http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v10i1.22

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Hematological profile of Beta Thalassemia Trait

Authors
Surya Dev Kumar Sah[1], Shanthala Devi AM[2]*
[1]St. John's Medical College and Hospital, Department of Transfusion Medicine and Immuno Hematology, Koramangala, Bengaluru, Karnataka 560034
[2]St. John's Medical College and Hospital, Department of Transfusion Medicine and Immuno Hematology, Koramangala, Bengaluru, Karnataka 560034
*Corresponding Author
Prof. Shanthala Devi A.M. MBBS, MD
Department of Transfusion Medicine and Immuno Hematology Koramangala, Bengaluru, Karnataka 560034

Abstract
Beta thalassemia trait is a heterozygous autosomal recessive form of beta thalassemia. Individual with beta thalassemia trait are clinically asymptomatic. The present study was retrospective in nature and was done over a period of five years from 2014-2018. In patients who have been diagnosed as beta thalassemia trait by HPLC, the Hb, RBC, PCV, MCV,MCH, MCHC, RDW(CV/SD), HPLC were correlated with patient history. Three discrimination index (Sir England and Fraser, Mentzer, Shine and Lal index) were used in this study and modified study criteria were calculated. Total 401 cases of Beta thalassemia trait were diagnosed by HPLC. Among various discrimination indices used, Shine and Lal(396 cases positive) showed highest sensitivity 98.75% followed by Dr. Mentzer (330 cases positive)82.29% and Sir England and Fraser(259 cases positive) 64.58%.When we have applied the modified study criteria (MCV <66fl, MCH<25pg and RBC count > 5million/mm^3)301 BTT cases were picked up out of 401 cases (sensitivity of 77.30%).Shine and Lal showed the highest sensitivity (98.75%)and that could be useful for screening the BTT efficiently. Modified study criteria (MSC) was applied, it has fairly good sensitivity 77.3% which is easily applicable as it does not involve any calculation. Application of discrimination indices in routine haematological practice of evaluating CBC and PBS leads to diagnosis of BTT cases which will considerably reduce the disease burden of Thalassemia major in the community.
Keywords: *Beta thalassemia minor, Red cell indices, Discrimination indices, High performance liquid chromatography, Peripheral blood smear.*

Introduction

Beta Thalassemia are a group of hereditary blood disorders characterized by anomalies in the synthesis of the Beta chain of Haemoglobin resulting in variable phenotype ranging from severe Anaemia to clinically Asymptomatic individuals. The Total annual incidence of symptomatic individuals is estimated at 1 in 100,000 throughout the world.[1]

The term Thalassemia is derived from the Greek, Thalassa (sea) and Heima (blood).

Beta Thalassemia includes 3 main forms:

Thalassemia Major, The Transfusion Dependent Form

Thalassemia Intermedia, who require Transfusion irregularly

Thalassemia Minor also called "Beta Thalassemia Carrier" or " Beta Thalassemia trait" or "Heterozygous Beta -Thalassemia", who are usually clinically Asymptomatic.[1]

Material and Method

The study was retrospective in nature and was done over a period of 5 years from 2014-2018. All

patients who have been diagnosed as beta thalassemia trait by HPLC. Hb, RBC, PCV, MCV,MCH, MCHC, RDW(CV/ SD), HPLC finding were correlated with patient history. Discrimination Indices were calculated.

The following discrimination Index were calculated.

a. Sir England and Fraser index [MCV-(5×Hb)-RBC-3.4] .
b. Mentzer index(MCV/RBC).
c. Shine and Lal index(MCV^2 ×MCH/100).
d. Modified study criteria (MSC) = MCV <66fl, MCH<25pg and RBC count > 5million /mm^3

Results

Data of 401 patients (211 Male and 190 Female) were collected. Out of 401 cases, 36 were≤10 years and 365 were > 10 years. Various discrimination Indices were applied. Using Shine and Lal index 396 were BTT and 5 were non BTT out of 401, it shows 98.75% sensitivity respectively. Similarly Dr. Mentzer index was applied, in which 330 were BTT and 71 were non BTT and the sensitivity is 82.29%. When we have applied Sr. England and Fraser index, it was found that 259 were BTT and 142 were non BTT and the sensitivity was 64.58%. Among all three indices Shine and Lal showed Highest sensitivity 98.75% followed by Dr. Mentzer 82.29% and Sr. England and Fraser 64.58%(Table 1).

