https://doi.org/10.34883/PI.2026.12.1.013

Safaa Jassim Mohammed[1], Yusur Farhan Bdaiwi[1], Maryam Moayad Tawfeeq[1], Zainab Alhatem[1], Mohammed Myasar Dawad[1], Ahmed Alshewered[2]✉
[1] Al-Hadbaa Blood & BMT Hospital, Nineveh Health Department, Ministry of Health, Nineveh, Iraq
[2] Misan Radiation Oncology Center, Misan Health Directorate, Ministry of Health, Misan, Iraq

Frequency of Haemoglobinopathy in Al-Hadbaa Blood and BMT Hospital in Nineveh Province after ISIS Invasion

Conflict of interest: nothing to declare.
Authors' contribution: all authors contributed equally to the article.

Submitted: 17.10.2025
Accepted: 12.12.2025
Contacts: ahmedsalihdr2008@yahoo.com

Abstract

Introduction. Haemoglobinopathy a group of inherited disorders in which there is abnormal production or structure of the hemoglobin molecule. It is one of the most popular inherited diseases worldwide.
Purpose. This study aimed to find Frequency of Haemoglobinopathies in al. Hadbaa Blood and BMT hospital (thalassemia center) in in Nineveh Province
Materials and methods. In this cross-sectional study, the subjects who go to al. Hadbaa Blood and BMT hospital in Nineveh province and the data were collected from hematological laboratory in al. Hadbaa Blood and BMT hospital (thalassemia center). The Hb value was analyzed by a high-performance liquid chromatographic (HPLC) method in hemolyzed full blood
Results. Total number of case was 326 new case (not previous diagnosis with hemoglobinopathy) where 172 of them is male and 154 of them is female, age of case is range from nine mouth to 70 years old. About 133 of case (34.6%) was normal HPLC and 213 of case had abnormal HPLC were Beta thalassemia trait was 69% of abnormal HPLC, sickle cell trait was 15% of abnormal HPLC, alpha trait was 15%, sickle cell disease was 15%, HbD 6% of abnormal HPLC, Beta thalassemia syndrome was 5% of abnormal HPLC and Hb E 1% of abnormal HPLC.
Conclusion. HPLC is a very useful and powerful technique; it quantifies HbA2, HbF and other Hb variants (HbS, HbD, HbE and HbH). So its best technique for screening and detection of hemoglobinopathy.
Keywords: High-performance liquid chromatographic (HPLC), hemoglobinopathy, inherited diseases, β-Thalassaemia, haemoglobin

Сафаа Джассим Мохаммед[1], Юсур Фархан Бдайви[1], Марьям Моаяд Тауфик[1], Зайнаб Альхатем[1], Мохаммед Мьясар Давад[1], Ахмед Альшеверед[2]✉
[1] Больница крови и трансплантации костного мозга «Аль-Хадбаа», Департамент здравоохранения Ниневии, Министерство здравоохранения, Ниневия, Ирак
[2] Центр радиационной онкологии Мисан, Управление здравоохранения Мисана, Министерство здравоохранения, Мисан, Ирак

Частота случаев гемоглобинопатии в больнице Аль-Хадбаа по переливанию крови и трансплантации костного мозга в провинции Ниневия после вторжения ИГИЛ

Конфликт интересов: не заявлен.
Вклад авторов: авторы внесли равный вклад в подготовку статьи.

