EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 8
87-94
Year: 2018

ACUTE PHASE REACTANT CORRELATES AMONG PREGNANT WOMEN IN PORT HARCOURT, NIGERIA

Chinyelu Obianuju Mba*[1], Teddy Charles Adias[2] and Evelyn M. Eze[3]

[1,3]Dept. of Medical Laboratory Science, Rivers State University, Nkpolu, Port Harcourt, Nigeria.
[2]Federal University Otuoke, Nigeria.

***Corresponding Author: Chinyelu Obianuju Mba**
Dept. of Medical Laboratory Science, Rivers State University, Nkpolu, Port Harcourt, Nigeria.

Article Received on 25/05/2018 **Article Revised on 15/06/2018** **Article Accepted on 06/07/2018**

ABSTRACT

Pregnancy is usually associated with many changes in a woman which can be physiologic or pathologic. This was a cross sectional study that was carried out with the aim of determining the acute phase reactant correlates among pregnant women in Port Harcourt, Nigeria. A total of 180 subjects were sampled, comprising of 90 pregnant and 90 non-pregnant women, within the age range of 16 to 45 years. Five milliliters of whole blood was collected from each subject at ambient temperature using standard venepuncture technique. Three milliliters was dispensed in EDTA bottle and was used for ESR assay, while 2 mililiters which was stored in plain bottle was used for CRP and albumin assays. C-reactive protein was analysed with reagents from BioCheck Inc, CA, USA using ELISA; ESR was analysed with Westergreen method; and Albumin was analysed with Bromocresolgreen method. The data obtained was coded and analysed using SPSS version 20. Comparison of pregnant women with controls using t-test, showed significant increase in ESR (10.97 vs 38.59 mm/hr, p <0.01) and CRP (0.000012 vs 0.00019 g/l, p <0.01), and decrease in albumin (45.80 vs 38.82 g/l, p<0.01). Comparison of the mean for the parameters within the three trimesters was done using ANOVA, and only albumin significantly varied (F=3.45, p=0.04). To identify the trimester pairs that had significant mean difference, Tukey's Post Hoc test was used. Albumin had a significant mean difference between the 1st and 3rd trimesters (p= 0.04). Using Pearson's correlation coefficient, ESR (r=0.47, p< 0.001) and CRP (r= -0.25, p< 0.01) negatively correlate with albumin; while ESR and CRP positively correlate with each other (r= 0.36, p< 0.01). Also, there was positive correlation of ESR and CRP in 2nd trimester (r=0.41, p=0.03). At least one acute phase reactant should be incorporated as a routine pregnancy screening test in conjunction with clinical assessment for prompt and efficient diagnosis of inflammatory disorders.

KEYWORDS: Acute Phase Reactants, correlates, pregnancy, Nigeria.

INTRODUCTION

Pregnancy is usually associated with many changes in a woman, which can be physiologic or pathologic. It is a state of both anti-inflammatory and pro-inflammatory reactions; the immune system responds differently in accordance with the nature of microorganism and stage of pregnancy, hence is modulated.[1]

Acute phase reaction or response is a collective term for many systemic, metabolic, behavioural, biochemical and nutritional changes that take place in the body, as a result of inflammatory stimulus.[2,3] The onset of acute phase response is within hours of inflammation,[3] it lasts for about 1 or 2 days, and normalcy is restored in the body within 4 to 7 days after resolution of the inflammatory stimulus.[4]

The occurrence of acute phase response can be sequel to one or combination of local or systemic instability that can arise from chemical, infection, neoplasm, surgery or trauma, tissue injury or immunological disorders.[5,6] The strength of the inflammatory response is proportional to the stimulus;[3] and it is mediated by cytokines such as tumor necrosis factor-alpha, interferon gamma, interleukin (IL)-6 and IL-1, which have proinflammatory functions.[7]

Acute phase proteins (APPs) are those whose plasma concentrations change (increase or decrease) by at least 25 percent during inflammatory disorders, [8] such as neoplasms, trauma, infections, acute arthritis, and systemic autoimmune disorders.[7] The level of change in the concentration of acute phase proteins is determined by the strength of the inflammatory stimulus, and it persists as long as the stimulus exist.[3] These proteins are useful indicators of stress and disease. The most commonly used acute phase reactants are C-

Reactive Protein (CRP) and Erythrocyte sedimentation rate (ESR).

