Original article

Acute coagulofibrinolytic and inflammatory changes in response to intramedullary nailing and its impact on outcome[☆] Venencia Albert^a, Arulselvi Subramanian^{a,*}, Vivek Trikha^b, Senthil Kumar Veerappan^b, Arul Jothi^b^a Departments of Laboratory Medicine, Jai Prakash Narayan Apex Trauma Centre, AIIMS, New Delhi, India^b Department of Orthopaedics, Jai Prakash Narayan Apex Trauma Centre, All India Institute of Medical Sciences, New Delhi, India

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1. Introduction

Intramedullary nailing is the preferred course of care for the definitive management of femoral shaft fractures. Despite the superior biomechanical advantages over other implants, its use has been debated due to its possible harmful systemic effects in the patient experiencing trauma. Systemic inflammatory response, also called “first hit,” after injury is followed by counter inflammatory response, which is a hypo-inflammatory reaction to counter severe inflammation. Any further thrust, by an extensive invasive surgical, can lead to “second hit,” ending with acute respiratory distress syndrome (ARDS) multiple organ failure (MOF) and death.¹ Inflammatory reactions in response to injury are exacerbated by femoral nailing resulting in a hyper inflammatory reaction which is followed by hypo inflammatory phase.²

2–3% of isolated fracture shaft of femur patients develop, respiratory failure (RF) secondary to fat embolism, ARDS, pulmonary embolism. Rate of respiratory failure increases and ranges from 10 to 75%, in fracture shaft of femur with associated injuries depending on the method of surgical management.³

Intravasation of bone marrow and intramedullary fat⁴, causes systemic intravascular coagulation and fibrinolysis with aggregation of platelets and formation of fibrin clots^{5–6}. Inflammation

potentiates coagulation with increased risk of thrombosis and down regulation of protein C anti-coagulant pathway.⁷

Excessive and uncontrolled activation of the coagulative, fibrinolytic and inflammatory pathways and hemodynamic changes have been implicated in some patients with isolated femoral shaft fractures, potentially worsened in those with concomitant injury. However, the pathophysiology of this condition remains incompletely understood.

The aim of this study was to examine the coagulative and inflammatory response following intramedullary nailing (IMN) procedure in fracture shaft of femur. Our hypothesis with the primary objective of evaluating the trends in the levels of thrombin/antithrombin, routine coagulation assays and Interleukin 6 (IL-6) following IMN & secondary objective was to compare the post-operative changes in these markers between the following study (I, II) and control (III) groups:- Study group: isolated fracture shaft of femur & polytrauma with fracture shaft of femur undergoing IMN and Control group: Patients undergoing plating of distal fracture femur.

2. Methods & methodology

2.1. Study design

Prospective observational cross sectional study

2.2. Level of evidence

Level II

[☆] This study was presented at TRAUMA 2014, 27th–30th Nov 2014 in New Delhi, India. This study was presented (poster) at 38th SICOT Orthopaedic World Congress 2017, 30th Nov to 2nd Dec 2017 in Cape Town, South Africa.

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2.3. Setting

This study was conducted in the Department of Laboratory Medicine and Orthopedics, of a Level I Trauma Care Center in northern India, over a period of two years (2012–2014). Patient recruitment was done in the emergency room by orthopedic surgeons, and followed up to one year in the outpatient department, following informed consent. Approval from the Institute Ethics Committee was obtained prior to conducting this study [IEC/OP-1/2013].

2.4. Participants

Sixty orthopedic trauma patients undergoing intramedullary nailing procedure admitted during study period, were included in the study and categorized as Group I (Isolated fracture shaft femur) and Group II (Polytrauma (Any other injury other than Isolated fracture femur and/or Injury to any other organ system) along with isolated fracture shaft femur) based on the type and severity of injury. Fifteen patients undergoing external fixation of distal fracture of femur formed Group III (control). Patients with prior H/O (1) open grade II and II femoral shaft fractures, pathological fractures other than osteoporosis, (2) severe hypoxia, hypotension, acidosis and/or traumatic brain injury at the time of admission, (3) presence of metabolic bone disease, liver and renal insufficiency, (4) presence of inflammatory pathologies, systemic disorders (SLE), solid or hematological malignancies, (5) previous operation on the injured limb, (6) also patient taking long term nonsteroidal anti-inflammatory drugs (NSAIDs), antiplatelets, anticoagulants, steroids, immunosuppressive agents, antiresorptive agents, and parathyroid hormone were excluded along with secondary admissions. Also patients with incomplete follow up were retrospectively excluded.

