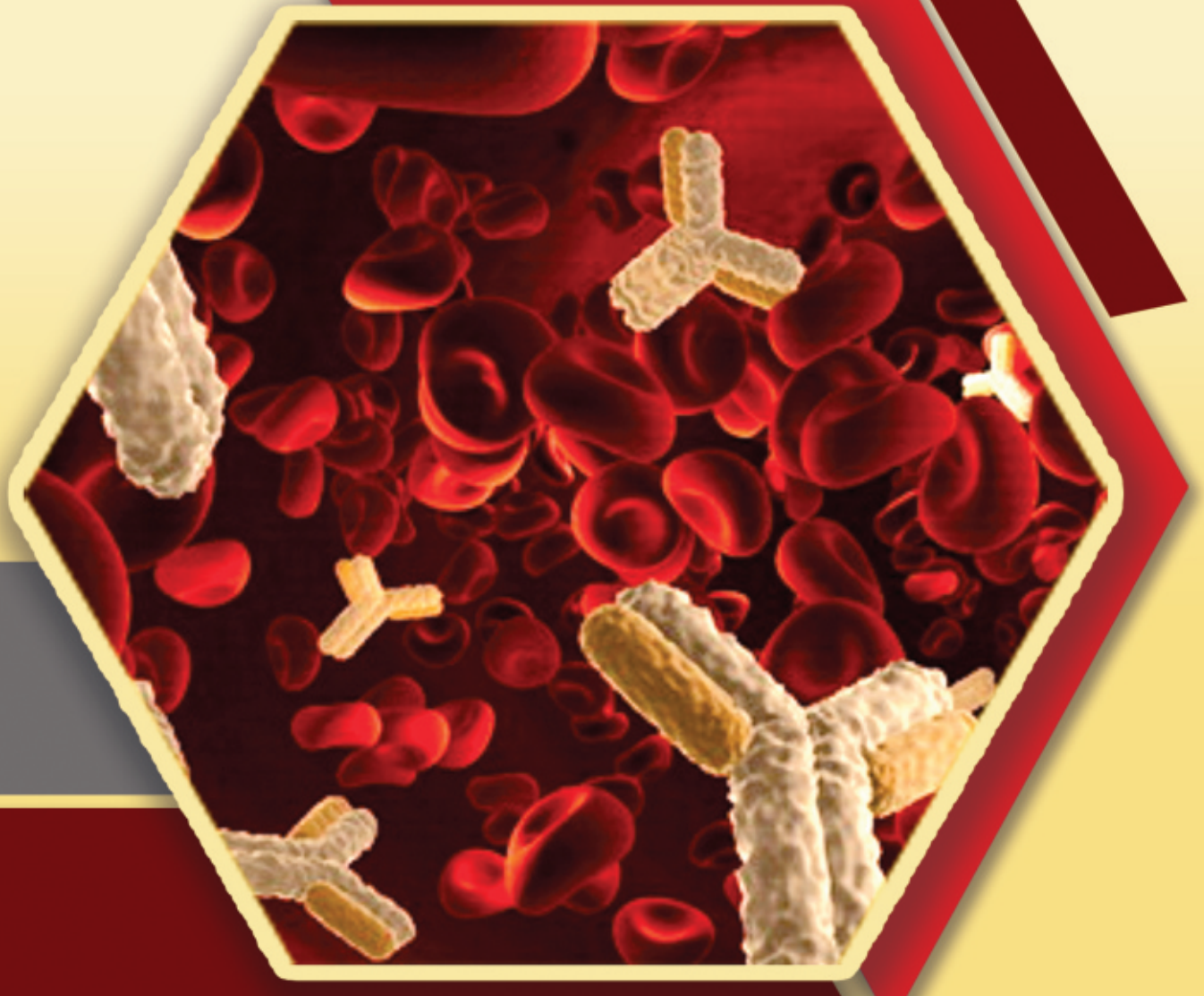
IMMUNOHAEMATOLOGY BULLETIN

Vol. 51 : No 1 Jan-April 2020



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Next-generation sequencing- Improves the diagnosis and management of patients with Congenital anemia

