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ABSTRACT

Severe infection and inflammation almost invariably lead to hemostatic abnormalities, ranging from insignificant laboratory changes to severe disseminated intravascular coagulation (DIC). The aim was to assess the effect of infection on coagulation parameters in infected burn wound that could predict for the development of DIC in those patients. This study included 60 patients (16 ♂ & 44 ♀), with mean age of 32.9 ± 10.5 years, they were treated in burn surgery unit Mansoura University Hospitals. They were classified into two groups, group I included 38 patients with burn wound infection, and group II included 22 patients with clean burn wound (control group). All cases were sub-

jected to through history taking and clinical examination. For cases with infected wounds, sterile swabs were used for aspiration of deeply seated wound pus for microbiologic examination. Blood samples were collected for prothrombin time (PT), activated partial thromboplastin time (APTT), platelet count and fibrinogen concentration detection. This study revealed females (73.3%) were mostly affected by burn insults than males (26.7%). Out of 60 studied cases 61.7% had 3rd degree of burn and 63.3% developed burn wound infection. The most frequently isolated organisms from infected wound (38) were pseudomonas aeruginosa (31.6%), E.coli (18.4%), proteus (13.2%), coagulase negative Staphylococci (coag. -ve

Staph) (10.5%), while the least were anaerobes (5.3%) and *Candida albicans* (2.6%). On comparing burn cases with infected wounds (gpl) to those with clean burn wound (gpII) for the hemostatic changes, there was highly significant increased both PT & APTT in gpl than gpII ($P \leq 0.001$ for each), while there was highly significant decreased both platelet count and fibrinogen concentration in gpl vs gpII ($P \leq 0.001$ for each). In conclusion sepsis decreases circulating platelets and interfere with hemostatic functions. Combinations of APTT, PT, fibrinogen level and platelet count are considered good screening tests for predicating DIC in those patients.

INTRODUCTION

Infection remains the leading cause of death among patients who are hospitalized for burns.(1) Burn wound represents a susceptible site for colonization by organisms either of endogenous or exogenous origin.(2)

Thromboembolic venous disease (TVD) is one of the most important causes of morbidity and mortality. It ranges from 5-7% in burn patients.(3) The activation of hemostatic factors and the long stays in bed have been

considered pathogenic factors of this complication(4).

The modification of routine hemocoagulative parameters in burn pathology is a fairly common finding. In addition, to the new regulatory mechanisms of coagulation system, it is now clear that the existence of a positive feed-back between inflammation and coagulation. As a result of marked imbalances in haemostatic equilibrium, there may be sometimes cases of severe hemorrhage which represent a grave clinical problem, possibly even leading to the death of the burn victim(5).

Because the pre-thrombotic state is frequently present in the burn patients, our aim was to assess the effect of infection on coagulation parameters and how could to predict for the development of pre DIC and DIC by using simple screening tests.

MATERIAL AND METHODS

This study was conducted on 60 patients (16 ♂ & 44 ♀) with burned Body surface area (BSA) over 30%. All of them had 2nd or 3rd degree burns. They were selected from burn Surgery Unit, Mansoura University Hospital. They were classified into

two groups, group I included 38 patients with infected burn wound, and group II included 22 patients with clean burn wound.

All patients are subjected to through history taking and clinical examination including classification of burn into either 2nd (partial thickness) or 3rd (full thickness) degree.

Burn wound was classified as wound cellulites which involves the unburned skin at the margin of the burn, or as an invasive wound infection, which is characterized by microbial invasion of viable tissue beneath the burn eschar. Clinical signs suggestive of burn wound infection include the progression of partial-thickness to full-thickness injury, changes in wound color (focal areas of red, brown, or black discoloration, green discoloration of the subcutaneous fat, violaceous discoloration and edema of wound margins and subeschar hemorrhage).

Effective topical antimicrobial therapy and daily wound inspection are necessary to monitor for infection, which may cause conversion of partial-thickness burns to full-thickness injuries.

Management of severe burn wounds is aimed at preventing the bacterial infections and progression of injury by maintaining adequate tissue oxygenation through aggressive volume repletion and early removal of necrotic tissue and the effective topical and systemic antimicrobial chemotherapies followed by wound closure by skin grafts.

