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STUDY TO IDENTIFY MODIFIABLE RISK FACTORS ASSOCIATED WITH ADVERSE OUTCOMES IN PATIENTS WITH FRACTURE HEALING

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ABSTRACT Adverse outcome continues to be one of the most important post fracture problem .It may need multiple hospitalisations and surgical interventions, with an impact on the health of the patient and his/her surrounding family members. More over there is an additional burden to the health care system and the society as a whole due to the increased socioeconomic/financial implications. Patients with prolonged treatment for non-union have been reported to not only suffer from the physical sequelae of the disease process but also from psychological disturbances.Understanding the causative factors of fracture adverse outcome leads to both prevention and improvements in treatment. The purpose of this study was to understand the clinical characteristics and causative factors of adverse outcome. Methods Two hundred and ninety-one patients with fracture of the long bone who were surgically and conservatively treated in our hospital over the last 2 years wereanalysed. Data were collected by reviewing medical charts. Radiographs were reviewed to classify the adverse outcome by radiographic appearance. Causative factors of adverse outcome were identified for each patient. Factors relating to inadequate mechanical stability or reduction and those relating to a decline in biological activity were investigated. Mechanical factors included inappropriate reduction, inappropriate surgical management, insufficient fixation, and conservative treatment. Surgical technical errors were identified through careful review by three experienced trauma surgeons. Biological activity factors included comminution and bone loss, open fracture, excessive surgical exposure, alcohol abuse, diabetes mellitus, smoking, and metabolic disease or Osteoporosis . We also classified the causative factors as patient-dependent or patient-independent factors. Results Of the 291 patient, at 1 year follow up 199 patient had normal union and 18 patient were with delayed union .74 patient were had non-union at 1 year follow up.However, patients having multiple risk factors like male gender with lower socioeconomic status with smoking and alcohol addiction with comorbidities like Hypertension and Anaemia were found to be more prone for nonunion of fractures.

KEYWORDS : Fractures , physiologyical affects , non union ,delayed union

INTRODUCTION

Adverse outcome continues to be one of the most important post fracture problem .It may need multiple hospitalisations and surgical interventions, with an impact on the health of the patient and his/her surrounding family members. More over there is an additional burden to the health care system and the society as a whole due to the increased socioeconomic/financial implications. Patients with prolonged treatment for non-union have been reported to not only suffer from the physical sequelae of the disease process but also from psychological disturbances. They often abuse narcotics and alcohol due to the chronic painful stimuli and not infrequently there is a break down into their family lives leading to separation from their partners. Identifying factors which are thought to contribute to fracture non-union is thus essential in order to attempt to prevent its development and to intervene early .In this study we wished to study the risk factors that are well accepted by the scientific community that have a negative influence onrepair process of long bones .Classifying the papers according to the level of evidence allowed us to understand the relative importance given in the literature to each one of the parameters assessed. Some factors were found to have more gravitas than others.Therefore the existing ranking of evidence for each studied risk factor, we developed a stratification scale, placing at the top of the scale the manuscripts with the highest level of evidence, Overall the factors that were placed at the top of the scale included: open method of reduction, open fracture, presence of post-surgical fracture gap, smoking, infection, wedge or comminuted types of fracture, high degree of initial displacement, lack of adequate mechanical strength given by the implant used and location of fracture in the tibia and femoral bone according to the vascularity of the zones that these bones have been divided .The above described nine risk factors have been assigned to contribute to an impaired fracture healing process established on studies.

The extent of the healthcare burden and costs associated with long bone fractures needs to be well understood to enhance the framework of decision making regarding treatment patterns and health security coverage, and to better evaluate the outcomes of non-union fracture prevention. –(1)

MATERIALS AND METHODS

This ia an observational study done at department of Orthopaedics of tertiary health care situated in Central India The study includes a total number of 291 Patient enrolled in the study Duration of study was 2 years, from August 2016

Case selection

We enrolled cases from all individuals registered in the hospital records who had a diagnosis of long bone fracture between year **2016and 2018** and who were age 18 years and above with one or multiple risk factor .

Diagnosis for fracture-healing complications are not fracture site-specific, we choose the most recent fracture diagnosis before or on the date of the first diagnosis of fracture-healing complication to reflect the eligible fracture site. We merged fracture sites into the following category: long bones (i.e, humerus, radius, ulna, tibia, fibula, and femur) at proximal middle and distal part. Long bones were classified together because they are alike with respect to mechanical properties, as they are primarily loaded with bending and are composed of mostly cortical bone.

