

**INTRODUCTION**

Erythrocyte sedimentation rate (ESR) is one of the most frequently ordered test in clinical medicine. In the present era ESR is losing its glory, because of availability of more specific and sensitive markers like CRP, fibrinogen and ferritin. The method of ESR estimation was first described in 1921 by R Fahraeus and A Westergren in pulmonary tuberculosis, and it rapidly became a common screening test worldwide.<sup>1,2</sup> Despite its limitations, the ESR remains a cost effective and widely used test for the screening and monitoring of infectious, autoimmune, malignant and other chronic inflammatory diseases, especially in developing country like India.

**PATHOPHYSIOLOGY OF ESR**

ESR is the rate at which the erythrocytes fall down by their own weight when anticoagulated blood is held in a straight column, in first hour. ESR is measured by Westergren and Wintrobe method. The International Committee for Standardization in Hematology (ICSH) recommended Westergren method as standard for measuring the ESR, which has now been accepted worldwide.<sup>3</sup> In addition to these methods there are now automated methods available which give readings in less than one hour but the results correlates to the standard 1hr Westergren reference method.

The ESR process in all can be divided into 3 phases. The first phase is the phase of rouleaux formation. During this phase the red cells owing to their discoid shape stack over each other. However due to a negative charge on their surface they repel each other and do not form rouleaux. The plasma proteins that neutralize this charge and enhance rouleaux formation are principally gammaglobulins and fibrinogen. Thus any factor that increases these proteins is going to increase the rate of rouleaux formation and thus the ESR. The common example to this is the increased ESR in chronic inflammation due to increase in fibrinogen as an acute phase reactant and increased gammaglobulins in multiple myeloma.

In addition to this another factor that determines this initial stage of ESR process is the shape of red cells. As described earlier the red cells stack over each other in a straight axis due to discoid shape. The conditions like sickle cell anemia is going to adversely affect this process as this new shape does not allow stacking and causes reduced ESR.

The second phase in the process of ESR is the stage of sedimentation where the rouleaux formed fall through

the plasma. However during the fall of each red cell group they form a negative retarding force of plasma. Thus if more red cells are present there will be more retarding force and thus reduced ESR (polycythemia) and the conditions where red cell mass is low there will be less retarding force causing increased ESR (anemia).

The third phase in ESR process is the stage of packing where the sedimented red cells pack within the space to give final readings. This component is principally affected by the abnormal shapes of the red cells causing the plasma to get trapped between the red cells and increase the ESR. This happens principally in anemia where there is a lot of anisopoikilocytosis, classic example of which is iron deficiency anemia.

Interpretation of ESR should be done carefully as it depends on many physiological and pathological factors as given in table 1 and 2.<sup>4</sup>

**ESR IN RHEUMATOLOGIC DISORDERS**

Rheumatoid arthritis is one of the most common disease in which ESR and/or CRP are used to measure disease activity. The DAS and DAS28 are the major clinical scoring systems used to measure the disease activity in RA wherein the ESR is an essential component.<sup>5</sup>

The patients with SLE relapse have raised ESR but normal CRP level, while with infection both are increased. Thus measuring both together is helpful in differentiating between infection and relapse.

In giant cell arteritis (GCA) increased ESR is a hallmark of undiagnosed disease and returns to normal following therapy. ESR of more than 50 mm 1<sup>st</sup> hr, is an essential component of this disease classification. Levels of ESR and/or CRP are also a useful marker of response to prednisone in GCA. Patients who have lower ESR are expected to show better response to prednisone.

**ESR IN MALIGNANT DISORDERS**

A high ESR has been found to correlate with overall poor prognosis for various types of cancer, including Hodgkin's

**Table 1: Normal values of ESR by Westergren method**

Age (Years)	Females (mm at 1 <sup>st</sup> Hr)	Males (mm at 1 <sup>st</sup> Hr)
<50	<12	<10
51-60	<19	<12
61-70	<20	<14
>70	<35	<30

**Table 2: Factors that influence the ESR**

Increased ESR	Decreased ESR	No clinically significant effect or questionable effect
Physiological		
Old age		Obesity
Female		Body temperature
Pregnancy		Recent meal
Menstrual cycle		Aspirin
<b>Pathological causes</b>		NSAIDs
Anemia	Acanthocytosis	Estrogen
RBC abnormalities	Polycythemia	OCP'S
Macrocytosis	Spherocytosis	Valproic acid
Elevated fibrinogen level	Sickle cell disease	Streptokinase
Infection	Hypofibrinogenemia	Phenobarbitone
Inflammation	Protein abnormalities	
Malignancy	Hypogammaglobinemia	
Atherosclerosis	Dysproteinemia with hyperviscosity state	

disease, gastric carcinoma, renal cell carcinoma, breast cancer, colorectal cancer and prostate cancer. In patients with breast carcinoma a combination of biochemical markers including CA15.5, CEA and raised ESR can be used to screen the metastatic disease in more than 90% patients. Also this combination with biochemical markers has shown to decrease the cost of treatment by up to 50% by preventing costly radiological workup. It has also been observed that no obvious cause is found in fewer than 2 percent of patients with a markedly elevated ESR.

### ESR IN CARDIAC DISORDERS & COPD

It has been shown that raised ESR is an important marker of atherosclerosis and a strong predictor of mortality from coronary artery disease (CAD). It is also a minor criterion for diagnosis of rheumatic fever by Jones criterion. In COPD patients the ESR is seen as a cheaper alternative to CRP in monitoring the disease activity. It increases in COPD as a response to rising levels of fibrinogen, gammaglobulins and in response to developing anemia.<sup>6</sup>

### ESR IN INFECTIONS

ESR is mostly raised in conditions like active tuberculosis and infective endocarditis. It also has been used as a marker of response to treatment in tuberculosis. However it may be normal in infections like typhoid fever and malaria. Increased ESR can be an early predictive marker of HIV seropositive progression towards AIDS. It also has been proposed by some authors that the ESR can be used as an inexpensive "sickness index" in the elderly.<sup>7</sup>

### EXTREME ELEVATION OF ESR

An extreme elevation of the ESR (defined as > 100 mm in 1st hour) is associated with a low false-positive rate for a serious underlying disease.<sup>8</sup> Most common causes are inflammatory disease like polymyalgia rheumatica, giant cell arteritis, multiple myeloma, JRA and metastatic malignant tumors. It can also be used to monitor the

disease activity and response to treatment in these disorders.

### ESR IN ASYMPTOMATIC PATIENTS

ESR should never be used as a screening tool in an asymptomatic patient. A normal ESR reassures the patient as well as the clinician that no underlying serious condition is present, especially when clinical suspicion of disease is low. A mild to moderate elevated ESR without obvious underlying disease should prompt repeat testing after several months rather than an expensive search for hidden diseases. However, an extremely high ESR even in asymptomatic patients should prompt the clinician to search for occult infections or inflammatory disease as stated above.

### CONCLUSION

- The ESR is an old, inexpensive yet still widely used test; although it's a non-specific but frequently ordered for diagnosis and monitoring of certain diseases.
- High ESR can be incidental finding in asymptomatic persons but it should be repeated after some months and to be correlated with clinical examination and other laboratory tests.
- Patient who have a markedly (>100 mm 1<sup>st</sup> hr) raised ESR are the one where probability of finding a serious disorder is quite high.
- The ESR also has important prognostic role in conditions such as malignancy, stroke, CAD and tuberculosis.
- The clinician should be aware that ESR is only one parameter that should be supported by other acute phase markers like CRP, fibrinogen or ferritin.
- It will always remain an important marker in developing country like India.

**REFERENCES**

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