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Assessment of Risk Factors Associated with Increased Incidence of Thalassemia in Najaf Governorate

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Abstract

General Background: Thalassemia is a common inherited hemoglobin disorder characterized by defective globin chain synthesis and widespread global distribution. **Specific Background:** The prevalence of thalassemia varies across regions and is influenced by demographic and hereditary factors, particularly in Middle Eastern populations. **Knowledge Gap:** Limited localized evidence exists regarding the specific risk factors contributing to thalassemia incidence in Najaf Governorate. **Aims:** This study aimed to identify demographic and genetic risk factors associated with increased thalassemia cases in Najaf. **Results:** A cross-sectional study of 167 patients revealed higher prevalence among males, children aged 1–10 years, and urban residents. Blood group O was most common, while Rh-positive status reflected general population trends. Parental consanguinity and positive family history showed strong associations with disease occurrence, and thalassemia major was more prevalent than minor forms. **Novelty:** This study provides localized epidemiological evidence highlighting the combined role of demographic and hereditary determinants in thalassemia distribution. **Implications:** The findings emphasize the importance of premarital screening, early diagnosis, and community awareness programs to reduce disease burden and improve health outcomes.

Keywords: Thalassemia, Risk factors, Consanguinity, Epidemiology, Najaf

Key Findings Highlights

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1. Introduction

Thalassemia is the most common inherited hematologic disease worldwide. It is characterized by low hemoglobin levels, attributed to the incomplete or complete suppression of the synthesis of alpha-type (in HbH disease) or beta-type globin chains (in beta-thalassemia). These globin chains are the major subunits of hemoglobin, which consists as separate tetramers throughout fetal to postnatal development including fetal Hb (HbF; $\alpha_2\gamma_2$), adult Hb (HbA; $\alpha_2\beta_2$) and Hgb A 2 ($\alpha_2\delta_2$), respectively (Weatherall et al., 2006).

The disease was initially clinically reported in 1925 when two different forms of the disorder were independently described in US and Italy. These respective phenotypes have now been identified as thalassemia major (TM) and thalassemia intermedia (TI) (Taher & Cappellini, 2018). However, advances in knowledge over the past 2 decades clarified that thalassemia can result from homozygosity or compound heterozygosity for affected allelic variants, and individuals with a single mutant allele generally present with a mild recessively inherited microcytic anemia defined as thalassemia minor (Munkongdee et al., 2020; Origa, 2021).

Due to genetic defects of alpha or beta globin polypeptides biosynthesis, thalassemia is now considered the commonest monogenic disease in all mankind. Although classically linked with Mediterranean populations, it is found widely across diverse geographic regions of sub-Saharan Africa, the Middle East, South and Southeast Asia and Western Pacific (Abu-Shaheen et al., 2020). Worldwide estimates suggest that 1.5% of world population are heterozygous for the thalassemia associated mutations based on epidemiological data reported by the World Health Organization. In addition, approximately 60000 infants are born every year having clinical severe types of the disease which includes homozygous beta-thalassemia, beta-thalassemia/hemoglobin E, homozygous alpha-thalassemia and other related hemoglobinopathies (Abu-Shaheen et al., 2020; Origa, 2017).

The introduction of historical population screening programs, aimed to identify carriers—associated with specific genetic counselling and prenatal diagnosis—has resulted in a marked decrease in affected births in several Mediterranean countries. These organized screening programs have started to be implemented in recent years in different populations of the Middle East and Asia (Origa, 2017). Prenatal diagnosis is possible after both pathogenic alleles have been molecularly characterized and can be made by the investigation of fetal DNA obtained invasively (chorionic villus sampling at 10-12 weeks of gestation, or amniocentesis at 15-18 weeks). Moreover, with preimplantation genetic diagnosis, couples have the possibility to give birth to unaffected babies. Novel non-invasive approaches, such as maternal blood analysis of cell-free fetal DNA, are expected to have an adherence in the future evolution of prenatal diagnostic procedures (Lee et al., 2021).

1.1 Research Objectives

This study aims to answer the following research questions:

1. Does gender influence the incidence of thalassemia ?
2. Does age affect the likelihood of developing thalassemia ?
3. Do blood group and Rh factor play roles in disease distribution?
4. Does consanguinity between parents increase the risk of thalassemia ?
5. Does family history and number of affected siblings influence disease occurrence ?

