


RESEARCH ARTICLE

Analysis of genotype distribution of thalassemia and G6PD deficiency among Hakka population in Meizhou city of Guangdong Province

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Abstract

Objective: The aim of the study was to explore genotype distribution thalassemia and G6PD deficiency in Meizhou city, China.

Methods: A total of 16 158 individuals were involved in thalassemia genetic testing. A total of 605 subjects were screened for common Chinese G6PD mutations by gene chip analysis. Genotypes and allele frequencies were analyzed.

Results: A total of 5463 cases carried thalassemia mutations were identified, including 3585 cases, 1701 cases, and 177 cases with α -, β -, and $\alpha + \beta$ -thalassemia mutations, respectively. $--^{SEA}$ (65.12%), $-\alpha^{3.7}$ (19.05%), and $-\alpha^{4.2}$ (8.05%) deletion were the main mutations of α -thalassemia, while IVS-II-654(C \rightarrow T) (40.39%), CD41-42(-TCTT) (32.72%), -28(A \rightarrow G) (10.11%), and CD17(A \rightarrow T) (9.32%) mutations were the principal mutations of β -thalassemia in Meizhou. There were significant differences in allele frequencies in some counties. Genetic testing for G6PD deficiency, six mutation sites, and one polymorphism were detected in our study. A total of 198 alleles with the mutation were detected among 805 alleles (24.6%). G6PD Canton (c.1376 G \rightarrow T) (45.96%), G6PD Kaiping (c.1388 G \rightarrow A) (39.39%), and G6PD Gaohe (c.95 A \rightarrow G) (9.09%) account for 94.44% mutations, followed by G6PD Chinese-5 (c.1024 C \rightarrow T) (4.04%), G6PD Viangchan (c.871G \rightarrow A) (1.01%), and G6PD Maewo (c.1360 C \rightarrow T) (0.51%). There were some differences of the distribution of G6PD mutations among eight counties in Meizhou.

Conclusions: The $--^{SEA}$, $-\alpha^{3.7}$, and $-\alpha^{4.2}$ deletion were the main mutations of α -thalassemia, while IVS-II-654(C \rightarrow T), CD41-42(-TCTT), -28(A \rightarrow G), and CD17(A \rightarrow T) mutations were the principal mutations of β -thalassemia in Meizhou. G6PD c.1376 G \rightarrow T, c.1388 G \rightarrow A, and c.95 A \rightarrow G were the main mutations of G6PD deficiency. There were some differences of the distribution of thalassemia and G6PD mutations among eight counties in Meizhou.

KEYWORDS

G6PD, genotype distribution, Meizhou city, southern China, thalassemia

Wu and Zhu equally contributed to this work.

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1 | INTRODUCTION

Hemoglobin disease and glucose-6-phosphate dehydrogenase (G6PD) deficiency are widespread human erythrocytogenetic diseases that affect millions of population.^{1,2} The geographical distribution of G6PD deficiency and thalassemia is closely related to the past and present epidemic of malaria, because it has the selective advantage of anti-malaria infection.^{3,4}

Thalassemia is an inherited autosomal recessive disease with microcytic hypochromic anemia resulting from reduced or absent synthesis of one or more of the globin chains of hemoglobin. As one of the commonest monogenic disorder in the world, thalassemia assumes diversity in clinical phenotypes varying from almost asymptomatic to lethal hemolytic anemia.⁵⁻⁷ Thalassemia is the most common monogenic disorder in the world and is especially prevalent in Mediterranean countries, Southeast Asia, Africa, Middle East, and in the Indian subcontinent. There are two main types of thalassemia, α and β .^{8,9} According to the reports of previous researches, thalassemia was mainly prevalent in the population of southern areas of the Yangtze River in southern China,¹⁰⁻¹³ especially in three most southerly provinces of Guangxi,¹⁴⁻¹⁶ Guangdong,¹⁷ and Hainan,^{18,19} in which individuals seems to be selective advantages to carry such mutations.

Hereditary G6PD deficiency is one of the most common genetic enzyme deficiency diseases in the world. G6PD deficiency is an X-linked incomplete dominant inherited disease. The *G6PD* gene is located on chromosome Xq28 which consists of 13 exons and 12 introns, encoding 515 amino acids. The deficiency is widely distributed and occurs in about 400 million people worldwide.²⁰ G6PD deficiency has an obvious geographical distribution in the mainland China, and it is higher in the provinces south of the Yangtze River, including Guangdong, Hainan, Guangxi, Yunnan, Guizhou, and Sichuan provinces.²¹⁻²³

Meizhou is a city located in the northeast of Guangdong Province, and most of the residents living in this area are Hakka

peoples. Hakka is an intriguing Han Chinese population that mainly inhabit in southern China who migrated to south originally from northern China.²⁴ Meizhou city consists of eight counties including Wuhua, Fengshun, Dabu, Jiaoling, Meijiang, Meixian, Pingyuan, and Xingning, where custom, lifestyle, and diet manifest some distinctions in certain extent.

Population screening and genetic counseling are important to prevent the birth of children with thalassemia major. Using genetic analysis for prenatal diagnosis can diagnose thalassemia major fetuses in early pregnancy and terminate pregnancy in time, so as to avoid the birth of thalassemia major patients, which is an effective method to prevent this disease at present. Precise mutation frequencies studies in different populations will help healthcare programs to control thalassemia.^{25,26} G6PD deficiency causes neonatal hyperbilirubinemia and chronic hemolytic anemia. Although most affected individuals are asymptomatic, exposure to oxidative stressors, such as certain drugs or infection, can elicit acute hemolysis.^{27,28} Meizhou is regarded as underdeveloped and backward city in Guangdong Province. As a social medical and health problem, thalassemia has brought great challenges to the development of Meizhou region. Here, we perform a survey of thalassemia and G6PD deficiency to analyze the feature of genotypes distribution and frequencies among eight counties of Meizhou area.

