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Risk factors of acute cellulitis in adult patients: A case-control study

Mohammad Nassaji[1,*], Raheb Ghorbani[2], Sanaz Ghashghaee[3]

[1]*Research Center for Social Determinants of Health, Faculty of Medicine,* ***Semnan University*** *of Medical Sciences, Semnan, Iran*
[2]*Research Center for Social Determinants of Health, Department of Community Medicine, Faculty of Medicine, Semnan University of Medical Sciences, Semnan, Iran*
[3]*Students' Research Committee, University of Medical Sciences, Semnan, Iran*

ABSTRACT

Cellulitis is a common medical condition with different severity varies from mild to life threatening disease. The identification of preventable risk factors could reduce morbidity and mortality from this disease and improve patient management. The aim of this study was to identify the risk factors associated with cellulitis in adult patients. We conducted a case-control study of 102 adult subjects with cellulitis and the same number of controls who were admitted to two university affiliated hospitals. Data were obtained with a questionnaire and from examination of patients. Two groups were matched based on age (p=0.717) and gender (p=0.661). The most common site of cellulitis was lower extremities (56.9%). The pack-year smoking and duration of smoking was significantly higher in patients with cellulitis (p=0<001). Logistic regression analysis showed that recent trauma (OR=55.8, 95% CI: 11.2-278.4, p<0.001), history of recent surgery (OR=6.3, 95% CI:1.7-23.7, p=0.006), body mass index(OR=1.38, 95% CI:1.22-1.57, p<0.001) and diabetes mellitus(OR=3.02, 95% CI:1.17-7.81, p=0.022) was significantly associated with development of cellulitis. No association was observed between corticosteroid use and risk of cellulitis (p=0.158). Our study showed that the most important risk factors for cellulitis in adult include trauma, recent surgery, high body mass index, diabetes mellitus and smoking. Therefore, it is recommended that protection against trauma, controlling of blood glucose levels, reducing body weight and smoking cessation may lead to reducing incidence of cellulitis.

Key Words: Cellulitis, risk factor, adult, case-control study

Introduction

Cellulitis is an inflammatory skin condition with an infectious origin involving the dermis and subcutaneous tissues. It is a common medical condition with different severity varies from mild to life threatening disease (1). Most commonly, cellulitis involves the lower extremities but may involve any parts of the body (2). The diagnosis of cellulitis is generally based on the morphologic features of the lesion and the clinical setting characterized by erythema, swelling, warmth, and pain. Fever and constitutional symptoms are often mild or absent in uncomplicated cellulitis (3).

Several risk factors for the cellulitis have been described. The most common of them are trauma, edema, superficial or deep venous insufficiency, prior radiation therapy, previous surgery and skin disorders that cause a potential portal of entry such as toe web intertrigo (4). Some other potential risk factors reported in studies including diabetes mellitus, prior malignancy, body mass index (BMI), smoking, alcoholism and ethnicity with controversial findings. Most of these previous studies reported that general risk factors have little role in the development of cellulitis (5-8).

The better identification of preventable risk factors for cellulitis has significant implications for reducing morbidity and mortality from this diseases and improving patient management. In addition differences findings in previous studies have suggested that there may be regional variations in risk factors and authors proposed more studies. So that we conducted a case control study to assess risk factors of cellulitis, particularly the roles of systemic risk factors.

Materials and methods

This case-control study was conducted from May 2013 to June 2014 in two university-affiliated

***Corresponding Author:** Mohammad Nassaji, Kowsar Hospital, Basij Blvd, Semnan, Iran, Tel: +98 2333437821, Mobile: +98 09121318640, Fax: +982333437837, E-mail: hnassaji@yahoo.com, mnzmohammad@gmail.com
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hospitals in Semnan, Iran. Adult patients (≥ 18 years) with diagnosis of acute cellulitis who admitted in hospitals or were visited outpatients considered for participation in the study. Control group were selected from adult outpatient and without history of cellulitis. Informed consent was obtained from all subjects before enrollment.

