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Evaluation of Growth Characteristics and Contributing Factors in Individuals with β-Thalassemia Major

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Abstract

Background: Growth problems are prevalent in children with β-thalassemia major and stem from a combination of various underlying causes. This study looked at height and weight status and what factors were linked to them in children with β-thalassemia major.

Methods: This was a cross-sectional study done with 80 children who have β-thalassemia major in Jiroft in 2024. We gathered information from their medical files using a checklist we created ourselves. It covered basic details about the children, their height and weight measurements, and serum ferritin levels. We used National Center for Health Statistics (NCHS) growth charts to evaluate the growth parameters. All analysis was done in SPSS version 22 with descriptive statistics and the right inferential tests; we took $p < 0.05$ as significant.

Results: The mean age of the participants was 12.1 ± 3.4 years. Overall, 78.7% of the children had a height-for-age below the 50th percentile, including 40.0% below the 5th percentile. Similarly, 87.6% had a weight-for-age below the 50th percentile, including 30.0% below the 5th percentile. Growth disorder was significantly associated with age (P = 0.006), whereas no statistically significant association was observed with sex (P = 0.246). Serum ferritin levels were ≥1,000 µg/L in 95.0% of the participants. Although the mean serum ferritin level was higher among children with growth disorder than among those without growth disorder, the difference was not statistically significant (P = 0.551).

Discussion: These results indicate a high rate of growth failure that worsens as the children get older. This likely reflects the cumulative effects of the disease and/or its treatment over time.

Conclusion: Growth impairment is highly prevalent among children with β-thalassemia major in Jiroft and becomes increasingly pronounced with age. Early and regular assessments, together with comprehensive management approaches, are essential to minimize potential long-term growth-related complications.

Keywords: Beta-Thalassemia, Growth Disorders, Child Development, Iron Overload, Ferritins.

1. Introduction

Approximately 5% of people worldwide have some kind of hemoglobin disorder, and thalassemia carriers account for about 1.7% of that group. It affects boys and girls equally, with roughly 4.4 new cases of

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thalassemia major occurring per 10,000 live births (1-3). Children and adults with thalassemia typically experience long-term severe anemia, impaired growth, enlarged liver and spleen, and bone changes—especially in the face and skull—that can significantly alter physical appearance (4-6). In Iran, the Thalassemia Association reports about 18,616 people living with thalassemia at present. The highest numbers are observed in Mazandaran and Fars provinces (7-10). In Mazandaran, nearly 2,500 patients are receiving regular care and treatment, and both official records and additional reports suggest the carrier rate for beta-thalassemia there is over 10% (11). Even with prevention programs and treatment efforts in place, new cases continue occurring in children and teenagers. That shows thalassemia continues to be a major public health issue requiring sustained attention (12)

. At the molecular level, thalassemia basically happens because the body makes much less of one globin chain—either alpha or beta—which throws off the balance between the two. That imbalance leads to extra unpaired globin chains piling up inside red blood cells, and that's really the starting point for a lot of the problems patients end up with (13, 14). One of the biggest and most common issues is iron overload, which plays a huge part in damaging organs over time (15-17). Iron builds up mostly because of three things: ineffective red blood cell production (ineffective erythropoiesis), all the repeated blood transfusions these patients need, and increased iron absorption from food in the gut—something that happens because of the ongoing anemia (18-20). Once transferrin—the main protein that carries iron in the blood—gets fully saturated, free iron starts floating around in the circulation and builds up in tissues. That free iron triggers the formation of very reactive oxygen species, like hydroxyl radicals. Those radicals cause oxidative stress, attacking lipids, proteins, and DNA, and basically messing up how cells normally work (21-23).

Cardiac issues are the main killer in thalassemia patients—over half of all deaths related to the disease come from heart problems (24, 25). Most of it stems from iron depositing in the heart muscle and the heart having to pump extra hard for years because of the anemia. The iron damages the heart directly, causing poor ventricular function. Then, the long-term extra workload leads to pulmonary hypertension and eventually right heart failure (26, 27). On top of heart problems, these patients often develop a tendency for blood to clot more easily (hypercoagulable state). This happens from ongoing red cell breakdown (chronic hemolysis), platelets getting activated, damaged blood vessel linings, and changes in clotting factors. All that puts them at higher risk for clots and thromboembolic events (28, 29). Repeated transfusions over the long term bring other risks too, like viral infections (hepatitis used to be common), but hepatitis B vaccination has really brought those numbers way down in recent years (30). Bone problems show up in almost every patient—osteoporosis is especially common. It leads to pain, fractures, and a much lower quality of life (31). The causes are mixed: hormone imbalances, poor nutrition, iron overload, bone marrow expanding from extra blood cell production, and lower bone density—particularly in the spine and hips during the growth years of puberty (32, 33). Another big transfusion-related issue is alloimmunization. Repeated blood transfusions can lead to alloimmunization, in which the recipient develops antibodies against minor red blood cell (RBC) antigens. These alloantibodies can cause delayed hemolytic transfusion reactions, complicate the identification of compatible blood for subsequent transfusions, and contribute to ongoing hemolysis, anemia, jaundice, and fatigue (34, 35). Endocrine problems are quite common in thalassemia too, and most of them come from iron building up in the endocrine glands—especially the anterior pituitary. Hypogonadism is by far the most frequent one, affecting over 70% of patients. It often leads to delayed puberty, trouble with fertility later on, and contributes to poor growth. Other endocrine issues that show up include hypothyroidism, hypoparathyroidism, diabetes, and problems with bone formation. The good news is that many of these can be partly or even fully fixed if caught early and treated properly (36, 37). Medical care has advanced considerably—better transfusion schedules, improved iron chelation drugs, and bone marrow transplants have significantly helped patients live longer and enjoy a better quality of life. Still, growth impairment remains one of the major ongoing concerns. It does not result from a single cause—it usually reflects a combination of chronic anemia, hypersplenism, iron overload, endocrine disturbances, micronutrient deficiencies (such as zinc deficiency), and sometimes adverse effects of chelation therapy. Regular monitoring of height and weight provides a useful indication of the patient's overall health status and whether the treatment plan is effective. Therefore, we conducted this study to examine height and weight in children with thalassemia major in Jiroft city. Our goal is to add some useful information about growth patterns and clinical outcomes in this group of kids who are particularly at risk.

