

Investigation on the Anxiety and Depression Status of Thalassemia Carriers After Genetic Counseling

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Purpose: Genetic disorders have psychological impacts on patients. We examined the status of anxiety and depression among thalassemia carriers after genetic counseling in Taizhou, Zhejiang Province, China.

Methods: From June 2017 to April 2021, 131 thalassemia carriers ≥ 12 years old received genetic counseling, and were issued questionnaires; among them, 82 (62.6%) questionnaires were completed and returned. We assessed anxiety and depression levels in thalassemia carriers using the Hospital Anxiety and Depression Scale (HADS) to obtain clinical indicators from the hospitals. We used nonparametric tests or Spearman correlation analysis to assess the correlations between anxiety, depression, and the independent variables.

Results: The frequencies of anxiety and depression were both 3.7%. Participants with more than a high school education had lower depression scores than those with less education ($P = 0.005$). Red blood cell count (RBC) counts was negatively correlated with depression scores ($r = -0.274$, $P = 0.043$). Furthermore, total cholesterol (TC) was negatively correlated with anxiety ($r = -0.374$, $P = 0.017$) and depression ($r = -0.379$, $P = 0.016$) scores.

Conclusion: The frequencies of anxiety and depression among thalassemia carriers receiving genetic counseling in Taizhou were both 3.7%, lower than those previously reported. These preliminary findings suggest a potential association between genetic counseling and reduced psychological distress. In addition, we found RBC and TC negatively affect mental status in thalassemia, these carriers need to pay attention to their diet and undergo regular monitoring.

Keywords: thalassemia carriers, anxiety, depression, HADS, genetic counseling

Introduction

Thalassemia is a single-gene, hereditary, recessive disease in which genetic mutations or deletions cause a range of clinical symptoms. Genetic detection techniques, including polymerase chain reaction (PCR), next-generation sequencing, and matrix-assisted laser desorption ionization time-of-flight mass spectrometry, have been widely used to diagnose thalassemia.^{1,2} There are more than 120 and 400 mutations³ involved in α and β thalassemia, respectively.

Genetic testing allows for the definitive diagnosis of several diseases; however, given the genetic results and properties, genetic testing is more closely related to patients' health and well-being, reproductive effects, and disease burden. Despite these benefits, patients undergoing genetic testing may experience psychological problems, including fear and anxiety.⁴ Positive genetic test results for cancer, Huntington's disease, and inherited heart disease can increase anxiety and depression.⁵⁻⁸ Negative psychological states can affect disease prognosis, treatment compliance, and quality of life.^{9,10}

Adequate pretest and posttest counseling is recommended worldwide when genetic testing is clinically considered.¹¹ Genetic counseling is widely used in cancer care, although its psychological benefits remain controversial. While some studies report reduced anxiety,^{5,12} others have found no significant improvement.¹³⁻¹⁵

Genetic counseling for parents of patients with mental disorders has been shown to reduce guilt, worry about family members, and anxiety.¹⁶ In two systematic reviews, 69% (40/59) and 43% (10/27) of the included studies, respectively, investigated patients' mental health status, including anxiety, depression, and worry, after genetic counseling.^{17,18} Although the results were inconsistent, most studies suggested that genetic counseling possibly alleviated anxiety and depression. During genetic counseling, understanding the changes in relevant laboratory indicators may facilitate the provision of targeted explanations. This can clarify the potential correlation between these indicators and anxiety or depression, thereby providing a basis for analyzing the physiological influencing factors of carriers' emotional issues. Furthermore, it enables a more comprehensive evaluation of the intervention value of genetic counseling.

In China, routine thalassemia screening has been implemented in provinces with a high incidence of thalassemia, such as Guangxi, Guangdong and Hainan provinces, while screening is mainly carried out in high-risk groups in other regions, and has not been widely used nationwide. In low-incidence areas, the conditions for thalassemia gene screening mainly target people with microcytic hypochromic anemia who have excluded iron deficiency and those with abnormal hemoglobin electrophoresis. And the intensity of screening is closely related to local policies and carrier rate.¹⁹

There are regional differences in genetic counseling for thalassemia in China. In high-incidence areas (such as Guangxi, Guangdong and Hainan provinces), a systematic counseling system has been established, covering pre-marital /pre-pregnancy screening subjects, carriers identified by public health programs, and parents of confirmed fetuses. In low-incidence areas, Genetic counseling is not carried out or is not conducted properly.¹⁹ Though our hospital provides genetic counseling to patients with thalassemia, their psychological status is not evaluated after the counseling. Therefore, we aimed to examine the status of anxiety and depression among thalassemia carriers who received genetic counseling in Taizhou, determine whether genetic counseling can alleviate anxiety and depression, and explore the relationship between anxiety/depression and laboratory indicators.

Methods

Study Design and Participants

This study utilized convenience sampling to survey thalassemia carriers from Taizhou Hospital, a public tertiary grade A hospital in Zhejiang Province, China.²⁰ Between June 2017 and April 2021, 243 thalassemia carriers who were diagnosed using genetic tests and underwent genetic counseling were included. Among these thalassemia carriers, we excluded individuals aged < 12 years ($n = 76$) and those who provided incorrect or out-of-use phone numbers ($n = 36$). We issued 131 questionnaires, and 82 thalassemia carriers responded (response rate: 62.6%). [Figure 1](#) illustrates this detailed process. [Table S1](#) shows the genetic counseling process. This includes, before genetic testing, the collection of clinical phenotypes, medical history, auxiliary examination, family history, possible inheritance mode, and signing of informed consent; and after genetic testing, interpretation of gene reports, notification of prognosis and treatment, and disease risk verification of family members.

This study was approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province (approval number: K20220126), which waived the requirement for informed consent. All the information was collected anonymously and confidentially. All data were de-identified prior to analysis, with direct identifiers (names, IDs) removed and indirect identifiers (dates, rare diagnoses) aggregated to prevent re-identification. Access to raw data was limited to authorized investigators under institutional data protection protocols. All programs adhered to the tenets of the Declaration of Helsinki and followed the standards of our ethics committee.

Data Sources

Questionnaire Delivery and Questionnaire Content

After undergoing standardized training, the investigators performed telephone follow-up interviews lasting ≥ 6 minutes. During these follow-ups, the investigators provided popular science and educational content; furthermore, they explained the study purpose, questionnaire content, and confidentiality of respondents' information. The questionnaire was designed using the WeChat-incorporated Wen-Juan-Xing platform (Changsha Ranxing Information Technology Co.,

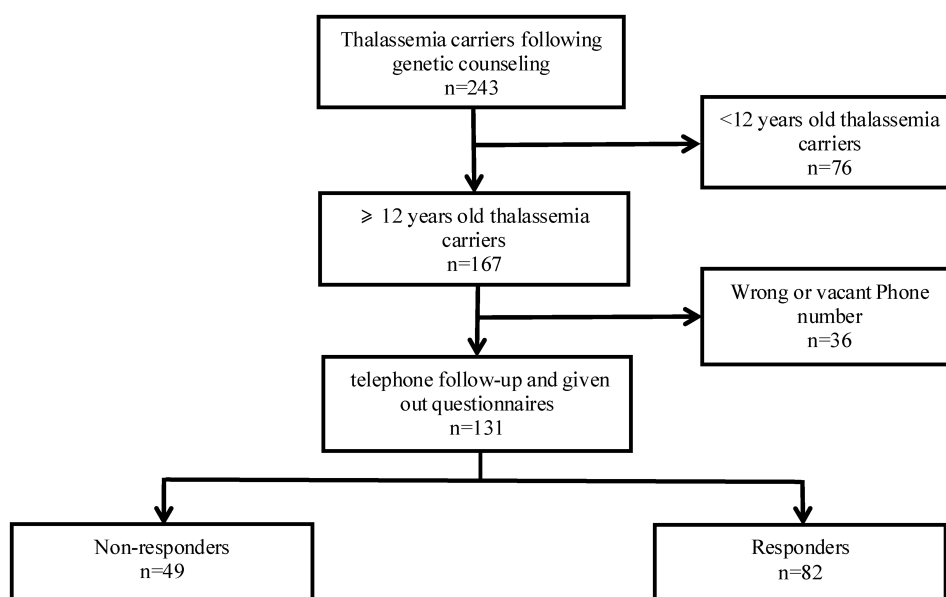


Figure 1 Flow chart.

