Changes in pattern of Erythrocyte Sedimentation Rate and C-Reactive Protein following major elective orthopaedic surgeries

R C Ezeh[1], K C Onyekwelu[2*], P O Egwim[2]

[1]*National Orthopaedic Hospital Enugu, Enugu State Nigerian and Department of Medical Biochemistry, Enugu State University of Science and Technology Teaching Hospital, Parklane, Enugu, Nigeria*
[2]*Department of Medical Biochemistry, College of Medicine, University of Nigeria, Enugu Campus, Nigeria*

ABSTRACT

Background and Objectives: Major surgeries are associated with various changes in the neuroendocrine and inflammatory cytokine system of the body. Most of these surgeries are performed with expensive implants and prostheses made of metals and their alloys. These metals are foreign bodies which when infected can lead to a disastrous outcome. Consequently, concerted effort is being made through the use of Erythrocyte Sedimentation Rate (ESR), C-reactive Proteins (CRP), and other acute phase proteins as a screening tool for early detection of deep surgical wound infections. The aim of this study was to determine the pattern of changes of ESR and CRP following major elective orthopaedic surgeries. **Patients and Methods:** This is a cross sectional study carried out over a period of six months. All patients that had major surgery within the period were noted and followed up. ESR and CRP levels were checked pre-operatively on day 0 and post-operatively on days 2, 4, 7 10, 14 and 42 using the modified Westergreen method and the High Sensitivity (HS) ELISA technique respectively. **Results:** The result showed a steep rise in both parameters (more than 300% constitutive levels) within 2 days post-operatively. The peak value for the mean serum CRP level was attained on day 4 post operatively with normalization to its pre-operative serum level on day 42 (P = 0.543), while the mean serum ESR reached its peak on day 7 and remained significantly higher than its pre-operative mean serum level even on day 42 post operatively (P = 0.003).**Conclusion:** ESR and CRP are both useful acute phase proteins for monitoring early post operative complications like surgical wound infections.

Keywords: ESR, CRP, Acute phase proteins

Introduction

The Acute Phase Response (APR) is part of the early-defense or innate immune system, which is triggered by different stimuli including trauma, infection, stress, neoplasia, and inflammation. The most important component of this response comprises the acute phase proteins (APP), which are a heterogeneous group of plasma proteins primarily synthesized by hepatocytes as part of the acute phase response [1,2]. The APR results in a complex systemic reaction with the goal of reestablishing homeostasis and promoting healing. APP, an integral part of the APR are used clinically as an aid to clinical diagnosis and the most important ones

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Correspondence
K C Onyekwelu
Department of Medical Biochemistry, College of Medicine, University of Nigeria, Enugu Campus, Nigeria
E Mail: emailkene@yahoo.com

of these acute phase reactants are ESR, CRP, fibrinogen and ferritin [3].Because the response is relatively non specific, the clinical value of measuring their concentration in the serum is to assess the extent of inflammation reflecting momentary disease activity [4]. Similar to tumor markers, acute phase proteins may be used to monitor the course of disease in response to therapeutic intervention. What makes ESR and CRP the markers of choice in monitoring acute phase reaction are the fact that they increase in concentration in the serum compared to basal values. Additionally, they have a relatively short lag time from the moment of stimulus [3].Although ESR is not used for establishing clinical diagnosis, it is a commonly used and cost efficient test, which can assist in following up with the progress and response to treatment of a disease [5,6]. ESR varies according to gender and age. In men, the value roughly equals to age (in year) / 2, in women age (in years) +10 / 2. In

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men, 15 mm/hour and in women, 20 mm/hour are considered as normal values [7]. Many factors like cell or tissue injury, infections, inflammatory disorders, myocardial infarction and others can cause increase in ESR and factors like sickle cell anemia, congestive heart failure, polycythemia can cause decrease in ESR [8].CRP is synthesized in the liver and is normally present as a trace constituent of serum or plasma at levels less than 0.3mg/dl [9], a value between 1-10 mg/dl is considered as mild and any value above 10 mg/dl is considered a very high increase [10, 11, 12]. CRP is one of the acute phase proteins, the serum or plasma levels of which rise during general, non specific response to a wide variety of diseases like bacterial infections, acute phase of rheumatoid arthritis, abdominal abscesses and inflammation of the bile ducts [13]. CPR is not specific for a certain disease as it shows inflammation and its degree. It is mainly useful for following the response to treatment [14, 15]. This study was therefore aimed at determining the pattern of changes of ESR and CRP following major elective orthopaedic surgeries.

