Association of Erythrocyte Sedimentation Rateto White Blood Corpuscles and Liver Enzymes

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ABSTRACT

Studies carried out in the past have shown that in infectious diseases there is increase in the levels of Erythrocyte Sedimentation Rate (ESR), White Blood Corpuscles (WBC) and liver enzymes Alanine Aminotransferase (ALT), Gamma GlutamylTransferase (GGT) and Lactate Dehydrogenase (LDH). There are other inflammatory markers like C reactive protein (CRP) and Procalcitonin, both of which are altered in several infectious diseases. This study is an attempt to find out the correlation of ESR to WBC and several analytes of liver function tests such as Aspartate aminotransferase (AST), ALT, ALP, GGT and Albumin. Results available for 100 patients attending the master health check up were used to find out the above associations. Very good correlations were observed between ESR and WBC for all patients ($p<0.0001$) and males & females ($p<0.01$). When the results for ESR was grouped as normal and abnormal, ESR showed association to ALT,AST and ALP ($p<0.05$) for normal patients and to only WBC for abnormal patients ($p<0.05$). The results obtained in this study confirms that ESR results always correlates with WBC and to some extend to liver function tests like ALT,AST and ALP and GGT. Further studies are required using a large number of patients and to extend such studies to find out association of ESR to various inflammatory markers.

Keywords:ESR, WBC, ALT, AST, ALP and GGT

INTRODUCTION

ESR and generally WBC correlates significantly in all bacterial infections. An extreme elevation of ESR is strongly associated with serious underlying disease, most often infection, collagen vascular disease or metastatic malignancy. The progression of disease was accompanied by increase of ESR, CRP and LDH levels. However only ESR and CRP values differed significantly in progression of cancer as compared to the clinical remission phase. In patients with bacteraemia. CRP was significantly higher among bacteraemic patients, whereas ESR, WBC and ALP were not. Although urinary nucleotide excretion, Copper, ALP and ESR reflect disease activity, they do not provide independent information beyond that of clinical assessment. ESR, LDH and GGT rose significantly in relapsing patients with Ewing's sarcoma. ESR was best correlated to disease activity. The inhibitory action of albumin on the ESR has clinical implications and must be known by physicians. It may help to interpret sedimentation rates more correctly and prevent misinterpreting presumed therapeutic successes or failures. Albumin had a synergistic effect on the ESR together with gamma-globulin, but not together with fibrinogen. Total leucocyte and absolute neutrophil counts were not correlated with either ESR or haematocritstandardized ESR. Studies interlinking ESR to liver enzymes are scarce and this study is an attempt to understand the association of ESR to liver enzymes.

REVIEW OF LITERATURE

Studies Show that ESR values vary with the nature of bacteria in meningitis[1].The mean ESR did not differ significantly between the bacterial and viral (Acute Lower Respiratory Infection (ALRI) neither did WBC or CRP. No combination of clinical signs and host responses or any cutoff values could be shown to differentiate reliably bacterial from viral Acute lower respiratory infection.[2] There was no significant differences in the WBC counts, the CRP concentrations and ESR levels between the bronchiolitis and bronchopneumonia cases. Respiratory Syncytical Virus (RSV) lobar pneumonia cases are coinfected with some bacterial organisms more heavily than in the RSV bronchiolitis and bronchopneumonia cases.[3] WBC, neutrophils and ESR are higher in patients with poor outcome than in those without clinical outcome. Both elevated WBC count and Neutrophil showed significantly positive association with poor clinical outcomes among patients with acute ischemic stroke at admission.[4]

Obese patients treated by Roux-en-y gastric bypass (RYGBP) showed sustained reductions in ESR, WBC, ALT, and GGT possibly due to reduced liver steatosis and increased Magnesium levels.[5] A significant increase of WBC with Febrile Convulsion (FC) have encountered and it

could be due to leucocytosis followed by convulsions.[6]ESR and differential leukocyte count are two valuable tests in febrile Urinary Tract Infection (UTI) and may be useful for localization of UTI level, but the total leukocyte count and CRP level as in qualitative methods are not useful, and many patients with febrile UTI do not have leukocytosis.[7]A significantly higher procalcitonin (PCT) level was observed in the septic group compared to those without sepsis. serum PCT level was a highly efficient laboratory parameter for the diagnosis of severe infectious complications after burn, but WBC, neutrophil, ESR and CRP levels were of little value.[8]Of the inflammatory markers simultaneously assessed in elderly population, only C3 was strongly associated with insulin resistance, independently of the components of the metabolic syndrome and abdominal and general obesity.[9]

