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Estimation of the prevalence of Hemoglobinopathies in Erbil governorate, Kurdistan region of Iraq

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Abstract:

BACKGROUND: Thalassemia syndromes and structural hemoglobin variants generate blood crisis of variable clinical symptoms, ranging from mild-to-moderate hematological disorder to severe, lifelong, transfusion-dependent anemia. The aim of current study was to uncover the prevalence of thalassemia and other hemoglobinopathies in the Erbil governorate, Kurdistan region of Iraq.

MATERIALS AND METHODS: The available data of thalassemia major, thalassemia intermedia, sickle cell disease, sickle cell trait, and HbH and HbE until the end of 2020 were collected retrospectively from Erbil Thalassemia Center in Erbil governorate, Kurdistan region of Iraq and analyzed by using Microsoft Excel (Version 2016).

RESULTS: An increase in the prevalence of thalassemia syndromes from 30.8/100,000 in 2015 to 37.3/100,000 individuals in the population in 2020 was revealed. The prevalence of all hemoglobinopathies combined increased from 31.9/100,000 to 42.7/100,000 individuals of the population. Thalassemia major was the predominant condition among the hemoglobinopathies with 758 (78.71%) cases out of 963 cases at the end of 2020.

CONCLUSION: This rise might be attributed to a large number of consanguineous marriages, the lack of effective prevention programs, and poor legislation. There is an emergent requirement for a preventive program, entailing identification of carriers, genetic counseling, guidelines to differentiate between other microcytic anemias with thalassemia traits, antenatal diagnosis, public education, and sustained legislation.

Keywords:

Erbil, hemoglobin, hemoglobinopathies, prevalence, sickle cell disorder, thalassemia

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Introduction

Hemoglobinopathies are a group of disorders rooted in structural and biosynthetic disturbances of hemoglobin synthesis resulting in a range of symptoms of varying severities. They are the most frequent type of monogenic disease worldwide.[1] They are among the world's significant health issues, with around 5% of the global population are carriers. There are about 42 million carriers and 12,000 newborns with severe and clinically significant hemoglobinopathy every year.[2] The global yearly thalassemia birth rate is projected to be approximately 60,000.[3] Thalassemia affects around 4.5 out of every 10,000 live births globally.[4]

The gene clusters for the synthesis of α and β globin chains are located on chromosomes 16 and 11, respectively. They are expressed in a coordinated and scheduled fashion according to the age of the individual.[5,6] Early in the embryonic life, three different Hbs are formed; ζ2,

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ε2 (Hb Gower-1), ζ2 γ2 (Hb Portland), and α2 ε2 (Hb Gower-2) between 4 and 14 weeks. After placental development, embryonic hemoglobins are replaced by hemoglobin F (HbF) (22).[7] In early infancy, the primary HbF expression shifts to adult hemoglobin (HbA), and by 2 years, (HbF, α2 γ2) accounts for 1% of HbA.[8] About 97% of an adult's hemoglobin (HbA, α2 β2) consists of two-and two-globin chains. 2%–3% is (HbA2, α2 δ2), α-and two δ-chains.[9]

Mutations in the gene clusters of both globin chains develop various hemoglobin abnormalities. The ensued disorder is dictated by the nature and location of the mutation. In general, there are two categories of disorders: Thalassemia syndromes (synthetic malfunction) and structural hemoglobin variants.[10] The common disorders include α-thalassemia, β-thalassemia, sickle cell disease, sickle cell trait, HbH, HbC, and HbE.[11]

Thalassemia is defined by the reduced or absent synthesis of at least one polypeptide globin chain (beta β, alpha α, gamma γ, and delta δ), resulting in imbalanced hemoglobin production, causing two main clinical forms: α-thalassemia and β-thalassemia.[12,13] The disturbed timely and sufficient production of any chain as programmed culminates in the accumulation of other globin chains in the developing red blood cell (RBCs) as long as there is no equivalent amount of the normally produced partner to attach with and assemble into a complete hemoglobin tetramer.[14] The clinical features of thalassemic patients include varying severity of anemia, bone deformities, hepatosplenomegaly, poor growth, yellow skin, and dark urine. Left untreated, thalassemia major patients die mostly from heart failure.[15]

