Hemoglobin Synthesis Dynamics In Inhabitants: A Comprehensive Study

Somia A. Nassar[1], Ghadi Albalawi[2], Rayanh Alshamikh[3], Ahmed Hjazi[4], Humood Al Shmrany[5], Munirah Saad Aldossari[6], Sultan f. Alqhatani[7] , Farhan R. Khan[8], Abdulkarim S.Binshaya[9*]

[1,2,3,4,5,9]*Department of Medical Laboratory Sciences, College of Applied Medical Sciences; Prince Sattam bin Abdulaziz University, Alkharj, 11942, Saudi Arabia
[,1]Department of Parasitology & Animal Diseases, National Research Centre, 33 Bohouth St., Dokki, Giza, 12622, Egypt
[6] Diabetic center, Al Adiriyah hospital, Riyadh, Saudi Arabia
[7]Laboratory Department, Aliman General Hospital, Riyadh 13782 , Saudi Arabia
[8]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Al- Quwayiyah, Shaqra University, Riyadh, Saudi Arabia

*** Corresponding Author**: Abdulkarim S.Binshaya
*Department of Medical Laboratory Sciences, College of Applied medical sciences, Prince Sattam bin Abdulaziz University, Alkharj, 11942, Saudi Arabia.Abd.ALDOSARI@psau.edu.sa

Abstract
Fetal hemoglobin (HbF) synthesis commences around the sixth week of gestation, sustaining high levels until the infant reaches two to four months of age. During the initial year of life, HbF levels precipitously decline, making way for the adult forms of hemoglobin. However, certain medical conditions, such as beta-thalassemia, can disrupt the normal transition to adult hemoglobin, leading to elevated HbF levels beyond infancy. Additionally, therapeutic interventions targeting HbF synthesis have been employed in the supervision of sickle cell anemia. This study presents a comprehensive analysis of data from 1,176 patients who underwent HbF analysis between 2018 and 2020 at the Medical Laboratory of Al Kharj Military Industries Corporation Hospital. Most patients exhibited healthy HbF levels. Among the patients, 85% demonstrated normal HbF levels relative to their ages and genders. Notably, 14% of patients exhibited HbF disturbances, with a higher incidence among females is 66%, aged 30 to 50 (56%) compared to males 34% and observed in age groups between 0 to 15 years. A limited subset of cases showed elevated levels of both HbF and adult hemoglobin (HbA). Furthermore, within the cohort exhibiting HbF disturbances, 64.5% demonstrated concurrent high HbF and the presence of hemoglobin S (HbS), in women (72%) it is more prevalent than in men (28%). In the pediatric population, 16 cases displayed elevated levels of both HbF and HbS, while 44 cases exhibited high HbF levels alone. Among one-year-old infants, HbF levels ranged from 0 to 2 percent in six cases, while 17 infants exhibited elevated HbF levels ranging from 3 to 36 percent. In conclusion, this study underscores the temporal dynamics of HbF levels during normal pregnancy and the first year of life, noting a significant increase in HbF levels that subsequently decline.

Keywords: Epidemiological, fetal hemoglobin, genetic disorders,

Introduction

During gestation, Hemoglobin F (HbF) is predominant. The production of HbF by erythroid precursor cells begins during pregnancy. Hemoglobin A (HbA) comprises 2- α and two beta components, while HbF has two γ proteins and two α proteins [1-3].

