

UNIVERSITI TEKNOLOGI MARA

**CLINICAL UTILITY OF
IMMATURE GRANULOCYTES
IN BACTERAEMIA**

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ABSTRACT

Background: The accuracy and clinical utility of automated white blood cell (WBC) differential counts have been validated in numerous studies, and these are widely used in routine practice. The immature granulocyte (IG) percentage is the new WBC differential count which potentially be a good, cost-effective parameter in patients with suspected bloodstream infection (BSI). In this study, we determined the clinical utility of IG and its correlation with other established inflammatory markers including C-reactive protein (CRP) and Absolute neutrophil count (ANC).

Methods: A 22-month cross-sectional study involved a total of 178 specimens from patients admitted to Pusat Pakar Perubatan Universiti Teknologi MARA (PPUiTM). Blood in an EDTA container was obtained for the results of differential count (IG and ANC) using the automated analyser Sysmex XN-550. Another sample in the present study involves CRP & Blood Culture and Sensitivity (C&S) results. The socio-demographic data was also gathered. The correlation between parameters (IG, CRP and ANC) were evaluated in the context of bacteraemia populations.

Results: Majority of the samples were from patients over the age of 50 years (81.5%), males (66.9%) and Malays (86%). Most bacteraemia patients had elevated IG (66%), ANC (76%) and CRP (90%) levels above the upper limit of normal. There was no significant difference in demographic characteristics (i.e. age groups, gender, and ethnicity) found with increases in IG, ANC, and CRP in bacteraemia. Based on Spearman correlation test the correlation of IG with CRP ($p < 0.001$) and IG with ANC ($p < 0.032$) were found to be significant, however the correlations were both weak ($r_s = 0.257$, $r_s = 0.16$).

Conclusions: The present study revealed that IG is comparable to ANC and CRP in patients with bacteraemia, thus potentiated to be an alternative inflammatory marker other than CRP and ANC. Incorporating the immature granulocyte assay into an algorithm that includes additional laboratory parameters may improve infection or bacteraemia prediction.

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CHAPTER ONE

INTRODUCTION

1.1 Background

Immature granulocytes (IG) incorporate immature cells of granulocytic lineages, including metamyelocytes, myelocytes, and promyelocytes, which are easily recognized and reported by automated haematology analysers as absolute IG count and percentage altogether. The IG is normally absent from peripheral blood, and an increased IG may occur with neutrophilia as a consequence of bacterial infection, inflammatory process, malignancy, trauma and pregnancy. The elevation of IG without neutrophilia may be seen in elderly patients, neonates and patients with myelosuppression. In these situations, an isolated increase in IGs (>2%) can be useful for recognizing an acute infection, even when the infection is not clinically suspected. (Buttarelli & Plebani, 2008).

Polymorphonuclear neutrophil (PMN) granulocytes are the first line of defence against infections. In bacteraemia, the invasion of the bloodstream by microorganisms has led to local proliferation and release of virulence factors into the bloodstream (Vijayan et al., 2017). Chemotactic factors produced by infectious agents, as well as those released as a result of their initial contact with phagocytes and other immune system components will signal the recruitment of additional PMN to infection sites during the inflammatory response (Nierhaus et al., 2013). Furthermore, the induction of granulocyte colony stimulating factor (G-CSF) during infection has increased the rate of proliferation of granulocytic progenitor cells including promyelocyte, myelocyte and metamyelocyte stages (Panopoulos and Watowich, 2008). This has led to the occurrence of circulating IG in the peripheral blood. Since healthy people do not have IG in their blood, the presence of IG in the peripheral circulation indicates significantly increased bone marrow activation, as seen in sepsis.

Bloodstream infections (BSIs) represent a growing public health concern. Early detection of bacteraemia facilitates the diagnosis of sepsis, timely initiation of antimicrobial therapy, reduces morbidity and mortality rate, and decreases healthcare expenses. A positive blood culture is an appropriate, acceptable standard in detecting