

## Effect of age on procoagulants in people with obesity at Sapele, Southern Nigeria

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### Abstract

**Background/Objectives:** Aged people with obesity are vulnerable to coagulation disorders arising from alterations in procoagulants. Therefore, this study aims to evaluate the effect of age on procoagulant such as: fibrinogen (FG), von willebrand factor (vWF), Soluble Vascular Cell Adhesion Molecules (sVCAM) tissue factor (TF), Tissue Plasminogen Activator (tPA) and Plasminogen Activator Inhibitor (PAI) in obese people.

**Materials and Method:** 312 subjects with age between 18 and 65years were enrolled for this study comprising of 111males and 201females who were further grouped into age ranges of 20-39years, 40-49years and 50-59years respectively. 4.5mls of venous blood was collected into Ethylene Diamine Tetra-acetic Acid (EDTA) container. Plasma obtained was analyzed using ELISA method.

**Results:** FG values in obese people within age range 20-29years was 100.59±209.23ng/ml while FG level of people within age range 40-49years and 50-59years were 71.14±64.24ng/ml and 41.83±15.63ng/ml respectively at p<0.05. PAI of those within age range of 20-39years was 411.65±349.88pg/ml while PAI of people in age range of 50-59years was 265.92±64.30pg/ml. sVCAM of people in the age range of 20-39years was 8.24±12.61u/l and people within the age range of 50-59years had sVCAM value of 4.42±1.17u/l. TF values of people within the age range of 20-39years was 82.03±54.21pg/ml while people in the age range of 50-59years had TF value of 74.54±20.05pg/ml at P<0.05. vWF of people within age range of 50-59years was 84.88±58.96u/l while younger people in the age range of 20-29years had vWF value of 74.59±55.32u/l at P<0.05.

**Conclusion:** Procoagulants such as: FG, PAI, sVCAM and TF were higher in younger people than in older people with obesity at Sapele southern Nigeria.

**Keywords:** Age; Obesity; Procoagulant; Sapele

### 1. Introduction

Obesity is a medical condition in which excess body fat has accumulated to the level that it produces adverse effect on health [1]. Uncontrolled weight gain is associated with many chronic diseases such as: cardiovascular disease, type 2 diabetes mellitus, asthma, sleep apnea, cancer, bone disease and reduction in life expectancy globally [2] and there is rising level of obesity in lower income countries resulting in poor health status and low economic productivity.

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A combination of too much food energy intake and sedentary life style are the major causes of obesity, which ultimately results in the formation of excess adipose tissue either in the visceral or in the subcutaneous cavity [3]. However, small number of cases are due principally to hereditary, medical issues, mental illnesses, Decreased variability in ambient temperature and interference with lipid metabolism [4].

In obesity, there is a chronic inflammatory state that is characterized by excess adipose tissue deposition and build-up of adipocytokines such as, inflammatory mediators and metabolic regulators. This inflammatory state results in alteration of procoagulant factors levels which interferes with normal blood coagulation [5]. Obesity and aging are key factors that affects procoagulants in humans and age induce variation in blood pressure may be attributed to changes in arterial and arteriolar stiffness due to aging [6]. Studies have reported that, arterial compliance reduces with ageing thereby, resulting in increased systolic blood pressure and diastolic blood pressure reduces or becomes more flattened usually after 50 years of age [7].

Procoagulants are precursors that promotes blood coagulation and there are reports that certain plasma procoagulant like von willebrand factor (vWF) increases with age [8]. The increasing plasma vWF levels expressed with aging can be connected to the increased oxidative stress via the stimulation of nuclear factor kappa light chain enhancer of activated B cells (NF-KB) signaling, that occurs during aging which is expressed by the bonding of the followings; (a) adhesion molecules, (b) macrophages to endothelial cells, (c) reduced compliance of connective tissues, (d) stiffness of vascular muscles and (e) tissue injury.

