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ORIGINAL ARTICLE

# Hematological Changes Associated with Illicit Drug Abuse in A City of Northern Nigeria

Amos Dangana, Idris Abdullahi Nasir, Jessy Thomas Medugu, Anthony Uchenna Emeribe

Amos Dangana, Department of Hematology, University of Abuja Teaching Hospital, PMB 228 Gwagwalada, FCT Abuja, Nigeria Idris Abdullahi Nasir, Department of Medical Laboratory Services, Unversity of Abuja Teaching Hospital, PMB 228 Gwagwalada, FCT Abuja, Nigeria

Jessy Thomas Medugu, Department of Medical Laboratory Science, College of Medical Sciences, University of Maiduguri, PMB 1069 Maiduguri, Borno State, Nigeria

Anthony Uchenna Emeribe, Department of Medical Laboratory Science, College of Medical Sciences, University of Calabar, PMB 1115 Calabar Cross River state, Nigeria

Correspondence to: Idris Abdullahi Nasir, Department of Medical Laboratory Services, University of Abuja Teaching Hospital, PMB 228 Gwagwalada, FCT Abuja, Nigeria.

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## **ABSTRACT**

**BACKGROUND AND OBJECTIVE:** Several illicit drugs have been linked to derangement of many hematological indices which can lead to host tissues and / or organs dysfunctions. The purpose of this study was to determine the effects of different psychoactive substances on hematological parameters of study subjects.

**METHOD:** The study included 200 substance abusers and 50 non-substance abusers comprising of 235 males and 15 females. All subjects were investigated routinely using hematological tests and urine toxicology parameters to assess the effects of psychoactive substance use. These subjects were grouped according to type of drug, and duration of substances they abuse. An association between urine toxicology results and changes in hematological parameters was evaluated for statistical significance.

**RESULTS:** There was statistical association between the number of substances abused with gender (p = 0.0169) but not with age of subjects (p = 0.9639). Findings from this study showed significant

difference between certain hematological parameters of nonsubstance users (NSU) and specific groups of substance abusers. The packed cell volume and eosinophil counts were significantly higher in substance abusers with increase in number of drug abuse compared to NSU (p = 0.02 and p = 0.0008 respectively). There was no statistically significant correlation between duration of substance abuse and hematological parameters studied.

**CONCLUSION:** Illicit substance abuse predisposes individuals to eosinophilia and relative increase in PCV. There is a need to promote awareness on the health related effects associated with illicit substance abuse

Key words: Substance Addiction; Psychoactive Drugs; Hematology

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## Keys

CAN: Cannabis

BDZ: Benzodiazepines

ALC: Alcohol CIG: Cigarettes

TRM: Tramadol

OPI: Opiates

BAR: Barbiturates

MTD: Methadone

COC: Cocaine

MOR: Morphine

PCV: Packed cell volume

WBC: Total white blood cell count

## INTRODUCTION

World Health Organization (WHO) referred to substance (drug) abuse as the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs and further posit that psychoactive substance use can lead to dependence syndrome. This syndrome refers to a cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use. This phenomena typically include a strong desire to take the drug, difficulties in controlling its use, persistence in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state<sup>[1]</sup>.

In 2009, the World Drug Report (WDR) evidences indicated that illicit drug use results from complex multifactorial interaction between repeated exposure to drugs, some biological and environmental factors. Demographical statistics and trends of drug (substance) abuse among population of different localities have been documented<sup>[1]</sup>.

Substance abuse and its sequelae place tremendous burden on individuals and society. At the individual level, substance use disorders are associated with anomalies ranging from impaired personal relationships, difficulties with work and school performance, to mental and physical health problems<sup>[2]</sup>. Grave consequences like parents loosing custody of their children, loss of jobs and assets, arrests and incarceration, and chronic illnesses such as HIV/AIDS, hepatitis C, hepatitis B, liver cirrhosis and mortality and morbidity are attributable to substance abuse<sup>[3-8]</sup>.

Drugs change the way our bodies functions by influencing endogenous constituents of the bodies<sup>[9]</sup>. When they are administered to the body (often by swallowing, inhaling, or injecting them), drugs find their way into our bloodstream and are transported to other parts of body where they exert their effects. In the brain, drugs may either stimulate or depress our alertness, and decrease sensitivity to pain<sup>[10]</sup>.