Erythrocyte sedimentation rate (ESR) is defined as the rate at which red blood cells settle in a vertical column of anticoagulated blood in one hour.[9] ESR does not establish the existence of a particular disease, but can serve as means of diagnosing a specific disease only when it is combined with the patient's history, physical examination and other laboratory findings.[3] Pregnancy is one of the physiologic conditions in which there is an elevation in the ESR.[10]

CRP was the first APP that was described, and its name was derived from its ability to precipitate the somatic C-polysaccharide of *Streptococcus pneumonia*.[8] In humans, chromosome 1 bears the CRP gene, and it codes for a mature 206 amino acid polypeptide.[11]

Human serum albumin is a nonglycosylated polypeptide with single chain, and has a molecular weight of 66,500 Da with 585 amino acids;[8] and a free thiol (Cys 34).[11] Albumin constitutes about 50-60% of total serum proteins and its normal range is 35-50g/L.[12] As an extracellular antioxidant, it binds to transition metals thus preventing them from catalyzing highly reactive biochemical reactions; it also inhibit the activities of hypochlorous acid (HOCl), peroxyl radicals and hydroxyl radicals.[12]

Many studies have demonstrated that the use of acute phase reactants is instrumental in management of different patient categories at various clinical settings.[13] In pregnancy, APRs can be used as biomarkers for the early diagnosis of preeclampsia, and this can significantly reduce both maternal and fetal mortality and morbidity.[14] Early detection of serum hsCRP in a pregnant woman has been shown to aid in identifying inflammatory cause that can affect the pregnancy outcome.[15] For these reasons, the aim of this research was to evaluate the acute phase reactant correlates among pregnant women in Port Harcourt, Nigeria.

MATERIALS AND METHODS

Study Design
This was an observational cross-sectional study.

Study Area
The study was carried out at Military Hospital, Port-Harcourt. The coordinates of Port Harcourt are 4.8129° N, 7.0900° E. Port Harcourt is the capital of Rivers State. It is also the largest city in the state. It lies along Bonny Rivers, and as at 2016 its estimated population was 1,865,000. Construction of the port was completed in 1912 but was named "Port Harcourt" by the Nigerian Governor of that time, in honour of the secretary of state, Lewis Vernon Harcourt. The port was to serve as an export channel for coal which was discovered in Enugu by Albert Ernest Kitson in 1916. The typical Port Harcourt climate is characterized by long heavy period of rainy season and short dry season, with less pronounced harmattan.[16] Port Harcourt is a major industrial city in Nigeria. Nigeria's first refinery was built there in 1965 at Alesa-Eleme.[17]

Study Population
The participants of this research were pregnant and non-pregnant women who obtained medical services at Military Hospital, Port Harcourt. Systematic sampling was employed in this study. Thirty pregnant women per trimester were sampled. The non-pregnant subjects were apparently healthy women who visited the health facility for other services such as family planning and immunization.

Inclusion criteria
The subjects who participated in this study were within the ages of 16 to 45 years old, apparently healthy, had no chronic illness, not on any medication that falsely elevate or reduce the level of acute phase reactants, and registered at Military Hospital.

Exclusion criteria
Sick women who had either acute or chronic ailments, those not within the stated age range, those on certain medications, and subjects who were not registered in the facility were excluded from this study. Also, women who were menstruating were also excluded from the control group.

Sample Size Determination
G-power version 3.0.10 was used to calculate the sample size; with parameters such as error of probability at 0.05, power (1-β error) at 0.95 (95%), and effect size of 0.15. This yielded sample size of 90 pregnant and 90 non-pregnant women (total of 180 subjects).

Ethical Consideration
Ethical approval was obtained from the Ethics Committee of Military Hospital, Port Harcourt. Informed consent of each participant was sought for verbally.

Sample Collection
Five milliliters of whole blood was collected from each subject at ambient temperature using standard venepuncture technique. Three milliliters was dispensed in ethylenediaminetetraacetic acid (EDTA) bottle and was used for ESR assay, while 2 mililiters which was stored in plain bottle was used for CRP and albumin assays.

Sample Analysis
Determination of C-Reactive Protein
Quantitative CRP assay was performed using high sensitivity Enzyme-linked Immunosorbent Assay (ELISA) Kit (BioCheck Inc, California, USA). The hsCRP ELISA is based on the principle of solid phase enzyme-linked immunosorbent assay.

Determination of Erythrocyte Sedimentation Rate
Westergreen method was used to determine the ESR.

Determination of albumin
This was done with Bromocresol green method (Standard method).