Подана: 17.10.2025
Принята: 12.12.2026
Контакты: ahmedsalihdr2008@yahoo.com

Резюме

Введение. Гемоглобинопатии – группа наследственных заболеваний, характеризующихся нарушением синтеза или структуры молекулы гемоглобина. Это одно из самых распространенных наследственных заболеваний в мире.
Цель. Определить частоту гемоглобинопатий в больнице переливания крови и ТКМ «Аль-Хадбаа» (центр талассемии) в провинции Ниневия.
Материалы и методы. В данном поперечном исследовании пациенты обращались в больницу переливания крови и ТКМ «Аль-Хадбаа» в провинции Ниневия. Данные были собраны в гематологической лаборатории больницы переливания крови и ТКМ «Аль-Хадбаа» (центр талассемии). Уровень гемоглобина анализировали методом высокоэффективной жидкостной хроматографии (ВЭЖХ) в гемолизированной цельной крови.
Результаты. Общее количество новых случаев составило 326 (без ранее диагностированной гемоглобинопатии), из которых 172 – мужчины, а 154 – женщины. Возраст пациентов варьировался от 9 месяцев до 70 лет. Примерно в 133 случаях (34,6%) результаты ВЭЖХ были нормальными, а в 213 случаях наблюдались отклонения от нормы: 69% – β-талассемия, 15% – серповидноклеточная анемия, 15% – α-анемия, 6% – HbD, 5% – синдром бета-талассемии и 1% – HbE.
Заключение. ВЭЖХ – очень полезный и мощный метод; он позволяет количественно определить HbA2, HbF и другие варианты Hb (HbS, HbD, HbE и HbH). Таким образом, это лучший метод для скрининга и выявления гемоглобинопатии.
Ключевые слова: высокоэффективная жидкостная хроматография (ВЭЖХ), гемоглобинопатия, наследственные заболевания, β-талассемия, гемоглобин

■ INTRODUCTION

Hemoglobinopathies (HBPs) are the most common of all monogenic autosomal-recessive diseases and the most severe include sickle cell disease and alpha/beta-thalassemia major. As carriers are typically asymptomatic and unaware of their carrier status, carrier couples often do not realize that with each pregnancy they face a 25% risk of a child with Hemogobionpathy [1].

Haemoglobins and their structure and function

The haemoglobin molecule contained within red blood cells is essential for human life, being the means by which oxygen is transported to the tissues. Other functions include the transport of carbon dioxide (CO2) and a buffering action [2].

Each molecule of normal adult haemoglobin A (Hb A, the dominant haemoglobin in blood after the age of 3–6 months) consists of four polypeptide chains, α2β2, each with its own haem group. Normal adult blood also contains small quantities of two other haemoglobins: Hb F and Hb A2. These also contain α chains, but with γ and δ chains, respectively, instead of β. The synthesis of the various globin chains in the foetus and adult [3].

Haemoglobin synthesis during human development

Haemoglobin is a tetrameric protein composed of two α-like and two β-like globin chains. The α- and β-globin genes are located in two separate clusters on different chromosomes. The duplicated α-globin genes (HBA1 and HBA2) are located on chromosome 16p in the α-globin gene cluster together with the embryonically expressed HBZ1. The β-globin gene cluster, located on chromosome 11p, harbours the prenatally expressed HBE, HBG1 and HBG2 and the postnatally expressed HBD and HBB genes. The embryonic, fetal and adult globin genes are organized along the genome in order of expression and regulated in a developmental stage- and tissue specific manner resulting in different types of haemoglobin, also called the haemoglobin switch. During the embryonic phase, the genes HBZ1 and HBE express the Hb Gower I (ζ2ε2), II (α2ε2) and Hb Portland (ζ2γ2), in the following 6 weeks the HBZ1 and HBE genes are switched off and HbF is expressed (α2γ2). Around birth there is a steep repression of γ gene expression in favour of the β-globin gene being expressed, resulting in a decrease in HbF level down to less than 0.5% and an increasing synthesis of HbA (α2β2) up to approx. 97–98%, which is completed approx. 6 months after birth. At the same time HBD is expressed and HbA2 (α2δ2) synthesized (2–3%), which has a diagnostic value in detecting β-thalassemia carriers for which the HbA2 levels are elevated (4–8%). Disease phenotypes associated with variants affecting the integrity of the β-globin gene are expressed approximately 6 months after birth [4].

Classification of the disorders of haemoglobin:

1. Mutations in the globin genes can cause a quantitative reduction.
2. Mutations in the globin genes can cause a qualitative changes.