Patients with chronic ulcer, abscess, necrotizing fasciitis and patients with a main diagnosis or a reason for hospitalization that was not cellulitis were excluded.

Cellulitis was defined based on clinical findings by a board-certified specialist in infectious diseases. The clinical criteria included of pain, warmth, edema and erythema without sharp demarcation from uninvolved skin with or without fever (3).

A structured data collection sheet was used to collate information about demographics, as well as local and systemic risk factors. Baseline data collected included age, gender, body mass index, smoking status, diabetes mellitus and congestive heart failure. History of recent trauma (<1 month), regional surgery in recent three month, corticosteroid consumption, and previous attack of cellulitis was also obtained. Location of cellulitis, extremity edema, dermatosis and toe web intertrigo, were detected by clinical examination.

BMI, defined as the weight in kilograms divided by the height in meters squared (kg/m^2). Diabetes mellitus was defined as self-reported history of diabetes mellitus and use of oral hypoglycaemic agents or insulin. Subjects were defined as cigarette smokers if they had smoked 3 or more cigarettes per day for at least 6 months. Patients were followed for response to treatment and divided as ≤ 3 or > 3 days responder.

The study protocol was approved by Research Council and Ethical Committee of the Semnan University of Medical Science.

Statistical analysis was performed by Kolmogorov-Smirnov, Chi-Square, Student's t, Mann-Whitney tests and logistic regression analysis using SPSS16.0. P-value less than 0.05 considered statistically significant.

Results

Of all patients admitted with diagnosis of cellulitis that were screened 102 met inclusion criteria and were enrolled. Same numbers of controls were selected. The mean (± SD) age of patients was 45.6 ±16.8 years and the controls was 46.5 ±16.8 that showed no statistically significant difference (p=0.717). 62.7% of cases and 65.7% of controls were male with no significant difference (p=0.661). Two groups were matched based on age and gender. Baseline characteristics and co-morbidities of two groups are showed in table 1.

Table 1. Basic characteristics of case and control groups

Characteristic	Study Group			
	Cellulites (n=102)		Control (n=102)	
	n	%	n	%
Age(years)				
<30	20	19.6	20	19.6
30-39	19	18.6	19	18.6
40-49	24	23.5	23	22.5
50-59	18	17.6	17	16.7
60-69	12	11.8	14	13.7
≥70	9	8.8	9	8.8
BMI* (Kg/m^2)				
<25	45	44.1	84	82.4
25-29.9	37	36.3	17	16.7
≥30	20	19.6	1	1.0
Co-morbidities				
-	64	62.7	63	61.8
Diabetes mellitus	28	27.5	14	13.7
CHF**	8	7.8	13	12.7
Corticosteroid use	7	6.9	13	12.7

*Body Mass Index **Congestive heart failure

The infection was located in the lower extremities in most the patients (Table 2).

Table 2. Anatomical location of cellulitis in patients

Site of infection	n	%
Lower extremities	58	56.9
Upper extremities	32	31.4
Thorax/trunk	5	4.9
Head/Face	5	4.9
Genital	2	2

Nineteen (18.6%) of patients had fever on admission. Eleven of the cellulite cases (10.8%) had previous episodes of cellulitis. Duration of response to treatment was ≤ 3 days in 28.4% and > 3 days in 71.6%.

From all patients 38.2% had history of trauma, whereas only 2% of control have positive history (p=0.001). Mean BMI (±SD) of patients was 25.8±4.1 and for control was 22.5±4.1 Kg/m^2. BMI of patients with cellulitis was significantly higher than controls (p<0.001).

Table 3. Logistic regression analysis for risk factors of cellulites in adult patients

Characteristic	Odds Ratio(OR)	95% Confidence Interval for OR	p-value
BMI*(Kg/m²)	1.38	1.22-1.57	<0.001
Co-morbidities			
-	1	-	-
Diabetes mellitus	3.02	1.17-7.81	0.022
CHF**	1.07	0.31-3.73	0.916
Pack- year smoking	1.13	1.00-1.29	0.056
Recent trauma	55.8	11.2-278.4	<0.001
Surgery	6.3	1.7-23.7	0.006

*Body Mass Index *Congestive heart failure

History of corticosteroid use was positive in 6.9% of patients and 12.7% of controls (p=0.158). Mean (±SD) duration of corticosteroid use was 8.7±8.0 and 2.4±8.0 in patients and controls respectively (p=0.056). From patients 27.5% and from control 13.7% had diabetes mellitus that was significantly difference (p=0.015).

