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SOME HAEMOSTATIC AND HAEMATOLOGICAL PARAMETERS OF PATIENTS WITH SNAKEBITE ENVENOMATION BEFORE, DURING AND AFTER TREATMENT IN KALTUNGO GENERAL HOSPITAL, GOMBE STATE, NIGERIA

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Abstract: **Snake bite envenomation is a global problem affecting mostly the rural communities living in the tropics, where basic health facilities are poor. This cross sectional prospective study was set out to evaluate the effects of envenomation and antivenom on some haematological and haemostatic parameters among patients with snakebite envenomation. In this study total of 286 participants were recruited comprising of 143 patients with snake bite who were treated with Anti-snake-Venom and 143 apparently healthy subjects as control. Blood samples were collected from all the participants and their Haematological parameters evaluated using sysmex KX-21N. The result showed reduced packed cell volume (PCV%) , platelets (Plts $10^9/_L$) and haemoglobin concentration (Hb) values of the study group on admission, when compared with the control ($p<0.05$). While the aPTT and PT levels of the study group were statistically signifcantly higher when compared with their control counterpart ($p<0.05$). The age, PDW, MPV, TWBC, RBC, Neutrophil, Lymphocyte, and mixed though differ between the control and study group but not statistically significant ($p>0.05$). The age group that was maximally affected by Snakebite was 18-30 years (55.9%) and the least affected were 0-10 years (3%) and 40 - 70 years (10%). Males had higher incidence (57.4%) as compared to females (42.6%). Farming and cattle rearing were the occupations with high snakebite incidence. In conclusion, PCV, Plt, HB concentration, aPTT and PT were affected significantly by envenomation. However, upon treatment with Anti-Snake-Venom (ASV) within 24 hours there were no significant increase on PDW, MPV RBC, TWBC, differrential (Neut, Lymph) and Mixed.**

Keywords: **global problem, haematological, haemostatic parameters.**

1. INTRODUCTION

The actual incidence and mortality associated with snakebite envenoming is poorly known, partly due to the lack of reliable information on this disease in many regions of the world (Gutiérrez *et al.*, 2010b: Harrison *et al*., 2009). Hence, encouraging studies on snakebite envenoming would provide a valuable information regarding motality, incidence and recovery rate of patients.

More so incidence is usually higher in men than women and children are also affected mostly due to their involvement in agricultural duties. Although health statistics, based on the reports of hospital cases to health authorities, are satisfactory in some countries like Brazil (De Oliveira *et al*., 2009), for many countries and regions this information is largely deficient (WHO, 2007a; Gutiérrez *et al*., 2010b). This is because health statistics are poor in many countries, and also that many people affected by snakebites do not seek medical attention and instead rely on local traditional healers, thus remaining invisible to health authorities (Otero *et al*., 2000; Habib *et al*., 2001;Sharma *et al*., 2004; Michael *et al*., 2010: Nasidi, 2007).

Some snake species will migrate from areas of low altitude, which is heavily saturated, to a preferred higher, drier habitat where they also come to breed and lay eggs. Many Nigerian farms have high altitude locations, with rocky, mountainous states at particular risk for snake encounters (Molesworth *et al*.,2003).

Occasionally, snakebite may lead to important complications such as amputation, blindness resulting from spitting cobra (*Naja nigricollis*) venom, opthalmia, fetal loss, and wound infection, tetanus and scarring with potential for malignant transformation, and psychological consequences e.g., excessive anxiety, stress, hysteria and worry (Abubakar *et al*., 2010). Although haematological and biochemical parameters of snakebite individuals were widely reported in Saudi Arabia (Al-Durihim *et al.,* 2010), in Rawalpindi (Afsheen *et al*., 2014), in India (Shubham *et al*., 2014), in Australia (Geoffrey *et al.,* 2013), in Benin Southern Nigeria (Eric *et al*., 2002) and in North-Eastern Nigeria (Habib and Abubakar, 2011), because of inadequate laboratory records on patients with Snakebite in Nigeria. Therefore, the present study set out to evaluate the effect of envenomation and antivenom on some Haematological and Haemostatic parameters of patients attending Snakebite Research, Training and Treatment Centre, General Hospital Kaltungo in Gombe State North-Eastern Nigeria.

