



## **Assessment of Inflammatory and Cardiac Status of *Echis ocellatus* Snake-bite Victims in Jos Metropolis, Plateau State, Nigeria**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Authors POM, GCJN, CCO and OEO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors GCJN, EEN, ECO and OSO managed the analyses of the study. Authors VIM, RSE, RCC and KEN managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** This study was designed to evaluate the inflammatory and cardiac status of snakebite victims using serum levels of C-reactive protein (CRP), troponin-I (TnI), total cholesterol (TC) and triglycerides (TG) as markers in *Echis ocellatus* snakebite victims before and after administration of EchiTab-G antivenom.

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**Materials and Methods:** A total of 80 subjects (40 *Echis ocellatus* bite victims and 40 apparently healthy individuals as test and control subjects respectively) were purposively recruited for this study. Venous blood samples were collected within 4 hours after bite. The whole blood clotting time (WBCT20) was determined immediately. Another batch of samples were collected from same snakebite victims, 2 days post administration of the anti-venom. CRP and Troponin-I levels were evaluated using the enzyme linked immunosorbent assay technique while serum total cholesterol, and triglyceride levels were assayed spectrophotometrically.

**Results:** The mean serum levels of troponin-I ( $2.98 \pm 5.75$ ) and CRP ( $36.64 \pm 29.01$ ) were significantly higher in *Echis ocellatus* bite victims before administration of anti-venom compared with control subjects ( $0.007 \pm 0.3$  and  $0.99 \pm 0.28$ ) and after post administration of anti-venom ( $0.16 \pm 1.39$  and  $15.96 \pm 17.36$ ) ( $P < 0.05$ ) respectively. Conversely, the mean plasma levels of total cholesterol and triglyceride were significantly lower ( $p < 0.05$ ) in snake bite subjects before anti-venom administration when compared with control and snake bite subjects after post administration of anti-venom. Furthermore, the mean serum levels of troponin-I and CRP correlated significantly positive when correlated between snake bite subjects before ( $r = 0.498$ ,  $p = 0.001$ ) and after ( $r = 0.430$ ,  $p = 0.006$ ) anti-venom administration respectively.

**Conclusion:** The research findings therefore suggest that *Echis ocellatus* envenomation triggers inflammatory reaction which could be the reason behind the alteration in cardiac markers as evidenced by the significant elevations in serum troponin-I and CRP levels amongst snake bite victims compared to the non-snake bite control groups thus, could cause cardiac arrest before anti-venom administration.

**Keywords:** *Echis ocellatus* venom; snakebite; inflammation; C-reactive protein; cardiac markers; troponin-I; total cholesterol; triglycerides.

## 1. INTRODUCTION

Snakebite is as old as History and its burden is a neglected tropical and public health issue (WHO, 2009). Moreso, studies have not been carried out globally on snakebite effects of which only few are documented but current emerging studies will be encouraging [1]. Snakebite envenoming comprises of a major public health problem among communities of the savanna region of West Africa, notably, Benin, Burkina Faso, Cameroon, Ghana, Nigeria and Togo [2]. Snakes, which are scientifically referred to as Serpentes are elongated, legless, carnivorous reptiles. Living snakes are found on every continent except Antarctica and on smaller land masses except in Ireland, New Zealand and many small Islands of the Atlantic and Central Pacific [3]. Most species of snake are non venomous and those that have venom use it primarily to kill and subdue prey rather than for self defense. There are about 2,900 species of snakes. Of these, 375 are venomous. Among others are constrictors which squeeze their prey [4].

