Serum Albumin Level in Second and Third Trimester Pregnancies in Makurdi, Nigeria

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Original Research Article

Abstract: Certain physiological changes occur during normal pregnancy. These changes when exaggerated could result to adverse maternal outcome. Adverse cardiovascular outcomes have been previously linked with hypoalbuminemia in the general population. Few reports exist about serum albumin level in second and third trimester of pregnancy. Our study aims at determining serum albumin level in second and third trimesters of pregnancy. This was a case-control study involving randomly selected 40 non pregnant and 77 pregnant women in Makurdi, Nigeria. The participants were subdivided into 3 comparable groups; control n=40, second trimester n=37 and third trimester n=40. Mean age, body mass index (BMI), and serum albumin in the study groups were compared using ANOVA. Associations of age, BMI, gestation age and albumin were determined using Pearson correlation analysis. Serum albumin level was significantly (P<0.0004) lower in the pregnant groups compared to the controls. A post hoc test reveals a significant (P<0.0001) lower serum albumin in third trimester group than in second trimester and controls. Conclusion: Knowledge about hypoalbuminemia during pregnancy will help distinguish pathological hypoalbuminemia during antenatal check-up.

Keywords: Albumin, Cardiovascular, Hypoalbuminemia, Pregnancy, Trimester.

INTRODUCTION

Serum albumin (SA) is a 65 KDa protein synthesized in the liver and associated with several vital physiological functions, such as maintenance of oncotic pressure and microvascular integrity, regulation of metabolic and vascular functions, provision of binding ligands for substances, antioxidant activities, and anticoagulant effects [1, 2].

Serum albumin is a powerful oxidant scavenger in human plasma which inhibits hydroxyl, peroxyl and hypochlorite radicals [3]. Høstmark reported that albumin as an extracellular antioxidant does have a cardioprotective role against lipid peroxidation [4]. Serum albumin is traditionally regarded as a biomarker for reliable risk prediction in various clinical settings. An increased risk in all-cause mortality and cardiovascular mortality has been shown to be associated with low SA concentration. Lower levels of serum albumin within the "normal" range are associated with increased risk of cardiovascular diseases [2]. Substantial evidence supports the significant inverse relation between serum albumin level and risk of coronary artery disease as well as all-cause mortality [5]. Evidence shows several underlying pathophysiologic mechanisms which hypoalbuminemia mediate adverse cardiovascular outcomes: a). Reduced vasodilatory, toxin binding, antioxidant and anticoagulation ability; b). Increased blood viscosity and vascular permeability [2].

Physiological changes occur during pregnancy to support fetal growth and development [6]. Maternal blood volume increases during pregnancy, due to increase in plasma, red cell, and white cell volumes [7]. The increase in plasma volume is characteristic of increased fluid retention [6, 8]. The exact mechanism of this hemodilution is unknown. However, hemodilution may explain the formation of edema in pre-eclampsia [9]. Preeclampsia is a multisystem disorder peculiar to human pregnancy, characterized by cardiovascular symptoms after the 20th week of pregnancy. Plasma albumin is the major contributor of the total colloid osmotic pressure of plasma [10]. Hypoalbuminaemia resulting from hemodilution reduces plasma oncotic pressure, predisposing to water accumulation in tissues [11]. Hormonal changes during pregnancy influences hemodynamics [12]. Mild systemic inflammation occurs during normal pregnancy due to a multitude secretion of inflammatory factors from the placenta into maternal circulation. Deregulation of these factors in which there is excessive systemic inflammation may precipitate preeclampsia [13]. Reduced plasma

concentration of albumin is a component of acute phase response of physiological pregnancy linked with systemic inflammation [14]. The nutritional status of pregnant women has been recognized as an essential determinant of fetal growth and survival [15]. Good nutritional status during pregnancy is one of the best predictors of optimal pregnancy outcome. However, under nutrition or protein energy malnutrition have been implicated as significant causes of various medical disorders in developing countries. Ogbodo *et al.,* observed a general decrease in nutritional parameters including serum albumin in pregnant women studied in a Nigerian population [16].

Previous studies exist regarding plasma proteins in pregnancy in Nigeria. However, scant reports are available about serum albumin level in second and third trimester of pregnancy. Therefore the present study aims at determining serum albumin level in second and third trimester pregnancies.

MATERIALS AND METHODS
Study Design
The case-control study compared serum albumin level in second and third trimester normal pregnancies with age matched non-pregnant women.

Study Area and Population
A sample of female participants aged 18-35 years, was randomly drawn from women attending the ante-natal clinic at the Federal Medical Centre Makurdi, Nigeria.

Sample Size
The sample size was determined using the formula for case-control studies that compare group means [17]; $n=1+2C(s/d)^2$, at a significance level of 5%, and statistical power of 90%.

Selection Criteria
Individuals were eligible to participate in the study if they: (a) were within the reproductive age of 18 to 35 years; (b) had no history of hypertension and were not using antihypertensive medications; (c) were free of any other major systemic illnesses (e.g. liver disease, cancer, diabetes mellitus); (d) were nonsmokers. All subjects were availed with informed consent, and the study was approved by the institutional ethical committee.