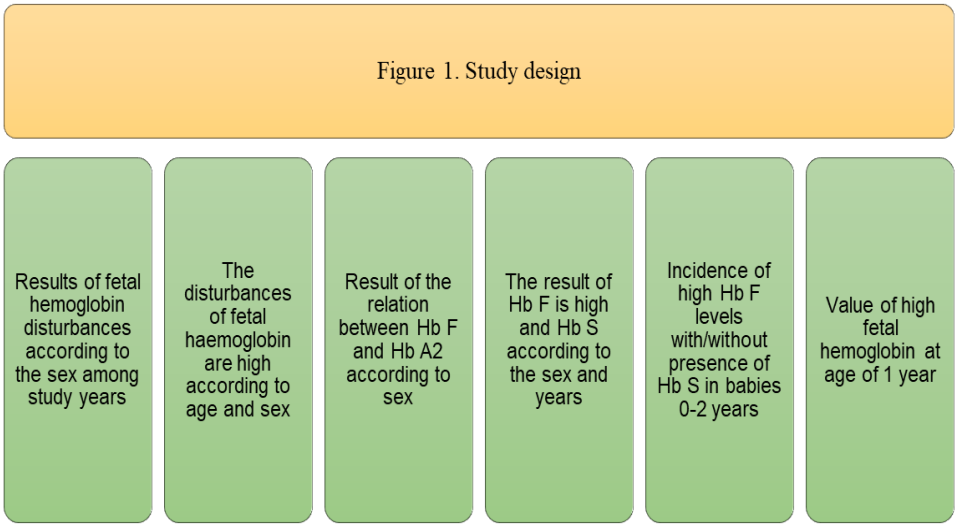
The transcription of the human globin locus causes the synthesis of mRNA precursors in the nucleus, which are later converted into mature globin mRNAs in the cytoplasm [4]. Enzymes and ribosomes, which are part of the cell's translational machinery in this instance, produce globins, which combine with heme to create the standard individuals Hb. HbF α2γ2 is the predominant hemoglobin throughout pregnancy, whereas HbA, α2β2 is the predominant hemoglobin during adulthood. A small Hb, hemoglobin A2 (HbA, α2δ2) often makes up less than 2% of the total amount of Hb [5]. Mice lack γ-globin genes, and the emergence of human γ-globin genes and HbF synthesis in prelates is rather new. HbF possesses a greater affinity for oxygen compared to HbA, which promotes oxygen delivery to the fetus within the placental circulation, is most likely a factor in the formation of -globin genes. A significant development in the biology of hemoglobin is the change from human γ to β-globin gene expression in late fetal life. Human disorders for example sickle cell anemia (SS disease) and β thalassemia are caused by the effects of this switch. [4, 5]. Although patients with these illnesses produce HbF during fetal life normally and optimally, the transition to mainly Birth-related HbA production is pathological. Haemoglobin S (HbS, α2βS2) is formed when βS accumulates due to the usual switch to β-globin gene expression in SS illness, which causes hemoglobin S (HbS) aggregation, hemolytic anemia, and small artery blockage [6]. The switch causes a reduction or absence of normal human β-globin and HbA synthesis, in human β thalassemia. As

a result, early erythroid cells experience excess α-globin buildup, precipitation, death, and inefficient erythropoiesis [1, 7, 8].
After the transition, inadequate HbF is formed in adult hematopoietic cells to make up for the absence of typical β-globin production in both SS and (Cooley anemia). Some SS and β thalassemia patients who received treatments with hydroxyurea and butyrate compounds experienced higher levels of HbF and clinical benefits [9-13]. A treatment for these diseases would be possible if the molecular processes behind hemoglobin switching were understood better and HbF could be completely restored in adult cells [14]. The objective of the study is to assess and record the incidence of fetal hemoglobin disturbances in various groups like pregnant women, non-pregnant women, babies, and children in Al Kharj City between 2018 and 2020. The primary objective of the study is to investigate the role of rising fetal hemoglobin levels in association with incidences of some diseases such as thalassemia, sickle cell anemia, or any other genetic disorder. To record the incidences of hemoglobin disturbances in pregnant, and non-pregnant women, babies, and children at Al Kharj Military Industries Corporation Hospital between 2018 and 2020. To determine the prevalence of high fetal hemoglobin concentrations in SS patients treated with hydroxyurea. To demonstrate the connection between fetal hemoglobin and both Hb A2 and Hb S. To record and observe the persistent elevation of HbF in young people older than one year.

Methods
The present study consists of 1176 individuals of both genders (i.e., male and female) and between 0-77 years of age. The participants visited medical clinics for HbEP testing using the capillary's 2 'flex piercing instrument. The equipment has Cap Piercing Mechanism to screen entire blood while maximizing laboratory productivity. Enhanced sample homogenization is provided by the inversion blending mechanism, which enhances the accuracy and precision of the outcomes. This multi-parameter device provides a thorough menu for testing proteins, immunotypes, hemoglobin, HbA1c, and CDT (carbohydrate deficient transferrin) on serum, urine, and whole blood.

The data were collected from the Laboratory department at Al Kharj Military Industries Corporation Hospital located in Al-Kharj City for the period from January 2018 to December 2020. The primary data showed that most patients were healthy people. Equivalent amounts for each hemoglobin zone are obtained by direct monitoring at 415 nm in capillaries. The data was obtained from Al-Kharj according to the patient data collection ethical protocol, which stated the privacy of patients and patients should not be identified for research purposes.

Applying the HPLC approach, the standards for each of the Capillary's 2 Flex-Piercing instrument's primary electrophoretic hemoglobin regions has been generated from a sample of 113healthy adults (men and women) with average hemoglobin values:
Hb A: among 96.7 and 97.8 %
Hb F: ≤ 0.5 % (*)
Hb A2: among 2.2 and 3.2 %
The data is classified as the following figure 1:



Statistical analysis
Statistical analysis for the hemoglobin data was analyzed using Microsoft Excel 2013 including the trend of prevalence and prevalence rate.