2. Materials and Methods

2.1 Study Design and Setting

A descriptive cross-sectional study was conducted in Najaf Governorate from January 1 to March 31, 2025. Collection of data have been performed at the Hematology/Thalassemic Center of Al-Zahraa Teaching Hospital in Al-Najaf City.

2.2 Study Population

The study population included 167 patients who had been previously diagnosed by a specialist of thalassemia. Eighty-six of these participants were male (52% of the total sample), and 81 were female (48%). Fairly proportioned gender distribution reflected and sufficient coverage of both, boys and girls in the study cohort which has reduced an interpretive bias associated with sex.

2.3 Data Collection

A structured data extraction form was used to obtain the following variables:

- Age
- Gender
- Place of residence
- Blood group and Rh factor
- Parental consanguinity
- Family history (number of affected siblings)
- Type of thalassemia (major/minor)

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2.4 Ethical Considerations

Patient confidentiality was strictly maintained.

3. Results and Discussion

3.1 . Gender Distribution

Figure.1. The distribution of patients according to gender

The current investigation shows a relatively equal sex ratio in the participants with respect to sex (52% males and 48% females). This slight male predominance parallels that observed in several local studies in Najaf province where a marginal higher rate of genetic blood diseases was recorded among males, of which thalassemia is the most common. For instance, Al-Hakim et al. (2020)], 53.437% of genetic blood disorders patients in their study were males. Furthermore, with the symptoms of the disease presenting themselves females in some families were visited at hospital comparatively less when comparing with males. This ignorance may further cause a late diagnosis or less tendency of healthcare-seeking behavior for female patients. Mikael and Al-Allawi (2018) also found that socio-cultural -preserving factors were affecting pre-diagnosis and PCC among Iraqi females.

