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Original Article

Acceptance towards giving birth to a child with beta-thalassemia major – A prospective study

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ABSTRACT

Objective: To explore the acceptance of pregnant Chinese women on giving birth to a child with beta-thalassemia major.

Materials and methods: Women's acceptance on having a child with beta thalassemia major was assessed using standard gamble metrics during an interviewer-administered survey on 309 women recruited in the antenatal clinic. Utility scores were determined and the association with sociodemographic factors was assessed.

Results: The median utility score for having a child with beta-thalassemia major was 0.5 (0–0.65). Women having either higher educational level or family income had significantly higher utility scores ($P < 0.05$) corresponding to a higher acceptance. During the interview 59.9% participants indicated that they would elect to undergo a termination of pregnancy if their fetus was diagnosed with beta-thalassemia major but 26.5% participants were unable to decide what action they would take.

Conclusion: Many Chinese pregnant women are ambivalent about giving birth to a baby with beta-thalassemia major. Women with higher educational level or higher family income had a higher acceptance towards the condition.

Introduction

Beta-thalassemia is a common inherited disorder of hemoglobin synthesis with a reported carrier frequency in Southeast and East Asia ranging from 2 to 9% [1]. Beta-thalassemia is caused by a mutation in the HBB gene located on the short arm of chromosome 11 which controls production of the beta-globulin protein. The loss or impaired production of beta-globulin results in red blood cell damage and anemia. In the homozygous state, marked reduction of functional hemoglobin levels results in transfusion dependent anemia, reduced growth, delayed development, bone abnormalities and hepatosplenomegaly. The mainstay of treatment currently is lifelong transfusion with concomitant iron chelation therapy to prevent the adverse effect of transfusion-mediated iron overloading and hemochromatosis, while successful allogeneic hematopoietic stem cell transplantation has been demonstrated in selected cases [2,3]. Mortality rates are reduced from 12.7 to 4.3 deaths per 1000 patient as therapies improved and life span has increased from 20 to 45 years since the 1970s [4].

Beta-thalassemia is an autosomal recessive inherited condition. Offspring of beta-thalassemia couple have a 25% chance of inheriting both mutations from the parents and being affected with beta-thalassemia major. Antenatal screening using mean corpuscular volume is effective in identifying asymptomatic carriers and at risk pregnancies [5]. Ultrasound screening however is unable to detect beta-thalassemia major prenatally because features of the disease only occur after birth unlike in the case of alpha-thalassemia major. Fetal diagnosis of beta-thalassemia major is reliant on genetic studies on fetal tissue obtained through either chorionic villus sampling or amniocentesis. Both of these diagnostic procedures are associated with procedure related fetal loss, with loss rates commonly quoted as ranging from 0.5 to 1% during counseling, although more recent studies have indicated rates as low as 0.1% [6–9].

The attitude towards giving birth to a child with abnormalities varies in different cultures. Chinese women who often find a handicapped child unacceptable have a low tolerance of fetal

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chromosomal abnormalities as demonstrated by the high proportion opting for elective termination of pregnancy for fetus diagnosed with Down syndrome [10,11]. In contrast to Down syndrome, our empirical observation would suggest that some Chinese women opted to continue pregnancies diagnosed with fetal beta-thalassemia major prenatally after counseling by Pediatric Hematologist on the prognosis and management options. We postulate that this may be because beta-thalassemia major is not associated with impaired intelligence unlike Down syndrome. There are no published studies on the acceptance of Chinese women's towards giving birth to a child with beta-thalassemia major. Since beta thalassemia is a relatively common inherited condition in our locality, understanding to what extent prospective parents accept, and the factors that could influence their choice, could help with effective prenatal counseling.

The method of Standard gamble metrics was previously used to assess the acceptance of Chinese women on having a Down syndrome baby and the metrics was well understood by the participants [11]. The study was able to demonstrate that Chinese women perceived having a Down syndrome baby a similar adverse life event as being blind and they had a much lower acceptance towards Down syndrome baby compared to Caucasian women [11]. Thus, standard gamble metrics was used in this study to assess Chinese women's acceptance on having a baby with beta-thalassemia major.