The snakes inject venom in their victims during bites. Snake venom contains diverse toxic components which results in diverse and multi factorial pathological consequences. Moreover, variables, such as the location of the bite site and

the amount of venom injected can contribute to the severity of clinical signs observed in snakebite victims [5]. While pathology can be limited to local effects surrounding the bite site such as pain, oedema and bruising, many envenomings also result in systemic manifestations, which can be severe and lethal if untreated. Clinical patterns of envenoming are classified into three groups: neurotoxic, cytotoxic and haemotoxic, although myotoxicity can also be present in certain cases [1]. Moreso, it is important to note that certain snake venoms are capable of causing combinations of these different toxicities and there are also examples of the same snake species causing different manifestations in human patients across different parts of their range [6,7]. Occasionally, snakebite may lead to important complications such as amputation, blindness, wound infection, tetanus and psychological consequences e.g excessive anxiety, stress and hysteria [8].

Snakebite envenoming may affect all body systems causing cardiac and hemodynamic abnormalities. The strongest predictor of mortality is central nervous system involvement with intracranial hemorrhage [9]. Snake venom is modified saliva delivered through fangs. Venom is a pre-digestant that initiates the breakdown of food into soluble compounds, facilitating proper digestion [10]. Venomous snakes that use

venoms usually have fangs in the front of their mouths, but some are located at the back of their mouths, curled backwards, which makes it difficult both for the snake to use its venom [11, 12].

Snake venoms are complex mixtures of proteins and are stored in venom glands at the back of the head, these glands open through ducts into grooved or hollow teeth in the upper jaw. These proteins can potentially be a mix of neurotoxins (which attack the nervous system), hemotoxins (which attack the circulatory system), cytotoxins, bungarotoxins that affect the body in different ways. The neurotoxic proteins isolated from various snake venoms are used *extensively as pharmacological tools because of their affinity for a particular target site* to gain insights into the function of the nervous system [13].

Four families of venomous snakes in Nigeria include: Actraspididae, Viperidae, Colubridae and Elapidae. Puff adder (*Bitisarietans*), Carpet viper (*Echis ocellatus*), Black-necked spitting cobra (*Najanigricollis*) and Black-necked spitting cobra (*Najanigricollis*) are the most important snakes associated with envenoming in Nigeria and they belong to the *Elapidae* family [14].

*Echis ocellatus* (*E. ocellatus*) envenomation is characterized by prominent local effects, including inflammation, necrosis, hemorrhage, edema, and pain, which develops rapidly after the envenomation and often result in permanent sequelae and systemic alterations such as hemorrhage, coagulopathy, and shock. Metalloproteinases has been implicated in both local and systemic effects of this snake venom [15].

Venomous snakes are believed to cause 2.5-3 million bites worldwide per year with 100,000-150,000 deaths [16,17]. The global mortality rates from snakebites appear to be about 5% of the victims [16]. The World Health Organization (WHO) estimates that approximately 2,500,000 venomous snakebites per year result in 125,000 deaths worldwide, 100,000 of which are in Asia and approximately 20,000 deaths in Africa [13, 18].

*Echis ocellatus* is a venomous viper specie endemic to West Africa [19]. Sexually mature females lay between 5-18 eggs, usually at the end of the dry season from February to March. The prevalence rate of *Echis ocellatus* bite in Nigeria is 2.5% [20]. In Nigeria, *Echis ocellatus*

bite can be identified either when killed or brought to the hospital, or by incoagulable blood using the 20mins Whole Blood Clotting Test (WBCT 20) [21].

Troponin-I (TnI) is the most specific and sensitive laboratory marker of myocardial cell injury and therefore could replace Creatine Kinase-MB as the gold standard [22]. The American Heart Association and the European Society of Cardiology (ESC) Taskforce Report on acute coronary syndromes without serum troponin-I elevation have attributed troponin measurements a central role in the diagnostic work up and therapeutic decision making. If injury persists and necrosis progresses, more troponin-I is released from the muscular pool [23]. Aside from patients with renal failure, there should be no difference in interpretation between troponin-T and troponin-I results, provided analytical guidelines and quality are followed.