3.2 . Age Distribution

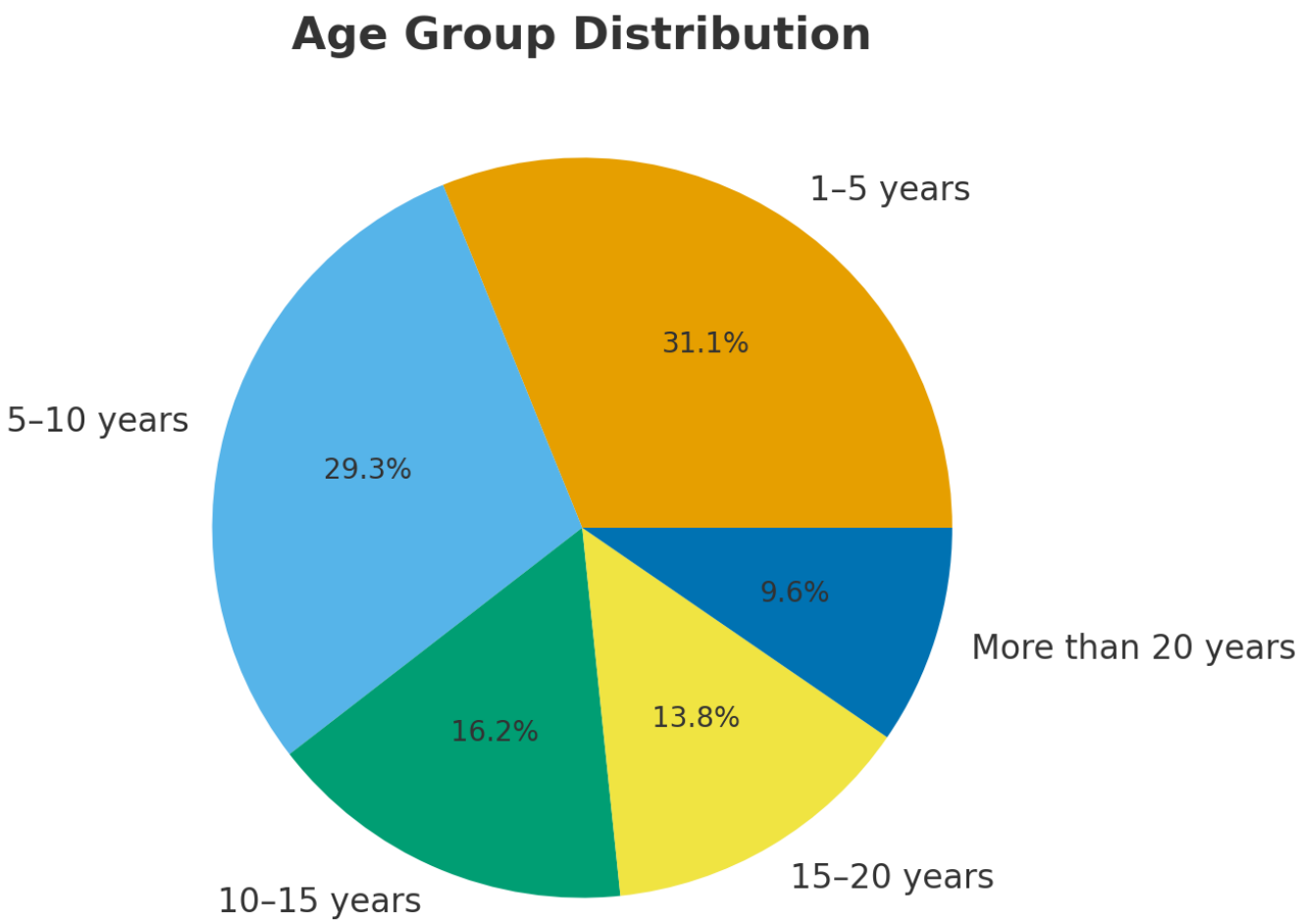

Figure 1.

Figure.2. The distribution of patients according to age group

The incidence was highest in children aged between 1and 5 years (31.1%) and 5 and 10 years (29.3%). This is consistent

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with previous studies that have reported severe presentations to occur during early childhood (Mikael & Al-Allawi, 2018). The lower rates among older patients probably reflect better survival with habitual transfusion therapy.

3.3 . Residence

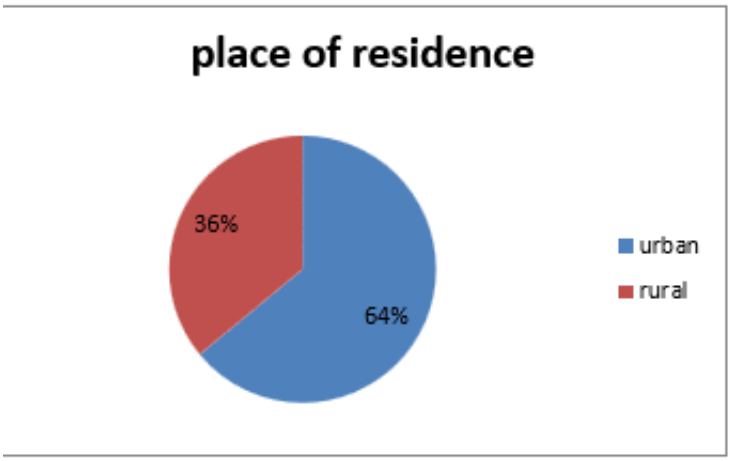

Figure 2.

Figure. 3. *The distribution of patients according to residence*

The distribution of study participants on the basis of their place of residence is presented in Figure It indicates that 64% were from urban and 36% came from rural. Part of these results are in line with the study by Al-Hakim et al. (2020) who found that the majority of patients suffering from hereditary blood diseases in Najaf were living in the city center 56.42% then rural areas in other townships in the governorate. However, Ali and Abdulla (2022) found 60% of their sample with thalassemia major patients were from rural areas. The discrepancy in the distribution of thalassemia and other related genetic blood disorders reported here stresses that the geographical distribution of thalassemia and other hereditary defects will vary among studies based on study population, sampling procedures, and demographic diversity within a particular governorate.

3.4 . Blood Group Distribution

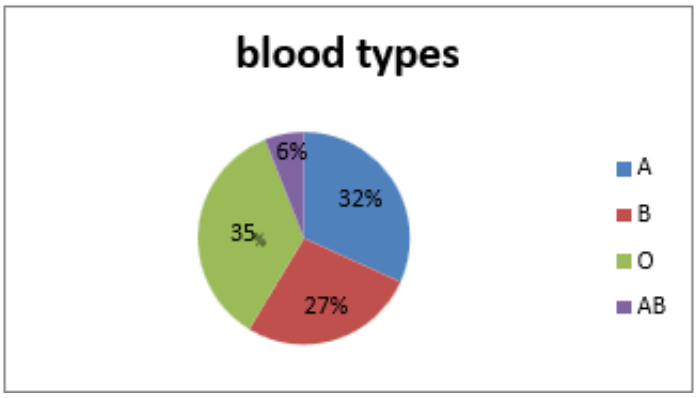

Figure 3.

