significantly more in diabetic patients. Stage 1 cellulitis is supposed to be managed conservatively. In Gopal et al series, it was seen that 38.5% of patients underwent unnecessary intervention whereas in this series, 5.6 % of patient underwent unnecessary surgical intervention.[20] In Gopal et al series, it was seen that as the stage of cellulitis increases, there was significant increase in need for surgeries.[20] Further, higher the stage of cellulitis, there was significantly higher chances of patients undergoing multiple surgeries.[20] In our

series, 42.9% of patients in stage 3 required re-surgeries and it was statistically significant.

Figure 5: Necrotizing fasciitis, this is stage 3 as per Amit Jain's staging system.

In Adimoolan et al series in non-diabetic cellulitis, 4% of them required amputation.[17] In Gopal et al series, 25.6% underwent amputation and 17.9% had major amputation which was significantly higher in stage 3 and 4 cellulitis.[20] In this series, all major amputations occurred in stage 4 where there was underlying myonecrosis. Myonecrosis is an important predictor of amputation which was not given importance in many scoring system and Amit Jain's surgical scoring system for diabetic foot was first scoring system which recognizes presence of myonecrosis as an important predictor of amputation.[9,10,29]

In Jain et al series, 3.85% had mortality and it was in stage 3.[26] In Gopal et al series, mortality was in 2.6% of cases and it was in stage 4.[20] In our series, 2.8% had mortality and it was in stage 3 cellulitis.

CONCLUSION

Cellulitis in lower limb is common both in diabetics as well as in non-diabetics though it is more severe in diabetics. Stage 1 cellulitis was common in non-diabetics whereas stage 1 and 2 were equally common in diabetics in this series. Further, debridement was more commonly done in diabetic cellulitis patients compared to non-diabetics. It was observed that patients with higher stages of cellulitis had more blisters, higher debridement's, re-surgeries, higher spectrum antibiotic usage and amputation rates and they were statistically significant. Amit Jain's staging system for cellulitis is a new, simple, easy to remember, practical, focal classification for cellulitis which can be used in lower as well as upper extremities and also in diabetics and non-diabetics. It provides a good guide to treatment and in predicting the outcomes. Recognition of cellulitis in early stages and timely intervention can have a good prognosis before it develops local and systemic complications.

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