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Study on risk factors affecting nonunion of fractures

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Abstract:

INTRODUCTION: Nonunion is one of the most common complications of fracture healing. The incidence of nonunion is believed to vary from 5% to 10%.

AIM: The aim of the research is to study the risk factors affecting nonunion of fractures and analyze the treatment taken, and it is bearing on nonunion.

MATERIALS AND METHODS: The study is a cross-sectional observational study with purposive sampling done in the orthopedic department. A total of 71 patients were selected, and a questionnaire was filled in with data obtained from the patient and medical records. Radiological evidence was also used to confirm the nonunion.

RESULTS: The sample included 48 men and 23 women. Of the females, 21 had attained menopause (91%). About 58% of the patients had taken treatment from Traditional Bone Setters (TBS), and 49% of the patients first went to a TBS before coming to the allopathic physician for fracture treatment. About 45% of the patients had a very short duration of immobilization of their fractures. A history of previous malignancy, bone cyst, or other illnesses lead to a longer time for recovery and return to work ($P = 0.0339$). Patients who had infected fractures had a significantly more number of surgeries than those without infection ($P = 0.015$). Nonsteroidal anti-inflammatory drugs use during treatment of fracture was also associated with nonunion ($P = 0.0077$), especially in allopathic medicine.

CONCLUSION: Nonunion continues to be a significant problem for all orthopedic surgeons despite their best ability to prevent them. A complete examination of the patient with relevant investigations and selection of the most suitable and appropriate treatment for each individual should be carried out; since each person is unique, and every fracture is not alike.

Keywords:

Fractures, nonunion, traditional bone setters

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Introduction

Fractures are one of the most common causes of disability and impairment. The annual fracture incidence in the United Kingdom is 3.6 fractures/100 people. The age-standardized lifetime prevalence of fractures is thought to be 38.2%.[1] The healing of fractures is a complex process which involves multiple factors working in tandem to bring about continuity of the structures and restore the bone to its original state. These factors are in equilibrium with each other, and there exists a fine balance between them. Any deficiency, disruption, or abnormality in any of the factors can lead to complications. Complications of fractures include delayed union, nonunion, malunion, joint stiffness, contractures, myositis ossificans, avascular necrosis, algodystrophy, osteomyelitis, growth disturbance, and deformity. Nonunion is one of the most common complications of fracture healing. The incidence of nonunion is believed to vary from 5% to 10%. However, a paucity of data on nonunion incidence and prevalence in the population and their risk factors were evident on review of literature.

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The risk factors that are associated with the development of nonunion include local and general factors. Local factors include type of fracture, severity, presence of infection, fixity, immobilization, radiation exposure, steroid use, time of removal of cast, and treatment method. In a study done by Karladani *et al*. soft-tissue conditions, high-energy trauma, fracture comminution, fracture displacement, treatment method, contamination, and associated injury were found to influence fracture healing.[2] However, a study done by Wu *et al*. found that female gender and fracture severity were not significantly associated with nonunion.[3] At the same time, increasing age and use of wire cerclage fixation had an increased risk of nonunions.

General factors analyzed include gender, age, metabolic, and nutritional status of the patient, general health, level of activity and muscle mass, smoking, and drug use. Shibuya *et al*. undertook an observational retrospective cohort study in 165 diabetic patients who were assessed for risk factors associated with nonunion, malunion, and delayed union. Hemoglobin A1c level more than 7%, peripheral neuropathy, surgery duration, were statistically significant and strongly associated with complications of fracture.[4] Dodson *et al*. showed that cigarette smoking, obesity, and diabetes were some of the factors linked with prognosis of ankle fractures.[5]

