I. INTRODUCTION

Southeast Asian Ovalocytosis (SAO) is a hereditary genetic disorder that is inherited in an autosomal dominant manner that impacts the red blood cell (RBC) membrane due to the deletion of codons 400-408 or 27 nucleotides in the exon 11 of the *SLC4A1* gene located on chromosome 17. This mutation results in the misfolding of the transmembrane domain of the SLC4A1 protein. Consequently, the deletion affects the protein's ability to act as an anion exchanger and ultimately disrupts the mechanical stability of RBC, resulting in a rigid RBC membrane (Kimura et al., 2006; Laosombat et al., 2005; Lavinya et al., 2021; Wrong et al., 2002; Yang et al., 2023). The disorder got its name due to its prevalence in numerous populations in Southeast Asia, especially in Thailand, Indonesia, Malaysia, and Papua New Guinea (Mgone et al., 1996; Nixon et al., 2018; Yusoff et al., 2003). A study by Mgone et al. (1996) detecting the occurrence of this genetic deletion recorded that the incidence rate ranges from 5-25% in Melanesia, Indonesia, Papua New Guinea, the southern part of Thailand, and the Philippines. Moreover, while SAO is generally asymptomatic and non-lethal in adult heterozygous individuals, the disorder may cause neonatal jaundice in newborns. It was thought to be lethal in a homozygous state towards both embryos and neonates, and recent papers have shown that some individuals experience mild jaundice, anemia, and gallstones (Bolton-Maggs et al., 2011; Flatt et al., 2020; Lavinya et al., 2021; Picard et al., 2014). Yet, SAO has been reported to confer protection against cerebral malaria, albeit the mechanism of how this benefit emerges is still largely unknown and immensely consists of conjectures (Allen et al., 1999; Kotepui et al., 2023).

The hallmark characteristic of SAO manifests in the presence of oval-shaped RBCs or ovalocytes, cup-shaped RBCs or stomatocytes, and triconcaves RBCs or knizocytes on the peripheral blood smear, which can be seen under the microscope (Garnett & Bain, 2012; Lesesve et al., 2012; Nixon et al., 2018). Although the method is accessible and cost-effective, microscopy is not a definitive diagnostic procedure for SAO for someone who is not properly trained to diagnose SAO, and thus similar to other genetic disorders, SAO detection would also require molecular analysis through

genotyping. A highly trained microscopist who is competent in differentiating RBC morphology and identifying SAO-related cell size and shape alterations is needed to screen for thin blood smears (Mgone et al., 1998; Nixon et al., 2018; O'Donnell et al., 1998). On the other hand, by directly targeting the molecular alteration in the *SLC4A1* gene that gave rise to the genetic disorder using polymerase chain reaction (PCR), the employment of genotyping in this research can act as the gold standard diagnostic approach for SAO (Liu et al., 1995; Yamsri et al., 2021; Wilder et al., 2009). Combining the two would allow an accurate and cost-effective diagnosis of SAO by confirming the presence of ovalocytosis and verifying the disorder's genetic source. Therefore, this research highlights the clinical significance and cost-effectiveness of proper SAO diagnosis and aims to provide prevalence data of SAO in Malinau, North Kalimantan. Along with this, the implementation of microscopy as the main SAO diagnosis method is still highly evaluated and sought for its easier application in areas with less accessibility to a laboratory. Thus, the data obtained from this research will also be utilized to assess the microscope as a diagnostic tool for SAO against PCR by calculating the test screening characteristics. From this, it can be predicted that a microscope will possess a comparable statistical screening characteristic result against PCR and thus, would become an alternative diagnostic tool for SAO.