Demographic data included age, sex, severity of injury, mode of injury, hospital length of stay, along with surgery related details such as: duration of surgery, time elapsed from injury to surgery, and whether the fracture site was opened during surgery or not, along with the clinical and laboratory investigations throughout hospital stay were recorded.

2.5. Surgical technique

Patients presenting at the emergency department were optimized according to the Advanced Trauma Life Support (ATLS) protocol, and were put on skeletal traction, if delay was anticipated, till the time of operation.

Isolated shaft femur fracture patients were operated at the earliest opportunity once they were optimized. Polytrauma patients were stabilized first with an external fixator within 48 h from injury and then operated for definitive fixation with reamed interlocking nail when deemed stable to undergo the procedure.

All the study patients were operated with standard closed antegrade IM nailing on fracture table under spinal or epidural anesthesia. Nails were locked both proximally and distally in all patients. Every attempt was made to perform the procedure closed however, in cases with delay if the reduction was not achieved mini open reduction of the two fragments was performed. Patients with distal femur fractures which were managed with external fixator initially and then definitively by plate were taken up as a control group. Plate application was also done once the patient was stabilized. Till then external fixator provided the splintage required.

2.6. Investigations

6 ml of blood samples were withdrawn preoperatively, post-operative at day 3, and 5 for all cases in group I and group II patients. For the group III (control) 6 ml of blood samples were withdrawn preoperatively and post-operative at day 3. Plasma based coagulation assay (prothrombin time, activated partial thromboplastin time, international normalized ratio, D-dimer & fibrinogen) along with ELISA analysis of Thrombin/Anti-thrombin complex (IMUBIND® TAT ELISA; catalog #ADG833, Sekisui Diagnostics GmbH) & Interleukin-6 (Human IL-6 Platinum ELISA, catalog #BMS213/2, eBiosciences, Vienna, Austria) were conducted as per manufacturer's instructions and data was maintained on a pre-designed pro-forma.

Any potential biased was addressed as the recruitment and laboratory investigations were performed by different individuals.

2.7. Outcome measure

The patients were mobilized from postoperative day one. Post-operative complications such as fat embolism syndrome, deep vein thrombosis, coagulopathy (defined as above than normal range of PT (16–2–16s), aPTT (28–36 s) and INR (<1.0)), sepsis (positive peripheral blood culture) and Acute respiratory distress syndrome (ARDS)⁸ were assessed throughout the course of hospital stay. After discharge, patients were scheduled for regular clinical, radiological and hematological follow-up in outpatient department at predefined time interval. Each patient underwent standard rehabilitation protocol; initial toe-touch weight bearing mobilization was commenced as tolerated from immediate post-operative period, which gradually progressed to partial weight bearing after 4 to 6 weeks. Full weight bearing mobilization was instituted after clinical and radiological confirmation of bony union, which was defined as union of 3/4 cortices on two orthogonal radiographs and absence of pain with weight bearing with/without support.

2.8. Statistical methods

Data was summarized as Mean $\pm$ S.D, differences within the groups were compared by *T*-Test/Mann Whitney test. Analysis of variance (ANOVA), followed by repeated measure analysis was applied to compare between study group (I & II) & control group (III) and between pre and post-surgery samples. *P* value of <0.05 was considered to be statistically significant. GEE population-averaged model was applied followed by repeated measure analysis to estimate the parameters of a generalized linear model with a possible unknown correlation between outcomes were done.

