Academia Open
Vol 9 No 2 (2024): December
DOI: 10.21070/acopen.9.2024.10066 . Article type: (Medicine)

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ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

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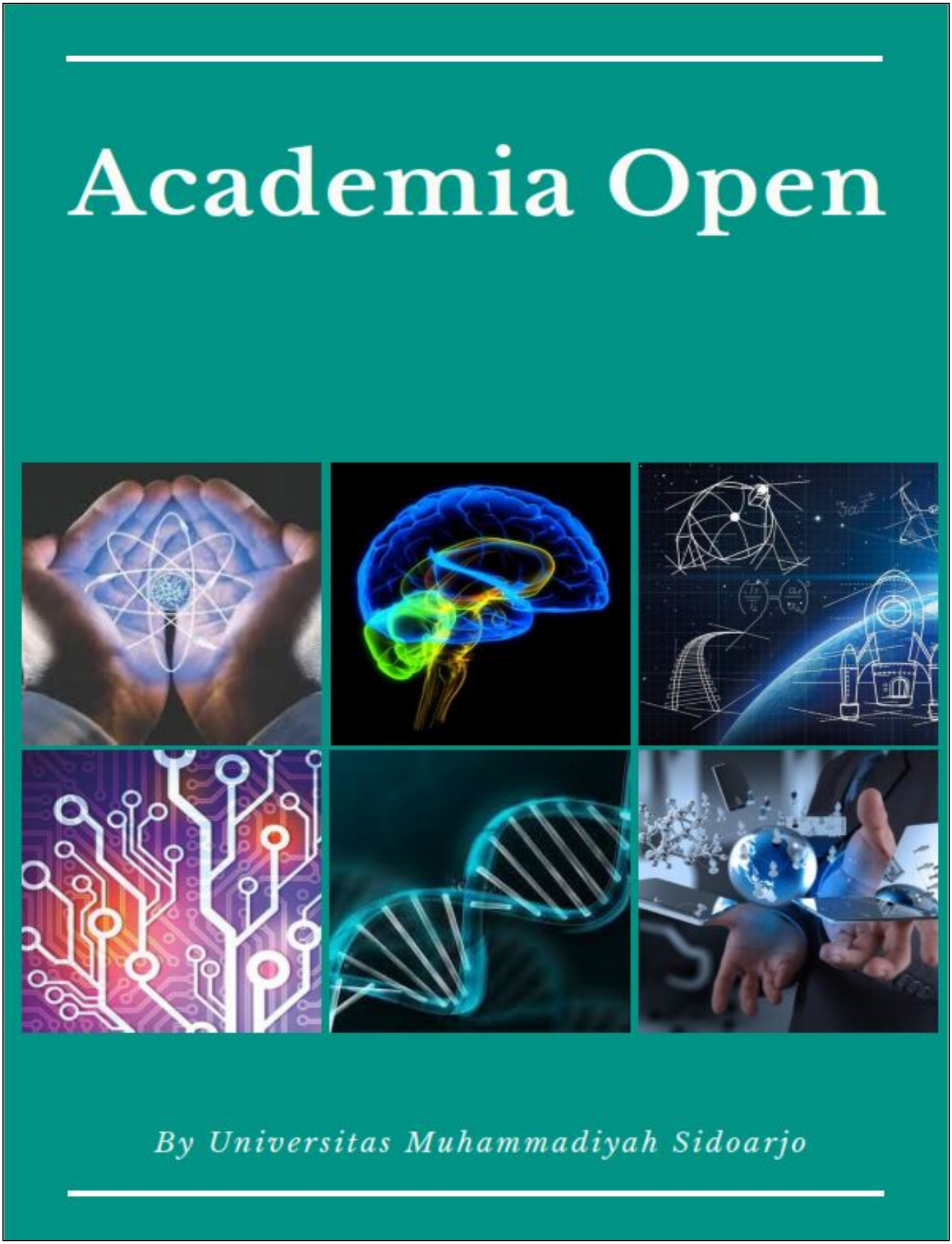

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Rising Cases of Hb H Disease in Iraq Highlight the Urgent Need for Pre-Pregnancy Screening

Meningkatnya Kasus Penyakit Hb H di Irak Menyoroti Kebutuhan Mendesak untuk Skrining Pra-Kehamilan

