Original Research Article

DISSEMINATED INTRAVASCULAR COAGULOPATHY; A CONDITION TO MON THE MANAGEMENT OF LEUKAEMIA PAT

ABSTRACT

Background: Disseminated intravascular coagulopathy is a consumption co which mostly results from an underlying disease. It occurs a coagulation cascade and hence leading to the formation of t due to the excessive consumption of platelet and coagulation factor associated with hypercoagulable state and increased ris complications and leukaemia is no exception. Bleeding mani leukemias, especially in blastic leukemia, and are prominent the disease. This study assessed disseminated intravascular patients in Nigeria.

Materials and Methods: One hundred and sixteen (116) subjects were study consisting of 58 leukaemic subjects (AML, CLL, and matched control subjects. The parameters estimated in this partial thromboplastin time with kaolin, integrated thrombin reagent time, D-dimer using Tina Quant Gen 2 on Roche Cobas C 1 by immunoturbidometry method, packed cell volume, platele were run on Abacus junior haematological auto analyser.

Was Acute Lymphoblastic Leukaemia (ALL) excluded? Or no single case of ALL was seen ?

Result: The mean ± SD of the parameters assessed in the leuk
3.74±3.13µg FEU/mL, 67.59±55.71seconds, 77.34±31.81secon
74±124.42 cells/mm3, 30.07±5.38% and 1.84±0.69 for D-dimer, PT, APTT, platelets,
PCV and INR respectively. The results display a significant statisti
leukemic and the control subjects (p<0.05).

Conclusion: The abnormality of these haemostatic parameters o
subjects (AML, CLL, and CML) is indicative of high incidence of disse
intravascular coagulopathy in these patients. This study the
intravascular coagulopathy can occur as a complication of various classes of leukae
studied especially if not properly managed and intervention commenced early.

Key Words: Disseminated intravascular coagulation, leukaemia, malignancy, h

INTRODUCTION

Disseminated Intravascular Coagulation (DIC) is an abnor
systemic intravascular activation of the coagulation system, simu
intravascular thrombi, distorting adequate blood supply to th
of exhaustion of the platelets and coagulation factors [1]. The clinical characteristics
include spontaneous or induced bleeding complications an
whereas multiple organ failure is a complication of intravascular fibri
formation. Also, the generation of multiple proteolytically a
cascade enzymes may initiate inflammatory activity, which may increase the s
syndrome [2].

Full stop comes BEFORE the Reference Number (or)
Reference number comes AFTER the full stop

Various disorders, including infections or inflammatory con
can cause activation of coagulation, also known as general activation of coagulation, that m
cause clinical complications and may not be detectable by routine laboratory ana

[3]. However, if activation of coagulation is sufficiently stron
and extension of global clotting may become [3]. The management of DIC
majorly directed at treating the underlying disease, but supp
care may involve supplementing the reduced coagulation
coagulations in addition to inhibiting coagulation by different anticoa
by exploiting the fibrinolytic system [4].

DIC could be initiated or be as a result of complication of sc
involve abnormal production of platelets and coagulation factors leukaemia
Is platelet production "normal" in DIC?
Also in APL-AML there may be abnormal production of procoagulant factors
Leukaemia is a group of malignancies that normally starts in
production of raised numbers of abnormal white blood cells [5]. Leukaemia can be
classified as acute or chronic and additionally be classified as myel
depending on the cell line that is affected. The cause of le
higher risk is associated with certain chemicals (benzene)
radiation, and infection with specific viruses (e.g., Epstein-Barr virus, human lymphot
virus). Smoking cigarettes and exposure to electromagnetic
as predisposing factors [6]. In patients with leukaemia, the prolifera
haematopoietic cells in the bone marrow with frequent spillage
to a decrease in the number of normal circulating blood cells
to anaemia, neutropenia and thrombocytopenia [7].

Acute Promyelocytic leukaemia (APL) has been associated with mu
is a subtype of AML and
abnormal bleeding [8]. Most, if not all, patients with APL have signs o
diagnosis. Patients with APL have an increased risk of deat
compared with patients with other forms of leukaemia, mostly

Unfortunately, outside of clinical trials the rate of early dea the advent of new therapies [9].

Disseminated intravascular coagulopathy is a critical condition that has been demonstrated in some individuals [10]. There is paucity of information on the presence of disseminated intravascular coagulopath leukaemia and other forms of chronic leukaemia in our environment. It is, therefore necessary to investigate DIC in individuals with the different fo the possibility of management of DIC alongside leukaemia in

MATERIALS AND METHODS

Who were the controls...
Non-leukaemic Haematological Malignancies?
Or non-Haematological Malignancies?
Or healthy subjects? Please specify

Subject Selection

One hundred and sixteen (116) subjects consisting of fifty eight (58) patients comprising 30 females and 28 males with acute myeloblastic leukaemia (AML), chronic lymphocytic leukaemia (CLL) and chronic myelocytic leukaemia (CML) who are currently und treatment and 58 age-sex matched **control** subjects who consented were recruited into th study from the Federal Teaching Hospital, Ido Ekiti, Nigeria and the University Coll Hospital, Ibadan, Nigeria. Ethical approval was obtained from the Federal Teaching Hospital Ido-Ekiti, Ekiti State.