Patients and Methods

This is a prospective observational cross sectional study involving twenty-three (23) adult Nigerian patients (10 Males and 13 Females) with a mean age of 53.95 years who underwent major elective orthopaedic surgeries at the National Orthopaedic Hospital, Enugu Nigeria. Such major surgeries includes: total joint replacement arthroplasty, open reduction with internal fixation using plate and screws and spinal decompression. Twenty-one (21) study subjects made up of adult Nigerian subjects (males 9, females 12) with a mean age of 49.61years working with the National Orthopaedic Hospital Enugu Nigeria were also recruited as negative control. All the 23 patients and 21 control adult subjects met the inclusion criteria.

Exclussion and Inclusion criteria

The following categories of patients were excluded from the study:

1. Patients without given consent for surgery or commitment to fully participate in the research.
2. Patient with evidence of acute or chronic infections.
3. Poorly controlled diabetic patients and those on immune suppressants.
4. Patient with known malignancies.
5. Pregnant women or women on contraceptive drugs**.**

6. Patient with pre -operative (day 0) ESR value of more than 50mm per 1st hour.

All subjects in this study (Patients and Controls) did not satisfy any of the exclusion criteria listed above, hence their inclusion/recruitment into the study.

Sample collection

Five (5) ml of venous whole blood was collected on each occasion (from the antecubital vein) for both ESR and CRP using EDTA bottles and plain bottles respectively. Samples were usually collected in the morning period. Two (2) ml of whole blood was put in the EDTA bottle while three (3) ml was put into the clean plain bottle. Each bottle was properly labeled with names, hospital number, sex, age and the day of collection. The patients (N = 23) underwent a series of ESR and CRP level estimations pre-operatively on day 0, and post operatively, on day 2, day 4, day 7, day 10, day 14 and day 42. Samples from the 21 healthy subjects (control group) were collected once and analyzed fresh together with the 161 frozen samples from the 23 patients.

ESR and CRP Estimation

The ESR estimation was done by the modified Westergreen method [16] and CRP estimation done using High Sensitive C-Reactive Protein Enzyme Immunoassay (HS CRP ELISA) kit produced by DRG International Inc., USA.

Statistical analysis

Patient's data and records were collected manually. Data statistical analysis was done using the Statistical Package for the Social Sciences (SPSS) version 17 (SPSS Inc. Chicago).The results were expressed in frequencies, means, percentages, tables, figures, and charts.

Ethics

The procedures followed in this study were in accordance with the ethical standards on human experimentation.

Result

A total of thirty five (35) patients who met the inclusion criteria as outlined above were recruited into the study. Out of this number only twenty- three (23) patients constituting 65.71% of the study group completed the research at 42 days post operative period. Other patients either refused to continue with

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the investigation because of the multiple vein punctures involved or were lost to follow up.

Age Distribution

The age range of the patients varied from 24 to 80 years with a mean age of 53. 95years. For the Control

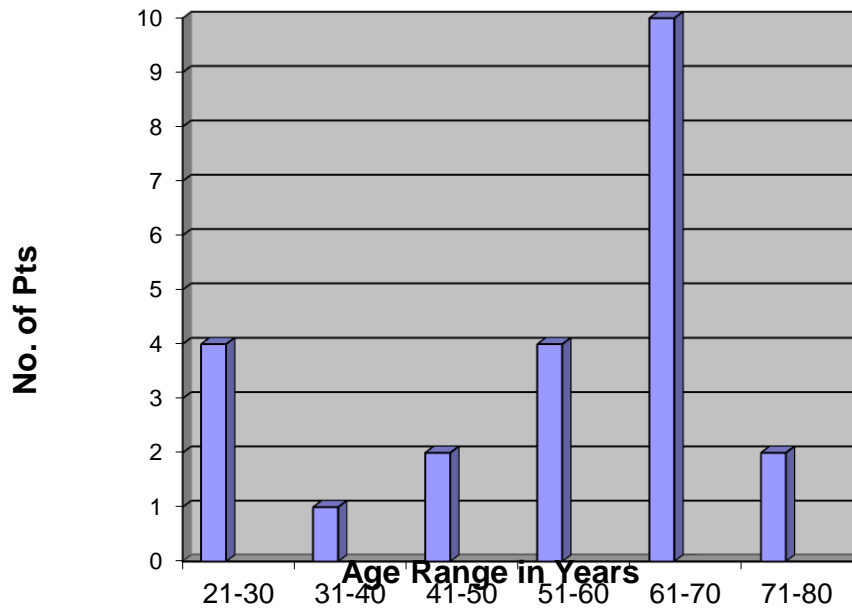group, the age range varied from 27 to 62 years with a mean age of 49.61years. Only 4 out of the 23 patients were below 30 years of age while 2 patients (8.7%) were above 71years of age (Figure 1).

