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CLINICAL USEFULNESS OF ESR AND PLATELETS IN HBSAG, HIV AND HCV INFECTIONS

Rajeswari S.[1], Anila Mathan[2] and Swaminathan S.*[3]

[1]Junior Technical Officer, Department of Biochemistry, Apollo Speciality Hospitals, Vanagaram
[2]Senior Consultant & Head, Department of Haematology & Blood Bank, Apollo Speciality Hospitals, Vanagaram
[3]Senior Consultant and Head, Department of Biochemistry, Apollo Speciality Hospitals, Vanagaram.

***Author for Correspondence: Dr. S. Swaminathan**
Senior Consultant and Head, Department of Biochemistry, Apollo Speciality Hospitals, Vanagaram

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ABSTRACT
Infection is still one of the leading cause of cirrhosis & Hepatocellular Carcinoma world wide. Many studies have shown that blood count indices are altered in infections involving HbsAg, HCV and HIV. However, only very few studies have found out an associations between individual counts and the infecting organism and majority of studies have found associations using count ratios. The outcome of this study has established strong associations between controls and patients for ESR in HbsAg & HIV (P <0.000001 & <0.05) and platelets in HCV & HIV infections (P<0.000001 & <0.01) respectively and only moderate inverse significance was observed for NLCR between controls and patients in the case of HbsAg infection. This study suggests that ESR and platelets values should be routinely monitored in infections involving HbAg, HCV and HIV.

KEY WORDS: HbsAg, HCV, HIV, NLCR.

INTRODUCTION

Generally all infections caused by HbsAg, HCV and HIV are said to alter several organ functions notably liver, kidney and heart as observed by increases in the metabolites released by such organs. Many studies have proved this observations. While total blood counts are generally altered, but its value may not be diagnostically useful unless individual counts are made use of for differential diagnostic purpose. This main aim of this study is to find out if any association exists between controls and patients for ESR, Platelet and NLCR.

HIV

Opioid receptors (OR) are involved in many physiological and pathological immune functions. During recent years, the treatment of opiate addiction with methadone in HIV-positive and HIV-negative patients have become widely accepted. However, little is known on the occurrence and course of OR on lymphocytes of these individuals. HIV seems to reduce OR particularly on lymphocytes and granulocytes regardless of the mode of HIV transmission. The quantification of OR on immune cells may help to elucidate the effects of opioid analogues in health and drug addiction.[1] Patients with HIV infection exhibited more pronounced decrease in the activity of all lymphocytic enzymes (neutrophil esterase, acidic phosphatase and succinate dehydrogenase), as well as in the activity of myeloperoxidase and the content of cation proteins and glycogen in neutrophils in comparison with patients having chronic active hepatitis.[2]

Preoperative peripheral blood Neutrophil-to-Lymphocyte Count Ratio (NLCR) has been proposed to predict prognosis of Hepato Cellular Carcinoma (HCC). However, the cutoff value of NLCR in several studies is not consistent. Some studies have shown that NLCR was associated with tumor size, clinical Tumor Node-Metastasis (TNM) stage, Portal Vein Tumor Thrombus (PVTT), distant metastasis, and Aspartate Aminotransferase (AST) in HCC. NLCR > 2.31, size of tumor > 5 cm, number of multiple tumors, III-IV of (TNM) stage, PVTT, distant metastasis, and AST > 40 U/L were predictors of poor Disease Free Survival (DFS) and Overall Survival (OS). Preoperative NLCR > 2.31 was an adverse predictor of DFS and OS in HCC after hepatectomy, suggesting that NLCR might be a novel prognostic biomarker in HCC after curative resection.[3]
Determine was the only rapid test that had a high enough sensitivity for detecting HIV exposure in early infancy, but it identified sero reversion later in life than the other tests indicating further investigations.[4]
Predictors of monocyte counts were gestational age, serum folate and season, while eosinophil counts declined with advancing gestation. Reference values adjusted or unadjusted for identified predictors were different from those of pregnant and non-pregnant white

women reported in the literature. Gravidity, season and micronutrient status influence White Blood Cells (WBC) counts during pregnancy and therefore are of physiological and clinical importance. WBC reference values in the literature were not applicable obviating the need for local reference values.[5] Hematopoietic disturbances are common in patients with HIV-1 infection. Activated immune cells and specific cytokines such as Interferon Gamma (IFN gamma) and Tumor Necrosis factor α (TNF-α) are involved inhibiting hematopoiesis.[6] The CD4 cell count was not a good surrogate for prediction of immunologic status of HIV-positive cancer patients during radio therapy.[7]