Ltd., Hunan, China); the link to the questionnaire was sent via text message, with the respondents completing the questionnaire online. For older patients who could not independently complete the questionnaire, it was administered via telephone after the consultation techniques, methods, and contents were discussed, revised, and finalized.

The questionnaire comprised three parts: first, demographic characteristics including age, sex, body mass index (BMI), education, marital status, and economic status; second, the procedures (Did you take iron supplementation? Were you tense when you were found to be anemic or confirmed as a thalassemia carrier? How long after the anemia diagnosis was a confirmed thalassemia carrier? Did you understand the diagnostic report? Did the doctors interpret the report for you?); and third, the Hospital Anxiety and Depression Scale (HADS).

Anxiety and depression were assessed using the HADS, which comprises 14 items divided into two seven-item subscales that measure anxiety (HADS-A) and depression (HADS-D). Even- and odd-numbered questions targeted depression and anxiety, respectively, on a scale of 0–3, with overall scores ranging from 0 to 21. The Chinese version of HADS is widely used^{21–24} and has shown good internal consistency and construct validity. The Cronbach's α coefficients of the anxiety and depression subscales were 0.68–0.93 (average 0.83) and 0.67–0.90 (average 0.82), respectively. Moreover, the validity ranged from 0.49 to 0.83, the sensitivity and specificity values were ≈ 0.8 ,²⁵ and a score ≥ 8 was indicative of anxiety or depression.²⁶

Laboratory Data

To explore the relationship between anxiety/depression and laboratory indicators, clinical laboratory parameters were collected. Laboratory blood routine and biochemical indices were extracted from patient records. Routine blood indicators were measured using a Mindray 6800Plus or Sysmex XE2100 Automatic blood cell analyzer. Biochemical indicators were measured using an Abbott ARCHITECT C1600 Automatic Biochemical Analyzer or the Beckman Coulter AU5800 Automatic Biochemical Analyzer. Anemia was defined as hemoglobin (Hb) levels of < 120 g/L and < 110 g/L in males and females, respectively. The presence of hypochromic microcytic erythrocytes was defined as a mean corpuscular volume (MCV) of < 82 fl and a mean hemoglobin content (MCH) of < 27 pg. For thalassemia gene detection, we further referred to whether there was a family history of hypochromic microcytic anemia and whether iron supplementation had no effect or no iron deficiency. Then, genomic DNA was isolated, followed by gap-PCR (Kit of Xiamen Zhishan Biotechnology Co., LTD) to detect the three common deletion types in α -thalassemia, including $-SEA$, $-\alpha 3.7$, and $-\alpha 4.2$ deletions. Reverse dot hybridization (Kit of Xiamen Zhishan Biotechnology Co., LTD) was used to detect the point mutations of 3 types of α -thalassemia (αCS , αQS and αWS)²⁷ and 17 types of β -thalassemia ($\beta^{IVS-II-654}$

(C→T), $\beta^{CD41-42(-TTCT)}$, $\beta^{CD17(A→T)}$, $\beta^{CD27-28(+C)}$, $\beta^{-28(A→G)}$, $\beta^{CD71-72(+A)}$, $\beta^{-29(A→G)}$, $\beta^{CD26(GAG→AAG)}$, $\beta^{CD31(-C)}$, $\beta^{-32(C→A)}$, $\beta^{IVS-1-1(G→T)}$, $\beta^{CD43(GAG→TAG)}$, $\beta^{-30(T→C)}$, $\beta^{CD14-15(+G)}$, $\beta^{int(ATG→AGG)}$, $\beta^{IVS-1-5(G→C)}$, and $\beta^{Cap+40-43(-AAAC)}$.²⁸

Statistical Analyses

Categorical variables were expressed as frequencies and percentages, while numerical variables were expressed as medians and percentiles (25th and 75th percentiles). Clinical and demographic characteristics were analyzed as independent variables. Anxiety and depression scores were analyzed as dependent variables. Correlations among anxiety, depression, and independent variables were assessed using nonparametric tests and Spearman correlation analysis. Statistical analyses were performed using the IBM SPSS 26 software (SPSS Inc., Chicago, IL, USA) and GraphPad Prism (V8.3.0). Statistical significance was set at $P < 0.05$.

Results

Table 1 shows the correlations between demographic characteristics, healthcare processes, anxiety, and depression. Among the 82 respondents, 66 (80.5%) were female and 16 (19.5%) were male. They were mainly aged 20–40 years (79.3%), and 65.9% of the respondents had a high school education or higher. Table 1 shows the proportions of BMI, marital status, family income, and medical history. Approximately 40.1% and 43.9% of the respondents were nervous upon the diagnosis of anemia and thalassemia, respectively. Approximately 81.7% of the respondents had received interpretation and education on genetic reports from doctors; moreover, only 3.7% of the respondents reported anxiety or depression (Table 1).

Table 1 The Description of Demographic Characteristics, Procedures and the Correlation Analysis Between Them and Anxiety, Depression Score

	Number (%)	Anxiety		Depression	
		Median (Q1–Q3)	Z (P)	Median (Q1–Q3)	Z (P)
Gender					
Male	16(19.5)	0.50(0–2.50)	–0.730(0.465)	2.00(0–4.50)	–0.684(0.494)
Female	66(80.5)	1.00(0–2.00)		1.00(0–4.00)	
Age (years)					
12–20	4(4.9)	1.50(0.25–7.25)	0.729(0.866)	1.00(0–5.75)	0.993(0.803)
20–40	65(79.3)	1.00(0–2.00)		1.00(0–4.00)	
40–60	9(11.0)	1.00(0–3.00)		1.00(0–4.00)	
>60	4(4.9)	1.00(0.25–2.50)		3.50(0.75–4.75)	
BMI (kg/m ²)					
<18.5	9(11.0)	1.00(0–4.50)	2.636(0.451)	4.00(0–5.00)	2.303(0.512)
18.5–23.9	50(61.0)	1.00(0–2.25)		1.00(0–3.25)	
24–27.9	18(22.0)	0(0–2.25)		0.50(0–3.00)	
≥28	5(6.1)	1.00(0–2.00)		1.00(0.50–7.50)	
Married					
Yes	74(90.2)	1.00(0–2.00)	–0.738(0.461)	1.00(0–4.00)	–0.631(0.528)
No	8(9.8)	1.50(0–6.50)		1.00(0–1.75)	
Education					
Under the high school	28(34.1)	1.00(0–3.00)	–1.431(0.153)	3.00(0–5.00)	–2.798(0.005)
High school and above	54(65.9)	1.00(0–2.00)		1.00(0–3.00)	
Occupation					
Student	5(6.1)	1.00(0–5.50)	3.404(0.638)	1.00(0–4.50)	4.614(0.465)
Officeholder	5(6.1)	2.00(0–3.50)		1.00(0.50–3.00)	
Teacher	9(11.0)	0(0–2.00)		0(0–3.00)	
Worker	14(17.1)	0(0–3.00)		2.50(0–4.25)	
Farmers/unemployed	25(30.5)	1.00(0–2.00)		2.00(0–4.50)	
Other	24 (29.3)	1.00(0–3.50)		1.00(0–3.00)	

(Continued)

Table 1 (Continued).