## What is already known on this topic

Alterations in hematological and liver function indices by substance abuse are indications of dyshematopoetic potential, pathological condition and impairment on the liver<sup>[11,12,13]</sup>. Many of the reports on the effects of substance abuse on hematological changes are done severally on substances including marijuana, alcohol, cigarette and volatile substances<sup>[14-17]</sup>. This is particularly true on the effects of excessive cigarette smoking on increased packed cell volume/poor red cell indices. Heavy alcohol consumption leads to bone marrow malfunctioning while volatile substances such as () leads to basophilia and eosinophilia<sup>[14-17]</sup>.

#### What this study adds to knowledge

Previous reports available rarely analyzed and compared hematological changes based on the number......(single, double, triple and multiple) of substance abused even in the face of unswerving rise in the trends of psychoactive substance abuse as documented by United Nations Office on Drugs and Crime<sup>[18]</sup>.

In this study, we investigated the effects of substance abuse on hematological parameters of drug abusers attending Federal Neuropsychiatric Hospital, Barnawa, Kaduna state, Nigeria.

## MATERIALS AND METHODS

## Study Area

This case-control study was conducted on 250 substance abusers attending Federal Neuropsychiatric Hospital, Barnawa, Kaduna state between January 2013 and January 2014. The Federals Neuropsychiatric Hospital, Kaduna in North-western part of Nigeria. Kaduna, the capital of Kaduna State is about 200 km from the Federal Capital Territory, Abuja. The hospital receives referral from

all states in the Northern Nigeria. Some patients and relatives travel for about 300-350 km to access our health care facility.

#### Sample collection and preparation

Five milliliters (5 mL) of blood was collected aseptically and gently dispensed into Ethylenediaminetetraacetic acid (EDTA) container while the remaining 2 mL was dispensed into plain vacutainer tubes. The tubes were then appropriately labelled with participants' ID number. The EDTA anticoagulated whole blood was stored at -4°C until laboratory analysis was conducted. Early morning urine samples were collected in clean urine containers and labelled with corresponding participants' ID number. The blood sample was used for complete blood count and white blood cell differentials, while the urine samples were investigated for the presence or absence of illicit drug and /or their metabolites.

#### Laboratory analytical procedures

Urine levels of toxicology parameters were determined using a HITACHI model 902 automatic analyzer (Hitachi High-Technologies Corporation, Roche Diagnostics) with an enzyme immunoassay (Microgenics CEDIA Fremont, California, USA, for urine toxicology). After hospitalization, each patient's first urine and blood sample before treatment were taken into account for comparison. Urine samples were tested simultaneously for heroin, morphine, opiate, tramadol, alcohol, cannabis, barbiturate, methadone and cocaine. Routine hematology parameters were measured using the Sysmex TM XP 300 (Sysmex diagnostics products) automatic hematology analyzer.

#### Ethical approval and informed consent

This study was approved by the ethical research committee of the Federal neuropsychiatric hospital, Barnawa, Kaduna state, Nigeria. All participants gave their written informed consent for inclusion before they voluntarily participated in the study. All data were analyzed anonymously throughout the study.

## **Statistical Analysis**

Statistical package for social sciences (SPSS) IBM 20.0 software (Chicago, Illinois, USA) was used for statistical analysis. Pearson's correlation and ANOVA was conducted on data. More so, Man-Whitney U tests-used for parameters were not normally distributed was used. *P*-values < 0.05 were considered as statistically significant.

#### **RESULTS**

The patients were grouped based on the number of substance abused, that is, Single Substance Users (SSU), Double Substance Users (DSU), Triple Substance Users (TSU) and Multiple (abusing  $\geq 4$ substances) Substance Users (MSU), while None Substance Users (NSU) are used as control in this study. The study shows that even though male (n = 235, 94%) are more in number than their female (n = 235, 94%) = 15, 6%) counterparts, they both indulge in random substance abuse regardless gender. Most of the men are single substance users (SSU, 19.6%) and double substance users (DSU, 19.6%) while most of the female are triple substance users (TSU, 1.2%) (Tables 1 and 2). Our study shows that people in the age group of 18-29 years have the highest participation in substance use with 11.2% involved in SSU, 11.2% in DSU, 12.4% in TSU and 12.0% in MSU, while those in age group 54-65 years have the least participation in substance use with 0.4% involved in SSU, 0.4% involved in MSU, and while 0.0% involved in DSU and TSU (Table 2). This study shows that there is significant difference between some hematological parameters of non-substance users (NSU) and specific groups of substance abusers (Table 3). Majority of the subjects were cigarette smokers, 130 (25%) , while cocaine (0.04%) and morphine (0.04%) were observed to be minimally abused (Figure 1). Duration of substance abuse, whether single, double, triple or multiple substance abuse did not correlate significantly with all hematological parameters studied (p > 0.05) (Table 4).