2 | MATERIALS AND METHODS

2.1 | Subjects

A total of 16 158 individuals who visited Meizhou People's Hospital (Huangtang Hospital) from January 2015 to May 2018 were involved in thalassemia genetic testing in this study. From February 2016 to May 2018, 605 subjects were screened for common Chinese G6PD mutations by gene chip analysis. The

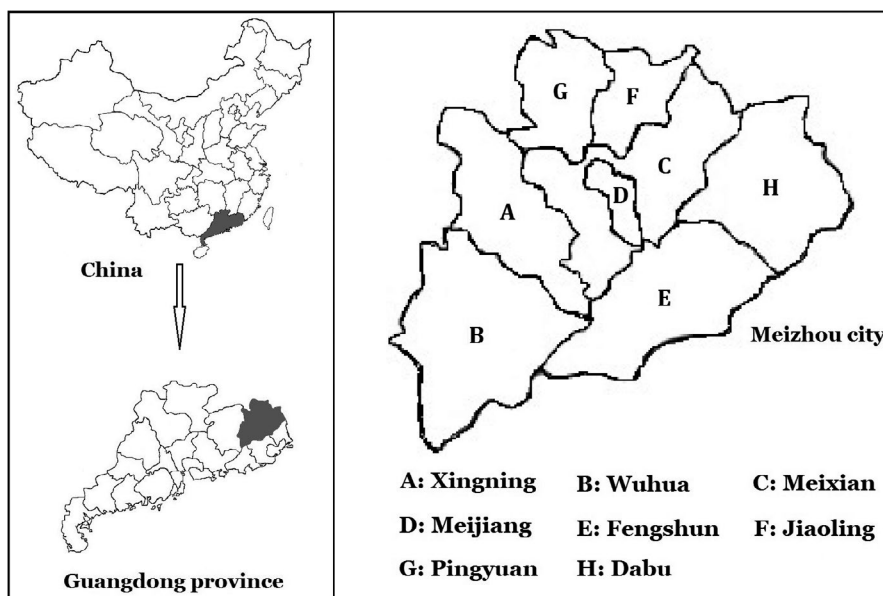


FIGURE 1 The geographical position of the eight counties in Meizhou

subjects included patients who went to cardiovascular disease center, prenatal diagnosis center, reproductive medicine center, physical examination center, pediatrics, gynecology, and other professional departments of our hospital, excluding patients with blood diseases. Figure 1 shows the location of the eight counties in Meizhou. This study was approved by the Ethics Committees of Meizhou People's Hospital (Huangtang Hospital), Meizhou Hospital Affiliated to Sun Yat-sen University (Guangdong Province, China) and was conducted according to the Declaration of Helsinki for biomedical research involving human participants. All participants provided written informed consent before enrollment in the study.

2.2 | Genetic testing for thalassemia

2.2.1 | Hematological studies and hemoglobin electrophoresis analysis

Samples were obtained via venipuncture of an antecubital vein, and then, 2 mL of peripheral blood was collected in EDTA anticoagulant tube. Sysmex XE-2100 blood analyzer (Sysmex Corporation of Japan, Block scientific Inc based on New York) was used to determine erythrocyte correlative indices following the standard operating procedures. Hemoglobin electrophoresis analysis was performed by Sebia capillary electrophoresis system (Sebia, Inc) compiling with standard operating procedures. Subjects detected to low mean corpuscular volume (MCV) values (<82 fL) and (or) lower mean corpuscular hemoglobin (MCH) values (<27 pg) were thought as suspicious thalassemia carriers. Subjects with low HbA₂ (<2.5%) were considered probable α -thalassemia carriers, whereas with high HbA₂ (>3.5%) were deemed possible β -thalassemia carriers.

2.2.2 | Molecular analysis

Peripheral blood was collected with EDTA anticoagulant tube, in which genomic DNA was extracted from leukocytes. DNA concentration was quantified using NanoDrop 2000™ Spectrophotometer (Thermo Fisher Scientific). Gap-polymerase chain reaction (gap-PCR) and flow-through hybridization technology (HybriBio Limited, Chaozhou, China) were used to detect α -thalassemia mutations, both deletional mutations ($-\alpha^{SEA}$, $-\alpha^{3.7}$, and $-\alpha^{4.2}$) and non-deletional mutations (Hb Constant Spring ($\alpha^{CS\alpha}$) (CD142,TAA \rightarrow CAA), Hb Quong Sze ($\alpha^{QS\alpha}$) (CD125,CTG \rightarrow CCG), and Hb Westmead ($\alpha^{WS\alpha}$) (CD122,CAC \rightarrow CAG)). Sixteen common non-deletional mutations in β -globin gene were detected by PCR and flow-through hybridization technology (HybriBio Limited, China): CD41-42(-TCTT), CD43(G \rightarrow T), IVS-II-654(C \rightarrow T), CD17(A \rightarrow T), CD14-15(+G), -28(A \rightarrow G), -29(A \rightarrow G), CD71-72(+A), CD26(G \rightarrow A), IVS-I-1(G \rightarrow T), IVS-I-1(G \rightarrow A), CD27-28(+C), IVS-I-5(G \rightarrow C), Cap + 40-43(-AAAC), initiation codon (T \rightarrow G), and CD31(-C).

2.3 | Genetic testing for G6PD deficiency

Genomic DNA was extracted from EDTA anticoagulant blood of subjects using the QIAamp DNA Blood Mini Kit (Qiagen). Amplification was performed using the G6PD Gene Typing Detection Kit (gene chip assay) (Sinochips Bioscience Co.). We detected the six mutation and one polymorphism sites in G6PD gene most commonly seen in the Chinese population by gene chip assay, including G6PD Gaohe (c.95 A \rightarrow G, 32 His \rightarrow Arg), G6PD Viangchan (c.871G \rightarrow A, 291 Val \rightarrow Met), G6PD Chinese-5 (c.1024 C \rightarrow T, 342 Leu \rightarrow Phe), G6PD Maewo (c.1360 C \rightarrow T, 454 Arg \rightarrow Cys), G6PD Canton (c.1376 G \rightarrow T, 459 Arg \rightarrow Leu), G6PD Kaiping (c.1388 G \rightarrow A, 463 Arg \rightarrow His), and one polymorphism (c.1311 C \rightarrow T, rs2230037).

2.4 | Statistical analysis

This study used SPSS statistical software version 20.0 (International Business Machines Corporation) to analyze data, and the results would be displayed with corresponding proportion. Descriptive analysis and Pearson chi-square test were used to compare the frequencies of genotype and allele among different counties in Meizhou region. $P < .05$ was considered to statistical difference.