	Number (%)	Anxiety		Depression	
		Median (Q1–Q3)	Z (P)	Median (Q1–Q3)	Z (P)
Monthly income(yuan)					
<3000	11 (13.4)	1.00(0–1.00)	1.234(0.745)	3.00(0–4.00)	5.000(0.172)
3000–5000	23 (28.0)	0(0–2.00)		1.00(0–4.00)	
5000–10,000	27 (32.9)	1.00(0–2.00)		2.00(0–4.00)	
>10,000	21 (25.6)	1.00(0–3.00)		1.00(0–2.00)	
Time(years)					
<1	27 (32.9)	1.00(0–2.00)	1.968(0.579)	1.00(0–4.00)	0.796(0.850)
1–5	26 (31.7)	1.00(0–3.00)		1.50(0–3.00)	
5–10	8 (9.8)	0.50(0–1.75)		2.00(0–2.75)	
≥10	21 (25.6)	1.00(0–4.00)		1.00(0–4.00)	
Medical history					
No	70 (85.4)	1.00(0–2.00)	–0.124(0.901)	1.00(0–3.25)	–0.692(0.489)
Yes	12 (14.6)	1.00(0–2.50)		2.00(0–5.75)	
Iron supplement					
No	46 (56.1)	0.50(0–2.00)	–1.695(0.090)	1.00(0–4.00)	–0.633(0.527)
Yes	36 (43.9)	1.00(0–3.00)		1.00(0–3.75)	
Understand the genetic report					
Yes	37 (45.1)	1.00(0–2.00)	–0.186(0.853)	1.00(0–4.00)	0.415(0.678)
No	45 (54.9)	1.00(0–2.50)		1.00(0–3.50)	
Interpretation and preaching					
Yes	67 (81.7)	1.00(0–2.00)	–0.660(0.509)	1.00(0–4.00)	–0.900(0.368)
No	15 (18.3)	1.00(0–1.00)		2.00(0–5.00)	
Tension when diagnosed anemia					
No	50 (59.9)	0.00(0–2.00)	6.410(0.041)	1.00(0–3.00)	3.281(0.194)
Occasionally	29 (35.4)	1.00(0–4.00)		2.00(0–4.00)	
Most of the time	3(3.7)	2.00(–)		1.00(–)	
Almost all the time	0 (0)	NA		NA	
Tension when diagnosed thalassemia carrier					
No	46 (56.1)	0(0–2.00)	8.504(0.014)	1.00(0–3.00)	1.939(0.379)
Occasionally	32 (39.0)	1.00(0–3.00)		2.00(0–4.00)	
Most of the time	4 (4.9)	3.00(1.25–7.00)		1.50(1.00–2.75)	
Almost all the time	0 (0)	NA		NA	
Anxiety					
Yes	3 (3.7)	9.00(–)	–3.069(0.002)	7.00(–)	–1.886(0.062)
No	79 (96.3)	1.00(0–2.00)		1.00(0–4.00)	
Depression					
Yes	3 (3.7)	3.00(–)	–1.774(0.076)	9.00(–)	–3.029(0.002)
No	79 (96.3)	1.00(0–2.00)		1.00(0–3.00)	

Notes: BMI, body mass index; Times: the time from finding anemia to the diagnosis of thalassemia carriers; iron supplement: iron supplement used prior to diagnosis. Q1–Q3: 25th and 75th percentiles. Bold values show a level of significance <0.05.

Thalassemia carriers with a high school education or above had lower depression scores than those with less education ($P = 0.005$). The nervousness level upon anemia diagnosis and confirmation in thalassemia carriers was positively correlated with anxiety scores. There were no significant differences in anxiety and depression scores according to age, sex, BMI, marital status, occupation, monthly income, duration from anemia detection to confirmation as a thalassemia carrier, medical history, understanding, interpretation, and education on genetic reports (Table 1).

Table 2 shows laboratory indicators and their correlations with anxiety and depression. Red blood cell (RBC) counts were negatively correlated with depression scores ($r = -0.274$, $P = 0.043$). Total cholesterol (TC) was negatively correlated with anxiety ($r = -0.374$, $P = 0.017$) and depression ($r = -0.379$, $P = 0.016$). High density lipoprotein

Table 2 The Description of Laboratory Index and Correlation Analysis Between Them and Anxiety, Depression Score

	Number	Median (Q1–Q3)	Anxiety		Depression	
			r	p	r	p
RBC($\times 10^{12}/L$)	68	4.72(4.16–5.46)	–0.222	0.069	–0.274	0.043
Hb(g/L)	68	104.00(89.25–119.25)	–0.177	0.148	–0.150	0.222
MCV(fl)	68	67.35(62.93–72.83)	–0.001	0.996	0.003	0.979
MCH(pg)	68	21.50(20.30–22.78)	0.054	0.664	0.085	0.493
MCHC(g/L)	68	320.00(310.25–326.00)	0.046	0.710	0.193	0.115
Hct(%)	68	32.45(28.93–37.20)	–0.219	0.073	–0.22	0.071
Hb/Hct	68	3.21(3.10–3.26)	0.063	0.610	0.191	0.118
Alb(g/L)	57	43.70(36.70–46.00)	–0.309	0.771	–0.079	0.558
Globulin(g/L)	57	28.40(25.80–30.75)	–0.125	0.352	–0.034	0.800
A/G	57	1.50(1.30–1.70)	0.075	0.580	0.001	0.992
TP(g/L)	57	69.50(65.55–74.95)	–0.061	0.651	–0.097	0.475
ALT(U/L)	58	12.50(9.00–19.75)	0.043	0.750	0.081	0.547
AST(U/L)	56	20.00 (17.00–23.00)	0.053	0.696	0.078	0.570
LDL(mmol/L)	39	2.25 (1.95–2.54)	–0.227	0.164	–0.108	0.514
HDL(mmol/L)	40	1.55(1.23–1.85)	–0.209	0.196	–0.238	0.139
TG(mmol/L)	40	1.96 (0.96–2.93)	–0.066	0.685	–0.166	0.305
TC(mmol/L)	40	4.44 (4.18–5.32)	–0.374	0.017	–0.379	0.016
IBIL($\mu\text{mol/L}$)	57	8.50 (6.00–11.25)	–0.001	0.995	0.066	0.628
DBIL($\mu\text{mol/L}$)	57	3.20(2.45–5.00)	0.028	0.836	0.039	0.771
TBIL($\mu\text{mol/L}$)	58	11.85 (9.33–17.22)	0.014	0.917	0.055	0.680
TBA($\mu\text{mol/L}$)	45	2.80(1.95–4.35)	0.038	0.805	–0.082	0.594
Anxiety	82	1.00(0–2.00)	1	0	0.574	<0.001
Depression	82	1.00 (0–4.00)	0.574	<0.001	1	0

Notes: Bold values show a level of significance <0.05 .

Abbreviations: RBC, red blood count; Hb, hemoglobin; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; Hct, hematocrit; Hb/Hct, hemoglobin-hematocrit ratio; Alb, albumin; A/G, albumin- globulin ratio; TP, total protein; ALT, alanine transaminase; AST, aspartate aminotransferase; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglyceride; TC, total cholesterol; IBIL, indirect bilirubin; DBIL, direct bilirubin; TBIL, total bilirubin; TBA, total bile acid.