Materials and methods

This was a prospective observational study conducted in a University unit in Hong Kong which offers universal first trimester combined screening test for Down syndrome [12]. Women who attended the clinic for assessment of fetal Down syndrome risk over a 4 month period were invited to participate in an interviewer-administered survey. All interviews were performed by a single individual with previous experience on administering the standard gamble technique [11]. Women who were non-Chinese or who did not speak Chinese were excluded from the study. The study was approved by the Institutional Ethics Committee and informed consent was taken from all subjects.

Before the survey was conducted, women were provided with written information on beta-thalassemia major including its genetic basis, cause, presentation and potential management options including regular blood transfusion, iron chelation therapy, and hemopoietic stem cell transplantation as well as current option to diagnose whether their fetus was affected. Women were informed that beta-thalassemia major could be diagnosed by an invasive diagnostic procedure with an associated risk of miscarriage of around 0.5–1%.

The survey was composed of two sections. The first section was designed to elicit relevant demographic information, including maternal age, marital status, educational history, family income level, obstetric history and family history. The women's attitude towards fetuses with beta thalassemia major and termination of pregnancy was assessed by the following question. 'Would you request a termination of pregnancy if your fetus is diagnosed with beta thalassemia major.'

The second section was designed to elicit patient acceptances using the standard gamble metrics. In a standard gamble test, subjects will be asked to choose from a guaranteed outcome (e.g. being blind for the rest of their life), or whether they would prefer an alternative state with some chance of a worst outcome (e.g. dying, '1-p') and a complementary chance of an ideal outcome (e.g. continue to live healthily, 'p'). The risks for the two situations are varied until the subject is indifferent to either of the two options, at which stage the 'utility' for the health state under consideration equals 'p'. This allows quantitative comparison of qualitatively different health states, which guides our understanding of the decision making process of the patients.

In order to ensure that our subjects understood the standard gamble metrics, the interviewer first assessed their utilities towards the health state of blindness. The subject was asked to make a decision starting with a probability of 100%, which was then reduced in steps of 5% until it reached 10% after which it was decreased at 1% interval until 2% and thereafter at 0.1% interval, until the subject was unable to make a choice between the two options. After ensuring that subjects understood the standard gamble methodology, the exercise was repeated and the utility towards pregnancy affected by Beta-thalassemia major is assessed using the same approach. The lower the utility, the lower was the patient's acceptance towards that health state.

Utility scores were summarized by median and interquartile range (IQR). Difference in scores between different patient groups was compared using Mann–Whitney U test. The Statistical Package for Social Sciences for Windows version 20 (IBM, Armonk, NY, USA) was used for statistical analysis of all data. A p-value of <0.05 was considered statistically significant.

Results

A total of 315 women who attended the clinic for first-trimester Down syndrome screening were invited to participate in the study, all agreed. Six women subsequently refused to complete the survey as they could not comprehend how the standard gamble assessment was performed, and were unable to complete the blindness standard gamble pre-assessment. These women were excluded from all further analyses. The 309 remaining participants were able to understand the standard gamble metrics and completed the survey.

The demographic characteristics of these 309 women are summarized in Table 1. Nine women were known to be alpha- ($n = 7$) or beta- ($n = 2$) thalassemia carriers prior to conducting the survey. A further 11 women were identified as alpha- ($n = 7$) or beta- ($n = 4$) thalassemia carrier after completing the survey by antenatal screening which indicated decreased MCV, and which was subsequently confirmed by hemoglobin pattern testing. The MCV of their partners were normal except that for the partner of one alpha-thalassemia carrier who was found also to have low MCV and was subsequently confirmed as being a beta-thalassemia minor carrier by hemoglobin pattern assessment.

Table 1
Demographic characteristics of the study population. Values are expressed as mean ± SD or as percentage.

Characteristic	
Age, years	31.9 ± 4.5
Married	92.6%
Education	
Secondary or below	55%
Tertiary or above	45%
Family income (HKD per month)[a]	
<50,000	80.6%
≥50,000	19.4%
Previous miscarriage	17.8%
Previous delivery	42.7%
Previous pregnancy termination	24.6%
Previous neonatal death	0
Previous stillbirth	0
Relative or friends with beta thalassemia	1.6%
Known thalassemia carrier	3.6%
IVF pregnancy	3.2%

[a] HKD 1 = USD 0.1281.