Sampling :

Samples were collected on EDTA for CBC and on sodium citrate for hemostatic tests.

Cases with infected burn wound, after cleansing the wound with sterile saline, sterile swabs were used for sample collection for aerobic culture. Syringes were used for aspiration of deeply seated infected wounds that were cultured anaerobically.

Procedures :

1- Hematological test :

- a) CBC was performed by automated cell counter system (Sysmex Corporation).
- b) Hemostatic tests including:
 - Prothrombin time (Diamed AG, 17855, Cressier S, Morat, Switzerland).
 - Activated partial thromboplastin

time (Diamed kit on automated Coagulometer Sysmex-CA 500).

- Fibrinogen level (DADE Behring New York, DE, 19 7/4 USA).

Normal values were established by pooled plasma collected from 15 healthy subjects.

2- Microbiological tests:

Swabs for aerobic culture were inoculated into blood agar plates and inoculated aerobically at 37°C for 24h. Specimens for anaerobic culture were inoculated into scheduler blood agar, inoculated anaerobically inside Mc- Intoch Jar with addition of anaerobic package (Oxoid) (Accumed International Ltd., USA). Isolated colonies were identified by gram stained smears, coagulase test for staphylococci and automated Sensititre system for gram negative bacilli.

This system utilizes fluorescence technology to detect the metabolic activity. The system is based upon the reactions activated with 32 biochemical tests prepared and directed into the Sensititre plates.

Aspirated syringe from deeply seated wounds was subjected to culture on Scheadler blood agar

plates (Oxoid, Unipath Limited, UK) and gram stained smear. Plates were incubated anaerobically in the McIntoch Jar after using anaerobic package (Oxoid), inspected daily and examined for isolated organisms.

RESULTS

General characteristics of the studied 60 patients with burn are shown in table (1): They were (16 ♂ and 44 ♀) with ages ranged from 17-54 years (32.9 ± 10.5). Out of the studied 60 cases, 23 (38.3%) had 2nd degree burn and 37 (61.7%) had 3rd degree burn, and 38 (63.3%) had infected burn wound and 22 (36.7%) cases had clean burn wound.

Isolated organisms from infected wounds (38 cases) are illustrated in table (2). The most frequently isolated organisms were pseudomonas aeruginosa (31.6%), E.coli (18.4%), proteus (13.2%), coag. -ve staph (10.5%), and enterococci (7.8%). This was followed by staphylococcus aureus, klebsiella, and anaerobes (5.3% for each), while the least was candida albicans (2.6%). Table (3) represents a comparison between cases with infected wounds (gpl) to those with clean burn wound (gpII), for different variables. There were insignificant

increased cases with infection in females (63.6%), then males (62.5%). Also, there was insignificantly increased percentage of infection in cases with 3rd degree burn than those with 2nd degree burn ($P=0.7$).

Impacts of wound infection on the hemostatic parameters are discussed in table (4). There was highly significant increased PT and APTT ($P\leq 0.001$ for each) in gpl vs gpil. However, each of fibrinogen level and platelet count was significantly de-

creased in gpl vs gpil ($P\leq 0.001$ for each).

In the patients who have infective complications, we observed a progressive deterioration of the hemocoagulative parameters, especially with regard to thrombocytosis. These modifications of haemostatic equilibrium and consequently the DIC seemed to be connected with the onset of sepsis. This modification was occurred much more with reported high incidence of the pseudomonas infection (12 out of the 38 patients).

Table (1): General characteristic of the studied 60 cases.

Sex	M (no & %)	16 (26.7%)
	F (no & %)	44 (73.3%)
Age	M \pm SD	32.9 \pm 10.5
Degree of burn	2 nd	23 (38.3%)
	3 rd	37 (61.7%)
Wound infection	-ve	22 (36.7%)
	+ve	38 (63.3%)

Table (2): Identification of isolated organisms in infected wound (38 cases).