Mutations in the globin genes can cause a quantitative reduction in output from that gene, alter the amino acid sequence of the protein produced or a combination of the two. Quantitative defects cause thalassaemia syndromes, whereas qualitative changes, referred to as haemoglobin variants, cause a wide range of problems, including sickle cell disease, unstable haemoglobins, decreased oxygen affinity, increased oxygen affinity, and

methaemoglobinaemia. Mutations in the globin gene complex might also alter the switch from fetal to adult haemoglobin synthesis, resulting in persistence of γ-globin expression, and hereditary persistence of fetal haemoglobin (HPFH) [5].

The thalassaemias and related disorders

The thalassaemias are the commonest single-gene disorders. Thalassaemia was first recognized by Cooley and Lee in 1925 as a form of severe anaemia associated with splenomegaly and bone changes in children. The term "thalassaemia" is derived from the Greek θαλασσα-(meaning "the sea") since many of the early cases came from the Mediterranean region [6].

Mutations in the globin genes can cause a quantitative reduction:

The β-thalassaemias

The β-thalassaemias pose by far the most important public health problems because they are common and usually produce severe anaemia in their homozygous and compound heterozygous states. Thalassemias are a common cause of hypochromic microcytic anemia which arises from the reduced or absent synthesis of the globin chain of hemoglobin. Thalassemias are a quantitative defect of hemoglobin synthesis. The highest prevalence of beta-thalassemia mutations is in people of Mediterranean, Middle Eastern, and Asian descent. Over 200 different thalassemia-causing mutations have been identified in the beta-globin gene, leading to the disease's wide genotypic and phenotypic variability [7].

The three classifications of beta-thalassemia are defined by their clinical and laboratory findings. Beta-thalassemia minor, also called carrier or trait, is the heterozygous state that is usually asymptomatic with mild anemia. Homozygosity or compound heterozygosity for beta-thalassemia mutations cause a more severe spectrum of anemias called beta-thalassemia intermedia and beta-thalassemia major. These two are distinguished clinically by transfusion dependence. Beta-thalassemia major requires routine transfusions, and intermedia does not [8].

Clinical diagnosis of beta-thalassemia major (TM) is made in children less than 2 years of age that present with microcytic anemia, mild jaundice, and hepatosplenomegaly. The complete blood count (CBC) of a patient with beta-thalassemia major will show microcytic hypochromic anemia with Hb levels less than 7g/dl, the mean corpuscular volume between (MCV) 50 and 70 fl, and mean corpuscular Hb (MCH) between 12 and 20pg. Beta-thalassemia intermedia presents with values of Hb between 7 and 10 g/dl, MCV 50 to 80 fl, and MCH 16 to 24pg. In beta-thalassemia minor, the red cell number is often elevated, reduced MCV, MCH, and the red cell distribution width (RDW) will typically show low elevations. The normal to mildly elevated RDW can help differentiate thalassemias from other microcytic hypochromic anemias, such as iron deficiency anemia and sideroblastic anemia where the RDW is typically very high. The peripheral blood smear will show microcytic hypochromic anemia with target cells, teardrop cells, and often coarse basophilic stippling. In severe forms of beta-thalassemia, there is anisopoikilocytosis with bizarre red cell morphology and numerous nucleated red blood cells [9].

The CBC and peripheral smear findings are non-specific. A diagnosis of beta-thalassemia requires hemoglobin electrophoresis or high-performance liquid chromatography (HPLC) to demonstrate abnormal percentages of HbA, HbA2, and sometimes HbF. The general pattern of beta-thalassemia is a decreased HbA percentage and a mildly increased

HbA2; less than 10% with variably increased HbF. A HbA2 above 10% suggests variant hemoglobin rather than beta-thalassemia. The magnitude of the HbA decrease depends on the genetic makeup of the affected individual. Patients with beta(+) alleles will have variably decreased HbA levels, and those that are homozygous beta(0) will produce no HbA. Beta-thalassemia minor characteristically has increased HbA2 (4–8%) with variably normal-to-low elevations of HbF. Beta-thalassemia major typically shows markedly elevated HbF (30-to-greater than 95%) with normal to mildly elevated HbA2. The distinction between beta-thalassemia major and intermedia is a clinical one and does not have diagnostic laboratory findings [8].

