ORIGINAL RESEARCH PAPER

Volume-7 | Issue-10 | October-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY ON THE USEFULLNESS OF ACTIVATED LYMPHOCYTES AND LYMPHOCYTE COUNT IN PREDICTING EPSTEIN-BARR VIRUS INFECTIOUS MONONUCLEOSIS.

Pathology

Dr. M. Indumathy Deputy Director, King Institute Of Preventive Medicine And Research, Guindy, Chennai. 600 026.

Dr. R. Muthukrishnan* Associate Professor Of Pathology, A.C.S. Medical College, Vellappanchavadi, Chennai. 600 077 *Corresponding Author

Dr. T. M. Karthikeshwaran DNB Paediatric Resident Vijaya Health Centre, Vadapalani, Chennai. 600 026.

Dr. Harshavardhini S Postgradute Student, Department of pathology, Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai. 600 116.

ABSTRACT

INTRODUCTION: Infectious mononucleosis (IM) is caused by Epstein-Barr virus(EBV) commonly among adolescents and children presenting with fever, malaise, sore throat, palatal petechiae, enlarged tonsils, cervical lymphadenopathy, lymphocytosis with atypical lymphocytes in blood, hepatosplenomegaly, jaundice and rarely splenic rupture. The present study analysed the predictive diagnostic accuracy of total leucocyte count, absolute lymphocyte count and percentage of atypical lymphocytes in the blood to diagnose IM

AIMS AND OBJETIVES:

- To evaluate the clinical usefulness and predictive value of blood parameters- lymphocytosis and presence of atypical lymphocytes in diagnosing Infectious mononucleosis.

METHODOLOGY: This study was conducted among 898 patients with serological report for EBV, blood count reports, and with clinical signs & symptoms suggestive of Infectious Mononucleosis over a 5 year period from January 2014 to August 2018.

CONCLUSION: Evaluation of blood parameters namely lymphocytosis, atypical lymphocytes, and WBC to lymphocyte ratio could significantly help in the diagnosis of Infectious mononucleosis but cannot replace serology.

KEYWORDS

Infectious mononucleosis (IM), Epstein-Barr virus (EBV), lymphocytosis, atypical lymphocytes, serological test (EBV- IgG-Elisa).

INTRODUCTION:

Infectious mononucleosis (IM) is a clinical syndrome common among adolescents and children in the age group of 10 to 30 years, caused by Epstein-Barr virus (EBV). Signs and symptoms of IM include fever, malaise, sore throat, palatal petechiae, enlarged tonsils, cervical lymphadenopathy, lymphocytosis with presence of atypical lymphocytes in blood, hepatosplenomegaly, jaundice[1] and rarely splenic rupture[2].

EBV is a Herpes virus, replicating predominantly in B-lymphocytes of the reticuloendothelial system and also in the epithelium of pharynx and salaivary glands[3]. Incubation period is 4 to 8 weeks and spread of infection is primarily by saliva. In acute infection, heterophile antibodies that agglutinate sheep erythrocytes are produced (Paul-Bunnell and Monospot tests). Antibodies to viral capsid antigen namely VCA-IgG and VCA-IgM are produced much earlier than heterophile antibodies, and these antibodies are more specific for EBV associated IM. The VCA-IgG antibody persists past the stage of acute infection and signals the development of immunity[4].

Diagnosis in primary care setting relies on physical examination looking for typical signs and symptoms combined with routine blood count. Hoagland's criteria[5] for the diagnosis of infectious mononucleosis are the most widely cited:

- At least 50 percent lymphocytes
- At least 10 percent atypical lymphocytes
- In the presence of fever, pharyngitis, and adenopathy confirmed by a positive serologic test.

Differential diagnosis for IM includes streptococcal pharyngitis, viral pharyngitides, acute CMV infection, toxoplasmosis and acute HIV infection and warrants appropriate serological testing since HIV, Toxoplasmosis and acute CMV are associated with significant pregnancy related complications.

The present study is to analyse the predictive diagnostic accuracy of blood parameters namely total leucocyte count, absolute lymphocyte count and percentage of atypical lymphocytes in the blood.