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Introduction

Congenital anaemia (CA) refers to a diverse group of genetically heterogeneous disorders characterized by a variable degree of anaemia ranging from relatively harmless to severe life-threatening, with often unexplained genotype-phenotype correlation [1]. The symptoms of CA include exchange transfusion during early infancy, recurrent blood transfusion, jaundice, hepatosplenomegaly, reticulocytosis, indirect hyperbilirubinemia, cholelithiasis, physical and mental retardation in few cases. CA is caused by mutations in more than 70 genes controlling red blood cell (RBC) production and structure. Mutations in these genes can lead to alterations in hemoglobin (Hb) levels, RBC differentiation, proliferation, RBC membrane structure, and defective activity of metabolic enzymes [1]. The usual diagnosis of CA is segregated into three steps. The first is based on clinical features- evaluation of complete blood count, positive familial history, and the observation of a peripheral blood smear. The second step comprises biochemical and highly specialized tests, such as the flow cytometry or ektacytometry for the diagnosis of erythrocytes membrane defects, which are available only in a few specialized laboratories in the world. The last step includes the molecular analysis of the causative gene by direct sequencing. Unfortunately, in several cases these investigations fail to achieve the correct diagnosis, especially when the family history is uninformative or when routine laboratory tests produce unclear data, as a result, even transfusion-dependent patients remained undiagnosed for many years.

Due to the limitation of the current diagnostic strategies, next-generation sequencing (NGS) is making its way to this field. The major current application of NGS in diagnostics is through disease-targeted tests for which multiple causative genes are known. Over the last few years, targeted NGS diagnostic panels were introduced into many haematology laboratories, thus offering a rapid and accurate diagnosis of patients with congenital anaemia.

Congenital anaemia, traditional diagnostics approaches, and their limitation

Congenital anaemia's can be broadly divided into hypoproliferative anaemia syndromes (such as Diamond-Blackfan anaemia), dyserythropoietic anaemias, inherited metabolic disorders (e.g. inherited sideroblastic anaemias), and haemolytic anaemias including inherited erythrocyte membrane disorders, enzymopathies, as well as thalassemia and hemoglobinopathies. Hemoglobinopathies and thalassemia are caused by a defect in the small gene (α, β, α1, α2) which can

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be detected by gene-by-gene sequencing approach, or by MLPA or GAP-PCR, and thus is not discussed further.

Red cell membrane disorder

Red blood cell membrane disorders may be caused due to the weakening of the cell membrane stability resulting in an irregular shape, increased fragility, and membrane loss, leading to morphological changes and haemolytic anaemia. The most common are Hereditary Spherocytosis, Hereditary Elliptocytosis, Hereditary Pyropoikilocytosis, Hereditary Stomatocytosis. The gene involved in these disorders is SLC4A1(BAND 3), EPB4.1(Protein 4.1), EPB4.2 (Protein 4.2), SPTB (Beta Spectrin), SPTA (Alpha Spectrin), PIEZO1 (Mechanosensitive PIEZO1 Ion Channel Protein), ANK1(Ankyrin), RHAG (Rh-associated glycoprotein) and few others.

Conventional diagnosis of hereditary spherocytosis is straightforward, based on the presentation of haemolytic anaemia and the presence of spherocytes in the peripheral blood smear. The confirmatory analysis is done by eosin 5' maleimide test using flow cytometry. Since most of the patients exhibit mild to moderate symptoms, molecular diagnosis is not usually preferred in the clinical setting.

Hereditary elliptocytosis (HE) is an autosomal dominant disorder resulting from mutations in SPTA1, SPTB, EPB4. The traditional diagnosis of HE usually relays on the presence of elliptocytes in the blood smear. Hereditary pyropoikilocytosis (HPP) is the extreme phenotype of HE, characterized by severe haemolytic anaemia associated with long-term transfusion-dependency. Poikilocytes and fragmented RBCs are seen on the blood smears. HPP is a recessive condition caused due to mutation in SPTA1 and SPTB. Critical analysis of CBC provides clear hints in diagnosis, for example, MCV is often reduced due to the large number of fragmented RBC in HPP. No conclusive results can be drawn by EMA in the case of HE and HPP. However, Imaging flow cytometry and ektacytometry can be used for diagnosis [17]. Unfortunately, very few laboratories have this facility.

Hereditary stomatocytosis are a wide range of membrane disorders but the most underdiagnosed one is characterized by alterations in ionic flux with increased cation permeability that results in inappropriate shrinkage or swelling of the RBC, and water lost or gained osmotically [18]. It includes dehydrated stomatocytosis (DHSt) and overhydrated stomatocytosis (OHSt) types. The associated genes are PIEZO1, RHAG, KCNN4, ABCB6, SLC4A1, SLC2A1, ABCG5, and ABCB8.

Traditional diagnostic approach of hereditary stomatocytosis and its limitations: Patients with DHSt present with haemolytic anaemia. A clue to the diagnosis is a high MCHC; the blood smears are usually not conclusive as stomatocytes may be scarce or not present at all. Diagnosis becomes further uncertain in transfusion-dependent patients. OHSt is characterized by a combination of high MCV and a low MCHC and prominent stomatocytes in the peripheral blood. Findings in osmotic gradient ektacytometry are diagnostic, except in transfusion-dependent patients. A molecular diagnosis is therefore the only way to reach a definite diagnosis in both types of Hst.