3. Results

3.1. Participants

A total of 86 orthopedic trauma patients were recruited in the study, however 10 were excluded due to incomplete follow-up. One polytrauma patient who developed acute pancreatitis following pancreatic and common bile duct injury with femoral fracture, died in the second week of the postoperative period cause of death being septic shock, was retrospectively excluded. 75 Patients were included, 58 men in the study group and 14 men in the control group, aged 27.1 ± 11.08 and 27.6 ± 11.5 years, respectively. ISS was 11.6 ± 3.85 for the study group and 10.7 ± 5.1 for control. The time from injury to admission was 2(1–19) days for the study group and 4.5 (1–30) days for control. The fractures were classified according to AO/OTA Classification. Study control had

additional injuries to the chest (n = 8) liver (n = 2) abdomen (n = 5) and other orthopedic fractures (n = 15). Average time from injury to IMN was 2(0–9) days for isolated fracture femur patients and 3(1–19) for fracture femur with other injuries [Table 1](#).

Hemoglobin levels, prior to surgical intervention were 10.6 ± 1.61 and 10.9 ± 1.94 for isolated fracture shaft femur and polytrauma with fracture shaft femur and 10.3 ± 1.94 for control. On admission anemia was seen in four patients in isolated femur fracture, seven in group polytrauma and two patients were anemic in control group [Table 1](#).

3.2. Coagulation markers

Routine plasma based coagulation assays i.e. prothrombin time (PT), activated partial thromboplastin time (aPTT), international normalized ratio (INR) and thrombin time (TT) was within normal range and did not vary across the two study groups and control on admission and post-surgical follow ups. Postoperative day 5 thrombin time was found to be significantly elevated in polytrauma patients in comparison to the isolated fracture patients. (p value 0.01). PT and INR were observed to be significantly elevated, prior to surgical intervention ($p < 0.0001$) as compared to post IMN surgery follow up samples in isolated fracture femur patients [Table 2](#).

In isolated fracture femur patient's fibrinogen levels elevated at day 1 and declined on postop day 3 & 5, approximately 60% of the patients in each of the groups had elevated d-dimer levels, however following fixation the percentage rose to 76.7% patients in group II and 79.7% on post op day 3, and later declined to 59.1% and 60% respectively on post op day 5 [Table 2](#).

Elevated concentrations of Thrombin-Antithrombin complexes (TAT) were observed in all three groups in response to trauma, however isolated fracture femur patient's had significantly higher TAT levels [99.1(2.2–219.4) vs. 76.3(1.6–212.4) & 16(1.1–79.6) respectively] compared to the other groups ($p < 0.001$)

TAT levels declined on postoperative day 1 (P value 0.009) and day 3 (P value 0.007) compared to the preoperative levels, although a statistically insignificant rise in TAT levels was observed on postop day 3 and day 5 compared to postoperative day 1 in isolated fracture femur patients [Fig. 1](#).

Similar trends in TAT levels were also observed in polytrauma patients, however it was statistically insignificant. In control a two

fold increase in the TAT levels was observed, although statistically insignificant.

3.3. Inflammation markers

Likely elevation in IL-6 Cytokine levels was observed in response to trauma, IL-6 levels in patients with isolated fracture femur was lowest compared to the polytrauma and control group [76.1(3.6–249.9) vs. 85.4(5.9–349) 181.6(2.4–356.3)], although statistically insignificant.

Postoperative elevation in the IL-6 levels were observed in isolated femur fracture and polytrauma patient groups, but was not statistically significant. A significant postoperative increase in polytrauma group (p 0.02), along with a significant follow up decline in IL-6 levels from postop day 1 to day 5 (P value 0.02) was observed; [Fig. 2](#)

3.4. GEE population-averaged model

To calculate the GEE model, log transformation of the data not following normal distribution was done, following repeated measure analysis, which showed statistically significant variation of the postoperative changes on day 3 for IL-6 amongst groups I & II and I & III, (p value 0.005). Preoperative levels of TAT were significantly higher in group I in comparison to groups II and III (p value < 0.001), however operative changes were only observed to be statistically significant between groups I & III (p value 0.04) [Table 3](#).