2. METHODOLOGY

Area of study

This study was carried out in General Hospital Kaltungo in Gombe State, North-Eastern Nigeria (a Snakebite Research, Training and Treatment Centre). The is a Case control study, subjects with snakebites and confirmed cases of snakebite envenomation who are yet to start treatment were recruited for the study. They subjects were "followed up" upon treatment to monitor the resolution of envenomation at 6 hours and 24 hours after antivenom intervention. They comprised of one hundred and forty three (143) snakebite subjects attending clinic in General Hospital Kaltungo and One hundred and forty three (143) apparently healthy subjects drawn from the general population as control subjects. Ethical clearance was sought and approval secured from the ethical Committee of Gombe state ministry of Health with reference number MOH/ADM/S/658/V.II/28 and consent was sought from the subjects, only those that gave approval were included in the study. The study duration was six months; from February– July, 2018.

Sample Collection

Nine (9) millilitres of blood was drawn from the subjects via venipuncture and 4.5ml was added into K_3EDTA bottle of 1.5mg for the analysis of blood count while the remaining 4.5ml was added into 3.2% sodium citrate container for the determination of PT and APTT levels. Three (3) sets of Blood samples were collected and processed at intervals from study subjects, for the above mentioned parameters as follows

(a) First sample: On admission before antivenom administration

(b) Second sample: After 6 hours of antivenom administration

(c) Third sample: After 24 hours of antivenom administration

SAMPLE ANALYSIS

The blood count was determined using automation-Sysmex Kx-21N 2008 while PT and APTT levels were carried out using Commercial test kits purchased and the manufacturer's instructions where strictly followed for the analysis

STATISTICAL ANALYSIS

The data collected were analyzed using Statistical Package for Social Sciences (SPSS Version 20) software. The values were expressed as Mean ± SD. ANOVA and Chi-square were used to test for significance. A p-value of ≤ 0.05 was considered as significant in all statistical analysis.

3. RESULT

The Socio-Demographic status of the study population and their control counterparts (Table 1). The most affected age bracket was 16-33 years (55%). More males were affected 57% then the females 42%. Farmers had the highest incident of snakebite 41.3% followed by Herdsmen 29.4% while others made up 27.9%. Rural dwellers constituted the highest number of affected individuals with 81.1% as against 17.5% of their urban counterpart. The most common site of snakebite was the lower limbs (Legs) 66.4%, followed by the upper limbs (Arms) with 29.4% cases while other sites had 2.8% cases. The most prevalent specie of snake in the study area was Carpet viper 81.8%, the unidentified snakes 11.3% while Cobra is 5.6%. The symptoms commonly expressed include swelling in all of affected subject, Pains in 95.1%, bleeding in 79.7 % and Hematemeis in 4.8% of the snake bit subjects. The antivenom (ASV) used were monovalent which account for 69.9% and polyvalent, 24.5%.

Table 1: Demographic characteristics of the study population

Parameter	Control Group (n=143)	Study Group (n=143)
Age (yrs)		
<15	49(34.3%)	32(22.4%)
16 – 33	96(67.1%)	78(55%)
>34	10(69.9%)	31(21.7%)
Sex		
Males	73(51%)	81(56.6%)
Females	82(57.3%)	60(42%)
Occupation		
Farmers	76(53.1%)	59(41.3%)
Herdsmen	32(22.4%)	42(29.4%)
Others	47(32.9%)	40(28%)
Residence		
Rural	120(83.9%)	116(81.1%)
Urban	35(24.5%)	25(17.5%)
Site of snakebite		
Leg	Nil	95(67.3%)
Arm	Nil	42(29.8%)
Others	Nil	4(2.9%)
Species of Snake		
c.viper	Nil	117(83%)
Cobra	Nil	8(5.7%)
Un-identified	Nil	16(11.3%)
Sign and symptoms		
Swelling	Nil	141(100%)
Bleeding	Nil	114(80.9%)
Pains	Nil	136(96.5%)
Hematemesis	Nil	7(5.0%)
Type of ASV		
Monovalent	Nil	100(70.9%)
Polyvalent	Nil	35(24.8%)

The comparism of haematological parameters of patients with snake bite on admission before intervention with anti-snake-venom (ASV) and the control group (table 2). The finding shows that PCV, Platelet and the Hb of the snake –bit subjects on admission before anti-snake-venom (ASV) intervention were significantly reduced when compared with the control

(p<0.05) group. On the other hand the aPTT and PT levels of the studied group were significantly prolonged when compared with their control counterparts (p<0.05). However the apparent numerical changes observed in age, PDW, MPV, TWBC, RBC, Neut, Lymph, and mixed cell values, between the control and the study groups were not statistically significant (p>0.05)

Table 2: Comparism of Haematological parameters of patients with snake bit and the control group