(HDL) and low density lipoprotein (LDL) levels did not correlate with anxiety or depression scores. Furthermore, anxiety and depression were positively correlated ($r = 0.574$, $P < 0.001$). The median hemoglobin level was 104 g/L. Hemoglobin levels did not correlate with anxiety or depression scores. Table 2 shows the correlations between other laboratory indicators and the anxiety and depression scores.

Figure 2 shows the time from confirmation of a thalassemia carrier questionnaire completion and some basic information. Three participants had anxiety or depression, respectively, and the frequency of both anxiety and depression was 3.7% (3/82). There were differences in the time from confirmation as a thalassemia carrier to the completion of the questionnaire. Figure 3 shows the genotype distribution; there is mainly β -thalassemia (66%). Six types of mutations were identified, most of which were IVS-II-654(C \rightarrow T) (26%), CD41-42(-TTCT) (20%). In cases of α -thalassemia carriers, 3 types of α -globin mutations were detected; –SEA/ $\alpha\alpha$ was the most common in the α -thalassemia, accounting for about 16%, followed by $-\alpha 3.7/\alpha\alpha$ (15%). The genetic diagnoses for the three patients with anxiety were IVS-II-654(C \rightarrow T), –SEA/ $\alpha\alpha$, and CD27/28(+C), respectively. The genetic diagnoses for the three patients with depression were IVS-II-654(C \rightarrow T), $-\alpha 3.7/\alpha\alpha$, and CD27/28(+C), respectively. Figure 4 shows the distribution of Hb, MCV, MCH, and mean corpuscular hemoglobin concentration (MCHC). Some carriers of thalassemia exhibited microcytic hypochromic anemia.

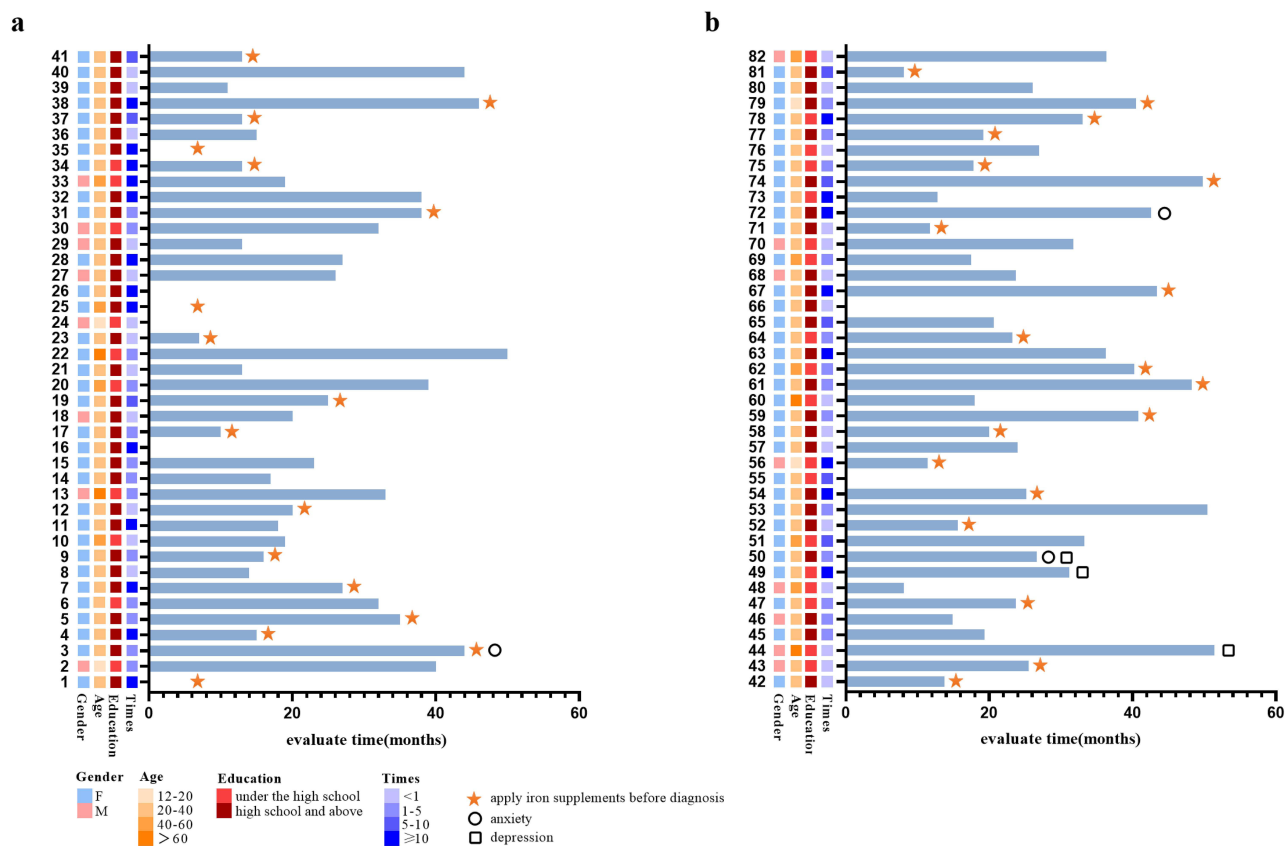


Figure 2 Basic information of the 82 thalassemia carriers.

Note: Times: the time from anemia diagnosis to the confirmation as a thalassemia carrier. Evaluation times: the time from confirmation as a thalassemia carrier to questionnaire completion. The thalassemia carriers are numbered from 1 to 82. (a) 1–41 subjects, (b) 42–82 subjects. Carriers 1, 16, 24–26, 55, and 66 were diagnosed in other hospitals, and the time of diagnosis was unknown. We did not obtain the real name of 35.

Discussion

In our study, the frequencies of anxiety and depression among thalassemia carriers were both 3.7%. Previous studies have investigated the psychological status of carriers of thalassemia. Eren et al²⁹ found a higher rate of anxiety and depression among patients with beta-thalassemia minor than among healthy participants ($P = 0.018$). Keşkek et al³⁰ found a higher rate of depression among patients with beta-thalassemia minor (81%) than among healthy participants ($P < 0.001$). Marvasti et al³¹ found a slightly higher rate of depression among patients with beta-thalassemia patients (39.3%) than among those without it ($P = 0.07$) (Table 3). Our study found lower anxiety/depression rates (3.7%) than prior reports,^{29–31} though direct comparisons were limited by methodological differences. While genetic counseling may contribute to this difference, natural psychological adaptation over time cannot be ruled out because of the variable follow-up intervals (Figure 2).