Among the cases, 24 (24.5%) of subjects were current regular cigarette smokers whereas in control group 19 (18.6%) were smoker. The mean (± SD) number of pack-year smoking was 16.4±20.3 in cases and 3.7±2.6 in control group that was significantly different (p<0.001). The mean (± SD) duration of smoking was 15.21±9.9 and 7.0±3.8 years in patients and control subjects respectively. There was significant difference in years of smoking between smoker subjects with and without cellulitis (p=0.001).

Logistic regression analysis showed that BMI (OR=1.38, 95% CI: 1.22-1.57, p<0.001), diabetes mellitus (OR=3.02, 95% CI: 1.17-7.81, p=0.022), history of recent trauma (OR=55.8, 95% CI: 11.2-278.4, p<0.001) and recent surgery (OR=6.3, 95% CI: 1.7-23.7, p=0.006), was significantly associated with development of cellulitis (Table 3).

Discussion

The role of some predisposing factors of cellulitis has not yet been elucidated. The prevalence of predisposing factors may vary between patient populations, and this may explain discordant findings among studies.

The anatomical distribution of cellulitis in our patients was similar to the most previous studies that reported most common site of involvement was the lower extremity (9-13). Local factors especially disruption of the cutaneous barrier seemed to be the most important risk factors for cellulitis across studies. Previous trauma and regional surgery were significantly associated with cellulitis in our study. In accordance with our findings some previous studies reported that traumatic wound and previous surgery were risk factors for cellulitis (7, 8, 14-16). Defects in cutaneous barrier caused by trauma and surgery facilitate the entry of pathogens to skin and development of infection. However, in a study participants with cellulitis had a lower incidence of recent trauma compared with controls (23% vs. 44%) (5).

Our findings showed that higher BMI was significantly associated with cellulitis which is in line with the results of some earlier studies. Dupuy et al. (6) in their study reported that being overweight was a risk factor associated with cellulitis of the leg. Similarly, obesity and higher BMI was independent risk factors for acute cellulitis in some other studies (8, 14, 17). In a prospective case-control study of 100 subjects with cellulitis and 200 control subjects, matched for age and sex, obesity was significantly more frequent in the case patient group, but being overweight was not (5).

Overweight and obesity has been suggested to be a risk factor for some infections. Several epidemiological investigations and emerging data indicate obesity may increases infection susceptibility in clinical settings (18). It is mediated by the effect of obesity on the immune response through a variety of immune mediators, which leads to susceptibility to infections (19).

Significant association between BMI and risk of cellulitis was not reported in some studies. To identify risk factors for acute lower limb cellulitis in the U.K.population, researcher found that systemic risk factors including obesity were not associated with cellulitis (7). Teerachaisakul et al. (20) evaluated risk factors of cellulitis in patients with lymphedema and reported that body mass index was not risk factor of cellulitis.

In most previously published studies, diabetes was not reported as risk factors of cellulitis (5-7, 17, 20). In contrast, we found that diabetes is an

independent systemic risk factor for cellulitis. Similarly, Mokni et al. (8) in their study reported that diabetes was associated with increased risk of cellulitis. Two studies conducted among hospitalized adults to evaluate the factors that contribute to the development of cellulitis. Diabetes mellitus was established underlying conditions in patients with cellulitis (9, 21). In a retrospective cohort study in Canada the risk ratios of having an infectious disease between those with and without diabetes were calculated. Rate of cellulitis was 1.81 time more common in patients with diabetes (22). Skin and soft tissue infections were significantly differences in the frequencies between diabetic and non-diabetic individuals in Suaya et al. (23) study.

