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POTENTIAL USE OF HAEMATOLOGICAL DATA IN THE DIAGNOSIS OF TUBERCULOSIS IN CHILDREN

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Abstract

ABSTRACT: Bacteriological/microbiological diagnosis of tuberculosis (TB) is often difficult in children and despite many recent advances in TB management, we have been unable to identify biomarkers predictive of disease. Previous studies have shown that haematological abnormalities especially anaemia is frequently found in children with TB and few recent studies have found that the ratio of monocytes to lymphocytes (ML ratio) and neutrophil to lymphocyte ratio (NL ratio) are associated with risk of TB disease. In this study we evaluated the haematological parameters of children with TB disease. In addition we describe the relationship between anaemia, ML ratio, NL ratio and clinical status of children with TB.

KEYWORDS : anaemia, ML ratio, haemoglobin, Tuberculosis

MAIN CONTENT

Diagnosing TB in children is often challenging due to paucibacillary nature of disease and the operational constraints of obtaining specimens from children who are unable to generate sputum.[1,2] Haematological indicators such as haemoglobin and other blood indices such as platelet and white blood cell (WBC) counts have been used to as diagnostic and prognostic markers in management of tuberculosis.[1,3,4] The blood monocyte-to-lymphocyte ratio (ML Ratio) and neutrophil to lymphocyte ratio (NL ratio), which are calculated from blood counts has been found to predict progression to TB in both children and adults.[5,6] Given the difficulty of diagnosing tuberculosis in children, we propose that a review of available haematological profiles serve as supplemental investigations and give useful information regarding the child's TB condition. We therefore, analysed the haematological parameters of children with TB disease and investigate the association between anaemia, ML ratio, NL ratio and clinical status. Between 2014 and 2019, we evaluated HIV-negative children aged 15 and under who had either confirmed or clinically diagnosed TB, from two hospitals in Chennai, Tamil Nadu, south India. The haematological indices [haemoglobin, total white cell count (WBC), total lymphocytes, total monocytes, total neutrophils], ML ratio, and NL ratio were analysed between children with TB disease and control children. Control children (n=393) had similar median age (6 years, IQR: 3 months – 15 years) and sex (male: 57%), had no signs and symptoms suggestive for TB disease and had negative Tuberculin skin test (TST). These children presented to hospital for elective surgeries or non-infective/ non-autoimmune conditions. We screened 2078 children of which 593 children were included in the analysis. The median age was 5.8 years (range 3 months–15 years) and 55% of children were under 6 years of age. 59% were males. Among the 593 children, 33.7% (200/593) were diagnosed with TB, of which 38% (76/200) were bacteriologically confirmed and 62% (124/200) were diagnosed clinically (radiological features and/or clinical features suggestive of TB). 32.4% (192/593) were anaemic. We found anaemia (Figure 1) was more common in children with TB [49% (98/200)] in comparison to children without TB [24% (94/393)] (p value <0.001). TB children also had elevated neutrophil count, monocyte count and lower lymphocyte count. (Table 1) Significant difference ($p < 0.001$) was also noted in Median ML ratio [0.2 (0.14 - 0.31) in TB disease and 0.15 (0.11 - 0.2) in controls] and NL ratio [1.43 (0.86 - 2.2) in TB disease and 0.86 (0.61 - 1.33) in controls] (Table 1). Other haematological parameters are shown in Table 1.

Table 1: Haematological profile

Haematological Parameter	Controls (n=393)	TB (n=200)	p-Value
Haemoglobin *median (IQR)*	11.9 (11 - 12.6)	11 (9.55 - 11.95)	<0.001
WBC *median (IQR)*	10.1 (8 - 12.3)	10.35 (8.5 - 12.9)	0.061
Lymphocytes *median (IQR)*	4.01 (3.19 - 5.44)	3.65 (2.71 - 4.8)	0.001
Monocytes *median (IQR)*	0.64 (0.48 - 0.86)	0.73 (0.53 - 1)	<0.001
Neutrophils *median (IQR)*	3.8 (2.72 - 5.34)	4.81 (3.6 - 6.52)	<0.001
M:L Ratio	0.15 (0.11 - 0.2)	0.2 (0.14 - 0.31)	<0.001
N:L Ratio	0.86 (0.61 - 1.33)	1.43 (0.86 - 2.2)	<0.001

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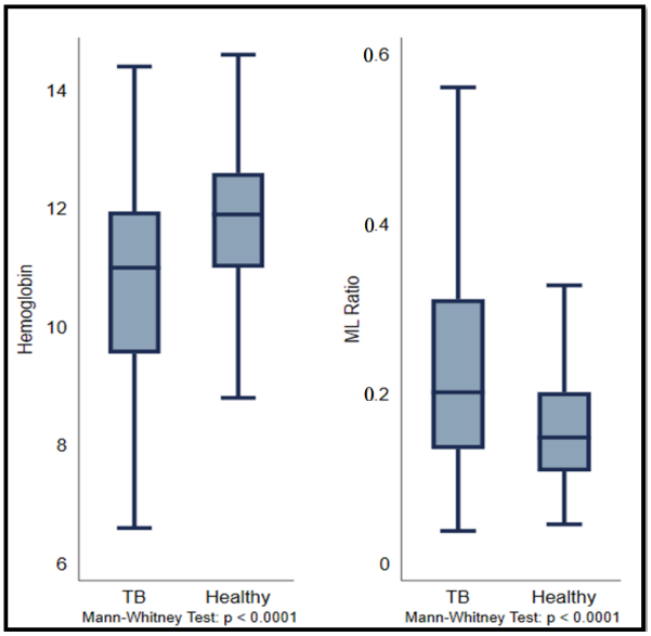

Figure 1 : Anaemia among TB and healthy children

Our findings demonstrate significant haematological abnormalities in children with TB, implying that these indices might be useful as additional tools in determining if a child has TB disease. This work further adds to the growing body of research on the ML and NL ratios as adjunct biomarkers for tuberculosis diagnosis in children, which is critical given the difficulty of obtaining respiratory samples for microbiologic diagnosis in children with Tuberculosis.[5-7] The ML and NL ratios, which may be easily calculated from standard differential complete blood counts, may be useful in the diagnosis of children with TB disease.

Our findings may not be applicable to all paediatric populations because our group was confined to children who presented to the hospital with any disease. We also excluded those with CNS tuberculosis. However, our ability to detect variations in haematological indices between the TB and unlikely TB groups was strong. Furthermore, including children with clinically diagnosed TB allowed us to investigate the efficacy of these markers in children with unconfirmed or presumptive TB.

In conclusion, haematological analysis, particularly ML ratio and NL ratio, might be a valuable adjunct diagnostic and predictive tool for TB disease in contexts where bacteriological confirmation is difficult to acquire.

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