Alpha thalassemia

Refers specifically to the abnormal or absent manufacturing of alpha-globin chains. These are associated with different genetic mutations. The severity of the clinical condition is based on the mutation type. The severity of mutation is based on which of the two alpha-globin loci is affected. Deletion or inactivation of one of the α-globin genes in the linked pair is designated α+-thalassemia; heterozygous α+-thalassemia when on one chromosome 16 (– α / α α), homozygous α+-thalassemia when on both chromosome 16 (– α / – α). Deletion or inactivation of both α-globin genes in the linked pair on the same chromosome 16 is referred to as α0-thalassemia (– – / α α). >40 α0-thalassemia mutations have been found and are usually designated by the region where the condition was first discovered; the most common α0-thalassemia deletion mutations include the Southeast Asia (– –SEA / α α), Filipino (– –FIL / α α), and Mediterranean (– –MED / α α) mutations. Hemoglobin H (HbH) disease occurs when 2 α-globin genes are deleted on one chromosome 16 and a third is either deleted, inactivated, or changed qualitatively on the other chromosome 16, leaving only one functional α-globin gene. Hemoglobin Barts (Hb Barts) hydrops fetalis syndrome occurs when all 4 α-globin genes are deleted or inactivated (homozygous α0-thalassemia) [10].

Haemoglobin Lepore

This is an abnormal haemoglobin caused by unequal crossingover of the β and δ genes to produce a polypeptide chain consisting of the δ chain at its amino end and β chain at its carboxyl end. The δβ-fusion chain is synthesized inefficiently and normal δ and β chain production is abolished. The Hb Lepore homozygotes show thalassaemia intermedia and the heterozygotes thalassaemia trait [3].

δβ-Thalassaemia

This involves failure of production of both β and δ chains. Hb F production is increased to 5–20% in the heterozygous state, which resembles thalassaemia minor haematologically. In the homozygous state, only Hb F is present and haematologically the picture is one of thalassaemia intermedia [3].

Mutations in the globin genes can cause a qualitative changes:

Qualitative abnormalities of Hb arise from mutations that change the amino acid sequence of the globin, thereby producing structural and functional changes in Hb.

There are 4 ways in which Hb can be qualitatively abnormal:

1) decreased solubility (eg, sickle hemoglobin [HbS]),
2) instability (eg, Hb Köln),

3) altered oxygen affinity (eg, HbM-Saskatoon),
4) altered maintenance of the oxidation state of the heme-coordinated iron (eg, HbM-Iwate) [11].

Sickle hemoglobin

The sickle cell mutation occurs when negatively charged glutamate is replaced by a neutral valine at the sixth position of the beta-globin chain. The mutation is transmitted via Mendelian genetics and is inherited in an autosomal recessive fashion [10]. A homozygous mutation leads to the severest form of Sickle cell disease, ie, SCA-also called HbSS disease. The coinheritance of beta-thalassemia and sickle cell mutation leads to HBS-thalassemia disease, which phenotypically behaves like HbSS disease [12].

A heterozygous inheritance leads to HbAS. Patients with HbAS are not considered within the spectrum of SCD as most of them never present with typical symptoms of SCA. They might only be detected during childbirth, blood donation, or screening procedures [13].

Pathophysiology Sickle cell anemia is characterized by two major components: Hemolysis and vaso-occlusive crises (VOC). The defect in the beta-globin gene makes the sickle hemoglobin (HbS) molecule susceptible to converting into rigid, elongated polymers in a deoxygenated state. The sickling process is cyclical initially, where sickle erythrocytes oscillate between the normal biconcave shape and the abnormal crescent shape (acquired under low oxygen pressure). However, there comes a time when the change becomes irreversible, and the sickle erythrocytes develop a permanent sickle shape, increasing the risk for hemolysis and VOC. All variants of SCD share the same pathophysiology leading to polymerization of the HbS component [14].