Total cholesterol is a steroid of high molecular weight and possesses the cyclopentanophenanthrene skeleton. Dietary cholesterol is partially absorbed and it is also synthesised by the liver and other tissues. Cholesterol is transported in plasma by lipoproteins. It is excreted unchanged into bile or after transformation to bile acids [24]. Increased total cholesterol values are associated with a progressively escalating risk of arteriosclerosis and coronary artery disease [25].

Triglycerides are esters derived from glycerol and three fatty acids. They are the main constituent of body fat in humans and animals, as well as vegetable fat [26]. In human body, high levels of triglycerides in the bloodstream have been linked to arteriosclerosis and by extension, the risk of heart disease and stroke [27].

C-reactive protein (CRP) is a phylogenetically highly conserved plasma protein, with homologues in vertebrates and invertebrates that participates in the systemic response to inflammation [28]. Characteristically, its plasma concentration increases in inflammatory states. CRP was discovered in Oswald Avery's Laboratory during the course of studies of patients with *Streptococcus pneumonia* infection. Minor CRP elevation has been observed in about two-thirds of the American population with plasma CRP levels under 3 µg/ml. Circulating CRP levels under 10 µg/ml have historically been regarded as clinically insignificant. In recent

years, a plethora of studies have demonstrated an association between slightly elevated CRP plasma levels, between 3µg/ml and 10µg/ml and the risk of developing cardiovascular disease [29].

### 1.1 Statement of the Problem

*Echis ocellatus* is a venomous viper specie endemic in West Africa. Several fatal cases after *E. ocellatus* bites are undocumented and not much studies have been carried out in this regard, but approximately 20,000 deaths annually have been reported in Africa, with Nigeria having 2.5% annual prevalent rate. *E. ocellatus* bites are serious public health challenge in the country. Its venom may severely affect the various organs and functions of the body [20]. There is therefore the need to provide information on the inflammatory and cardiac status of *Echis ocellatus* bite victims before and after administration of anti-snake venom. This information may be valuable as a guide for policy makers in public health.

### 1.2 Justification of the Study

Snake envenoming may have significant effect on various organs and functions of the body. These may include the cardiac, inflammatory and coagulatory functions. Prompt assessment of these parameters may provide valuable information in the proper management of *E. ocellatus* bite victims. The aim of this study was to assess the cardiac and inflammatory status of *Echis ocellatus* envenomation using troponin-I, total cholesterol, triglyceride and C-reactive protein levels as markers in *Echis ocellatus* bite victims.

## 2. MATERIALS AND METHODS

### 2.1 Research Design

This is a longitudinal study designed to assess the serum levels of troponin-I, total cholesterol, triglyceride and C-reactive protein in *Echis ocellatus* bite victims in Jos metropolis, Plateau State, Nigeria. Subjects were recruited by purposive sampling. Samples were collected within four (4) hours after bite. The whole blood clotting time (WBCT20) was evaluated immediately. Another batch of blood samples were collected from same snake bite victims, two (2) days post administration of the anti-venom.

### 2.2 Study Area

The sample collection was carried out in Plateau State Specialist Hospital, Jos, Plateau State, while the research analysis was performed at the Research Laboratory, Nnamdi Azikiwe University, Nnewi, Anambra State, Nigeria. Ethical approval for this study was obtained from the Ethics Committee of the Faculty of Health Sciences and Technology, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Nnewi, Anambra State.

### 2.3 Study Population

A total of 80 individuals were recruited for this study which included 40 subjects of *Echis ocellatus* bite victims and 40 apparently healthy individuals that served as controls. Subjects with renal disorder, inflammatory and autoimmune diseases such as systemic lupus erythematosus (SLE), scleroderma, Sjögren's syndrome, mixed connective tissue disease, polymyositis/dermatomyositis, rheumatoid arthritis, history of cardiac disease such as coronary heart disease, ischaemic heart disease etc and coagulatory disorders were excluded from this study. Informed written consent was sought and obtained from the study participants prior to specimen collection.