3 | RESULTS

A total of 16 158 blood samples were obtained and analyzed from eight counties of Meizhou area. A total of 8701 cases with microcytosis (MCV < 82 fL and/or MCH < 27 pg) were found, and corresponding percentages of microcytosis in Xingning, Wuhua, Meixian, Meijiang, Fengshun, Jiaoling, Pingyuan, and Dabu were 56.96% (1792/3146), 56.87% (1750/3077), 51.29% (1407/2743), 55.14% (1025/1859), 48.76% (1023/2098), 48.33% (652/1349), 55.54% (536/966), and 55.98% (515/920), respectively. The corresponding abnormal ratio of hemoglobin in Xingning, Wuhua, Meixian, Meijiang, Fengshun, Jiaoling, Pingyuan, and Dabu were 52.64% (1656/3146), 52.00% (1600/3077), 46.34% (1271/2743), 47.98% (892/1859), 47.47% (996/2098), 44.48% (600/1349), 48.96% (473/966), and 50.98% (469/920), respectively.

The result of the incidence rate of α - and β -thalassemia of eight counties in Meizhou area is shown in Table 1. A total of 5463 cases of thalassemia were identified including 3585 cases of α -thalassemia, 1701 cases of β -thalassemia, and 177 cases of α -compound β -thalassemia. The total prevalence of thalassemia in Meijiang (31.84%, $P = .043$) was lower than other counties in Meizhou area. However, the relative proportions of α - and β -thalassemia did not differ greatly among eight counties. The prevalence of α -thalassemia in Meijiang (20.73%, $P = .046$) was lower than other counties in Meizhou area. The prevalence of Hb H disease in Wuhua (2.31%, $P = .008$) was higher than other counties in Meizhou area, while in Jiaoling (0.89%, $P = .015$) was lower than other counties.

TABLE 1 The prevalence of α - and β -thalassemia in different counties of Meizhou area

Variable	Case number (n = 16 158) (percentage, %)									
	Xingning (n = 3146)	Wuhua (n = 3077)	Meixian (n = 2743)	Meijiang (n = 2098)	Fengshun (n = 1859)	Jiaoling (n = 1349)	Pingyuan (n = 966)	Dabu (n = 920)	Total (n = 16 158)	
α -thalassemia	693 (21.96)	703 (22.85)	615 (22.42)	435 (20.73) ^a	411 (22.11)	295 (21.87)	230 (23.81)	203 (22.07)	3585 (22.19)	
α -thalassemia silent	188 (5.98)	174 (5.65)	142 (5.18)	95 (4.53)	99 (5.33)	84 (6.23)	60 (6.21)	46 (5.00)	888 (5.50)	
α -thalassemia trait	454 (14.43)	458 (14.88)	423 (15.42)	316 (15.06)	277 (14.90)	199 (14.75)	150 (15.53)	139 (15.11)	2416 (14.95)	
HBH disease	51 (1.62)	71 (2.31) ^a	50 (1.82)	24 (1.14)	35 (1.88)	12 (0.89) ^a	20 (2.07)	18 (1.96)	281 (1.74)	
β -thalassemia	338 (10.74)	336 (10.92)	275 (10.03)	218 (10.39)	184 (9.80)	144 (10.67)	111 (11.49)	95 (10.33)	1701 (10.53)	
β -thalassemia trait	333 (10.58)	330 (10.72)	273 (9.95)	214 (10.20)	182 (9.79)	142 (10.53)	111 (11.49)	93 (10.11)	1678 (10.38)	
β -thalassemia major	5 (0.16)	6 (0.19)	2 (0.07)	4 (0.19)	2 (0.11)	2 (0.15)	0 (0)	2 (0.22)	23 (0.14)	
α -compound β -thalassemia	40 (1.27)	40 (1.30)	29 (1.06)	15 (0.71)	20 (1.08)	12 (0.89)	7 (0.72)	14 (1.52)	177 (1.10)	
Total	1071 (34.04)	1079 (35.07)	919 (33.50)	668 (31.84) ^a	615 (33.08)	451 (33.43)	348 (36.02)	312 (33.91)	5463 (33.81)	

The shaded cells show that there are statistically significant differences compared with other counties.

^aManifests that compared with other counties, $P < .05$.

Allele frequencies of α - and β -thalassemia of eight counties in Meizhou area are exhibited in Table 2. A total of 5952 mutant chromosomes including 4063 α -thalassemia mutant chromosomes and 1889 β -thalassemia mutant chromosomes were identified. Compared with other counties, Wuhua assumed higher allele frequencies in both α -thalassemia (13.39%, $P = .032$) and $-\alpha^{3.7}$ deletion (2.75%, $P = .045$), and higher frequencies in $\alpha^{WS}\alpha$ allele of Xingning (0.60%, $P = .001$), in $-\alpha^{4.2}$ deletion of Jiaoling (1.45%, $P = .023$), in $\alpha^{CS}\alpha$ allele of Dabu (0.98%, $P = .006$), and in IVS-II-654(C \rightarrow T) allele of Pingyuan (3.16%, $P = .018$) were showed compared with other counties separately. IVS-II-654(C \rightarrow T) mutation was found dominance in most of these counties, while Meixian and Fengshun had a higher percentage in CD41-42(-TCTT) (1.99% and 2.27%, respectively) allele. The β -thalassemia mutations in the order of allele frequency between eight regions of Meizhou, the mutations were IVS-II-654(C \rightarrow T) > CD41-42(-TCTT) > -28(A \rightarrow G) > CD17(A \rightarrow T) in Xingning, Meijiang, Jiaoling and Pingyuan (similar to Jiangxi), IVS-II-654(C \rightarrow T) > CD41-42(-TCTT) > CD17(A \rightarrow T) > -28(A \rightarrow G) in Wuhua and Dabu (similar to Fujian), CD41-42(-TCTT) > IVS-II-654(C \rightarrow T) > CD17(A \rightarrow T) > -28(A \rightarrow G) in Meixian and Fengshun.