GEE population-averaged model depicts that overall declining trend in the levels of inflammatory markers IL-6 following fixation is statistically significant between control & isolated femur fracture also between control & polytrauma. For coagulation marker TAT although there is an overall increase in response to trauma (preoperative) between the control and study groups, which significantly higher levels in isolated femur fracture patients followed by polytrauma and lastly control, there is however no variation in the TAT levels in patients with isolated fracture and polytrauma following intramedullary nailing.

Table 1
On admission demographic & clinical details.

Parameters		Patient groups			
		External fixation (n = 10)	Isolated ^b femur IMN (n = 30)	Polytrauma IMN (n = 30)	p-value
Age		27.6 ± 11.5	26.4 ± 10.7	32.4 ± 8.3	0.20
Gender ^b	Male	14(93.3)	28(93.3)	30(100)	0.41
	Female	1(6.67)	2(6.67)	0(0)	
Mode of Injury ^b	RTA	7(50)	27(90)	22(73.3)	0.02
	Fall	6(42.8)	3(10)	7(23.3)	
	Miscellaneous	1(7.2)	0(0)	1(3.3)	
Injury severity score		10.6 ± 6.0	9 ± 0.1	14.3 ± 3.9	<0.001
Time taken from injury to surgery(days) ^a		4.5(1–270)	2(0–9)	3(1–19)	0.40
Haemoglobin(gms/dl)		10.6 ± 1.61	10.9 ± 1.94	103 ± 1.94	0.42
Haematocrit (%)		32.1 ± 5.55	33.4 ± 6.02	31.9 ± 6.24	0.60
Red blood cell count		3.6 ± 0.61	3.6 ± 0.74	3.3 ± 0.67	0.23
Platelet (/cu mm) ^a		179(100–544)	184(45–328)	177(45–639)	0.90
Total leukocyte count (x/cu mm) ^a		8200(4500–19700)	10250(4200–14900)	8850(4500–65900)	0.65
Coagulopathy ^b	No	14(93.3)	13(43.3)	14(46.7)	0.002
	Yes	1(6.7)	17(56.7)	16(53.3)	
Sepsis ^b	No	12(85.7)	28(93.3)	26(86.6)	0.69
	Yes	2(14.3)	2(6.7)	4(13.4)	

Bold values depict statistical significance (p value < 0.05).

Data expressed as Mean ± SD;

^a Median (min–max).

^b Frequency (%).

Table 2

Changes in the levels of conventional coagulation assays.

Parameters		Patient Group			p-value
		External fixation (n = 10)	Isolated ^a femur IMN (n = 30)	Polytrauma IMN (n = 30)	
Prothrombin time (12–16 s)	Pre-op	15.2 ± 1.88	16.2 ± 3.67	15.6 ± 2.53	0.58
	Day 1	–	15.6 ± 2.86	15.5 ± 2.29	0.94
	Day 3	14.2 ± 0.89	14.2 ± 2.04	14.7 ± 1.97	0.52
	Day 5	–	14.3 ± 1.61	16.7 ± 8.26	0.14
	p-value		<0.001 ^b	0.41	
Activated partial Thrombin time (28–36 s)	Pre-op	28.0 ± 3.47	28.7 ± 5.03	28.5 ± 3.76	0.86
	Day 1	–	29.5 ± 4.39	27.5 ± 4.42	0.08
	Day 3	29.1 ± 3.95	28.8 ± 5.39	27.7 ± 6.06	0.66
	Day 5	–	28.6 ± 5.46	32.2 ± 14.45	0.22
	p-value		0.83	0.14	
INR	Pre-op	1.1 ± 0.18	1.2 ± 0.44	1.1 ± 0.26	0.45
	Day 1	–	1.1 ± 0.29	1.1 ± 0.24	0.82
	Day 3	1.0 ± 0.08	1.0 ± 0.02	1.10 ± 0.19	0.43
	Day 5	–	1.0 ± 0.16	1.3 ± 1.03	0.19
	p-value		<0.001 ^c	0.53	
Fibrinogen (150–400 mg/dl)	Pre-op	471.2 ± 161.52	368.7 ± 193.81	383.8 ± 153.38	0.15
	Day 1	–	422.1 ± 160.82	390.3 ± 163.61	0.45
	Day 3	434.7 ± 184.4	390.5 ± 205.5	415.5 ± 171.69	0.74
	Day 5	–	370.188.34	392.9 ± 168.64	0.63
	p-value		0.54	0.59	