Statistical Analysis
The data generated was coded, entered and analyzed using Statistical Package for Social Science (SPSS) version 20. Normality of data was tested by the Kolmogorov–Smirnov test. The descriptive data was presented as means ± Standard Deviation (SD). Comparison of the ESR, CRP and albumin among pregnant and non-pregnant women was done with T-test at Confidence Interval of 95%. The difference in mean ESR, CRP and albumin at various trimesters was determined by One-way Analysis of Variance (ANOVA). Tukey Post Hoc test was used to identify the trimesters that had significant mean difference. Pearson correlation was used to determine the association of the ESR, CRP and albumin. Data were considered significant at $p \leq 0.05$.

RESULTS

Acute Phase Reactants of Subjects
Variations in the mean of the assayed APRs among the pregnant and non-pregnant women were compared using T-test. There was significant difference in the mean of all between the two groups ($p < 0.001$). The mean ESR and CRP of pregnant women (38.59 mm/hr. and 0.00019 g/l, respectively) were higher than that of the non-pregnant women (10.97 mm/hr. and 0.00001 g/l); while that of albumin was lower in pregnancy (38.82 g/l) when compared to the controls (45.80 g/l). These are highlighted in Table 1.

Table 1: Comparison of the Mean of Acute Phase Reactants among the Subjects.

	Non-pregnant (n=90)	Pregnant (n=90)		
Parameter	**Mean ± SD**	**Mean ± SD**	**t**	**p-value**
ESR (mm/hr)	10.97 ± 3.56	38.59 ± 9.38	-26.11	<0.01*
CRP (g/l)	0.000012 ± 0.000010	0.00019 ± 0.00033	-5.18	<0.01*
Albumin (g/l)	45.80 ± 5.74	38.82 ± 5.97	7.99	<0.01*

***Key**: SD – Standard Deviation, ESR – Erythrocyte Sedimentation Rate, CRP – C-reactive Protien, * - Significant.*

APRs of Controls and Different Trimesters of Pregnancy
The possible variations in the means of the measured APRs in the three trimesters, from baseline, were compared using one-way analysis of variance (ANOVA). All significantly varied ($p<0.05$). The results are displayed in Table 2.

Table 2: Comparison of APRs between Controls and Different Trimesters of Pregnancy.

		Gestational age			F	p-value
	Control (n=30)	1st trimester (n=30)	2nd trimester (n=30)	3rd trimester (n=30)		
Parameters	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**		
ESR (mm/hr)	11.00 ± 3.67	37.30 ± 9.70	39.97 ± 9.94	38.50 ± 8.57	82.03	<0.01*
CRP (g/l)	0.0000032 ± 0.0000015	0.00013 ± 0.00017	0.00027 ± 0.00041	0.000185 ± 0.00036	4.51	0.01*
Albumin (g/l)	47.90 ± 5.71	40.87 ± 4.87	38.67 ± 6.08	36.93 ± 6.38	20.78	<0.01*

***Key**: APR – Acute Phase Reactants, SD – Standard Deviation, ESR – Erythrocyte Sedimentation Rate, CRP – C-reactive Protien, * - Significant*

Acute Phase Reactant Changes at Different Trimesters
The possible variations of the means of all the measured parameters in the three trimesters were compared using one-way analysis of variance. Albumin is the only APR whose mean significantly varied in the three trimesters ($F= 3.45$, $p= 0.04$). This is shown in Table 3.

Table 3: Analysis of Variance (ANOVA) Showing APR changes at Different Trimesters.

	Gestational age			F	p-value
	1st trimester (n=30)	2nd trimester (n=30)	3rd trimester (n=30)		
Parameters	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**		
ESR (mm/hr)	37.30 ± 9.70	39.97 ± 9.94	38.50 ± 8.57	0.60	0.55
CRP (g/l)	0.00013 ± 0.00017	0.00027 ± 0.00041	0.00018 ± 0.00036	1.35	0.27
Albumin (g/l)	40.87 ± 4.87	38.67 ± 6.08	36.93 ± 6.39	3.45	0.04*

***Key**: APR – Acute Phase Reactants, SD – Standard Deviation, ESR – Erythrocyte Sedimentation Rate, CRP – C-reactive Protein, * - Significant*

Multiple Comparisons of Parameters among the Trimesters

Post hoc test was carried out to identify the trimesters which had significant mean difference. There was no significant change in the mean of ESR and CRP; while albumin had a significant mean difference between the 1st and 3rd trimesters (p= 0.04). These are shown in Table 4.

Table 4: Post Hoc Test Showing Multiple Comparisons.