An extreme elevation of the ESR is strongly associated with serious underlying disease, most often infection, collagen vascular disease or metastatic malignancy. When an increased ESR is detected with no obvious clinical explanation, it is important to repeat the test after an appropriate interval rather than pursue an exhaustive search for occult disease.[10]Headache, epigastric pain, nausea, decreased appetite together with fever in the evening or at night with normal/decreased leukocyte count and abnormal liver function tests are the most common clinical symptoms found in typhoid subjects.[11] The progression of disease was accompanied by increase in ESR, CRP and LDH levels, however only ESR and CRP values differed significantly in progression of cancer as compared to the clinical remission phase. Among analysed markers, only LDH level at diagnosis proved to be an independent prognostic factor for the overall survival rate. It has been demonstrated that ESR, CRP and LDH determinations in children suffering from cancer may serve as useful markers both in diagnostics and monitoring of the disease course. Moreover, the pre-treatment LDH level appeared to have an important role in the prognosis of the overall survival rate.[12]The 8-hydroxydeoxyguanosine (8-OHdG) level in circulating leukocytes is a reliable marker of oxidative stress occurring in the liver of individuals with chronic Hepatitis C Virus (HCV) infection. Deoxyribonucleic acid (DNA) oxidative damage appears to be an early and unique event in the natural history of HCV-related hepatitis. This injury increases the risk of genomic damage and may be one of the important factors involved in the carcinogenic process in cases of HCV-related chronic liver disease.[13] These findings are considered to be characteristic of RA, and suggest the existence of latent or subclinical hepatobiliary involvement and an association between the expansion of hepatobiliary involvement and the mechanism of disease activation. Thus measurement of the serum levels of ALP and its isoenzymesin rheumatoid arthritis (RA) is considered to be important.[14]

In patients with bacteraemia. CRP was significantly higher among bacteraemic patients, whereas ESR, WBC and ALP were not. The area under receiver operator characteristic curve for CRP was within significance level (P<0.05). None of the markers could reliably diagnose bacteraemia. CRP alone was significantly higher among bacteraemic patients.[15] Patients with metastatic prostate cancer (PCa) can be divided into three statistically significantly different prognostic risk groups for PCa-specific mortality by using the binary classified pretreatment variables ALP, Prostate Specific Antigen (PSA), ESR and age.[16] In patients with RA bone metabolism is affected. In active disease, there was decreased bone formation, while bone resorption was increased. The therapy of weekly low dose Methotrexate (MTX) had improved bone resorption, suggesting that in patients with RA, MTX might have a bone protective effect by controlling disease activity.[17] Although urinary nucleotide excretion , Copper, ALP and ESR reflect disease activity, they do not provide independent information beyond that of clinical assessment.[18]Pre-operative high ESR, but not ALP, was a significant predictor for cancer-specific survival among renal cell cancer patients. Anaemia increases the risk of death from other illness.[19] Urinary Pyridinoline levels are elevated in patients with Ankylosing spondylitis (AS). Gender, duration of disease and ESR also have an impact on urinary excretion of these collagen compounds. Bone turnover in patients with AS reflects normal osteoblastic activity and high osteoclastic activity.[20]

ESR, LDH and GGT rose significantly in relapsing patients with Ewing's sarcoma. ESR was best correlated to disease activity.[21]Besides the common liver manifestation of primary biliary cirrhosis, systemic involvement and overlaps with other Connective tissue diseases (CTDs) are not infrequent in Chinese patients. When overlapping with other CTDs, primary biliary cirrhosis (PBC) patients manifested some special clinical and laboratory features which may have effect on the prognosis.[22] The influence of albumin on erythrocyte aggregation is complex and depends on the technique used; low shear viscosity is increased, but ESR under no flow conditions is decreased. The inhibitory action of albumin on the ESR has clinical implications and must be evaluated by physicians. It may help to interpret sedimentation rates more correctly and prevent misinterpreting presumed therapeutic successes or failures.[23] The ESR increased linearly with the concentrations of fibrinogen or gammaglobulin (IgG) when these exceeded normal thresholds. The ESR was slightly decreased by increasing concentrations of albumin. Albumin had a synergistic effect on the ESR together with gamma-globulin, but not together with fibrinogen.[24] Albumin levels showed a strong direct relationship with haematocrit which accounted for the inverse correlation found between albumin and ESR. The haematocritstandardised ESR showed no significant correlation with albumin levels. Total leucocyte and absolute neutrophil counts were

not correlated with either ESR or haematocritstandardised ESR. The high correlation found between fibrinogen and haematocritstandardised ESR suggests that differences in this acute phase protein influence the degree of red cell aggregation and rouleaux formation in the horse.[25]

MATERIALS AND METHODS

Samples received from Master Health Check up were analyzed. ESR was processed byCaretinum XC-A30 auto analyzer, WBC in fully automated ADIVA 2120i analyzer and Liver enzymes were processed by DIRUI CS400 fully automated analyzer. Results available for 100 MHC patients in the age group of 1-78 years consisting of 58 males (age group 8-78 years) and 42 females (age group 1- 73 years) were used for this study.

Inclusion Criteria

Patients attending routine MHC and the results available for analytes like ESR, WBC, AST, ALT, ALP, GGT and Albumin were used for this study.