Nonunion for a prolonged period can lead to growth disturbance of the bone, impaired function of the limb or area, stiffness, osteoarthritis, injury to the surrounding nerves and tendons. Hence, timely treatment of fractures and nonunion itself is required to prevent these complications. Otherwise, it can lead to marked disability and physically challenged for the patient resulting in socioeconomic and psychological problems and rehabilitation of such patients is a long drawn-out process. There are three categories of patients presenting to us with nonunion. Adequately treated and followed up patients who present with nonunion shown by radiographs. Most of these patients may not feel any pain and will be symptomless. Another group includes patients who were not adequately treated and followed. The final group includes patients who have never consulted a doctor. In addition to the above, in India, we have a fourth set of patients who believe in the traditional bone setters for treatment. This presents another challenge to the physician during the treatment of fractures. The basis of traditional bone setting (TBS) and its relation to nonunion is not yet fully understood. Panda and Rout conducted a study on Puttur kattu (Bandage), a popular means of fracture reduction in this part of India. Most of the patients had direct contact with the traditional bone setters or had been old cases. They followed this treatment due to cheap and quicker services and traditional skill and fame. About 71% of the patients were satisfied with the treatment provided and 60% regarded allopathic practice as a costly option. It showed that out of 52 cases followed up, only 1 patient reported nonunion while 2 had delayed union and 3 patients had malunion.[6] One of the objectives this study aims to establish is the relationship between the practice of traditional bone setting and the appearance of nonunion.

There are many treatment modalities for reduction of fractures, but invariably due to many factors nonunion occurs. The management of the patient is also one of the factors which have a bearing on nonunion. In a study done by Calori *et al*. (2007) it was concluded that certain types of fractures have high risk of nonunion. They include fractures of scaphoid, clavicle, naviculus, fifth metatarsal, proximal humerus, and tibia. 90% of long bone nonunion can be successfully treated by a single operative procedure, but patients with infected nonunions required more than one procedure.[7]

A comprehensive research on factors affecting fractures from a gross perspective was found to be deficient, and therefore, this study was done to find the risk factors affecting all types of fractures leading to nonunion. Most studies focused on the fracture of individual bones and their consequences.

Materials and Methods

The study is a descriptive cross-sectional observational study. It was carried out in one of the largest tertiary care hospitals in South India. Patients presenting to the orthopedic department with nonunion of fractures were recruited for the study after giving written consent. The sample included adults of both genders, above the age of 18 years, undergoing treatment for nonunion with sufficient medical records and informed consent and radiological evidence of nonunion. The study excluded patients without sufficient medical records, on steroids and without informed consent. On an average, a total of 40–50 cases of fracture are reported in the outpatient department. Out of these, 5%–10% of the patients develop nonunion, and the study recruited one or two cases of nonunion coming to the hospital per day.

A questionnaire was filled in with data obtained from the patient and medical records. X-rays were also used to confirm the nonunion. The data collected were entered into the Microsoft Excel computer program and checked for any inconsistency. The results were presented in proportions/percentages. Mean, standard deviation, percentage, and coefficient of variation calculations were done. The statistical test used was Chi-square test.

Results

A total of 71 cases of nonunion were identified, including 48 men and 23 women. Of the females, 21 had attained menopause (91%). Age-wise distribution showed that patients in the age group of 30–40 years of age had the highest representation of 56% followed by 40–60 years of age at 22%. Based on the occupation, nonskilled workers included 35% of the sample, followed by farmers and unemployed at 22% each. Semi-professionals and skilled are at 7.05% each and professionals at 5.33%. Both urban (44%) and rural (56%) were equally present in the study. About 45% of the patients belonged to the middle class and 55% belonged to the lower class [Figure 1].

Habits such as alcohol and smoking are present in 42.5% and 35.21% of the patients, respectively, and those with diseases such as diabetes and tuberculosis form 36.62% and 11.27%, respectively. Previous history of bone cysts and malignancy was found in 33% of the patients, whereas 51% did not have any previous illnesses [Figure 2].

Open fractures accounted for 35% and closed fractures for 65% of the nonunions. 82% of the fractures were noncomminuted and 18% were comminuted fractures. Associated injuries along with the fracture were present in 42% of the patients. Both right- and left-sided fractures were equally involved in nonunion formation. The tibia was found to be the most common bone undergoing nonunion, followed by, fibula, femur, and humerus. Lower limb fractures were the most common at 69% followed by the upper limb at 28% [Figure 3].