Dependent Variable	Trimester(I)	Trimester(J)	Mean Difference (I-J)	p-value
ESR (mm/hr)	1st trimester	2nd trimester	-2.67	0.55
		3rd trimester	-1.20	0.89
	2nd trimester	1st trimester	2.67	0.55
		3rd trimester	1.47	0.83
	3rd trimester	1st trimester	1.20	0.89
		2nd trimester	-1.47	0.83
CRP (g/l)	1st trimester	2nd trimester	-0.00014	0.27
		3rd trimester	-0.00006	0.81
	2nd trimester	1st trimester	0.000140	0.27
		3rd trimester	0.000084	0.62
	3rd trimester	1st trimester	0.000056	0.81
		2nd trimester	-0.00008	0.62
Albumin (g/l)	1st trimester	2nd trimester	2.20	0.35
		3rd trimester	3.93	0.04*
	2nd trimester	1st trimester	-2.20	0.35
		3rd trimester	1.73	0.52
	3rd trimester	1st trimester	-3.93	0.04*
		2nd trimester	-1.73	0.52

***Key**: SD – Standard Deviation, ESR – Erythrocyte Sedimentation Rate, CRP – C-reactive Protien, * - Significant*

Correlation of the Acute Phase Reactants

There was correlation analysis of the acute phase reactants in pairs among all participants, in pregnancy, at different trimesters and among the control group, using Pearson's correlation coefficient. Among all the participants, the parameters are significantly correlated. ESR (r=0.47, p< 0.001) and CRP (r= -0.25, p< 0.01) negatively correlate with albumin; while ESR and CRP positively correlate with each other (r= 0.36, p< 0.01). There was no significant correlation among the parameters among all pregnant women, all non-pregnant women, in first trimester, and in third trimester. In the second trimester, ESR and CRP were positively correlated (r= 0.41, p= 0.03). The details of this correlation analysis are fully stated in Table 5. The Scatter Plot graphs for the correlation of these three APRs are shown in Figures 1-3.

Table 5: Pearson's Correlation Analysis of the Acute Phase Reactants.

	ESR (mm/hr) and CRP (g/l)		ESR (mm/hr) and Albumin (g/l)		CRP (g/l) and Albumin (g/l)	
Pregnancy status	**r**	**p-value**	**r**	**p-value**	**r**	**p-value**
Pregnant and non-pregnant (n=180)	0.36	<0.01*	-0.47	<0.01*	-0.25	<0.01*
Pregnant (n=90)	0.09	0.39	-0.04	0.69	-0.10	0.33
1st trimester (n=30)	-0.04	0.82	0.33	0.08	-0.03	0.86
2nd trimester (n=30)	0.41	0.03*	-0.20	0.29	0.04	0.83
3rd trimester (n=30)	-0.29	0.12	-0.15	0.44	-0.25	0.18
Non-pregnant (n=90)	0.11	0.32	-0.04	0.74	-0.13	0.21