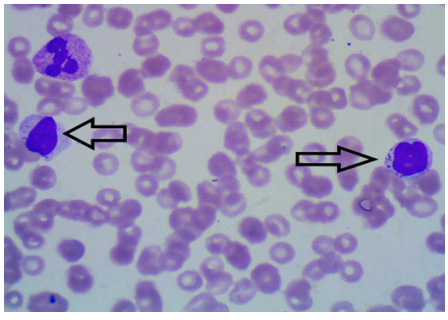

FIGURE-1: Activated/ atypical lymphocytes shown by arrows – 100x magification

AIM OF THE STUDY:

To evaluate the clinical usefulness of blood parameters of lymphocytosis and presence of atypical lymphocytes in diagnosing Infectious mononucleosis.

OBJECTIVES:

To ascertain the predictive value of blood parameters –lymphocytosis and atypical lymphocytes in the diagnosis of IM.

MATERIALS AND METHODS:

This study was conducted among 898 patients with serological report for EBV , blood count reports, and with clinical signs & symptoms suggestive of Infectious Mononucleosis (Inclusion criteria for this study), over a period of last 5 years from January 2014 to August 2018. Patients' records with positive serology but without blood counts were not included in this study (Exclusion criteria).

The lymphocyte count (>4000 cells/uL)[6], %atypical lymphocytes (>10%)[7], and total leucocyte counts (>11,000 cells/uL) of serology positive and negative patients were collated & tabulated.

The data was statistically analysed using Microsoft Excel for positive and negative predictive diagnostic values of total count, absolute lymphocyte count, and percentage atypical lymphocytes for the diagnosis of Infectious Mononucleosis and the results were presented.

RESULTS:

Of the 898 patients 62 patients (6.9%) tested positive for EBV IgG-Elisa .Of the 62 patients 32 were males and 30 were female with ratio of 1: 1.06. The mean age of serology positive patients was 22 years (range: 9 to 56 years). Of the 62 cases, 41(66%) had elevated total leucocyte count, 49(79%) had an elevated absolute lymphocyte count and 49(79%) had an elevated percentage of atypical lymphocytes. (Table-1)

Table- 1: Distribution of sero positive and sero negative patients according to haematological parameters.

HEMATOLOGICAL PARAMETERS	SERO POSTIVE		SERO NEGATIVE	
	Above reference range	Within reference range	Above reference range	Within reference range
TOTAL COUNT-TLC	41	21	108	728
ABSOLUTE LYM COUNT-ALC	49	13	42	794
ATYPICAL LYMP %	49	13	50	786

The data was analysed and sensitivity, specificity and positive and negative predictive values were calculated as follows (Table-2)

Table-2 Sensitivity, Specificity and Positive and Negative Predictive Values of parameters considered

HEMATOLOGICAL PARAMETERS	POSITIVE PREDICTIVE VALUE	NEGATIVE PREDICTIVE VALUE	SENSITIVITY	SPECIFICITY
TOTAL LYMPHOCYTE COUNT	27.5	97.1	66.1	87.1
ABSOLUTE LYMPHOCYTE COUNT	53.8	98.4	79.0	95.0
ATYPICAL LYMPHOCYTE %	49.5	98.4	79.0	94.0

All the three haematological parameters considered in this study were found to be significantly associated with infectious mononucleosis as shown by significant p value (<0.05) (Table-3)

Table-3: p values of haematological parameters

HEMATOLOGICAL PARAMETERS	p value	Interpretation
TOTAL LYMPHOCYTE COUNT	1.66 x 10-7	Significant
ABSOLUTE LYMPHOCYTE COUNT	1.77 x 10-77	Significant
ATYPICAL LYMPHOCYTE %	2.92 x 10-70	Significant

DISCUSSION:

Infectious mononucleosis (IM) is a clinical syndrome caused by Epstein-Barr virus (EBV). It is common among adolescents and children in the age group of 10 to 30 years.[1] IM is conventionally diagnosed via serological tests - IgG ELISA for viral capsid antigen.[8]

The limitation of serological studies include cost, prolonged turnaround time due to pooling of test samples in specialised laboratories, availability of test in rural and semi urban areas and logistics involved in transportation of samples to referral labs.[9] Hence alternative methods for the diagnosis of IM become imperative.