Data Collection
Participants provided information on their demographic characteristics, detailed medical history, dietary and lifestyle habits.

Body mass index (BMI)
Body weight to the nearest 0.1 kg and height to the nearest centimeter were measured and BMI was calculated as weight (kilograms)/height (meters squared).

Blood sample collection
Participant's blood samples were collected into plain vacutainer tubes and centrifuged at 3000 rpm for 10 min within 1 h of blood collection. Blood in plain vacutainers was used for the determination of serum albumin immediately after separation.

LABORATORY METHODS
Determination of serum albumin
The reagent kit for the determination of serum albumin was obtained from Randox Laboratories Limited, United Kingdom. Serum albumin was determined by the bromocresol green (BCG) end point method. The measurement of serum albumin was based on its quantitative binding to the indicator BCG. The intensity of the colored albumin‑BCG‑complex is proportional to the concentration of albumin in the sample [18]. The intensity of the deep green colored solution obtained was spectrophotometrically measured at a wavelength of 578 nm to obtain the absorbances of the serum, standard, and control solutions. The concentrations of albumin in these samples were determined using the formula: Absorbance of serum solution/Absorbance of standard solution × Conc. of Std. (46.7 g/l).

Statistical Analysis
The statistical package IBM Armonk, New York, United States SPSS version 21 was used in analyzing the data generated. Descriptive statistics were used in determining the mean and standard deviation of the parameters measured. The one way analysis of variance (ANOVA) followed by a post hoc test was used in comparing the mean of the parameters in the study groups. Pearson correlation analyses were done to test the association between parameters measured in the study groups. Two-tailed $P < 0.05$ was considered statistically significant.

RESULTS
Table-1 shows age, BMI, serum albumin in control, second and third trimester pregnancies. There was no significant ($P>0.05$) difference in maternal age of the groups compared. A significant ($P<0.0001$) higher BMI was observed in the pregnant groups compared with the non pregnant group. Serum albumin level was significantly ($P<0.0001$) lower in the pregnant groups compared to the controls. A post hoc test revealed a significant ($P<0.0001$) lower serum albumin in third trimester group than in second trimester and controls. Table-2 shows Pearson correlation coefficients of age, BMI and albumin in non pregnant controls. A significant ($P<0.01$, r=0.413) correlation was observed between age and BMI in the control group, while a non significant ($P>0.05$) correlation was found between age and albumin, BMI

and albumin. Table-3 presents Pearson correlation coefficients of age, BMI, albumin and gestation age in the pregnant group. A significant ($P<0.01$, $r= -0.506$) inverse correlation was observed between albumin and gestation age. While BMI and age correlated significantly ($P<0.01$, $r= 0.391$), an insignificant ($P>0.05$) correlation was observed between age and albumin, BMI and albumin, BMI and gestation age in the pregnant group.

Table-1: Age, BMI, serum albumin in control, second and third trimester pregnancies

Parametres	Non pregnant (NP) n=40		Second trimester (ST) n=37		Third trimester (TT) n=40	F-value		P-value	
AGE years	26.78±6.52		27.43±4.62		28.80±4.30	1.543		0.218	
BMI kg/m²	24.80±3.72		27.87±6.27		28.93±3.68	56.568		<0.0001*	
ALB	42.20±2.91		38.67±3.17		35.65±2.12	8.395		<0.0004*	
Post Hoc	**NP**	**ST**	**P**	**NP**	**TT**	**P**	**ST**	**TT**	**P**
AGE	26.78±6.52	27.43±4.62	0.584	26.78±6.52	28.80±4.30	0.088	27.43±4.62	28.80±4.30	0.256
BMI	24.80±3.72	27.87±6.27	0.005*	24.80±3.72	28.93±3.68	<0.0002*	27.87±6.27	28.93±3.68	0.322
ALB	42.20±2.91	38.67±3.17	<0.0001*	42.20±2.91	35.65±2.12	<0.0001*	38.67±3.17	35.65±2.12	<0.0001*

*significant difference, BMI-body mass index, ALB-albumin

Table-2: Pearson correlation coefficients between age, BMI, and albumin in non pregnant women

R	AGE	BMI	ALB
AGE	1	0.413**	0.066
BMI		1	-0.272
ALB			1

**.Correlation is significant at the 0.01 level (2-tailed), BMI-body mass index, ALB-albumin

Table 3: Pearson correlation coefficients between age, BMI, albumin, and gestation age in pregnant women

R	AGE	BMI	ALB	Gest. Age
AGE	1	0.391**	-0.073	0.109
BMI		1	0.025	0.149
ALB			1	-0.506**
GEST. AGE				1

**Correlation is significant at the 0.01 level (2-tailed), BMI-body mass index, ALB-albumin, Gest Age-gestation age

DISCUSSION

Serum albumin, the major determinant of plasma oncotic pressure is regarded as a biomarker for reliable risk prediction in various clinical settings. Physiological changes and under nutrition during pregnancy may affect plasma levels of albumin, exposing pregnant women to adverse cardiovascular outcomes. The effect of maternal plasma volume, systemic inflammation and under nutrition on plasma concentration of albumin influenced our choice of measurement of this protein in predicting pre-eclampsia. The present study determined plasma albumin levels in second and third trimester normal pregnancies to provide evidence that an extreme change in plasma albumin level may be implicated in pre-eclampsia.