The procoagulants considered in this study are: fibrinogen (FG), von willebrand factor (vWF), Soluble Vascular Cell Adhesion Molecules (sVCAM) tissue factor (TF), Tissue Plasminogen Activator (tPA) and Plasminogen Activator Inhibitor (PAI).

In addition, aged people (i.e above 50years of age) with obesity are more vulnerable to thrombotic disease and coagulation abnormalities as a result of alterations in procoagulants. Therefore, the aim of this study is to evaluate Effect of Age on procoagulant in people with obesity at Sapele, Southern Nigeria.

Sapele is a city located in central part of Delta State, Southern Nigeria. It is positioned at a height of 9meters above sea level at latitude of 5.89<sup>o</sup> and a longitude of 5.68<sup>o</sup>. Sapele has a population of about 174,273 (Population census, 2006) and accommodates different tribes such as: Okpe, Urhobo, Itsekiri, Ibo, Ijaw, Isoko, Hausa, Edo, Yoruba, Ibibio, Nupe, Tiv, Fulani. The common diets in this locality are starch, yam, garri, rice, beans, plantain, palm oil, fish, meat, periwinkle etc.

It is believed that, providing information on the effects of obesity on the above listed procoagulants will help in formulation of appropriate strategies and program for maximum healthcare to people with obesity in Sapele and indeed Nigeria at large.

### **1.1. Inclusion Criteria**

Obese adults who fell within the age ranges of 18 and 65 years and resident in Sapele and its environ were recruited into the study.

### **1.2. Exclusion Criteria**

Pregnant women, known hypertensive patient, patient with demonstrable ascites, intra-abdominal masses, malignancy, renal disease, Liver disease, Diabetes mellitus, HIV infection, current oral anticoagulant use, recent surgery (<3 months), and those who refused consent were excluded from this study.

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## **2. Materials and Method**

This cross sectional and descriptive study was carried out at Central Hospital, Sapele, General Hospital, Oghara and Biomed Diagnostic Centre, Sapele all in Southern Nigeria. 312 subjects with age between 18 and 65years were enrolled for this study comprising of 111males and 201females which were further grouped into age ranges of 20-39years, 40-49years and 50-59years respectively.

### **2.1. Sample Collection**

Four and half milliliters (4.5mls) of venous blood was collected from all participant into EDTA container. The blood sample was analyzed within one hour of collection using Enzyme Linked Immuno-Sorbent Assay (ELISA) method.

## 2.2. Ethical Approval

Ethical Clearance for this study was obtained from the Ethics committee of Central hospital, Sapele Medical Zone, Sapele, on 8<sup>th</sup> of December, 2016 with Reference number SNZ/A.31VOL.3/54. Informed consent was also obtained from individuals as well as completed structured questionnaire.

## 2.3. Sample Analysis

4.5mls of venous blood was collected and dispensed into EDTA container. Samples was further allowed to stand and centrifuge at 3000 rpm for 10 minutes to obtain a clear plasma, which was kept at - 20°F until time for analysis. The blood sample was analyzed using ELISA method. Collated data were analyzed using Student's t-test, One-way ANOVA, LSD post-hoc test and results were expressed as mean  $\pm$  standard deviation.

## 2.4. Elisa Method's Principle

Standard solutions and samples were added to antibody specific pre coated microelisa stripplate wells, when combined with the specific antibody, then reacted with biotinylated detection antibody specific for correspondent human proagulant and Avidin-Horseradish Peroxidase (HRP) conjugate after incubation to produce specific colored solution with substrate solution, which changes color with the addition of stop solution. The Optical Density (OD) was measured spectrophotometrically at wavelength of 450nm, The OD value was proportional to the concentration of a given procoagulant.

## 3. Results

The Fibrinogen (FG) values of younger people with obesity within age range 20-29years was 100.59 $\pm$ 209.23ng/ml while FG level of older people of age range 40-49years and 50-59years was 71.14 $\pm$ 64.24ng/ml and 41.83 $\pm$ 15.63ng/ml respectively at p<0.05.