Overall, 185 out of 309 (59.9%) participants indicated that they would elect to terminate the pregnancy if their fetus was diagnosed with beta-thalassemia major. Forty-two (13.6%) participants would continue their pregnancy even if the fetus was affected with beta-thalassemia major. The remaining participants (26.5%) indicated that they were unable to decide what action they would take. There was no statistical significance difference between those who would continue or terminate the pregnancy in most of the demographic characteristics. However, 66.7% of women who had only received secondary education or below indicated they would terminate an affected fetus in contrast to 49.3% women with tertiary education or above ($P < 0.05$). Also, 75.6% of women with a previous history of termination of pregnancy would terminate a beta-thalassemia major affected fetus compared to 53.6% of women with no previous history ($P < 0.05$).

The median utility score was 0.4 (IQR: 0.05–0.55) for blindness and 0.5 (IQR: 0–0.65) for a beta-thalassemia major affected birth. The results of univariate analysis of relationship between subject characteristics and Utility scores are summarized in Table 2. The utility score for beta-thalassemia major affected birth was significantly higher in subjects with tertiary educational level or above and higher family income ($P < 0.05$). The utility score for beta-thalassemia major affected birth was significantly lower for subjects who indicated that they would terminate a pregnancy affected with beta-thalassemia major. Patients whose pregnancy was conceived via IVF procedures had a higher difference in utility score for a beta-thalassemia major affected birth and being blind compared to women who had conceived spontaneously ($P < 0.05$).

Table 2
Univariate analysis of relationship between subject characteristics and Utility scores.

Characteristics	Utility scores for blindness (IQR)	Utility scores for a beta thalassemia affected birth
Maternal age		
<35 (n = 221)	0.35 (0.05–0.55)	0.45 (0–0.6)
≥35 (n = 88)	0.4 (0–0.5)	0.5 (0–0.65)
Previous delivery		
No (n = 177)	0.4 (0.05–0.55)	0.5 (0–0.65)
Yes (n = 132)	0.35 (0–0.5)	0.4 (0–0.6)
Previous miscarriage		
No (n = 254)	0.4 (0.05–0.55)	0.5 (0–0.65)
Yes (n = 55)	0.4 (0–0.55)	0.45 (0–0.65)
Previous pregnancy termination		
No (n = 233)	0.4 (0.05–0.55)	0.5 (0–0.65)
Yes (n = 76)	0.3 (0–0.5)	0.45 (0–0.6)
Educational level		
<tertiary (n = 170)	0.35 (0–0.5)	0.43 (0–0.6)[b]
≥tertiary (n = 139)	0.4 (0.16–0.55)	0.5 (0.05–0.65)
Family income[a]		
<HK$50,000 (n = 249)	0.35 (0.03–0.55)	0.45 (0–0.6)[b]
≥ HK$50,000 (n = 60)	0.4 (0.16–0.5)	0.5 (0.3–0.7)
Will terminate if fetus diagnosed with Beta thalassemia major		
No (n = 42)	0.37 (0.2–0.5)	0.5 (0.43–0.7)[b]
Yes (n = 185)	0.35 (0–0.55)	0.45 (0–0.6)
Marital status		
Single (n = 23)	0.4 (0.15–0.6)	0.5 (0–0.5)
Married (n = 286)	0.37 (0.05–0.65)	0.45 (0–0.65)
Known thalassemia carrier		
No (n = 300)	0.4 (0.05–0.55)	0.5 (0–0.65)
Yes (n = 9)	0.4 (0.15–0.63)	0.3 (0–0.6)
IVF pregnancy		
No (n = 299)	0.4 (0.05–0.55)	0.45 (0–0.6)
Yes (n = 10)	0.33 (0–0.54)	0.73 (0.34–0.8)

[a] HKD 1 = USD 0.128.
[b] Denote $P < 0.05$ (Mann–Whitney *U* Test).

