

## Protein C Level and Activated Partial Thromboplastin Time in Neonatal Sepsis

**Albara Ahmed<sup>1</sup>, Babiker Mohammed<sup>2</sup>, Abdelhalim Nasr<sup>3</sup>, Wafa Elhag<sup>4</sup>, Awadelkareem Abass<sup>5</sup> and Mosab Nouraldein Mohammed Hamad<sup>6\*</sup>**

<sup>1</sup>Assistant Professor, Department of Haematology, Alfajr College for Sciences Technology, Medical Laboratory Science Program, Khartoum, Sudan

<sup>2</sup>Professor of Pathology, Department of Pathology, Faculty of Medicine, Karari University, Omdurman, Sudan

<sup>3</sup>Associate Professor, Department of Microbiology, Faculty of Medical Laboratory Sciences, Al Neelain University, Khartoum, Sudan

<sup>4</sup>Associate Professor of Neonatology, Department of Pediatrics, Faculty of Medicine, University of Bahri, Sudan

<sup>5</sup>Assistant Professor, Department of Haematology, Faculty of Medical Laboratory Science, University of Khartoum, Khartoum, Sudan

<sup>6</sup>Lecturer of Medical Parasitology, Department of Medical Laboratory Science, Phylum of Parasitology and Medical Entomology, Alfajr College for Sciences Technology, Khartoum, Sudan

**\*Corresponding Author:** Mosab Nouraldein Mohammed Hamad, Lecturer of Medical Parasitology, Department of Medical Laboratory Science, Phylum of Parasitology and Medical Entomology, Alfajr College for Sciences Technology, Khartoum, Sudan.

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### Abstract

**Aim:** The researchers intended to evaluate Activated Partial Thromboplastin Time (APTT) and Protein C (PC) amongst Sudanese neonates with sepsis (Cases) in Omdurman maternity hospital, Sudan related with healthy neonates (controls) for recognizing haemostatic alteration in APTT and PC amongst neonatal sepsis which cumulative yearly in Sub Saharan African countries along with incessant home-grown efforts by governmental bodies and NGOs.

**Results:** An overall of 100 neonates alienated similarly into septic cases and healthy controls, died neonates were constituted 10 (20%) while 40 (80%) were recovered between case group.

APTT showed noteworthy continuation in septic neonates compared to controls (mean; 47.8 and 37.5 sec for cases and controls, respectively) P-value was 0.00. Amongst patients group: dead neonates exhibited significant prolongation matched recovered (mean; 61.5 and 44.4 sec) P-value 0.00. PC showed noteworthy reduction in dead neonates compared to recovered (mean; 25.4 and 36.2% for dead and improved). P-value 0.04.

Insignificant change in PC was found amid case and control group. None of the sex, gestational age, delivery method, sepsis onset, and causative agent displayed noteworthy correlation with APTT and PC. APTT&PC can be valuable as indicator of neonatal sepsis mortality.

**Conclusion:** APTT was meaningfully prolonged in neonatal sepsis (P-value 0.00). APTT also prolonged considerably in deceased septic neonates matched to recovered one (P-value 0.00). PC reduced expressively in dead neonates compared to recover in case group (P-value 0.04). Prolonged APTT and reduce PC can be valuable as a marker for neonatal sepsis mortality.

**Keywords:** Neonatal Sepsis; Mortality; APTT; PC; Sudan

### Introduction

Neonatal sepsis is a worldwide encounter leading to high morbidity and mortality in neonates [1-4]. Though numerous microorganisms can be a source of neonatal sepsis, bacteria are the most frequent cause of neonatal sepsis in the world [2,4]. In all regions where statistics on hospitalization for sepsis are accessible, numbers amplified progressively [5]. In the U.S sepsis accounts for far more mortalities; its mortality frequency is far more than prostate and breast cancer as well as AIDS combined [6]. In unindustrialized countries; sepsis represents for 60 - 80% of lost lives yearly, influencing about 6 million newborns and kids [7]. Pathophysiological tool of sepsis is not fully understood, but coagulation changes are hallmark of the syndrome [8]. Together inflammation and hemostasis are unified pathophysiologic processes that significantly affect each other, inflammation leads to activation of hemostatic system that in turn also greatly influences inflammatory activity [9].

The study intended to evaluate activated partial thromboplastin time (APTT) and Protein C (PC); the first parameter screen intrinsic coagulation pathway and the other measures natural inhibitor PC system amongst Sudanese neonates with sepsis (case group) compared to healthy neonates (control) and to correlate sex, delivery method, and gestational age with such coagulation parameter between both groups. Moreover, to correlate APTT and PC with outcome, sepsis onset, and Gram stain typing of the causative agent between patients in order to study variations amid both parameters among neonates with sepsis.

### Methods

The study was prospective cross sectional hospital based study, conducted at Omdurman Maternity hospital, Sudan from June 2013 to April 2015 on 100 Sudanese neonates divided into; cases (neonates with proven sepsis by blood culture), and controls (healthy neonates) after ethical approval has been obtained from the ethical committee in Omdurman maternity hospital and neonatal mothers. Blood culture for recognition of microorganism was done, positive culture comprised as patient sample. Then directly venous neonatal blood collected and plasma prepared for APTT and PC valuation.

