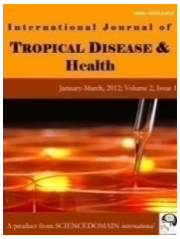

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# Effect of Alcohol Consumption on Platelet, Prothrombin Time and Activated Partial Thromboplastin Time of Alcoholics in Birnin Kebbi, Kebbi State, Nigeria

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***Authors' contributions***

*This work was done in collaboration with all authors. Authors OE, AY, IZI and ALS were responsible for study design, recruitment of subjects and ethical clearance application. Authors AW, ACE, AM and BAI performed the statistical analysis. Authors EKU, FU, TCA and IPI did all the laboratory testing. Authors DI, FA and OOI managed the analyses and report writing. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** Alcoholism is a global public health problem with significant socioeconomic implications. The aim was to investigate the effect of alcoholism on the haematological

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and haemostatic parameters of consecutively recruited alcoholics in Birnin Kebbi, Kebbi State and North Western Nigeria.

**Study Design and Methodology:** This prospective case-control study included one hundred adults alcoholics [≥18 years), aged range (18-60), mean age (38.46 ± 13.26) and made up of 68 males (68%) and 32 females (32%)]. Fifty gender and age matched non-alcoholics were monitored as controls. Ethical approval was obtained from the research and ethics committee in the Faculty of Medical Laboratory Science of the Usmanu Danfodiyo University Sokoto, North Western Nigeria. Written informed consent was obtained from all study subjects after counselling.

**Place and Duration of Study**: This study was carried out at the service laboratory in the Department of Haematology, Faculty of Medical Laboratory Science in Usmanu Danfodiyo University in Sokoto North Western Nigeria between May 2011 to February, 2012.

**Result:** Participants for this study included 50 heavy alcoholics and 50 moderate alcoholics (subjects) and 50 age and gender –matched non-alcoholics (controls). Platelet count of non-alcoholics, moderate and heavy alcoholics was; 260.7 ± 48.17, 253.3 ± 43.16 and 130.6 ± 6.79 respectively. Platelet count was significantly lower among heavy alcoholics compared to non-alcoholics (p=0.0001). Although marginally higher, there was no statistically significant difference in the platelet count of moderate alcoholics and non-alcoholics (p=0.10). We observed a negative correlation between platelet count and duration of alcoholism (r=-0.62). The mean prothrombin time (PT) and activated partial thromboplastin time (APTT) values of non-alcoholics, moderate alcoholics and heavy alcoholics was; (14.46 ± 0.97 and 34.82 ± 13.71), (15.74 ± 1.26 and 35.78 ± 3.50) and (19.46 ± 0.93 and 43.42 ± 5.13) respectively. Prothrombin time and activated partial thromboplastin time values were significantly lower among heavy alcoholics compared to non-alcoholics (p=0.0001). PT and APTT were marginally higher among moderate alcoholics compared to non-alcoholics but the difference however was not statistically significant (p= 0.08 and 0.62 respectively). We observed a positive correlation between duration of alcoholism and prolonged prothrombin time and activated partial thromboplastin time (r = 0.46 and 0.55 respectively).

**Conclusion:** Our study has shown that alcoholism produces a significant adverse effect on some haematological and haemostatic parameters. Evidenced data generated from this study can facilitate the development of a policy on the effective management of haematological and haemostatic complications associated with alcoholism. There is need to enact laws that regulate the production, sales and consumption of various alcoholic beverages to prevent abuse and protect the health of citizens.

*Keywords: Haematology; haemostasis; alcoholism; Kebbi State; Nigeria.*

## 1. INTRODUCTION

Alcoholism has been defined as an individual's dependence on alcohol, alcohol misuse or uncontrolled drinking habit, which adversely interferes with his biological, social and mental well-being [1]. The WHO estimates that there are 140 million people with history of alcoholism worldwide [2]. Alcohol is the most available and widely abused substance. Beer alone is the world's most widely consumed alcoholic beverage and it is the third-most popular drink overall, after water and tea [3,4].