Red blood cell enzyme disorder

RBC enzyme deficiencies are mostly inherited in an autosomal recessive form with haemolysis occurring only in homozygous or compound heterozygous individuals, some enzyme deficiencies are also X-linked. The most common is glucose-6-phosphate dehydrogenase (G6PD) and pyruvate kinase (PK) deficiencies; however, several other much less frequent enzyme disorders cause haemolytic anaemia without specific abnormalities in the morphology of the RBC. Diagnosis is based on the detection of reduced specific enzyme activity, but errors can be made in the interpretation of results because of the instability of the enzyme, high reticulocyte count, or recent blood transfusions. Hence, molecular diagnosis is the only way to rule out the defects. G6PD deficiency is identified based on a simple DPIP dye decoloration method, measurement of enzyme activity, and DNA Sanger's sequencing. Since variants in the G6PD gene are identified by gene by gene sequencing method, as are only three variant most prevalent (G6PD Mediterranean, G6PD Orissa, and G6PD Kelara-Kalyan contribute 80% of Indian populations)so it is not discussed further.

Pyruvate kinase deficiency

Pyruvate kinase deficiency (PKD) is the second most common cause of congenital non-spherocytic haemolytic anaemia followed by G6PD deficiency [5]. Pyruvate kinase catalyzes the conversion of phosphoenolpyruvate (PEP) to pyruvate with phosphorylation of adenosine triphosphate (ATP) [9]. Thus, PK deficiency leads to a reduction in ATP and shortened reticulocyte and red cell lifespan, due to an inability to maintain the red cell electrochemical gradient and membrane integrity, leading to clearance in the spleen. PK deficiency is transmitted as an autosomal recessive disorder. Over 200 mutations have been described in the PKLR gene [9,10]. The severity of anaemia is highly variable and PBS is non-conclusive. The measurement of enzyme activity is helpful for diagnosis.

The traditional method of diagnosis of PKD and its limitation: The conventional diagnosis of PKD is based on the presence of pathological symptoms of congenital haemolytic anaemia with insight into blood smear and measurement of pyruvate kinase enzyme activity. Tests of RBCs enzymes are not widely available and, also, recent blood transfusions and elevated reticulocyte count interfere with the results [9]. However, due to the non-specific clinical presentation, the misdiagnosis of PKD seems to be common. In 3 centers performing NGS panels for congenital anaemias (18, 24, 25), out of 15 patients eventually diagnosed with PKD, only one patient was referred with the correct diagnosis, while 11 were referred with a pre-test diagnosis of CDA and 3 with unknown haemolytic anaemia.

Glucose phosphate isomerase deficiency

Glucose phosphate isomerase (GPI) is the third most common type of erythroenzyme deficiency. GPI plays an important role in catalyzing isomerization reaction between glucose 6-phosphate and fructose 6- phosphate in the second step of glycolysis. To date, only 55 cases have been reported in the world literature [8]. The deficiency of the GPI enzyme is caused due to homozygous or compound heterozygous mutation in the GPI gene. This enzyme is ubiquitously present in most organisms and

expressed in all tissues. GPI also plays an important role as neuroleukin (NKL), autocrine motility factor, maturation factor, and myofibril bound serine proteinase inhibitor [8]. Hydrops fetalis and mental retardation are also associated with GPI deficiency [8]. Diagnosis is fulfilled by measurement of enzyme activity.

The traditional method of diagnosis of GPI def and its limitation : Similar to PKD, GPI def is conventionally diagnosed based on symptoms of congenital haemolytic anaemia, physical or mental retardation, family history, scanning of a peripheral blood smear, and enzyme activity. However, diagnosis is difficult due to the intervention of recent blood transfusion and reticulocyte count. The usefulness of NGS in the diagnosis of GPI deficiency and rare enzyme deficiency have been described in the various laboratory [1,2,7,8,20].

Diamond Blackfan Anaemia

Diamond Blackfan Anaemia (DBA) is congenital anaemia characterized by pure red cell aplasia and associated with congenital bone abnormalities including short stature, craniofacial anomalies, thumb anomalies, and genito-urinary and cardiac congenital abnormalities [11]. Generally, the onset within the first year of life, with macrocytic anaemia, low reticulocyte counts, and hyperproliferative erythroid lineage. DBA is mostly inherited in an autosomal dominant inheritance although few cases with the autosomal recessive patterns are also reported. DBA has an occurrence rate of 1 in 500000 live births [12]. DBA occurs as a result of genetic mutation in ribosomal protein gene. The gene codes for both large and small units of ribosomal protein. More than 20 ribosomal genes are known to be associated with DBA, of which RPS19 is commonly affected [12]. Variable clinical presentation in patients and multiple gene association makes it difficult to diagnose in the routine laboratory.