Fig 1: Age Distribution of Patients

Diagnosis/Surgical procedure

Out of the 23 patients admitted for surgery 18 patients (78.26%) had severe osteoarthritis of the Hip/knee joints requiring Total Joint Arthroplasty (TJA) of the affected joints, 3 patients (13.04%) had old fracture non union requiring open reduction and internal fixation with plate and screws (ORIF), while the remaining 2 patients (8.79%) with spinal pathology had laminectomy (LAM) (Figure 2).
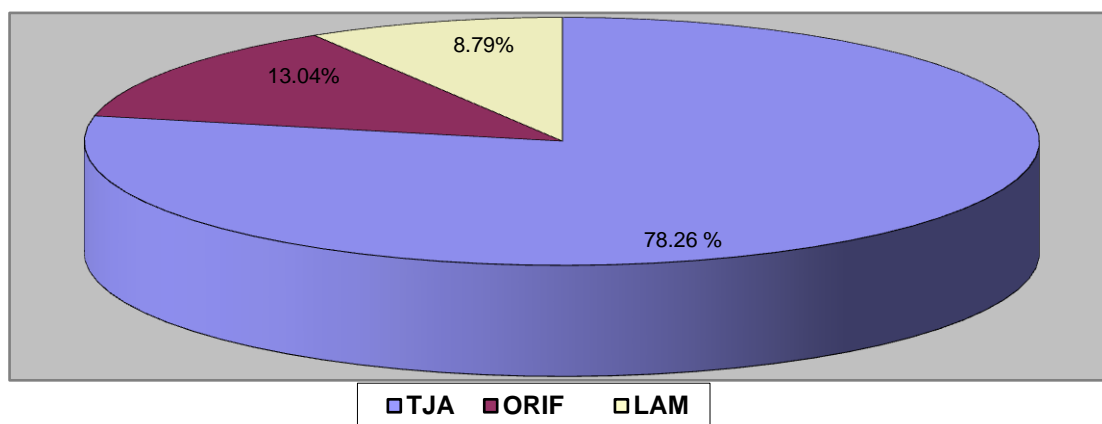

Fig 2: Profile of Diagnosis/Surgical Procedure

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Basal Serum ESR Levels:

The breakdown of mean basal ESR values according to individual sex reveals a mean basal ESR value of 10.8mm/1st hr and 11.8mm/1st hr for male patient and control respectively and 20mm/1st hr and 21.25mm/1st hr for female patients and control respectively (Figure 3).
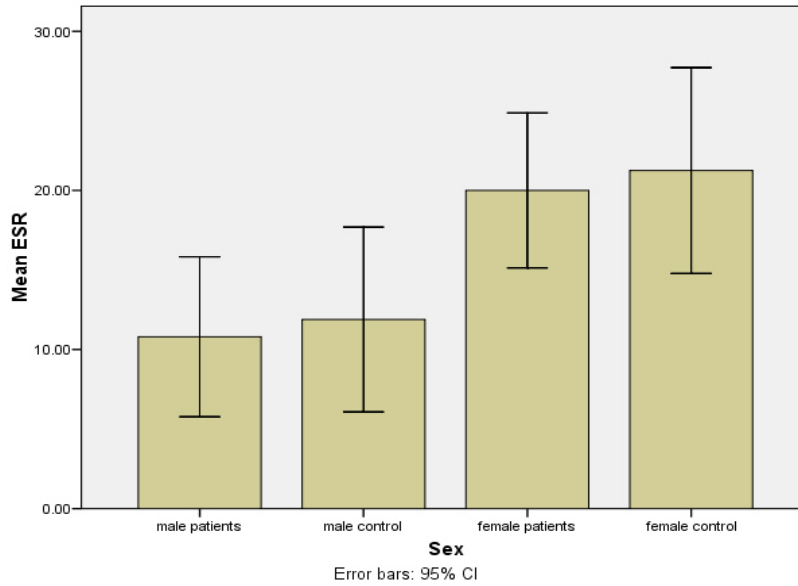