The diagnosis of the sickle cell syndromes is made by the identification of HbS in erythrocyte hemolysates. Historically, cellulose acetate electrophoresis at alkaline pH was used to separate HbA, HbA2, and HbS, and citrate agar electrophoresis at acidic pH was used to separate comigrating HbD and HbC from HbS and HbA2, respectively [11].

Hemoglobin E

Structural change is a substitution of glutamic acid by lysine at the 26th position of the betaglobin chain. The mutation is also thalassemic because the single-base GAG/AAG substitution creates a cryptic splicing site, which results in abnormal mRNA processing and reduction of mRNA that can be translated. HbE is also slightly unstable in the face of oxidant stress and is sometimes referred to as a thalassemic hemoglobinopathy [15].

Individuals with hemoglobin E trait are asymptomatic with or without mild anemia (hemoglobin >12 g/dL), and mild microcytosis. Peripheral smear may be normal or may show hypochromia, microcytosis, target cells, irregularly contracted cells, and basophilic stippling. HbE usually makes up 30% or less of total hemoglobin. The compound heterozygous state, HbE b thalassemia, results in a very variable phenotype ranging from thalassemia trait, NTDT, to TDT, depending on the beta-mutation [16].

Hemoglobin C

HbC is the third most common mutant hemoglobin, after HbS and HbE. The hemoglobin mutant results from the substitution of lysine For glutamic acid as the sixth amino acid of beta-globin, the consequence of a single nucleotide substitution (GAG/AAG) in the sixth codon. The resultant positive-to-negative charge difference on the surface of the HbC

tetramer results in a molecule with decreased solubility in both the oxy and deoxy forms, which may undergo intraerythrocytic aggregation and crystal formation [17, 18].

Laboratory studies in HbCC show a mild hemolytic anemia, microcytosis, and slightly elevated reticulocyte counts. The MCHC is elevated because of the effect of HbC on cellular hydration. The peripheral blood smear shows prominent target cells, microcytosis, and irregularly contracted red cells. Confirmation of the diagnosis requires identification of HbC, which comigrates with HbA2, HbE, and HbOArab on cellulose acetate electrophoresis and isoelectric focusing. Thus, HbC must be distinguished by citrate gel electrophoresis or HPLC. Specific treatment for patients with HbCC is not generally necessary [19].

Hemoglobin D

HbD is usually diagnosed incidentally. (HbDPunjab) results from the substitution of glutamine for glutamic acid at the 121st position of the beta-chain. Patients who are homozygous (HbDD) may have a mild hemolytic anemia. Individuals who are heterozygous (HbAD) are clinically normal, with normal blood counts and a peripheral smear with the occasional target cells. The major clinical relevance of HbD is with compound heterozygous inheritance with HbS, resulting in a form of sickle cell disease, perhaps as a result of the low affinity of HbD promoting hemoglobin deoxygenation. The diagnosis of HbAD (D trait) or HbDD is made by hemoglobin electrophoresis. HbS and HbD have similar electrophoretic mobility on alkaline cellulose acetate electrophoresis and isoelectric focusing. They can be differentiated by acid citrate agar electrophoresis, HPLC, or solubility studies. This distinction is important for genetic and prognostic counseling [20].

■ MATERIALS AND METHODS

Study Population

In this study, the subjects who go to al. Hadbaa Blood and BMT hospital in Nineveh province and the data were collected from hematological laboratory in al. Hadbaa Blood and BMT hospital (thalassemia center).