Organism	Frequency	%
Pseudomonas	12	31.6
E.coli	7	18.4
Proteus	5	13.2
Staph. -ve	4	10.5
Enterococci	3	7.8
Staph. aureus	2	5.3
Klebsiella	2	5.3
Anaerobes	2	5.3
Candida	1	2.6
Total	38	100

Table (3): Comparison between infected (gpI) and non infected (gpII) wounds in the studied 60 cases.

		gpI 38 (63.3%)	gpII 22 (36.7%)	Sig. Test	P
Age	M ± SD	33.1 ± 11.3	32.9 ± 9.0	t 0.168	0.8
Gender	M	10 (62.5%)	6 (37.5%)	X ² 0.007	0.9
	F	28 (63.6%)	16 (36.3%)		
Burn degree	2 nd	14 (36.8%)	9 (40.9%)	X ² 0.097	0.7
	3 rd	24 (63.2%)	13 (59.1%)		

Table (4): Effect of wound infection on hemostatic parameters of the gpI vs gpII.

		gpI 38 (63.3%)	gpII 22 (36.7%)	Sig. Test	P
PT	M ± SD	16.3 ± 2.3	12.5 ± 0.6	t 7.1	≤0.001
APTT	M ± SD	42.2 ± 7.1	30.1 ± 2.0	t 7.6	≤0.001
Fibrinogen	M ± SD	16.8 ± 72.9	606 ± 215.5	Z 5.8	≤0.001
Platelet	M ± SD	107.5 ± 27.2	228.0 ± 55	Z 6.3	≤0.001

DISCUSSION

The burn injury causes mechanical disruption to the skin, which allows environmental microbes to invade the deeper tissues. The usual skin barrier to microbes is replaced by a moist, protein-rich, avascular eschar that fosters microbial growth. The avascularity of the eschar prevents migration of immune cells and restricts the distribution of systemically administered antibiotics. Furthermore, toxic intermediaries released by the eschar can impede the immune response.⁽⁶⁾ The burn wound surface is sterile immediately following injury; however, it is repopulated quickly with gram-positive organisms from hair follicles, skin appendage, and the environment during the first 48 hours. More virulent gram-negative organisms replace the gram-positive organisms after 5-7 days. Gram negative organisms have greater motility, possess many antibiotic resistance mechanisms, and have the ability to secrete collagenases, proteases, lipases, and elastases, enabling them to proliferate and penetrate into the subeschar space.⁽⁷⁾

The proinflammatory cytokines produced by sepsis act directly to affect organ function or they may act indirectly through secondary mediators.

Endotoxin can also cause the release of tissue-factor by endothelial cells leading to fibrin and activation of the coagulation cascade depletes the patient's ability to make clot resulting in hemostatic abnormalities, ranging from insignificant laboratory changes to severe disseminated intravascular coagulation (DIC).⁽⁸⁾ On the other hand, increased production of plasminogen-activator inhibitor-I from vascular endothelium suppresses the fibrinolytic activity. These procoagulant changes are further accelerated by decreased circulating levels of antithrombin III, protein C, and protein S⁽⁹⁾.

It was mentioned by Mousa⁽¹⁰⁾ and Revathi et al⁽¹¹⁾ that organisms most frequently isolated from burn are *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Klebsiella pneumoniae*, *Aspergillus* species, and *Candida albicans*. *Pseudomonas aeruginosa*, which is the most important and dangerous bacterium in burn sepsis.⁽¹²⁾

In our study, the frequently isolated organisms were *Pseudomonas aeruginosa* (31.6%), *E. coli* (18.4%), *Proteus* (13.2%), *Staphylococci coagulase negative* (10.5%), while the least were anaerobes (5.3%) and

Candida albicans (2.6%). Among the modification of coagulation parameters that occurred in infected burnt patients (38), 12 patients were infected by *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* are the agents most likely to cause infections in burn that would be accompanied by activation of coagulation and fibrinolysis.⁽¹³⁾

Recent advances in understanding the pathogenesis of sepsis declared that bacterial products such as endotoxins, in gram -ve bacteria, or cell wall fragments, in gram +ve bacteria, are able to trigger the inflammatory and coagulation pathway directly or indirectly through inflammatory cells to produce inflammatory cytokines.⁽¹⁴⁾

Corral et al.⁽¹⁵⁾ suggested that activation of coagulation by endotoxins is severe in sepsis. On the other hand, Arora et al.⁽¹⁶⁾, in a similar study, found that there was no significant difference on coagulation parameters in gram positive and gram negative infection.