On multivariate analysis, low NLCR remained a significant predictor for HIV infection (odds ratio, 0.49; 95% confidence interval, 0.264-0.912; p=0.024). No significant differences were observed in clinical manifestations, radiographic findings, and indirect hemagglutination titer between the 2 groups. HIV-infected patients with amoebic liver abscess tended to have a lower NLCR than non-HIV-infected comparators.[8] The Receiver-Operating Characteristic (ROC) curve for NLCR predicting mortality showed an Area Under the Curve (AUC) of 0.701. This was better than the AUC for the neutrophil count, WBC count, lymphocyte count and CRP level (0.681, 0.672, 0.630 and 0.565, respectively). NLCR on admission at the emergency department predicts severity and outcome of Community Acquired Pneumonia (CAP) with a higher prognostic accuracy as compared with traditional infection markers.[9] Recently, the derived NLCR has been proposed as an easily determinable prognostic factor in cancer patients. Further validation of this easily available parameter in prospective studies and as a potential stratification tool in clinical trials are required. Glasgow Prognostic Score (GPS), mGPS, Prognostic Index (PI) and Prognostic Nutritional Index (PNI) are independent prognostic factors for survival of HIV patients with Nonhodgkin Lymphoma (NHL).[10]

HbsAg

Hepatitis B Virus (HBV) infection continues to be a serious global health problem. During the course of HBV vaccination, C-Reactive Protein (CRP) are elevated in term infants without sepsis. HBV vaccine is responsible for CRP elevation in term infants after vaccination at birth. Evaluating CRP response to HBV vaccine at birth in term infants should be considered in differentiation of early neonatal sepsis to avoid unnecessary antibiotic use.[11] HBV infection is still one of the leading causes of cirrhosis and HCC worldwide. Liver biopsy is the gold-standard method to assess the severity of liver fibrosis, but the invasive nature of this method limits its usage. Currently, noninvasive parameters are utilized to estimate liver histology. Mean Platelet Volume (MPV) and Red Cell Distribution Width (RDW) values are significantly higher in HBV infected patients, associated with severity, and can be defined as independent predicting factors in hepatic fibrosis. Further studies are required to determine the associations between MPV and the severity of fibrosis in HBV infected patients.[12]

The HBV infected and control group showed no difference in NLCRs while there was a significant difference in terms of Aspartate Aminotransferase to Platelet Ratio Index (APRI) scores ($P < 0.001$). Multiple logistic regression analysis revealed that the only independent predictive factor for liver fibrosis in Chronic Hepatitis B (CHB) was platelet count. APRI score was significantly higher in cirrhotic than in non-cirrhotic patients. However, this significance was not confirmed by multiple logistic regression analysis. The optimum APRI score cut-off point to identify patients with cirrhosis was 1.01 with sensitivity, specificity, positive predictive value and negative predictive value of 62% (36%-86%), 74% (62%-83%), 29% (13%-49%) and 92% (82%-97%), respectively. In addition, correlation analyses revealed that NLCR has a negative and significant relationship with Histological Activity Index (HAI). NLCR ratio was negatively correlated with HAI. APRI score may be useful to exclude cirrhosis in CHB patients.[13] Mean NLCR ratio levels were notably lower in patients with advanced fibrosis when compared with patients with no/minimal fibrosis. The mean value of APRI was markedly higher in cases with advanced fibrosis compared to those with no/minimal fibrosis. Reduced levels of the peripheral blood NLCR ratio were found to give high sensitivity, specificity and predictive values in CHB patients with significant fibrosis. The above observations suggests that the NLCR ratio could be used as a novel noninvasive marker of fibrosis in patients with CHB.[14]

NLCR has been proposed to predict prognosis of HCC. However, the cut-off values are empirical. Preoperative elevated NLCR significantly increases the risk of recurrence in patients who underwent Liver Transplant (LT) for HCC. Patients with both NLCR≥3 and tumor number >3 are not a good indication for LT. Score model may aid in the selection of patients that would most benefit from transplantation for HCC.[15] Univariate and multivariate analysis demonstrated that NLCR ≥ 4, is a significant predictors of tumor recurrence in HCC patients. A preoperative elevated NLCR significantly increased the risk for tumor recurrence in HCC patients after LT.[16]

HCV

Significant rise of CD8+, CD28- cells, Natural Killer (NK) cells and NK-T lymphocytes was demonstrated in hepatitis group. Several correlations were noticed between various cell subsets studied in virus C infected children. Studies show that HCV infection affects child immunity at systemic level. Cellular alterations are detectable by means of Flow Cytometry. Evaluation of its parameters might have predictive value in antiviral treatment.[17] HCV infection may be associated with thrombocytopenia and increased iron stores in patients receiving medical care. Previously undiagnosed HCV

seropositivity has little effect on the CBC and body iron stores but appears to perturb the response to an inflammatory stimulus, causing reduced rather than increased circulating CRP concentrations and increased rather than decreased transferrin concentrations.[18]

