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Comparative Analysis of *Neutrophil Counts* in Haemoglobin Variants (AA, AS, SC and SS)

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Abstract:
Objective*: The study was a follow-up to an earlier study done to compare the haematological indices of some Hb Genotype variants. The range of neutrophil counts of subjects with different haemoglobin genotypes was the subject of the present study. The objective was to highlight the differences in a single haematotlogical index in the Hb genotype variants which may help in identifying points of departure in the pathophysiology of such variants. Secondly, to help in planning interventions and predicting outcomes.*
Study Design*: The same outpatient population base employed for the earlier study was analyzed. The study covered the period between 2012 and 2022 (20 years). The total and differential white blood counts of three hundred randomly selected patients (150 males and 150 females) aged between 1 and 25 years were scrutinized. Only patients presenting with (confirmed) malaria were included for comparable morbidity. Patients with co-existing persistent HbF were excluded to avoid misinterpretation of the generated data.*
Results*: There were significant differences between the neutrophil counts of the haemoglobin genotype variants reviewed in the study.*
Conclusion*: Haemoglobin genotyping should be routinely ordered alongside the other tests in areas of high prevalence of haemoglobinopathies and the results interpreted with reference to the Hb Genotype.*
Key words: *Neutrophil Count; Neutrophilia; Haemoglobin Genotype;*

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I. Introduction:

The present study was a follow-up to an earlier (pilot) study on comparison of the haematological indices in haemoglobin genotype variants (1). Observations coupled with literature review during the past two decades since the earlier study showed that neutrophil counts vary in the different haemoglobin genotypes under similar conditions (2). Some studies have considered specific haematological indices in relation to Hb genotype variants (3). However, there is still a relative paucity of comparative studies simultaneously analyzing the haematological indices of different haemoglobin genotypes. Moreover, in many centres, total and differential white cell counts are usually performed without reference to the haemoglobin (Hb) genotype and vice versa except in obvious cases such as HbSS. In areas where haemoglobinopathies are rampant, such as Africa, knowledge of genotype related differences in haematological profiles may be an additional tool in planning interventions and predicting outcomes.

II. Materials And Methods:

Three hundred and sixty (360) individual results of haemoglobin genotype, total and differential white blood counts were obtained from data generated by a standard laboratory.

III. Results:

The genotype and neutrophil counts were the indices of interest. They were retrieved from the available records,collated and tabulated (Table 1).

Statistical Analysis:
The results were subjected to statistical analysis using ANOVA and Student's t-test. The neutrophil counts were presented graphically as a function of the respective haemoglobin genotypes and displayed in form of column charts (Figure 1) for clarity of comparison. Table 1 shows the average values of the neutrophil counts obtained for the different haemoglobin genotypes.

IV. Discussion:

Sickle cell disease (SCD) is a blood disorder characterized by the presence of abnormal haemoglobin (Hb) molecules resulting in abnormally shaped (sickled) red blood cells (RBCs) with greatly reduced life span (4). It is considered the most common single gene mutation affecting millions of people worldwide (5). In several studies, the severity of sickle cell disease (SCD) has been found to be significantly associated with elevated leukocytes count (6). The studies have however been largely general rather than comparative as in the present study although a few studies have also compared the leucocyte counts in HbAA, HbAS and HbSS patients (7).
In the present study, Hb AA subjects had the lowest average neutrophil counts while the HbSS variants had the highest average neutrophil counts respectively.

Haemoglobin genotypes and Neutrophil Counts:

The results obtained in the present study correlated significantly with those earlier reported (8). For instance, the neutrophil count was observed to correlate well with results obtained in earlier studies. The highest level was consistently observed in HbSS subjects (1). This observation has been attributed to some factors intrinsic to the HbSS genotype such as: a) Continuous bone marrow stimulation as a result of the perennial haemolysis.
b) Frequent infections due to the poor handling of encapsulated bacteria by HbSS subjects.
c) Immune mediated responses of granulocytes to various pathogens (9)

The average neutrophil count in Hb SC subjects in this study was higher than that in HbAS but lower than the average value for HbSS. The neutrophil counts in AA and AC variants were not significantly different and were within normal limits (Table 1 and Figure 1). However, there were significant differences between the HbAA group and the other variants. Generally, the neutrophil count was in the following ascending order in the corresponding variants: HbAA < HbAC< HbAS< HbSC < HbSS. These observations seem to suggest that the presence of the HbS allele plays a significant role in the pathophysiological processes leading to elevations of the neutrophil count. On the contrary, the HbA allele seems to have a moderating effect on the pathological processes triggered by the presence of the HbS allele and hence on the neutrophil count as well.

V. Conclusion:

Observed differences in haematological indices among the population could be partly explained based on genotype differences among other factors. Reasonably accurate predictions of possible profiles and interpretations of the haematological indices of subjects with the various Hb genotypes could also be made. The Hb genotype should be routinely ordered alongside the other tests and the results interpreted with reference to the Hb Genotype. For instance, a relatively high neutrophil count may not necessarily translate to acute infection if the genotype is known to be SS and the patient is clinically stable. Such individual may be an HbSS patient in the steady state. There is need for further investigations designed to address other specific haematological indices in relation to the genotypes. It is believed that the results obtained in the present study should be reproducible in larger studies and other settings.

Table 1: Average Neutrophil Counts in Hb Genotype Variants

HBG	NEUTROPHIL COUNT (%)
AA	**45.62**
AC	**46.00**
AS	**48.41**
SC	**50.00**
SS	**51.88**

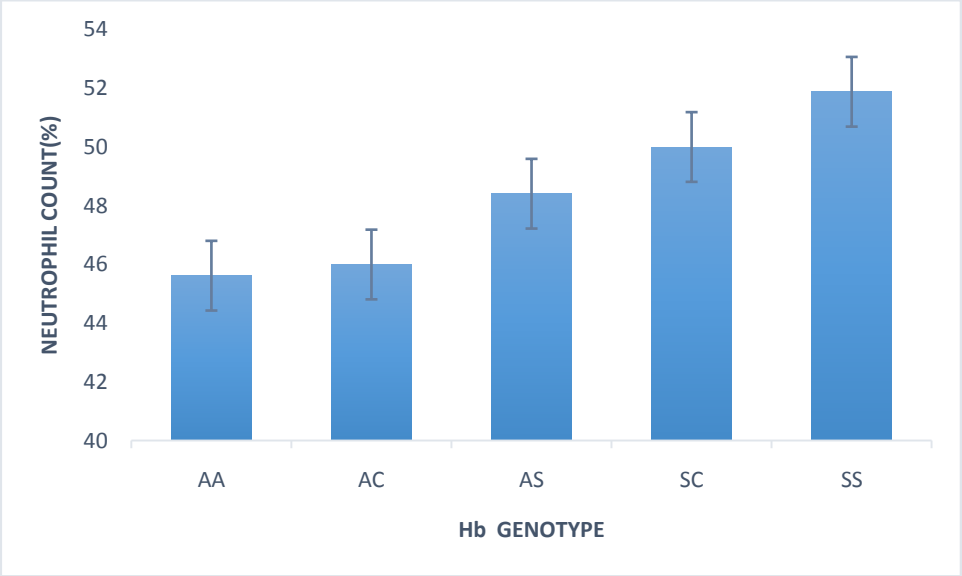

FIGURE 1: Column chart showing neutrophil count of various Hb genotype variants.

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