Individuals with diabetes have a greater frequency and severity of infections. The reasons for this include abnormality in cell mediated immunity and phagocyte functions associated with hyperglycemia (24, 25). Also diabetes causes some abnormality in skin condition that leads to disruption of integrity of skin, abnormal proprioception and neuropathy that predisposes to cellulitis (26).

The difference in these findings might at least partly be explained by differences in the study design, patients' selection, number of samples and confounding variables.

The result of study shows that patients with cellulitis have had significantly more pack-years of smoking than controls. Also, duration of smoking was significantly higher in patients with cellulitis. In accordance with this, a case-control retrospective study was conducted to evaluate potential risk factors for development of recurrent cellulitis. Authors found that tobacco use was significant independent predictors of cellulitis (17). In a study on patients who underwent abdominoplasty, postoperative wound infection was more common in smokers than non smoker. Both number and duration of smoking increased risk of infections (27). In another study smoking was significant risk factors for surgical site infections in orthopedic patients (28).

The currently available literature suggests that smoking exerts deleterious effects on both morphological and functional aspects of the microcirculation of skin and compromise perfusion of skin. The mechanisms of this phenomenon include compromised endothelial-dependent vasorelaxation, thickening of the walls of arterioles, platelet aggregation and endothelial cell dysfunction (29). In addition; collagen synthesis and the deposition of mature collagen in the extracellular matrix are reduced by smoking. This phenomenon leads to an imbalance between biosynthesis and degradation of dermal proteins (30). In contrast some other studies did not show any association between smoking and risk of cellulitis (5-8).

Most studies about cellulitis did not evaluate the role of corticosteroid use. Corticosteroid therapy did not appear to increase the risk of cellulitis in our patients. Similarly Kumar et al. (31) reported that corticosteroid administration did not increase the risk of postsurgical wound infection in their patients.

Our findings are strengthened by the case-control study design, age and gender matched groups and inclusion of both inpatients and outpatients. There are a few limitations to our study that deserve mention. First, the eligible patient number is relatively small in this study. Second, we assessed patients in university affiliated hospital, so that referral bias may be occurred.

In this study we found that beside of local risk factors, general risk factors including diabetes mellitus, body mass index and smoking are possible risk factors for development of cellulitis. Therefore, it is recommended that protection against trauma, controlling of blood glucose levels, reducing body weight and smoking cessation may lead to reducing incidence of cellulitis. Further prospective studies with larger samples are needed to better identification the role of these risk factors in acute cellulitis.

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Conflict of interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

References

1. Gunderson CG. Cellulitis: definition, etiology, and clinical features. Am J Med 2011; 124: 1113-1122.
2. Swartz MN. Clinical practice. Cellulitis. N Engl J Med 2004; 350: 904-912.
3. Bailey E, Kroshinsky D. Cellulitis: diagnosis and management. Dermatol Ther 2011; 24: 229-239.
4. Stevens DL, Eron LL. Cellulitis and soft-tissue infections. Ann Intern Med 2009; 150: ITC11.
5. Björnsdóttir S, Gottfredsson M, Thórisdóttir AS, et al. Risk factors for acute cellulitis of the lower limb: a prospective case-control study. Clin Infect Dis 2005; 41: 1416-1422.

