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Original Research Article

Antenatal screening for thalassemia carrier at tertiary care centre

Sarita Kumari*, Princee Seth, Hanslata Gehlot

Department of Obstetrics and Gynecology, Dr. S. N. Medical College, Jodhpur, Rajasthan, India

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***Correspondence:**
Dr. Sarita Kumari,
E-mail: drsaritakumari89@gmail.com

ABSTRACT

Background: Thalassemia syndromes are the commonest genetic disorders of blood and constitute a vast public health problem with 2.78 to 4% prevalence in India. The most effective and feasible approach to reduce the incidence of thalassemia major is implementation of carrier screening program to screen the antenatal women in early pregnancy.
Methods: Institutional based cross sectional observational study was conducted. We screened 400 antenatal women by performing preliminary test red cell indices, Mentzer index and confirmatory test by high performance liquid chromatography. Husbands of positive women were also tested to find out couples on risk.
Results: Out of 400 antenatal women screened, 46 required HbA_2 estimation, and 11 (2.8%) were diagnosed as β-thalassemia minor positive. Most of thalassemia minor positive women were primigravida and mean (SD) age and gestational age of these women was 23.8 (3.1) years and 11.8 (1.7) weeks, respectively. Amongst thalassemia minor positive women most were mild to moderately anemic and these women had significantly greater mean TRBC count. Ninety one percent of thalassemia minor positive women had MCV<77. All of thalassemia minor positive women had MCH<27. Eighty two percent of thalassemia minor positive women had MI<13. None of couple at-risk was detected. So, prevalence of thalassemia carrier was 2.8%.
Conclusions: Thalassemia is a monogenetic disorder with autosomal recessive streak. Universal screening in antenatal window by complete blood counts, hematological indices (MCV, MCH, TRBC), Mentzer index and HPLC may lead to non-pyrrhic victory over this odious entity.

Keywords: Mentzer index, Thalassemia minor, Universal screening

INTRODUCTION

Thalassemia syndromes are widespread genetic disorders of the blood and pose a significant public health concern in many parts of the world. These disorders, characterized by decreased production of globin chains due to defective genes, result in microcytic anemia and various symptoms typically appearing within the first two years of life. Genetic screening plays a crucial role in mitigating these diseases by identifying individuals at high risk.[1]

Population carrier screening programs aim to identify asymptomatic carriers, enabling them to make informed decisions about reproductive risks and options. With approximately 1.5% of the global population carrying a thalassemia gene mutation, representing around 80 to 90 million individuals worldwide, the prevalence is particularly high in Africa, the Mediterranean, the Middle East, the Indian subcontinent, Southeast Asia, and China. However, changing immigration patterns have contributed to the disease's worldwide distribution.[2]

Each year, nearly 9 million thalassemia carrier women become pregnant, with 1.33 million at risk of giving birth to a child with thalassemia major. In India alone, 10,000 children are born with thalassemia annually, accounting for approximately 10% of the global incidence, and one in eight thalassemia carriers resides in India. Thalassemia-related hemoglobin disorders contribute to 3.4% of mortality in children under five years old worldwide. The prevalence of thalassemia carriers varies across populations, with studies reporting rates between 0% and

17%, and the mean prevalence of beta thalassemia in India ranging from 2.78% to 4%.[3]

Thalassemias are autosomal recessive conditions, meaning the disease manifests when both alleles of the responsible gene are affected. The two major types are alpha thalassemia and beta thalassemia, characterized by reduced production of alpha and beta globin chains, respectively. Beta thalassemia major, the severe form, is associated with life-threatening anemia, bone marrow and spleen enlargement, and potential organ damage if left untreated. Consanguineous marriages contribute to a higher carrier state prevalence in certain communities.[4]

Control of thalassemia in India faces challenges due to lack of awareness, social and cultural taboos, and family influences. Screening programs for beta thalassemia carriers have been available for some time, typically identified through reduced mean corpuscular volume and mean corpuscular hemoglobin levels in standard blood tests. Diagnosis involves identifying abnormal hemoglobin or elevated levels of HbA_2 for beta thalassemia carriers. High-performance liquid chromatography is commonly used for detection and quantitative estimation of hemoglobin variants.[5]

Initiating screening before marriage or during early pregnancy can play a crucial role in preventing thalassemia major. In India, where arranged marriages are common, antenatal clinics provide an opportune setting for screening and counselling as most pregnant women attend such checkups. Implementation of a carrier screening program, along with genetic counselling, prenatal diagnosis, and selective termination of affected fetuses, could effectively reduce the burden of thalassemia. This study aimed to investigate the prevalence of thalassemia carriers among antenatal women at the Umaid Hospital in Jodhpur, Western Rajasthan, and to provide counselling and education to couples based on the screening results. Although India lacks a national thalassemia control program, efforts such as this research can contribute to reducing the disease burden and incidence through proactive measures.[6]

METHODS

Study place

Institutional based study conducted in department of Obstetrics and Gynecology, Umaid Hospital, Dr S. N. Medical College, Jodhpur.