WHEN were these samples taken for analysis? Was it at first presentation before institution of supportive care or chemotherapy? Or during chemotherapy? Or post chemotherapy???

Blood samples collection and analysis

Four millilitres (4 ml) of peripheral blood was collected from each subjects that have given consent to participate in the study with 2 ml into the 0.25ml of trisodium citrate anticoagulant (anticoagulant to blood ratio studies; while 2 ml dispensed into EDTA contained vials for the comp The citrated blood for coagulation studies was separated by centrifugation for 15 minutes to obtain platelet rich plasma which was analysed or frozen at -20°C until

The parameters estimated in this study were prothrombin ti with kaolin, international normalised ratio, D-dimer using Dimer Quanta Gen 2 D-dimer reagent on Roche Cobas C 111 analyser by imm while packed cell volume, platelet and white blood cell counts haematological auto analyser.

Statistical Analysis

The data generated was expressed as mean ± SD. A p-value < 0.05 was considered the significant level of statistical analysis using SPSS version 20

What was the distribution ? How many patients had AML? How many with CML or CLL? What of sex distribution? Age range? No biodata

RESULTS

The mean ± SD of various parameters estimated in participants involved in this study represented in Table 1 reflects significant difference between the compared with the control subjects, with the patients demonstrating prolonge as well as elevated counts (p < 0.05) than the controls. Platelet counts however were re

What counts were elevated?

What number/ % of patients had Thrombocytopenia???

significantly in the patients than the control subjects.

The p-value was 0.07 → that is NOT significant

Additionally, the PT and PTTK among the D-dimer level in the leukae subjects represented in Table 2. It was observed that 86% of the patients had incre dimer and prolonged PT while 48% with D-dimer and prolonged PTTK 5% having a prolonged PT, PTTK, INR and increased D-dimer level.

Did these 5% have Thrombocytopenia??? Not stated

Figure 1 demonstrates the correlation between the coagulat leukaemia. Chronic lymphocytic leukaemia (CLL) displayed a strong relationship with 32 of cases (32), being CLL patient, having increased D

How many of the patients ACTUALLY had DIC??? Not stated

Table 1: Mean±SD of estimated clotting parameters and platelet count in patients and control subjects.

Parameter	Patients Mean±SD	Control Mean±SD	t-test	p-value
D-dimer(µg FEU/mL)	3.47±3.13	0.31±0.1	5.888	0.001
PT(second	67.59±55.7	13.10±1.	5.266	0.001
PTTK(seco	77.34±31.8	31.19±2.	7.796	0.001
Platelet co (cells/mm^3)	193.62±10	233.69±5	1.818	0.074
WBC(cells/mm^3)	74±124.42	5.08±1.3	3.506	0.001
PCV (%)	30.07±7.38	37.80±4.	5.870	0.001
INR	1.84±0.09	1.11±0.0	7.705	0.001

PCV (Packed Cell Volume), WBC (White Blood Cell Count), PT (Partial Thromboplastin Time with Kaolin), INR (International Normalised Ratio)

Table 2: Distribution of D-dimer levels among the PT and PTTK levels in subjects.

	D-dimer		
	NORMA	HIGH	P val

Again, WHEN were these samples taken for analysis? Was it at first presentation before institution of supportive care or chemotherapy? Or during chemotherapy? Or post chemotherapy???

- the mean PCV seems high for patients with leukaemia, also the platelet count... were these samples taken after treatment or transfusion had commenced? If so they may not give a true picture of their coagulation status

Moreover, platelets are consumed in DIC, but the platelets for the Leukaemics does not show thrombocytopenia AND there was no statistical difference between the platelets for the Leukaemics and the controls- therefore

INR should come after PT

PT	NORMA	0	2(3.5	0.731
	HIGH	6(10.3	50(86	
PTTK	NORMA	0	4(6.9	0.619
	HIGH	6(10.	48(82	

123 PT (Prothrombin Time), PTTK (Partial Thromboplastin Time w

124

125 FIGURE 1: Correlation between the type of leukaemia and co

126 PT (Prothrombin Time), PTTK (Partial Thromboplastin Time with Kao

127 (International Normalised Ratio)

128 DISCUSSION

129 Disseminated intravascular coagulation (DIC) is a dynami

130 performed shows only the conditions at a [illegible] given moment

131 circumstances associated with this disorder repeating these

132 diagnosis. Analysis performed in assessing the haemostatic

clinical course and the diagnosis is established based on clinical suspicion and supp laboratory analysis [11]. The analyses performed in laboratory include parameters indica procoagulant and fibrinolytic substance activation, inhibitor or failure [12]. Prothrombin time (PT), partial thromboplastin time with kaol thrombocyte count show the consumption [11] and activation of th

Malignancy is associated with a hypercoagulable state thrombohemorrhagic complications. Clinical complications can range from lo thrombosis to bleeding of varying degrees of severity becau coagulation (DIC), with life-threatening bleeding being frequent in a particularly in acute promyelocytic leukemia (APL) [13]. Laboratory assessments profound hemostatic imbalance in this condition, with activa and nonspecific proteolysis systems [13].