***Key**: SD – Standard Deviation, ESR – Erythrocyte Sedimentation Rate, CRP – C-reactive Protien, * - Significant.*

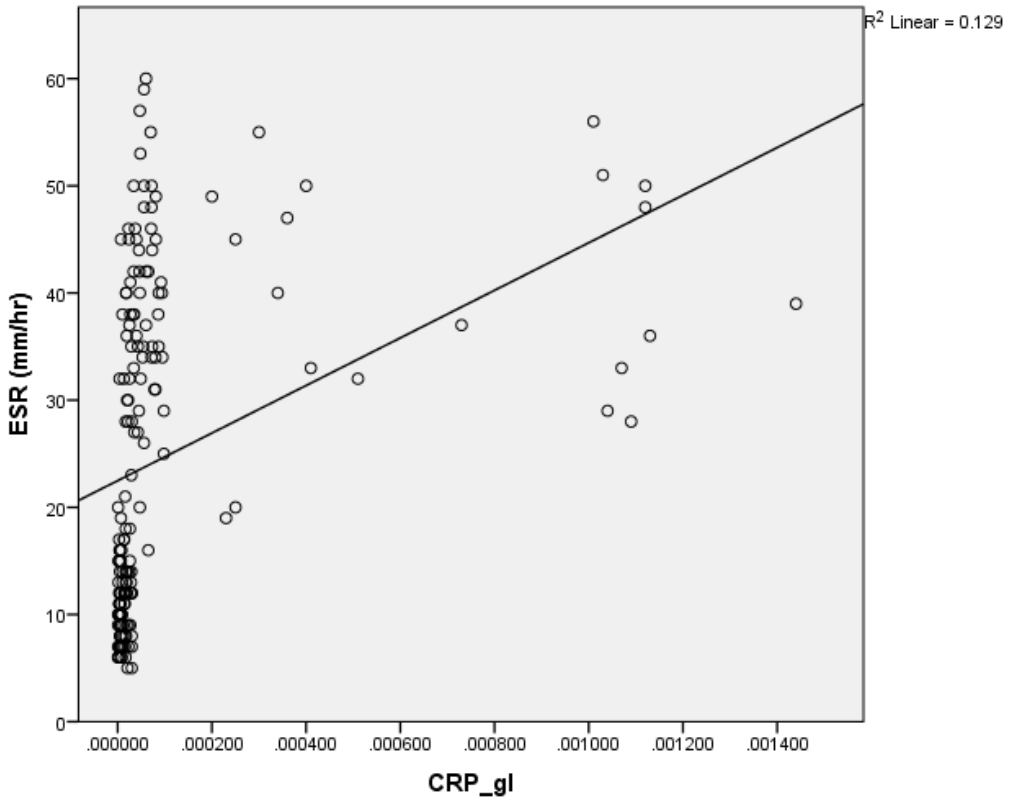

Fig. 1: Scatter Plot Showing Relationship between CRP (g/l) and ESR (mm/hr).

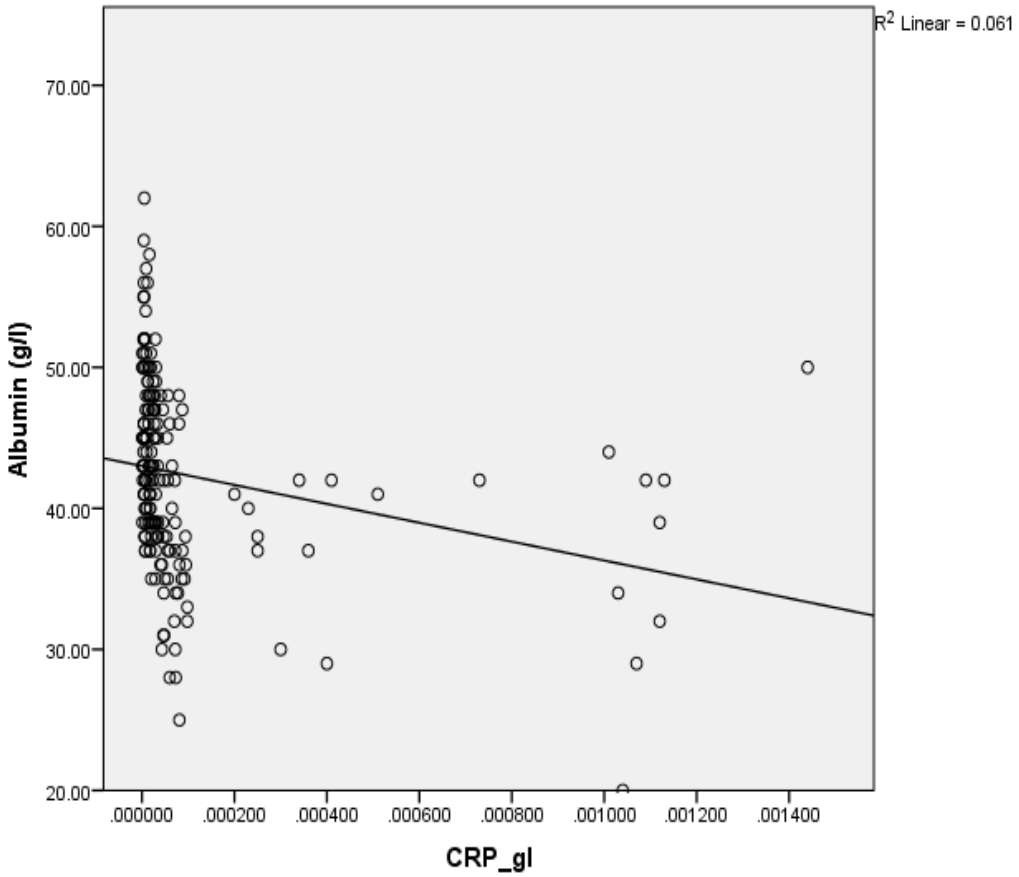

Fig. 2: Scatter Plot Showing the Relationship between CRP (g/l) and albumin (g/l).