Traditional diagnosis of DBA and its limitation: Diagnosis of DBA is established by characteristic laboratory findings including persistent macrocytic anaemia, high levels of hemoglobin-F, elevated RBC adenosine deaminase (ADA) (13). Bone marrow (BM) aspiration reveals the paucity of erythroid precursors. Ribosomal RNA analysis can also validate the diagnosis of DBA by differentiating between defects in the small and large ribosomal subunits. The most commonly mutated genes in DBA are RPS19, RPL5, RPS26, and RPL11, which can be studied using Sanger sequencing. However, the gene-by-gene sequencing approach for > 20 possibly mutated genes is time-consuming, expensive, and in many cases fails to identify the underlying defect.

Congenital dyserythropoietic anaemia

Congenital dyserythropoietic anaemias (CDAs) are a group of rare disorders marked by ineffective erythropoiesis [14]. CDA patients exhibit different degrees of anaemia, from asymptomatic to fetal hydrops, varied class of hyporegenerative anaemia with insufficient reticulocyte count, ineffective erythropoiesis, and variable intensity of haemolysis [14]. Patients frequently present jaundice, splenomegaly, cholelithiasis, and iron overload as a consequence of transfusion, ineffective erythropoiesis, and increased peripheral cell destruction.

CDAs are classified into four types based on the morphology of bone marrow erythroblasts and associated causative gene [14]. CDA type I is characterized by hypercellularity and erythroid hyperplasia in bone marrow smear, binucleated erythroblasts of different size and shape, thin chromatin bridges between nuclei of erythroblasts, dense heterochromatin with vacuoles or spongy appearance [14]. CDA type I is further subdivided into type Ia and type Ib based on causative gene CDAN1 and C15ORF41 respectively. CDA type II is characterized by bi/multinucleated erythroblasts of equal size, peripheral double membranes of erythroblasts, and hypoglycosylation of band 3 membrane protein as a biochemical hallmark [14]. CDA type II is caused by variants in the SEC23B gene. CDA type II patients mimic hereditary spherocytosis which can be differentiated by measuring CD44 antibody [15]. CDA type III is characterized by the presence of multinucleated erythroblasts in bone marrow smear, intranuclear clefts into heterochromatin and autophagic vacuoles. CDA type III is caused by one variant in the KIF23 gene. CDA type IV presents dyserythropoietic morphology similar to CDA I and II types: binucleated erythroblasts, rare immature erythroid cells with marked heterochromatin [14]. CDA type IV is caused by variants in the KLF1 gene. Recently, a CDA variant has been described: X-linked thrombocytopenia with dyserythropoietic anaemia (XLTDA) caused by a defect in the GATA1 gene (chromosome: Xp11.23) is categorized as CDA type V. CDA types I and II are inherited in an autosomal recessive manner, CDA types III and IV in an autosomal dominant manner, and XLDTA is expressed in X-linked pattern. The actual incidence of these anaemias is unknown due to their clinical heterogeneity, the presence of asymptomatic forms, and the misdiagnosis.

Traditional diagnosis of CDA and its limitation: Since last decade, the diagnosis of CDA majorly relies on bone marrow morphology, and in the case of CDA II glycosylation analysis of RBC membrane proteins [15]. These studies are available only in a few specialized laboratories, and as a result, many patients remained undiagnosed for years. Based on recent targeted NGS studies of patients with congenital anaemias, it was found that CDA is indeed a commonly misdiagnosed disease. Kedar et al pointed out of the six patients referred with a clinical diagnosis of CDA but only one patient was diagnosed with CDA with the NGS panel [7]. Russo et al, also found CDA to be the most difficult for diagnosis [1].

Congenital Sideroblastic Anaemia

Congenital Sideroblastic anaemia (CSA) is a rare type of inherited anaemia marked by the presence of ring sideroblasts in the bone marrow. The most frequent form is X-linked sideroblastic anaemia (XLSA), caused by a mutation in the ALAS2 gene [16]. 5- aminolevulinic acid synthase (ALAS-2) is rate-limiting enzymes in heme -synthesis and is expressed specifically in erythroid tissue [16]. It may also show in few cases, autosomal dominant, recessive, and mitochondrial patterns of inheritance. Other lesser-known genes involved in heme synthesis, iron-sulfur cluster, or mitochondrial protein synthesis are also associated with CSA [16]. However, pathogenesis and prevalence of the disease are still unknown.

Traditional diagnosis of CSA and its limitation: CSA patients are largely diagnosed by the presence of ring sideroblast in bone marrow smear and iron deposition. Anaemia in CSA may be microcytic, normocytic, or macrocytic. Diagnosis majorly relies on molecular findings due to the association of > 10 genes in CSA. However, very few laboratories have facilities for molecular study.