Parameters	Control	Patients	cat t	Pvalue
Age	26.8±11.44	25.6± 10.93	0.106	>0.05
PCV	38.04± 2.81	35.5± 7.0	7.31	<0.05
Platelet	224.56±54.96	184± 60.4	2.51	<0.05
PDW	14.80±2.25	15.58± 2.17	7.03	>0.05
MPV	11.47±1.50	11.55±1.20	0.70	>0.05
HB	12.66±0.89	11.14±2.06	2.32	<0.05
TWBC	6.15±1.73	7.74± 3.19	1.34	>0.05
RBC	3.98± 0.86	3.95± 0.77	0.08	>0.05
N	55.55±3.87	56.21±17.52	0.64	>0.05
L	33.30±4.01	33.91±12.47	0.69	>0.05
MIXED	11.04±2.66	9.11±2.55	1.72	>0.05
APTT	34.05±2.09	114±10.63	8.56	<0.05
PT	11.51± 1.00	112.4±14.0	2.04	<0.05

The result showed that 21 persons upon admission at 0 hour had their platelet count ≤100x10^9/L (table 3**)**. ASV intervention at 6th hour revealed 26 person while at 24th hour post intervention only 12 persons were observed to have their platelets count still less than ≤100x10^9/L. 131 of the snake bite persons had their aPTT values prolonged beyond 50 ses at 0 hour admission. Upon interventions with ASV at 6th and 24th hours greatly reduced the number of persons to 18 & 6 with prolonged aPTT respectively. The PT of 118 subjects were prolong upon admission at 0 hour. The number reduced to 10 persons at 6th intervention and 4 persons at 24th hour intervention.

TABLE 3: Resolution rate of the haemostatic parameters of the snake bit patients at 0th Hour, 6th Hour and 24th Hour of interventions.

S/n	Parameter	Intervention at 0thhour (n=143)	Intervention at 6thhour n=143)	Intervention at 24thhour (n=143)
1.	**PLT(109/L)**			
	<100 ((10$^{9/}$)	21(14.6)%	26(18.2%)	12(8.4%)
2	**APTT (sec)**			
	Normal (36-50 sec)	10(7.0%)	114(79.7%)	135(94.4%)
	Prolonged(>50 sec)	131 (91.6%)	27(18.9%)	6(4.3%)
3	**PT(sec)**			
	Normal (11-16 sec)	28(19.6%)	131(91.6%)	137 (95.8%)
	Prolonged (>16sec)	118(82.5%)	10(7.0%)	4 (2.7%)

Comparison of some haematological parameters of snakebite patients at 0th hour, 6th hour and 24th hour respectively of ASV post interventions (table 4). The mean values of PCV, plt, TWBC aPTT and PT of the subjects upon admission at 0th hour were significantly raised when compared with ASV post intervention at 6th hour and 24th hours (p<0.05) respectively. The study also revealed that PDW, MPV, Hb, RBC, Neut, Lymph and mixed cells after the intervention with ASV at 6th hours and 24th hour were similar(p>0.05).

Table 4: comparison of some haematological parameters of snakebite patients at 0th hour, 6th hour and 24th hour respectively of ASV post interventions

Means ± Standard Deviation of Patients				f-value	p-value
Parameters	**Intervention at 0 hour (n=143)**	**Intervention at 6 hour (n=143)**	**Intervention at 24 hour (n=143)**		
PCV	35.5±7.0*	31.9±7.2	32.4±6.9	6.95	**.001**
PLT	184±60*	150.6±64.1	154.3±40.3	12.58	**.000**
PDW	15.58±2.17	15.63±1.84	15.21±1.72	1.25	**.289**
MPV	11.55±1.20	11.55±1.29	11.73±1.41	.598	.550
HB	11.14±2.06	10.32±2.51	11.12±3.05	1.08	.342
TWBC	7.73±4.1*	6.66±2.91	6.35±63.1	6.48	**.002**
RBC	3.95±0.77	3.69±0.89	3.71±0.83	1.98	**.139**
Neut (%)	56.21±17.52	57.10±12.18	55.38±10.57	0.587	**0.557**
Lymp (%)	33.92±16.83	33.08±11.56	34.92±19.97	.689	**0.503**
Mix (%)	9.12±2.30	9.80±3.51	9.73±3.22	1.88	**.153**
APPT(sec)	114.4±10.63*	69.56±56.57*	39.61±12.7*	248.9	**0.000**
PT (sec)	112.46±14.0*	49.35±36.46*	15.33±4.59*	396.0	**0.000**