The result of genotypes of different counties in Meizhou area is shown in Table 3, showing subtle differences among each county. There were higher genotype frequencies in $-\alpha^{4.2}/\alpha\alpha$, β^N/β^N of Jiaoling (2.45%, $P = .002$), in $--^{SEA}/-\alpha^{3.7}$, β^N/β^N (1.55%, $P = .030$) and $\alpha\alpha/\alpha\alpha$, $\beta^{IVS-II-654}/\beta^N$ (5.80%, $P = .015$) of Pingyuan, in $\alpha^{CS}\alpha/\alpha\alpha$, β^N/β^N of Meixian (0.95%, $P = .010$), and in $--^{SEA}/\alpha^{CS}\alpha$, β^N/β^N of Dabu (1.20%, $P < .001$) compared with other counties. There are lower frequencies in $\alpha^{CS}\alpha/\alpha\alpha$, β^N/β^N of Xingning (0.25%, $P = .006$) and in $\alpha\alpha/\alpha\alpha$, β^{-28}/β^N of Dabu (0.22%, $P = .019$) compared with other counties.

For G6PD deficiency, there were six G6PD mutations and 19 genotypes were detected, including six kinds of heterozygotes, six kinds of hemizygotes, and seven kinds of homozygotes. The result of allele frequencies of G6PD in different counties of Meizhou area is shown in Table 4. The six G6PD mutations including G6PD Canton (c.1376 G \rightarrow T)(45.96%), G6PD Kaiping (c.1388 G \rightarrow A)(39.39%), and G6PD Gaohe (c.95 A \rightarrow G)(9.09%) account for 94.44% of mutations, followed by G6PD Chinese-5 (c.1024 C \rightarrow T)(4.04%), G6PD Viangchan (c.871G \rightarrow A)(1.01%), and G6PD Maewo (c.1360 C \rightarrow T) (0.51%). There were higher frequency in G6PD c.1376 G \rightarrow T allele of Wuhua (18.18%, $P = .004$) and lower frequency in G6PD c.1376 G \rightarrow T allele of Meijiang (4.49%, $P = .032$) compared with other counties. The mutations were c.1376 G \rightarrow T > c.1388 G \rightarrow A > c.95 A \rightarrow G in Xingning and Dabu, c.1376 G \rightarrow T > c.1388 G \rightarrow A > c.95 A \rightarrow G in Wuhua and Meixian, c.1388 G \rightarrow A > c.1376 G \rightarrow T > c.1024 C \rightarrow T in Meijiang, c.1388 G \rightarrow A > c.1376 G \rightarrow T > c.95 A \rightarrow G in Fengshun, c.1388 G \rightarrow A > c.1376 G \rightarrow T > c.1024 C \rightarrow T in Jiaoling, and c.1376 G \rightarrow T > c.1388 G \rightarrow A > c.1360 C \rightarrow T in Pingyuan. In addition, we detected 55 patients (9.09%) with the polymorphism (c.1311 C \rightarrow T).

Among these cases, 130 cases were simultaneously performed on genetic testing for thalassemia and G6PD deficiency, among them, 70 cases with G6PD deficiency mutations, 27 cases carried

TABLE 2 Allele frequencies of α - and β -thalassaemia in different counties of Meizhou area

Mutant chromosomes	Allele number (percentage, %)										Total (n = 32 316)
	Xingning (n = 6292)	Wuhua (n = 6154)	Meixian (n = 5486)	Meijiang (n = 4196)	Fengshun (n = 3718)	Jiaoling (n = 2698)	Pingyuan (n = 1932)	Dabu (n = 1840)			
α -thalassaemia	790 (12.56)	824 (13.39) ^a	693 (12.63)	478 (11.39)	473 (12.72)	322 (11.93)	253 (13.10)	230 (12.50)	4063 (12.57)		
(-35A)deletion	515 (8.18)	521 (8.47)	458 (8.34)	329 (7.84)	295 (7.93)	202 (7.49)	169 (8.75)	157 (8.53)	2646 (8.19)		
(- $\alpha^{3.7}$)deletion	154 (2.45)	169 (2.75) ^a	135 (2.46)	82 (1.95)	95 (2.56)	57 (2.11)	49 (2.53)	33 (1.79)	774 (2.40)		
(- $\alpha^{4.2}$)deletion	67 (1.06)	63 (1.02)	49 (0.89)	39 (0.93)	33 (0.89)	39 (1.45) ^a	22 (1.14)	15 (0.82)	327 (1.01)		
α^{CS} (CD142,TAA → CAA)	13 (0.21)	31 (0.50)	38 (0.69)	18 (0.43)	25 (0.67)	13 (0.48)	5 (0.26)	18 (0.98) ^a	161 (0.50)		
α^{WS} (CD122,CAC → CAG)	38 (0.60) ^a	29 (0.47)	10 (0.18)	9 (0.21)	15 (0.40)	6 (0.22)	8 (0.41)	5 (0.27)	120 (0.37)		
α^{OS} (CD125,CTG → CCG)	3 (0.05)	11 (0.18)	3 (0.05)	1 (0.02)	9 (0.24)	5 (0.19)	0 (0)	2 (0.11)	34 (0.11)		
(- α^{HIS})deletion	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.03)	0 (0)	0 (0)	0 (0)	1 (0.01)		
β -thalassaemia	382 (6.07)	380 (6.17)	305 (5.56)	237 (5.65)	201 (5.41)	156 (5.78)	119 (6.16)	109 (5.92)	1889 (5.85)		
IVS-II-654(C → T)	157 (2.50)	144 (2.34)	108 (1.97)	97 (2.31)	75 (2.02)	75 (2.78)	61 (3.16) ^a	46 (2.50)	763 (2.36)		
CD41-42 (-TCTT)	103 (1.64)	142 (2.31)	109 (1.99)	70 (1.67)	85 (2.27)	42 (1.56)	32 (1.66)	35 (1.90)	618 (1.91)		
-28(A → G)	54 (0.86)	34 (0.55)	28 (0.51)	22 (0.52)	14 (0.38)	17 (0.63)	17 (0.88)	5 (0.27)	191 (0.59)		
CD17 (A → T)	40 (0.64)	43 (0.70)	31 (0.57)	20 (0.48)	17 (0.46)	8 (0.30)	7 (0.36)	10 (0.54)	176 (0.54)		
CD27-28 (+C)	10 (0.16)	1 (0.02)	6 (0.11)	7 (0.17)	0 (0)	4 (0.15)	2 (0.10)	8 (0.43)	38 (0.12)		
CD26 (G → A)	2 (0.03)	1 (0.02)	9 (0.16)	10 (0.24)	6 (0.16)	8 (0.30)	0 (0)	2 (0.11)	38 (0.12)		
CD71-72 (+A)	8 (0.13)	7 (0.11)	4 (0.07)	2 (0.05)	1 (0.03)	2 (0.07)	0 (0)	1 (0.05)	25 (0.08)		
Cap+40-43 (-AAAC)	0 (0)	3 (0.05)	5 (0.09)	6 (0.14)	2 (0.05)	0 (0)	0 (0)	2 (0.11)	18 (0.06)		
CD14-15 (+G)	2 (0.03)	0 (0)	1 (0.02)	1 (0.02)	1 (0.03)	0 (0)	0 (0)	0 (0)	5 (0.02)		
-29 (A → G)	5 (0.08)	3 (0.05)	2 (0.04)	1 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	11 (0.03)		
CD43 (G → T)	1 (0.02)	2 (0.03)	1 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (0.01)		
IVS-1-1	0 (0)	0 (0)	1 (0.02)	1 (0.02)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.01)		