Fig 3: Mean basal ESR values of both patients and control with reference to sex

Basal serum CRP levels

The breakdown of mean basal CRP values according to sex shows mean basal CRP levels of 11.65 and 7.887 mg/L for male patient and control respectively and 7.63 and 3.05 mg/L for female patient and control respectively (Figure 4).
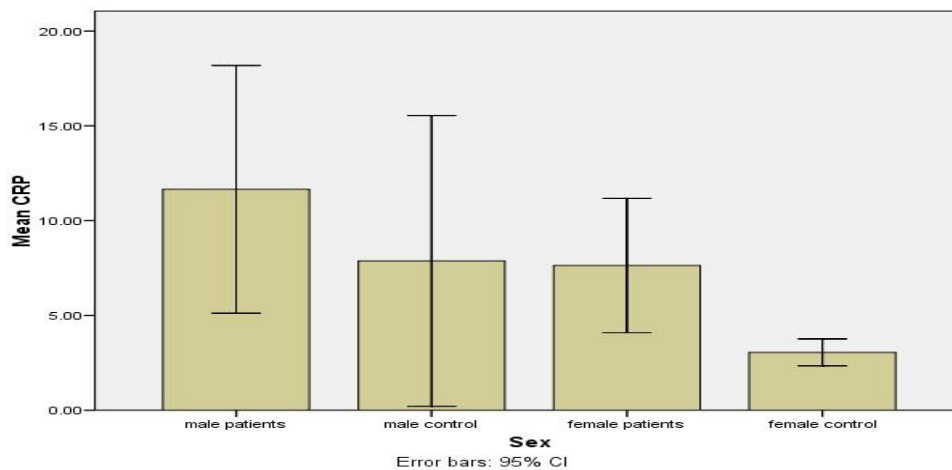

Fig 4: Mean basal CRP values for both patients and control with reference to sex

Pattern of Changes of ESR

The serum ESR in the immediate post operative period shows a remarkable change in pattern. It rises from its mean basal serum level of 16.00mm/1st hr to 51.84mm/1st hr on day 2, peaks on Day 7 at 83.70mm/1st hr and gradually falls to 24.13mm/1st hr on day 42 (Figure 5).
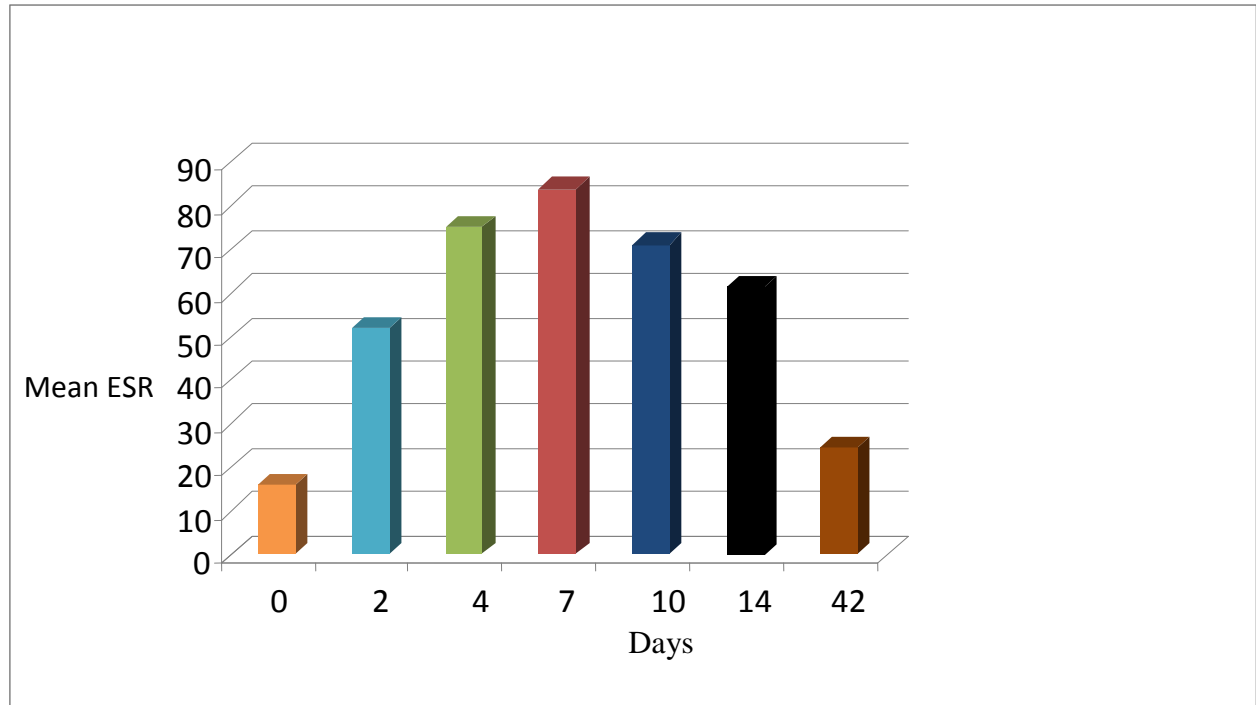