Results

Refer to the analysis of collected data from 20182020 according to disturbances of fetal hemoglobin in female and male; the result showed that in 2018 there was 361 patients with fetal hemoglobin 312 were of normal fetal hemoglobin (female 282 and male 30), while 49 patients were high fetal hemoglobin (female 35 and male 14). In 2019, the result showed there were 425 patients with fetal hemoglobin 370 were of normal fetal hemoglobin (female 341 and male 29), while 51 patients were high fetal hemoglobin (female 41 and male 10). In 2020 the result showed there was 390 patients with fetal hemoglobin 325 were of normal fetal hemoglobin (female 311 and male 14), while 66 patients were high fetal hemoglobin (female 35 and male 31). (Table 1)

Table 1: Fetal hemoglobin disturbances according to the gender among study years

Years	Total patient		Normal Patient		Female		Male		Hb F (High)		Female		Male	
	No.	%			No.	%	No.	%			No.	%	No	%
2018	361	100	312	86.5	282	90.4	30	9.6	49	13.5	35	71.4	14	28.6
2019	425	100	370	87.1	341	92.2	29	7.8	51	12.9	41	80.4	10	19.6
2020	390	100	325	83	311	95.7	14	4.3	66	17	35	53	31	47

Regarding to the age distribution among females and males disturbances of fetal hemoglobin, the collected data from 2018 – 2020 showed that at age of 0-5 years there were 66 patients with high fetal hemoglobin (female 26 and male 40), at ages of 5-15 years there were 28 patients with high fetal hemoglobin (13 female and male 15), at age 15-30, there were 30 patients with high fetal hemoglobin (female 30), at age 30-50, there were 90 patients with high fetal hemoglobin (female 90), while at age 50-70, there were 2 patients with high fetal hemoglobin (female 2).(Table and figure 2)

Table 2: The disturbances of fetal hemoglobin according to age and sex

Age	Female	Male	Total patient
0-5	26	40	66
5-15	13	15	28
15-30	30	-	-
30-50	90	-	-
50-70	2	-	-

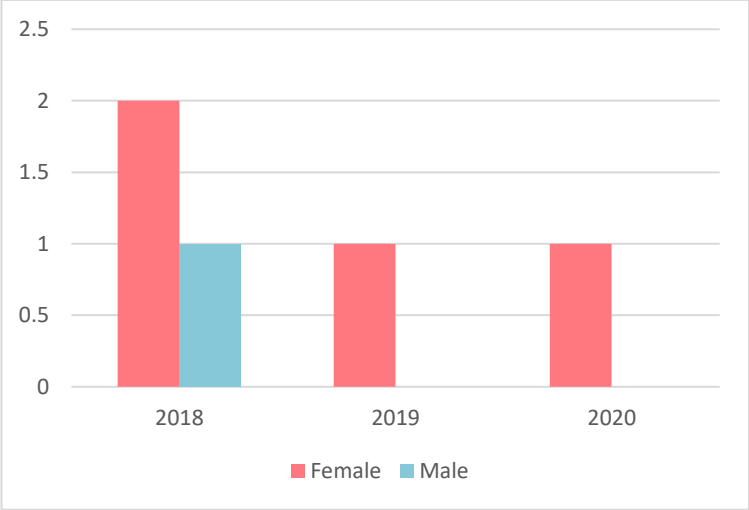


Figure 2: Hb F and Hb A2 according to sex

As shown in table and figure 3 there were only 5 cases that revealed a high concentration of both Hb F and Hb A2 and the result showed that in 2018 there was 3 patients with Hb F and HbA2 (female 2 and male 1). While in 2019 there was 1 patient of Hb F and HbA2 (female 1), and in 2020 there was 1 patient of Hb F and HbA2 (female 1).