Key: ($p \leq 0.05$) is considered statistically significant

4. DISCUSSION

The incidence and mortality associated with snakebite envenomation is poorly known, partly due to lack of reliable information on this disease in many regions of the world (Gutierrez *et al.*, 2010b). The present study was designed to investigate the effect of envenomation and antivenom on some haemostatic and haematological parameters of patients with snake bite attending snake bite research and treatment centre, Gombe State, Nigeria which comprised of more middle aged and male patients whom where mostly farmers, Residending in Rural communities. These patients were observed to record significantly decreased PCV, Platelet concentration and Heamoglobin concentration while their APTT and PT values where significantly increased when compared to control subjects. However, the APTT and PT of these patients were observed to have more prolonged resolution rate at the 0th hour intervention compared to the 6th and 24th with a significant variation that occurred when compared with all three intervention hours but the platelets had more resolution rate at <100 at the 6th hour with a significant elevated means value at 0 hr of intervention for the platelet , PCV and TWBC values when compared across the all intervention timing.

It could be inferred that mild anaemia may have occurred in this patients as a result of the significant ($p<0.05$) decrease PCV that was observed when compared with control group. However, this decrease in PCV was mild due to quick intervention with ASV at 0 hour which was observed to have a significant ($p<0.05$) variation when compared across other ASV intervention hours. This finding was similar to the outcome of Graham *et al.*, (2010). This variation could have been due to Hemolysis in RBC occuring due to direct or indirect poisonous effect on RBC membrane and level of hematocrit is reduced (Masci *et al.*,2000). Hemolysis occur due to the action of phospholipids enzyme A2, which is present in all snakes venome and specific factor present in some snakes. Phospholipids A2 directly effect on the cell membrane or producing plasma lysolocithine (Norris *et al.*, 2005). However, this observation is in contracts with some results of Radha,(2018) who observed some increased PCV in some patients and this may be laboratory fault or due to hemolysis and obligatory blood formation. The rise in PCV on ASV at 0 hour could have been due to angiotensin II which produces a significant decrease in the blood volume and an increase in the extravascular fluid.

It was also observed that a significant ($p<0.05$) decrease in the mean platelet count of patients (184±60.4) was recorded when compared with control (224.56±54.99) subject. It was also observed that due to intervention with ASV at 0 hour, the decreased platelet count was mildly alleviated as a significant ($p<0.05$) boast was recorded (184±60.4) when compared with intervention at 6 hour (150.6±64.0) and intervention with ASV at 24 hour (154.3±40.3). This rise on ASV could been due to could be due to hemoconcentration caused by a massive release of catecholamines (Freire-maia and Campos,2017) and angiotensin II (Radha, 2018). The results after antivenom administration showed a definite reversal. These changes could be due to a fall in angiotensin II level, leading to hemodilution.

The findings of observed in table 2 revealed a significant ($p<0.05$) slight decreased Heamoglobin concentration in patients with snake bit when compared with their control group. It was observed that due to intervention with ASV at 0 hour, Total white blood cell (TWBC) of patients was significantly slightly increased when compared to 6th and 24th hour intervention. This finding was similar to the outcome of Graham *et al.*, (2010). The rise could have been due to angiotensin II which produces a significant decrease in the blood volume and an increase in the extravascular fluid, leading to peripheral circulatory failure and pulmonary edema (Douglas, 1995). Angiotensin II also stimulates the release of catecholamines. Catecholamines and angiotensin II may synergize or amplify each other's action and these may act, at least in part, at similar sites (Douglas,1995), resulting in hematological changes.

Furthermore, aPTT and PT levels of patients on admission at 0th hour when compared with 6th hour and 24th hours were deranged but at intervention with ASV, picked up and resolved completely. This could be due to due to the effect of venom on liver and finally impaired the synthesis of coagulating factor or denaturization of these factors and it may be due to impairment in coagulating factors (Gray, 2003). Amozegari et al have also indicated that Vipera Leptina venum (Ahwaz, Iran) inactives coagulation factors (Amozegari et al., 1999). The RBC and the differentials (Neut, Lymph and mixed) when compared were not statistically significant ($p>0.05$) which was also observed by Moriarity *et al.*, 2012.

5. CONCLUSION

Snakebites is common in rural areas. Snakebites mainly affect the agricultural and herdsmen workers.Mostly young people are affected(16-33years)The deranged PT and aPTT levels were normalized within 24 hours post ASV intervention even though not all. We concluded that envenomation improved Platelet, PT, aPTT, TWBC, and HB respectively upon treatment with Anti-Snake-Venom (ASV) and the most prevalent specie of snake in the study area was Carpet viper with 83 cases.

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