### 2.4 Sample Collection

A total of 10 ml of venous blood was collected aseptically from all the subjects and dispensed into a plain container for the determination of the levels of troponin-I, cholesterol, triglyceride and C-reactive protein. The samples were centrifuged at 4,000 rpm for 10 minutes and the serum separated was refrigerated until analyzed.

### 2.5 Determination of Whole Blood Clotting Time (WBCT20)

Estimation of WBCT20 was performed using the method as described by Kornalik and Blomback [30].

#### 2.5.1 Principle

The coagulation time of whole blood is the length of time required for a measured amount of blood to clot under certain specified conditions [30].

### 2.6 Evaluation of Cardiac Troponin-I (cTnI) Level

The method of Peter and Eva [31] was adopted for the determination of Cardiac troponin-I levels.

This is essentially an enzyme-linked immunosorbent assay (ELISA) technique.

### 2.6.1 Principle

Antibodies specific for human cTnI are located on an electrochemical sensor fabricated on a silicon chip. The enzyme bound to the antibody/antigen/antibody sandwich cleaves the substrate releasing an electrochemically detectable product. The electrochemical sensor measures this enzyme product which is proportional to the concentration of cTnI within the sample.

### 2.7 Determination of Serum Total Cholesterol Level

The evaluation of serum cholesterol was done using enzymatic method as described by Meattini [32].

#### 2.7.1 Principle

Free and esterified cholesterol in the sample originates in the presence of cholesterol oxidase and peroxidase resulting to a coloured complex that can be measured by spectrophotometry [32].

### 2.8 Evaluation of Serum Triglyceride Level

The spectrophotometric method of Tietz [33] was applied for the evaluation of serum triglyceride

#### 2.8.1 Principle

The triglycerides are determined after enzymatic hydrolysis with lipases. The indicator is a quinoneimine formed from hydrogen-peroxide, 4 aminophenazone and 4 chlorophenol under the catalytic influence of peroxidase.

### 2.9 Estimation of C-reactive Protein Level

The method as described by Pepys [34] was utilized for the estimation of C-reactive protein levels.

#### 2.9.1 Principle

The simple Step ELISA employs an affinity tag labeled capture antibody and a reported conjugated detector antibody which immunocapture the sample analyte in solution. The entire complex is in turn immobilized via

immunoaffinity of an anti-tag antibody coating the well.

### 2.10 Statistical Analysis

Data collected was analyzed using the independent students' t-test and Pearson's correlation coefficient was utilized for correlation studies. Values were recorded significant at  $p < 0.05$ .

## 3. RESULTS

Table 1 shows the serum levels of troponin-I, total cholesterol (TC), triglyceride (TG) and C-reactive protein (CRP) in *Echis ocellatus* bite victims before and post administration of anti-venom and control.

There was a significant increase in the mean serum levels of troponin-I, triglyceride and c-reactive protein in *Echis ocellatus* bite victims pre-administration of anti-venom compared with those of the non-victims (controls) ( $P < 0.05$ ). However, a significant decrease was observed in the mean serum level of total cholesterol in *Echis ocellatus* bite victims pre-administration of anti-venom compared with that of non-victims ( $P < 0.05$ ). There was also a significant increase in the mean serum levels of troponin-I and c-reactive protein only and a significant decrease in the mean serum levels of total cholesterol and triglyceride in the test subjects pre-administration of anti-venom compared with those of the test subjects post administration of anti-venom ( $P < 0.05$ ). Furthermore, serum levels of triglyceride and c-reactive protein were significantly higher in test subjects post administration of anti-venom compared with those of the control subjects ( $P < 0.05$ ).

Table 2 shows the correlation of the levels of troponin-I with the levels of total cholesterol (TC), triglyceride (TG) and C-reactive protein (CRP) in *Echis ocellatus* bite victims pre-anti-venom administration.