The shaded cells show that there are statistically significant differences compared with other counties.

^amanifests that compared with other counties, $P < .05$.

TABLE 3 The mutant genotypes of different counties in Meizhou area

Mutant genotype	Case number (n = 16 158) (percentage, %)									Total (n = 16 158)
	Xingning (n = 3146)	Wuhua (n = 3077)	Meixian (n = 2743)	Meijiang (n = 2098)	Fengshun (n = 1859)	Jiaoling (n = 1349)	Pingyuan (n = 966)	Dabu (n = 920)		
α -thalassaemia	693 (22.03)	703 (22.85)	615 (22.42)	435 (20.73) ^a	411 (22.11)	295 (21.87)	230 (23.81)	203 (22.07)	3585 (22.19)	
$^{-SEA}/\alpha\alpha, \beta^N/\beta^N$	435 (13.83)	425 (13.81)	394 (14.36)	298 (14.20)	248 (13.34)	181 (13.42)	146 (15.11)	129 (14.02)	2256 (13.96)	
$^{-\alpha^{3.7}}/\alpha\alpha, \beta^N/\beta^N$	115 (3.66)	114 (4.68)	99 (3.61)	60 (2.86)	68 (3.66)	47 (3.48)	34 (3.52)	28 (3.04)	565 (3.42)	
$^{-\alpha^{4.2}}/\alpha\alpha, \beta^N/\beta^N$	46 (1.46)	42 (1.36)	34 (1.24)	28 (1.33)	18 (0.97)	33 (2.45) ^a	18 (1.86)	14 (1.52)	233 (1.44)	
$^{-SEA}/\alpha^{3.7}, \beta^N/\beta^N$	26 (0.83)	37 (1.20)	21 (0.77)	16 (0.76)	15 (0.81)	6 (0.44)	15 (1.55) ^a	5 (0.54)	141 (0.87)	
$\alpha^{CS}/\alpha\alpha, \beta^N/\beta^N$	8 (0.25) ^a	17 (0.55)	26 (0.95) ^a	14 (0.67)	14 (0.75)	11 (0.82)	4 (0.41)	7 (0.76)	101 (0.62)	
$\alpha^{WS}/\alpha\alpha, \beta^N/\beta^N$	27 (0.86)	18 (0.58)	9 (0.33)	7 (0.33)	13 (0.70)	4 (0.30)	8 (0.83)	4 (0.43)	90 (0.56)	
$^{-SEA}/\alpha^{4.2}, \beta^N/\beta^N$	17 (0.54)	11 (0.36)	14 (0.51)	6 (0.29)	10 (0.54)	4 (0.30)	4 (0.41)	1 (0.10)	67 (0.41)	
$^{-SEA}/\alpha^{CS}, \beta^N/\beta^N$	4 (0.13)	14 (0.45)	11 (0.40)	2 (0.10)	7 (0.38)	2 (0.15)	1 (0.10)	11 (1.20) ^a	52 (0.32)	
$\alpha^{OS}/\alpha\alpha, \beta^N/\beta^N$	3 (0.10)	7 (0.23)	2 (0.07)	1 (0.05)	9 (0.48)	5 (0.37)	0 (0)	2 (0.22)	29 (0.18)	
$^{-SEA}/\alpha^{WS}, \beta^N/\beta^N$	4 (0.13)	5 (0.16)	4 (0.15)	0 (0)	2 (0.11)	0 (0)	0 (0)	1 (0.10)	16 (0.10)	
Others	8 (0.25)	13 (0.42)	1 (0.04)	3 (0.14)	7 (0.38)	2 (0.15)	0 (0)	1 (0.11)	35 (0.22)	
β -thalassaemia	338 (10.74)	336 (10.92)	275 (10.03)	218 (10.39)	184 (9.90)	144 (10.67)	111 (11.49)	95 (10.33)	1701 (10.53)	
$\alpha\alpha/\alpha\alpha, \beta^{WS-11-654}/\beta^N$	142 (4.51)	123 (4.00)	101 (3.68)	92 (4.39)	67 (3.60)	69 (5.11)	56 (5.80) ^a	37 (4.02)	687 (4.25)	
$\alpha\alpha/\alpha\alpha, \beta^{CD41-42}/\beta^N$	94 (2.99)	127 (4.13)	97 (3.54)	64 (3.05)	77 (4.14)	39 (2.89)	31 (2.30)	34 (3.70)	563 (3.48)	
$\alpha\alpha/\alpha\alpha, \beta^{CD17}/\beta^N$	37 (1.18)	40 (1.30)	26 (0.95)	19 (0.91)	17 (0.91)	7 (0.52)	7 (0.72)	10 (1.09)	163 (1.01)	
$\alpha\alpha/\alpha\alpha, \beta^{28}/\beta^N$	36 (1.14)	26 (0.84)	26 (0.95)	15 (0.72)	12 (0.65)	17 (1.26)	15 (1.55)	2 (0.22) ^a	149 (0.92)	
$\alpha\alpha/\alpha\alpha, \beta^{CD27-28}/\beta^N$	8 (0.25)	1 (0.03)	5 (0.18)	6 (0.29)	0 (0)	3 (0.22)	2 (0.19)	4 (0.43)	29 (0.18)	
$\alpha\alpha/\alpha\alpha, \beta^E/\beta^N$	1 (0.03)	0 (0)	4 (0.15)	9 (0.43)	6 (0.32)	5 (0.37)	0 (0)	2 (0.22)	27 (0.17)	
$\alpha\alpha/\alpha\alpha, \beta^{CD71-72}/\beta^N$	7 (0.22)	6 (0.19)	4 (0.15)	2 (0.10)	0 (0)	2 (0.15)	0 (0)	1 (0.11)	22 (0.14)	
$\alpha\alpha/\alpha\alpha, \beta^{Cap}/\beta^N$	0 (0)	2 (0.06)	5 (0.18)	4 (0.19)	2 (0.11)	0 (0)	0 (0)	2 (0.22)	15 (0.09)	
$\alpha\alpha/\alpha\alpha, \beta^{29}/\beta^N$	5 (0.16)	3 (0.10)	2 (0.07)	1 (0.05)	0 (0)	0 (0)	0 (0)	0 (0)	11 (0.07)	
$\alpha\alpha/\alpha\alpha, \beta^{CD14-15}/\beta^N$	2 (0.06)	0 (0)	1 (0.04)	1 (0.05)	1 (0.05)	0 (0)	0 (0)	0 (0)	5 (0.03)	
Others	6 (0.19)	8 (0.26)	4 (0.15)	5 (0.24)	2 (0.11)	2 (0.15)	0 (0)	3 (0.33)	30 (0.19)	

