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Factors associated with long bone fracture healing complications (delayed union, nonunion and malunions) in Arar, Saudi Arabia: A case control study

Basem M M Salama[1]✉, **Awwad Alenezy**[2], **Majed Alrowaili**[3]

[1]Department of Family & Community Medicine, Faculty of Medicine, Northern Border University, Saudi Arabia; and Community Medicine Department, Damietta Faculty of Medicine, Al-Azhar University, Egypt.
[2]Department of Family & Community Medicine, Faculty of Medicine, Northern Border University, Saudi Arabia
[3]Department of Surgery (Orthopedic Division), Faculty of Medicine, Northern Border University, Saudi Arabia

✉**Corresponding author**
Department of Family & Community Medicine, Faculty of Medicine, Northern Border University, Saudi Arabia; and Community Medicine Department, Damietta Faculty of Medicine, Al-Azhar University, Egypt;
Email: drbasemsalama@yahoo.com

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ABSTRACT

Background: Bone fractures are the commonest cause of hospitalized trauma. Fracture healing complications (FHC) is frequently associated pain, restricts the patient's activities, increases dependency and financial burden. This study aimed to identify factors which can affect fracture healing. *Subject and methods*: A nested case-cohort hospital-based study conducted patients (above the age 20 years) who were treated for acute fractures of long bones. 31 patients diagnosed with FHC (delayed union fracture) were chosen as cases and 124 Patients with normal fracture healing were included as controls. *Results*: By logistic regression analysis, smoking, age of the patient, gender, open fracture and diabetes were found to be independently associated with FHC. *Conclusion:* Smoking, age of the patient, gender; open fracture and diabetes were found to be the important risk factors of FHC.

Keywords: Fracture, bone, healing, risk, union.

1. INTRODUCTION

Bones are providing the body its shape, mechanical support, and protection and facilitating its movement (Oryan et al., 2015). Bone Fractures is the commonest cause of hospitalized trauma. Fracture healing consists of a cascade of cellular events and biochemical

factors finally leading to complete structural regeneration and functional restoration of the injured skeleton (Sadighi et al., 2015). Any disturbance during fracture healing stages, lead to an impaired healing process defined as healing complication (delayed union, nonunion or malunion) (Indu et al., 2014, Saoji et al. 2020). Delayed union was defined as fracture heals after four to six months or a fracture that has not united within a period of time that would be considered adequate for bone healing (Pountos et al., 2013). Nonunion was defined as a fracture has no possibility of healing without more specialized intervention (Pountos et al., 2013) or lack of boney bridging of a fracture after 6–12 months (Liu et al., 2018).

Healing complication is frequently associated pain, restricts the patient's activities, increases dependency and financial burden. It difficult to treat and may be requiring numerous surgical intervention to treat (Rupp et al., 2018). Fracture healing complication is a critical challenge facing both patients and healthcare and its treatment are very costly result in healthcare burden (Copuroglu et al., 2013). In the first six months' post-injury the direct costs for loss of productivity due to disability resulted from fracture and treatment costs up to $23,000 per isolated limb fracture, (Hak et al., 2014). Rates of FHC is 2- 10% of all diaphyseal fractures, varying according to study type sample size, patient sociodemographic character, injury site and severity and method of management (Ekegren et al., 2013). Fracture healing complications was (1.9%) in Scotland and 8% in Australia, of patients who had fractures and admitted to hospital per year (Mills & Simpson, 2014), while the overall incidence was among adult population (Beck et al., 2018).

Fracture healing restores the original physical and mechanical properties of the tissue of fracture part and is affected by a many of systemic and local factors. A number of risk factors are known to impair fracture healing, which can be classified as patient-related or patient independent. Factors related to Patient including age, sex, smoking, nutritional status, diabetes, and other comorbidities and nonsteroidal anti-inflammatory (NSAIDs) use. Patient nonrelated factors include fracture site, pattern and displacement, the degree of soft tissue injury, severity of bone loss, presence of site infection or not, and quality of fracture management (Leiblein et al., 2019; Lee et al., 2018; Westgeest et al., 2016).

This study aimed to identify factors which can affect fracture healing, enabling for appropriate targeting of patient monitoring and treatment.

2. PATIENTS AND METHOD

A nested case-control hospital-based study conducted from March 2018 to May 2019. The study was included 752 patients (above the age 20 years) who were treated for acute fractures of long bones (humerus, ulna, radius femur, tibia, and fibula) attended the orthopedic department. Patients were followed up at routine postoperative intervals to evaluate union based on radiographic evidence and clinical examinations. 31 patients diagnosed with FHC (delayed union fracture) were chosen as cases and 124 Patients with normal fracture healing were included as controls (3controls for everyone case).

A predesigned interviewing questionnaire was used to collect study variables from the participants such as age, sex, smoking habits, comorbidities like diabetes, hypertension, history of prolonged intake of NSAIDS or corticosteroid s, fracture type (open or closed), cause of fracture (motor vehicle accident or fallen), and infection of the fracture site.