Alcoholism is a worldwide social problem with severe effects on public health. It accounts for about 10%-15% of all patients admitted into general hospital [5]. Chronic alcoholism is a

disease that is often progressive and fatal. It is one of the numerous wide spread non-communicable diseases that is ravaging the world, and poses serious threat to the global health sector particularly due to its associated rising morbidity and mortality rate [6]. In Western countries about 10% of the general public of age not less than 15 years are affected by alcoholism giving rise to poor job performance, legal problems, social and inter-personal problems [7]. Alcoholism is associated with negative consequences from drinking such as significant financial burden, unemployment, loss of family, accidental injury or death [8]. In the United States about 63,718 deaths in the year 2000 were attributed to harmful drinking [9]. In Nigeria and other developing countries in the world so many alcohol - related accidents and mortality may have occurred without reliable documentation. Chronic alcoholism is the third leading cause of mortality even though many alcohols related death go unrecorded particularly in developing countries [10]. Chronic alcoholism has significant serious consequences on the haematopoietic systems involving the various blood cells, their progenitors in the bone marrow and clotting components [11]. Chronic alcoholism have a significant effect on the liver enzymes (aspartate aminotransferase and gamma glutamyl transferase) and coagulation parameters (prothrombin time and activated partial thromboplastin time) and blood coagulation [12,13]. However, there is paucity of data on the effect of alcohol on haematological and haemostatic parameters of alcoholics in Nigeria. History of a consumption of a locally brewed alcoholic beverage (Burukutu) is high in Kebbi State. The aim of this study is to investigate the effects of alcoholism on some haematological and haemostatic parameters. Evidenced data generated can facilitate the development of a policy on the effective management of haematological and haemostatic complications associated with alcoholism.

## 2. MATERIALS AND METHODS

### 2.1 Subjects

This prospective case-control study included one hundred adults (≥18 years) aged range (18-60 years) and mean age (45.25 ± 11.50) who were alcohol dependent (subjects) and fifty age and gender -matched non-alcoholics (controls). Alcoholics were classified into 2 groups; heavy (50 participants) and moderate alcoholics (50 participants). Inclusion criteria included; age ≥ 18 years, no history of present or past 2 weeks medication use prior to the collection of samples and willingness to give a written informed consent after counseling. Exclusion criteria included; pregnancy, age < 18 years, history of haematological diseases, malignancies or infections, chronic illnesses such as tuberculosis and diabetes mellitus. Controls included age and gender- matched non-alcoholics with neither current nor past history of regular alcohol drinking.

The aim of this study was to investigate the effect of chronic alcoholism on some haematological and haemostatic indices of chronic alcoholics and the non-alcoholics. The haematological and haemostatic values of subjects and control participants were compared statistically. Confirmation of alcoholism was established on the basis of the Short Michigan Alcoholism Screening Test (SMAST) [14]. The SMAST is a 13-item, self-reporting and effective diagnostic instrument developed from the Michigan Alcoholism Screening Test (MAST) questionnaire. It gives a better sensitivity and diagnostic accuracy on chronic alcohol consumption and thus does not have the tendency for false positive as does the MAST [15]. Subjects for this cross-sectional study were all outpatients selected based on a random-cluster sample of different suburban drinking bars in Birinin Kebbi where subjects meet to drink a locally brewed alcoholic beverage (Burukutu). Subjects were of low

socioeconomic class. They were predominantly unemployed men and women on low income. Burukutu is a popular alcoholic drink among indigenes of the Northern region of Nigeria. It is a local brew made from fermented sorghum and other protein enriched grains. Previous report indicates that the % v/v of alcohol in burukutu is 3.2% [16]. The age long drink serves as an affordable source of alcohol for those who lack the financial means to patronize refined brew like beer and other foreign or imported alcoholic drinks [17]. For the purpose of this study, a moderate alcoholic was defined based on USDA/DHHS Dietary guidelines as one who drinks not more than one unit of alcoholic drink per day for women and no more than two alcoholic drinks per day for men. A heavy alcoholic is someone who regularly drinks more than 3-4 units of alcohol a day for men and 2-3 units for women [18]. To exclude of the text: Chronic alcoholism is characterized by impaired control over drinking, preoccupation with the drug alcohol, use of alcohol despite adverse consequences, and distortions in thinking, most notably denial [19]. For the purpose of this study, drink volume was 473 ml and the bar glass volume is 44.4 ml.