The shaded cells show that there are statistically significant differences compared with other counties.

^amanifests that compared with other counties, $P < .05$.

TABLE 4 Allele frequencies of G6PD in different counties of Meizhou area

Variable	Allele number (percentage, %)								Total (n = 805)
	Xingning (n = 185)	Wuhua (n = 154)	Meixian (n = 119)	Meijiang (n = 89)	Fengshun (n = 102)	Jiaoling (n = 46)	Pingyuan (n = 52)	Dabu (n = 58)	
c.1376 G → T	19(10.27)	28 (18.18) ^a	12 (10.08)	4 (4.49) ^a	10 (9.80)	2 (4.35)	9 (17.31)	7 (12.07)	91 (11.30)
c.1388 G → A	16 (8.65)	14 (9.09)	12 (10.08)	13 (14.61)	12 (11.76)	4 (8.70)	4 (7.89)	3 (5.17)	78 (9.69)
c.95 A → G	7 (3.78)	4 (2.60)	4 (3.36)	1 (1.12)	1 (0.98)	0 (0)	0 (0)	1 (1.72)	18 (2.24)
c.1024 C → T	1 (0.54)	1 (0.65)	2 (1.68)	2 (2.25)	0 (0)	1 (2.17)	0 (0)	1 (1.72)	8 (0.99)
c.871G → A	1 (0.54)	0 (0)	1 (0.84)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.25)
c.1360 C → T	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1.92)	0 (0)	1 (0.12)
Total	44 (23.78)	47 (30.52)	31 (26.05)	20 (22.47)	23 (22.55)	7 (15.22)	14 (26.92)	12 (20.69)	198 (24.60)

The shaded cells show that there are statistically significant differences compared with other counties.

^amanifests that compared with other counties, $P < .05$.

thalassemia mutations were identified, and 13 cases with both thalassaemia and G6PD deficiency mutations and 46 cases did not carry thalassaemia and G6PD deficiency mutations. Due to the small number of cases, we cannot analyze the relationship of thalassaemia and G6PD deficiency. Of course, further studies are required to reveal the relationship, which is one of our next major research goals.

4 | DISCUSSION

Thalassaemia is an inherited autosomal recessive disease that is mainly prevalent in Guangdong, Guangxi, and Hainan provinces. Thalassaemia major places a heavy financial burden on some families.^{10-12,29} Meizhou located in the northeastern part of Guangdong Province is an underdeveloped city, in which the vast majority of permanent residents are Hakka. In result of geography, culture, and customs, the proportion of intermarriage between Hakka people in Meizhou and other regions is relatively small,²⁴ which consequently triggered higher genetic frequency of thalassaemia. In broad terms, due to the higher prevalence and some differences from other cities of Guangdong Province, to make sure whether the eight counties of Meizhou city have some differences is necessary.

In this study, the total incidence of thalassaemia in Meizhou region was 33.80%, of α -thalassaemia was 22.17%, of β -thalassaemia was 10.53%, and of α -compound β -thalassaemia was 1.10%. Compared with previous studies, our research presented relatively higher prevalence of thalassaemia because our subjects were hospitalized patients.

The statistics and analysis of molecular characteristics and morbidity of thalassaemia in different regions have increasingly enriched in many studies. For example, frequency of carriers for α -thalassaemia is 15% and β -thalassaemia carriers comprise 4.8% in Guangxi Province, while 46.7% of α -thalassaemia with the main genotype of $--^{SEA}/\alpha\alpha$ and 39.4% of β -thalassaemia with the main genotype of CD41-42(-TCTT) and IVS-II-654(C → T) (5.8%) ranked the fifth position.¹⁴ The Li people in Hainan Province presented 53.45% of α -thalassaemia with chief genotype of $-\alpha^{4,2}$, $-\alpha^{3,7}$ deletion, 3.83% of β -thalassaemia with lead genotype of CD41-42(-TCTT) mutation, while the Han people in Hainan Province presented 12.16% of α -thalassaemia with chief genotype of $--^{SEA}$, $-\alpha^{3,7}$ deletion, 6.11% of β -thalassaemia with the main mutation is CD41-42(-TCTT).¹⁹ As for Guangdong Province, the carrier rate of α -thalassaemia was 8.53% in which $--^{SEA}$ and $-\alpha^{3,7}$ deletion were the main genotypes with frequencies 46.9% and 36.5%, respectively, while the carrier rate of β -thalassaemia was 2.54% in which CD41-42(-TCTT) (36.4%) and IVS-II-654(C → T) (24.8%) were the principal genotypes.¹⁷ There are also many differences in terms of the interior of the Guangdong Province. Shenzhen assumed 4.34% of α -thalassaemia, in which the primary genotype was $--^{SEA}$ deletion (74.85% of mutations), 1.99% of β -thalassaemia in which CD41-42(-TCTT) and IVS-II-654(C → T) played a dominant role with frequencies 41.25% and 27.50%, respectively.³⁰ Shaoguan manifested the prevalence was 10.44% of α -thalassaemia, in which $--^{SEA}$ deletion was 3.44%, 3.97% of β -thalassaemia with chief