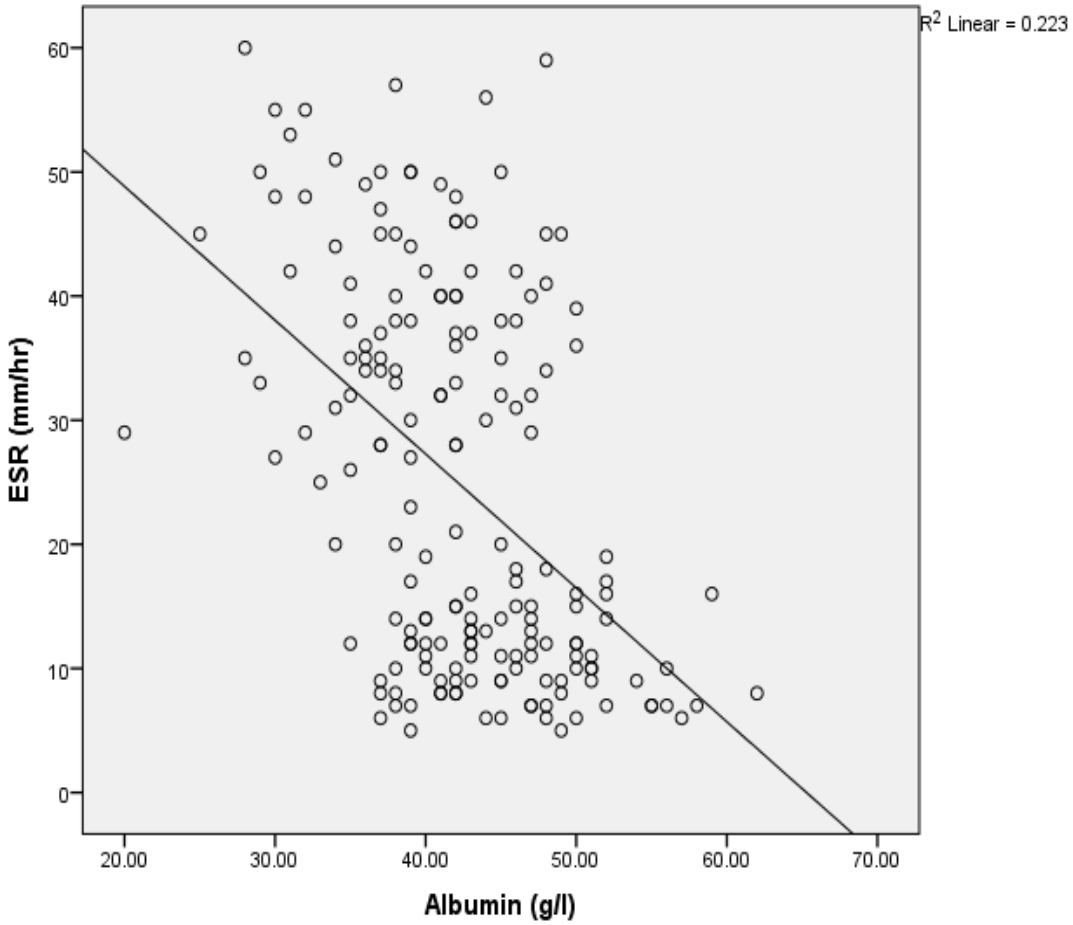

Fig. 3: Scatter Plot Showing the Relationship between Albumin (g/l) and ESR (mm/hr).

DISCUSSION

This study set out with the aim of assessing the acute phase reactant correlates among pregnant women in Port Harcourt, Nigeria. However, the key findings were obtained from comparison of the parameters among pregnant and non-pregnant women, inter-trimester comparison, and correlation of the APRs.

Erythrocyte sedimentation rate and c-reactive protein were significantly higher among the pregnant women unlike albumin which was lower. The elevated ESR corroborates similar findings made at some parts of Nigeria like Ile-Ife,[18] Yenogoa,[19] and other parts of the world.[20,21,22] Higher CRP in pregnancy is consistent with previous research.[23,24] Albumin, which is a negative APR, was lower, in line with the findings of other studies.[25,26,27]

Increase in the indicators of acute phase reaction among pregnant women is of particular concern because it has been reported to have a significant association with intrauterine growth restriction, low birth weight and neonatal complications.[28] There is need for these tests to be carried out in pregnancy especially for women who have a higher risk of having preeclamsia – chronic hypertension, obesity and diabetes; since it has a correlation with the disease severity.[29]

All the APRs assayed in the study, had significant change when the mean for the three trimesters and controls (from baseline to third trimester) were compared using ANOVA. The concentration of albumin progressively decreased, and this concurs with the findings of another study where there was a progressive decline with increasing gestational age ($p<0.01$).[27] Both ESR and CRP was increased from baseline to 3rd trimester.