As previously mentioned, genetic counseling can contribute to the relief of psychological burden. The United States was the first country to initiate genetic counseling approximately 50 years ago. In 2019, Marvasti et al³⁴ found that Iran and Turkey lacked information regarding genetic counseling. Moreover, although there are relevant certifications, institutional registrations, and genetic counseling committees in China, there are no relevant data regarding the annual number of trained genetic counselors and training programs. There has been a recent rapid development in domestic genetic counseling; however, the number of genetic counselors remains relatively small. Two months after the establishment of the Genetic Counseling Committee in 2015, China actively conducted multifield training courses on genetic counseling, established multiple top hospitals as genetic counseling training institutions, and trained individuals such as registered physicians, students attending medical or life science schools, laboratory technicians, and non-genetic professionals to become competent in genetic counseling.³⁵ Our hospital implemented a similar model by conducting numerous training sessions for genetic counselors and clinicians, which provided the hospital with the capacity for pre-

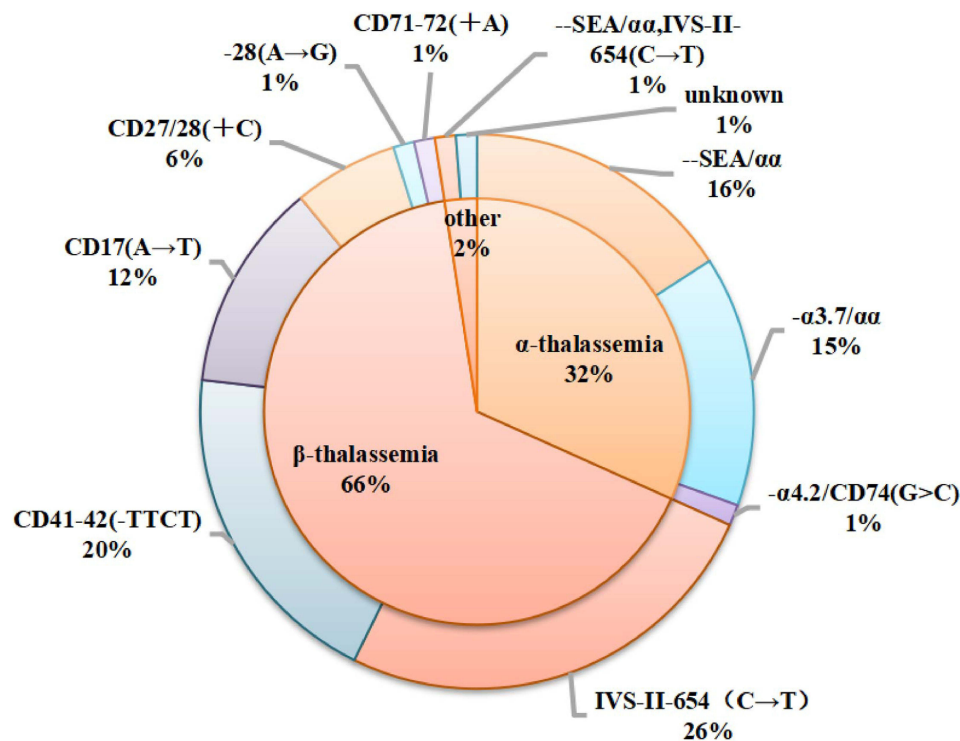


Figure 3 Gene distribution among thalassemia carriers.

and post-test genetic counseling, including popular science education, genetic risk assessment, and measures for addressing psychological changes and the needs of consultants during the consultation process.

Genetic counseling increases knowledge, improves the perception of personal control, promotes positive health behaviors among thalassemia carriers and it provides them with humanistic care and social support.^{18,36} This could be attributed to genetic counseling improving anxiety and depression in thalassemia carriers as well as the use of different assessment scales, regional differences, and differences among the included populations.

In 2006, the National Society of Genetic Counselors defined genetic counseling as a process of helping people understand and adapt to the medical, psychological, and family effects of genetics on a disease.³⁷ It is a patient-centered, educational, and supportive communication process. Previous studies have shown that genetic counseling contributes to a broader field of psychotherapy.^{38,39} In genetic counseling, chronic disease management and smoking cessation, cognitive behavioral theory (CBT) is widely used;^{40,41} further, online psychological interventions based on the CBT model have been found to relieve depression, anxiety, and general pain symptoms in patients with chronic diseases.⁴² Reciprocal engagement in genetic counseling personalizes the counseling process, which may improve emotional control in patients receiving genetic test results.¹² Additionally, there is worldwide lobbying for adequate pre- and posttest counseling in genetic testing.¹¹ Janssens found that this was not often provided.⁴³ A previous study reported that only 12% of genetic analyses in Italy were accompanied by pre- or posttest counseling,⁴⁴ indicating challenges in the widespread implementation of genetic counseling.

Regarding the influence of demographic characteristics on anxiety and depression in thalassemia carriers, in our study, depression scores were higher among participants with below high school education than among those with high school education or above. Thalassemia carriers with a low education level could have difficulty understanding medical knowledge regarding diseases, which could impede them from correctly understanding their own diseases and lead to negative psychological factors, such as anxiety or depression. In our study, the proportion of males (19.5%) was significantly lower than that of females (80.5%). Some studies have reported that women have a higher incidence of anxiety and depression than men.^{45,46} However, Marvasti et al⁴⁷ reported a higher incidence of depression in men living in poverty than in corresponding women. Additionally, anxiety and depression are influenced by marital status,

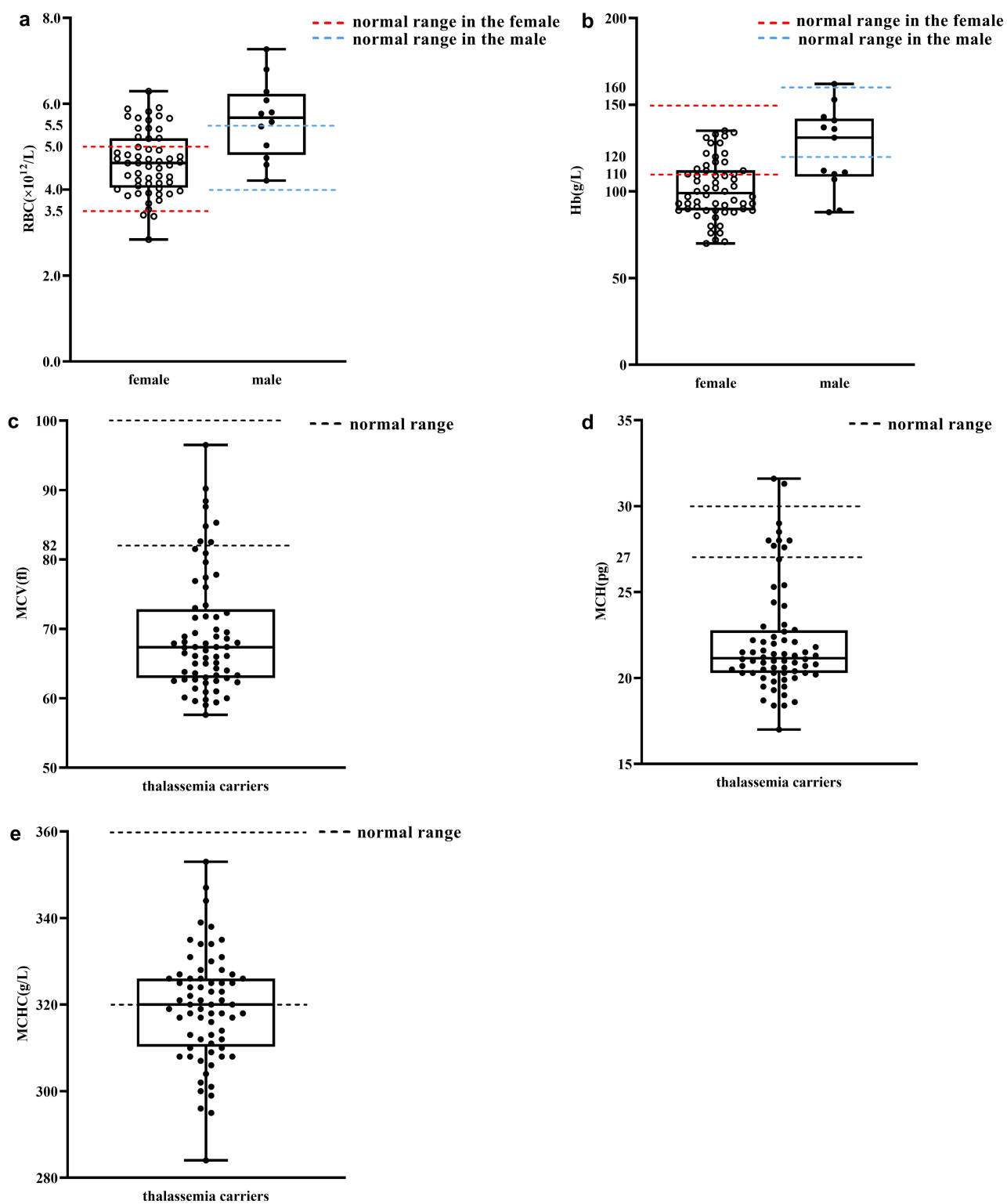


Figure 4 The distribution of RBC (a), Hb (b), MCV (c), MCH (d), and MCHC (e) among thalassemia carriers.

unemployment, and low income. Moreover, adults people tend to be more prone to anxiety and depression.⁴⁸ However, Blomen⁴⁹ reported no correlation between mental health status and sex, economic status, or marital status among young people aged 20–40 years. Follow-up studies should expand the sample size.