Fig 5: Pattern of Changes of ESR

Pattern of Changes of CRP

The serum CRP changes after major elective orthopaedic surgical procedure shows a steep increase from its mean basal level of 9.38 mg/L to 30.15 mg/L on day 2 and 31.37mg/L on day 4 when it peaks. This is followed by a steady decline in the serum CRP levels until day 42 when it has almost normalized to its pre-surgery serum level (10.10mg/L) (Figure 6).
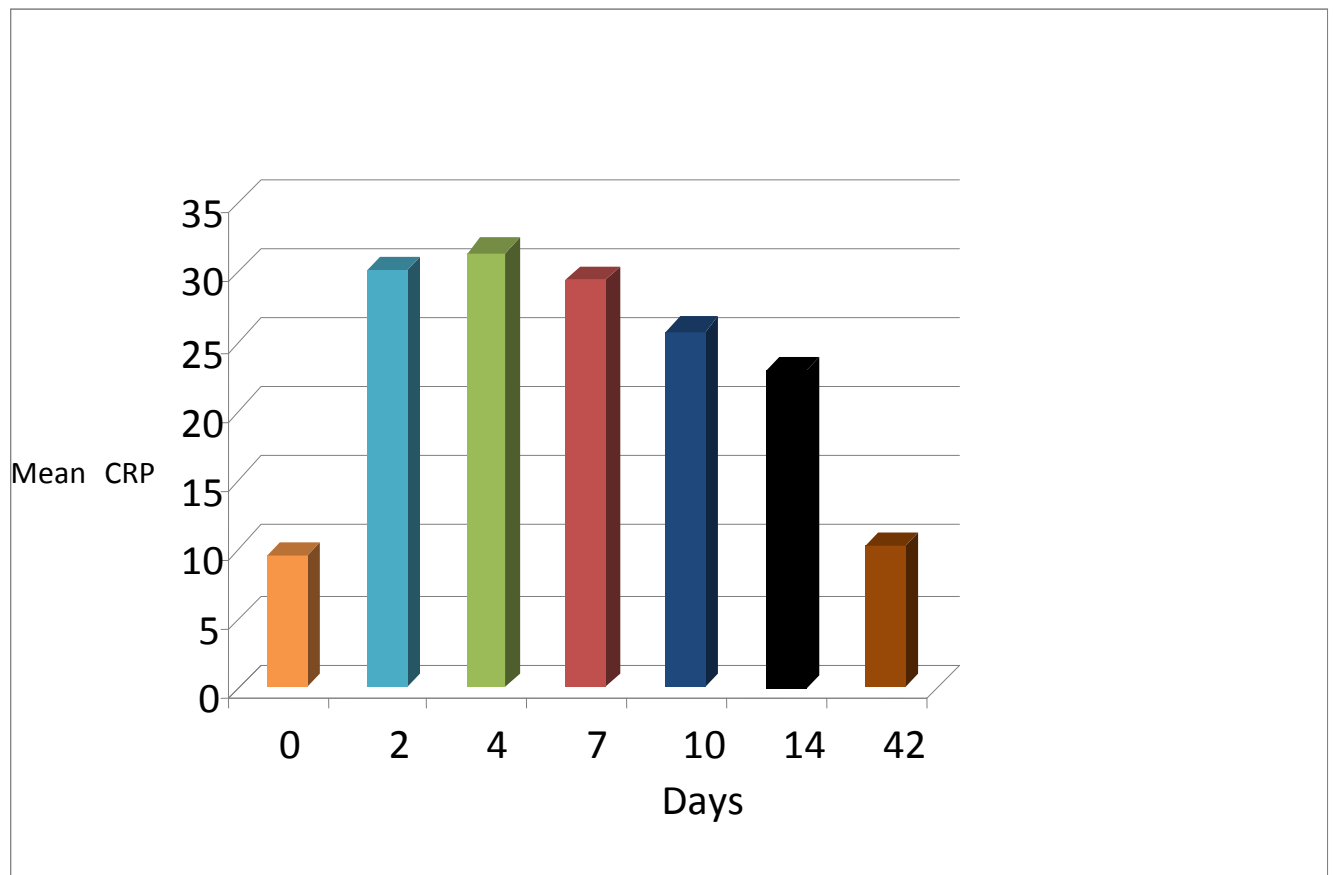
Fig 6:Pattern of Changes of CRP