Next-generation sequencing

Due to the failure of the current diagnostic workflow to find a definitive and correct diagnosis of congenital anaemia, next-generation sequencing (NGS) is making its way to this field. In the last decade, whole-exome sequencing (WES) has been widely used for the diagnosis of patients with congenital anaemias. The major current application of NGS in diagnostics is through disease-targeted tests for which multiple causal genes are known. Some studies have already demonstrated the usefulness of the targeted-NGS (t-NGS) approach in the investigation of specific subtypes of congenital anaemia patients. This method, in which NGS is followed by capturing of genes of interest, is advantageous over WES as it requires simpler bioinformatics analyses and provides a deeper sequencing coverage [3]. However, it needs to be continuously updated to include newly discovered genes. Besides, it does not allow the identification of novel genes. The multi-gene panels include a gene set ranging from 28 to 70 loci causative of CDA, DBA, haemolytic anaemia's due to enzymatic defects, hereditary membrane defect, hemoglobinopathy, and sideroblastic anaemia. One of the main caveats of NGS, whether WES or gene-panel based, is the difficulty to interpret sequence variants. It is advisable to adopt the American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology guidelines on variant classification. A variant may be pathogenic or benign polymorphism. The main challenge is the interpretation of variants of unknown significance (VOUS). Online bioinformatics tools -Polyphen-2 (http://genetics.bwh.harvard.edu/pph2/), SIFT (http://sift.jcvi.org/), PROVEAN (http://provean.jcvi.org), Mutation Taster (http://www.mutationtaster.org/, Mutation Assessor (http://mutationassessor.org/r3/), PMUT (http://mmb.irbbarcelona.org/PMut/analyses/new/), MutPred (http://mutpred.mutdb.org/), PANTHER (http://pantherdb.org/tools/csnpScoreForm.jsp) are utilized in interpreting the nature of the variants. Databases such as the Genome Aggregation Database (https://gnomad.broadinstitute.org/), Human Gene Mutation Database (http://www.hgmd.cf.ac.uk/ac/index.php), and ClinVar (https://www.ncbi.nlm.nih.gov/clinvar/) provides accurate frequency and previous reports (if any) of the variants. When it is difficult to determine the significance of detected variance as disease-causing, it is advisable to perform family segregation analysis. When available, it is also highly important to confirm the genetic findings with functional tests. Therefore, the advances of genetic testing do not obliviate the importance of functional tests; both direct the molecular work-up and confirm the genetic results.

EXPERIENCE AT NIIH

In collaborative study of NIIH with Japanese group of researchers, we included 21 undiagnosed severe transfusion-dependent (suspected) congenital anaemia patients. We have developed a very

systematic flowchart for the diagnosis of unexplained hemolytic anemia cases. (Figure-1) Among total 21 tested, we succeeded in providing a diagnosis to 17 patients (77%). The genetic diagnosis was performed by gene capture followed NGS of 76 genes known to cause anaemia syndromes. Five cases were diagnosed with red cell