From the above chart, it is seen that 58% of the patients had taken treatment from traditional bone setters after fracture. In addition, 49% of the patients first went to a TBS before coming to the allopathic physician for fracture treatment. Previous studies have attributed this to the inhibition of the patient to surgery and the cost involved. In part among those treated at the hospital, 60% of the patients had to undergo operative procedures for fracture reduction. In those who underwent operative procedures, 58% underwent two surgeries and 31% underwent one operative procedure [Table 1].

Chi-square = 1.155, degree of freedom 1, $P = 0.239$.

In upper limb fractures, duration of immobilization was <12 weeks, but in the lower limb, it was more than 12 weeks for majority of the patients. Since inadequate immobilization is one of the risk factors for nonunion, from the pie chart, it is seen that 45% of the patients had a very short duration of immobilization of their fractures. Fractures of the scaphoid, ulna, and femur require longer duration of immobilization than others.

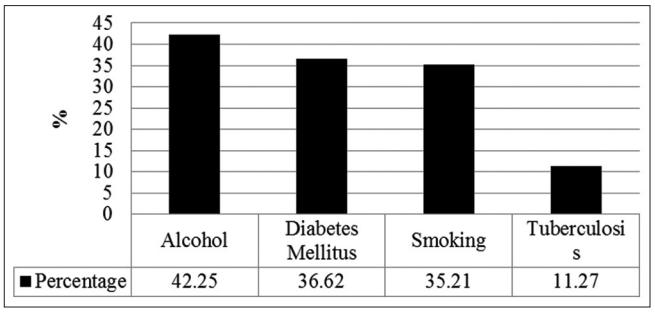

Figure 1: Habits and past illnesses

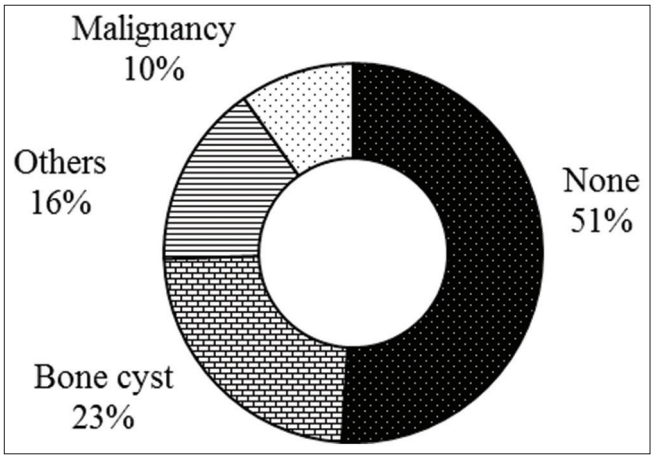

Figure 2: Previous illnesses

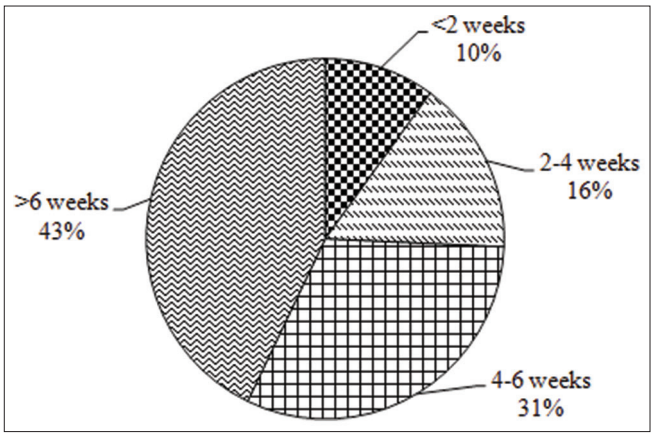

Figure 3: Time of removal of cast

Similarly, fractures of the axial skeleton, such as those of the ribs, scapula, clavicle and pelvic ring heal well without need for much immobilization. The opposite is also true, in the sense that excessive immobilization does more harm than good, especially fractures of the metacarpals and phalanges can lead to permanent joint stiffness [Figure 4].