## 2.2 Study Area

Birnin Kebbi, town and capital of Kebbi state, Northwestern Nigeria. It is the site of a federal university, state polytechnic, college of education and a government rice-research station. As of 2007 the city has an estimated population of 125,594 (National Population Commission (NPC) [20].

## 2.3 Methods

Six milliliters of blood sample was drawn aseptically using the S-Monovette vacutainer blood collection system (Sarstedt, Numbrecht, Germany) from the median antecubital vein for all the subjects and control participants into a citrate and an EDTA- anticoagulated bottle. The citrated sample was centrifuged for 5 minutes at 1000 rpm to obtain the citrated plasma. Citrated plasma was used to determine Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) using standard manual laboratory methods within 4 hours of sample collection. PT and APTT reagent manufactured by Diagen, (UK) was testing for PT and APTT. Test procedures were conducted according to the instructions in the manufacturer's standard operating manual. The EDTA anticoagulated blood was used for platelet count and blood film determination. Blood film was made by the push wedged method, dried and stained using a Rowmanowsky stain (Leishman stain).

## 2.4 Statistical Analysis

Data were entered and analyzed using statistical package SPSS version 9 (SPSS Inc., Chicago, IL). Statistical analysis included descriptive analysis of mean, standard deviation. A p- value of $\leq 0.05$ was considered to be statistically significant in all statistical analyses.

## 3. RESULT

Subjects were classified into two groups (50 heavy and 50 moderate alcoholics) Platelet count for the non-alcoholics, moderate and alcoholics was; $260.7 \pm 48.17$, $253.3 \pm 43.16$ and $130.6 \pm 6.79$ respectively. Platelet count was significantly lower among heavy chronic alcoholics compared to non-alcoholics ($p=0.0001$). Although marginally lower, there was no statistically significant difference in the platelet count of moderate alcoholics and non-alcoholics ($p=0.10$). We observed a negative correlation between platelet count and duration

of alcoholism (r=-0.62). The mean PT and APTT values of non-alcoholics, moderate alcoholics and heavy alcoholics was; (14.46 ± 0.97 and 34.82 ± 13.71), (15.74 ± 1.26 and 35.78 ± 3.50) and (19.46 ± 0.93 and 43.42 ± 5.13) respectively. PT and APTT values were significantly lower among heavy alcoholics compared to non-alcoholics (p = 0.0001). Table 1 shows the Mean and standard deviation of PLC, PT, APTT and among subjects and controls. PT and APTT were marginally higher among moderate alcoholics compared to non- alcoholics. This difference however was not statistically significant (p= 0.08 and 0.62 respectively). We observed a positive correlation between duration of alcoholism and PT and APTT and (r=0.46 and 0.55 respectively). The examination of peripheral blood smears indicated a high prevalence of macrocytosis, target cells and stomatocytes among alcoholics compared to non- alcoholics.

## 4. DISCUSSION

Alcoholism has been a major menace and cause of morbidity and mortality in Nigeria [21]. Its perception as a disease and its effects particularly on the haemopoietic system has not been fully elucidated particularly in Kebbi State in North Western Nigeria. In this present study, we observed that history of chronic alcoholism has a significant effect on the platelet count. The platelet counts of heavy alcoholics were significantly lower than those of non-alcoholics. Our finding is consistent with previous reports [22-24] which indicated that heavy drinking have a significant effect on haematological parameters. Alcohol consumption causes hypocellularity leading anaemia, leucopenia, thrombocytopenia and their relative sequelae [25]. Chronic alcoholism has been linked to insufficient availability of iron and other vital micronutrients such as vitamin B12 and folate for erythropoietic activities [26]. This is probably due to the inability of the ethanol irritated sticky intestinal mucosa to absorb these essential blood forming micronutrients, which eventually result in impaired haemopoiesis. We observed significant negative correlation between history of alcoholism and platelet count. Decrease in the number of platelets as well as abnormal platelets function seems associated with chronic alcoholism. Previous reports have shown that when blood ethanol concentration rises to 0.10%, platelet production, number and function may be affected [25-27].