Out of the three APRs assayed in the study, only albumin had significant change when the mean for the three trimesters only were compared using ANOVA. Its concentration progressively decreased. This agrees with the findings of another study where there was a progressive decline with increasing gestational age ($p<0.01$).[27] This is a quite anticipated finding because albumin is a negative APR so it was expected to be decreasing as pregnancy progresses. Sequeal to the ANOVA for multiple trimester mean comparison, the post hoc test was carried out to highlight the trimesters which had significant mean differences. Albumin is the only APR that had significant result; and this lies in the mean difference of the 1st and 3rd trimesters.

The correlation analysis of the APRs has interesting findings. As anticipated, there was significant correlation

of all the APR pairs among both pregnant and non-pregnant women. ESR and CRP were positively correlated. That is to say, they both increase simultaneously, probably because they are both positive APRs. [4] Albumin had a significant negative correlation with both ESR and CRP; which means that as its concentration is decreasing, that of the latter will be increasing. This finding is not out of line considering the fact that albumin is a negative APR.[30] There was no significant correlation of these APR in the following categories of subjects: pregnant women, 1st trimester, 3rd trimester and non-pregnant women. However, ESR and CRP had significant positive correlation in the 2nd trimester.

There is little or no article on the correlation of acute phase reactants, especially in pregnancy. The only research we could use to compare our correlation result is a study of the correlation of CRP, ESR and albumin among diabetics in Bayelsa State, Nigeria.[31] They recorded significant positive correlation of CRP with ESR. Albumin had no correlation with both ESR and CRP. This might be because the analysis was done for diabetics only, without the controls.

CONCLUSION

The findings of this study recorded a significant increase of acute phase reaction in pregnancy; with increased levels of ESR and CRP, accompanied by decreased albumin level in comparison with the control group. Unlike ESR and CRP, albumin level significantly varied within the three trimesters, it progressively decreased. For the multiple comparisons among the trimesters, albumin had a significant mean difference between the 1st and 3rd trimesters.

Generally, both ESR and CRP negatively correlate with albumin; while they positively correlate with each other. The APRs have no correlation among pregnant women, non-pregnant women, in first trimester, and in third trimester; but ESR and CRP positively correlate in the second trimester.

RECOMMENDATION

At least one acute phase reactant should be incorporated as a routine pregnancy screening test in conjunction with clinical assessment for prompt and efficient diagnosis of inflammatory disorders; especially for hypertensive, diabetic and obese women who have a higher risk of developing complications in pregnancy.

REFERENCES

1. Mor G, Cardenas I. Review Article: The Immune System in Pregnancy: A Unique Complexity. Am J Reprod Immunol, 2010; 63(6): 425-33.
2. Khan FA, Khan MF. Inflammation and Acute Phase Response. Int J Appl Biol Pharm, 2010; 1(2): 312-21.
3. Kilicarslan A, Uysal A, Roach EC. Acute Phase Reactants. Acta Med, 2013; 2: 2–7.
4. Chu ST, Lee YC. Characterization of Acute-Phase Proteins (Apps). Proteins (APPs), 2012; 1: 6.
5. Gruys E, Toussaint MJM, Niewold TA, Koopmans SJ. Acute Phase Reaction and Acute Phase Proteins. J Zhejiang Univ Sci B, 2005; 6(11): 1045-56.
6. Moore MM, Chua W, Charles KA, Clarke SJ. Inflammation and Cancer: Causes and Consequences. Clin Pharmacol Ther, 2010; 87(4): 504-8.
7. Markanday A. Acute Phase Reactants in Infections: Evidence-Based Review and a Guide for Clinicians. Open Forum Infect Dis, 2015; 2(3): ofv098.
8. Jayachandran C, Suchetha A, Mundinamane DB, Apoorva SM, Bhat D, Lalwani M. Acute Phase Proteins. J Chem Pharm Res, 2016; 8(2): 365-70.
9. Jeremiah ZA, Emelike FO. Clinical Utility of the Erythrocyte Sedimentation Rate Test and Haemoglobin Electrophoretic Patterns among Premarital Couples in Port Harcourt, Nigeria. Orient J Med, 2010; 22: 1-4.
10. Quinn JG, Tansey EA, Johnson CD, Roe SM, Montgomery LEA. Blood: Tests Used to Assess the Physiological and Immunological Properties Of Blood. Adv Physiol Educ, 2016; 40: 165–75.
11. Ahmed MS, Jadhav AB, Hassan A, Meng QH. Acute Phase Reactants as Novel Predictors of Cardiovascular Disease. ISRN Inflamm, 2012; 2012: 1-18.
12. Lim PS, Cheng YM, Yang SM. Impairments of the Biological Properties of Serum Albumin in Patients on Haemodialysis. Nephrology, 2007; 12(1): 18–24.
13. James TR, Reid HL, Mullings AM. Are Published Standards for Haematological Indices in Pregnancy Applicable Across Populations: An Evaluation in Healthy Pregnant Jamaican Women. BMC Pregnancy Childbirth, 2008; 8(1): 8.
14. Kameswaramma K. Estimation of C - Reactive Protein, Magnesium and Uric Acid Levels in PreEclampsia Patients in Comparison with Normal Pregnant Women. Sch J App Med, 2014; 2(2B): 628-32.
15. Dhok A, Daf S. Role of High Sensitivity C – Reactive Protein in Adverse Pregnancy Outcome. J Mahatma Gandhi Inst Med Sci, 2010; 15(i): 27–31.
16. Wikipedia (2018). Port Harcourt. https://en.wikipedia.org/wiki/Port_Harcourt.
17. Encyclopaedia Brittanica (2018). https://www.britannica.com/place/Port-Harcourt#accordion-article-history.
18. Oke OT, Awofadeju SO, Oyedeji SO. Haemorheological Profiles in Different Trimesters among Pregnant Women in South West Nigeria. Pak J Physio, 2011; 7(2): 17- 9.
19. Eledo BO, Buseri FI, Akhogba AO. Evaluation of Some Haematological Parameters among Pregnant Ijaw Women: An Indigenous West African Tribe. J Health Medicine Nursing, 2015; 13: 10-7.