Time of removal of cast was found to be taking more than 6 weeks in 43% of the patients while it was between 4 and 6 weeks for 31% of the patients and between 2 and 4 weeks for 16% of the patients. The cast was removed

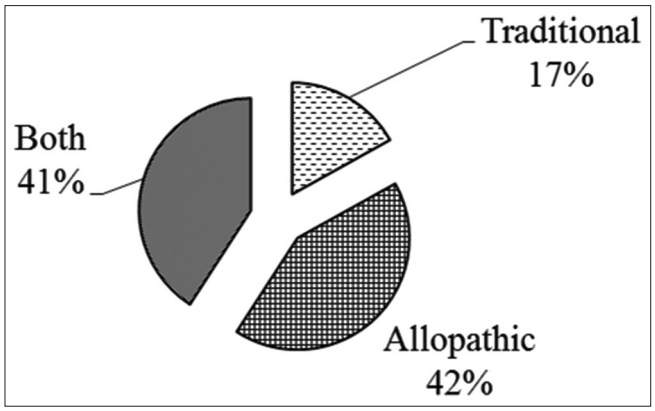

Figure 4: Type of treatment

within 2 weeks for only 10% of the patients. Time of removal of cast correlated with their time of return to work in most patients with 72% returning to work after 6 weeks. However, this long duration of employment will have an effect on the economic status of the patient since most of the patients belong to the lower and middle socioeconomic group [Figure 5].

The use of nonsteroidal anti-inflammatory drugs (NSAIDs) was found to be higher (67%), and it was calculated that alcoholic patients were also more likely to have used NSAIDs than nonalcoholics ($P = 0.0126$).

Discussion

From the data obtained, it is seen that 91% of the women presenting with nonunion had attained menopause. This could be attributed to the decreased protective effect of estrogen, which could be corrected by giving calcium and Vitamin D supplements. A history of previous malignancy, bone cyst or other illnesses lead to a longer time for recovery and return to work ($P = 0.0339$). Studies have shown that radiotherapy decreases fracture healing and causes changes in the biochemical and histological parameters [Table 2].[8-10]

Chi-square 11.9037, degree of freedom 2, $P = 0.0026$.

Traditional bonesetters were mostly preferred by patients belonging to the lower socioeconomic status ($n = 33$) when compared to those from middle class ($n = 26$). A study in Nigeria showed that most patients patronized traditional bone setters due to inexpensive treatment and quicker results.[11] Patients with closed fractures also chose traditional bone setters while those with open fractures came for allopathic treatment ($P = 0.0026$). The Puttur kattu was mostly used by patients who were illiterate and those with secondary and higher secondary education. The graduate people only comprised 20% of the patients at the Puttur Clinic.[6] Creating awareness among the people and encouraging them to come to

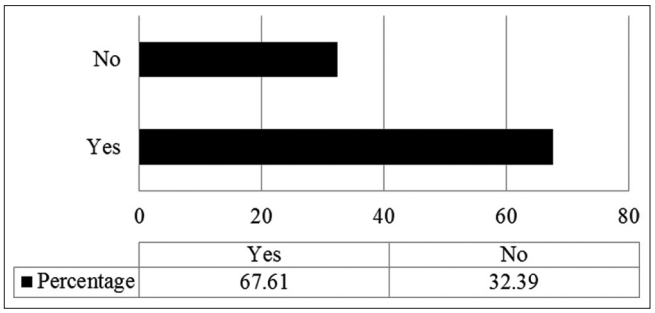

Figure 5: Nonsteroidal anti-inflammatory drugs use

Table 1: Duration of immobilisation versus site of fracture

Site	Duration of Immobilisation	
	<12 weeks	>12 weeks
Upper limb	11	9
Lower limb	20	29

