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Comparative Analysis of C - reactive protein and Erythrocytes Sedimentation Rate among Hypertensive Patients Attending Gwako Primary Health Care Centre

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Abstract

Background: Hypertension (HTN or HT), also known as high blood pressure or arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. Blood pressure is expressed by two measurements, the systolic and diastolic pressures. ***Purpose/Aim*:** To investigate the usefulness of C-reactive protein and ESR as biomarkers for the diagnosis of hypertension among hypertensive patients attending gwakor primary health centre. ***Methods***: The study investigated the levels of ESR and CRP among hypertensive subjects. Qualitative and semi quantitative C-reactive protein was carried out on serum and ESR was also done using whole blood. ***Result*:** Of the 200 subjects recruited for the study the age distribution of C-reactive protein seropositivity among the study subjects shown that the age between 21-30 had a seropositivity 1(5.6%) with a total Number of 18 within the group, and the age group between 31-40 shown a seropositivity of 5(9.8%) with total number tested within the age group 51, also the age range between 41-50 shown a seropositivity of 6(24.0%) with total number tested to be 25, and the age range between 51-60 had no seropositivity with total number tested were 4, while >60yrs showed 2(100.0%) with total number tested were 2. the highest number of seropositivity observed was in the age range of >60yrs and above, followed by 41-50 with 24%. The highest value observed among the age group of >60yrs was not surprised because this age group are prone to degenerative diseases because of age related conditions as individual aged as shown in table 4.1. The difference observed among the age distribution of CRP seropositivity among the study subjects showed a significance difference which was statistically significant. The sex distribution among the study subject showed that men had seropositivity of 10(19.6%) with a total number of 51 tested, while female showed 4(8.2%) with total number of 49 tested. ***Conclusion*:** The findings in this study confirmed that CRP and ESR are good inflammatory markers in the management of hypertensive patients, also CRP is a more sensitive and specific marker compared to ESR, and it also reveal that as individual is aging the risk of developing hypertension is high because elderly people are more expose compared to younger persons.

Keywords: Hypertension, C-Reactive, Protein, Erythrocytes, Sedimentation, Rate.

INTRIDUCTION

Inflammation is recognized as a main pathogenic element in the development of hypertension. Schermuly, *et al*., (2011): Price, *et al*., (2012). With several studies showing a significant association between systemic inflammatory markers and hypertension Yildiz *et al*, 2013; Özpelit, *et al.*, (2015). Inflammation is also a precursor for the development and progression of atherosclerosis and systemic hypertension (sHTN). The association between C-reactive protein (CRP) and sHTN hasGG been established in multiple cross-sectional studies Ford E. and S., Giles, 2000. Rohde *et al.*, 1999; Bermudez E,2002; Chae, *et al.*, 2001, in particular after the advent of high sensitivity CRP (hs-CRP) assays capable of detecting levels that were earlier considered to be normal. Higher levels of CRP may contribute to the development of sHTN through the reduction of endothelium-defendant relaxation by reducing nitric oxide production in endothelial cells. Yamada, *et al*.,

2001 Venugopal, 2002, resulting in vasoconstriction and increased production of endothelin. CRP may also promote atherosclerosis through upregulating angiotensin type 1 receptor expression. Wang, *et al*., 2003. Another marker of systemic inflammation is albumin which is an acute phase reactant that is influenced by multiple factors mainly including malnutrition and inflammation which may reduce albumin levels irrespective of the patient's nutritional status. Lyons, *et al.*, 2009. Other inflammatory markers include erythrocyte sedimentation rate (ESR), ferritin, angiotensin-converting enzyme (ACE), and 25 OH vitamin D.

Sarcoidosis is a systemic inflammatory disease that is associated with higher incidence of PH not only in cases with evidence of advanced parenchymal fibrosis, but also in cases without significant interstitial lung disease. In fact, anti-inflammatory therapies can have an impact on the progression of sarcoidosis-associated PH. Rodman, *et al.*, 2014. The relationship between chronic granulomatous inflammatory disease and systemic hypertension had not been previously explored. C-reactive protein is one of the acute phase proteins that increase during systemic inflammation. Individuals without inflammation usually have CRP levels below 1 μg/mL; however, patients with bacterial infections, autoimmune diseases, and cancer frequently have CRP level as high as 100μg/mL or even higher. It is clear that a high CRP level has no specificity in differentiating disease entities from one another. Despite its lack of specificity, CRP has now emerged as one of the most powerful predictors of cardiovascular risk. Even more remarkable, CRP's predictive power resides in the range between 1 to 5 μg/mL, which was previously regarded to be normal in the era preceding the high-sensitivity CRP test. In fact, tests showing serum CRP levels greater than 10 μg/mL in apparently healthy men or women should be repeated to exclude occult infection or other systemic inflammatory process. To understand CRP's transition from an acute phase protein to a most useful inflammatory biomarker for predicting future cardiovascular events, we must know more about the role of the immune system in the pathogenesis of atherosclerosis. Albert, *et al*., 2001.