There were moderate positive correlations between the levels of troponin-I (TnI) and TC ( $r = 0.278$ ;  $P > 0.05$ ) and C-reactive protein (CRP) ( $r = 0.498$ ;  $P < 0.05$ ), however, no correlation existed between cTnI and TG ( $r = 0.007$ ) in *Echis ocellatus* bite victims pre-administration of anti-venom.

**Table 1. Mean serum levels of troponin-I, total cholesterol (TC), Triglyceride (TG) and C-reactive protein (CRP) in *Echis ocellatus* bite victims before and post administration of anti-venom and control**

Groups	Troponin-I (ng/ml)	TC(mmol/l)	TG(mmol/l)	CRP (mg/l)
Pre anti-venom administration(A)	2.98±5.75 <sup>b</sup>	3.65±0.83 <sup>b</sup>	0.87±0.11 <sup>a</sup>	36.64±29.01 <sup>a</sup>
Post anti-venom administration (B)	0.16±1.39 <sup>b,c</sup>	4.28±0.79 <sup>b,c</sup>	0.92±0.15 <sup>a</sup>	15.96±17.36 <sup>a</sup>
Control (C)	0.007±0.3 <sup>b,c</sup>	4.28±0.56 <sup>b,c</sup>	0.77±0.10 <sup>a</sup>	0.99±0.28 <sup>a</sup>
f- value	8.244	9.904	15.236	34.303
p-value	<0.001	<0.001	<0.001	<0.001
A vs B	0.008	0.001	0.027	<0.001
A vs C	0.001	0.001	0.027	<0.001
B vs C	1.000	1.000	0.027	0.002

KEYS: <sup>a</sup>= significant difference across the groups (AvsB, AvsC and BvsC), <sup>b</sup>= significant difference between groups (AvsB and AvsC), <sup>c</sup>= non-significant difference between groups. TC= Total cholesterol, TG= Triglyceride, CRP= C-reactive protein

**Table 2. Correlation of the levels of troponin-I with the levels of total cholesterol (TC), triglyceride (TG) and C-reactive protein (CRP) in *Echis ocellatus* bite victims pre-anti-venom administration**

Parameters	N	R-value	P-value
Troponin-I vs TC	40	0.278	0.082
Troponin-I vs TG	40	0.007	0.964
Troponin-I vs CRP	40	0.498	0.001

Key: TC= Total cholesterol, TG= Triglyceride, CRP= C-reactive protein

**Table 3. Correlation of the levels of troponin-I with the levels of total cholesterol (TC), triglyceride (TG) and C- reactive protein (CRP) in *Echis ocellatus* bite victims post anti-venom administration**

Parameters	N	R	P-value
Troponin-I vs TC	40	0.750	0.650
Troponin-I vs TG	40	-0.212	0.194
Troponin-I vs CRP	40	0.430	0.006

Key: TC= Total cholesterol, TG= Triglyceride, CRP= C-reactive protein

Table 3 shows the correlation of the levels of troponin-I with the levels of total cholesterol (TC), triglyceride (TG) and C- reactive protein (CRP) in *Echis ocellatus* bite victims post anti-venom administration.

A strong positive correlation existed between the levels of troponin-I and TC ( $r= 0.750; P>0.05$ ) while a moderate positive correlation existing between the levels of cTnI and CRP ( $r= 0.430; P<0.05$ ). However, a weak negative correlation was obtained between the levels of cTnI and TG ( $r= -0.212; P>0.05$ ).

#### 4. DISCUSSION

*Echis ocellatus* is regarded as the most medically important snake specie in West Africa and causes both public health and severe economic problems, especially to farming communities [35]. It is a venomous viper specie, responsible for human fatalities [36]. In humans, envenoming

by *Echis ocellatus* causes local inflammation, with severe blistering, oedema and tissue necrosis at the bite site and life threatening systemic effects including haemorrhage, coagulopathy and occasionally hypovolaemic shock [37]. Snake antivenom is the only specific therapy for treating snake bites. This antivenom contains polyclonal antibodies that are generated by immunizing animals (horses and sheep) with small amounts of snake venom. The resulting antibodies are purified from serum or plasma and formulated into intact IgG or Fab fragment therapies, which are administered intravenously following snakebite [38].