Qualitative hemoglobin disorders are caused by mutations that distort the normal globin 3-dimensional structure.[16] The glutamate to valine at the sixth amino acid position on the β-globin subunit. When exposed to deoxy-state, it causes the polymerization of Hb, forming hemoglobin S (HbS). This condition subsequently results in the RBC deforming into a crescent or sickle shape and sickle disease. Sickled RBCs obstruct the circulation from blood, inducing tissue hypoxia, leading to severe ischemic pain and stroke.[17]

Hemoglobin E (HbE) is another structural hemoglobin aberration caused by glutamate to lysine substitute at the 26th amino acid position on β-globin, which frequently occurs throughout various countries of Asia.[18,19] Although HbE does not lead to any substantial clinical issues on its own, when interacting with diverse types of α-and β-thalassemia causes a broad range of clinical syndromes of varying severity.[19]

Thalassemias are seen in the regions of the world that were once endemic for malaria.[13] β-thalassemia is the most common hemoglobin disorder in the mediterranean region, the Middle East, and Asia. α-thalassemia is common in South-east Asia, and sickle-cell anaemia predominates in Africa. However, increased migration has imported hemoglobin disorder into regions that were not originally endemic.[20]

The α-thalassemia is more prevalent in Southeast Asia, notably Laos and Thailand, than the rest of the world, with until 40% of genetic traits identified in Thalassemia traits (TTs) (1%–30%).[4,13,4,13] The TT affects between 2% and 3% of black people.[13]

β-thalassemia is frequent in the Mediterranean, the Middle East, Central East Asia, Far East Asia, India, Southern China, and South America.[21] The prevalence in such regions might be as high as 10%. Because there is no efficient screening procedure in place, the exact number of thalassemia-affected patients in the United States is unclear.[22] The genetic incidence of β-thalassemia worldwide is 2%–18% in the Eastern Mediterranean and 0%–11% in South-east Asia.[4] Around 1.5% of the population worldwide are β-thalassemia carriers.[23] According to the registration in Iraq, 16 (out of 19) accessible Thalassemia centers in untill the end of 2015, the total number of Thalassemia patients was 11,165, constituting 66.3% of all hereditary anemias recorded in these centers. Between 2010 and 2015, the thalassemia prevalence was elevated from 33.5/100,000 to 37.1/100,000. β-thalassemia major accounted for 73.9% of all thalassemia forms. Approximately 66.0% of the patients were < 15 years old; 78.8% were offspring of related parents, and 55.9% had a minimum of one complication.[23]

Thalassemia is becoming a significant economic issue across developing countries because lifelong treatment required infants with infection and malnutrition originated from Thalassemia. It has also been observed that the global economy has improved over the last 50 years, and the total mortality rate of newborns has decreased.[24,25]

Many reports on the frequency of these disorders in middle–eastern countries have been published. In Erbil and neighboring provinces, many studies have been conducted that studied the molecular pattern of thalassemia.[26,27] However, no accurate prevalence figures of the different hemoglobinopathies in Erbil province exist.

The current study aims to reveal the prevalence of Thalassemia in addition to other hemoglobin disorders in the Erbil governorate, Kurdistan region of Iraq.

Materials and Methods

In the current study, we collected the available data of Thalassemia, in addition to other types of haemoglobin disorders retrospectively, from Erbil Thalassemia Center in 2020, and the total population in Erbil city, from the Kurdistan Region Statistics Office. To compare the number of cases in different years, we showed the number of cases in six succesive years, starting from 2015 to 2020. However, the patients were registered before 2015. The data were analyzed using Microsoft Excel 2016.

The collected data comprised the following:

- Thalassemia major
- Thalassemia intermedia
- Sickle cell disease
- Sickle cell trait
- HbH and HbE are available as "variable types."