Erythrocyte sedimentation rate; Inflammation; Coronary atherosclerosis; Cardiac mortality; Risk factors; Ischemic heart disease Introduction Histopathologic studies have consistently shown that inflammatory cells not only participate in the initiating events leading to plaque formation (adesion of monocytes to activated endothelial cells, migration into subendothelial layers, and transformation into macrophages), but also affect the subsequent evolution of the lesion. Activated T lymphocytes are present in the lipid core of atherosclerotic lesions and, through the release of cytokines, stimulate macrophage migration and activation, inhibit collagen synthesis, and induce neovascularization.1 Thus, various indices of systemic inflammation (white blood cell count, serum interleukin-6, fibrinogen, C-reactive protein, and albumin concentrations) have been reported to predict ischemic heart disease (IHD) development both in healthy subjects and in at-risk patients.2 Whether inflammation is a risk factor for IHD because it favours the occurrence of clinical events (e.g. through plaque destabilization and/or blood clotting) or because it heralds the presence of a more extensive coronary atherosclerosis (ATS), is unknown. Similarly, the notion that rheologic characteristics of blood contribute to the pathogenesis of IHD is gaining growing support. The major components of blood viscosity are the blood cell mass (i.e. the hematocrit), the intrinsic resistance of the plasma to flow (commonly measured by capillary viscometry), and red blood cell aggregability, which can be estimated through the erythrocyte sedimentation rate (ESR).

MATERIALS AND METHOD

Study Area:

This study was conducted at the Gwako Primary health care centre gwagwalada, Federal Capital Territory (FCT) Abuja, gwako is in Gwagwalada area council is about 60 km away from the FCT. It is one of the settler's towns of the FCT. The town is close to the Nnamdi Azikwe international airport along the Abuja – Lokoja Express way, it is located between latitude 8°55' and 9°00'N and longitudinal 7°00' and 7°05'E.

The centrality of this town in relation to other area councils' headquarters make it influential and important in various socio-economic activities. The climate condition of this town is not far-fetched from that of the tropics having several climatic elements in common; most especially the wet and dry season characteristic. The temperature of the area ranges from 30°C to 38°C yearly, with the highest temperature experienced in the month of March and mean total rainfall of approximately 1650 mm/annum.

About 60% of this rain falls between the months of May to August. The area council is an industrial zone of FCT that stands out as the second most cosmopolitan city of the FCT, after the capital city with 10 political wards. These have brought about the inflow of people into the council. 75% of the residents live in close proximity with poor drainage system, several pot-holes on their streets and indiscriminate environmental dumpsites.

Study Population:

The study population for this study includes 200 confirmed hypertensive patients (subject) and ages-matched was recruited in the Clinic Gwako primary health care Abuja, North-Central Nigeria.

Inclusion Criteria

- Patients who meet the following inclusion criteria were recruited in the study

- Hypertensive patients attending clinic at gwako primary health care centre.
- Patients who gave informed consent in the clinic and agreed to be included in the study.

Exclusion Criteria

The following were excluded from participating as subjects in the study.

- Non-hypertensive patients
- Hypertensive patients who did not give informed consent to be included in the study

Sample Size Determination

The sample size was determined using the standard formula for calculation of minimum sample size:

$(n=z^2\ pq/d^2)$

n =minimum sample size

z =standard normal deviation and probability.

p=prevalence of value to be estimated from previous studies.

q=Proportion of failure (= 1 - p)

d=precision, tolerance limit, the minimum is 0.05.

Therefore $n=z^2\ pq/d^2$

Where Z =95% (1.96)

P=6.2 % (0.048) (Aliyu *et al.*, 2011).

q = 1 - 0.048 (=0.952)

d = 5% (0.05)

Therefore $n = (1.96)^2\ (0.062)\ (0.952) / (0.05)^2$

n=201

The minimum Number of study subjects was 201

Ethical Clearance and Informed Consent:

Ethical clearance was obtained from the Head of health Gwagwalada area council, FCT Abuja. Informed consent was also be obtained from all participating subjects in accordance with the standards of human experimentation and with the Helsinki Declaration of 1975, as revised in 70. This will be done via informed consent from study participants.