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Abstract

General background: Hemoglobin H (Hb H) disease results from mutations in three of the four α-globin genes, leading to α-thalassemia. **Specific background:** In Iraq, this condition is rare among alpha-thalassemia cases. The disease presents significant hematological abnormalities, impacting quality of life. **Knowledge gap:** Despite its rarity, few studies have characterized the hematopathological features and prevalence of Hb H disease in specific Iraqi regions. **Aims:** This study aimed to assess the hematological parameters and prevalence of Hb H disease among patients in Diyala province, Iraq. **Results:** A total of 81 patients with Hb H disease (53.18% male, 46.91% female) were registered at the Baqubah Teaching Hospital in 2023. Median patient age was 21.8 years (range 4-48). Hematological analysis revealed consistently low levels of hemoglobin (Hb) and hematocrit (HCT) compared to standard values. Mean corpuscular volume (MCV) was also significantly reduced, with 58.02% of patients presenting Hb levels below 10 g/dL. The 21-40 age group had the highest incidence (46.91%). **Novelty:** This study is among the few to investigate Hb H disease prevalence and hematopathological characteristics in Diyala province, revealing an unexpectedly high incidence in the 21-40 age group. **Implications:** These findings suggest that hematological parameters, including MCV and Hb levels, should be considered in thalassemia screening programs, particularly in pre-pregnancy assessments, to prevent the birth of children with severe forms of alpha-thalassemia and reduce Hb H disease prevalence.

Highlights:

1. Hb H disease shows low hemoglobin and MCV abnormalities.
2. Highest incidence occurs in patients aged 21-40 years.
3. Pre-pregnancy screening reduces severe alpha-thalassemia risk.

Keywords: Hb H disease, alpha-thalassemia, hematological parameters, Diyala province, prevalence

Published date: 2024-09-11 00:00:00

ISSN 2714-7444 (online), https://acopen.umsida.ac.id, published by Universitas Muhammadiyah Sidoarjo

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Introduction

A class of autosomal recessive hemoglobinopathies known as thalassemias are characterized by defective generation of normal alpha- or beta-globin chains. These hemoglobinopathies can cause anemia, premature red blood cell death, and inefficient erythropoiesis. While abnormal globin chain synthesis is the cause of sickle cell disease and other prevalent hemoglobinopathies [1]. One of the most prevalent monogenic diseases in the Mediterranean, Middle East, East and Southeast Asian regions, and in nations where these people have migrated is alpha thalassemia [2, 3]. Alpha globin anomalies can present clinically as silent carrier states, when one α-globin gene has been deleted, or as lethal hydrops fetalis, where all four α-globin genes are missing [4]. The disorder known as hemoglobin H (Hb H) occurs by the absence of three α-globin genes (compound heterozygous α +/ α 0,– α /– –), in which one alpha globin gene remains functioning, the patient produces a hemoglobin variant known as Hb H, which is made up of four β-chains (β4) [5, 6]. Even in patients with similar genotypes, the clinical severity of Hb H disease varies, possibly as a result of genetic and environmental modifiers [7]. Over 95% of α-thalassemia syndromes occur by deletional defects, with point mutations responsible for the remaining cases [8]. Mild-to-moderate microcytic hypochromic anemia and Hb levels that often fall between 8 and 10 g/dL are the hallmarks of Hb H disease; however, the degree of anemia varies based on the genetic abnormality, with Hb extremes reported between 2.6 and 13.3 g/dL [9]. For instance, Hb H Constant Spring is a non-deletional type of the disease that, compared to deletional Hb H, has a more severe anemia and disease course, with complications showing up by the time a person is ten years old [10, 11]. With Hb H illness, there may be varying degrees of jaundice and symptoms of impaired growth in children. Hb H disease is the most dangerous but nonfatal form of sickness hemoglobin-related [9]. In Iraq, in general, HbH illness is regarded as a rare disease in all individuals with alpha-thalassemia [12]. So, the present study focused on knowing the number of patients with Hb H disease in Diyala province and Hematological parameters for the patients.

Methods

This study included patients with the HB H disease registered in the Baqubah teaching hospital, Iraq from the 1st of January 2023 until the 31st of December 2023. The study excluded individuals with sickle cell anemia and those whose HPLC profile was consistent with the beta thalassemia characteristic. A total of 81 patients with Hb H thalassemia were registered. Information was obtained from the center registries and patient files. For the whole study population, the center used high performance liquid chromatography (HPLC) and Bio-Rad method HbA2/F to test for abnormal hemoglobins. Hematological parameters including RBC, HCT, Hb, MCV WBC and PLT were measured by the center and the standard values and ranges for hematological parameter analysis used as shown in the table 1.

