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PLATELET FUNCTIONS IN PATIENTS WITH MENINGOCOCCAL MENINGITIS AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI

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## PLATELET FUNCTIONS IN PATIENTS WITH MENINGOCOCCAL MENINGITIS AT THE KENYATTA NATIONAL HOSPITAL, NAIROBI

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### ABSTRACT

**Objective:** To determine platelet abnormalities in patients with meningococcal meningitis.

**Design:** Case control study.

**Subjects:** Fifty seven cases of meningococcal meningitis based on a cerebrospinal fluid gram stain for gram negative diplococcus or positive culture were recruited. Fifty-seven controls matched for age and sex were also recruited. The following platelet functions tests were performed; platelet counts, platelet adhesiveness, platelet aggregation and clot retraction.

**Results:** Fifty seven patients (41 males and 16 females) with meningococcal meningitis were studied. Their mean age was  $25.5 \pm 8.32$  years with a range of 15 to 45 years. Five patients had purpura, four peripheral gangrene, eight conjunctival haemorrhages and one was in shock. There was a statistical significant difference in the platelet aggregation and clot retraction between the patients and controls at p-values of 0.0001 and 0.0002 respectively. There was no significant difference in the platelet count and adhesiveness between the patients and the controls at a p-value of 0.203 and 0.22 respectively. No association was found between the platelet functions and the clinical presentations.

**Conclusion:** Patients with meningococcal meningitis have abnormalities in the platelet functions mainly in aggregation and adhesiveness.

### INTRODUCTION

Acute meningococcal infection in man pursues a variable course. Usually the patient survives a severe illness which is characterised by meningitis and occasionally a petechial rash(1-4). However certain patients may die in profound and unresponsive shock hours after the onset of illness despite prompt and adequate medication. Disseminated intravascular coagulopathy (DIC) has been well demonstrated in patients with meningococcal meningitis(4-6).

The spectrum of abnormalities which may occur in the haemostatic mechanism during severe bacterial infection extends from isolated thrombocytopenia to disseminated intravascular coagulation(3,4). Marked thrombocytopenia alone may cause a haemorrhagic tendency. Thrombocytopenia can be caused by direct damage by endotoxin(5). It may also occur in vasculitis due to adherence of platelets to the damaged vascular surface (4). Platelets may also be reduced through an immune mediated platelet destruction mononuclear phagocytic system(7). Thrombocytosis may also occur in infection as a result of inflammation(5). Qualitative platelet abnormalities have been reported in infections. Pareti *et al*

demonstrated acquired platelet dysfunction due to "exhausted platelet" in patients with DIC(8).

The aim of this study was to investigate platelet abnormalities in patients with acute meningococcal meningitis.

### MATERIALS AND METHODS

Between May and July 1995, 63 consecutive adult patients admitted with a diagnosis of acute meningococcal meningitis were recruited after approval from the Ethics and Research Committee of the Kenyatta National Hospital. Three patients were excluded due to aspirin ingestion and three due to renal failure. Only 57 satisfied the inclusion criteria and form the basis of this study. The inclusion criteria were patients with meningitis who either had cerebrospinal fluid positive on Gram stain for gram-ve diplococci or culture positive for neisseria meningitidis. We excluded all patients who had taken aspirin, those in renal, hepatic failure, diabetes mellitus and alcoholics. Patients demographic data was obtained, a history with specific emphasis on bleeding tendency such as haematemesis, haematuria epistaxis and easy bruisability and rash was obtained. Clinical examination was then performed with emphasis to blood pressure, purpura, sub-conjunctival haemorrhage and gangrene.

All the patients had a full blood count, liver function test, random blood sugar and urea and electrolytes performed.

### Platelet Function

- Platelet Count:* This was done according to the method of Brecher and Cronkite(9).
- Platelet adhesiveness:* This was done by the modified glass bead column test according to Obrien and Solzman(10,11).
- Platelet aggregability to ADP:* This was done according to the method of Chandler(12).
- Clot retraction:* This was done according to the method of Mcfarlane(13).

*Controls:* Age and sex matched controls that had not been on aspirin or drugs that affect platelet, non smokers, non diabetics, not in hepatic failure or renal failure were selected from the medical and surgical wards. The patients were those who had been admitted for minor elective surgery like hernia repair, lipoma removal, deviated nasal septum etc. who did not require transfusion prior or after. The blood sample was taken prior to surgery.

## RESULTS

Fifty seven patients 41 males and 16 females were recruited. Their mean age was  $25.56 \pm 7.62$  years with a range of 13 to 45 years. Most of the patients were from Kibera slum area.

Apart from features of meningitis the following haemostatic clinical findings were found (Table 1).