**Table 1** Comparison of Mean  $\pm$ SEM of some procoagulant parameters with age of people with obesity

Variables	Obese(n=312)	Normal(n=103)	t-test	p-value
	Mean $\pm$ SEM	Mean $\pm$ SEM		
<b>20-29 years</b>	<b>n=75</b>	<b>n=22</b>		
FG(ng/ml)	100.59 $\pm$ 209.23	37.01 $\pm$ 15.02	3.084	0.002**
vWF( $\mu$ /l)	74.59 $\pm$ 55.32	58.12 $\pm$ 17.87	2.839	0.005**
sVCAM( $\mu$ /l)	8.23 $\pm$ 12.61	4.07 $\pm$ 1.40	3.338	0.001**
tPA(pg/ml)	363.92 $\pm$ 602.05	186.76 $\pm$ 82.50	2.965	0.003**
PAI(pg/ml)	335.36 $\pm$ 88.61	249.36 $\pm$ 86.61	4.705	0.001**
TF(pg/ml)	82.03 $\pm$ 54.21	66.69 $\pm$ 21.47	1.932	0.049**
<b>30-39 years</b>	<b>n=99</b>	<b>n=33</b>		
FG(ng/ml)	99.44 $\pm$ 209.23	36.01 $\pm$ 15.02	3.085	0.002**
vWF( $\mu$ /l)	73.59 $\pm$ 55.32	57.12 $\pm$ 17.87	2.739	0.005**
sVCAM( $\mu$ /l)	8.24 $\pm$ 12.61	4.08 $\pm$ 1.40	3.348	0.001**
tPA(pg/ml)	360.92 $\pm$ 602.05	183.76 $\pm$ 82.50	2.975	0.003**
PAI(pg/ml)	345.05 $\pm$ 153.31	259.36 $\pm$ 88.61	4.715	0.001**
TF(pg/ml)	80.04 $\pm$ 54.21	64.70 $\pm$ 21.47	1.922	0.049**
<b>40-49 years</b>	<b>n=90</b>	<b>n=30</b>		
FG(ng/ml)	71.14 $\pm$ 64.24	68.80 $\pm$ 34.51	0.113	0.910

vWF( $\mu$ /l)	93.79 $\pm$ 79.09	72.10 $\pm$ 26.66	0.860	0.392
sVCAM( $\mu$ /l)	7.69 $\pm$ 7.63	5.24 $\pm$ 1.35	1.010	0.315
tPA(pg/ml)	354.75 $\pm$ 313.34	253.20 $\pm$ 55.66	1.019	0.310
PAI(pg/ml)	411.65 $\pm$ 349.88	284.00 $\pm$ 45.02	1.148	0.253
TF(pg/ml)	108.45 $\pm$ 86.03	71.40 $\pm$ 19.77	1.353	0.179
<b>50-59 years</b>	<b>n=48</b>	<b>n=18</b>		
FG(ng/ml)	41.83 $\pm$ 15.63	30.75 $\pm$ 0.87	1.396	0.174
vWF( $\mu$ /l)	84.88 $\pm$ 58.96	40.50 $\pm$ 0.58	1.482	0.150
sVCAM( $\mu$ /l)	4.42 $\pm$ 1.17	3.25 $\pm$ 0.29	1.956	0.061
tPA(pg/ml)	229.83 $\pm$ 82.54	192.50 $\pm$ 20.21	0.887	0.383
PAI(pg/ml)	265.92 $\pm$ 64.30	295.00 $\pm$ 5.77	-0.890	0.382
TF(pg/ml)	74.54 $\pm$ 20.05	62.50 $\pm$ 14.43	1.144	0.263