Sampling Method:

5 milliliters of blood sample was collected from each subject aseptically using the venipuncture technique. The blood was collected into tubes containing dipotassium ethylenediamine tetra-acetic acid (K2EDTA) anticoagulant, was mixed thoroughly. Also, 3ml of blood was collected into plain bottle and the samples were left undisturbed at room temperature and later centrifuged at 3000rpm for 5minutes to obtain clear non- haemolysed serum. The serum was transferred into sterile labelled test tubes and assayed (in batches) for C-reactive protein and ESR.

Laboratory investigation

C -Reactive Protein

Test Principle:

Spectrum CRP latex reagent is a suspension of polystyrene particles sensitized with anti-human CRP. When the latex reagent is mixed with a serum containing C-reactive protein, visible agglutination occurs. The latex reagent has been produced so that agglutination will take place only when the level of CRP is greater than 6 mg/L.

Procedure Qualitative Test (Screening)

1. Bring all reagents and specimens to room temperature.
2. Place one drop (50 µl) of the positive control and 50 µl of the patient serum into separate circles on the glass slide.
3. Shake the CRP latex reagent gently and add one drop (45 µl) on each circle next to the sample to be tested and control.
4. Mix well using disposable stirrer spreading the mixture over the whole test area and tilt the slide gently. Agitate for about 2 minutes with rotator or by hand and observe for the presence or absence of agglutination.

RESULTS AND INTERPRETATION

Negative Result:

No agglutination of the latex particles suspension within two minutes. Positive result: An agglutination of the latex particles suspension will occur within two minutes, indicating a CRP level of more than 6 mg/L.

Semi-Quantitative Test

1. Serum to be titrated is serially diluted (1:2, 1:4, 1:8 etc) in 0.9 g/L saline solution.
2. Place one drop of positive control on slide. Do not attempt to dilute the CRP positive control serum for comparative or other purposes as no correlation exists between actual titre of the control and titre of unknown sera.
3. Place 50 µl of each serum dilution individually in successive circles on the slide and proceed as in screening methodology.

Results and Interpretation

The serum CRP titre can be defined as the highest dilution showing a positive result. The approximate CRP level (mg/L) present in the sample can be obtained by the following formula: CRP Titre (mg/L) = Highest dilution with positive reaction x Reagent sensitivity (6 mg/lL) e.g. if the agglutination is present up to a titre 1:8, the approximate serum CRP level is 8 x 6 = 48 mg/L.

Erythrocytes Sedimentation Rates (ESR)

Westergren's Method

Principle of ESR

When anticoagulated blood is allowed to stand in a narrow vertical glass tube, undisturbed for a period of time, the RBCs – under the influence of gravity- settle out from the plasma. The rate at which they settle is measured as the number of millimeters of clear plasma present at the top of the column after one hour (mm/hr). This mechanism involves three stages:

Procedure:

- Mix the anticoagulated blood thoroughly.
- Draw the blood into the tube upto 0 mark with the help of rubber bulb.
- Wipe out blood from bottom of the tube with cotton.
- Set the tube upright in stand. Make sure the pipette fits snugly to eliminate possible leakage and that the pipette is in vertical position.
- Leave the tube undisturbed for 1 hour.
- At the end of 1 hour, read the result.

Statistical Analysis:

Data obtained will be entering into a statistical package (such as SPSS version 22) on a computer to define the nature of the distribution of data for each group. Statistical differences of data will be analyzed using series of statistical analysis such as mean, standard deviation, Chi –square, student's t-test, ANOVA depending on the nature (categorical or continuous) and distribution of data (normal or non-normal). Pearson's correlation was used to determine the relationship between sets of data. Probability ($p \leq 0.05$) was used to determine the level of significant for all statistical analysis.

RESULTS

Table 4.1: Age- and Sex-Distribution of C-Reactive Protein Seropositivity among Subjects

Variable	No. of Subject Tested	No. Seropositive	Chi-square	*p* value
Age (years)			16.8	0.002*
21 – 30	18 (18.0)	1 (5.6)		
31 – 40	51 (51.0)	5 (9.8)		
41 - 50	25 (25.0)	6 (24.0)		
51 – 60	4 (4.0)	0 (0.0)		
>60	2 (2.0)	2 (100.0)		
Sex			2.69	0.101
Male	51 (51.0)	10 (19.6)		
Female	49 (49.0)	4 (8.2)		

*#significant association determined by two tailed Chi-squared test

Table 4.2: Comparison of Erythrocyte Sedimentation Rate with the C-Reactive Protein Reactivity and Sex of Subjects

Erythrocyte Sedimentation rate (mm/Hour)		t value	*p* value
CRP Sero-reactivity (mean± SEM)			
Seropositive (n=14)	Seronegative (n=86)		
100.07±5.36	19.43±1.87	15.8037	<0.0001*
Sex (mean± SEM)			
Male (n= 51)	Female (n= 49)		
37.18±5.54	24.00±3.35	2.0154	0.04*

