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Erythrocyte Sedimentation Rate Revisited: Evaluation Of The Clinical Relevance Of Elevated Erythrocyte Sedimentation Rate And Its Correlation With The Final Diagnosis.

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ABSTRACT

The erythrocyte sedimentation rate, ESR is one of the most frequently used laboratory investigations. The usefulness of the erythrocyte sedimentation rate is becoming limited as a result of low sensitivity and specificity and emergence of new methods of evaluating disease. The aim of the current study was to assess the clinical relevance of a simple, rapid, cost-effective diagnostic tool, the elevated ESR and its correlation with the final diagnosis in the present day routine clinical practice. A cross-sectional, observational, prospective and retrospective study was conducted in the department of clinical pathology providing laboratory services to a tertiary care centre in coastal India. Of the total 11674 patients, whose samples were sent for estimation of ESR, a total of 270 patients with ESR above 50 mm/hr were evaluated and ESR was compared with age, sex and final diagnosis. The ESR was found to be more elevated in the elderly as compared to the younger age groups. The mean ESR was found to be significantly higher in males as compared to females (p=0.031.) In our study, 210 patients had ESR in the range of 50-100mm/hr and 60 had ESR above 100mm/hr. Out of the 210 patients, the leading cause for elevated ESR was chronic systemic diseases like chronic liver disease, chronic obstructive pulmonary disease, followed in frequency by acute inflammatory conditions like abscess, cellulitis. Malignancy and tuberculosis had a higher percentage of patients in the ESR group >100mm/hr as compared to chronic inflammatory disease where more patients had elevated ESR in the range of 50-100mm/hr.

Keywords: Erythrocyte sedimentation rate, clinical relevance, chronic inflammatory disease**,** tuberculosis, malignancy.

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INTRODUCTION

The erythrocyte sedimentation rate (ESR) is one of the oldest and most frequently utilised laboratory methods [1-4]. The ESR is a commonly performed laboratory test with intriguing antecedents extending back to the classical period of Western medicine. Although this background was appreciated by the physicians who popularized the test in the early part of this century, it has been largely forgotten. There has always been a lack of consensus about the role of the ESR as a nonspecific indicator of inflammation and tissue injury. The usefulness of the sedimentation rate has decreased as new methods of evaluating disease have been developed. The basic factors influencing the sedimentation rate were understood by the early decades of this century and the most satisfactory method of performing the test was introduced by Westergren in 1921 [5].

The ESR has been found to be of clinical significance in the follow up and prognosis of non-inflammatory diseases such as prostate cancer, coronary artery disease and stroke. ESR may be useful in monitoring HIV/AIDS disease [6]. Therefore the ESR is important in the diagnosis of inflammatory conditions and in the prognosis of non-inflammatory conditions, making this old test far from obsolete in either the near or distant future, especially in a resource poor population. The ESR is helpful in the specific diagnosis of a few conditions, notably temporal arteritis, polymyalgia rheumatica and possibly rheumatoid arthritis. It may predict relapse in patients with Hodgkin's disease. An extreme elevation of the ESR is strongly associated with serious underlying disease. When an increased ESR is encountered with no obvious clinical explanation, the physician should repeat the test after an appropriate interval rather than pursue an exhaustive search for occult disease. The usefulness of the ESR is becoming limited as a result of low sensitivity and specificity and emergence of new methods of evaluating disease. Nevertheless, it still remains a key diagnostic criterion for a few conditions [1].

Hence this study is undertaken to provide further information on the etiological relationship of elevated ESR in patients in a tertiary care centre and its relevance in current clinical practice.

MATERIALS AND METHODS

After approval of the institutional research and ethics committee, a cross-sectional, observational, prospective and retrospective study was conducted in the department of clinical pathology providing laboratory services to a tertiary care centre in coastal India. Two hundred and seventy consecutive patients with the ESR≥ 50 mm/hour from non-repetitive, out patients and in-patients from the surgical, medical and gynaecological departments were included in the study.

All patients aged ≥12 years with ESR equal to or more than 50mm/hour and only those patients with adequate further investigations to arrive at a final diagnosis were included. Those patients who did not have follow up investigations to support a final clinical diagnosis were excluded. The clinical data of the patients were collected along with the available relevant laboratory tests used to arrive at a final diagnosis. The patients were subcategorised into two groups:

Group A: Those patients whose ESR was more than 50mm/hour and less than 100mm/hour.
Group B: Those patients with ESR ≥100mm/hour.

The ESR at this laboratory is carried out on whole blood samples obtained through standard venous venepuncture techniques in 1.2 ml Vacu-tec tubes (Diesse Diagnostic Senese) containing 0.2ml sodium citrate or 4ml EDTA coated Vacutainer tubes (Becton Dickinson).The ESR test was performed by manual Westergren method using 0.4ml of 3.8% of sodium citrate and 1.6ml EDTA blood using the Vacuette (Greiner bio-one) tubes or using an automated Vesmatic 20 (Diesse Diagnostic Senese). Results between 0-149mm/hour were reported as exact figures whereas those having ESR equal to or more than 150 were reported as ≥150mm/hour.