Table 2: Type of treatment vs type of fracture

	Traditional	Allopathic	Both
Open fracture	4	17	4
Closed fracture	8	13	25

Table 3: Type of treatment versus socioeconomic conditions

Socioeconomic class	Initial Treatment		Total
	Traditional	Allopathic	
Lower	17	15	32
Upper	18	21	39
Total	35	36	71

Table 4: Nsaid's used versus type of treatment

Type of treatment	NSAIDS	
	Used	Not Used
Traditional	5	7
Allopathic	4	26
Both	17	12

trained orthopedist can prevent nonunion formation. At the same time, including the TBS for follow-up of the patients and [Table 3] patients who had infected fractures had a significantly more number of surgeries than those without infection ($P = 0.015$). The duration of immobilization was also significantly prolonged for older individuals with $P = 0.0235$. NSAID's use during treatment of fracture was also associated with nonunion ($P = 0.0077$), especially in allopathic medicine. Odds ratio for NSAID use was 2.6, in a similar study done by Hernandez *et al*.[12] Therefore, prudent use of NSAIDs during the recovery from fractures could lead to a decrease incidence of nonunion [Table 4].

Chi-square 9.7326, degree of freedom 2, $P = 0.0077$.

Giannoudis *et al*. proposed a theory for fracture healing called the "Diamond concept." According to this concept, there are four important factors involved in bone restoration. They include growth factors, scaffolds, mesenchymal stem cells, and the mechanical environment.[13] Hence, in the treatment of nonunion due diligence must be given to all the four factors. Underrepresentation of any one of these factors can lead to delayed union or nonunion.

Newer methods for fracture reduction include bone grafting, graft substitutes, bone morphogenetic protein (BMP), and platelet-rich plasma concentration (PRP). Autologous bone grafting currently remains the gold standard for the treatment of nonunion. However, due to complications arising out of donor graft tissue and further research, newer studies indicate possible use of BMPs, especially BMP-7.[14] Ongoing long-term studies have shown that it has been successful in relative terms when compared to other treatment methods. There is a failure rate of 6.2% compared to 38.5% for PRP. Three out of 12 cases of autologous iliac crest bone grafting (ICBG) required revision surgery when compared to one in 15 cases of BMP-7 use. Even in financial terms, BMP therapy was found to be more cost-effective than ICBG. The average hospital stay was 10.66 for ICBG versus 8.66 days for BMP-7 and time-to-union was 6.9 months for ICBG compared to 5.5 months for BMP-7.[15] However, sometimes, monotherapy alone is not enough to bring about union hence some surgeons recommend polygenic therapy which includes use of all three elements of the diamond concept.[16]

Limitations

Fracture healing being a continuous multiagency process, it is not possible to elucidate all the factors involved in the restoration of continuity. Further studies in this topic are required to reveal the confounding factors and determine the relation between various factors and bone growth and remodeling. Many other factors taking part have also not been examined in this study which would be carried forward to future research in this topic. This study is also limited by the lack of a control group to measure the strength of the association of risk factors. The sample size of this study is also small. There is also an inadequate amount of data on the prevalence and incidence of nonunion, therefore as sequel to this study; a prospective cohort study can be done to calculate the incidence of nonunion in fractures.

Conclusion

Nonunion continues to be a significant problem for all orthopedic surgeons despite their best ability to prevent them. Some of the risk factors that have been found associated with nonunion in this study include postmenopausal state, history of illnesses such as bone cyst and malignancy, patronage of TBS, site of the fracture, and NSAID use. The development of nonunion not only is due to patient practices and treatment inadequacy but also depends on the fracture etiology and local and systemic factors at play during the healing process. A complete examination of the patient with relevant investigations and selection of the most suitable and appropriate treatment for each individual based on their socioeconomic condition is in the best interest of both the parties; since each person is unique and every fracture is not alike.

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Conflicts of interest

There are no conflicts of interest.

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