In this study we did not carry out direct or indirect assessment of the mean corpuscular volume. We had used the morphometric method to monitor macrocytosis. The examination of peripheral blood smears usually provides excellent clues to the aetiology of diseases. We observed that macrocytosis, target cell and stomatocytes was significantly higher among heavy and moderate alcoholics compared to non -alcoholics. Our finding is consistent with a previous report which indicated that peripheral blood pictures from alcoholic patients typically divulged round macrocytes and stomatocytes [25]. Laboratory test play a major role in the health monitoring of alcoholics [28]. Previous report suggest that in order to get the most accurate picture of the effect of drinking on laboratory parameters, regular follow up test including liver enzymes and blood count is important [29]. Laboratory markers are well suited for outcome evaluation of drinking behavior of alcoholics after inpatient treatment for alcoholism or other comparative periods of abstinence [30].

**Table 1. Mean and standard deviation of PLC, PT, APTT and among subjects and controls**

| Parameter | Heavy alcoholics[(a)] | Moderate alcoholics[(b)] | Non-alcoholics controls [(c)] | t-value | p-value |
|---|---|---|---|---|---|
| PLC count ($x\ 10^9$/L) | 130.6 ± 6.79 | 253.3± 43.16 | 260.7 ± 48.17 | $17.2^{a+b}$<br>$19.01^{a+c}$<br>$1.66^{b+c}$ | $0.0001^{a+b}$<br>$0.0001^{a+c}$<br>$0.10^{b+c}$ |
| PT (Seconds) | 19.46 ± 0.93 | 15.74 ± 1.26 | 14.46 ± 0.97 | $23.16^{a+b}$<br>$25.0^{a+c}$<br>$1.46^{b+c}$ | $0.0001^{a+b}$<br>$0.0001^{a+c}$<br>$0.08^{b+c}$ |
| APTT(Seconds) | 43.42 ± 5.13 | 35.78 ± 3.50 | 34.82 ± 13.71 | $11.54^{a+b}$<br>$10.96^{a+c}$<br>$0.50^{b+c}$ | $0.0001^{a+b}$<br>$0.001^{a+c}$<br>$0.62^{b+c}$ |

*PLC= Platelet count; PT= Prothrombin time; APTT= Activated partial thromboplastin time.*
*a, b = Comparism of mean values between mean values of heavy and moderate alcoholics*
*a, c= Comparism of mean values between mean values of heavy and non- alcoholics*
*b, c = Comparism of mean values between mean values of moderate alcoholics and Activated Partial Thromboplastin Time*

We observed that haemostatic parameters of PT and APTT were significantly higher among heavy alcoholics compared to non-alcoholics. We observed a significant positive correlation between duration of alcoholism and deranged PT and APTT. Alcohol consumption seems to have a negative effect on the liver with attendant negative impact on the synthesis of coagulation factors. Previous report indicates that alcoholic hepatitis and alcohol- associated liver cirrhosis are the eminent causes of decreased production of blood clotting factors [31-34]. There is significant evidence that links alcoholism to decreased levels of fibrinogen and selected other coagulation factors. A recent report indicates that consumption of commonly ingested quantities of alcohol correlated with the development of a hypocoagulable state in men [35]. Similarly, a previous report [36] indicates that ethanol has multiple effects on haemostasis, affecting platelets and coagulation factors. Although conflicting results exist in literature, growing evidence seems to point to the fact that ethanol and its metabolites causes a partial platelet activation generating poorly functioning platelets, decreased levels of fibrinogen and selected other factors. Platelet count and basic coagulation investigation (PT and APTT) are readily available in most health facilities in Nigeria. Low platelet count and poor coagulation results can be used as readily available, simple and affordable methods, which can be used regionally to help in the early identification of serious alcohol-related liver disease in *Nigeria.*

## 5. LIMITATIONS

The major limitation of this study is that we did not include monitoring of subjects for biochemical evidence of liver damage in our study design. Biochemical evidence of liver damage is essential because liver injuries can greatly affect PT and APPT and also the number of platelets. There is high probability of severe liver injury, including alcoholic hepatitis and cirrhosis in alcoholics.

## 6. CONCLUSION

This report has shown that alcoholism has multiple negative effects on platelets and coagulation factors. Evidenced data generated in this study can facilitate the development of a policy on the effective management of alcohol –related effect on platelets and coagulation factors. There is need to enact laws that regulate the production, sales and consumption of various alcoholic beverages to prevent abuse and protect the health of citizens.

## CONSENT

Authors may use the following wordings for this section: "All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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