Some coagulation parameters were estimated to assess coagulopathy in leukaemia patients in this study. The parameters estimated are; I time (PT), INR, partial thromboplastin time with kaolin (PTTK), pla (PCV), and white blood cell counts (WBC). It was observed that PCV had a lower ($p<0.05$) and platelet values ($p>0.05$) when compared with values obtained subjects (Table 1). Anaemia of chronic disease in the leukemic p or as a result of cytotoxic therapy. This finding is similar to that established by a previous study carried out by Akanmu et al. (2014) [10] where significant difference observed in PCV values of leukemia patients compared with controls.

The reduced mean±SD platelet observed is suggestive of excessive consumption which is indicative of the occurrence of DIC, resulting in the platelets being used u bleeding. In a similar study by Sadek et al. (2014) [14], a multicenter analysis where

Platelets 193.62±102.79 ... i.e. most of the platelet counts were between 90.83 to 296.41 and in Africans normal Reference range for platelets is lower than Caucasian values - 90-400... therefore did the patient actually have thrombocytopenia ? Either from the Leukaemia itself or the DIC?

but the mean/SD platelet of your cases does not reflect thrombocytopenia

they specified that the most frequent encountered abnormal laboratory listed as thrombocytopenia, increased fibrin degradation products, PTTK and low fibrinogen. Also, this study corroborates a study carried out by Lafc et al (2006) [31] where it was reported that activation and excessive consu platelets and clotting factors result in paradox, which leads to signs of DIC. The previous reports corroborates with the results of this study

The PT, PTTK and INR of the leukaemic patients in this study were found to be significantly prolonged (p<0.05) than those of the controls which were within normal range (Table 1). This is observed to be due to the exhaustion of some coagulation factors involved in the extrinsic pathway in the leukaemic subjects suggestive of DIC. This finding is similar to another report of study carried out by [14] et al (2017) where they discovered the leukaemic subjects to be prolonged compared to the controls (p<0.0 Sadek et al (2015) [41] also concluded that prolonged PT, PTTK and INR is a common finding in DIC.

The increased D-dimer level in the studied patients along with the increased PT, PTTK observed in this study indicates an increased fibrinolytic activity due to th deposition by coagulation process in the leukaemia subjects. D-dimer is a fibrin degradation product and an increased D-dimer level is ~~a~~ feature diagnostic factor of DIC.

The mean ± SD distribution of WBC, platelet and other haemostatic parameters carried out in this study displays an insignificant difference between male and female subjects which infers that gender has no effects on these parameters. However, there was a measured statistically significant difference (p<0.05) in the PCV thus showing that gender plays a major role in the PCV of the subjects

This should have come in the results section. There was no mention of it in the results section therefore should not be discussed here without prior mention in the results.

Avoid repeating figures that were stated in the results all over again in the discussion. Just go ahead and discuss the findings without repeating the results

Furthermore, 86% of the patients were observed to have increased D-dimer and prolonged PT while 48% had increased D-dimer and prolonged (PTTK) indicating the development of DIC and 5% having a prolonged PT, PTTK, D-dimer level establishing the onset of DIC symptoms which is evidence experienced by the patients. This is corroborated by a study that stated prolonged PT/PTTK and D-dimer as diagnostic tools [11] for DIC.

Did these 5% have thrombocytopenia? If not that is not in keeping with DIC

This study also revealed a strong relationship between the coagulation type of leukaemia (Figure 1) establishing that the leukaemia patients with abnormalities in laboratory analysis of blood coagulation, even without cl demonstrating varying degrees of blood clotting activat hypercoagulable state [18].

This statement is not clear- please rephrase..

Avoid making One-Sentence Paragraphs

In conclusion, the majority of the haemostatic parameters in the leukaemic patients observed to be abnormal, with PT, PTTK, INR being very prolonged and D-dimer level elevated while the platelet count below the normal level in most subjects. These trends of results are characteristic of DIC and indicative of the condition result of impaired haemostatic activity in the subjects recruited in the study. This study therefore revealed strong possibility of DIC in individuals suffering from various types of leukaemia (AML, CLL and CML) of their gender and treatments.

Not stated

Was it AML or ALL??

There can't be DIC without thrombocytopenia!

It is therefore recommended that the management of patients with leukaemic disseminated intravascular coagulopathy should be carefully and monitored in order to possibly detect its occurrence at the onset to adequate management of the DIC disorder should also be monitored alongside the treatment and management of le could be life-threatening.

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How does this apply?

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Are your case DOGS or Humans???...

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Note!!
References highlighted in RED are outdated/ too old!
Try to keep the references within the past 5-10 years.