The exact number of HbH and HbE cases was not available from the source. Otherwise, it existed as combination under the name of "variable types". Other data were as follows:

- The distribution of the cases according to gender
- Death in a year and the average age of the deaths
- The number of expatriates
- The number of blood pints used
- The number and types of tests done and the age distribution of the patients.

The study was approved by the Ethical Committees of both general directorate health of Erbil and Erbil Polytechnic University scientific committee.

Results

The data of thalassemia syndromes and other hemoglobinopathies collected from Erbil Thalassemia Center by the end of 2020 was as follows: Thalassemia major (n = 758), Thalassemia intermedia (n = 84), sickle cell disease (n = 60), sickle cell trait (n = 37), and the variable types (n = 24). The sum of all cases of conditions mentioned above was 963. The number of each recorded condition mentioned above increased year after year. Thalassemia major and intermedia, both increased from 601 and 18 cases in 2015 to 758 and 84 cases by the end of 2020, respectively. The number of sickle cell disease, sickle cell trait, and variables types have also increased from 14,7 and 3 cases in 2015 to 60,37 and 24 cases at the end of 2020, respectively [Figure 1].

The prevalence of hemoglobinopathies has increased from 31.9 in 2015 to 42.7 in 2020/100,000 individuals in populations [Table 1].

According to the data obtained, Thalassemia major was the predominant condition, estimated to be 758 out of a total of 963 cases, which represents 78.71% of all cases [Figure 2].

The prevalence of thalassemia syndromes, apart from other conditions, had also increased from 30.8/100,000 in 2015 to 37.3/100,000 individuals of the population by the end of 2020 [Table 2].

The distribution of the cases by gender was 48.75% for females and 51.25% for males. The age group with the highest number of recorded cases was 6–15 years with 44.45%. The second and third top age groups were 1–5, with 23.20% and 16–25, with 21.60%, respectively. Other age groups are followed [Figure 3].

The number and the average age of the deaths, the number of blood pints used, and the expatriates, all are shown in Table 3.

There were 527,735 tests done during the 6 years included in our study, with an average of 87,955.83/year. Biochemical and hematological tests were predominant, comprising 50.8% and 40.34%, respectively [Figure 4].

Discussion

According to the collected data, the prevalence of all hemoglobinopathies combined increased from 31.9/100,000 in 2015, to 42.7/100,000 individuals of the population to the end of 2020 [Table 1]. The increase in the prevalence of hemoglobinopathies is more rapid than the growing population number. Thus, population expansion is not the exclusive reason for the increased prevalence.

Thalassemia syndromes, especially thalassemia major, were the most frequent hemoglobinopathy in the current study [Figure 1]. The prevalence of thalassemia syndromes had increased from (30.8/100,000 in 2015) to (37.3/100,000 individuals in 2020) [Table 2]. The higher rate of thalassemia in Iraq might be defined by the high number of consanguineous marriages,

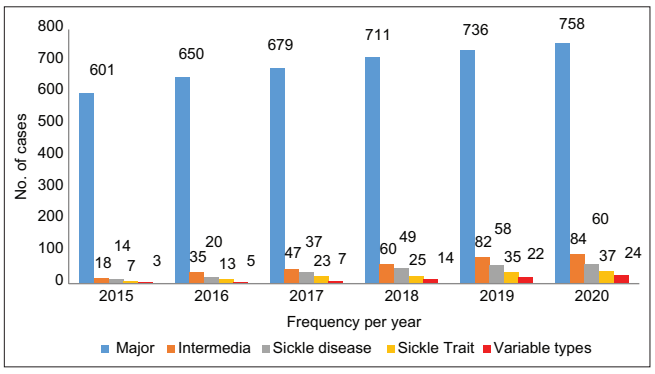

Figure 1: The number of cases of different hemoglobin disorders from 2015 to 2020

Table 1: The prevalence of haemoglobinopathies

Year	*n*	Total population	Prevalence/100,000
2015	643	2,009,637	31.9958281
2016	723	2,062,380	35.05658511
2017	793	2,113,391	37.52263542
2018	859	2,162,509	39.72237803
2019	933	2,209,569	42.22542948
2020	963	2,254,422	42.71604873