Table 3: The relation between Hb F and Hb A2 according to sex

Years	HB F (high) HB A2 (high)	Female	Male
2018	3	2	1
2019	1	1	-
2020	1	1	-

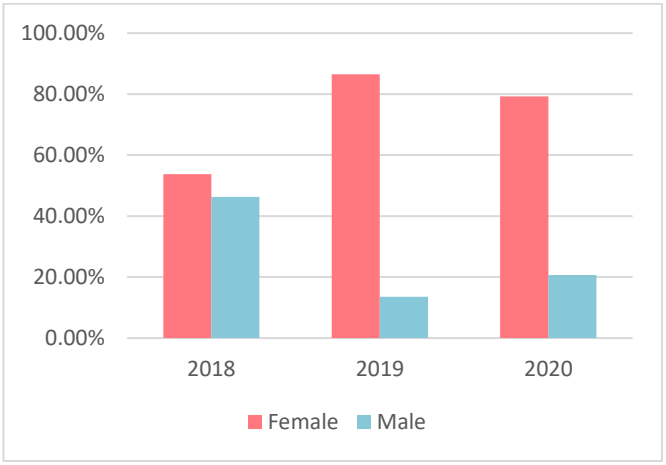


Figure 3: Hb F is high and Hb S according to sex and years

Regarding to the relation between Hb F disturbances and HB S among the years of collected data, results showed that in 2018 the total cases were 41, 22 (53.7%) were female while 19 (46.3%) were male, while in 2019 the total cases were 37, 32 (86.5%) of the were female and 5 (13.5%) were male, and in 2020 the total number of cases was 29, 23 (79.3%) of the were female while 6 (20.7%) were male. (Table and figure 4)

Table 4: Hb F disturbances in the presence of Hb S according to gender and study year.

Years	HB F (high) HB S (present)		Female		Male	
2018	41	100%	22	53.7%	19	46.3%
2019	37	100%	32	86.5%	5	13.5%
2020	29	100%	23	79.3%	6	20.7%

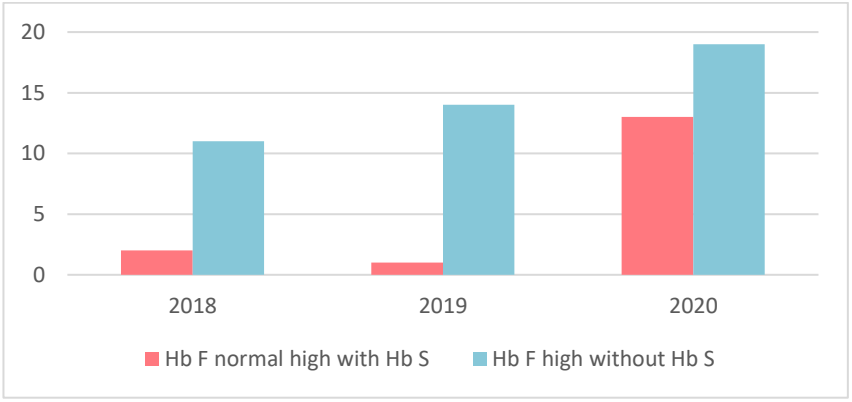


Figure 4: Normal high Hb F with Hb S & high Hb F without in babies 0-2 years

Table 5 showed the increase of Hb F level among babies which was always high either alone or with a level of Hb S in babies suffering from sickle cell anemia as recorded in 2018 there were 2 babies have high HbF and HbS, and 11 recorded high levels of Hb F only. In 2019 there was only one baby with high level of both Hb F and Hb S and 14 had a higher level of Hb F only. While in 2020, 13 babies recorded a high of both Hb F and HbS and 19 has high HbF only.

Table 5: Incidence of high Hb F levels with/without presence of Hb S in babies 0-2 years

Years	Hb F normal high with HbS	Hb F high without Hb S
2018	2	11
2019	1	14
2020	13	19

Figure 5 showed the result of Hb F level in 23 patients of one year age, 6 babies were normal (0 to 2 %) while 17 babies recorded a high level of Hb F ranging from 3% -36%.