Table 3 Related Articles About on the Anxiety and Depression of the Thalassemia Carriers

Author	Year	Country	Subjects	Method	Result	Discussion
Eren R ²⁹	2021	Turkey	39 BTm subjects 25 healthy controls	Gender, age, BMI, educational status and marital status were completed; BTm and controls were drew blood and filled out the questionnaire of FSS, HADS. T test and Chi-square test for data analysis	51.3% BTm subjects and 20.0% control subjects are anxiety ($p = 0.018$), 51.3% BTm subjects and 24.0% control subjects are depression ($p = 0.039$)	Reasons for this anxiety: (1) genetic inheritance and the possibility of having a child with major thalassemia. (2) health anxiety.
MarvastiVE ³¹	2006	Iran	280 BTT group 200 non-BTT group	Two groups filled out the Beck depression inventory questionnaire (BDI), T test and Chi-square test for data analysis	39.3% (110) BTT subjects were depression, which were constituted of 60.9% (67) male and 39.1% (43) female. BTT subjects is slightly higher than non-BTT subjects in the depression ($p=0.07$)	The role of cholesterol level and developing major depression are still many controversies. β -thalassemia trait subjects can be more prominent depressed in higher ages.
Keşkek SO ³⁰	2013	Turkey	53 BTm participants; 53 healthy subjects	The chi-square, T test or Mann Whitney U-test for data analysis. Pearson correlation coefficient(r) with p value and 95% CI for correlation analysis.	81% (43) BTm subjects and 51.5% (22) were depression ($p<0.001$)	Low cholesterol concentrations, a defect on chromosome 11 may be the reasons.
Bocchetta A ³²	2005	Sardinia	1014 consecutive patients diagnosed according to modified Research Diagnostic Criteria (RDC)	The chi-square, OR, 95% CI for date analysis.	16.4% among bipolar and 9.9% among non-bipolar subgroups were heterozygous β -thalassemia ($p = 0.01$; relative risk = 1.65).	The relevance of heterozygous β thalassemia as a susceptibility factor in mood disorder may due to the linkage disequilibrium between the globin gene and a mood disorder gene closely located in chromosome 11p15 or a direct effect of heterozygous β thalassemia in clinical presentation (microcytic anemia).
Graffeo L ³³	2018	Italy	4943 Tm and 21,063 controls	Logistic Penalised Regression Model (LPRM), Kaplan-Meier curves and Cox regression model for date analysis	Tm is a risk factor for health expectation, particularly, in the cirrhosis, kidney disorders, cholelithiasis, mood disorders.	The cause of mood disorders in Tm individuals is expounded.

Abbreviations: BTm, β -thalassemia minor, BTT, β -thalassemia trait, Tm, thalassemia minor, FSS, fatigue severity scale, HADS, Hospital Anxiety and Depression Scale, OR, odds ratio, 95% CI, 95% confidence interval.

In addition, we found a negative correlation between total cholesterol and anxiety and depression scores, consistent with previous findings.^{50,51} Although, total cholesterol reduction is a protective factor against cardiovascular diseases, low total cholesterol concentrations may reduce serotonin activity in the brain, leading to depression.⁵² Therefore, psychological evaluation during genetic counseling for thalassemia carriers with low total cholesterol levels requires more attention.

A systematic review revealed a close relationship between a significant decrease in HDL and the occurrence of major depression.⁵³ Conversely, some studies have indicated that a reduction in LDL helps inhibit anxiety and depressive emotions.⁵⁴ However, no correlation was observed between HDL or LDL and anxiety/depression in the present study. This may be attributed to two main factors: first, the sample size of this study was relatively small; and second, the changes in HDL and LDL levels among patients with thalassemia were minor, failing to reach a statistically significant correlation. Future studies should expand the sample size to further verify this relationship.

Erythrocyte levels are negatively correlated with depression/anxiety,⁵⁵ which is consistent with our findings. Thalassemia carriers often exhibit the phenomenon of “reduced RBC lifespan (chronic mild hemolysis).” These abnormalities may lead to elevated levels of oxidative stress in the blood.⁵⁶ Furthermore, this process may increase the risk of anxiety and depression through the “oxidative stress-neuroinflammation-emotional disturbance” pathway.⁵⁷ While we found a negative correlation between red blood cell count and anxiety/depression, we observed no correlation between hemoglobin and anxiety/depression scores, which is consistent with a report by Demircan et al.⁵⁸ This result may stem from two potential reasons: first, patients with thalassemia mostly present with microcytic hypochromic anemia, a type of anemia characterized by reduced hemoglobin synthesis and a compensatory increase in red blood cells

—leading to a disproportionate relationship between red blood cell count and hemoglobin levels,^{59,60} second, the relatively small sample size of this study may also have influenced the results of the correlation analysis.

Doctors should take a biological-psychological-social medicine approach rather than just focusing on patients' physical health. Psychological problems, including anxiety and depression, can affect a patient's quality of life and increase the economic burden on society and family. Therefore, preventing and reducing anxiety and depression is crucial. Genetic counseling is a personalized process, and further experience is required to optimize its benefits.

This study has several limitations. First, based on the convenience sampling approach, the study population not only introduces selection bias, but also the Hawthorne effect is inevitable.⁶¹ Follow-up studies can be conducted using random sampling, and the measurements should be repeated for further verification. Second, we did not include a control group, such as patients with severe thalassemia and iron-deficiency anemia, or their own before and after controls, which limits the indication of the role of genetic counseling. Follow-up studies should be conducted with a control group and psychological assessments before and after genetic counseling. Third, this was a single-center, small-sample study. However, there may be differences between cities and regions. The sample size should be expanded in further studies. Future studies in other areas are required to validate our findings. Fourth, there was no standardized time for the psychological status assessment. As anxiety and depression may decrease over time,⁶² this may have affected the observed incidence rates of anxiety and depression. Moreover, we did not explore which types of patients with thalassemia are more prone to developing anxiety and depressive symptoms, which is an important future research direction.

Conclusions

The frequencies of anxiety and depression among thalassemia carriers receiving genetic counseling in Taizhou were both 3.7%, which was lower than previously reported. These preliminary findings suggest a potential association between genetic counseling and reduced psychological distress. In addition, we found that RBC and TC negatively affect mental status in thalassemia; these carriers need to pay attention to their diet and undergo regular monitoring.

Data Sharing Statement

The datasets generated and analyzed during this study are available from the corresponding author Bo Shen upon reasonable request.

Ethics Approval

The study was exempted from informed consent and approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province (Approval number: K20220126).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare.