Exposures of interest

We chose to study patient-related risk factors including patient characteristics (age, sex, body mass index), blood investigations (Hb gm%), unprescribed drug (smoking, alcohol use and tobacco chewing), comorbidities (Hypertension, Diabetes mellitus, asthma and anemia), use of prescribed medications (steroids, NSAIDs, anticoagulants), and external factors (house hold injury, motor vehicle accident, work place injury). We assessed the presence of comorbidities, fall, and medication use in the year before the fracture date.

Clinical history along with co-morbidities, abuse of unprescribed drug, previous history of fracture, complications, duration of nonunion. Socio-economic and mode of injury.

Socio economic status of patient is measured with help of modified Prasad classification .osteoporosis taken in account with help of Singh's index of osteoporosis and X ray of pelvis with both hip antero-posterior view.

Patient were reviewed at 3rd,6th , 9th month and 1 year interval in clinic for analysis fracture healing , by clinical and radiological on basis of x rays.

Table-1 : Comparison of outcomes at follow-up at different time intervals

Outcomes	Follow-up							
	at 3 month		at 6 month		at 9 month		at 1 year	
	Number	%	Number	%	Number	%	Number	%
Healed	42	14.4%	104	35.7%	191	65.6%	199	68.4%
Healing	118	40.5%	60	20.6%	0	0.0%	0	0.0%
Delayed healing	131	45.0%	127	43.7%	291	100.0%	18	6.2%
Non union	0	0.0%	0	0.0%	0	0.0%	74	25.4%
Total	291	100.0%	291	100.0%	291	100.0%	291	100.0%

The proportion of healed cases increased significantly follow-up at 1 year (68.4%) as compared to healed cases at 3 month (14.4%)

RISK FACTORS ASSOCIATED WITH ADVERSE OUTCOMES:
Table-2: Adverse outcome and habit of smoking of the patients

Habit of smoking	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	9	26	73	108
Row %	8.3	24.1	67.6	100.0
Col %	50.0	35.1	36.9	37.2
No	9	48	125	182
Row %	4.9	26.4	68.7	100.0
Col %	50.0	64.9	63.1	62.8
TOTAL	18	74	198	290
Row %	6.2	25.5	68.3	100.0
Col %	100.0	100.0	100.0	100.0

there was significant association between habit of smoking and adverse outcome of the patients .Thus adverse outcomes were mostly prevalent among smokers as compared to non-smokers.The risk of adverse outcome (Delayed union or Nonunion) was 1.46 times more among the smokers as compared to the non-smokers and the risk was significant

Table-3: Adverse outcome and habit of tobacco chewing of the patients

Habit of tobacco chewing	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	11	43	120	174
Row %	6.3	24.7	69.0	100.0
Col %	61.1	58.1	60.3	59.8
No	7	31	79	117
Row %	6.0	26.5	67.5	100.0
Col %	38.9	41.9	39.7	40.2
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

Thus adverse outcomes were mostly prevalent among tobacco chewers as compared to non- tobacco chewers.The risk of adverse outcome (Delayed union or Nonunion) was 1.63 times more among the tobacco chewers as compared to non- tobacco chewers and the

risk was significant

Table-4 : Adverse outcome and habit of drinking of alcohol of the patients

Habit of drinking of alcohol	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	6	21	31	58
Row %	10.3	36.2	53.4	100.0
Col %	33.3	28.4	15.6	19.9
No	12	53	168	233
Row %	5.2	22.7	72.1	100.0
Col %	66.7	71.6	84.4	80.1
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

There was significant association between habit of drinking of alcohol and adverse outcome of the patients .Thus adverse outcomes were mostly prevalent among alcoholic patients as compared to nonalcoholic patients.

The risk of adverse outcome (Delayed union or Nonunion) was 1.63 times more among the alcoholic patients as compared to nonalcoholic patients and the risk was significant.

Table-5: Adverse outcome and diabetes mellitus of the patients

Diabetes mellitus	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	7	28	63	98
Row %	7.1	28.6	64.3	100.0
Col %	38.9	37.8	32.0	33.9
No	11	46	134	191
Row %	5.8	24.1	70.2	100.0
Col %	61.1	62.2	68.0	66.1
TOTAL	18	74	197	289
Row %	6.2	25.6	68.2	100.0
Col %	100.0	100.0	100.0	100.0

There was significant association between diabetes mellitus and adverse outcome of the patients . Thus adverse outcomes were mostly prevalent among the patients with diabetes mellitus as compared to the patients without diabetes mellitus.