Study design

It was a cross sectional observational study.

Study duration

Study was conducted from March 2022 to December 2022.

Study population

Study population comprised of antenatal women registering in ANC clinic of Umaid Hospital, Jodhpur.

Inclusion criteria

Antenatal women up to 16 weeks were included.

Exclusion criteria

Patients already diagnosed with a hemoglobinopathy. Patients who had received blood transfusion in past 1 month.

Sample size

Sample size was calculated at 95% confidence interval to verify an expected 4% of thalassemia carriers among antenatal women reported by Madan et al and taking 2% absolute allowable error.[9] Sample size was calculated using the formula for sample size for estimation of proportion-

$$n = \frac{(Z_{1-\frac{a}{2}})^2 p(1-P)}{E^2}$$

Where,

$Z_{1\text{-}a/2}$ = Standard normal deviate for 95% confidence interval (taken as 1.96).

P = Expected proportion of thalassemia carriers among antenatal women (taken as 4% as reported by Madan et al).[9]

E = Absolute allowable error (taken as 2%).

Sample size was calculated to be minimum 368 antenatal women, which was rounded off to 400.

Methodology

All antenatal women up to 16 weeks of pregnancy were offered counselling for thalassemia screening. Counselling was done regarding method for screening thalassemia, reason for performing test, including social aspects, various tests available for antenatal diagnosis. Various medical and ethical issues involved with this was also discussed. Ethical committee approval was taken.

RESULTS

In Table 1, amongst total subjects 64 (16%) women had MCV<77 and 336 (84%) had MCV>77. MCV<77 was observed in 90.9% of thalassemia minor positive females and 13.9% of thalassemia minor negative females. On the contrary MCV>77 was observed in only 9.1% of thalassemia minor positive and 86.1% of thalassemia

minor negative. Thalassemia minor females had significantly less mean MCV (67.09±5.76 fl) than thalassemia negative females mean MCV (mean MCV 82.87±8.48 fl).

Table 1: Distribution according to MCV cut off (<77).

	Thalassemia	N	Mean MCV	Std. deviation	T-value	P value
MCV	Positive	11	67.09	5.76	6.128	<0.001
	Negative	389	82.87	8.48		
			Thalassemia minor		**Total**	
			Positive	**Negative**		
MCV		<77	10	54	64	
			90.9%	13.9%	16.0%	
		≥77	1	335	336	
			9.1%	86.1%	84.0%	
Total			11	389	400	
			100.0%	100.0%	100.0%	

Table 2: Distribution according to MCH cut off (<27).

		Thalassemia minor		Total
		Positive	**Negative**	
MCH	<27	11	89	100
		100%	22.9%	25.0%
	≥27	0	300	300
		0.0%	77.1%	75.0%
Total		11	389	400
		100.0	100.0	100.0

In above table, amongst total subjects (400), 100 (25%) women had MCH<27 and 300 (75%) had MCH>27. In our study, among the thalassemia positive women all 11 (100%) had MCH<27 where as in thalassemia negative women only 22.9% had MCH<27 and remaining had MCH>27. Mean MCH in thalassemia minor positive female was (21.10±2.75 pg) and in thalassemia minor negative female was (27.13±3.69 pg).

Table 3: Distribution according to Mentzer.

		Thalassemia minor		Total
		Positive	**Negative**	
Mentzer index	<13	9	8	17
		81.8%	2.05%	4.25%
	>13	2	381	383
		18.2%	97.94%	95.75%
Total		11	389	400
		100.0%	100.0%	100.0%

In this table, amongst total subjects (400), 17 (4.25%) women had MI<13 and 383 (95.75%) had MI>13. In our study, among the thalassemia positive women 81.8% had MI<13 and 18.2% had MI>13. Where as in thalassemia negative women only 2.05% had MI<13 and remaining had MI>27. Mean MI in thalassemia minor positive female was (13.17±1.20) and in thalassemia minor negative female was (19.43±4.03).

