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CHARACTERIZATION OF RED BLOOD CELL PARAMETERS IN SOUTHEAST ASIAN OVALOCYTOSIS (SAO) AND NON-SOUTHEAST ASIAN OVALOCYTOSIS (NON-SAO) WITH OR WITHOUT THALASSAEMIA/ HAEMOGLOBINOPATHIES

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ABSTRACT

Background: SAO and thalassaemia/haemoglobinopathy traits are phenotypically mild. Coinheritance of these diseases may produce severe hemolysis and ineffective erythropoiesis. This study aims to identify the haematological differences and association between SAO and non-SAO groups with and without thalassaemia/haemoglobinopathy. **Methods:** A cross-sectional comparative study was performed on 424 subjects investigated for thalassaemia/haemoglobinopathies. 212 SAO subjects were selected based on classical SAO morphology from peripheral blood film (PBF). An equal 212 non-SAO subjects were selected by the absence of SAO morphology. The demographic data, complete blood count, haemoglobin analysis, and molecular result testing were reviewed. Data analysis was performed by Chi-square test, student's t-test, and one-way ANOVA. *P*-value < 0.05 was considered significant. **Results:** SAO group had a significantly lower RBC count and higher MCH, MCHC, and RDW as compared to the non-SAO group (4.89 $x10^{12}$/L vs 5.31 $x10^{12}$/L, 24.4-pg vs 23.2 pg, 33.8 g/dL vs 31.8 g/dL, 17.9% vs 15.6%). SAO and thalassaemia/ haemoglobinopathy coinheritance demonstrated significantly higher RBC count and lower MCV and MCH as compared to SAO without the coinheritance (5.03 $x10^{12}$/L vs 4.17 $x10^{12}$/L, 70.4 fL vs 81.1 fL, 23.8 pg vs 28.1 pg). Hb comparison among SAO and thalassaemia/haemoglobinopathy coinheritance revealed non-significant differences except for SAO/β^{+} demonstrated a notable Hb, MCV, and MCH reduction, and RDW increment. **Conclusion:** SAO with β-thalassaemia trait increases the severity of anaemia, hypochromic, and microcytosis. All suspected SAO from PBF with hypochromic and microcytosis should have further testing to exclude thalassaemia/haemoglobinopathy coinheritance as early detection and proper genetic counseling can be offered.

KEYWORDS: Southeast Asian Ovalocytosis (SAO), thalassaemia, haemoglobinopathy, coinheritance, morphology

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CHAPTER ONE
INTRODUCTION

1.1 Research Background

Southeast Asian Ovalocytosis (SAO) and thalassaemia/haemoglobinopathy are two common heritable red cell disorders encountered in Southeast Asian countries[1-5]. SAO arises from a heterozygous mutation in the *SLC4A1* gene that results in defective Band 3 protein on the red cell membrane[6-7]. The homozygous SAO is known to be lethal in utero. Few neonates who survived ex-Utero required intensive intervention[8-9]. Thalassaemia/ haemoglobinopathy, on the other hand, arises from a defective globin gene producing either a quantitative defect (thalassaemia) or a qualitative defect (haemoglobinopathy) in the production of haemoglobin molecules[9-10].

SAO and thalassaemia/haemoglobinopathy, when inherited separately as heterozygous states, are phenotypically mild and do not require any form of treatment[1-3,9-10]. Previous studies suggest a mild presentation[11-12]. Researchers conducted a comparative study among SAO children, who reported a significantly higher incidence of anaemia and increased degree of anisocytosis among SAO children with β-thalassaemia trait[13]. There was a case report on a Malay family with coinheritance of SAO and β-thalassaemia trait, where the mother presented with symptomatic anaemia (shortness of breath, dizziness, quickly fatigue). Subsequently, two of her children were diagnosed with similar coinheritance. The anaemic symptoms affected their quality of daily life[1]. There are other reports on SAO adults with β-thalassaemia traits who had significant hemolysis associated with gallstone disease and haemosiderosis[14-15]. The severity of the complications worsens with age. Younger adults with this coinheritance did not develop clinically significant anaemia; however, complications of ineffective erythropoiesis developed in adulthood, and the older patient had more severe haemosiderosis[14].

Previously, a significantly higher incidence of anaemia in older children and significant complications in adults with concomitant inheritance was observed. This has suggested the importance of excluding concomitant SAO among patients with thalassaemia/ haemoglobinopathy. Medical practitioners should address precautions in populations with a higher prevalence of these conditions, especially when the clinical phenotype is more severe than the expected heterozygous [14]. These patients may benefit from early identification,