In this study, a significant increase in the mean serum levels of troponin I, triglyceride and c-reactive protein was observed in *Echis ocellatus* bite victims pre-administration of antivenom, compared with those of the non-victims (controls) ( $P<0.05$ ). However, a significant decrease was

also observed in the mean serum level of total cholesterol in *Echis ocellatus* bite victims pre administration of anti-venom compared with that of non-victims ( $P < 0.05$ ). There was also a significant increase in the mean serum levels of troponin I and C-reactive protein in the test subjects pre-administration of anti-venom compared with those of the test subjects post administration of anti-venom ( $P < 0.05$ ) and a significant decrease in the mean serum levels of total cholesterol and triglyceride in the test subjects pre-administration of anti-venom compared with the test subjects post administration of anti-venom. Furthermore, serum levels of triglyceride and C-reactive protein were significantly higher in test subjects post administration of anti-venom compared with those of the control subjects ( $P < 0.05$ ).

This could be attributed to hypovolemic shock, hypercoagulability, toxic myocarditis and coronary artery spasm as possible mechanisms for myocardial infarction and the elevated troponin-I levels in snakebite victims. The possible first report of myocardial infarction after a snake bite was described by Brown and Dewar [39]. These researchers reported a significant increase in troponin-I levels and other cardiac markers in myocardial infarction from *Echis ocellatus* bite, and ventricular tachycardia also due to snake bite. Troponin-I is a cardiac and skeletal muscle protein useful in the laboratory diagnosis of heart attack [40]. It is a part of the troponin protein complex, that binds to actin in thin myofilaments to hold the actin-tropomyosin complex in place. In this condition, myosin cannot bind actin in relaxed muscle [41]. Troponin-I is presented in cardiac muscle tissue by a single isoform with molecular weight 23.9 K Da and it consists of 209 amino acid residues [40].

Onyeama et al. [42], used albino wistar rats as experimental animals and reported that the serum level of total cholesterol was significantly elevated in the venom treated group of rats compared with the controls. However, another study by Sun et al. [43] differed from that of Onyeama et al. [42] by concluding that viper venom has little effect on the regression of atherosclerosis, but prolongs blood clotting and lowers serum cholesterol level. Serum levels of total cholesterol may be decreased in snakebite victims due to transcapillary lipoprotein leakage and this could affect lipoprotein transport and metabolism. This therefore is in contrast to the findings of Onyeama et al. [42] who observed a

significant increase in the serum levels of triglyceride in experimental animals treated with viper venom compared with the control.

In our work, there was a significant decrease in the mean serum levels of triglyceride in *Echis ocellatus* bite victims pre-administration of anti-venom when compared with the mean serum levels of triglyceride in the victims post administration of anti-venom. Furthermore, a significant increase was observed in the mean serum levels of triglyceride post administration of anti-venom compared with that of the non victims of *Echis ocellatus* bite. According to Onyeama et al, anti-snake venom was able to lower serum lipid levels in envenomated rats with elevated plasma lipid levels before anti-venom administration [42]. Triglycerides are major components of very low density lipoprotein and chylomicrons that play important role in metabolism as energy sources and transporters of dietary fat. They contain more than twice as much energy as carbohydrates [44].

*E. ocellatus* produces a haemotoxic venom that can cause cardiovascular effects among other conditions [45]. Cardiovascular effects are best characterized by a dramatic fall in blood pressure and this can be caused by a number of different venom toxins. For example, SVMPs (Snake Venom Metalloproteinases) indirectly contribute to hypotension by increasing vascular permeability via the degradation of capillary basement membranes, resulting in leakage and reductions in blood pressure [45]. This is in accordance to the finding of Onyeama et al. [42].