Figure .4. The distribution of patients according to the blood type factor

The frequency of ABO blood group of the samples are shown in (figure 4) with blood type O (35%) being most common, followed by types A (32%), B(27%) and AB(6%). This distribution suggests an over representation of blood group O in thalassemia patients in Najaf. To the best of our knowledge, this distribution might not represent ABO blood group pattern in people residing in Najaf Governorate or even for Iraqis as a whole. It has been reported by various studies that blood groups differ with respect to geographic region and ethnic races. In population based-studies in Iraq, blood group O was most common followed by A and then B, while AB is the least common. This observation is consistent with the result of Hassan (2016) but contrasts the conclusion obtained by Abid and Ereiby (2019). This could be attributed to variations in the study population, sample size, regional demographics and genetic factors responsible for distribution of blood group.

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3.5 . Rh Factor

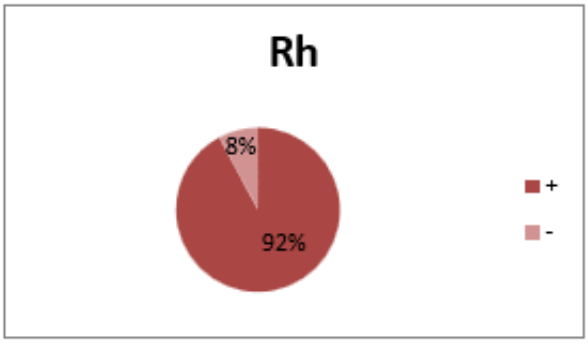

Figure 4.

Figure.5. The distribution of patients according to the of Rh factor

The distribution of the Rh factor among the studied patients is shown in Figure (5) which indicates that most of the patients were Rh positive (92%) and only 8% were Rh negative. In the current research, these results show that most of the patients with thalassemia are Rh positive and this is consistent with the distribution of Rh factor in general Iraqi population. Rh positive Iraqis account for 85–95% of population (Mohssin and Mahmood 2015).

There is no direct evidence supporting a causal association between the Rh factor and thalassemia, as thalassemia is a hereditary disorder resulting from mutations in hemoglobin genes, whereas the Rh factor is determined by an entirely different genetic system. Therefore, the high prevalence of Rh-positive individuals among thalassemia patients merely reflects its predominance in the general population and does not indicate that the Rh factor represents a risk factor for the development of thalassemia.

3.6 . Parental Consanguinity

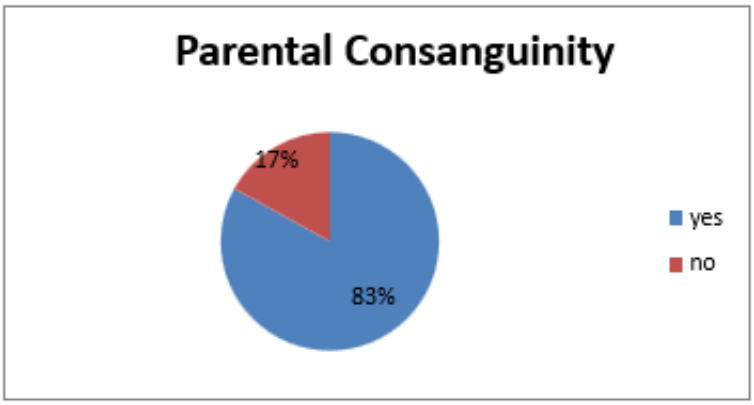

Figure 5.

Figure .6. The distribution of patients according to the Parental Consanguinity

Figure (6) illustrates the rate of consanguinity in patients' parents. Results: We revealed that the percentage of patients with consanguineous parents was 83%, and that of patients with nonrelated parents was 17%. This result illustrates a very high prevalence of consanguinity in thalassemia patients' families in Najaf; hence the possible role of consanguineous marriage in increasing the risk of genetic disorders like thalassemia. The high proportion of thalassemia (83%) compared to other spectrum of genetic disease (consanguineous marriage being established as causing rise in both autosomal recessive genetic disease) strongly supports the scientific literature that clearly indicates the prevalence of autosomal recessive genetic disorder in the offsprings of consanguineous marriages. This increases the likelihood that a child will inherit both recessive alleles that cause the disease. Such practical implications from the findings highlight the need for health education and creativeness in plans and giving presentations for local community awareness concerning the risks of consanguineous marriage and its contribution to the incidence of genetic disorders. Such a result reinforces the findings reported by Al-Hakim et al. (2020).