\*\*Significant (p<0.01) \*Significant (p<0.05) † Not Significant

On the other hand, PAI of younger people with age range of 20-39years was 411.65 $\pm$ 349.88pg/ml while the PAI of older people in the age range of 50-59years was 265.92 $\pm$ 64.30pg/ml. Furthermore, sVCAM of people at the age range of 20-39years was 8.24 $\pm$ 12.61u/l and people at the age range of 50-59years had sVCAM value of 4.42 $\pm$ 1.17u/l. on the other hand, People in the age range of 30-49years had no significant difference in procoagulant values. Nevertheless, TF values of people within the age range of 20-39years was 82.03 $\pm$ 54.21pg/ml while older people in the age range of 50-59years had TF value of age 74.54 $\pm$ 20.05pg/ml at P<0.05 as shown in table 1. Furthermore, Nevertheless, vWF of older people was 84.88 $\pm$ 58.96u/l while younger people in the age range of 20-29years was 74.59 $\pm$ 55.32u/l at P<0.05.

Nevertheless, the correlation of some procoagulant was shown in table 2 below such that vWF, tPA and TF had a significant correlation with age in people with obesity at Sapele. While, FG, sVCAM and PAI had no significant correlation with procoagulants in respect to age as shown in table 2.

**Table 2** Correlation of age with procoagulants

Parameter	Correlation (r)	P values
Age vs. Fib	0.059	0.456†
Age vs. vWF	0.180	0.022*
Age vs. sVCAM	0.078	0.325†
Age vs. tPA	0.178	0.041*
Age vs. PAI	0.112	0.157†
Age vs. TF	0.159	0.044*

\*\*Correlation Significant (p<0.01) \*correlation significant (p<0.05) †correlation not significant

#### 4. Discussion

The procoagulant in people with obesity have been analyzed in respect to age and it was discovered that, in this study vWF value of older people was higher than that of the younger people. This implies that plasma vWF level increases with aging. This result is in line with earlier reported by Mariachiara, in 2017 [8], which showed that vWF level increase progressively and significantly with aging particularly in individual without vWF related gene mutated diseases. The increasing plasma vWF levels expressed with aging can be connected to the increased oxidative stress via the stimulation of nuclear factor kappa light chain enhancer of activated B cells (NF-KB) signaling that occurs during aging, which is also expressed by the bonding of adhesion molecules, macrophages to endothelial cells, reduced compliance of connective tissues, stiffness of vascular muscles and tissue injury. On the other hand, sVCAM reduces with Age which is in conformity with findings of Yani *et al.*, in 2006 [9], that reported upregulation of sVCAM associated with aging and its

expressions during aging were elicited by increased oxidative stress via the activation of NF-KB signaling that occurs during aging in a study carried in mice.

Aged subjects and obese patients are more vulnerable to thrombotic disease linked with stress. The report also observed that restraint stress induces the TF expression in a tissue specific and cell type specific manner. Obese Subjects were hyper responsive to restraint stress in the induction of TF gene, particularly in their livers and adipose tissues. Stress induced micro thrombi development was common in renal glomeruli and within the vasculature in the adipose tissue of aged subjects and the pre administration of mice with anti TNF alpha antibody partly attenuated the stress mediated induction of TF gene in adipose tissues in these mice [10]. These reports indicated that the induction of TF gene may increase the risk of stress connected with thrombosis in older subjects and obese individuals.

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## 5. Conclusion

The values of procoagulants such as: Fibrinogen (FG), Plasminogen Activator Inhibitor (PAI), Soluble Vascular Cell Adhesion Molecules (sVCAM) and TF were higher in younger people with obesity when compare with the values in older obese people. On the other hand, von willebrand factor (vWF), was higher in older obese people than in younger people with obesity at Sapele southern Nigeria.

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## Compliance with ethical standards

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### *Disclaimer*

The views expressed in this article are that of the authors not an official position of any hospital or institution.

### *Disclosure of conflict of interest*

This article has not been submitted to any journal for purpose of publication except the one being considered now. There is no conflict of interest regarding this work among the authors.

### *Ethical Approval*

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### *Statement of informed consent*

Informed consent was also obtained from individual participants included in the study as well as completed structured questionnaire.

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