genotype of CD41-42(-TCTT).³¹ The genotypes and allele frequencies of Meizhou show some differences from Guangdong. --^{SEA}/ $\alpha\alpha$ was the most common α -thalassemia genotype, accounted for 62.93% of α -thalassemia. $\alpha^{WS}\alpha$ (CD122, CAC \rightarrow CAG) accounted for 0.37% (120/32316) of α -thalassemia and was relatively lower than the proportion of in Guangdong Province reported in the previous study. The main genotype of β -thalassemia in Meizhou is IVS-II-654(C \rightarrow T), whereas the counterpart in Guangdong is CD41-42(-TCTT); however, CD41-42(-TCTT) showed higher proportion in Fengshun and Meixian.

A person who is a carrier of --^{SEA} deletion is potentially at risk of begetting infants with HbH disease or the Hb Bart's hydrops fetalis syndrome, depending upon the α -globin genotype of his/her partner, which would exhibit range from hypochromic anemia to hydrops fetalis. According to previous researches, most of regions indicated a similar feature with higher genotype of --^{SEA} deletion. Our results are consistent with those reported in most other regions. Nonetheless, the distributions and proportions in different areas regarding β -thalassemia genotype seem to be subtly difference. Our research may not fully represent the epidemiology of thalassemia in this region related to the randomization and sample capacity of study subjects possibly as for most of our subjects were hospitalized patients.

G6PD deficiency gene carrying incidence rate was 5.41% in Guangdong Province.^{32,33} The c.1388 G \rightarrow A (30.4% mutations) and c.1376 G \rightarrow T (25.5% mutations) were the most common G6PD mutations in Hakka population of Guangdong Province studied by Yu et al.³⁴ G6PD c.1376 G \rightarrow T, c.1388 G \rightarrow A, and c.95 A \rightarrow G account for 78.05% mutations in Ganzhou region, Jiangxi Province,³⁵ 75.3% in Han and Zhuang people in Guangxi Province,³⁶ and 85.2% in Fujian Province.³⁷ G6PD c.1376 G \rightarrow T, c.1388 G \rightarrow A, and c.95 A \rightarrow G were the main type of G6PD gene mutations in Chinese population, which generally accounts for more than 50%. In this study, c.1376 G \rightarrow T, c.1388 G \rightarrow A, and c.95 A \rightarrow G mutations accounted for 94.44% of the total mutation types, and the mutation distribution was consistent with the results in other places.

It is reported that the G6PD enzyme activity in patients with G6PD deficiency compound thalassemia may be higher than that of G6PD deficiency patients, due to an increase in the number of newborn erythrocytes and increase in the activity of G6PD in the chronic hemolysis of the G6PD deficiency compound thalassemia patients.³⁸⁻⁴⁰ The patients with G6PD deficiency compound thalassemia may have normal G6PD activity, so such patients may be missed in the screening of G6PD activity. We are collecting data from different types of thalassemia genotypes with G6PD gene mutations, and next study may reveal the correlation between thalassemia and G6PD deficiency.

The genotype distribution and frequencies of thalassemia and G6PD deficiency in Meizhou area have regional characteristics, and there are also significant differences in different counties. Local governments can formulate corresponding measures and detection projects to prevent and control thalassemia major and G6PD

deficiency according to the genotype distribution and frequencies, effectively saving costs and enhancing social benefits.

5 | CONCLUSION

In conclusion, --^{SEA}, - $\alpha^{3.7}$, and - $\alpha^{4.2}$ deletion were the main mutations of α -thalassemia, while IVS-II-654(C \rightarrow T), CD41-42(-TCTT), -28(A \rightarrow G) and CD17(A \rightarrow T) mutations were the principal mutations of β -thalassemia in Meizhou. Genetic testing for G6PD deficiency, c.1376 G \rightarrow T, c.1388 G \rightarrow A, and c.95 A \rightarrow G were the main mutations of G6PD deficiency in this region. In addition, there were some differences of the distribution of thalassemia and G6PD mutations among eight counties in Meizhou.

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REFERENCES

- Howes RE, Piel FB, Patil AP, et al. G6PD deficiency prevalence and estimates of affected populations in malaria endemic countries: a geostatistical model-based map. *PLoS Medicine*. 2012;9(11):e1001339.
- Millimono TS, Loua KM, Rath SL, et al. High prevalence of hemoglobin disorders and glucose-6-phosphate dehydrogenase (G6PD) deficiency in the Republic of Guinea (West Africa). *Hemoglobin*. 2012;36(1):25-37.
- Taylor SM, Fairhurst RM. Malaria parasites and red cell variants: when a house is not a home. *Curr Opin Hematol*. 2014;21(3):193-200.
- Taylor SM, Cerami C, Fairhurst RM. Hemoglobinopathies: slicing the Gordian knot of *Plasmodium falciparum* malaria pathogenesis. *PLoS Pathog*. 2013;9(5):e1003327.
- Muncie HL Jr, Campbell J. Alpha and beta thalassemia. *Am Fam Physician*. 2009;80(4):339-344.
- Weatherall DJ, Clegg JB. Inherited haemoglobin disorders: an increasing global health problem. *Bull World Health Organ*. 2001;79(8):704-712.
- Weatherall DJ. The thalassemia syndromes. *Tex Rep Biol Med*. 1980;40(5):323-333.
- Cohen AR, Galanello R, Pennell DJ, Cunningham MJ, Vichinsky E. Thalassemia. *Hematology Am Soc Hematol Educ Program*. 2004;1:14-34.
- Weatherall DJ. Thalassemia: the long road from bedside to genome. *Nat Rev Genet*. 2004;5(8):625-631.
- Chan V, Chan TK, Cheng MY, Leung NK, Kan YW, Todd D. Characteristics and distribution of β thalassemia haplotypes in South China. *Hum Genet*. 1986;73(1):23-26.
- Ye BC, Zhang Z, Lei Z. Molecular analysis of alpha/beta-thalassemia in a southern Chinese population. *Genet Test*. 2007;11(1):75-83.