The data were computed using Microsoft Excel 2007 and analysed by descriptive statistics. Total numbers, percentage and mean values of different groups of patients were calculated. Further statistical evaluation of the data was performed using the chi square test and statistical package for the Social Sciences version 15.0 (SPSS vs.15). $p<0.05$ was taken as significant.

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RESULTS

A total of 270 patients were evaluated and ESR was compared with age, sex and final diagnosis. In this study, mean ESR was found to be higher in the age group of 70-80 as compared to the other age groups and it was found to be least elevated in the age group 20-30 and below 20 (Table 1). The sex distribution is shown in Table 2 and the mean ESR was found to be significantly higher in males as compared to females in this study with p=0.031.

Table 1: Mean ESR vs age group

Age group	Number of patients	Mean ESR	Std. Deviation	Minimum	Maximum
<20	10	77.6000	25.51340	50.00	114.00
20 -30	27	77.5185	24.30158	50.00	140.00
30 -40	24	78.8333	21.35755	50.00	140.00
40 -50	49	85.2245	29.14709	50.00	140.00
50 -60	68	84.1471	26.70416	51.00	140.00
60 -70	49	81.1429	19.57145	50.00	140.00
70 - 80	35	89.9714	23.52281	50.00	140.00
>80	8	78.5000	18.03964	54.00	105.00

Table 2: Mean Elevated ESR and Gender distribution

Sex	Number of patients	Mean ESR	Std. Deviation	t
Male	141	86.1064	26.19970	2.17300
Female	129	79.6202	22.48061	p=.031 significant

Out of the 270 patients whose ESR were assessed 210 patients were found to have ESR in the range of 50-100 and 60 patients were found to have ESR above 100. Out of the 210 patients, 41.4% (87) of the patients had chronic systemic diseases like diabetes mellitus (DM), chronic renal failure, chronic liver disease, chronic obstructive pulmonary disease (COPD), 18.6% (39) of the patients had acute conditions which included infections- cellulitis, abscess, peritonitis, pancreatitis, 7.6% (16) had pneumonia, 7.1%(15) had urinary tract infection (UTI), 6.7%(14) had malignancy, 6.2%(13) had bone disorders like arthritis. A smaller percentage of the patients were found to have tuberculosis (TB) (5.2%), lower respiratory tract infection (LRTI) (4.3%) and cirrhosis (2.9%).

Out of the 60 patients who had ESR above 100, higher percentage of patients had chronic systemic diseases (31.7%) followed by acute systemic diseases (16.7%), malignancy (13.3%), UTI (11.7%) and TB(10%).

Mean ESR was found to be highest among TB patients (Mean ESR-96.17) followed by malignancy (Mean ESR-91.95) and UTI (89.23) as shown in Table 3.

On evaluation of these patients over a period of three months, the follow up showed significantly decreased value in patients with acute diseases such as pneumonia, LRTI, cellulitis, etc. In patients whose condition deteriorated there was an increase in ESR but not significantly. There was no significant change in ESR in those with chronic diseases. Patients with malignancy were followed up for six months, those who responded to chemotherapy did show a decrease in ESR.

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Table 3: Correlation of mean elevated ESR with the diagnosis

	N	Mean	Std. Deviation	Minimum	Maximum
TB	17	96.1765	34.41881	50.00	140.00
Malignancy	22	91.9545	29.77771	52.00	140.00
UTI	22	89.2273	19.87085	52.00	140.00
Pneumonia	21	83.1905	22.01731	55.00	140.00
Acute conditions (abscess, cellulitis)	49	81.5510	21.92512	50.00	140.00
Chronic systemic diseases	106	80.3868	22.88088	50.00	140.00
Cirrhosis	8	80.1250	29.61388	51.00	140.00
LRTI	11	78.4545	33.85665	50.00	140.00
Bone disorders	14	73.0714	18.27762	51.00	107.00

DISCUSSION

Edmund Biernacki and Robin Fahreus have been credited with the discovery of ESR although it had been described much earlier by John Hunter [7]. The ESR is a simple and relatively inexpensive laboratory tool and is known as an acute phase reactant test as it reacts to acute conditions such as infection or trauma in the body [8]. The test measures the distance that erythrocytes have fallen after one hour in a vertical column of anticoagulated blood under the influence of gravity. This test has been widely used for the documentation of inflammatory, infectious and neoplastic processes in regions with limited resources. The ESR is commonly used as a non specific indicator of certain inflammatory and malignant conditions, both as a diagnostic screening test and in the assessment of disease activity.