The present study shows that plasma albumin levels were reduced in normal pregnancy compared to non pregnant controls. Plasma levels of albumin reduced as the pregnancies advanced from second to third trimester. Maternal age and BMI did not influence serum albumin levels observed in the study. The results of this finding corroborates with that of Zannat et al., [11] ogbodo et al., [16] Gohel et al., [19] Maryam et al., [20] Mahdi et al.,[21] Das et al.,[22] Zannat et al., showed that the serum albumin levels decreased significantly both in first and third trimester and maximal decrease observed in the third trimester [11]. Obgodo et al., observed a decrease in serum albumin level in second and third trimesters pregnancies compared to non pregnant women [16]. The study of Gohel et al., observed a progressive decrease in serum albumin from the first, through the

second and third trimesters of pregnancy compared with non-pregnant women [19]. Maryam *et al.*, revealed that serum albumin level decreased in the first trimester and continuously as the pregnancy advanced [20]. In a sample population of a Nigerian community, a study conducted by Das *et al.*, serum albumin value was significantly lowered particularly in second and third trimester pregnancy compared to the non-pregnant women [22]. The observed pattern of plasma albumin in normal pregnancy is explained by an increase in plasma and interstitial volume, and possibly by an increase in albumin metabolism [23]. Olooto *et al.*, found low serum albumin in preeclamptic women compared to normal pregnancies albumin [24]. Ghazali *et al.*, found lower serum albumin in women with preeclampsia compared to healthy pregnant women and further observed a positive correlation between plasma albumin and severity of the disease [25]. Gojnic et al., in the third trimester of pregnancy observed a correlation between low albumin and severity of pre-eclampsia [26]. Increased capillary permeability secondary to endothelial damage is explained to be partly responsible for the findings of low plasma albumin observed in preeclampsia [27].

Concentration of serum albumin is influenced by several factors, including its synthetic rate, catabolic rate, extravascular distribution, and exogenous loss. Nutritional status and systemic inflammation affect the synthesis of serum albumin [2]. Hemodilution in pregnancy could be partly responsible for decrease in serum albumin level [28]. In pregnant state, the elevation in plasma volume is in response to an underfilled vascular system resulting from systemic vasodilatation and increase in vascular capacitance [29].

Arterial under-filling in pregnancy leads to the stimulation of arterial baroreceptors, activating the rennin-angiotensin-aldosterone system (RAA) and the sympathetic nervous systems. Activation of the RAA system leads to increased plasma levels of aldosterone, resulting in a non-osmotic release of arginine vasopressin (AVP) from the hypothalamus and subsequent salt and water retention in the kidney distal tubule and collecting duct. This creates a hypervolaemic, hypoosmolar state characteristic of pregnancy [12]. Extracellular volume increases by 30–50% and plasma volume by 30–40%. Maternal blood volume increases by 45% to approximately 1200 to 1600 ml above non-pregnant values. By the late third trimester the plasma volume increases by more than 50–60%, with a lower increase in red blood cell mass and therefore plasma osmolality falls by10 mosmol/kg. The increase in plasma volume plays a critical role in maintaining circulating blood volume, blood pressure and utero-placental perfusion during pregnancy [30].

Reduction in serum albumin levels in the pregnant group may be due to hepatic impairment of albumin synthesis. During pregnancy, hormones like estrogen, progesterone is found to be increased and reach maximum level during the third trimester of pregnancy [6]. These hormones affect metabolic, synthetic and excretory functions of liver [31].

Hypoalbuminemia observed could be due to inflammatory responses during pregnancy. The activation of inflammatory response leads to a relevant change in plasma proteins, cytokines, and complements. Serum albumin is a negative-phase protein whose concentration decreases in response to inflammation [2]. Although the mechanisms are not completely clear, it is presumed that a large proportion of amino acid is utilized to synthesize positive-phase proteins rather than albumin in the liver during an inflammatory response [32].

Linking the observed low serum albumin in the pregnant women partly to under nutrition need not be over emphasized since the sample population is obtained from a developing nation like Nigeria whose citizenry are prone to under nutrition.

The use of small sample size, failure to measure inflammatory factors and nutritional indices to assess systemic inflammation and nutritional status in the participants are limitations of our study

CONCLUSION

Physiological changes during pregnancy are maternal adaptation for survival of the baby. In this present study hypoalbuminaemia during pregnancy could be due to hemodilution, inflammation and under nutrition. Exaggerated changes should be monitored and identified during antenatal check-ups to prevent pathological states that may endanger maternal outcomes.

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