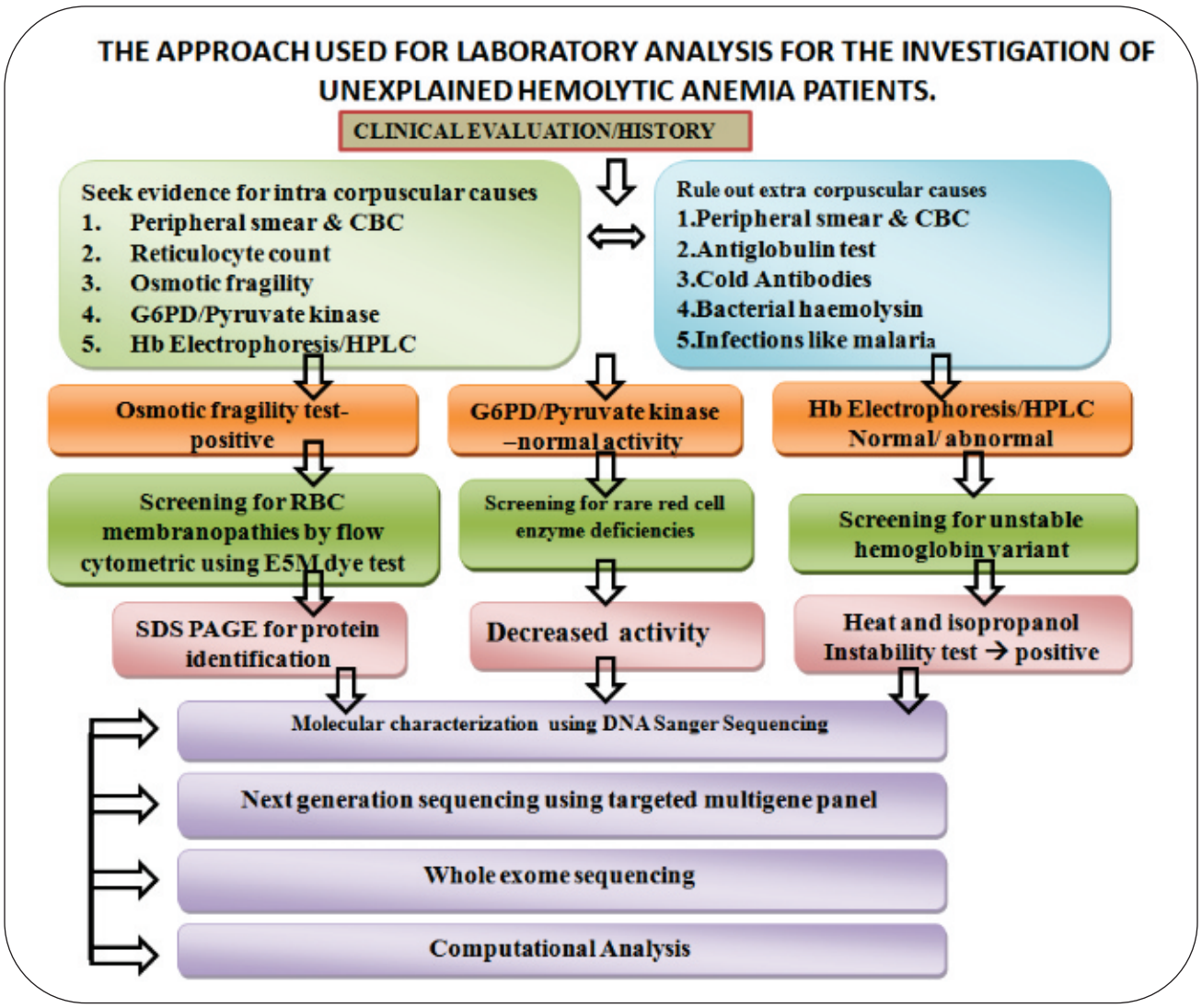

FIGURE-1: THE APPROACH USED FOR LABORATORY ANALYSIS FOR THE INVESTIGATION OF UNEXPLAINED HEMOLYTIC ANEMIA PATIENTS

membrane protein defects, six with red cell metabolic enzyme defect, three cases confirmed combined membrane and enzyme defect, two cases with Diamond–Blackfan anaemia (DBA), and one with CDA type II. The 21 out of 26 identified mutations were novel. In seven patients, the genetic diagnosis differed from the previously presumed diagnosis. Earlier these seven cases were presumed to be a case of CDA or DBA, but later diagnosis confirmed them with red cell membrane protein defects or rare red cell enzymopathies. However, four cases remained undiagnosed. [7]. Table 1 showed the summary of the genetic defect identified at our centre.

Sr. No.	Related disorders	No of cases
1	Thalassemia	11 case
2	RBC Membrane defect	35 case
3	GPI deficiency	32 case
4	PK deficiency	51 case
5	HK deficiency	2 case
6	AK deficiency	3 case
7	Pyrimidine 5' Nucleotidase deficiency	3 case
8	Congenital dyserythropoietic anemia (CDA)	7 case
9	Diamond blackfan Anemia (DBA)	10 case
10	Congenital Sideroblastic anemia (CSA)	4 case
11	Fanconi anemia	1 case
12	ABCG8 (Sitosterolemia)	1 case
13	LRBA (PID)	1 case
14	Rare etiology of CHA	8 cases
15	NO pathogenic variant detected	4 cases

Table-1: Targeted Multi-gene next generation sequencing panel identified molecular defects in congenital anemias

The major drawback of NGS/t-NGS is the failure to identify large base deletions or mutation in pseudogenes. This requires alternative approaches such as copy number analysis, array-based genome hybridization, or MLPA. Also, it is important to study the epigenetic causes in undiagnosed cases where genetic findings could not sufficiently provide a reason for the manifestation of the disease. Previously, we have also used targeted next-generation sequencing diagnosis for two unusual cases of haemolytic anaemia and identified novel variant in adenylate kinase (AK1) gene and glucose phosphate isomerase (GPI) gene [8,20,21]. Recently, we have utilized NGS in supplementing the diagnosis of DHSt patients[19].

Conclusion

In conclusion, the complete work plan for diagnosis must include the past -present medical history of

patient and family, ethnic background, clinical data, biochemical test records, molecular and genetic information(if available). We also recommend the incorporation of NGS panels (targeted/ whole) for the diagnosis of patients with congenital anaemia as part of the routine work-up, to decrease the gap from presentation to diagnosis. A timely diagnosis will direct towards specific therapeutic approaches, will define the appropriate work-up and follow-up plans, and allow necessary genetic counselling.