Blood collection

Blood samples were collected and Testing of samples was carried at the department of Laboratory of al. Hadbaa Blood and BMT hospital Teaching Hospital (thalassemia center): start 26/December/2023 to End: 14/November 2024. The material used to determine CBC 5-part difference and Hb-Varaint was about 2 ml of venous blood collected in vacuum tubes with an anticoagulant EDTA (Ethylene Diamine Tetracetic Acid).

The Hb value was analyzed by a high-performance liquid chromatographic (HPLC) method in hemolyzed full blood.

The exclusion criteria included subject with iron deficiency anemia or previous diagnosis with hemoglobinopathy.

Ethical approval

The Medical Ethical Committee of Department of Patho-hematology, "Al-Hadbaa" Blood & BMT Hospital approved this study (no. 5 on 2023).

Statistical analysis

Statistical Package Version 24 for Social Sciences (SPSS Inc.) software used to analyze data. Nominal variables described as frequency and percentage.

Show number and percentage of hemoglobinopathy

Haemoglobinpathy	No.	%
Beta- thalassemia trait	147	69
Sickle trait	15	7
Suggested Alpha trait [a]	15	7
Beta-thalassemia syndrome [b]	5	2.4
Sickle cell disease [c]	15	7
HbH	6	2.8
Hb-Lepor	3	1.5
Hb-D	6 (5 trait &1 homozygous state)	2.8
Hb-E	1 (trait state)	0.5
Other Hboglobinopathy (Hb-Cand O-Arab)	0	0
Total	213	100

Notes: [a] suggested by abnormal CBC (low MCV, MCH and high RBC count) with normal iron study and normal or low HbA2; [b] include thalassemia major and intermediate; [c] include HbSS and sickle-thalassemia.

■ RESULTS

Total number of case was 326 case where 172 (52%) of them is male and 154 (47%) of them is female. The age was ranged from nine mouth to 70 years old. About 133 of cases (34.6%) was normal HPLC and 213 (65.4%) of cases had abnormal HPLC. The number and percentage of hemoglobinopathy is show in table.

■ DISCUSSION

Alpha- and beta-thalassemia are the most popular single gene heamoglobin disorder in the world. These disorder which generally confined to certain area, religion and cast, are now widely spread over all the world and because of global human migration the formula and marriage between all different societies and internal collective norms, it has contributed significantly to large cumulative case of heamoglobinopathy worldwide.

In this study 326 case where 172 (52%) of them is male and 154 (47%) of them is female, M : F ratio is 1.1 : 1 and this Similar results were also reported Yonus et al. [21] and Kready et al. [22].

In this study show most frequent hemoglobinpathy is beta-thalassemia trait fallowed by sickle trait and sickle cell disease and then other hemoglobiopathy included (HbH, HbD, Hb-lepore and Hb E).

Similar frequency and rate of hemoglobinopathy results were also reported Warghade et al. [23].

While Yonus et al. [21] Al-Allawi et al. [24] and Polus [25] reported most frequency of hemoglobinopathy is beta-thalassemia trait which is same results of this study but differed from this study by rate number because this study is done in thalassemia center while previous studies done in primary health care centers for routine premarital investigations.

■ CONCLUSION

HPLC is a very useful and powerful technique; it quantifies HbA2, HbF and other Hb variants (HbS, HbD, HbE and HbH). So its best technique for Screening and detection of hemoglobinopathy.