**Table 1**

*Features of haemostatic failure in patients with meningococcal meningitis*

	No.	%
Conjunctival haemorrhage	8	14
Purpura	5	8.8
Gangrene	4	7
Epistaxis	4	7

\* some patients had more than one sign

**Table 2**

*Comparison of haematological and biochemical parameters between the patients and controls*

Parameter	Patients	Controls	P-value
Haemoglobin/(g/dl)	11.8(2.4)	12(2.5)	NS
WBC count(X10)	12.2(3.2)	5.8(1.7)	0.0001
Urea mmol/L	5.2(2.7)	4.87(2.2)	NS
Creative umol/L	112.4(5.4)	103.3(4.8)	NS
Bilirubin umol/L	12.3(2.4)	12.6(2.3)	NS
ALT U/L	30.2(1.8)	29.8(1.5)	NS
ALT U/L	32(3.2)	28.6(2.7)	NS

There was no significant difference in the haematological and biochemical parameters between the patients and controls apart from the total white cells which were significantly higher in those with meningococcal meningitis at a p-value 0.001 (Table 2).

*Platelet count:* Ten (17.5%) of the patients had thrombocytopenia and three had platelet counts above 450 000. Overall there was no statistical significant difference in the platelet count between the cases and the controls (Table 3).

**Table 3**

*Platelet function tests in patients with meningococcal meningitis*

Parameter	Cases N=57	Controls N=57	Significance
Platelet count	227,234 (108,877)	261,800 (105,471)	p = 0.203
Platelet aggregation (seconds)	27(11.8)	12.66(5.2)	p = 0.0001
Platelet adhesiveness	34(16.225)	37.7(13.0)	p = 0.22
Clot retraction(%)	53.6(12.8)	45.9 (8.101)	p = 0.0002

() standard deviation

There was no association between the clinical features and platelet functions.

## DISCUSSION

This study illustrates the various haemostatic defects that may occur in patients with meningococcal meningitis. The clinical signs of impaired haemostatic defects ranged from conjunctival haemorrhages to gangrene. Four of the patients had gangrene of the toes with one requiring amputation. This shows the severity of this complication. Gangrene of the extremities has been reported to be a rare complication of meningococcal meningitis often in association with DIC but may also occur due to vasculitis(14).

The overall platelet count in this study was not significantly different from that of the controls. However ten patients had thrombocytopenia. The cause of thrombocytopenia in patients with infections are multiple(3-6). Although it is mostly related to disseminated intravascular coagulation it is often observed in patients without evidence for DIC(5). Thrombocytopenia is an early and prominent finding in patients with septicaemia. Its incidence has been reported to range from 63% to 77% in septicaemic patients(3,5,6). There is evidence that thrombocytopenia is associated with accelerated peripheral destruction of platelets(5). Bacteria may cause endothelial damage, leading to platelet adhesion and aggregation or their products may bind directly to platelets leading to their aggregation and clearance from the circulation.

Kelton *et al.* have demonstrated elevated platelet associated IgG in the thrombocytopaenic patients with septicaemia(7). This entails that an immunological process could destroy the platelets. Infection can result in both thrombocytopaenia and thrombocytosis, this may have levelled of the effect of the total platelet count. Serial platelet counts have demonstrated that platelet count varies in the course of illness(5,15). In one study the platelets reached the minimum levels on day two to four culminating in a thrombocytosis 10 days later(4). It is possible that we may have had more patients with thrombocytopaenia had we carried out a serial study. Another factor which may also be related to thrombocytopaenia is infection with the HIV which was not investigated in this study.

Platelet aggregation were found to be significantly increased in our patients as compared to the controls. Pareti *et al* found defective platelet aggregation in patients with disseminated intravascular coagulopathy(8). As has been noted previously meningococcal infection is associated with endothelial damage which are known to activate the coagulation cascade and lead to reduced platelet count. The other explanation for the prolonged aggregation could be due to the antibiotic treatment. All the patients in this study were already on high doses of penicillin G by the time the platelet function tests were performed. Platelet function abnormalities have been documented in patients on B- lactam antibiotics which may lead to severe bleeding tendency especially if they are given at high doses(16-19). These abnormalities may appear from day one to four weeks. The maximum effect is third to fourth day. The beta lactams inhibit platelet aggregation, prolong bleeding time and secretion and adhesion to sub-endothelial and collagen surfaces(18). High doses block the binding sites of different agonists epinephrine, ADP, Von Willebrand factor to the platelet surface(16-19).

We did not find any correlation of the platelet aggregation with the clinical parameters such as gangrene, vasculitis, sub-conjunctival haemorrhage.

The other significant abnormality noted in our patients was the prolonged clot retraction This is dependent upon the platelet numbers and the fibrinogen levels with the platelet contractile protein, thrombosthenin, responsible for the mechanical work. Since these test is dependent upon the platelet numbers and fibrinogen levels it was not surprising that defects were noted.

This study illustrates the various qualitative and quantitative platelet abnormalities in meningococcal meningitis. Recognition of these abnormalities is important in the management of these cases.

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