The risk of adverse outcome (Delayed union or Nonunion) was 1.50 times more patients with diabetes mellitus as compared to the patients without diabetes mellitus and the risk was significant .

Table-6: Adverse outcome and hypertension of the patients

Hypertension	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	11	31	104	146
Row %	7.5	21.2	71.2	100.0
Col %	61.1	41.9	52.3	50.2
No	7	43	95	145
Row %	4.8	29.7	65.5	100.0
Col %	38.9	58.1	47.7	49.8
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

There was significant association between hypertension and adverse outcome of the patients. Thus adverse outcomes were mostly prevalent among the patients with hypertension as compared to the patients without diabetes mellitus.

The risk of adverse outcome (Delayed union or Nonunion) was 1.81 times more patients with hypertension as compared to the patients without hypertension and the risk was significant .

Table-7: Adverse outcome and asthma of the patients

Asthma	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	0	7	20	27
Row %	0.0	25.9	74.1	100.0
Col %	0.0	9.5	10.1	9.3
No	18	67	179	264
Row %	6.8	25.4	67.8	100.0
Col %	100.0	90.5	89.9	90.7
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

There was no significant association between asthma and adverse outcome of the patients . Thus adverse outcomes were more or less equally distributed among the patients with asthma and the patients without asthma.

Table-8: Adverse outcome and anemia of the patients

Anemia	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	10	24	65	99
Row %	10.1	24.2	65.7	100.0
Col %	55.6	32.4	32.7	34.0
No	8	50	134	192
Row %	4.2	26.0	69.8	100.0
Col %	44.4	67.6	67.3	66.0
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

There was significant association between anemia and adverse outcome of the patients . Thus adverse outcomes were mostly prevalent among the patients with anemia as compared to the patients without anemia.

The risk of adverse outcome (Delayed union or Nonunion) was 2.01 times more patients with anemia as compared to the patients without anemia and the risk was significant .

Table-9: Adverse outcome and osteoporosis of the patients

Osteoporosis	Adverse outcome			TOTAL
	Delayed union	Non union	Union	
Yes	5	31	97	133
Row %	3.8	23.3	72.9	100.0
Col %	27.8	41.9	48.7	45.7
No	13	43	102	158
Row %	8.2	27.2	64.6	100.0
Col %	72.2	58.1	51.3	54.3
TOTAL	18	74	199	291
Row %	6.2	25.4	68.4	100.0
Col %	100.0	100.0	100.0	100.0

There was significant association between osteoporosis and adverse outcome of the patients. Thus adverse outcomes were mostly prevalent among the patients with osteoporosis as compared to the patients without osteoporosis.

The risk of adverse outcome (Delayed union or Nonunion) was 1.14 times more patients with osteoporosis as compared to the patients without osteoporosis and the risk was significant .

DISCUSSION
In this study, risk factors related with fracture healing complications, in patients with fractures of long bones were observed.

Non Prescribed Drugs:
• **Smoking and tobacco**
37.1% of the patients were having habit of smoking and 62.9 % were nonsmokers. The results can be compared with study by Hernandez RK et al(1) in which 42% patients were smokers and 58 % were nonsmokers and W-Dahl A et al (54) in which nonsmoker cases were more than smokers.

On cross tabulation between smoking and adverse healing outcome, we found that There was significant association between habit of smoking (tobacco) and adverse outcome of the patients (p=0.017). Thus adverse outcomes like delayed union and nonunion were mostly prevalent among smokers as compared to non-smokers.Hernigou J et al (61) concluded that smoking (tobacco use) was significantly associated with nonunion, whether the fracture was open or closed (p<0.01) and similar observation were also W-Dahl A et al (54) and M.S.Gaston et al (31) who suggested the risk for smoker developing adverse healing complication was 2.5 times higher than that of nonsmoker . Castillo, Renan C et al (62) also stated that Smoking places the patient at risk for increased time to union and complications.Thus it was concluded that smoking and tobacco chewing was a risk factor for adverse healing outcome.