20. Verma A, Chaudhary H. Study of Haematological Parameters in Advanced Pregnancy. International Journal of Recent Trends in Science and Technology, 2013; 7(1): 16-9.
21. Krishnaveni A, Lakshmi ANR, Paramjyothi P. Erythrocyte Sedimentation Rate in Pregnancy. Int J Biomed Sci, 2014; 5(08), 474-5.
22. Chaudhari SJ, Bodat RK. Are There any Difference in Haematological Parameters in Pregnant and NonPregnant Women? Nat J Community Med, 2015; 6(3): 429-32.
23. Raoof IB. Assessment of Some Biochemical Markers in Pregnant Women in Iraq. Int J Curr Microbiol Appl Sci, 2015; 4(12): 692-8.
24. Mei Z, Li H, Serdula MK, Flores-Ayala RC, Wang L, Liu J, Grummer-Strawn LM. C-Reactive Protein Increases with Gestational Age During Pregnancy Among Chinese Women. Am J Hum Biol, 2016; 28(4): 574-9.
25. Adedeji AL, Adedosu O T, Afolabi OK, Badmus JA, Ehigie LO, Fatoki JO, Adelusi TI. Serum Protein Profile in Nigerian Women: An Analysis by Gestation Age. Researcher, 2012; 4: 38-42.
26. Prasad VD, Shireen S, Ramana GV, Gupta S. Assessment of Copper, Ceruloplasmin, Total Proteins and Albumin in Gestational Hypertension. IOSR Journal of Dental and Medical Sciences, 2014; 13(4): 101-4.
27. Zannat MR, Nessa A, Ferdousi S. Serum Albumin in First and Third Trimester of Pregnancy. Dinajpur Medical College Journal, 2016; 9(2): 216-20.
28. Ernst GD, de Jonge LL, Hofman A, Lindemans J, Russcher H, Steegers EA, Jaddoe V W. C-Reactive Protein Levels in Early Pregnancy, Fetal Growth Patterns, and the Risk for Neonatal Complications: the Generation R Study. Am J Obstet Gynecol, 2011; 205(2): 132-e1.
29. Mahmoud A G, Mostafa SM, Mervat MH, Amany AAA. Predictive Value of Maternal Serum C-Reactive Protein Levels With Severity Of Preeclampsia. Zagazig University Medical Journal, 2016; 22(2): 70-81.
30. Jain S, Gautam V, Naseem S. Acute-Phase Proteins: As Diagnostic Tool. J Pharm Bioallied Sci, 2011; 3(1): 118.
31. Adias TC, Eze EM, Dick DP. Acute Phase Reactant Correlates and Erythrocyte Sedimentation Rate Among Type 2 Diabetes Mellitus Patients in Yenagoa, Nigeria. IOSR Journal of Nursing and Health Science, 2018; 7(1): 63-70.