## DISCUSSION

Illicit substance abuse are usually associated with aplastic anemia, bone marrow suppression, and elevated levels of inflammation may cause a wide range of systemic disorders which warrant careful clinical attention.

There was significant statistical difference between the packed cell volume (PCV) of the substance abusers and the non-substance abusers (p-value= 0.02). The PCV of substance abusers were observed to be significantly higher (SSU, 39.6  $\pm$  4.5; DSU, 41.0  $\pm$ 3.9; TSU, 41.2  $\pm$  4.5; and MSU, 41.1  $\pm$  5.1) than that of the nonsubstance abusers (NSU,  $38.9 \pm 3.2$ ). This may be due to increased MCV (macrocytosis). This concurs with the findings of Basime and colleagues who reported higher PCV values among abusers as against non-non-abusers<sup>[16]</sup>. However, this is in contrast with findings by Dasofunjo and colleagues who demonstrated a significant decrease in hematocrit value of rats administered with single substance and double/mixed substances<sup>[14]</sup>. This contrasting findings could illustrate the heterogeneity between humans and rodent systems. Secondary erythrocytosis results from either inadequate tissue oxygenation or from abnormal /premature stimulation of erythropoiesis. Erythrocytosis increases oxygen-carrying capacity of the blood, but at high hematocrit levels increased blood viscosity may result in decreased tissue oxygen delivery.

Our study shows that there is significant difference between the eosinophils counts of the study subjects (p-value = 0.0008). Eosinophils counts of substance abusers (Mean  $\pm$  SD) was significantly higher than that of non-substance abusers (NSU, 2.0  $\pm$  1.1). There is however, no significant difference between the total leucocyte counts (p-value = 0.31) and other fractions of differential leucocyte counts (neutrophils, lymphocytes and monocytes with p-values = 0.92, 0.96 and 0.15 respectively) for the substance

abusers and non-substance abusers. This study in some part agrees and in most parts disagrees with the work carried out by Mustafa et al among homeless children (6-18 years) exposed to chemical intoxication in Khartoum. In their study they reported marked decrease in hematocrit (anemia), normal total leucocyte counts with marked lymphocytosis, eosinophilia and monocytosis among the subjects<sup>[19]</sup>.

This study illustrated that there is no significant correlation between the number of substance abused and the hematological

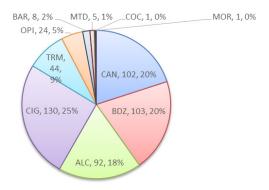




Figure 1 Frequency of substance abuse.

Gender	SSU (%)	DSU (%)	TSU (%)	MSU (%)	NSU (%)	Total (%)
Male	49 (19.6)	49 (19.6)	47 (18.8)	48 (19.2)	42 (16.8)	235 (94.0)
Female	1 (0.4)	1 (0.4)	3 (1.2)	2 (0.8)	8 (3.2)	15 (6.0)
Total	50 (20.0)	50 (20.0)	50 (20.0)	50 (20.0)	50 (20.0)	250 (100.0)

Age group, yr	SSU (%)	DSU (%)	TSU (%)	MSU (%)	NSU (%)	Total (%)
18 - 29	28 (11.2)	28 (11.2)	31 (12.4)	30 (12.0)	27 (10.8)	144 (57.6)
30 - 41	20 (8.0)	20 (8.0)	17 (6.8)	17 (6.8)	19 (7.6)	93 (37.2)
42 - 53	1 (0.4)	2 (0.8)	2 (0.8)	2 (0.8)	2 (0.8)	9 (3.6)
54 - 65	1 (0.4)	0 (0.0)	0 (0.0)	1(0.4)	2 (0.8)	4(1.6)
Total	50 (20.0)	50 (20.0)	50 (20.0)	50 (20.0)	50 (20.0)	250 (100.0)