• **Alcohol**
19.9% of the patients were having habit of drinking of alcohol which was comparable with study of Askew A et al (55)in which population of alcoholic abuser(40%) was less as compared to non-alcoholic's abusers(60%).

On correlation of adverse outcome and alcoholism, the risk of adverse outcome (Delayed union or Nonunion) was 1.63 times more among the alcoholic patients as compared to nonalcoholic patientsand the risk was significant.Kanis JA et al (50) concluded alcohol intake was associated with an increased risk of any fracture. Askew A et al (55) concluded that The mean fracture healing time inalcoholics was approximately twice that in non-alcoholic's and this difference was highly significant. The frequency of delays in fracture healing in alcoholics was also significantly greater than in non-alcoholic's .as well as Chakkalakal et al (27) andM.S.Gaston et al (31) also concluded healing complication were more in alcoholic than nonalcoholic abuser's .Thus it was concluded that Alcoholism was a risk factor for adverse healing outcome

Comorbid conditions:
• **Diabetes mellitus**
There was significant association between diabetes mellitusand adverse outcome of the patients (p=0.0114). The risk of adverse outcome (Delayed union or Nonunion) was 1.50 times more inpatients with diabetes mellitus as compared to the patients without diabetes mellitus and the risk was significant. Similarly Hernandez RK et al (1)concluded that there is significant association between diabetes mellitus and adverse outcome. M.S.Gaston et al (31) clinical studies have demonstrated a significantly higher incidence of delayed union ,nonunion and a doubling of the time to healing of fracture in diabetic compared to non-diabetic patient . Sadighi A et al (43) also concluded Prevalence of nonunion in diabetic patients with fracture undergoing orthopaedics surgery is higher than the healthy individuals

• **Hypertension**
The risk of adverse outcome (Delayed union or Nonunion) was 1.81 times more patients with hypertension as compared to the patients without hypertension and the risk was significant. **Relatively similar studies were done by S. Yang et al (2014)**[36]stated Results **Women with hypertension** were more prone to fracture and delayed healing those without the disease. **Ilić et al (2013)(37)**study also had similar results.

• **Asthma**
There was no significant association between asthma and adverse outcome of the patients (p=0.371).T.P.Van staaet al (63) stated that oral steroid is used more commonly in asthma (40%) and observed dose dependent fracture risk .

• **Anemia**
The risk of adverse outcome (Delayed union or Nonunion) was 2.01

times more patients with anemiaas compared to the patients without anemia and the risk was significant.M.S.Gaston et al (31) also stated that a decrease in blood volume associated with anemia delayed healing .

• **Osteoporosis**

There was significant association between osteoporosis and adverse outcome of the patients (p=0.0131). The risk of adverse outcome (Delayed union or Nonunion) was 1.14 times more patients with osteoporosis as compared to the patients without osteoporosis and the risk was significant. Hernandez RK et al (1) obtained the similar result.Calori GM et al (48)described it as one of general risk factor contributing to nonunion.

Hence, comorbidities like DM, hypertension, anemia and osteoporosis was found to be a risk factor for adverse fracture healing outcome.

To observe the adverse effects of risk factors on the process of healing, the study group was divided into 2 categories i.e. patients having single risk factor and patients having multiple risk factors. Proportion of patients having multiple risk factors (83.2%) was significantly higher than that of patients having a single risk factor (16.8%). At the first, second and third follow ups, delayed healing was more prevalent in patients having multiple risk factors. On cross tabulation of final outcome and risk factor, it was found that non-union and delayed union of long bone fractures were mostly prevalent among the patients with multiple risk factors. The risk of non-unionwas 2.18 times more patients with multiple risk factors as compared to the patients with single risk factors and the risk was significant.

CONCLUSION
• There are number of risk factors which lead to delayed healing in spite of adequate management of fracture.
• Some of these risk factors are modifiable and attempt should be made for the benefit of the patient
• Risk factor are alcohol, tobacco chewing, smoking, diabetes mellitus, hypertension, asthma, anemia, and osteoporosis.
• In presence of multiple risk factors in a given patient as against single risk factor healing is delayed.
• Non prescribed risk factor like consumption of alcohol, tobacco chewing, and lack of nutrition in poor socio-economic group has adverse outcome in term of fracture healing.
• Our results are in conjunction with the finding available in the literature. Hence, it is advised to correct modifiable risk factors to the best possible extent.

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