In our previous study conducted in this hospital MCV <66fl, MCH<25pg and RBC count > 5million/mm^3 were applied and the ability to segregate the potential BTT cases were studied. This was called Modified study criteria (MSC). This criteria was applied in present study to examine its sensitivity. In the study period 2014-2018 using MSC picked up 310 out 401 cases of BTT with sensitivity of 77.30% .MSC had less sensitivity than shine & Lal and Mentzer index, but sensitivity is more than England & Fraser (Table 1).

Modified cut off and sensitivity

When the cut off value of Dr. Mentzer index was increased to <13.5, its sensitivity also increased to 86.28%(346/401), however when cut off value decreased to <12.45 and <12.5 its sensitivity also decreases to 80.04%(321/401) and 77.80% (312/401) respectively. Similarly When the cut off value of England & Fraser index was increased to <5.3 and <6.5, its sensitivity also increased to 80.54%(323/401) and 82.54%(331/401) -, however when cut off value decreased to ≤-1.39 its sensitivity also decreases to 56.85%(228/401) .Similarly when the cut off value of Shine and Lal index was increased or decreased to <1083, <1004, and ≤595 its sensitivity decreased to 95.78% (384/401), 92.51%(371/401) and 17.70% (71/401) respectively.

Table 1: Discrimination indices, Modified cut off & its sensitivity

RBC INDEX	Accepted Cut Off	BTT		NON BTT		Sensitivity %	Modified Cut Off	BTT	Sensitivity (%)
		True positive	%	False Negative	%				
Dr. Mentzer	<13	330/401	82.29%	71/401	17.70%	82.29%	<12.5	312/401	77.80%
							<12.45	321/401	80.04%
							<13.5	346/401	86.28%
England & Fraser	<0	259/401	64.58%	142/401	35.41%	64.58%	≤-1.39	228/401	56.85%
							<5.3	323/401	80.54%
							<6.5	331/401	82.54%
Shine & Lal	<1530	396/401	98.75%	5/401	1.25%	98.75%	≤595	71/401	17.70%
							<1004	371/401	92.51%
							<1083	384/401	95.78%
Modified study	RBC>5 million/ mm^3 MCV<66 fl MCH<25pg	310/401	77.30%	91/401	22.69%	77.30%			

Table 2: Comparison of Each Discrimination index with Different studies

Study	England & Fraser Sensitivity	Dr . Mentzer Sensitivity	Shine & Lal Sensitivity
Fakher [5](IN 2009) 323 CASES	71%	93%	100%
Aysel[6] (IN 2014) 290 CASES	66.2%	98.7%	100%
Mehdi [7](IN 2015) 504 CASES		75.7%	87.6%
Sanjay [8](IN 2016) 225 CASES	61.1%	94.4%	100%
Saud.M[9](in 2007) 153 cases	100%	74.4%	97.8%
Nikitha T [10](in 2015) 848 cases	43.78%	90%	100%
Sirdah Mahmoud [11] (in2018)800 cases	97.53%	83.75%	50.96%
Present study 401 Cases	64.58%	82.29%	98.75%

Discussion

Beta thalassemia is the commonest inherited hemoglobinopathy. Prevalence of beta thalassemia trait (BTT) varies from 1.0% -14.9% in various region of India. The classical heterozygote carriers of BTT is usually asymptomatic.[2] The diagnosis is made through evaluation of positive family history or during population screening.[3]Through family history of thalassemia is important, a significant number of patients do not have previously affected family member[4]. Given the seriousness of homozygous □- thalassemia, correct identification of BTT is important to enable family screening & genetic counselling.[2]

The aim of this study was to evaluate the sensitivity of various cost effective screening tools like discrimination indices and modified study criteria of RBC indices of □ thalassemia trait before subjecting the suspected microcytosis cases for an expensive technique like HPLC and estimation of HbA, HbA_2 & HbF which is confirmatory.

Many cases were asymptomatic (40%) and were diagnosed during family screening or routine Peripheral smear (PBS) examination. Symptomatic individuals also presented for other illness like jaundice, tuberculosis etc and were picked up during PBS examination. This is indicative of the role played by routine haematological examination in presumptive diagnosis of BTT.