Hematological parameters (Common Abbreviations)	Units	Values
Erythrocytes (RBC)	10^6/uL	4.06 – 5.30
Haematocrit (HCT)	%	38 - 52
Hemoglobin (Hb)	g/dL	12.0 – 16.0
Mean Corpuscular Volume (MCV)	fL	76 - 96
Leukocyte (WBC)	10^3/uL	3.70 – 11.00
Platelet Count (PLT)	10^3/uL	155 - 450

Table 1. *Standard values and ranges for hematological parameter analysis*

Result and Discussion

Result

According to the current study, (HPLC) of the patients with Hemoglobin H (Hb H) disease demonstrated low level of HbA2 (1.3) Figure 1. of the 81 patients with Hb H disease consisted of 38 (53.18%) men and 43 (46.91%) women with a median age of 21.8, range 4 - 48 years Figure 2. In the study, age was divided into three groups 0-20 years, 21-40 years and ≥41 years. Hb H disease was high in the age group 21-40 years 36 (46.91%) followed by 0-20 years with 38 (44.44%) and the age group ≥41 years was the lowest with 7 (8.64%) Figure 3.

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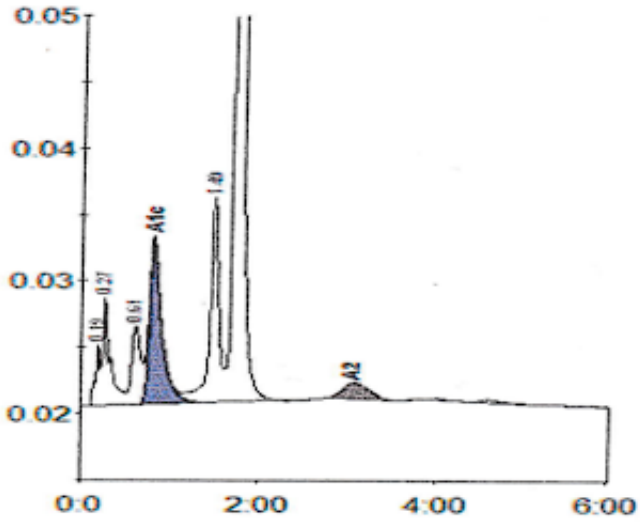

Peak table - ID: 101841

Peak	R.time	Height	Area	Area %
A1a	0.19	4574	15677	1.1
A1b	0.27	8218	47074	3.4
LA1c/CHb-1	0.61	5922	42935	3.1
A1c	0.81	12457	123970	11.0
P3	1.49	15542	106702	7.6
A0	1.72	252280	1041379	74.3
A2	3.05	1150	24360	1.3 *
Total Area:		1402096		

Concentration:	%
A1c	11.0
A2	1.3 *

Figure 1.

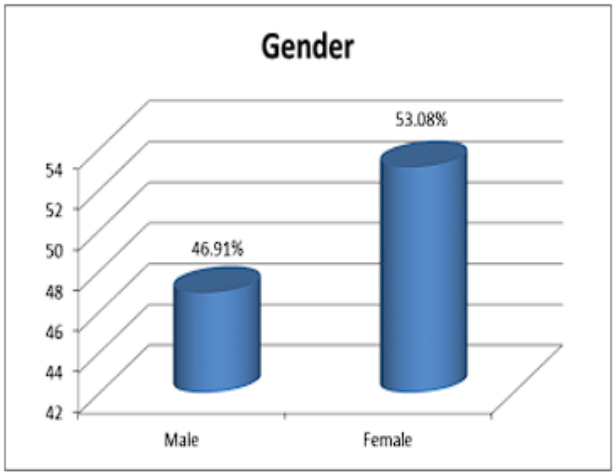

Figure 2: Rates of Hb H disease according to the gender

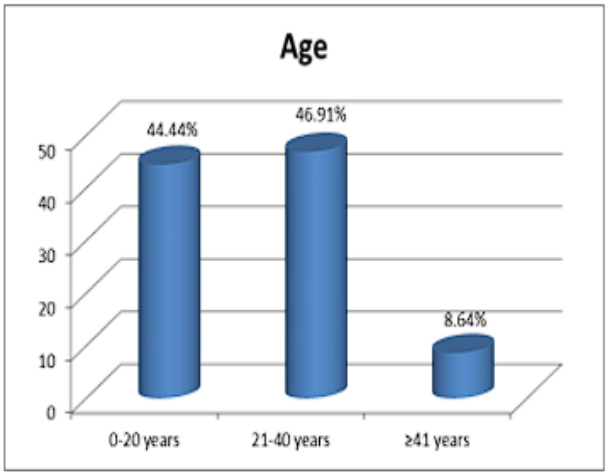

Figure 3: The distribution of the patients with Hb H disease by age

Figure 2.