Comparative Changes in serum ESR and CRP levels

The comparative changes in the pattern of serum ESR and CRP following major elective orthopaedic surgical procedures are presented in figure 7. The graph shows that the CRP peaks faster on day 4 and has almost completely normalized by day 42, (p value 0.543). The ESR on the other hand continues to rise from its pre-injury level (day 0) to day 7 when it peaks. It then starts a gradual fall which is still significantly higher than its pre-injury levels at day 42, (p value = 0.003).
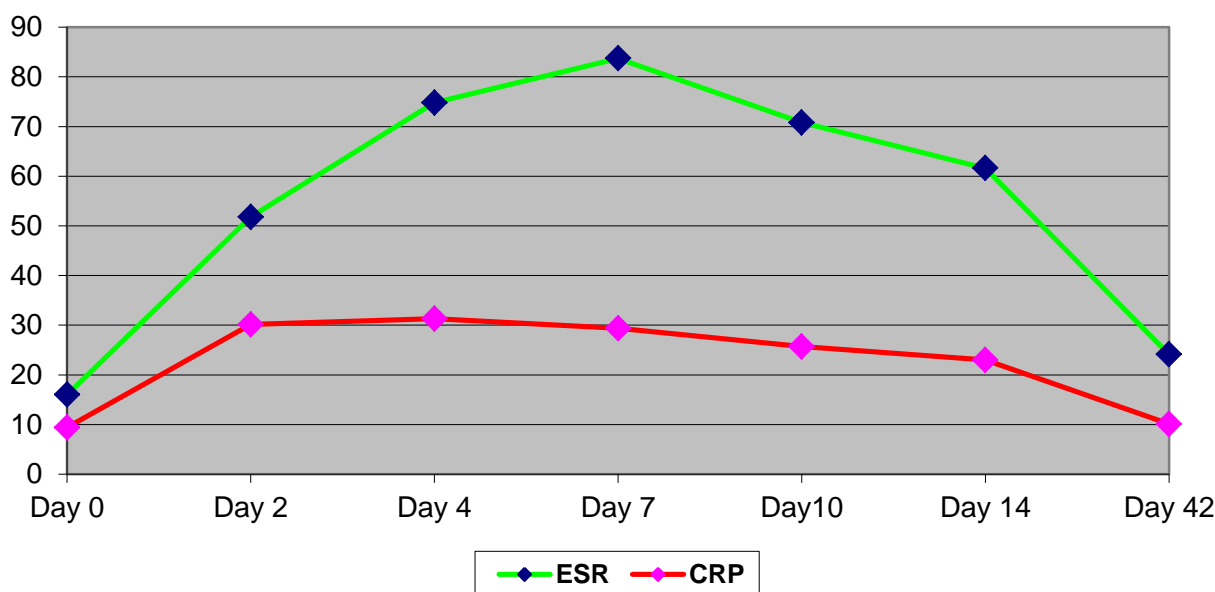
Fig 7:Comparative Plots of Changes in Serum ESR and CRP