Table 2: The prevalence of Thalassemia syndromes (Thalassemia major and Intermiedia)

	Major	Intermedia	Sum	Total population	Prevalence/100,000
2015	601	18	619	2,009,637	30.80158257
2016	650	35	685	2,062,380	33.21405367
2017	679	47	726	2,113,391	34.35237493
2018	711	60	771	2,162,509	35.65303081
2019	736	82	818	2,209,569	37.02079455
2020	758	84	842	2,254,422	37.34881934

shortage of effective prevention programs, and poor legislation.[23,28] Another study also concluded a significant difference between families with consanguineous and nonconsanguineous marriage for the prevalence of thalassemia.[28]

According to the Iraq Family Health Survey, about 63.0% of all marriages in Iraq were between relatives in central and southern governorates and about 45.0% in northern governorates (Kurdistan region).[23] Another reason for the predominance of transfusion-dependent thalassemia is the higher necessity of blood transfusion of these patients compared to other types of hemoglobinopathy.[29] The changing patterns of the prevalence of Thalassemia in different parts of the world are affected mainly by changes in the birth number of new patients. They are primarily influenced by population migration, prevention programs, and different survival rates of patients with β-thalassemia.[30]

There were no data of thalassemia minor in the current study which is attributed to the less requirement for blood transfusion and much milder symptoms of anemia in comparison to thalassemia intermedia and major. Therefore, they do not visit the centers of related disorders to be treated.[31] Furthermore, the morphological findings in both the β-TT and iron deficiency anemia are at times so close that it is challenging to distinguish one from the other[32-34]

The variables types here are to demonstrate HbH and HbE conditions together. Unfortunately, we could not harvest the exact number of each condition individually from the data source. However, both were the least form of hemoglobinopathies among patients, combined and presented as variable types. The number of expatriates decreased from 278 in 2015 to 25 cases in 2020.