References

1. Munkongdee T, Chen P, Winichagoon P, et al. Update in Laboratory Diagnosis of Thalassemia. *Front Mol Biosci.* 2020;7:74. doi:10.3389/fmolb.2020.00074

2. Zhang J, Liu Z, Chen R, et al. A MALDI-TOF mass spectrometry-based haemoglobin chain quantification method for rapid screen of thalassaemia. *Ann Med.* 2022;54(1):293–301. doi:10.1080/07853890.2022.2028002
3. Tesio N, Bauer DE. Molecular Basis and Genetic Modifiers of Thalassaemia. *Hematol Oncol Clin North Am.* 2023;37(2):273–299. doi:10.1016/j.hoc.2022.12.001
4. Biesecker B. Genetic Counseling and the Central Tenets of Practice. *Cold Spring Harb Perspect Med.* 2020;10(3):a038968. doi:10.1101/cshperspect.a038968
5. Nelson HD, Pappas M, Cantor A, et al. Risk Assessment, Genetic Counseling, and Genetic Testing for BRCA- Related Cancer in Women. *JAMA.* 2019;322(7):666. doi:10.1001/jama.2019.8430
6. Oliveira FFB, de Barros Silva PG, de Sant'Ana RO, et al. How does genetic testing influence anxiety, depression, and quality of life? A hereditary breast and ovarian cancer syndrome suspects trial. *Support Care Cancer.* 2021;29(7):3521–3530. doi:10.1007/s00520-020-05867-2
7. Oliveri S, Ferrari F, Manfrinati A, Pravettoni G. A Systematic Review of the Psychological Implications of Genetic Testing: a Comparative Analysis Among Cardiovascular, Neurodegenerative and Cancer Diseases. *Front Genet.* 2018;9:624. doi:10.3389/fgene.2018.00624
8. Bordet C, Brice S, Maupain C, et al. Psychosocial Impact of Predictive Genetic Testing in Hereditary Heart Diseases: the PREDICT Study. *J Clin Med.* 2020;9(5):1365. doi:10.3390/jcm9051365
9. de Groot M, Golden SH, Wagner J. Psychological conditions in adults with diabetes. *Am Psychol.* 2016;71(7):552–562. doi:10.1037/a0040408
10. Lwin MN, Serhal L, Holroyd C, Edwards CJ. Rheumatoid Arthritis: the Impact of Mental Health on Disease: a Narrative Review. *Rheumatol Ther.* 2020;7(3):457–471. doi:10.1007/s40744-020-00217-4
11. Bowdin S, Gilbert A, Bedoukian E, et al. Recommendations for the integration of genomics into clinical practice. *Genet Med.* 2016;18(11):1075–1084. doi:10.1038/gim.2016.17
12. Yuen J, Lee SY, Courtney E, et al. Evaluating empowerment in genetic counseling using patient-reported outcomes. *Clin Genet.* 2019;97(2):246–256. doi:10.1111/cge.13646
13. Hickey KT, Sciacca RR, Biviano AB, et al. The effect of cardiac genetic testing on psychological well-being and illness perceptions. *Heart Lung.* 2014;43(2):127–132. doi:10.1016/j.hrtlng.2014.01.006
14. Larsson MU, Luszcz MA, Bui T-H, Wahlin T-BR. Depression and suicidal ideation after predictive testing for Huntington's disease: a two-year follow-up study. *J Genet Couns.* 2006;15(5):361–374. doi:10.1007/s10897-006-9027-6
15. Manchanda R, Loggenberg K, Sanderson S, et al. Population testing for cancer predisposing BRCA1/BRCA2 mutations in the Ashkenazi-Jewish community: a randomized controlled trial. *J Natl Cancer Inst.* 2014;107(1):379. doi:10.1093/jnci/dju379
16. Austin JC, Honer WG. Psychiatric genetic counselling for parents of individuals affected with psychotic disorders: a pilot study. *Early Interv Psychiatry.* 2008;2(2):80–89. doi:10.1111/j.1751-7893.2008.00062.x
17. Athens BA, Caldwell SL, Umstead KL, et al. A Systematic Review of Randomized Controlled Trials to Assess Outcomes of Genetic Counseling. *J Genet Couns.* 2017;26(5):902–933. doi:10.1007/s10897-017-0082-y
18. Madlensky L, Trepanier AM, Cragun D, et al. A Rapid Systematic Review of Outcomes Studies in Genetic Counseling. *J Genet Couns.* 2017;26(3):361–378. doi:10.1007/s10897-017-0067-x
19. Haishan J, Ying P. Expert consensus on carrier screening, prevention and control for thalassaemia. *J Int Neurol Neurosurg.* 2024;51(05):43–50.
20. Bowen X, Feng Y, Zhao Y, et al. Decent work, work engagement, and turnover intention among registered nurses: a cross-sectional study. *BMC Nurs.* 2024;23(1):31. doi:10.1186/s12912-023-01662-6
21. Wang H, Huang D, Huang H, et al. The psychological impact of COVID-19 pandemic on medical staff in Guangdong, China: a cross-sectional study. *Psychological Medicine.* 2020;1–9.
22. Yang Z, Huang X, Liu X, et al. Psychometric Properties and Factor Structure of the Chinese Version of the Hospital Anxiety and Depression Scale in People Living With HIV. *Frontiers in Psychiatry.* 2019;10:346. doi:10.3389/fpsy.2019.00346
23. Zhang D, Fan Z, Gao X, et al. Illness uncertainty, anxiety and depression in Chinese patients with glaucoma or cataract. *Sci Rep.* 2018;8(1):11671. doi:10.1038/s41598-018-29489-1
24. Liu CL, Liu L, Zhang Y, et al. Prevalence and its associated psychological variables of symptoms of depression and anxiety among ovarian cancer patients in China: a cross-sectional study. *Health Qual Life Outcomes.* 2017;15(1):161. doi:10.1186/s12955-017-0738-1
25. Bjelland IDA, Haug TT, Neckelmann D, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res.* 2002;52(2):69–77. doi:10.1016/S0022-3999(01)00296-3
26. Stern AF. The Hospital Anxiety and Depression Scale. *Occup Med.* 2014;64(5):393–394. doi:10.1093/occmed/kqu024
27. Xi H, Liu Q, Liu J, et al. Expert consensus on clinical genetic counseling of α -thalassaemia gene analysis. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi.* 2024;41(6):669–676. doi:10.3760/cma.j.cn511374-20240131-00079
28. Writing Group For Practice Guidelines For D, Treatment Of Genetic Diseases Medical Genetics Branch Of Chinese, Medical A, Shang X, Wu X, et al. Clinical practice guidelines for beta-thalassaemia. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi.* 2020;37(3):243–251. doi:10.3760/cma.j.issn.1003-9406.2020.03.004.
29. Eren R, Karışmaz A, Aslan C, et al. Beta Thalassaemia Minor: patients Are Not Tired but Depressed and Anxious. *Med Princ Pract.* 2021;30(1):69–72. doi:10.1159/000508981
30. Keşkek SO, Kirim S, Turhan A, Turhan FG. Depression in subjects with beta-thalassaemia minor. *Ann Hematol.* 2013;92(12):1611–1615. doi:10.1007/s00277-013-1851-9
31. Marvasti VE, Dastoori P, Karimi M. Is beta-thalassaemia trait a risk factor for developing depression in young adults? *Ann Hematol.* 2006;85(12):873–874. doi:10.1007/s00277-006-0154-9
32. Bocchetta A. Heterozygous beta-thalassaemia as a susceptibility factor in mood disorders: excessive prevalence in bipolar patients. *Clin Pract Epidemiol Ment Health.* 2005;1(1):6. doi:10.1186/1745-0179-1-6
33. Graffeo L, Vitrano A, Scodotto S, et al. beta-Thalassaemia heterozygote state detrimentally affects health expectation. *Eur J Intern Med.* 2018;54:76–80. doi:10.1016/j.ejim.2018.06.009
34. Abacan M, Alsubaie L, Barlow-Stewart K, et al. The Global State of the Genetic Counseling Profession. *Eur J Hum Genet.* 2019;27(2):183–197. doi:10.1038/s41431-018-0252-x
35. Sun L, Liang B, Zhu L, et al. The rise of the genetic counseling profession in China. *Am J Med Genet C Semin Med Genet.* 2019;181(2):170–176. doi:10.1002/ajmg.c.31693