The present study compares the useful of haematological parameters like total leukocyte count, absolute lymphocyte count and percentage of atypical lymphocytes in the diagnosis of IM. Increased absolute lymphocyte count and percentage of atypical lymphocytes have high sensitivity (79%) while absolute lymphocyte count has highest specificity (95%). This finding is similar to findings of study by Biggs TC et.al[6] and Lennon et.al[10]

The importance of early diagnosis of IM lies in the fact that it can lead to massive enlargement of the spleen which in turn can be ruptured in those involved in contact sports. Splenic rupture can result in massive intra-abdominal bleed with high mortality rate.[11] (Figure 2)

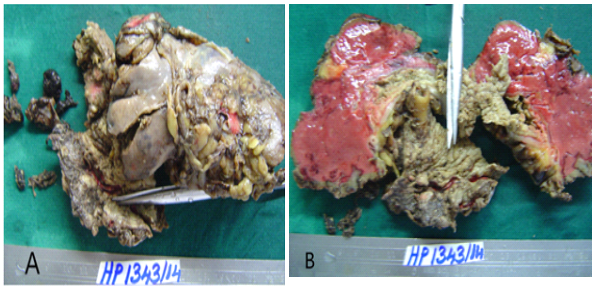

FIGURE 2 A & B – RUPTURED SPLEEN, EXTERNAL AND CUT SURFACE

CONCLUSION:

Evaluation of blood parameters namely lymphocytosis, atypical lymphocytes, and WBC to lymphocyte ratio could significantly help in the diagnosis of Infectious mononucleosis and to rule out non EBV associated IM and reduce the need for confirmatory serological tests which do have the constraints of cost, availability of the test and logistics involved in transporting sample to the specialised laboratories. Moreover should the clinical condition warrants, serological tests can be done with the retained stored blood sample. Further appropriate counselling can be provided to the patients suspected to have been infected with EBV and having splenomegaly by advising them to avoid participating in collision sports and thus avoiding splenic rupture

REFERENCES:

1. Jenson HB, Epstein Barr Virus, In: Kleigman RM, Stanton BF, St Geme J, Schor NF, ed. Nelson Textbook of Paediatrics, 20th edition. Philadelphia; WB Sanders 2015; 1586-1590
2. Dommerby H, Stangerup SE, Stangerup M, Hancke S. Hepatosplenomegaly in infectious mononucleosis, assessed by ultrasonic scanning. J Laryngol Otol 1986; 100:573-9.
3. Andersson JP. Clinical aspects of Epstein-Barr virus infection. Scand J Infect Dis Suppl 1991;80:94-104.
4. Aronson MD, Komaroff AL, Pass TM, Ervin CT, Branch WT. Heterophil antibody in adults with sore throat: frequency and clinical presentation. Ann Intern Med 1982; 96:505-8
5. Hoagland RJ. Infectious mononucleosis. Prim Care 1975; 2:295-307
6. Biggs TC, Hayes SM, Bird JH, Harries PG, Salib RJ. Use of the lymphocyte count as a diagnostic screen in adults with suspected epstein–barr virus infectious mononucleosis. The Laryngoscope. 2013 Oct;123(10):2401-4
7. Sumaya CV, Ench Y. Epstein-Barr virus infectious mononucleosis in children: I. Clinical and general laboratory findings. Pediatrics. 1985 Jun 1;75(6):1003-10
8. Tcherniaeva I, den Hartog G, Berbers G, van der Klis F. The development of a bead-based multiplex immunoassay for the detection of IgG antibodies to CMV and EBV. Journal of immunological methods. 2018 Jul 26.
9. Kasifoglu N, Oz S, Dinleyici EC, Us T, Bor O, Durmaz G, Akgun Y. Comparison of Methods Used for the Diagnosis of Epstein-Barr Virus Infections in Children. Polish Journal of Microbiology. 2018 Jan 1;67(1):81-8
10. Lennon P, O'Neill JP, Fenton JE, O'Dwyer T. Challenging the use of the lymphocyte to white cell count ratio in the diagnosis of infectious mononucleosis by analysis of a large cohort of Monospot test results. Clinical Otolaryngology. 2010 Oct;35(5):397-401.
11. O'Connor TE, Skinner LJ, Kiely P, Fenton JE. Return to contact sports following infectious mononucleosis: the role of serial ultrasonography. Ear Nose Throat J 2011;90:E21–E24.