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नई पीढ़ी की अनुक्रमण विधि (NGS): जन्मजात रक्ताल्पता (एनीमिया) रोग के निदान एवं उचित प्रबंधन हेतु एक बेहतर तकनीक

श्री सोमप्रकाश धनगर

जन्मजात रक्ताल्पता (एनीमिया) आनुवंशिक रूप से विभिन्न विकारों के एक विविध समूह का प्रतिनिधित्व करता है जो कई रूपों (हल्के रोग से लेकर मृत्युदायक तक) में मरीजों में दिखाई देता है। साथ ही इस रोग में अक्सर अस्पष्ठ जीनोटाइर्प-फेनोटाइप सहसंबंध देखने को मिलता है। इसके सामान्य लक्षणों में बाल्यावस्था के दौरान पूर्ण रक्त आधान एवं बारम्बार रक्त आधान की आवश्यकता का होना पीलिया यकृत एवं तिल्ली का बढ़ना अविकसित लाल रक्त कोशिकाओं का बढ़ना (रेटिकुलोसाइटोसिस), अप्रत्यक्ष पित्तवर्ण का बढ़ना (हाइपरबिलीरुबिनमिया), पित्तपथरी (कोलेलिथियसिस), शारीरिक और मानसिक मंदता (कुछ मामलों में) आदि शामिल हैं। जन्मजात रक्ताल्पता को मोटे तौर पर कम प्रसार रक्ताल्पता रोग समूह जैसे कि, डायमंर्डब्लैकफैन एनीमिया, जन्मजात एनीमिया, हेमोलिटिक एनीमिया, जन्मजात लाल रक्त कण झिल्ली विकार तथा एन्ज़ाइमोपथिस एवं चयापचय संबंधी विकार (सिडरोब्लास्टिक रक्ताल्पता) के रूप में विभाजित किया जा सकता है। जन्मजात अरक्तता का कारण लाल रक्त कोशिकाओं के कोशिकीय कार्य और उत्तरजीविता में शामिल विभिन्न पार्थवे (एनारोबिक ग्लाइकोलिसिस, हेक्सोज मोनोफॉस्फेट शंट, ग्लूटाथियोन चयापचय और न्यूक्लियोटाइड सालवेज) एवं इनमे भाग लेने वाले किसी भी किण्वक में उपस्थित दोष हो सकते है। इन दोषो का मुख्य कारण लाल रक्त कोशिकाओं के निर्माण और संरचना को नियंत्रित करने वाले 70 से अधिक जीनों में उत्परिवर्तन होता है। चूँकि इस रोग पर अनुसन्धान अभी जारी है अतः कारक जीनों की इस सूची को अभी पूर्ण नहीं माना जा सकता है। इन जीनों में उत्परिवर्तन हीमोग्लोबिन के स्तर लाल रक्त कोशिकाओं विभेदन तथा प्रसार लाल रक्त कोशिकाओं झिल्ली संरचना और चयापचय एंजाइमों की दोषपूर्ण गतिविधि को जन्म देता है। अतः जन्मजात अरक्तता रोग के सटीक निदान हेतु ज्ञात कारक जीनो में उत्परिवर्तन का पता लगाना आवश्यक है।

परंपरागत रूप से शिरा रक्त स्मीयर (रक्त लेपित एवं रंजीत कांच की पट्टी का सूक्ष्मदर्शी द्वारा अध्ययन करना) शरीर में लोह तत्व की मात्रा का अनुमापन और हीमोग्लोबिन वैद्युत कण संचरण (इलेक्ट्रोफोरेसिस) जैसी सरल प्रयोगशाला तकनीक के द्वारा जन्मजात रक्ताल्पता का निदान किया जाता है। इसके अलावा भी कुछ परम्परांगत तकनीकों जैसे क्रोमैटोग्राफी वैद्युत कण संचरण (इलेक्ट्रोफोरोसिस), आसमाटिक फ्रेजिलिटी और ईओसिन-5 मेलामाइन रंजक के आधार पर विभिन्न जन्मजात रक्त सम्बन्धी रोगो का निदान किया जा सकता है हालांकि उन्नत प्रौद्योगिकी और विशेषज्ञता की अनुपलब्धता के कारण कुछ रक्त सम्बन्धी जन्मजात रोगो जैसे लाल रक्त कोशिका के झिल्ली प्रोटीन में दोष (जैसे स्टामाटोसाइटोसिस), लाल रक्त कोशिकाओं में किण्वक की कमी (जैसे ग्लाइकोलाइटिक किण्वक की कमी) और हीम निर्माण विकार (जैसे सिडरोब्लास्टिक रक्ताल्पता) सहित अन्य दुर्लभ विकारों का निदान करना मुश्किल होता है।