Exclusion criteria

Results available from patients attending other clinics such as cardiac and endocrine were excluded for this study.

Statistical Analysis

For statistical analysis of data, a software downloaded from the website http://www.vassarstats.net was used to calculate correlation coefficient (r), students 't' distribution (t) and probability (p) between ESR and WBC and to liver function tests AST, ALT, ALP, GGT & Albumin

RESULTS AND DISCUSSION

Table IStatistical Parameters (r, t & p) for all patients (n=100)

S.no	Group	Pairs Compared	r	t	p
1	All patients (n=100)	ESR vs WBC	0.3701	3.944	<0.0001
		ESR vs Albumin	-0.3415	-3.597	<0.001
2	Males (n=58)	ESR vs WBC	0.3180	2.51	<0.01
		ESR vs GGT	0.3957	3.224	<0.01
		ESR vs Albumin	-0.5007	-4.329	<0.001
3	Females (n=42)	ESR vs WBC	0.4193	2.921	<0.01
		ESR vs Albumin	-0.3330	-2.234	<0.05

Based on the ESR values, the patients were grouped as normal (50 patients with ESR <20) and abnormal (50 patients with ESR >20).

Table I shows the statistical parameters obtained for r, t & p for all the 100 patients, 58 males and 42 females (All groups contains both normal and abnormal). ESR showed a very good positive association to WBC (p<0.0001) and significant negative association to albumin (p<0.001). All other liver function tests such as ALT, AST and ALP did not show any correlation. In the case of

male patients, ESR showed positive and good association to WBC and GGT (P<0.01), while its association to Albumin is inverse but highly significant (P<0.0001). However, in the case of female patients while ESR shows a positive association to WBC, its association to albumin was found to be inverse. (<0.02 &<0.05 respectively).

Table II: Statistical Parameters (r, t & p) for all normal & abnormal patients (n=50)

S.no	Group	Pairs Compared	r	t	p
1	Normal patients (n=50)	ESR vs ALT	-0.26762	-1.975	<0.05
		ESR vs AST	-0.24101	-1.863	<0.05
		ESR vs ALP	0.32922	2.404	<0.05
2	Abnormal patients (n=50)	ESR vs WBC	0.25810	1.851	<0.05

In the case of 50 normal patients ESR showed significant negative association to AST and ALT, but a positive association to ALP (P<0.05). In the case of abnormal patients, ESR showed a significant positive association only to WBC (p<0.05).

Previous studies have shown that increase in ESR is accompanied by an increase in CRP and LDH, but we could not find an association between ESR and LDH.[12] As we did not measure CRP and PCT, we are unable to correlate ESR values with those two inflammatory markers.[9] In patients with metastatic cancer, ALP may be an useful liver function test and is associated with ESR and this observations is in consistent with our study.[16] Measurements of ESR, LDH and GGT was found to be useful in detecting relapse of osteosarcoma and our study support this earlier observation.[21] The correlation of ESR to albumin proved in this study is in consistent with earlier observations.[23] Increase in ESR has been linked to both fibrinogen and IgG, but we did not measure these two analytes. Fibrinogen, IgG and PSA may serve as additional diagnostic tool to link with ESR in various types of infections. In this study, ESR shows good associations to WBC, GGT, albumin indicating that both GGT and albumin are altered in infectious diseases.[23,24]

Many previous studies have shown that measurements of ESR and WBC will be useful for laboratory diagnostic purposes to evaluate infectious diseases. However in recent times, clinicians are investigating liver function tests along with PCT & CRP. In majority of infections elevation in the levels of PCT along with CRP is a common findings. We did not measure these inflammatory markers, as facilities for testing these analyteswere not available. Previous studies have shown that progression of disease state was correlated with elevation in the levels of ESR and CRP. We have proved in this study that increase in ESR is always associated with WBC [1] as well as to LDH and GGT but this study could not find an association of ESR to LDH [12,21]. However, ESR was found to be association to albumin and this observations is consistent with previous studies [24,25]. Hence linking ESR results to WBC, liver function tests such as AST, ALT, ALP, GGT, Albumin

along with inflammatory markers such as PCT, Fibrinogen, IgG, Interleukins and CRP may help in the total diagnosis and treatment of patients suffering from infectious diseases.

CONCLUSION

This study demonstrates that ESR is associated with WBC irrespective of whether the patients ESR results are normal or elevated. ESR values correlate with Liver Function tests and shows good correlations to AST, ALT, ALP, GGT & Albumin. The correlation of ESR to inflammatory markers like Procalcitonin, CRP, Fibrinogen, Interleukins and immunoglobulins was not studied. From this study testing of ESR, WBC, AST, ALT, ALP, GGT& Albumin would guide the clinicians in the diagnosis of whether liver function is affected or not due to infections. Further studies are necessary with a larger sample size to link ESR to inflammatory markers.

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