C-reactive protein (CRP) is a pentameric protein found in blood plasma whose level rises in response to inflammation. CRP is synthesized by the liver in response to factors released by macrophages and fat cells [46]. It is used mainly as a marker of inflammation. Apart from liver failure, there are few known factors that affect CRP production. Interferon alpha inhibits CRP production from liver cells which may explain the relatively low levels of CRP found during viral infections compared to bacterial infections [47]. CRP, just like Tumour necrosis factor-alpha (TNF- $\alpha$ ), is a pro inflammatory cytokine produced mainly by activated macrophages or monocytes and plays an important role in diverse cellular events, such as the production of other cytokines, cell proliferation, differentiation and apoptosis [48]. Inflammatory effects from *Echis ocellatus* bite include local swelling (edema), pain and bleeding at the site of the bite. Systemic effects include; coagulopathy, spontaneous

systemic hemorrhage, gum bleeding, hematuria, hematemesis, hemolysis and the non-specific symptoms, nausea and vomiting with abdominal pains [49].

Furthermore, there were moderate positive correlations between the levels of troponin-I (Tnl) and C-reactive protein (CRP); TC and no correlation between Tnl and TG in *Echis ocellatus* bite victim's pre-administration of anti-venom. There was also a strong positive correlation between the levels of troponin-I and TC while a moderate positive correlation existed between the levels of Tnl and CRP. C-reactive protein (CRP) levels were elevated in *Echis ocellatus* bite victim's pre-administration of anti-venom. This data shows a possible *Echis ocellatus* venom action on acute phase reactants, interacting with target cells like macrophages releasing inflammatory mediators such as interleukin-6 (IL-6) and interleukin-8 (IL-8). CRP, just like IL-6 also, acts on the liver increasing the production of CRP [50]. *E. ocellatus* venom plays major roles in the development of inflammation, oedema and other responses to inflammation in different systems of the body. Due to the presence of the metalloproteinases in the *E. ochellatus* venom, it is able to induce edema with hemorrhage, unlike the Elapids (cobra) venom once they lack metalloproteinases [50].

Elevated serum levels of troponin-I and CRP are also associated with severe cardiovascular mortality cases. In a study by James et al. [50], to evaluate c-reactive protein (CRP) and troponin-I (Tnl) as predictors of risks of the individual end points of mortality and myocardial infarction (MI) in a large cohort of patients with acute coronary syndrome (ACS), it was discovered that in ACS, baseline levels of Tnl and CRP were independently related to increased rate of mortality. Thus, any detectable elevation of Tnl, with or without corresponding elevation of CRP is also associated with an increased risk of myocardial infarction. Regarding to mortality, both markers are related and provide risk stratification than one alone. This is in line with the findings of Veselka et al. [51], who investigated the correlation between troponin-I (Tnl) and C-reactive protein (CRP) in a multivariate analysis performed to identify the predictors of myocardial infarction (PMI).

## 5. CONCLUSION

The research findings therefore suggest that *Echis ocellatus* envenomation triggers

inflammatory reaction which could be the reason behind the alteration in cardiac markers as evidenced by the significant elevations in serum troponin-I and CRP levels amongst snake bite victims compared to the non-snake bite control groups thus, could cause cardiac arrest before anti-venom administration. Anti-venom tends to improve response to treatment when administered promptly. Early assessment of the levels of cardiac and inflammatory markers in snakebite victims will be an invaluable tool for effective management of this life threatening condition.

## CONSENT

As per international standard informed and written participant consent has been collected and preserved by the authors.

## ETHICAL APPROVAL

The ethical approval has been obtained by the authors from The College of Health Sciences Nnamdi Azikiwe University, NNEWI campus, Nigeria, bearing authorization number: ERC/FHST/NAU/2018/58.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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