In the present study an algorithm was used to segregate cases of BTT from non BTT by simple, cost effective screening test. Therefore the use of red cell indices in the form of discrimination indices were used. Sensitivity of Shine & Lal was highest (98.75%) followed by Mentzer (82.29%). England &Fraser (64.58%) which is similar to the findings of different studies listed below (Table 2)

In the previous study conducted by Fakher (323 cases), Aysel (290 cases), Sanjay (225 cases) and Nikitha T (848 cases) and they have also applied Shine and Lal Discrimination Indices and reported that its sensitivity was 100% which is very close to our result. When Dr Mentzer indices was used by the authors mentioned in the table 2, the sensitivity was higher than what we have found in our present study, except Mehdi (504 cases) and Saud M (153) and the results are shown in table 2. Similarly comparison of Sr. England and Fraser index with all comparison groups ,all have highest sensitivity than present study except Sanjay 225 cases(61.1%) and Nikitha T 848 cases (43.78%) which is less sensitivity than present study (64.58%).

Conclusion

The haematological parameters of Beta thalassemia traits were analysed in the 5yr period from 2014 to 2018 in St Johns Medical College Hospital. A total of 401 cases were diagnosed in this period. The haematological parameters showed a low normal or mildly decreased Hb, increased RBC count and low MCV and MCH. Mean Hb was 10.92gm/dl, mean RBC count was 5.67 million/mm^3, mean MCV was 61.85fl, mean MCH was19.85pg. The various discrimination indices were applied to ascertain their sensitivity. The Mentzer index, England and Fraser index and Shine and Lal index were applied. The Shine and Lal index had the highest sensitivity of 98.75%. Modified study criteria (MSC) of RBC count > 5million /mm^3, MCV< 66fl and MCH< 25 pg was applied to evaluate the sensitivity. It had fairly good sensitivity of 77.3% which is easily applicable as it does not involve any calculation. Application of discrimination indices in routine haematological practice of evaluating CBC and PBS leads to diagnosis of BTT cases which will considerably reduce the disease burden of Thalassemia major in the community.

Acknowledgement

The author would like to acknowledge St. John's Medical College and Hospital for providing the facilities for the research work.

References

1. Danjou F, Anni F, Galanello R. Beta-thalassemia: from genotype to phenotype. Hematological 2011; 96(11): 1573–1575.
2. Madan N, Meera S, Satendra S , et al. Red cell indices and discrimination function in the detection of □- thalassemia trait in a population with high prevalence of iron deficiency Anemia. Indian j patholmicrobiol 1999;42(1):55-61.
3. Caterina B, Galanello R. Thalassemia and related disorder : quantitative disorder of haemoglobin synthesis. John Gree(editor). Wintrobes clinical hematology, 11thedn, Lippincott Williams and wilkins, 2004;1319-1366.
4. Louise L, sylivia TS. Thalassemia currents approach to an old disease pediatrclin N Am 2002; 49:1165-1191.
5. Fakher Rahim, Bijan Keikhaei. Better differential diagnosis of iron deficiency anemia from beta-thalassemia trait. Research Center of Thalassemia & Hemoglobinopathies. Turk J Hematol 2009; 26: 138-45 .
6. Aysel, Gamze, Ay Gegul, et al. Hematological Indices for Differential Diagnosis of Beta Thalassemia Trait and Iron Deficiency Anemia. Hindawi Publishing Corporation Anemia Volume 2014; Article ID 576738, 7 pages http://dx.doi.org/10.1155/2014/576738 .
7. Mehdi, Elahe, Beth. Reliability of Different RBC indices and Formulas in discriminating between □-Thalassemia minor and other Microcytic Hypochromic cases.Mediterr J Hematol Infect Dis www.mjhid.org 2015; 7: Open Journal System .
8. Sanjay P, Manas, Rahul ,et al. Evaluation of Various Discrimination Indices in Differentiating Iron Deficiency Anemia and Beta Thalassemia Trait: A Practical Low Cost Solution. Annals of Pathology and Laboratory Medicine. December 2016 ;Vol. 03, No. 06.
9. Suad M, AI Fadhli, Anwar M,AL-A wadhi, et al. Validity Assessment of Nine Discrimination Function Used for the Differentiation between Iron deficiency Anemia & Thalassemia minor: Oxford University press.13 Dec 2006; vol 53,no2,93-97.
10. Nikita Tripathi, Jai Prakash, Pranavkumar, Manish Verma. Role of Haemogram parameters & RBC indices in Screening & Diagnosis of beta thalassemia trait in microcytic, Hypochromic Indian children:

international journal of Hematological Disorders;2015, vol2,no2,43-46.

11. Mohmoudsirdah, Khaled Al Mghari,Ali H, Abuzaid, et al. Should sex differences be considered when applying mathematical indices & formulas for discriminating beta thalassemia minor from iron deficiency: practial