The probability of disease at any age increases with increased ESR and becomes more significant when the ESR exceeds 50mm/hr [3]. Extremely elevated ESR (EEESR) defined as equal to or greater than 100mm per hour is associated with a low false positive rate and a 90% predictive value for serious underlying disease, most often infection, collagen vascular disease, or metastatic malignancy [8].

The erythrocyte sedimentation rate (ESR) can be used to identify low-grade inflammation that contributes to future vascular events [9-14]. Measurement of the ESR is commonly accepted to be of diagnostic value if certain diseases are suspected on clinical grounds, e.g. polymyalgia rheumatica or plasmocytoma [2].

In order to understand the limitations of ESR measurement for the differentiation between 'healthy' and 'sick', one has to recall that the ESR, unlike most other laboratory tests, reflects the interaction of numerous blood components, not all of which have been fully recognized. Basically, the two major determinants of ESR are erythrocyte aggregation and haematocrit [5]. Red blood cell aggregation, in turn, is influenced by plasma proteins, which reduce the negative electrostatic forces between red cells, causing aggregation and faster sedimentation. If one considers the enormous variability in plasma protein composition and interaction, it is clear that a high variability of test results must ensue. Accordingly, it has been found that ESR, in the absence of any disease, is influenced by obesity [4], age [15] and race [16]. ESR is always slightly raised in anaemia a fact that is not appreciated in many patients, as well as due to the influence of drugs [15,16]. Fibrinogen, the most abundant acute-phase reactant, has the greatest effect on the elevation of the ESR when compared with other acute-phase reactants [3].

In our study, mean elevated ESR was found to increase with increasing age and it was found to be the highest in the age group 70-80.This result is similar to previous studies where there was a significant increase

in ESR and fibrinogen with increasing age although which was non-significant or marginally significant for ESR when they adjusted for fibrinogen differences [9].

In the current study, mean ESR was found to be higher in males as compared to females. Sex has an important role in defining normal values for the ESR. In another study, sex had significant statistical interactions with all of the major determinants of the ESR, demonstrating an additive effect on the ESR and on its components [9].

In this study a large percentage of the patients having elevated ESR amounting to a total of 106 patients (39.3%) were suffering from chronic diseases like diabetes mellitus, COPD, chronic liver disease, cholecystolithiasis, inflammatory bowel disease, chronic renal failure. Diabetes being one of the commonest chronic conditions, in this study also diabetic foot was the commonest chronic disease with elevated ESR. In a study done by Ford ES the data showed that participants who developed diabetes had a higher erythrocyte sedimentation rate and leukocyte count than participants who remained free of diabetes in addition to other factors [17].

Acute inflammation like cellulitis, abscess.etc with a total of 49 patients (18.1%) was the next common cause for elevated ESR. Among the acute infections, abscess was the commonest case. In this study 22(8.1%) patients had urinary tract infection, 17(6.3%) patients had tuberculosis and 14(5.2%) patients had bone disorders like septic arthritis. Similarly in a study done by Yousuf et al infection(38.6%) was the leading cause for elevated ESR. The main infections included tuberculosis(5.5%), osteomyelitis, septic arthritis(3.1%), urinary tract infection(4.7%) and sepsis of unknown origin [8].

Pneumonia was found in 16(7.6%) patients and LRTI in 11(4.1%) patients. In a study done by Hopstaken et al, ESR and c-reactive protein in addition to other criteria were significant predictors of pneumonia [18].

In our study it was found that ESR was elevated in 22(8.1%) patients having malignancy. Monig et al found that in hospital patients with elevated ESR, malignancy were found in 25% of all cases which was not significantly different from the incidence of malignancies in patients with normal ESR [2]. Yousuf et al in their study found that elevated ESR was found in 15.4% of the patients having malignancy [8]. Cankurtaran et al in their study found that malignancy was the leading cause (21.6%) for elevated ESR, followed by infectious disorders (10.1%), collagen vascular diseases (9.4%), and non-neoplastic hematologic disorders (5.0%) [19].

The patients having malignancy and TB had a higher percentage of patients in the ESR group->100mm/hr as compared to chronic systemic disease where more patients have elevated ESR in the range of 50-100mm/hr. Also in the present study the mean elevated ESR was found to be the highest in TB. In pneumonia also the mean ESR was high which could be because only those patients were included whose ESR was high and other patients with normal ESR were not taken into account therefore giving this result.

CONCLUSION

The ESR is an inexpensive yet still widely used test though the indications of ESR have decreased as the sophistication of laboratory testing has increased. However in a limited resource population, it can be used as a measure of the acute phase response, is a helpful indicator of the presence and extent of inflammation or tissue damage and response to treatment as well as malignancy. The ESR can also play a role in non-inflammatory conditions such as coronary artery disease. Thus, we continue to rely on this often used test and its role in everyday clinical practice cannot be underrated.

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