Informed consent

All participants were given the right to participate or not in the study. Informed consent was taken from all participants shared in this study.

Statistical Analysis

Data entered and analysis using SPSS software, version 20.0 (SPSS Inc., Chicago, IL, USA). Using bivariate analysis; Chi square ($\chi 2$) or Fisher's exact tests were taken to compare categorical variables of interest. While multivariate logistic regressions analysis (enter approach) was performed to determine the independent factors affecting FHC. A p-value < 0.05 (95% CI) was interpreted as statistically significant.

3. RESULTS

During a 14-month period, 752 patients who received conservative treatment of fracture were prospectively evaluated. Of the 752 patients, 31 suffered from the delayed union. There were no cases of mal-union or un-union. 31 patients with the delayed union were chosen to serve as cases and 124 patients with normal healing were chosen as controls (3 controls for everyone case) for the purpose of statistical analysis.

Table 1 shows that, regarding sociodemographic factors, gender was significantly associated with fracture healing complications (FHC) and males were at more risk of (FHC) than females (OR = 3.4, 95% CI = 1.4-8.1) and Age > 45 years, compared with age <45, was linked with greater risk of (FHC) (OR = 6.3, 95% CI = 2.6-14.9). Comparing case to control group, smoking was associated with

greater risk (FHC) (OR = 2.3, 95% CI = 1.1-5.2to 15.5). Also diabetes associated with greater risk of (FHC) (OR = 2.6, 95% CI = 1.1-6.5) and prolonged intake of (NSAIDs) associated with more risk of (FHC) (OR = 2.4, 95% CI = 1.1-5.8).

Patients who had a fracture due to motor vehicle accidents were at more risk of (FHC) (OR = 3.4, CI: 1.5-7.9). Also, fracture's wound infection linked with greater risk of (FHC) (OR = 3.5, 95% CI = 1.1-10.9). Patients who had open fracture were more likely to suffer from (FHC) (OR = 3.4, 95% CI = 1.5-7.9). There was no statistically significant difference (P >0. 05) between cases and controls groups as regards the history of hypertension and prolonged intake of corticosteroid.

Logistic regression analysis revealed that, smoking, patient age, gender, open fracture and diabetes were found to be independently associated with (FHC) (OR =8.1, CI = [2.3-29.1], OR =7.8, CI = [2.5-24.3], OR =7.1, CI = [2.1-24.1], OR =7.9, CI = [2.1-30.1], OR =6.5, CI = [1.6-26.6] respectively) (Table 2 & figure 1).

Table 1 Comparison between cases and control regarding patient and fracture characteristics

	Cases N=31	Controls N=124	Odd ratio	95% CI	P value
Age: >45 years	16 (52%)	18 (15%)	6.3	2.6-14.9	0.001
≤45 years	15 (48%)	106 (85%)			
Sex: male	23 (74%)	57 (46%)	3.4	1.4-8.1	0.005
Smoking: Yes	20 (65%)	55 (44%)	2.3	1.1-5.2	0.045
Diabetes: Yes	10 (32%)	19 (15%)	2.6	1.1-6.5	0.03
Hypertension: Yes	5 (16%)	30 (24%)	0.6	0.2-1.7	0.3
NSAIDS: Yes	11 (36%)	23 (19%)	2.4	1.0-.8	0.04
corticosteroids: Yes	10 (32%)	34 (27%)	1.3	0.6-3.0	0.5
open fracture: Yes	14 (45%)	24 (19%)	3.4	1.5-7.9	0.003
Cause of fracture					
Motor vehicle accident	20 (65%)	53(43%)	2.4	1.1-5.5	0.03
Falls	11 (35%)	71 (57%)			
Fracture site Infection: Yes	6 (19%)	8 (7%)	3.5	1.1-10.9	0.03

Table 2 Multivariate logistic regression analysis of risk factors of FHC

	P-value	Adj. OR	CI (95%)
Smoking	0.001	8.1	2.3-29.1
Age	0.001	7.8	2.5-24.3
Gender	0.002	7.1	2.1-24.1
Open Fracture	0.002	7.9	2.1-30.1
Diabetes	0.009	6.5	1.6-26.6
Cause Of Fracture (Motor Vehicle Accident)	0.06	3.1	0.9-9.8
NSAIDs	0.08	3.1	0.6-10.9
Hypertension	0.42	1.8	0.5-6.9
Corticosteroid	0.44	1.6	0.5-5.6
Fracture Site Infection	0.82	1.2	0.3-6.2

4. DISCUSSION

Regarding gender and age, the study reported no significant difference between case and control group (Cheung et al., 2016; Stewart, 2019). Zura et al., 2016 found a difference between genders (rate of healing complication risk among males 5.4% compared with a 4.6% for females). This explained by vigorous activities of males, which my lead to higher energy fractures compared to females. Also more osteoblasts and good blood flow in the periosteum of children and young adults. Our results illustrated that smoking is associated withmore risk of FHC. This supported by similar findings of other studies, which proved that negative effect of smoking on fracture healing (Hernigou & Schuind, 2019; Pearson et al., 2016). Smoking activates the cholinergic anti-inflammatory,

which inhibits the secretion of TNF-alpha. In addition it reduces the oxygen carrying capacity of blood and acts as a vasoconstrictor leading decrease of tissue perfusion, hypoxia and ischaemia of the peripheral tissue which deteriorated bone healing (Xu et al., 2020).