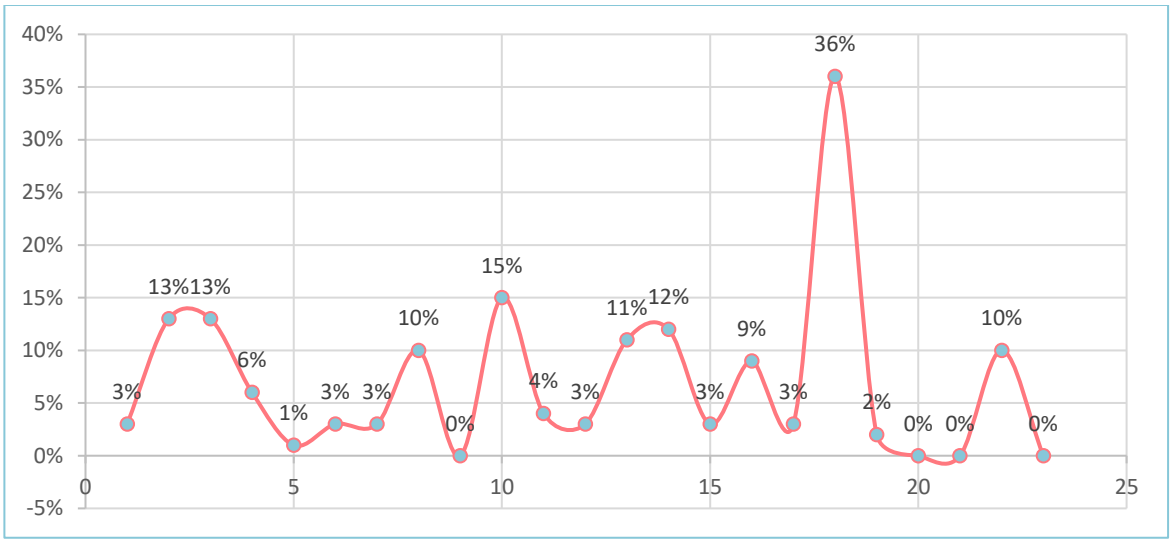


Figure 5: Values of high fetal hemoglobin at age of 1 year

Discussion

The primary oxygen carrier molecule in fetal RBCs, fetal hemoglobin, is in charge of carrying oxygen from mom's circulatory to the fetus' organs and body tissues. It begins to form at roughly sixth week of pregnancy, and its levels continue to be high even after delivery. Compared to the adult types of hemoglobin, HbF has a distinct composition that makes it more effective at binding oxygen. It describes how the placenta, which is located in the womb of the mother, allows the growing baby to absorb oxygen through its mom's blood. According to Table 1, fetal hemoglobin, which is primarily present in the fetus from the 10th to 12th week of being pregnant until six months after birth and is produced by erythroid precursor cells, may explain why females experience Hb F disturbances more frequently than males. Hemoglobin A, the primary type of adult hemoglobin, is created within the first year [15, 16] . As recorded in Table 2 the disturbances of HbF - according to age and sex - showed a high level of hemoglobin F in males, especially at the age of 0-15 years old. These results may be due to that; in the first year after birth, the Hb F is still being high until it is replaced by HbA. However, the high level of HbF after the age of 1 year may be due to either thalassemia or sickle cell anemia [17, 18]. The most common susceptible age of increasing level of Hb F in female present at 15-45 years old as at this age women has the tendency to pregnant [19, 20]. or may be due to genetic factors such as thalassemia, sickle cell anemia, or the use of some medications as hydroxyurea which cause an increase in HbF [18]. Table 3 showed 5 cases 4 female and 1 male - among the 3 years of the collected data - recorded high amount of both Hb F and Hb A2. These may be due to illnesses for example β-thalassemia, that disturb mechanisms of the adult hemoglobin and cause HbF amount rises. [17].

Results recorded in Table 4 show that there was a relation between high levels of HbF and the presence of Hb S which was recorded in a patient suffering from sickle cell anemia and this may be due to that the patients were treated with hydroxyurea, that endorses the generation of fetal Hb and lessens the early bursting of RBCs [18, 21]. Due to its ability to inhibit the production of HbS chains within RBCs, HbF is crucial in decreasing the impact of such conditions [22]. Curiously, greater amounts of HbF were linked to a decrease in the incidence of painful instances, leg ulcers, and overall intensity of the sickness, as well as these symptoms, as well as the recovery of these symptoms [23]. The results recorded in table 7 represent the incidence of high levels of Hb F in babies within 0-2 years old which is a normal phenomenon. Until one year of age of child the HbF level is greater [24] while the greater amount of HbF after that may be due to the presence of HbS which means “babies suffering from sickle cell anemia”. The elevated levels of HbF are protective for newborns with SCD at birth [25]. If the HbF stays relatively elevated after being born, sickle-cell disease sufferers will experience fewer painful episodes, which will improve their scenario [26] as HbF reduce the ability to disrupt HbS formation within red blood cells [22]. The different values of HbF in the first 1 year of age which means When a baby is born, the process of switching from manufacturing HbF and HbA to HbF (50–95%) begins. HbA predominates at 6 months of age; however, some hereditary illnesses can develop as a result of gene mutations that code for elements in HbF. HbF is produced rather than haemoglobin A due to alterations in the areas that act as the HBG1 and HBG2 promoters (hereditary persistence of HbF) [27-29].

Conclusion

Based on the results obtained from this study, we can draw the conclusion that a normal pregnancy and infants at the age of one year are linked to a notable rise in HbF levels, which subsequently experience a relative decrease.

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