REFERENCES

1. Van Vliet ME, Kerkhoffs JLH, Harteveld CL, Houwink EJF. Hemoglobinopathy prevention in primary care: a reflection of underdetection and difficulties with accessibility of medical care, a quantitative study. *European Journal of Human Genetics [Internet].* 2022 Jul 1;30(7):790–4.
2. Bain BJ. *Haemoglobinopathy diagnosis*. Hoboken, Nj: Wiley Blackwell; 2020.
3. Hoffbrand V. *Hoffbrands Essential Haematology.* 2024.
4. Harteveld CL, Achour A, Arkesteijn SJG, et al. The hemoglobinopathies, molecular disease mechanisms and diagnostics. *International Journal of Laboratory Hematology.* 2022 Sep;44(S1):28–36.
5. Hoffbrand AV, Higgs DR, Keeling DM, Mehta AB. Postgraduate Haematology. 7th ed. Chichester, West Sussex; Hoboken, Nj: Wiley Blackwell; 2016.
6. Rees DC. The beginnings of molecular medicine. *Haematologica [Internet].* 2022 Sep 1 [cited 2024 Mar 8];107(9):2009–10.
7. Cao A, Galanello R. Beta-thalassemia. *Genetics in Medicine [Internet].* 2010 Jan 21;12(2):61–76.
8. Needs T, Gonzalez-Mosquera LF, Lynch DT. Beta Thalassemia [Internet]. PubMed. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK531481/
9. Origa R. β-Thalassemia. *Genet Med.* 2017 Jun;19(6):609–619.
10. Esio N, Bauer DE. Molecular Basis and Genetic Modifiers of Thalassemia. *Hematology/Oncology Clinics of North America [Internet].* 2023;37(2):273–99.
11. American. Ash-Sap. 2021. https://ashpublications.org/books
12. Ehsan M, Maruvada S. Sickle Cell Anemia [Internet]. Nih.gov. StatPearls Publishing; 2023.
13. Vincent O, Oluwaseyi B, James B, Saidat L. Coinheritance of B-Thalassemia and Sickle Cell Anaemia in Southwestern Nigeria. *Ethiopian Journal of Health Sciences.* 2016 Nov 11;26(6):517.
14. Kato GJ. Priapism in sickle-cell disease: a hematologist's perspective. *J Sex Med.* 2012 Jan;9(1):70–8.
15. Avery's Diseases of the Newborn [Internet]. Elsevier eBooks. Elsevier BV; 2023 [cited 2024 Nov 16].
16. Fucharoen S, Weatherall DJ. The Hemoglobin E Thalassemias. *Cold Spring Harbor Perspectives in Medicine [Internet].* 2012 Aug 1;2(8):a011734–4.
17. Kundrapu S, Janaki N, Meyerson HJ. Compound Heterozygosity for Hb D-Ibadan (HBB: c.263C>A) and Hb C (HBB: c.19G>A). *Hemoglobin.* 2018 Jul;42(4):269–271.
18. Zacharia G, Maronge GF, Brazda FW, Boulmay BC. Hemoglobin SO-Arab and α-thalassemia diagnosed in an adult: A case-based review of the hemoglobinopathies. *Am J Med Sci.* 2013 Oct;346(4):325–7.
19. Bachir D, Galacteros F. Hemoglobin C [Internet].
20. Gupta V, Aggarwal P. Profile of Hemoglobin D (HbD) Disease in Eastern Uttar Pradesh: A Single-Center Experience. *Cureus.* 2022 Oct 27.
21. Adnan B, Kashmoola M, Alhatem Z. Frequency of Haemoglobinopathies in Premarital Screening in Nineveh Province. *Annals of the College of Medicine, Mosul.* 2021 Dec 1;43(2):157–63.
22. Kready HO, Mohammed M, Salim Al-Karawi A, Al-Jindeel TJ. Epidemiology of thalassemia in Baghdad, Iraq: A Single Center Experience. *BNIHS.* 2020 May 2;140(02):2211–5.
23. Warghade S, Britto J, Haryan R, et al. Prevalence of hemoglobin variants and hemoglobinopathies using cation-exchange high-performance liquid chromatography in central reference laboratory of India: A report of 65779 cases. *Journal of Laboratory Physicians.* 2018 Jan;10(01):073–9.
24. Al-Allawi NA, Al-Dousky AA. Frequency of Haemoglobinopathies at premarital health screening in Dohuk, Iraq: implications for a regional prevention programme. *EMHJ.* 2010;16(4):381–385.
25. Polus RK. Prevalence of Haemoglobinopathies among marrying couples in Erbil province of Iraq. *Iraqi J Hematol.* 2017;6(2):90–93.