Bold values depict statistical significance (p value < 0.05).

ANOVA applied; followed by regression analysis with Bonferroni's post hoc analysis was done. Data expressed as Mean ± SD.

^a Frequency (%).^b pre-op vs. day3: 0.012; pre-op vs. day5: 0.008; day1 vs. day3: 0.012; day1 vs. day5: 0.013.^c pre-op vs. day3: 0.009; pre-op vs. day5: 0.008; day1 vs. day3: 0.010; day1 vs. day5: 0.022. **Fig. 1.** Temporal changes in the plasma levels of coagulation marker Thrombin Antithrombin complex in femur fracture patients with or without surgical intervention.

3.5. Outcome

Union occurred in all cases within the expected course of healing, except for 3 cases which went into delayed union and required minor corrective procedures like dynamization of the screws for fracture femur, and were healed within the following six months. Coagulopathy was observed in 16.7% of the patients with isolated femur fracture, 13.4% in polytrauma and 7.4% in external fixation, discordantly lower number of patients with isolated fracture femur developed sepsis defined as blood culture positivity, i.e. 6.7% compared to 13.4% in polytrauma and 14.2% in external fixation. 13.3% developed postoperative complications in group I, 23.3% in group isolated femur fracture, with one patient who

developed fat embolism syndrome with hemodynamic dysfunction, and one developed acute respiratory distress syndrome, 6.6% in group polytrauma group.

These variations were not for to be statistically significant with the type of procedure performed and/or with polytrauma/isolated fracture femur

4. Discussion

Operative procedures subsequent to traumatic injuries, represent a secondary insult to an already overwhelmed on-going physiological system, steering the patient with a primed inflammatory response towards increased odds of morbidity and mortality. Early IMN of long bone fractures in severely injured patients has been reported as beneficial, but has also been associated with increased inflammation, hemodynamic instability, as it may lead to further activation of inflammatory pathways, blood loss, or episodes of tissue hypoperfusion, hypoxia or fat embolization which may trigger development of ARDS^{8–11}.

The following are the major findings of our study on role of intramedullary nailing of long bone fractures as secondary inflammatory insults by assessing the coagulative and inflammatory response to IMN, using biomarkers of coagulation and inflammation

- Standard plasma based coagulation assays were within the normal range for patients in the study groups as well as study control, also no clinically significant elevation or decline in these investigations were observed succeeding intramedullary nailing
- There was a general marked elevation in the levels of thrombin-antithrombin complexes in response the orthopedic injury, and the highest elevation was seen in patients with isolated femur

Fig 2. Temporal changes in plasma proinflammatory IL-6 levels in femur fracture patients with or without surgical intervention.

Table 3

GEE population-averaged model, after log transformation to follow normal distribution.

Parameters	Patient Group				p-value
		External fixation (n = 10)	Isolated # femur IMN (n = 30)	Polytrauma IMN (n = 30)	
IL-6 (<12.7 pg/mL)	Pre-op	4.7 ± 1.39	4.02 ± 1.26	4.4 ± 0.85	Group 1 vs. Group2: <0.001 Group 1 vs. Group3: 0.006 Group 2 vs. Group3: 1.05
	Day 1		4.4 ± 1.16	4.4 ± 0.88	
	Day 3	4.9 ± 0.78	3.7 ± 1.34	3.9 ± 1.1	
	Day 5		3.8 ± 1.44	3.7 ± 1.03	
Thrombin/Antithrombin Complex (TAT) (<1.2–3.3 ng/mL)	Pre-op	2.1 ± 1.77	4.3 ± 1.12	4.0 ± 1.19	Group 1 vs. Group2: 0.039 Group 1 vs. Group3: 0.039 Group 2 vs. Group3: 0.02
	Day 1		3.9 ± 0.70	3.9 ± 1.08	
	Day 3	3.1 ± 1.31	3.8 ± 0.90	3.9 ± 0.89	
	Day 5		3.9 ± 1.10	3.9 ± 1.04	