Table 3 Association between sequences of substance abuse with hematological indices.									
Parameter		<i>p-</i> value <sup>α</sup>							
	SSU (n = 50)	DSU (n = 50)	TSU(n = 50)	MSU (n = 50)	NSU (n = 50)	p-value			
PCV (%)	39.6 ± 4.5	41.0 ± 3.9	41.2 ± 4.5	41.1 ± 5.1	38.9 ± 3.2	0.0247*			
WBC ( $\times 10^9/L$ )	5.5 ± 1.7	$5.4 \pm 1.3$	$5.3 \pm 1.3$	$5.0 \pm 1.2$	5.5 ± 1.1	0.3115			
Neutrophils (%)	51.7 ± 11.8	$51.6 \pm 11.4$	$51.3 \pm 11.6$	$50.2 \pm 11.0$	$50.2 \pm 12.6$	0.9285			
Lymphocytes (%)	38.7 ± 10.1	$38.7 \pm 11.6$	$38.7 \pm 9.9$	$39.4 \pm 10.4$	$40.0 \pm 11.6$	0.9665			
Eosinophils (%)	$3.2 \pm 3.5$	$3.0 \pm 2.2$	$4.4 \pm 4.0$	$4.2 \pm 3.9$	$2.0 \pm 1.1$	0.0008*			
Monocytes (%)	$6.3 \pm 3.6$	$6.6 \pm 5.2$	$5.9 \pm 3.3$	$6.3 \pm 2.7$	$7.6 \pm 2.9$	0.1572			

<sup>&</sup>lt;sup>a</sup> Determined by one-way ANOVA, \* Significant difference between the NSU and other groups; Dunnett's Multiple Posttest determined difference between NSU and specific groups. \* Observation: Eosinophil count steadily increasing with the number of substances abused.

Table 4 Correlation between duration of substance abuse and hematological parameters.									
Parameter <sup>a</sup>	1-3 years $(n = 50)$		4- 6 yea	4- 6 years $(n = 50)$		7-9 Years $(n = 50)$		$\geq$ 10 years (n = 50)	
1 arameter	r	<i>p</i> -value	r	<i>p</i> -value	r	<i>p</i> -value	r	<i>p</i> -value	
PCV (%)	0.163	0.257	0.254	0.075	-0.155	0.281	0.102	0.479	
Total WBC (x109/L)	-0.027	0.855	0.016	0.913	0.159	0.270	-0.116	0.422	
Neutrophils (%)	-0.007	0.962	0.084	0.563	-0.205	0.153	-0.095	0.513	
Lymphocytes (%)	-0.042	0.774	0.030	0.837	0.273	0.055	0.047	0.748	
Eosinophils (%)	0.257	0.071	-0.144	0.317	-0.140	0.331	-0.059	0.686	
Monocytes (%)	0.163	0.257	-0.058	0.691	0.046	0.750	0.267	0.061	

<sup>&</sup>lt;sup>a</sup> Pearson's correlation (*r*). Observation: duration of abuse of these substances, whether single, double, triple or multiple substance abuse does not correlate significantly with the hematological parameters.

parameters but illustrates that certain number of substance abused weakly correlate with some hematological parameters. The DSU weakly correlated with PCV (r = 0.254, p-value = 0.07), the TSU weakly correlated with lymphocyte counts % (r = 0.73, p-value = 0.05), the SSU weakly correlated with eosinophils counts (r = 0.257, p-value = 0.07) while MSU on the other hand, weakly correlated with monocyte counts (r = 0.267, p-value = 0.06). The blood monocyte is in transit between the marrow and tissues, where it transforms into a macrophage. It participates in virtually all inflammatory and immune disorders. Monocytosis may occur in some patients with cancer and several unrelated conditions, such as, depression and increase endogenous cytokine provocation (e.g. by illicit drug metabolites). However, the unpredictability in the monocyte response is a function of its relatively small blood pool size, the dampening effect of a large tissue pool, and the ability to expand macrophage numbers by local mitosis in tissues. It is difficult, though, to precisely delineate a single causative factor for abnormal hematological indices.

## CONCLUSION

This report confirms that illicit substance abusers do show some hematological abnormalities; however; more detailed surveillance is necessary with prolonged follow-up. Routine hematology parameters can be used to predict the need for intensive monitoring programs especially in individuals on multiple drug abuse. There is a need to promote awareness on various hematological and other health-related effects associated with illicit substance abuse. Health education programs at community levels should be delivered for these individuals, this may empower them to make informed choices.

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## **Authors contributions**

Amos Dangana conceptualized the study design and conducted the study as well as developed the initial draft manuscript. Jessy Thomas Medugu and Idris Abdullahi Nasir gave input into the design and statistical aspects of the study, and revised the manuscript critically for publication. Anthony Uchenna Emeribe provided guidance on study design and development of the study. All authors read and approved the final manuscript.

## CONFLICT OF INTEREST

Authors declare that there are no conflicts of interest associated with this manuscript

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**Peer reviewer:** Yusuke Furukawa, MD, Professor and Director, Division of Stem Cell Regulation, Jichi Medical University, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan.