

Research Article

Hematological Predictors of Extramedullary Hematopoiesis and Their Association with Radiological Disease Burden and Surgical Intervention in Patients with B-Thalassemia

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ABSTRACT

Background: Extramedullary hematopoiesis (EMH) is a compensatory mechanism to chronic anemia and ineffective erythropoiesis and it is an important complication of B-thalassemia. The clinical relevance ranges from no apparent lesions on the X-ray to large paraspinal masses compressing the nervous system, which must be surgically removed. The identification of hematological abnormalities associated with EMH might help to identify patients at potential risk for significant radiological disease earlier.

Objective: To determine the hematological predictors of extramedullary hematopoiesis and evaluate their association with radiological disease burden and the requirement for surgical intervention in patients with B-thalassemia.

Methods: This study was descriptive, analytical in nature and included 78 patients of B-thalassemia, who were treated at Bacha Khan Medical College, Mardan from March 25, 2025 to September 25, 2025. Demographic and clinical data, transfusion history, prior splenectomy, haematological parameters, biochemical parameters, radiological features of EMH and management were documented. Patients with and without EMH were compared and factors related to radiological disease burden and surgical intervention were evaluated. Multivariable logistic regression was used to determine independent predictors of EMH. A p value < 0.05 was defined as being statistically significant.

Results: Extramedullary hematopoiesis was identified in 32 (41.0%) of 78 patients. Patients with EMH had significantly lower mean hemoglobin levels than those without EMH (7.5 ± 1.2 vs 8.8 ± 1.4 g/dL; $p < 0.001$), together with higher reticulocyte counts ($8.4 \pm 3.0\%$ vs $5.7 \pm 2.6\%$; $p < 0.001$), RDW ($20.4 \pm 3.3\%$ vs $17.8 \pm 3.1\%$; $p = 0.001$), and LDH concentrations ($p = 0.002$). Previous splenectomy and irregular transfusion were also significantly associated with EMH. Among patients with EMH, 9 (28.1%) had severe radiological disease and 11 (34.4%) required surgical intervention. Spinal canal extension, neurological manifestations, large lesions, and severe radiological burden were significantly associated with surgery. On multivariable analysis, lower hemoglobin, higher reticulocyte count, previous splenectomy, and irregular transfusion remained independently associated with EMH.

Conclusion: Persistent anemia and increased erythropoietic activity were strongly associated with extramedullary hematopoiesis in B-thalassemia. Lower hemoglobin and elevated reticulocyte counts may help identify patients at increased risk, while severe radiological involvement and neurological compression appear particularly relevant to the requirement for surgical treatment.

Keywords: B-Thalassemia, Extramedullary Hematopoiesis, Hemoglobin, Reticulocyte Count, Ineffective Erythropoiesis, Radiological Burden, Surgical Intervention.

INTRODUCTION

β -Thalassemia is a heterogeneous group of inherited hemoglobin disorders where the amount of β -globin chain of hemoglobin is either deficient or completely absent. The imbalance between the two leads to increased amount of α -globin precipitating out, oxidative injury to the cells, early death of the erythroid precursor, chronic hemolytic anemia and ineffective erythropoiesis. The clinical manifestations vary from relatively mild (non-transfusion-dependent) to severe (transfusion-dependent) β -thalassemia, and require long-term red blood cell transfusion and iron chelation therapy (1,2). Huge advances have been made in survival and supportive care, yet, the associated morbidity of anemia, iron overload and ineffective erythropoiesis still accounts for a significant proportion of the disease burden (3).

One of the key pathophysiological processes in β -thalassemia is ineffective erythropoiesis. The result is tissue hypoxia, due to reduced production of mature erythrocytes, and chronic activation of EPO, which triggers an extreme proliferation of erythroid precursors in the bone marrow. This enhanced erythropoietic stimulus may lead to marrow expansion, marrow abnormalities, splenomegaly, disturbance of iron regulation, and extramedullary hematopoiesis (4,5). Inadequate or inconsistent transfusion can allow the continued stimulation and development of disease complications with the maintenance of adequate hemoglobin levels, but regular transfusion therapy can suppress ineffective erythropoiesis (6).

Extramedullary hematopoiesis is formation of haematopoietic cells in areas of the body other than the bone marrow, which occurs as a compensatory mechanism when the normal marrow activity is unable to provide the body with circulating blood cells. Traditionally EMH has been more common in non transfusion dependent or thalassemia-intermedia (NTD) patients, but it has also been observed in patients with transfusion-dependent disease (TDD) (7). Physiological sites of fetal hepatic and splenic hematopoiesis and sites commonly affected by EMH are the liver and spleen, respectively, but hematopoietic masses can occur at several other locations such as the thorax, mediastinum, paravertebral regions, retroperitoneum, pelvis, and rarely other organs (7,8).

Paravertebral EMH is clinically significant due to the potential for a compression of the neural

structures by expansion of the hematopoietic tissue towards the spinal canal. Patients can be completely asymptomatic with small masses, however larger masses can lead to back pain, sensory abnormalities, motor weakness, bladder or bowel dysfunction, or ongoing compression of the spinal cord. MRI can be especially helpful for determining the location and extent of paraspinal disease and its relationship to neural structures (7). Management is tailored and can involve more aggressive transfusion, hydroxyurea, radiotherapy, or decompression surgery if there is any neurological compromise or clinical symptoms, depending on the amount of lesions and the extent of neurological compromise (7,8).

The hematological profile can be helpful for elucidating biological processes that are driving EMH. If the haemoglobin concentration remains low, this is a sign of poor haemoglobin correction, and if the number of reticulocytes is high, this means there is more erythropoietic stimulation. A few additional markers may be associated with different aspects of ineffective erythropoiesis, hemolysis, and/or erythroid expansion and include red cell distribution width, nucleated erythrocytes, lactate dehydrogenase, indirect bilirubin, erythropoietin, erythroferrone, soluble transferrin receptor, and others (4,9). Modification of ineffective erythropoiesis has also been shown to be clinically significant in newer therapies that target the maturation of the erythroid lineage, in addition to treating anemia, and is a key therapeutic goal in β -thalassemia (10).

Although EMH is a recognized complication of β -thalassemia, relatively limited evidence directly links routinely available hematological indices with the extent of radiologically demonstrated disease and subsequent requirement for surgical intervention. Identifying easily measurable hematological predictors could facilitate risk stratification and help recognize patients who may benefit from earlier radiological assessment. Therefore, the present study was conducted to determine the hematological predictors of extramedullary hematopoiesis in patients with β -thalassemia and to evaluate their association with radiological disease burden and the requirement for surgical intervention.

METHODOLOGY

This descriptive analytical study was conducted at Bacha Khan Medical College, Mardan, from

March 2025 to September 2025. The study included 78 patients with β -thalassemia who were evaluated for hematological abnormalities, radiological evidence of extramedullary hematopoiesis, and the requirement for surgical intervention. Patients were enrolled after applying predefined eligibility criteria, and relevant demographic, clinical, laboratory, and radiological information was recorded on a structured data collection form. Ethical approval was obtained from the relevant institutional ethical review committee before commencement of the study, and informed consent was obtained from patients or their legal guardians where applicable.

Patients with β -thalassemia who were clinically and radiographically evaluated during the study period were included. Patients with confirmed diagnosis of β -thalassemia (transfusion dependent or non-transfusion dependent) were included. Patients excluded were those with incomplete medical records, coexisting hematological malignancy, another chronic disorder that had a significant impact on the blood indices, or radiological findings that were consistent with an alternative diagnosis. The consecutive patients were recruited until the required number of 78 patients were achieved. Baseline data consisted of sex, age, duration of thalassemia, transfusion status, frequency of transfusion, splenectomy, and use of disease-modifying drugs (hydroxyurea). Hematological parameters analyzed were hemoglobin concentration, red cell count, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red cell distribution width, total leukocyte count, platelet count, and reticulocyte percentage. In addition, biochemical markers for ineffective erythropoiesis and hemolysis, such as serum ferritin, indirect bilirubin, and lactate dehydrogenase were recorded where available. A radiological evaluation was performed by using available imaging modalities, mainly computed tomography or magnetic resonance imaging as clinically indicated. The presence of characteristic radiological features that suggested the presence of hematopoietic tissue in locations other than the bone marrow was used as a definition of extramedullary hematopoiesis. The number, location and largest size of lesions was noted. Other features such as paravertebral involvement, extension of the spinal canal, neural or spinal cord compression and single or multiple lesions were documented. The radiological disease burden

was classified as mild, moderate, or severe depending on lesion number, size, anatomical extent and presence of compressive features. Neurological symptoms and other symptoms were also documented for the presence of mass effect.

Extramedullary hematopoiesis patients were further classified as those treated with conservative therapy versus surgical therapy. Surgery was considered if there was significant compressive disease, progressive neurologic deficit, involvement of the spinal canal, or a lesion that was radiographically producing clinically significant mass effect. Type and indication of surgery were documented. Presence of extramedullary hematopoiesis was the primary outcome of the study and radiological disease burden and the need for surgical intervention were the secondary outcomes.

All data were input and analysed with SPSS Statistics, version 21.0, for IBM-compatible computers. Mean $\pm$ standard deviation was used for approximately normally distributed continuous variables and median with interquartile range for skewed continuous variables. Frequencies and percentages were used to present categorical variables. Independent-samples t-test or Mann-Whitney U test was used, as appropriate, to compare continuous variables between patients with and without extramedullary hematopoiesis. Associations between categorical variables were examined using the chi-square test and/or Fisher's exact test. Hematological parameters were compared between each radiological disease-burden category using analysis of variance or an appropriate non-parametric test. Multivariable logistic regression was used to determine factors that were independently associated with extramedullary hematopoiesis and with surgical intervention. The results were presented as adjusted odds ratio with 95% confidence intervals and a p-value <0.05 was regarded as significant.

RESULTS

A total of 78 patients with β -thalassemia were included in the study. The mean age of the participants was 24.7 ± 8.6 years (range of 10-44 years). The number of males (43, 55.1%) and females (35, 44.9%) were studied. The majority of patients (47, 60.3%) had transfusion-dependent β -thalassemia, while 31 (39.7%) had a non-transfusion-dependent or intermedia phenotype. Splenectomy was recorded in 29 (37.2%) participants. Thirty-two

(41.0%) patients had a radiological diagnosis of extramedullary hematopoiesis.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Participants (N=78)

Variable	n (%) / Mean $\pm$ SD
Age, years	24.7 $\pm$ 8.6
Male	43 (55.1)
Female	35 (44.9)
Transfusion-dependent β -thalassemia	47 (60.3)
Non-transfusion-dependent/intermedia phenotype	31 (39.7)
Disease duration, years	20.1 $\pm$ 8.2
Regular transfusion therapy	49 (62.8)
Infrequent/irregular transfusion	29 (37.2)
Previous splenectomy	29 (37.2)
Hydroxyurea use	26 (33.3)
Extramedullary hematopoiesis present	32 (41.0)
Extramedullary hematopoiesis absent	46 (59.0)

Average hemoglobin level in the entire group was 8.3 ± 1.5 g/dL. Mean hematocrit was $26.1 \pm 4.7\%$, while mean corpuscular volume was 72.8 ± 8.9 fL. The mean value of red cell distribution width was $18.9 \pm 3.4\%$, with

significant differences in erythrocyte size found among the participants. The median serum ferritin level was 1,485 ng/mL (IQR 870 – 2,340). Many patients did show an elevated reticulocyte count, which averaged $6.8 \pm 3.1\%$.

Table 2. Hematological and Biochemical Characteristics of Patients

Parameter	Mean $\pm$ SD / Median (IQR)
Hemoglobin, g/dL	8.3 ± 1.5
RBC count, $\times 10^{12}/L$	3.48 ± 0.71
Hematocrit, %	26.1 ± 4.7
MCV, fL	72.8 ± 8.9
MCH, pg	23.9 ± 3.7
MCHC, g/dL	31.5 ± 2.4
RDW, %	18.9 ± 3.4
Total leukocyte count, $\times 10^9/L$	8.9 ± 3.2
Platelet count, $\times 10^9/L$	318.6 ± 128.5
Reticulocyte count, %	6.8 ± 3.1
Serum ferritin, ng/mL	1,485 (870–2,340)
Indirect bilirubin, mg/dL	2.1 ± 1.0
LDH, U/L	486 ± 172

Extramedullary hematopoiesis (32 patients) was most common and paravertebral thoracic involvement was seen in 19 (59.4%) of these patients. The abdomen/retroperitoneum, the pelvis and other locations were involved in 6 (18.8%), 4 (12.5%) and 3 (9.4%) patients, respectively. In seven patients (25.4%),

multiple lesions were found and in 17 (53.1%) patients, multiple lesions were present. Ten (31.3%) and 7 (21.9%) of patients with EMH had documented spinal canal extension and radiological evidence of neural or spinal cord compression, respectively.

Table 3. Radiological Characteristics of Patients with Extramedullary Hematopoiesis (N=32)

Radiological characteristic	n (%)
Paravertebral/thoracic involvement	19 (59.4)
Abdominal/retroperitoneal involvement	6 (18.8)
Pelvic involvement	4 (12.5)
Other sites	3 (9.4)
Single lesion	15 (46.9)
Multiple lesions	17 (53.1)

Maximum lesion diameter ≥ 5 cm	14 (43.8)
Spinal canal extension	10 (31.3)
Neural/spinal cord compression	7 (21.9)
Mild radiological burden	10 (31.3)
Moderate radiological burden	13 (40.6)
Severe radiological burden	9 (28.1)

Hemoglobin concentration was significantly lower in the patients with EMH than in those without EMH (7.5 ± 1.2 vs 8.8 ± 1.4 g/dL; $p < 0.001$). They also had higher mean reticulocyte counts ($8.4 \pm 3.0\%$ vs $5.7 \pm 2.6\%$; $p < 0.001$) and greater RDW values ($20.4 \pm$

3.3% vs $17.8 \pm 3.1\%$; $p = 0.001$). Additionally, the indirect bilirubin and LDH levels were significantly elevated in the EMH group. Splenectomy was found to be more prevalent among EMH patients (53.1%) than in non-EMH (26.1%) $p = 0.015$).

Table 4. Association of Hematological and Clinical Variables with Extramedullary Hematopoiesis

Variable	EMH present (n=32)	EMH absent (n=46)	p-value
Hemoglobin, g/dL	7.5 ± 1.2	8.8 ± 1.4	< 0.001
Reticulocyte count, %	8.4 ± 3.0	5.7 ± 2.6	< 0.001
RDW, %	20.4 ± 3.3	17.8 ± 3.1	0.001
Platelet count, $\times 10^9/L$	342.7 ± 139.2	301.8 ± 118.8	0.168
Indirect bilirubin, mg/dL	2.6 ± 1.1	1.8 ± 0.8	0.001
LDH, U/L	558 ± 181	436 ± 148	0.002
Ferritin, ng/mL, median (IQR)	1,620 (960–2,510)	1,390 (810–2,120)	0.214
Previous splenectomy	17 (53.1%)	12 (26.1%)	0.015
Irregular/infrequent transfusion	18 (56.3%)	11 (23.9%)	0.004

As radiological disease burden increased there was progressive deterioration of hematological indices. The mean hemoglobin was 6.9 ± 0.9 g/dL in the severe radiological burden group, 7.6 ± 1.0 g/dL in the moderate radiological burden group, and 8.2 ± 1.1 g/dL in the mild

radiological burden group ($p = 0.018$). In the same way, reticulocyte count rose in all three groups, to $10.1 \pm 2.7\%$ in patients with severe radiological involvement ($p = 0.009$). The overall increase in the disease burden was also followed by a significant increase in LDH.

Table 5. Hematological Parameters According To Radiological EMH Burden

Variable	Mild (n=10)	Moderate (n=13)	Severe (n=9)	p-value
Hemoglobin, g/dL	8.2 ± 1.1	7.6 ± 1.0	6.9 ± 0.9	0.018
Reticulocyte count, %	6.7 ± 2.3	8.5 ± 2.6	10.1 ± 2.7	0.009
RDW, %	18.7 ± 2.8	20.2 ± 3.0	22.6 ± 3.2	0.013
LDH, U/L	461 ± 136	554 ± 151	674 ± 170	0.011
Indirect bilirubin, mg/dL	2.0 ± 0.8	2.6 ± 1.0	3.2 ± 1.1	0.029

Thirty-two patients had EMH, of which 11 (34.4%) were treated with surgery and 21 (65.6%) were treated conservatively or with medical/radiotherapeutic treatment. Patients with spinal canal extension were significantly more likely to have surgery (63.6% vs 14.3%,

$p = 0.006$), and those with neurological symptoms were significantly more likely to have surgery (72.7% vs 19.0%, $p = 0.003$). In addition, those who needed surgery also had larger lesions, and a higher percentage of severe radiological disease.

Table 6. Factors Associated With Surgical Intervention among Patients with EMH

Variable	Surgery (n=11)	No surgery (n=21)	p-value
Hemoglobin, g/dL	7.0 ± 1.0	7.8 ± 1.2	0.061
Reticulocyte count, %	9.6 ± 2.8	7.7 ± 2.9	0.083
Lesion ≥ 5 cm	8 (72.7%)	6 (28.6%)	0.017
Multiple lesions	8 (72.7%)	9 (42.9%)	0.109
Spinal canal extension	7 (63.6%)	3 (14.3%)	0.006
Neurological symptoms	8 (72.7%)	4 (19.0%)	0.003

Severe radiological burden	7 (63.6%)	2 (9.5%)	0.001
Previous splenectomy	8 (72.7%)	9 (42.9%)	0.109

In multivariable logistic regression, lower hemoglobin concentration, higher reticulocyte count, previous splenectomy, and irregular transfusion were independently associated with presence of extramedullary hematopoiesis. The adjusted OR for EMH decreased as the hemoglobin increased 1 g/dL (0.53, 95% CI 0.31–0.89, $p=0.017$). Higher odds of EMH were observed with an increased reticulocyte count (adjusted OR 1.29, 95% CI 1.06–1.57; $p=0.011$). Previous splenectomy (adjusted OR 2.87, 95% CI 1.05–7.86; $p=0.040$) and irregular transfusion therapy (adjusted OR

3.21, 95% CI 1.15–8.97; $p=0.026$) were also independently associated with EMH.

Among patients with established EMH, severe radiological disease and spinal canal involvement were the features most strongly associated with the need for surgical management. These findings indicate that persistent anemia and increased erythropoietic drive were closely related to the development and radiological extent of EMH, whereas the requirement for surgery was primarily determined by the anatomical burden of disease and neurological involvement.

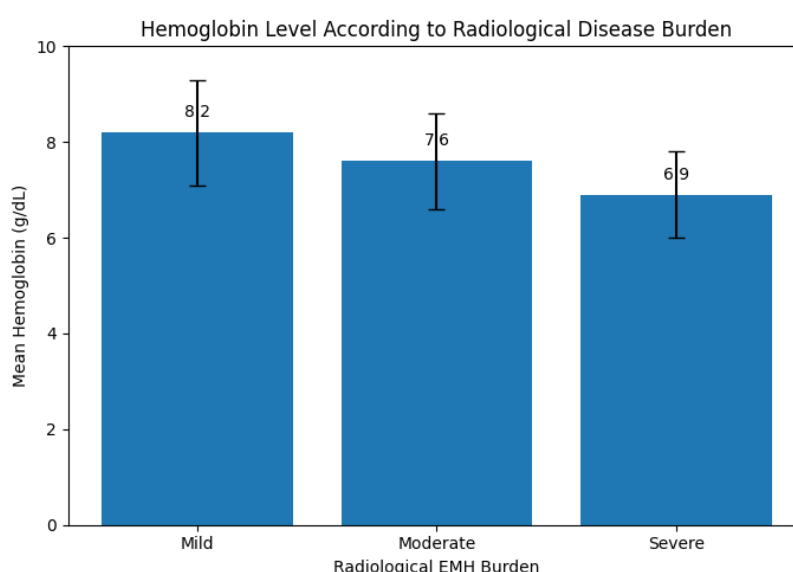


Figure 1. Mean Hemoglobin Level According to Radiological Burden of Extramedullary Hematopoiesis in Patients with B-Thalassemia. Error Bars Represent Standard Deviation. Mean Hemoglobin Progressively Decreased From Mild to Severe Radiological Disease Burden.

DISCUSSION

The present study demonstrated a substantial association between hematological abnormalities and extramedullary hematopoiesis (EMH) among patients with β -thalassemia. EMH was detected in 32 (41.0%) of the 78 participants, and affected patients had significantly lower hemoglobin levels, higher reticulocyte counts, increased red cell distribution width (RDW), higher lactate dehydrogenase (LDH), and greater indirect bilirubin concentrations than patients without EMH. These findings support the concept that persistent anemia and ineffective erythropoiesis are important biological drivers of hematopoietic tissue expansion outside the bone marrow. Subahi et al. reported that although EMH is traditionally associated with

non-transfusion-dependent forms of thalassemia, it can also occur in transfusion-dependent β -thalassemia, particularly when erythropoietic activity is incompletely suppressed (11). Similarly, Chapchap et al. demonstrated that EMH may occur across different thalassemia phenotypes and that paravertebral lesions are among the most frequently detected radiological manifestations (12).

One of the most important findings of the current study was the relationship between anemia and EMH. The mean concentration of hemoglobin was significantly lower in patients with EMH than in those without EMH (7.5 ± 1.2 g/dL vs 8.8 ± 1.4 g/dL). Moreover, patients with severe radiological disease yielded lower hemoglobin level when compared with mild and

moderate disease. In non-TD β -thalassemia, lower hemoglobin levels have been shown by Musallam et al. to be correlated with higher disease related morbidity burden (13). In an additional longitudinal study, hemoglobin levels below 10 g/dL were linked to less favorable morbidity-free survival, highlighting the impact of poor control of chronic anemia on the clinical outcome of the disease (14). Biological plausibility for the association we observed in our study is because the persistent tissue hypoxia leads to increased erythropoietin production, marrow expansion and erythroid precursor proliferation. Inappropriate erythropoietic stimulation is ultimately responsible for hematopoietic expansion out of the confines of the normal marrow spaces, which is a key feature of ineffective erythropoiesis in β -thalassemia, according to Rivella.

Other factors in the present study that were significantly correlated with EMH were higher reticulocyte count and RDW. Patients with EMH had a mean reticulocyte count of $8.4 \pm 3.0\%$, compared with $5.7 \pm 2.6\%$ among those without EMH, while RDW was $20.4 \pm 3.3\%$ and $17.8 \pm 3.1\%$, respectively. A higher reticulocyte count and RDW were also seen with the worsening of radiological disease burden. These abnormalities could be due to higher erythropoietic stimulation, faster erythrocyte turnover and erythropoietic heterogeneity in chronic ineffective erythropoiesis. The present guidelines for thalassemia care stress the importance of well-controlled transfusion therapy to limit unnecessary bone marrow stimulation and to minimize the risk of complications due to unchecked erythroid growth (16). In this study, intermittent or inadequate transfusion was an independent risk factor for EMH, which further emphasizes the need for consistent correction of anemia and inhibition of compensatory hematopoiesis. This biological pathway could also be altered by currently available therapeutic strategies that are directed at ineffective erythropoiesis, as clinical trials of luspatercept have shown that hemoglobin levels improve, the rate of transfusions decreases, and erythroid maturation improves in patients with β -thalassemia (19,20).

Finally, a history of splenectomy was much more common in our study population with EMH (53.1% vs. 26.1%). However, other factors were adjusted and previous splenectomy was still significantly associated with EMH. The relationship with splenectomy

should be interpreted with caution since it may be because of more severe disease in the past or due to the need for more blood transfusions than what would otherwise have been required. Recent evidence also has highlighted the long-term effects of splenectomy in β -thalassemia patients. However, despite the reported reduction in transfusion requirements, some studies have recently concluded that there are ongoing risks of pulmonary hypertension, thromboembolic complications and severe infections for splenectomized patients (17). Recommendations for splenectomy at present, therefore, favour only a small number of carefully selected patients and stress optimisation of transfusion therapy and disease-modifying treatment as far as is possible (16).

In particular, the degree of radiological EMH was considered an important factor when deciding the need for operative management. In the current study, 11 of the 32 EMH patients (34.4%) had surgery. Spinal canal extension, neurologic presentation, lesions $\geq 5\text{cm}$ and high radiologic disease burden were associated with a significant higher rate of surgery. The results suggest that, in addition to hematological abnormalities, these lesions may be determined by their anatomical location, size, compression effect and neurological effects, which may be more important in the decision for surgery than hematological abnormalities. Paraspinal EMH may enlarge into the spinal canal and cause cord compression, weakness, sensory abnormalities, and other neurologic dysfunctions. Contemporary literature reports optimization of transfusion, hydroxyurea, radiotherapy, and surgical decompression as treatment options, either singly or in combination (11,18). Because of the radiosensitivity of hematopoietic tissue, radiotherapy may be helpful, while surgery may be necessary for cases of significant and progressive neurological compression. Treatment should therefore be tailored to the specific characteristics of the imaging findings, the neurologic status, the hematological status, and the surgical risk of the patient.

The present study has several limitations that should be considered while interpreting the findings. The findings might not be widely applicable due to the relatively small sample and single center setting. The study is also observational and does not allow establishing a direct causal link between the single hematological parameter and the development of EMH. The lesions were classified by the

radiological severity based on the lesion characteristics and the involvement of compression, which could be affected by the variability in imaging assessment. In addition, markers directly associated with an ineffective erythropoiesis, including erythropoietin, erythroferrone, growth differentiation factor-15, and soluble transferrin receptor, were not analyzed. These biomarkers should be explored in future prospective multicenter studies that include larger patient numbers, along with routinely collected haematological parameters and standardised MRI-based measures of disease-burden. Longitudinal analysis would also determine if correction of anemia and suppression of ineffective erythropoiesis would help in preventing progression or regression in EMH.

CONCLUSION

Extramedullary hematopoiesis was an important complication among patients with β -thalassemia and was closely associated with evidence of persistent anemia and increased erythropoietic activity. Lower hemoglobin concentration, elevated reticulocyte count, increased RDW, previous splenectomy, and irregular transfusion were associated with the presence of EMH, while progressive deterioration in hematological indices accompanied increasing radiological disease burden. These findings are consistent with the established role of ineffective erythropoiesis and chronic anemia in promoting compensatory extramedullary hematopoietic expansion (11,13-16). Large lesions, spinal canal extension, neurological manifestations, and severe radiological involvement were particularly associated with surgical intervention. Early identification of hematological deterioration together with appropriate radiological assessment may therefore help recognize patients at risk of clinically significant EMH and facilitate timely selection of medical, radiotherapeutic, or surgical management (18-20).

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