Discussion

At present, this is the only study that has assessed the acceptance of Chinese pregnant women on having a baby with beta-thalassemia major. We have previously reported the Chinese women's acceptance of having a child with Down syndrome using standard gamble metrics and found very low acceptance towards Down syndrome with a utility score of 0.2 [11]. Our current study indicated that Chinese women were ambivalent about their acceptance towards a child with beta-thalassemia major. The median utility score of 0.5 demonstrated that half of the participants were unable to decide when the choice is an equal chance of having a child with beta-thalassemia major or death. Only 59.9% women indicated that they would request termination of pregnancy if their fetuses were affected by beta-thalassemia major. About 14% of participants would keep the pregnancy if it is affected with beta-thalassemia major and one-third of participants were indecisive about their action at the time of interview. This was in contrast with our previous study on willingness to continue with a Down syndrome affected pregnancy [11]. More than 80% of participants in our earlier study on Down syndrome had already decided for termination of pregnancy during the interview solely based on hypothetical survey [11].

For individuals affected by beta thalassemia major, even though life-long medical treatment was required, intelligence was not affected and the individual could lead an independent life in adulthood. Prospective parents might thus find a child with beta-thalassemia major a less distressing life event compared to conditions that could lead to intellectual disability such as Down syndrome. With the advancement in iron chelation therapy and the possibility of definitive treatment such as hematopoietic stem cell transplantation, acceptance towards a pregnancy with fetal beta-thalassemia major might be further increased [13,14].

Acceptance towards beta-thalassemia major affected birth was lower amongst women with lower educational level and lower family income as shown by a lower utility score. Women with lower educational level also had a higher acceptance for termination of a fetus affected by beta-thalassemia major. In contrast, the acceptance of a beta-thalassemia major affected birth was higher for women who had conceived via an IVF procedure as demonstrated by a higher difference in utility score for an affected birth and being blind compared to women conceived spontaneously ($P < 0.05$). Significant differences in utility score for women with different educational level, family income or mode of pregnancy were not demonstrated in our previous study that assessed women's acceptance on having a Down syndrome affected birth [11]. Although qualitative studies are required to evaluate the underlying reason for women's choice, our findings suggest that women's acceptance towards having a child with severe medical condition but normal intelligence might be influenced by their social circumstances and financial ability to take care of a child with disability. While the acceptance towards having a child with Down syndrome that is associated with learning disability is generally low among Chinese population irrespective of their background.

In summary, our study demonstrated that Chinese pregnant women are ambivalent towards a child with beta-thalassemia major and their acceptance could be influenced by their socioeconomic backgrounds. Although Chinese pregnant women are generally considered to have a low tolerance to fetal anomalies, our findings suggested that their acceptance towards beta-thalassemia major might be dependent on their family capacity to take care of a child affected with medical illness only. The decision of pregnancy management could thus be largely affected by the content of the counseling after the diagnosis of fetal beta-thalassemia major. Treatment options for individuals with hematological illness are improving rapidly and Obstetricians generally have limited experience in managing children with beta-thalassemia major. We

recommend to offer parental counseling on the prognosis and management options for having an offspring with beta-thalassemia major by a Pediatric Hematologist in order to provide the most updated information for the couple to guide decision on pregnancy management.

A limitation of our study is that only a small percentage of participants were known to be carriers of thalassemia during the survey. Since the survey was performed during first trimester which is also the time for antenatal screening for thalassemia, many women in our cohort were uncertain about their thalassemia status at the time of survey and consider themselves as a possible silent carrier. Thus their response in the gambling scenario could still reflect the acceptance in the antenatal population. Another limitation in our study is that many women were not familiar with beta-thalassemia major and the management options. Although general information was given to respondents before the survey, women with low educational level might still have limited understanding on the disease particularly about the merits of curative treatment such as hemopoietic stem cell transplantation that may have influenced their acceptance towards the condition. Future study should be performed on beta-thalassemia couple to understand their acceptance and socioeconomic factors that influences their choices.

In conclusion, Chinese women were ambivalent towards giving birth to a baby with beta-thalassemia major. Women with higher educational level or higher family income have higher acceptance towards the condition.

Conflicts of interest statement

The authors have no conflicts of interest.

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