#### APTT procedure

APTT measured by clotting procedure; 50 microliter of plasma gotten, then a metal ball added, then 50 microliter of cephaloplastin added, and incubated for 180 seconds, then 0.02M calcium chloride added (all reagent were pre-warmed at 37°C for 15 minutes), then directly clotting time counted by semi-automated coagulometer (Stago Stat-4. France), calibrator (Uricalibrator, Stago. France) used as control.

#### PC procedure

50 microliter of 1/10 diluted (with Owren-Koller buffer) plasma obtained, then a metal ball added, then 50 microliter of PC deficient plasma (protein C deficient plasma, Stago. France) added, 50 microliter of PC activator (highly purifies extract of Agkistrodon contortirx venom. Stago. France) was added and incubated for exactly 180 seconds, then 0.02M of STA calcium chloride added (all reagent pre-warmed at 37°C for 15 minutes), then clotting time counted using semi-automated coagulometer (Stago Stat-4. France), calibrator (STA Uricalibrator. Stago. France) used as control.

#### Data analysis

Collected data analyzed by SPSS (statistical program for social and science) IBM SPSS Statistics version 20.

**Ethics approval**

Ethical approval gotten from the research ethical committee of Omdurman maternity hospital. Main investigator got an informed consent form from the neonates’ parents who involved in the study prior to going on.

**Results**

100 venous neonatal blood specimens (50 for both groups) were involved. Sex distributions were: 26 females (52%) and 24 males (48%), 27 females (54%) and 23 (46%) for case and control group respectively. 17 neonates were term (37 week or more) (34%) and 33 were preterm (less than 37 week) (66%), 1 term neonate (2%) and 49 preterm (98%) for case and control. No significant difference was found between case and control group in term of gestational age.

Clusters were considered rendering to delivery mode: caesarean section and normal vaginal delivery neonates. 17 delivered normally (34%) and 33 delivered by cesarean sections (66%), 7 delivered normally (14%) and 43 delivered by cesarean sections (86%) for case and control. No important change was found among case and control group in term of delivery mode.

Among patient, dead septic neonates constituted 10 (20%) and 40 were recovered (80%).

Among case group: early onset (0 - 7 days) septic neonates represented 17 (34%) and late onset (7 - 28 days) represented 33 (66%).

Gram stain typing of causative agent among case group were classified; Gram negative 41 (82%), Gram positive 9 (18%). Mortality among sepsis onset distributed among case group into; early 4 (40%) and late onset 6 (60%). No significant difference was found between case and control group in term of Gram stain typing of causative agents.

APTT protracted in patient group compared to control (47.9 and 37.5 second) (P-value 0.00).

PC reduced in patients compared to control (34.4 and 36.8%) (P-value 0.41) (Table 1).

Parameter	Mean	P-value
APTT (case)	47.8 sec	0.000
APTT (control)	37.5 sec	
PC (case)	34.3%	0.412
PC (control)	36.8%	

**Table 1:** APTT and PC mean and P-value among both groups.

Neonatal outcome showed significant correlation of APTT and PC among case group. (P-value; 0.00 and 0.04 respectively) Amongst patients; APTT expressively protracted and protein C was meaningfully reduced in dead neonates compared to recovered (Table 2).

Parameter	Mean	P-value
APTT (Dead)	61.5 sec	0.00
APTT (Recovered)	44.4 sec	
PC (Dead)	25.4%	0.04
PC (Recovered)	36.2%	

**Table 2:** APTT and PC mean and P-value considering outcome among case group.

None of the gender, delivery mode, Gram stain typing of causative bacterial gent and sepsis onset, showed significant correlation with APTT and PC. Considering gender; P-value 0.24 and 0.90 for APTT and PC. Mode of delivery; 0.12 and 0.70. Gram stain typing; 0.27 and 0.16. Sepsis onset; 0.82 and 0.56.

### Discussion

Generalized systemic inflammation followed by coagulation system stimulation, and equally, mechanisms of coagulation system meaningfully influence inflammatory response [10]. Important protracted APTT was in line with Krishna I, *et al.* [11] and Angraini D, *et al.* [12] who establish found APTT in sepsis patients. APTT meaningfully reduce in dead neonates, this conclusion was in line with Christian Niederwanger, *et al.* [14] and Benediktsson S., *et al.* [13] who noticed APTT protraction in patients with severe sepsis is accompanied with amplified mortality. The result correlate with PC, dead septic neonates have significant lower PC than recovered, this outcome was in line with Bhat R, *et al.* [15] who decided significant correlation between PC reduce and sepsis deaths. Prolongation of APTT and reduced PC designates stimulation of intrinsic coagulation proteins and PC with continuance of activation of both, consume APTT (intrinsic factors) and PC, these goes in line with Disseminated Intravascular Coagulation (DIC), which is one of main etiologies of sepsis deaths.

### Conclusion

APTT was meaningfully protracted in neonatal sepsis (P-value 0.00). APTT also protracted meaningfully in dead septic neonates in comparison to recovered one (P-value 0.00). PC reduced significantly in dead neonates in comparison to recovered in persons (P-value 0.04). Prolonged APTT and reduce PC can be valuable as an indicator for neonatal sepsis mortality.

### Limitation of the Study

Initially, incomplete funds locally, in term of capability (financial) resources, and personnel (nurse, phlebotomist, and other health profession) in Neonatal Intensive Care Unit (NICU) and the equipment facility (the study is self-funded). Then, lack of sufficient health education and awareness, low educational level, and poor socio-economics of families of the participants. Lastly, Limited local data of previous studies on similar parameter among Sudanese population.

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