As shown in figures 4 and 5, Hb, and HCT were significantly lower in Hb H patients than in normal values. The Hb value was lower than 10 g/dLwith 47 (58.02%) and more than 16 g/dL with 3 (3.7%). RBC was high in 65(80.25%) patients and WBC was in normal range in 52 (64.2) Hb H patients Figures 6 and 7 respectively.

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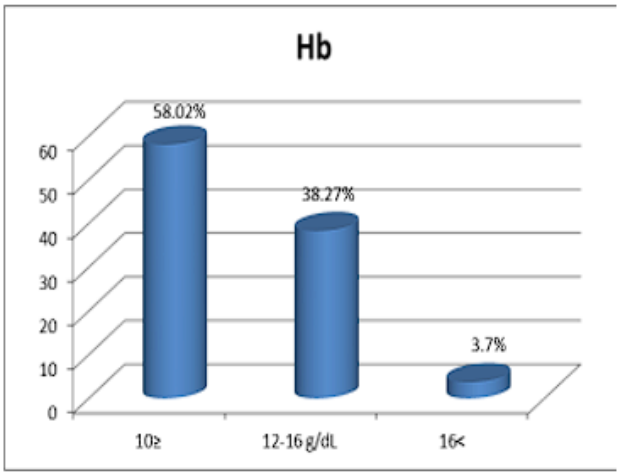

Figure 4: Hb values in patients with Hb H disease

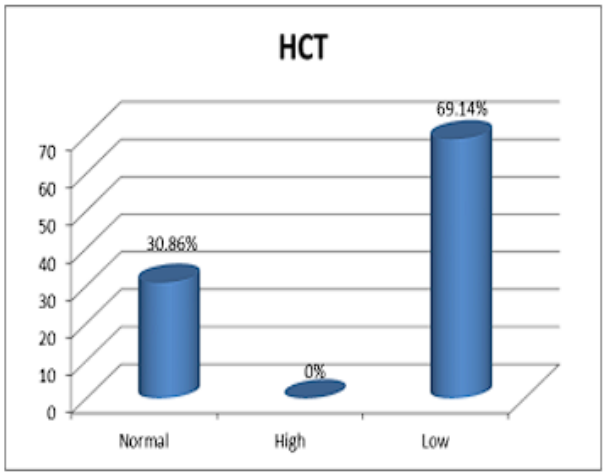

Figure 5: Distribution of HCT values in patients with Hb H disease

Figure 3.

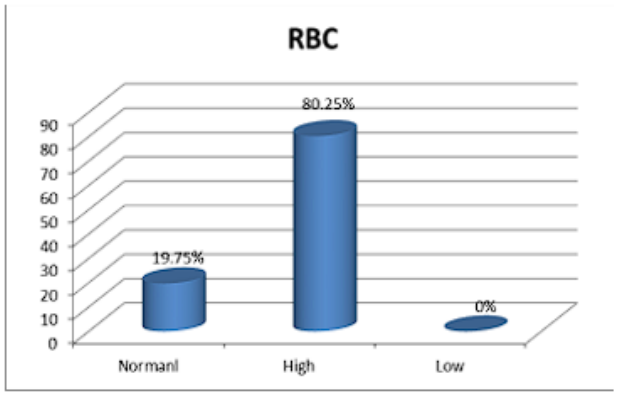

Figure 6: Rates of RBC in patients with Hb H disease

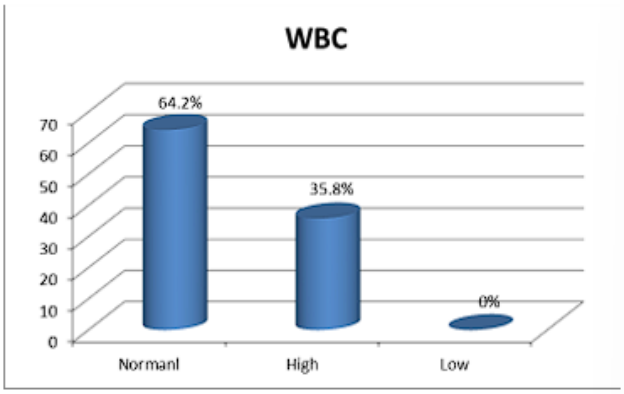

Figure 7: Distribution of WBC values in patients with Hb H disease

Figure 4.