नई पीढ़ी की अनुक्रमण विधि की उपयोगिता (नेक्स्ट्जेनेरेशन सिक्वेंसिंगः NGS)

जीनोम अनुक्रमण (Genome Sequencing) के तहत डी. एन. ए. के भीतर न्यूक्लियोटाइड के सटीक क्रम का पता लगाया जाता है। केंद्रित जीनोम अनुक्रमण {टार्गेटेड अनुक्रमण (NGS)} भी इस तकनीक का एक भाग है। इस तकनीक में संपूर्ण जीनोम का अनुक्रमण न करके केवल ज्ञात कारक जीनो का ही अनुक्रमण किया जाता है। जिससे परिक्षण कम समय और लागत में पूर्ण हो जाता है। इसके साथ ही यह तकनीक एक गहन अनुक्रमण कवरेज प्रदान करती है। केंद्रित जीनोम अनुक्रमण {लक्षित (टार्गेटेड) एनजीएस} तकनीक के विकास से दुर्लभ आनुवांशिक विकारों जैसे जन्मजात अरक्तता का निदान तीव्र सटीक और लागत प्रभावी हो गया है।

हमारे संस्थान के वैज्ञानिको द्वारा किये गए शोध के आधार पर यहाँ सलाह दी जाती है की जन्मजात अरक्तता रोग के सटीक निदान हेतु आवश्यक सूचना जैसे रोगी और उसके परिवार का इतिहास जातीय पृष्ठभूमि जैव रासायनिक परीक्षण अभिलेख आणविक और आनुवंशिक जानकारी होना आवश्यक है। क्योकि ये सभी सूचना नयी पीढ़ी के अनुक्रमण के परिणामो का विश्लेषण करने में उपयोगी होती है। जन्मजात रक्ताल्पता बीमारी की शुरुआत और निदान तक के अंतराल को कम करने के लिए नई पीढ़ी की अनुक्रमण विधि पैनल (लक्षित/ संपूर्ण) को शामिल करने की सलाह हमारे संस्थान के वैज्ञानिको द्वारा दी जा रही हैं। राष्ट्रीय प्रतिरक्षा रुधिर विज्ञान संस्थान में नई पीढ़ी की अनुक्रमण विधि का प्रयोग असाधारण अनुवांशिक विकार के निदान के लिए किया जाता है। आज नई पीढ़ी की अनुक्रमण विधि (NGS) का उपयोग दुनिया भर की उन्नत प्रयोगशालाओं में विभिन्न बीमारियों जैसे कर्क रोग प्रतिरक्षा की कमी और आनुवांशिक रोगो के निदान में किया जा रहा है तथा भारत में भी नियमित रूप से इस तकनीक को नैदानिक प्रक्रिया के हिस्से के रूप में जोड़ने हेतु भारतीय आयुर्विज्ञान अनुसन्धान संस्थान के वैज्ञानिको द्वारा भरसक प्रयास किये जा रहे है। राष्ट्रीय प्रतिरक्षा रुधिर विज्ञान संस्थान (मुंबई) के वैज्ञानिको द्वारा अस्पष्ठ (अनएक्सप्लेंड) हिमोलिटिक रक्ताल्पता के निदान हेतु एक नैदानिक यथा प्रवाह तालिका का विकास किया है। जिसके माध्यम से चिकित्सक जन्मजात रक्ताल्पता का निदान आसानी से कर सकते है।

Women's day celebration on 8th March, 2020. Dr. Vasantha Muttuswami, Former Senior DDG, BMS division, ICMR was felicitated for her contribution in Science. The theme for Women's day was “I am Generation Equality: Realizing Women's Right”. Dr. Padma Deostali, Director, Centre for Health and allied themes (CEHAT) delivered a lecture on topic “Why genders matter in Medicine?”

Dr. HM Bhatia oration award was given to Dr. Neelam Giri from Clinical genetics branch, Division of Cancer Epidemiologyand genetics, National Cancer Institute, Rockville, USA on 6th Feburary, 2020.

Annual training program in Immunohaematology for Blood bank medical officers & technicians from 1-18th March, 2020

Training program in Immunohaematology for M.D D.M students from 1-10th March, 2020

SPORTS DAY CELEBRATION

FOUNDATION DAY

Annual Sports 21th to 28th Jan, 2020

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Immunohaematology Bulletin is brought out by:

ICMR-NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY
13th floor, New multi-storeyed Building, K.E.M. Hospital Campus,
Parel, Mumbai- 400012 (INDIA). Web: www.niih.org.in