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CORRESPONDENCE

Inadequate Pre-conception Counseling is a Major Challenge for Antenatal Management of β-Thalassemia: Experience from a Referral Centre in India

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β-Thalassemia (β-thal) is a common autosomal recessive monogenic disorder caused due to mutations in the *HBB* gene. It is a major public health burden in India with the prevalence ranging from 1.5 to 4% [1–3]. The high prevalence calls for a robust system to manage β-thal in the prenatal stage. This study aimed at identifying the bottlenecks that encumber the prenatal genetic diagnosis of β-thal.

We analyzed the medical records of all the couples (n = 93) referred to the Department of Medical Genetics at Manipal Hospital, Bangalore, India, for prenatal diagnosis of β-thal during the period January 2014–June 2019. Complete sequencing of the *HBB* gene was offered to all the couples. Firstly, we analyzed the basis for referral (Fig. 1a). The major referral reason was the presence of β-thal offspring in the family (58.6% with one β-thal major offspring; 4.6% with two β-thal major offsprings). The second common referral reason was the hematological diagnosis of the β-thal trait in the couple (29.9%). Referral due to the presence of β-thal major in a first-degree relative was seen in a small fraction of patients (6.9%). Secondly, we analyzed the referral stage (Fig. 1b). Majority of the referrals were in the antenatal stage (92.6%), a small percentage in the preconception stage (7.4%), and none in the neonatal stage.

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The main findings of our analysis are: (1) presence of a β-thal offspring in the family was the most common reason for referral and (2) referrals were mostly in the antenatal stage.

Appreciation of the clinical indications is the major factor that influences the effectiveness of prenatal management of a genetic disorder. Referral due to the presence of β-thal affected offspring in the family was about two times higher than that due to the diagnosis of the β-thal trait in the couple (58.6 vs. 29.9%). Also, all the referrals were from obstetricians and none from pediatricians. The lower frequency of referral due to β-thal trait appears to underline inadequate parental screening. Microcytic hypochromic anemia in routine blood analysis is an indication for β-thal. However, this can be confounded by iron deficiency anemia which affects nearly half of the pregnant women in India [4]. Inadequate work-up of hypochromic microcytic anemia probably due to the cost of hemoglobin and ferritin tests may be responsible for fewer referrals. A recent study from Sri Lanka found that nearly a third of anemia during pregnancy was related to α and β-thal trait. Thus the suggestion for investigating the causes of anemia in women of childbearing age and during pregnancy in addition to providing universal iron supplementation [5]. Population screening, awareness building programmes and prenatal testing of β-thal began in India from around 1980 [1]. The lower frequency of referral due to β-thal trait indicates incomplete coverage of these programmes.

Appropriateness of the referral stage is another parameter that influences the effectiveness of prenatal management of a genetic disorder. Genetic analysis often requires longer turn-around-time. Clinicians appear to be unaware of this issue since the majority of the referrals were in the antenatal stage than in the preconception stage. From experience, most of the referrals were after 12 weeks of

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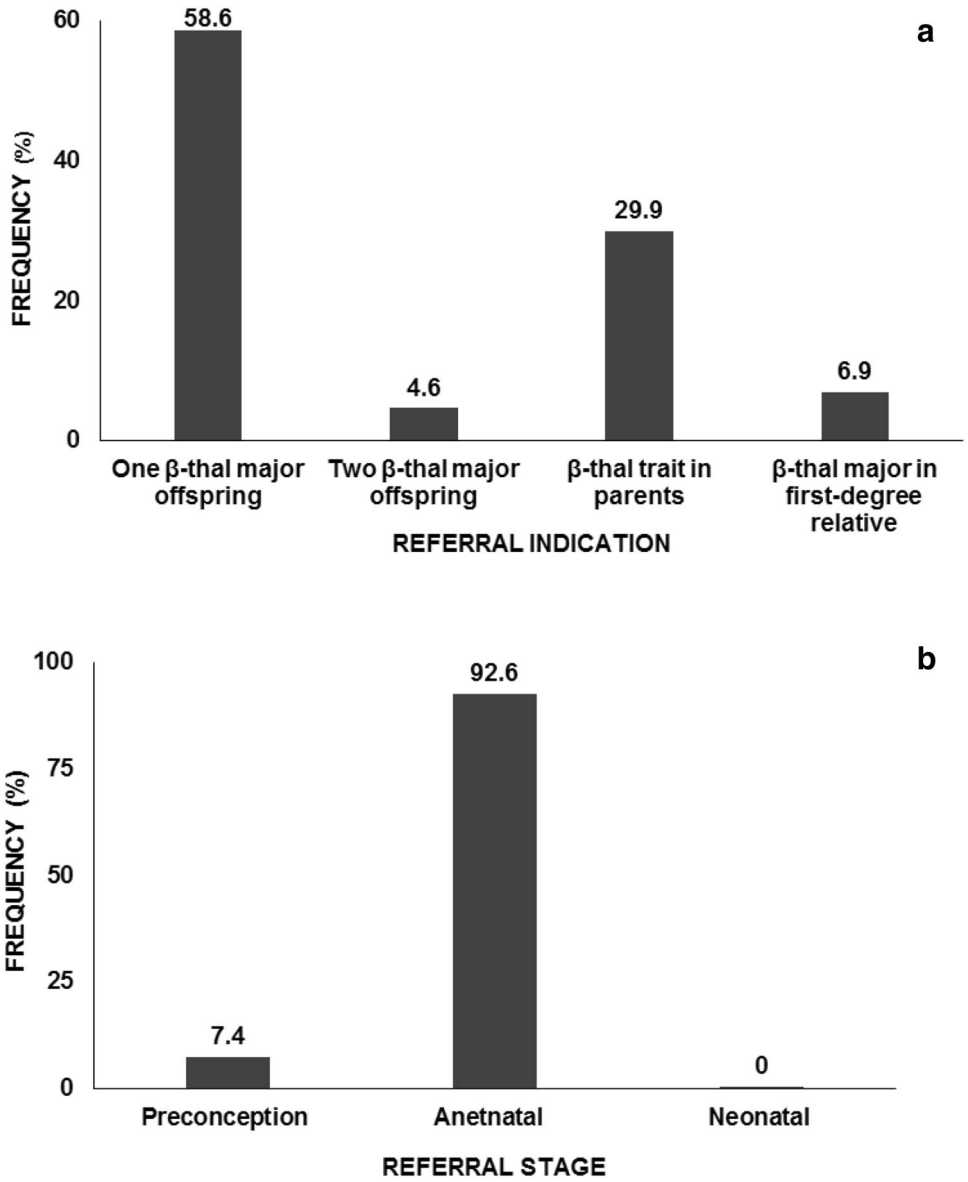

Fig. 1 Graphical representation of types and frequency of **a** referral indications and **b** referral stage

gestation. The referral timeline planning appears to be guided by the 12 weeks rule applicable to fetal sampling.

Our analysis shows that prenatal management of β-thal is mainly complicated by the lack of preconception and early antenatal screening. This warrants awareness-building programmes among clinicians on the implications of an affected child on the reproductive future of the parents and also the importance of early antenatal referral for genetic work-up.

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Compliance with Ethical Standards

Conflict of interest All authors declare that they have no conflict of interest.

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