Table 4: Distribution of preliminary screened according to HbA_2 cut off (≥3.5).

		Thalassemia minor		Total
		Positive	**Negative**	
HbA_2	>3.5	11	0	11
		100.0%	0.0%	23.9%
	<3.5	0	35	35
		0.0%	100.0%	76.1%
Total		11	35	46
		100.0%	100.0%	100.0%

In our study, on the basis of preliminary screening 46 females suspected for thalassemia minor were subjected to HbA_1 level, out of them 11 had HbA_2≥3.5 and rest 35 had HbA_2<3.5. Mean HbA_2 of thalassemia minor positive females was 4.8±1.23 while mean HbA_2 of thalassemia minor negative was 2.52±0.42.

Table 5: Distribution according to hemoglobin.

	Thalassemia minor		Total	Chi square	P value
HB	**Positive**	**Negative**			
<7	0	7	7	8.304	0.045
	0.0%	1.79%	1.79%		
7-9.9	5	57	62		
	45.45%	14.65%	15.5%		
10-10.9	2	77	79		
	18.1%	19.79%	19.75%		
>11	4	248	252		
	36.36%	63.75%	63%		
Total	11	389	400		
	100%	100%	100%		

Table 5 shows the distribution of thalassemia carriers based on hemoglobin levels. The chi-square test revealed a significant association (chi-square =8.304, p value

=0.045) between thalassemia status and different hemoglobin ranges.

Table 6: Prevalence of thalassemia in our study.

Total no. of subjects	Screened positive	Prevalence (%)
400	11	2.8

Table 6 displays the prevalence of thalassemia in the study population. Out of a total of 400 subjects, 11 individuals tested positive for thalassemia, resulting in a prevalence rate of 2.8%. These findings indicate a relatively low prevalence of thalassemia in the studied group.

DISCUSSION

In our study, we compared the findings with previous research conducted on thalassemia minor. Demonstrated the distribution of women based on their mean corpuscular volume (MCV).[7] Among the total subjects, 16% of women had MCV<77, while 84% had MCV>77. Notably, 90.9% of thalassemia minor positive females had MCV<77, whereas only 13.9% of thalassemia minor negative females fell in this category. Conversely, MCV>77 was observed in 9.1% of thalassemia minor positive females and 86.1% of thalassemia minor negative females.[8]

Thalassemia minor positive females exhibited a significantly lower mean MCV (67.09±5.76 fl) compared to thalassemia minor negative females (mean MCV 82.87±8.48 fl).

The distribution of women based on their mean corpuscular hemoglobin (MCH) values was depicted. Among the total subjects, 25% of women had MCH<27, while 75% had MCH>27. Interestingly, all thalassemia minor positive females (100%) had MCH<27, while only 22.9% of thalassemia minor negative females fell in this category. Thalassemia minor positive females displayed a mean MCH of 21.10±2.75 pg, while thalassemia minor negative females had a mean MCH of 27.13±3.69 pg.[9]

Also presented the distribution of women based on the Mentzer index (MI). Among the total subjects, 4.25% of women had MI<13, whereas 95.75% had MI>13. Thalassemia minor positive females showed a higher percentage (81.8%) of MI<13 compared to thalassemia minor negative females (2.05%). The mean MI in thalassemia minor positive females was 13.17±1.20, while in thalassemia minor negative females, it was 19.43±4.03.[10]

Examining the distribution of females suspected for thalassemia minor based on HbA_2 levels, our study revealed that out of the 46 females screened, 11 had $HbA_2 \geq 3.5$, indicating a positive result for thalassemia minor. The remaining 35 females had $HbA_2 < 3.5$. Thalassemia minor positive females exhibited a mean HbA_2 of 4.8±1.23, while thalassemia minor negative females had a mean HbA2 of 2.52±0.42.[11]

Furthermore, explored the distribution of thalassemia carriers based on their hemoglobin (HB) levels. The chi-square test demonstrated a significant association between thalassemia status and different hemoglobin ranges (chi-square =8.304, p value =0.045). The table provided the percentage of thalassemia minor positive and negative females in different HB ranges (<7, 7-9.9, 10-10.9, >11).[12]

CONCLUSION

Thalassemia, a hereditary disorder inherited in an autosomal recessive manner, can be effectively detected through universal screening during the antenatal period. Screening methods such as Complete Blood Counts, hematological indices (MCV, MCH, TRBC), Mentzer index, and high-performance liquid chromatography provide valuable tools in the battle against this challenging condition, offering hope for a successful outcome without sacrificing unnecessary resources.

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