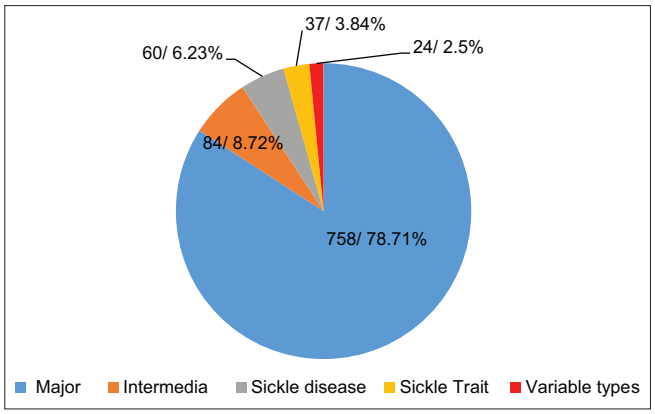

Figure 2: The percentage of each type of hemoglobin disorders

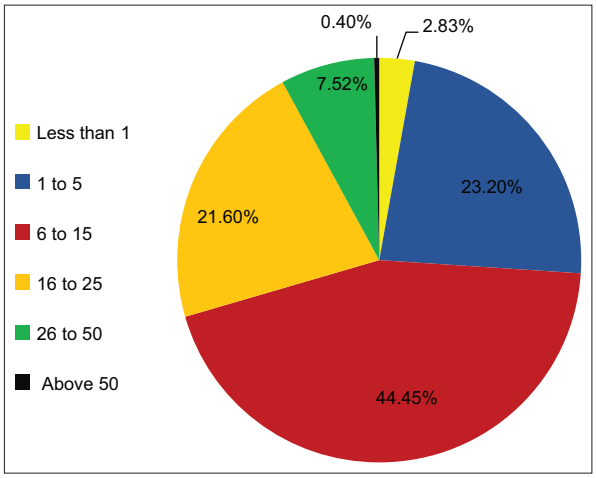

Figure 3: The age distribution of patients

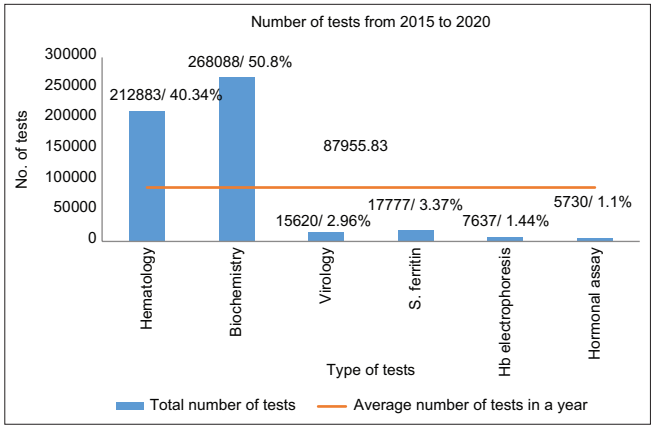

Figure 4: The number of different tests. The blue bars depict different test categories, and the orange line shows the average number of tests per year

Nonetheless, no contrary impact was observed on the increasing prevalence of hemoglobinopathies.

Roughly half (44.45%) of patients included in the study were between 6 and 15 years of age, 23.20% were between 1 and 5 years, 21.60% were between 16 and 25, and 7.92%

Table 3: The number of deaths in a year, the average age of death, the sum of blood pints used, and the number of Expatriates

	2015	2016	2017	2018	2019	2020	Average	Sum
Number of deaths in a year	9	8	15	6	7	10	9.16	55
Average age of death	23	23	22	18	23	21	21.6	
Sum of blood pints used in a year	10,765	10,765	10,765	10,682	11,482	12,284	11,124	66,743
Expatriates	278	301	323	147	19	25	182.16	1093

of patients were over 25 years old. In a study conducted in Iraq, the age distribution of thalassemic patients was 3% below 1 year, 21.70% was between 1 and 5 years, 41.70% was between 6 and 15 years, 20.40% was between 16 and 25 years, 12.30% was between 26 and 50 years, and 0.80% was between > 50 years old.[23]

The sum of deaths was 55 cases, and the average age of death was about 21.6 years old from 2015 to 2020. Unfortunately, the exact age of death was not available in the collected data. This number is equal to only 1.1% of the total cases included in the study. Further follow-up studies are required to determine the survival rate of patients. An Iranian study reported that 99% of the thalassemia patients lived until 10 years of age, 97% till 15, 95% up to 20, and 92% continued until 25 years of age. The difference in survival rates across cities may have been due to variations in the timeliness of diagnoses, available health-care services, accurate and regular treatment measures, and regular follow-up and monitoring by medical teams.[35]

A bulk number of blood pints were used, and tests were done at the Erbil Thalassemia center throughout the 6 years. During 2015–2020, 66,743 blood pints were used for blood transfusion, with an average of 11,124 blood pints/year. Furthermore, there were 527,735 tests done during the 6 years included in our study, with an average of 87,955.83/year. This high number of blood components usage and tests cause a substantial economic burden on the government and patients' families due to the high cost of therapy.

Conclusion

Thalassemia and other inherited hemoglobin disorders are subject to becoming a serious community health problem, causing significant financial and psychological issues on the families and sizable burdens on the financial status in any region in the absence of an effective prevention program.

As a preliminary step, the current study aimed to show the prevalence of hemoglobinopathies till the end of 2020, in the Erbil City-Kurdistan Region. As a result, an increase in the prevalence the hemoglobin disorders was revealed.

The abundance of consanguineous marriages due to cultural reasons, the lack of constitutive and effective prevention programs, and poor legislation might explain this rise.[23]

The study recommends that there is an emergent and strict need for an immediate and effective preventive program encompassing the diagnosis of TT (Carriers) in the community, specified guidelines to discriminate between iron-deficiency anemia and TT, premarriage identification of carrier couples, genetic counseling, and antenatal diagnosis. Furthermore, it is imperative to set constitutive guidelines for educating the population regarding Thalassemia and other inherited disorders with unequivocal legislation.

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Conflicts of interest
There are no conflicts of interest.

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