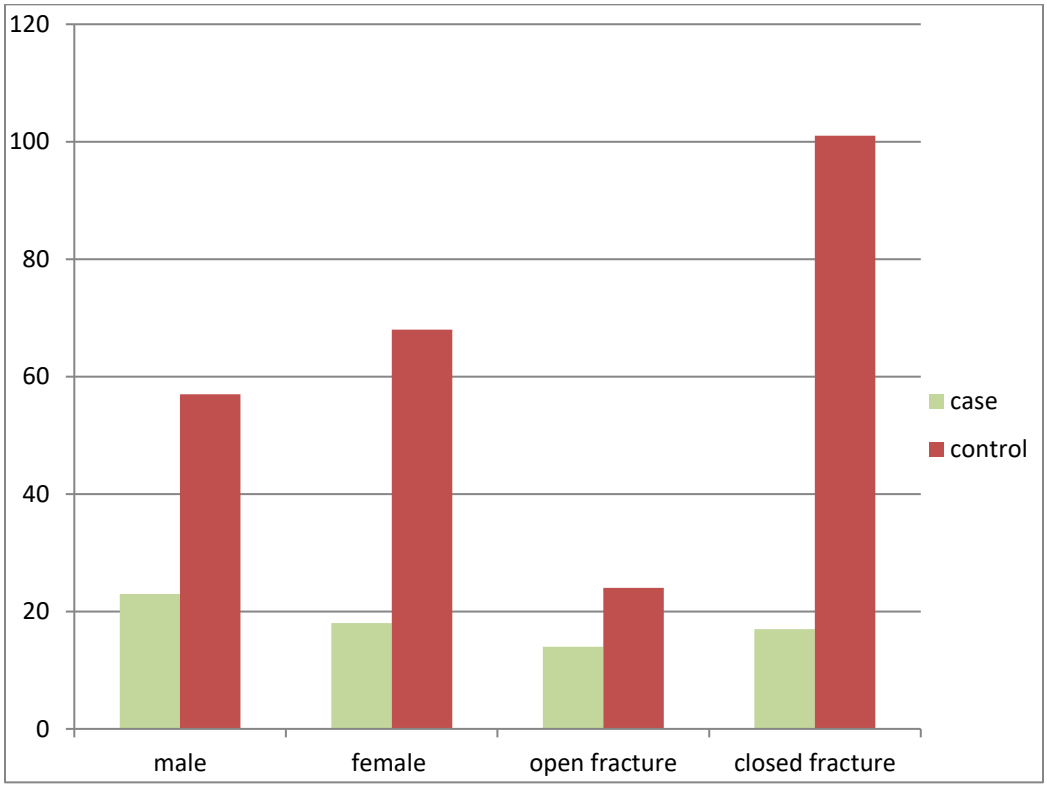

Figure 1 type of fracture and gender difference between cases and control groups

Diabetes mellitus associated with a risk of FHC. This in agreement with others (Sadighi et al., 2015; Marin et al., 2018) they found high risk of nonunion in diabetes mellitus patients (2-3 times more than non-diabetic patients). Diabetes often impaired shaft vascularization (Jiao et al., 2015). This study revealed that CRC was significantly associated with prolonged use of NSAID. This is coincides with other studies (Wang & Bhattacharyya, 2015; Kurmis et al., 2012), while it in contrary to (Indu et al., 2014) results. NSAID inhibits COX-2 factors which reducing osteoclastic activity leading to inhibition of fracture healing.

Our study revealed an association of open wound fracture and risk of FHC, this in line with previous studies finding (Mills et al., 2017; Nandra et al., 2016). Open fractures lead to soft tissue erosion and injury to the periosteal blood vessels impairing vascularity resulting in necrotic surfaces which inhibit the normal fracture healing. A significant association was seen between fracture site infections (p-value 0.002, OR= 6.11) and FHC. These in consistent with many studies (Kortram et al., 2017; Ebraheim et al., 2013; Sørensen, 2012) reported the same finding. Infection may lead to instability at the fracture site. Also, a vascular necrotic bone at the fracture site and osteolysis due to infection produce poor bony contact resulting in a delayed bony union.

5. CONCLUSION

This study concluded that smoking, age of the patient, gender; open fracture and diabetes were the only independent risk factors of FHC. Therefore, take proactive efforts to intervene early in high-risk patients.

Recommendation

More measurers to prevent smoking

Good control of diabetes and good care of open fracture.

Ethical approval

The study was approved by the Medical Ethics Committee of Northern Border University, Saudi Arabia (ethical approval code: A-37-10).

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Conflict of Interest

The authors have no conflict of interest.

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Data and materials availability

All data associated with this study are present in the paper.

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