Bold values depict statistical significance (p value < 0.05).

Data expressed as Mean ± SD.

- fracture, however these levels declined subsequent to intramedullary nailing in both isolated and polytrauma femur fracture patients. Also Postsurgical TAT levels were lower in isolated femur fracture patients compared to the polytrauma
- iii Similar to TAT levels traumatic injury also resulted in a surge in cytokine Interleukin-6 levels, but unlike TAT, IL-6 levels were lowest in isolated femur fracture patients. 24 h following intramedullary nailing there was a rise in the cytokine levels which later declined in the subsequent follow up days.
 - iv ARDS was only seen in one polytrauma patient post IMN, incidence of coagulopathy, sepsis and mortality was low and did not statistically vary among the study groups.

The embolic load produced during most nailing procedures is mild and it is assumed that these responses are normally self-limiting and homeostatically controlled, so that most pass unnoticed when measured by standard clinical markers.¹²

Our results suggest that there is a direct need of specific markers for the monitoring hemodynamic status of orthopedic patients that may help make the optimum surgical and treatment decisions in a trauma care set up. An elevated concentration of TAT and IL-6 in all three groups indicates their predisposition towards thrombosis and enhanced inflammation. Although literature suggests that surgical procedures may act as a second insult and may precipitate late multiple organ dysfunction syndrome if they

are performed in patients with multiple trauma while they still have an increased level of posttraumatic inflammation. On contrary we report a subsequent decline in TAT and IL-6 levels following nailing, indicating IMN does not directly trigger a second hit phenomenon, and that inflammation, hemodynamic instability following IMN is directly associated with high severity of injury as evident by the high postsurgical TAT and IL-6 levels in polytrauma patients compared to isolated femur fracture. Also when compared to other interventions IMN doesn't enhance inflammation as seen by the highly elevated IL-6 following external fixation, compared to IMN.

Robinson et al.¹² aimed to quantify the coagulative and cardiorespiratory response to nailing of isolated fractures, using sensitive, invasive monitoring, in 84 patients who had intramedullary nailing for isolated traumatic fractures of the tibia (group I, 34 patients) or of the femur (group II, 27 patients). Group III comprised 23 patients with pathological fractures of the femur. Within all groups there was a significant postoperative increase in PT, D dimers, PF1 + 2 and β -TG and a decrease in platelets and fibrinogen when compared with preoperative levels, they report

that reamed nailing is associated with the activation of coagulation and fibrinolysis along with the activation and consumption of platelets.

Husebye et al.¹³ evaluated the impact of primary femoral IMN on coagulation, fibrinolysis, inflammatory and cardiopulmonary responses in 12 polytrauma patients. The IMN operating time was 106 ± 7 (range 60–155) minutes. A marked activation of the coagulation and fibrinolytic systems was seen at hospital admission, but no significant procedure-related effect could be detected. Systemic activation of the coagulation system, represented by arterial TAT level increase, was present at patient admission to the hospital. The high TAT levels were mainly related to the injury. No increase of arterial TAT plasma concentration related to the IMN procedure was observed. They also report The IL-6 levels >200 pg/mL, elevated IL-6 levels in their study was in agreement with our study demonstrating a post injury association between increased levels of IL-6, and high ISS and postoperative complications.