Discussion

The age distribution of the patients ranges from 24 years to 80 years with a mean age of 53.95 years (Figure 1).   The highest concentration of patients; N=10 (43.48%) was seen in the 61-70 years age group. Incidentally all the patients in this group had total joint replacement arthroplasty for degenerative osteoarthritis. Also of note is that four (4) patients (17.39%) were below 30 years of age (Figure 1). Three (3) out of the 4 patients below 30 years have sickle cell arthropathy of the hip joints requiring early total joint replacement surgery while the fourth patient had open reduction and internal fixation with plate and screws for an old fracture non union. Interestingly, the majority of the patients (69.56%) who participated in the study were above 50 years of age. This is not surprising considering the fact that most of the patients who were recruited into the study presented with degenerative osteoarthritis which is an age related disease. Of the 23 patients who completed the study, 18 (78.26%) had severe osteoarthritis of the hip and knee joints (Figure 2).   The predominance of the patients with degenerative osteoarthritis was because it was convenient for the research since the hospital was operating on them in batches at the time of the study. Of the 18 patients with severe osteoarthritis, 12 were of the hip joints while 6 affected the knee joints. The distribution was also a purely chance occurrence as more hip surgeries were done at the Hospital at the commencement of the programme than knee replacement procedures. The basal serum ESR level showed a higher mean basal ESR values in females in both patients and control groups. It could be clearly seen that there is no significant difference in the mean basal serum ESR levels for both patients and control with respect to individual sex. The significantly higher mean basal ESR levels in females compared to their male counterparts is in keeping with earlier published works of Bottiger and Svedberg [17] and Obi [18]. The basal serum CRP levels show that the mean serum CRP level is significantly higher in males than females. The higher mean serum CRP level in males is in keeping with the works of Milkan et al [19] and Yamada et al. [20]. However, this finding contrast with most published articles from the West. For instance Shaffer [21] and Harlan [22] in a population based Dallas study showed that the median CRP values were higher in females. One explanation for this higher CRP level in females is that the dysfunctional adipose tissue, as indicated by elevated Triacylglycerol (TAG) levels, appears to accelerate inflammation in women compared to men. Also noted in this study was a significant difference in the mean serum CRP levels (unlike for the ESR) between the patients and control. This observation may be due to some undiagnosed inflammatory arthritis in some of the patients. The mean serum ESR level (figure 5) increased from its pre-surgery (day 0) level, peaked on day 7 and dropped by day 42. This significant rise and fall of ESR

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following major surgeries is in keeping with the earlier works of Johnson et al [23], Okafor and Maclellan [24], Larson et al [25]. The acute rise and fall of ESR following elective surgeries can be explained by the high post operative (post traumatic) level of serum fibrinogen which has a direct correlation with serum ESR level. Also the reduction in the serum fibrinogen level with the resolution of the inflammatory process within seven days explained the subsequent peaking within 4-7 days and gradual normalization within 42 days in the absence of infection. The mean serum CRP level (figure 6) also rises from its pre-surgery basal (day 0) level, continues to rise until day 4 when it peaks and subsequently falls back to its basal level on day 42. This acute rise and subsequent fall of serum CRP level is in keeping with works of Waleczek et al. [26] and Niskanen et al. [27]. Following major surgeries/trauma the serum mononuclear cells especially the macrophages are recruited and activated to release increased levels of interleukin II, VI and even some amount of tumour necrosis factor α. These factors stimulate the liver to produce increased level of Acute Phase Proteins including the CRP. Subsequent resolution of inflammation (absence of wound complications like infections) leads to the normalization of serum CRP level. The CRP and ESR values (figure 7) rises from there mean basal levels, peak at day 4 and day 7 respectively and decline gradually with the CRP almost falling to their pre-surgery level on day 42. The initial rise and peaking of CRP on day 4 is faster than for ESR, and so could be a better indicator of early post operative complications such as infections than ESR whose initial rise is also rapid, but with a slower and irregular fall.

Conclusion

ESR and CRP are both useful acute phase proteins for monitoring early   post operative complications like surgical wound infections. CRP attains its peak faster (day 4) compare to ESR (day 7) and its fall is also more rapid and regular; therefore it could be a better indicator/predictor of early post-operative complications than ESR.

Authors Contribution

ERC, OKC, EPO - Conception, design, data collection and analysis, laboratory analysis, literature search, preparation of the manuscript and critical revision of the manuscript.

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