12. Zhang JZ, Cai SP, He X, et al. Molecular basis of beta thalassaemia in south China. Strategy for DNA analysis. *Hum Genet.* 1988;78(1):37-40.
13. Chan V, Chan TK, Chebab FF, Todd D. Distribution of beta-thalassaemia mutations in south China and their association with haplotypes. *Am J Hum Genet.* 1987;41(4):678-685.
14. Pan HF, Long GF, Li Q, et al. Current status of thalassaemia in minority populations in Guangxi. *China. Clin Genet.* 2007;71(5):419-426.
15. Cai R, Liu J, Wang L, et al. Study on molecular epidemiology of the alpha-thalassaemias in Liuzhou City, Guangxi Autonomous Region, China. *Hemoglobin.* 2009;28(4):325-333.
16. Zhu L, Luo RG, Zhou TH. Genotypes of β Thalassaemia in Guangxi. *Military Med J South China.* 2009;23(2):41-43.
17. Xu XM, Zhou YQ, Luo GX, et al. The prevalence and spectrum of α and β thalassaemia in Guangdong Province: implications for the future health burden and population screening. *J Clin Pathol.* 2004;57(5):517-522.
18. Zeng YT, Huang SZ. Alpha-globin gene organisation and prenatal diagnosis of alpha-thalassaemia in Chinese. *Lancet.* 1985;1(8424):304-307.
19. Yao H, Chen X, Lin L, et al. The spectrum of α - and β -thalassaemia mutations of the Li people in Hainan Province of China. *Blood Cells Mol Dis.* 2014;53(1-2):16-20.
20. Lee J, Park J, Choi H, et al. Genetic profiles of Korean patients with glucose-6-phosphate dehydrogenase deficiency. *Ann Lab Med.* 2017;37(2):108-116.
21. Lai HC, Lai MPY, Leung KSN. Glucose-6-phosphate dehydrogenase deficiency in Chinese. *J Clin Pathol.* 1968;21(1):44-47.
22. Chiu DT, Zuo L, Chao L, et al. Molecular characterization of glucose-6-phosphate dehydrogenase (G6PD) deficiency in patients of Chinese descent and identification of new base substitutions in the human G6PD gene. *Blood.* 1993;81(8):2150-2154.
23. Ainoon O, Alawiyah A, Yu YH, et al. Semiquantitative screening test for G6PD deficiency detects severe deficiency but misses a substantial proportion of partially-deficient females. *Southeast Asian J Trop Med Public Health.* 2003;34(2):405-414.
24. Li SM. Population migration regional economic growth and income determination: a comparative study of Dongguan and Meizhou China. *Urban Studies.* 1997;34(7):999-1026.
25. Li B, Zhang XZ, Yin AH, et al. High prevalence of thalassaemia in migrant populations in Guangdong Province, China. *BMC Public Health.* 2014;14(1):905.
26. Lai K, Huang G, Su L, He Y. The prevalence of thalassaemia in mainland China: evidence from epidemiological surveys. *Sci Rep.* 2017;7(1):920.
27. Nkhoma ET, Poole C, Vannappagari V, Hall SA, Beutler E. The global prevalence of glucose-6-phosphate dehydrogenase deficiency: a systematic review and meta-analysis. *Blood Cells Mol Dis.* 2009;42(3):267-278.
28. He M, Lin K, Huang Y, et al. Prevalence and molecular study of G6PD deficiency in the Dai and Jingpo Ethnic Groups in the Dehong Prefecture of the Yunnan Province. *Hum Hered.* 2018;83(2):55-64.
29. Kazazian HH Jr, Dowling CE, Waber PG, Huang SZ, Lo WH. The spectrum of β -thalassaemia in China and South-East Asia. *Blood.* 1986;68(4):964-966.
30. Li Z, Li F, Li M, Guo R, Zhang W. The prevalence and spectrum of thalassaemia in Shenzhen, Guangdong Province, People's Republic of China. *Hemoglobin.* 2006;30(1):9-14.
31. Chen YJ, Jia SQ, Chen PY, et al. Molecular Epidemiology Survey of α - and β -thalassaemia in Shaoguan City of Guangdong Province. *J Hunan Normal Univ.* 2005;2(1):40-45.
32. Du CS, Xu YK, Hua XY, Wu QL, Liu LB. Glucose-6-phosphate dehydrogenase variants and their frequency in Guangdong, China. *Hum Genet.* 1988;80(4):385-388.
33. Zhong YH, Wu CH, Chen GL, Liu JF, Qu YX, Hospital YP. The correlation analysis of G6PD and pathological jaundice of newborn in northern Guangdong. *Chin J Birth Heal Hered.* 2016;31(1):32-35.
34. Yu GL, Jiang WY, Cs DU, et al. Identification of G6PD gene variants from Hakka population in Guangdong province. *Chin J Med Genet.* 2004;21(5):448-451.
35. Hu R, Lin M, Ye J, et al. Molecular epidemiological investigation of G6PD deficiency by a gene chip among Chinese Hakka of southern Jiangxi province. *Int J Clin Exp Pathol.* 2014;8(11):15013-15018.
36. Yan T, Cai R, Mo O, et al. Incidence and complete molecular characterization of glucose-6-phosphate dehydrogenase deficiency in the Guangxi Zhuang autonomous region of southern China: description of four novel mutations. *Haematologica.* 2006;91(10):1321-1328.
37. Liu P, Jiang WY, Zhang XX, et al. Glucose-6-phosphate dehydrogenase gene mutations in She Nationality, Fujian province. *Chin J Hematol.* 2005;26(10):612-615.
38. Chen D, Chen HP, Liang L. The significance of the G6PD activity detection in thalassaemia diagnosis. *Chin J Birth Heal Hered.* 2007;15(1):27-28.
39. Chen D, Chen HP, Wang Y, Liang L, Rong KB. The activity range of G6PD in thalassaemia combined G6PD deficiency in Lab and it's clinical significance. *Chin J Birth Heal Hered.* 2006;14(5):28-30.
40. Magnani M, Stocchi V, Canestrari F, et al. Redox and energetic state of red blood cells in G6PD deficiency, heterozygous beta-thalassaemia and the combination of both. *Acta Haematol.* 1986;75(4):211-214.

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