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REVIEW

A Systematic review on diagnostic methods of red cell membrane disorders in Asia

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Abstract

Membranopathies are a group of inherited blood disorders where the diagnosis could form a challenge due to phenotype-genotype heterogeneity. In this review, the usage and limitations of diagnostic methods for membranopathies in Asian countries were evaluated. A systematic review was done using articles from PubMed, Google Scholar, and EBSCO from 2000 to 2020. Thirty-six studies conducted in seven Asian countries had used different diagnostic methods to confirm membranopathies. In 58.3% of studies, full blood count (FBC), reticulocyte count, and peripheral blood smear (PBS) were used in preliminary diagnosis. The combination of the above three with osmotic fragility (OF) test was used in 38.8%. The flowcytometric osmotic fragility (FC-OF) test was used in 27.7% where it showed high sensitivity (92%–100%) and specificity (96%–98%). The eosin-5-maleimide (EMA) assay was used in 68.1% with high sensitivity (95%–100%) and specificity (93%–99.6%). About 36.1% of studies had used sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) as a further diagnostic method to detect defective proteins. Genetic analysis to identify mutations was done using Sanger sequencing, next-generation sequencing (NGS), and whole-exome sequencing (WES) in 33.3%, 22.2%, and 13.8% of studies, respectively. The diagnostic yield of NGS ranged from 63% to 100%. Proteomics was used in 5.5% of studies to support the diagnosis of membranopathies. A single method could not diagnose all membranopathies. Next-generation sequencing, Sanger sequencing, and proteomics will supplement the well-established screening and confirmatory methods, but not replace them in hereditary hemolytic anemia assessment.

KEYWORDS
Asia, diagnostic methods, hereditary hemolytic anemia, membranopathies, next-generation sequencing

1 | INTRODUCTION

Hereditary hemolytic anemias (HHA) are a heterogeneous group of genetic disorders characterized by increased destruction of circulating red blood cells (RBC), causing mild-to-severe chronic anemia. The intrinsic red cell defects in HHA are due to red cell membrane disorders (membranopathies), red cell enzyme deficiencies (enzymopathies), and hemoglobin disorders (hemoglobinopathies).[1] HHA is clinically characterized by jaundice, recurrent anemia, cholelithiasis, splenomegaly, and hepatomegaly, with variable age at onset and severity.[2,3] In developing countries, HHA is an important cause of morbidity and mortality secondary only to malnutrition and infections.[4]

The RBC membrane cytoskeleton is a multiprotein complex that interacts with phospholipid bilayer via vertical and horizontal interactions. The mutation in genes coding for membrane proteins results in a decrease in RBC permeability and impaired RBC deformability.

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