3.7 . Family History

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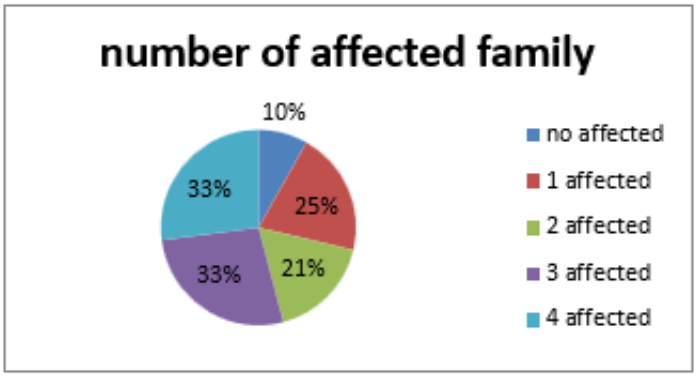

Figure 6.

Figure.7. The distribution of patients according to the number of family individuals affected by the disease

Distribution of thalassemia patients as per the number of affected siblings in the same family, representing interfamilial inheritance (Figure) From the results, 90% of patients had one or more affected siblings and only 10% of patients had all their unaffected siblings. Families with one affected sibling had the second highest proportion (25%), followed by two affected siblings (21%), three affected siblings (33%), and four affected siblings (11%). These results corroborate the autosomal recessive nature of thalassemia, as the disease occurs when an individual inherits impaired thalassemia alleles from both parents. When marriages are consanguineous, the probability that both parents carry the same recessive gene is much higher, as is the proportion of affected children in a family. The large percentage of families with more than one sibling affected especially those with three or more (44%) highlight the immediate need for premarital genetic screening and the advent of early diagnosis programs to prevent new cases from being born. These findings are in accordance with the previous studies (**Weatherall and Wiley-Blackwell, 2001; Modell and Darlison, 2008**).

3.8 . Type of Thalassemia

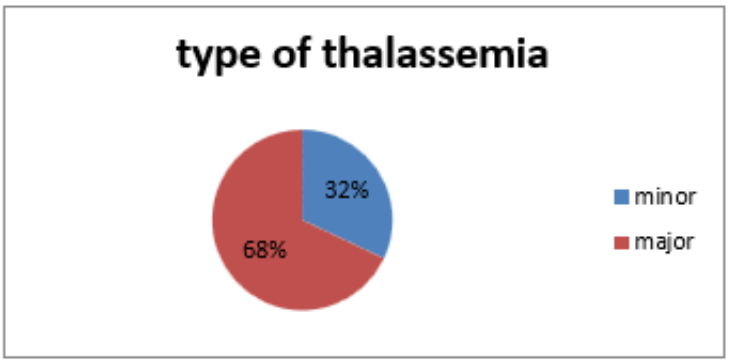

Figure 7.

Figure.8. The distribution of patients according to the type of thalassemia

The character of shows the types of thalassemia in the sample under study (figure 8). Results also demonstrated that thalassemia major was the most common, contributing 68%, thalassemia minor 32%. This result shows that most patients in the sample have the more advanced (more severe) form of the disease. These findings are similar to the results obtained from the study conducted by Mikael and Al-Allawi (2018), where a higher percentage of people with thalassemia major were higher. Thalassemia major is considered the more serious form which usually requires repeated blood transfusions and more intensive medical management, while thalassemia minor usually has little or no clinical symptoms.

4. Conclusion

Thalassemia is one of the most common hereditary disorders in Najaf Governorate and its incidence is affected by various demographic and genetic factors. The results show the significant attribution of consanguinity, positive family history and younger age groups to the disease burden. The aim is to reduce the incidence rate of new cases and improve outcomes by strengthening premarital screening programs, improving community awareness, and expanding initiatives for early diagnosis.

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