6. Dupuy A, Benchikhi H, Roujeau JC, et al. Risk factors for erysipelas of the leg (cellulitis): case-control study. BMJ 1999; 318: 1591-1594.
7. Halpern J, Holder R, Langford NJ. Ethnicity and other risk factors for acute lower limb cellulitis: a U.K.-based prospective case-control study.Br J Dermatol 2008; 158: 1288-1292.
8. Mokni M, Dupuy A, Denguezli M, et al. Risk factors for erysipelas of the leg in Tunisia: a multicenter case-control study. Dermatology. 2006; 212: 108-112.
9. Koutica P, Mylonakis E, Boyce J. Cellulitis: evaluation of possible predisposing risk factors in hospitalized patients. Diagn Microbiol Infect Dis 1999; 34: 325-327.
10. Lazzarini L, Conti E, Tositti G, de Lalla F. Erysipelas and cellulitis: clinical and microbiological spectrum in an Italian tertiary care hospital. J Infect 2005; 51: 383-389.
11. Pavlotsky F, Amrani S, Trau H. Recurrent erysipelas: risk factors. J Dtsch Dermatol Ges 2004; 2: 89-95.
12. Perelló-Alzamora MR, Santos-Duran JC, Sánchez-Barba M, et al. Clinical and epidemiological characteristics of adult patients hospitalized for erysipelas and cellulitis. Eur J Clin Microbiol Infect Dis 2012; 31: 2147-2152.
13. Krasagakis K, Valachis A, Maniatakis P, et al. Analysis of epidemiology, clinical features and management of erysipelas. Int J Dermatol 2010; 49: 1012-1017.
14. Karppelin M, Siljander T, Vuopio-Varkila J, et al. Factors predisposing to acute and recurrent bacterial non-necrotizing cellulitis in hospitalized patients: a prospective case-control study. Clin Microbiol Infect 2010; 16: 729-734.
15. Roujeau JC, Sigurgeirsson B, Korting HC, Kerl H, Paul C. Chronic dermatomycoses of the foot as risk factors for acute bacterial cellulitis of the leg: a case-control study. Dermatology 2004; 209: 301-307.
16. Inghammar M, Rasmussen M, Linder A. Recurrent erysipelas--risk factors and clinical presentation. BMC Infect Dis 2014; 14: 270.
17. Lewis SD, Peter GS, Gomez-Marın O, Bisno AL. Risk factors for recurrent lower extremity cellulitis in a US Veterans medical center population. Am J Med Sci 2006; 332: 304-307.
18. Falagas ME, Kompoti M. Obesity and infection. Lancet Infect Dis 2006; 6: 438-446.
19. Milner JJ, Beck MA. The impact of obesity on the immune response to infection. Proc Nutr Soc 2012; 71: 298-306.
20. Teerachaisakul M, Ekataksin W, Durongwatana S, Taneepanichskul S. Risk factors for cellulitis in patients with lymphedema: a case-controlled study. Lymphology 2013; 46: 150-156.
21. Serdar ZA, Akçay SŞ, Inan A, Dağlı O. Evaluation of microbiological spectrum and risk factors of cellulitis in hospitalized patients. Cutan Ocul Toxicol 2011; 30: 221-224.
22. Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. Diabetes Care 2003; 26: 510-513.
23. Suaya JA, Eisenberg DF, Fang C, Miller LG. Skin and soft tissue infections and associated complications among commercially insured patients aged 0-64 years with and without diabetes in the U.S. PLoS One 2013; 8: 60057.
24. Jackson LA. Evaluating diabetes mellitus as a risk factor for community-acquired infections. Clin Infect Dis 2005; 41: 289-290.
25. Gupta S, Koirala J, Khardori R, Khardori N. Infections in diabetes mellitus and hyperglycemia. Infect Dis Clin North Am 2007; 21: 617-638.
26. Oumeish OY. Skin disorders in patients with diabetes. Clin Dermatol 2008; 26: 235-242.
27. Araco A, Gravante G, Sorge R, et al. Wound infections in aesthetic abdominoplasties: the role of smoking. Plast Reconstr Surg 2008; 121: 305-310.
28. Jain RK, Shukla R, Singh P, Kumar R. Epidemiology and risk factors for surgical site infections in patients requiring orthopedic surgery. Eur J Orthop Surg Traumatol 2015; 25: 251-254.
29. Lehr HA. Microcirculatory dysfunction induced by cigarette smoking. Microcirculation 2000; 7: 367-384.
30. Thomsen SF, Sørensen LT. Smoking and skin disease. Skin Therapy Lett 2010; 15: 4-7.
31. Kumar S, van Popta D, Rodrigues-Pinto R, et al. Risk factors for wound infection in surgery for spinal metastasis. Eur Spine J 2015; 24: 528-532.