Morley et al.¹⁴ observed very high IL-6 levels pre & post IMN (median 3947 at opening and 15,903 pg/mL after IMN), providing evidence that intramedullary reaming can cause a significant local inflammatory reaction

Giannoudis et al.¹⁵ studied the effect of femoral reaming on the inflammatory process as implicated in the pathogenesis of acute respiratory distress syndrome (ARDS) and multiple-organ failure

(MOF), by assessing the changes in the levels of serum interleukin-6 (IL-6) in 32 patients with femoral fractures treated by nailing. They found that the levels of serum IL-6 rose significantly during the nailing procedure indicating a measurable 'second hit'.

Hietbrink et al.¹⁶ studies il-6 surge in 45 isolated femur fracture and femur fracture in polytrauma patients. Eighteen hours after intramedullary nailing, plasma IL-6 levels were significantly increased in patients with isolated femur fractures but not polytrauma. They concluded that the inflammatory cellular response deficit to the development of ARDS appears to be mainly determined by the initial injuries and not the additional insult by IMN.

The timing of fracture fixation and the presence of associated injuries have been stated to influence the development of RF after femoral fractures but the contribution of these variables remains controversial³. Late fixation was identified as a risk factor by some authors¹⁷, but this was disputed by others¹⁸.

Low incidence of post-operative complications in our study group also supports our results, and thus we recommend early intramedullary nailing for patients with isolated femur fracture, and for patients who have other associated injuries, hemodynamic stability should be a priority than fixation, especially in a country such as India where in the primary responders to a site of traumatic incident are mostly bystanders and police personnel and not certified paramedics, that may provide appropriate trauma care to accident victims during this 'Golden Hour' of injury, thereby preventing fatalities. In our study the polytrauma patients were first stabilized by using less invasive surgical techniques, postponing fixation until they are hemodynamically stable with subsided inflammation and later scheduled for fixation, decrease the rate of postoperative organ failure. Damage control orthopedics concentrates on prevention of this severe inflammatory reaction, or second hit, while simultaneously stabilizing fractures to prevent further damage.²

Pape et al.¹⁹ randomized multiple injured patients (n = 165) with femoral shaft fractures to either initial (<24 h) intramedullary femoral nailing (n = 94) or external fixation and later conversion to an intramedullary nail (n = 71). The reported odds of developing acute lung injury were 6.69 times greater in borderline patients who underwent intramedullary nailing in comparison with those who underwent external fixation. They concluded that for multiple injury patients in a clinically stable condition, early intramedullary nailing of the femoral shaft fracture continues to be the gold standard for treatment, contrast to a higher incidence of systemic complications seen, if intramedullary nail fixation is performed for immediate stabilization of the femur fracture in patients who present in a borderline clinical condition. Thus they recommended in patients who present with an unclear status, the type of surgical procedure for fixation of a femoral shaft fracture should be carefully selected, according to the initial assessment of the clinical condition. In borderline patients, an external fixator should be applied for temporizing purposes.

4.1. Limitations

(i) On admission sampling was not done, therefore a true baseline could not be established (ii) Sampling was not done after damage control in polytrauma patients, which could have further asserted our results.

5. Conclusions

This is the first study of its kind which clinically and biochemically assess the effect of surgical treatments on inflammation and coagulation in fracture shaft of femur in India. Routine plasma based coagulation assays are not sufficient to assess

hemodynamic instability following orthopedic injuries and surgical procedures, as they failed to capture coagulation changes in all study group at all time points. Specific markers targeting thrombosis should be evaluated to monitor coagulation abnormalities, as seen by the decline in plasma TAT levels following IMN regardless of associated injury. Post-surgical TAT and IL-6 in isolated fracture femur were observed to be lower than polytrauma patients, suggesting that inflammation, hemodynamic instability following IMN is directly associated with severity of injury.

Damage control is a better proposition in polytrauma patients than early fixation, as the post-surgical IL6 levels of both isolated femur fracture group and polytrauma did not vary across the groups, and were significantly lower than external fixation group on day 3. Therefore emphasis should be given on hemodynamic stabilization prior to surgical management of orthopedic patients.

Conflict of interest

None.

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