As shown in Figure 8, Mean Corpuscular Volume (MCV) was significantly lower in Hb H patients than in normal values. While, Platelet Count (PLT) was in normal range in 58 patients as shown in Figure 9.

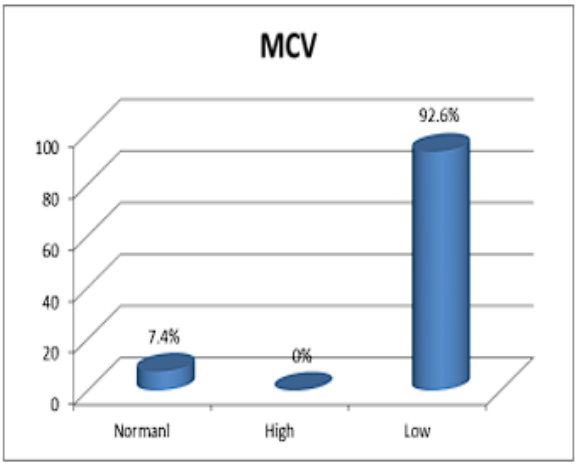

Figure 8: MCV values in patients with Hb H disease

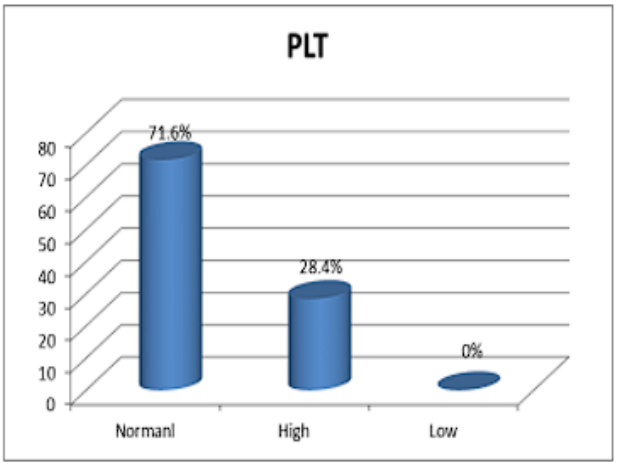

Figure 9: PLT values among patients

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Figure 5.

Discussion

Around the world, thalassemia has been recognized as the most common monogenetic disorder. 5.2% of people worldwide carry a significant hemoglobin disease variant, such as β or α0 thalassemia, and about 20% of people are carriers of α + thalassemia [13]. The percentage of people with the β-thalassemia gene in Iraq varies between 3.7 and 4.6 percent. Even Nevertheless, there are no published data on the carrier proportion of α-thalassemia in Iraq [14]. The most widely used basic hematological measures include measurements of MCV, MCH, and the amount of Hb A2 and HbF, as well as knowledge of the hematological characteristics of the many kinds of thalassemia genes and their interactions. In patients with Hb H deletion, the red cell MCV is significantly lower [3]. The current investigation supported previous results that Hb H patients had considerably lower Mean Corpuscular Volumes (MCV) than normal values. Also, Leukocyte (WBC) and Platelet Count (PLT) were within normal range which degree with a case report study that reported low level of WBC and PLT in Hb H patient [15]. of the 81 patients with Hb H disease in the study, involved of 38 (53.18%) male and 43 (46.91%) female and this is acceptable with a study performed on 145 patients with Hb H disease consisting of 70 (48.3) female and 75 (51.7) male [16]. According to analysis, the coinheritance of Hb H disease may have an impact on HbA2 levels in addition to the hematological parameters (Hb, MCV, and MCH). The low level of HbA2 in each case demonstrates this [17]. The investigation has shown that HPLC has many limitations despite being a useful first-level test. In particular, it has been noted that some patients may have a positive genetic test result but a negative HPLC result. Other measures, such as MCV, RBC count, MCVr, and reticulocyte count, may be suggestive of underlying mutations in the globin genes in addition to low levels of Hb and HPLC abnormalities. Thus, a study suggests that these blood count criteria be used as an essential tool for determining whether patients require full genetic testing [18]. The most severe types of thalassemia may be avoided if at-risk couples are identified by hematologic characteristics prior to pregnancy, particularly if they are belonging to a group at risk for α0 thalassemia (- -/αα) [19].

Conclusion

The results on this study suggest that using Hematological parameters which including MCV, WBC, PLT and Hb values as well as anemia symptoms patients could be in consideration prior to pregnancy. And then, avoiding born child with such a risky kind of alpha thalassemia which leads to an increase the prevalence of Hb H disease.

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