*# Significant difference determined by Unpaired Student T- test

Table 4.3: Comparison of Erythrocyte Sedimentation Rate with Age of Subjects

Erythrocyte Sedimentation Rate (mm/Hr)					F value	*p* value
Age (Years) Mean ±SD						
21 – 30 (n=17)	31 – 40 (n= 50)	41 – 50 (n=26)	51 – 60 (n=5)	>60 (n=2)		
21.2 ± 23.1	27.0±27.8	36.0 ± 39.9	52.0 ± 44.38	101.0± 1.41	3.805	0.007*

*# significant difference determined by One-way ANOVA

DISCUSSION

Hypertension has become a chronic condition and a major public health problem that adversely affects health status of individuals, families and communities. Worldwide hypertension is estimated to cause 7.1 million premature deaths and 4.5% of the disease burden. The population of global disease burden attributable to hypertension is substantial.

This study investigated the levels of ESR and CRP among hypertensive subjects. Of the 200 subjects recruited for the study the age distribution of C-reactive protein seropositivity among the study subjects shown that the age between 21-30 had a seropositivity 1(5.6%) with a total Number of 18 within the group, and the age group between 31-40 shown a seropositivity of 5(9.8%) with total number tested within the age group 51, also the age range between 41-50 shown a seropositivity of 6(24.0%) with total number tested to be 25, and the age range between 51-60 had no seropositivity with total number tested were 4, while >60yrs showed 2(100.0%) with total number tested were 2 . the highest number of

seropositivity observed was in the age range of >60yrs and above, followed by 41-50 with 24%. The highest value observed among the age group of >60yrs was not surprised because this age group are prone to degenerative diseases because of age related conditions as individual aged as shown in table 4.1.

The difference observed among the age distribution of CRP seropositivity among the study subjects showed a significance difference which was statistically significant.

The sex distribution among the study subject showed that men had seropositivity of 10(19.6%) with a total number of 51 tested, while female showed 4(8.2%) with total number of 49 tested. The difference observed among male and female were not statistically significant at p>0.05 as shown in table 4.1. This also implies that the individual has chances of developing cardiovascular disease and atherosclerosis is high because CRP been an acute phase reactant and also an inflammatory marker.

Table 4.2 shows the comparison of ESR with CRP reactivity and sex of the study subjects.

The seropositivity of n=14 shows a mean and standard error of mean 100.07±5.36 and a Seronegative of n=86 which also shown a mean and standard error of mean of 19.43±1.87, there is a significance different between the mean and standard error of mean of the seropositivity and seronegative which was statistically significant at p>0.05 of 95% confidence interval. The mean and standard error of mean between male and female study subjects also shown a significant difference. The male N=51 shown a mean and standard error of mean 37.18±5.54, while that of female counterpart N=49 was 24.00±3.35. the difference observed was statistically significant at p>0.05, which implies that both male and female study subjects are at risk of developing systemic hypertension which may likely progress atherosclerosis, because there is an association between the two inflammatory markers which can lead to vasoconstriction and increase production of endothelin and the resultant effects will be myocardial infarction and stroke.

Table 4.3 shows the comparison of ESR with age of study subjects. The age between 21-30, shown a mean and standard deviation of 21.2±23.1with a total of 17 study subjects in the age group, and between the age range of 31-40 showed a mean and standard deviation of 27.0±27.3 with a total number of 50 study subjects in the age group, and between 41-50 showed a mean and standard deviation of 36.0±39.9 with a total number of 26 study subjects while 51-60 showed a mean and standard deviation of 52.0±44.38 with a total number of 5 study subjects in the age group and >60yrs showed a mean and standard deviation of 101.0±1.41 with a total number of 2 study subjects in the age group. The difference observed between the age groups in the study subjects were statistically significant at p>0.05 which implies that the chances of study subjects developing myocardial infarction, atherosclerosis and cardiovascular diseases is high and as such they needs to be very vigilant and the physician managing such patients need to monitored them very closely in order to avoid any crisis of cardiovascular diseases which may lead to heart failure.

Fig1 showed the pattern of seropositivity of CRP among the study subjects which shows that 14% and about 86% are seronegative among the study participants which may likely develop and inflammatory reaction or response which may be as a result of non-communicable diseases.

CONCLUSION AND RECOMMENDATIONS

In conclusion, the findings in this study confirmed that CRP and ESR are good inflammatory markers in the management of hypertensive patients, also CRP is a more sensitive and specific marker compared to ESR, and it also reveal that as individual is aging the risk of developing hypertension is high because elderly people are more expose compared to younger persons .its therefore recommended that research be carried out in other inflammatory markers as it will give more and a better insight into the management of hypertension and other non-communicable diseases.

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