In the subgroup analysis, higher NLCR (≥1.42) (odds ratio, 0.494, P = 0.038) was an independent poor predictor of Sustained Virological Response (SVR) in genotype 2 patients but was not in genotype 1 patients. NLCR is a simple and easily accessible marker to predict response to peginterferon plus ribavirin therapy for chronic hepatitis C genotype 2.[19]

MATERIALS AND METHODS

50 patients in the age group of 28-68 years consisting of males and female were selected for this study. All 50 patients attended the Infectious Diseases clinic and the control group patients were selected from those attending the routine Master Health Check up. The main aim of this study was to find out the association between each Viral infection viz HbsAg, HCV and HIV and haematological parameters, WBC, ESR, PLT and NLCR ratio between patients and normal controls.

Vitros EQI analyser was used for screening HbsAg, HCV and HIV. Siemens Advia 2120i analyser was used to measure CBC and the results obtained were validated using controls supplied by the company.

Inclusion Criteria

Patients who attended infectious diseases clinic and who have viral infections like HbsAg, HCV and HIV and routine Master Health Checkup patients who were investigated for CBC were included in the study.

Exclusion Criteria

All other patients attending the infectious diseases clinic and who were not infected by HbsAg, HCV and HIV were excluded.

STATISTICAL ANALYSIS

Critical ratios (CR)[20] were calculated using sample mean and Standard Deviation (SD) in comparison with population mean.

CR was calculated using the formula

$$CR = \frac{\text{Difference in Means}}{\text{Estimate of the standard Error of Mean}}$$

RESULTS

Table I Statistical Parameters Mean, SD, CR & P (Controls Vs Patients)

	Analytes	Control Mean	Patient		Critical ratio	Probability
			Mean	SD		
HbsAg (n=50)	WBC	7.93	8.12	2.73	0.49	>0.10
	ESR	7.31	19.92	26.47	3.371	<0.000001
	PLT	257.12	237.08	76.68	0.733	>0.10
	NLCR	2.28	3.99	4.84	-2.496	<0.02
HCV (n=15)	WBC	7.9	7.79	1.94	0.219	>0.10
	ESR	7	18.57	18.17	2.46	<0.01
	PLT	193.4	261.87	50.37	5.260	<0.000001
	NLCR	3.43	2.15	0.63	1.445	>0.10
HIV (n=15)	WBC	7.79	7.95	3.46	0.1797	>0.10
	ESR	7	22.5	26.85	2.23	<0.05
	PLT	261.87	222.27	61.12	2.51	<0.01
	NLCR	2.15	2.26	1.66	0.256	>0.10

Table I shows the statistical parameters Critical Ratio and probability along with Mean & SD. A higher significant association was found for ESR in HbsAg infection (P <0.000001) and a moderate association in the case of HCV and HIV infections (P<0.02 and <0.05 respectively). While no significant exists for WBC in all types of infections, PLT shows a highly significant correlation in the case of HCV and a moderate significant in HIV infection. These observations indicate that ESR and PLT are indeed useful haematological indices for the diagnosis of HbsAg, HCV and HIV infected patients. NLCR was found to be useful only in the diagnosis of HbsAg as it shows an inverse correlation (P<0.02)

DISCUSSION

Generally haematological indices are altered in infections involving HbsAg, HCV & HIV. There are also many other inflammatory markers such as CRP, CD counts to diagnose infections involving the above viruses. Lymphocytic enzymes are said to decrease in all HIV infections, but this study was only to evaluate the clinical usefulness of ESR & PLT in the diagnosis of HbsAg, HCV and HIV infections. [2] NLCR remains as a significant predictor of HIV infection and it is found to be a usual marker to predict severity of infection on admission and also found to be useful in cancer patients.[10] However, this study finds its usefulness only in the case of HbsAg infection. Studies have shown that APRI is a more useful parameter than NLCR in general infections, but this study has found its usefulness only in the diagnosis of HbsAg infections.[13] NLCR is also found to be useful to diagnose in tumor recurrence in HCC patients.[16] This study has strongly established the

clinical usefulness of ESR and PLT in the diagnosis of infection caused HbsAg, HIV and HCV.

CONCLUSION

The outcome of this study strongly suggests that among the various individual counts done in haematology in infections involving HbsAg, HCV and HIV, ESR and platelets indices are found to be more useful for diagnostic and prognostic purposes as they show associations to such infections between controls and patients. Further the above associations were strongly observed as per the increase in ESR in HbsAg and HIV and increase in platelets in case of HCV. Alterations in NLCR was observed with significant increase in HbsAg and decrease in HCV infections. More studies are requested to confirm our observations with large number of patients and to suggest a definitive routine haematological tests for the diagnosis of infectious diseases involving the above three viruses.

Conflict of Interest: None

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