36. Nishigaki M, Tokunaga-Nakawatase Y, Nishida J, Kazuma K. The effect of genetic counseling for adult offspring of patients with type 2 diabetes on attitudes toward diabetes and its heredity: a randomized controlled trial. *J Genet Couns.* 2014;23(5):762–769. doi:10.1007/s10897-013-9680-5
37. National Society of Genetic Counselors', Definition Task F, Resta R, Biesecker BB, et al. A new definition of Genetic Counseling: national Society of Genetic Counselors' Task Force report. *J Genet Couns.* 2006;15(2):77–83. doi:10.1007/s10897-005-9014-3.
38. Austin J, Semaka A, Hadjipavlou G. Conceptualizing genetic counseling as psychotherapy in the era of genomic medicine. *J Genet Couns.* 2014;23(6):903–909. doi:10.1007/s10897-014-9728-1
39. van Langen IM, Hofman N, Tan HL, Wilde AAM. Family and population strategies for screening and counselling of inherited cardiac arrhythmias. *Ann Med.* 2004;36(1):116–124. doi:10.1080/17431380410032526
40. Kurniawan MH, Handiyani H, Nuraini T, et al. A systematic review of artificial intelligence-powered (AI-powered) chatbot intervention for managing chronic illness. *Ann Med.* 2024;56(1):2302980. doi:10.1080/07853890.2024.2302980
41. Goh KW, Ming LC, Al-Worafi YM, et al. Effectiveness of digital tools for smoking cessation in Asian countries: a systematic review. *Ann Med.* 2024;56(1):2271942. doi:10.1080/07853890.2023.2271942
42. White V, Linardon J, Stone JE, et al. Online psychological interventions to reduce symptoms of depression, anxiety, and general distress in those with chronic health conditions: a systematic review and meta-analysis of randomized controlled trials. *Psychol Med.* 2020;2020:1–26.
43. Janssens S, Chokoshvili D, Vears DF, et al. Pre- and post-testing counseling considerations for the provision of expanded carrier screening: exploration of European geneticists' views. *BMC Medical Ethics.* 2017;18(1). doi:10.1186/s12910-017-0206-9.
44. Giardino D, Mingarelli R, Lauretti T, et al. Survey of medical genetic services in Italy: year 2011. *BMC Health Serv Res.* 2016;16(1). doi:10.1186/s12913-016-1340-7.
45. Araya R, Rojas G, Fritsch R, et al. Treating depression in primary care in low-income women in Santiago, Chile: a randomised controlled trial. *Lancet.* 2003;361(9362):995–1000. doi:10.1016/S0140-6736(03)12825-5
46. Hinz A, Herzberg PY, Lordick F, et al. Age and gender differences in anxiety and depression in cancer patients compared with the general population. *Eur J Cancer Care (Engl).* 2019;28(5):e13129. doi:10.1111/ecc.13129
47. Premawardhena A, Arambepola M, Katugaha N, Weatherall DJ. Is the beta thalassaemia trait of clinical importance? *Br J Haematol.* 2008;141(3):407–410. doi:10.1111/j.1365-2141.2008.07071.x
48. Dong L, Freedman VA, Mendes de Leon CF. The Association of Comorbid Depression and Anxiety Symptoms With Disability Onset in Older Adults. *Psychosom Med.* 2020;82(2):158–164. doi:10.1097/PSY.0000000000000763
49. Blomen CL, Pott A, Volk AE, et al. Communication processes about predictive genetic testing within high-risk breast cancer families: a two-phase study design. *Sci Rep.* 2021;11(1). doi:10.1038/s41598-021-98737-8.
50. Altinoz MA, Ince B. Hemoglobins emerging roles in mental disorders. Metabolic, genetical and immunological aspects. *Int J Dev Neurosci.* 2017;61(1):73–85. doi:10.1016/j.ijdevneu.2017.06.007
51. Fiedorowicz JG, Palagummi NM, Behrendtsen O, Coryell WH. Cholesterol and affective morbidity. *Psychiatry Res.* 2010;175(1–2):78–81. doi:10.1016/j.psychres.2009.01.001
52. Arango V, Underwood MD, Mann JJ. Serotonin brain circuits involved in major depression and suicide. *Prog Brain Res.* 2002;136:443–453.
53. Almulla AF, Thipakorn Y, Algon AAA, et al. Reverse cholesterol transport and lipid peroxidation biomarkers in major depression and bipolar disorder: a systematic review and meta-analysis. *Brain Behav Immun.* 2023;113:374–388. doi:10.1016/j.bbi.2023.08.007
54. Landaverde-Mejia K, Dufoo-Hurtado E, Camacho-Vega D, et al. Pistachio (*Pistacia vera* L.) consumption improves cognitive performance and mood in overweight young adults: a pilot study. *Food Chem.* 2024;457:140211. doi:10.1016/j.foodchem.2024.140211
55. Shafiee M, Tayefi M, Hassanian SM, et al. Depression and anxiety symptoms are associated with white blood cell count and red cell distribution width: a sex-stratified analysis in a population-based study. *Psychoneuroendocrinology.* 2017;84:101–108. doi:10.1016/j.psyneuen.2017.06.021
56. Longo F, Piolatto A, Ferrero GB, Piga A. Ineffective Erythropoiesis in β -Thalassaemia: key Steps and Therapeutic Options by Drugs. *Int J Mol Sci.* 2021;22(13):7229. doi:10.3390/ijms22137229
57. Elbakary N, Al-Khuzaei N, Hussain T, et al. Inflammatory biomarkers as predictors for unlocking antidepressant efficacy: assessing predictive value and risk stratification in major depressive disorder in a prospective longitudinal study. *J Affect Disord.* 2025;387:119545. doi:10.1016/j.jad.2025.119545
58. Demircan F, Gozel N, Kilinc F, et al. The Impact of Red Blood Cell Distribution Width and Neutrophil/Lymphocyte Ratio on the Diagnosis of Major Depressive Disorder. *Neurol Ther.* 2016;5(1):27–33. doi:10.1007/s40120-015-0039-8
59. Sankaran VG, Weiss MJ. Anemia: progress in molecular mechanisms and therapies. *Nat Med.* 2015;21(3):221–230. doi:10.1038/nm.3814
60. Musallam KM, Cappellini MD, Coates TD, et al. Alpha-thalassemia: a practical overview. *Blood Rev.* 2024;64:101165. doi:10.1016/j.blre.2023.101165
61. Yeh M-Y, Wu S-C, Tung T-H. The relation between patient education, patient empowerment and patient satisfaction: a cross-sectional-comparison study. *Appl Nurs Res.* 2018;39:11–17. doi:10.1016/j.apnr.2017.10.008
62. Wevers MR, Ausems MG, Verhoef S, et al. Does rapid genetic counseling and testing in newly diagnosed breast cancer patients cause additional psychosocial distress? results from a randomized clinical trial. *Genet Med.* 2016;18(2):137–144. doi:10.1038/gim.2015.50

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