In this work, on comparing burn cases with infected wounds (group I) to those without infection (group II) as regards the changes in hemostatic par-

ameters, there was highly significant increase in both PT & APTT in infected cases ($P \leq 0.001$ for each). While there was significantly decreased fibrinogen concentration and platelet count in infected than those with clean burn wound ($P \leq 0.001$ for each) however in a study by Arora et al. they found that platelet count was not significantly decreased, while fibrin/fibrinogen degradation products were significantly higher in cases with sepsis. In a study of association between sepsis and the changes in hemostatic molecular markers by Iba et al.⁽¹⁷⁾, they mentioned that low fibrinogen levels though specific for DIC were present in only low percent of their studied cases and were normal in some cases with septicemia. They added that combination of $APTT > 38$ sec., with $PT > 15$ sec. and low platelet count were good screening tests for developing DIC. In cases of severe sepsis in burn injury, the sequelae of the imbalance between inflammatory mediators and their antagonists can lead to endothelial injury, and dynamic alterations in the coagulation and fibrinolysis, and so-called DIC. The changes in blood coagulation, fibrinolysis, they help to cast light on the various phenomena that occur in haemostasis, regarding both coagulation

and fibrinolysis; any modification of these parameters could be a warning signal of a condition which from an initial subclinical level might evolve towards a *more serious condition like DIC.*

In conclusion, the purpose of our study is to identify, if possible, among the data that will accumulate from a routine use of these tests a correlation with the survival of burn patients. We hope that these procedures will provide us with information on the basis of which it will be possible to draw up a protocol of clinical and laboratory control enabling us to formulate predictions regarding hemocoagulative conditions, i.e. to foresee the turning point towards conditions of hypercoagulation when there is still time to initiate correct therapy including early excision of necrotic tissue and skin grafting that might coincide with study by Still and Law⁽¹⁸⁾ to decrease the frequency of burn wound sepsis and consequently DIC.

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الإعتبرارات المبدئية لمشاكل التجلط الناتجة عن الحروق

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وحدة جراحة التجميل وقسم الباثولوجيا الإكلينيكية

كلية الطب - جامعة المنصورة

من المعروف أن العدوى الميكروبية والإلتهابات يصاحبها تغيرات فى أرقام الدم تتراوح بين تغيرات

معملية بسيطة الى حدوث جلطات الأوعية الدموية.

يهدف البحث الى دراسة تأثير العدوى الميكروبية على أرقام الدم والذي قد يساعد فى توقع حدوث

جلطات الأوعية الدموية.

ضم البحث ٦٠ مريضاً (١٦ ذكور و٤٤ أنثى) تم اختيارهم من وحدة جراحة التجميل والحروق تم أخذ التاريخ المرضى والكشف الإكلينيكي وقسم المرضى الى مجموعتين، المجموعة الأولى تشمل ٣٨ من المرضى المصابين بتلوث الحروق والمجموعة الثانية تشمل ٢٢ مصاباً بالحروق بدون تلوث .

أخذت عينات الدم لعمل صور الدم واختبارات زمن البروثرومبين وزمن الثرمبولاستين الجزئى النشط وتعيين نسبة الفيبيرينوجين فى الدم كما أخذت من المجموعة الأولى مسحات لعمل المزارع الميكروبيولوجية.

أسفر البحث عن أن معظم الميكروبات التى تم عزلها من حالات الحروق الملوثة من أنواع سيدومونس.

وعند مقارنة الحالات المصابة بتلوث الحروق بغير المصابة وجد زيادة ذو دلالة إحصائية فى كل من زمن

البروثرومبين الجزئى النشط بينما كان هناك إنخفاضاً ذو دلالة إحصائية فى كل من عدد الصفائح الدموية

ونسبة الفيبيرينوجين فى الدم ويستخلص من هذا البحث: أن مجموعة الإختبارات المكونة من زمن البروثرومبين

والثرمبولاستين الجزئى النشط وعدد الصفائح الدموية ونسبة الفيبيرينوجين فى الدم تعد من الإختبارات

البسيطة السهلة التى يمكن الإستعانة بها كاختبارات مسح أولى تمكن من توقع حدوث جلطات الأوعية

الدموية فى حالات الحروق الملوثة .