2. Methods

Study Design, Population and Sampling

This descriptive-analytical cross-sectional study was conducted in Jiroft, Iran, during 2024. The study

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population consisted of patients with a confirmed diagnosis of transfusion-dependent β-thalassemia major who were registered and receiving regular care in Jiroft during the study period. Participants were identified from the available patient records and were included if they met the predefined eligibility criteria and had sufficient clinical, anthropometric, and laboratory information for the variables evaluated in the study. A total of 80 eligible participants were included in the final analysis. The study sample therefore represented the eligible patients available in the study setting during the defined study period. Because the study was based on the available eligible population and medical records during the study period, an a priori sample size calculation was not performed. All available eligible participants who met the study criteria and had sufficient data for the required analyses were included. In this study, the term "β-thalassemia major" refers to transfusion-dependent β-thalassemia requiring regular blood transfusion therapy.

Inclusion and Exclusion Criteria

Participants were selected based on explicit criteria derived from patient records, including a confirmed diagnosis of thalassemia major as documented in medical files, initiation of the first blood transfusion at or before the age of 2 years to reflect the early onset typical of the condition, and a history of receiving regular monthly blood transfusions prior to the study enrollment period to indicate ongoing management of the disease; additionally, implicit criteria based on the study design and data collection methods encompassed being a child aged approximately 6 months to 15 years, as inferred from reference ferritin values and the target population description of children with thalassemia major, residency in Jiroft city during the study period in 2024 to align with the defined study population, and availability of complete or sufficiently detailed patient records to allow extraction of required demographic information such as age, sex, height, and weight, along with paraclinical findings such as ferritin levels via the researcher-designed checklist for accurate and complete data extraction. We applied several practical exclusions during both sampling and data extraction to maintain a focused study population. We excluded patients who did not have a confirmed diagnosis of thalassemia major (including thalassemia minor or intermedia, since the study focused exclusively on major cases). We also excluded anyone outside the typical pediatric range—adults or infants younger than 6 months—because ferritin reference values change considerably in very young infants, and the emphasis was on children. Incomplete records were also excluded: if key information was missing—such as demographic details, height/weight measurements, or ferritin levels—and we could not obtain the missing information even after attempting to contact families using the phone numbers in the files, those cases were excluded. We limited the population to children actually living in Jiroft city during 2024, so anyone not residing there was excluded. Finally, we excluded any records showing non-compliance with transfusion requirements—such as irregular transfusions (not monthly) or first transfusion after age 2—which were inconsistent with our inclusion criteria.

Data Collection Tools and Procedures

We collected all the data straight from the patients' medical records using a checklist that one of the researchers put together. This checklist was based on what was already in the standard patient files and covered basic demographics (age, sex, height, weight) plus lab results (specifically serum ferritin levels). For assessing growth, we compared height and weight against the standard curves from the US National Center for Health Statistics (NCHS). The NCHS growth references were used because these charts were the standard growth references routinely available and used in the clinical assessment and documentation of children at the study setting during the study period. Height-for-age and weight-for-age measurements were interpreted according to age- and sex-specific NCHS percentiles. Therefore, the prevalence of growth impairment reported in this study should be interpreted relative to the NCHS reference population. We used separate curves for boys and girls: weight-for-age and height-for-age. All data were handled with full confidentiality—no names or identifying details were recorded or shared anywhere. The checklist had three main parts: Part One was simple: just the basic demographics such as age and gender. Part Two covered the anthropometric measurements. We used a spring scale for weight, a wall-mounted stadiometer for height, the NCHS growth charts, an interview sheet, and the designated thalassemia patient file. Weight was measured with the child standing barefoot in light clothing. Height was taken standing straight against the wall meter. After measuring, we plotted the values on the NCHS curves and calculated how the child's height and weight compared to the standard percentiles for their age and sex. Serum ferritin levels were obtained from the participants' medical records or laboratory results recorded during the study period. Serum ferritin concentrations were reported in µg/L and were used as an indicator of body iron burden. For descriptive analysis, ferritin levels were categorized as <1,000 µg/L, 1,000–2,500 µg/L, and >2,500 µg/L. For the purpose of the association analyses, growth disorder was classified according to the predefined criteria used in the study database. Participants were

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categorized as having or not having a growth disorder based on their recorded anthropometric assessment. Height-for-age and weight-for-age were evaluated using age- and sex-specific NCHS reference percentiles.

Statistical Analysis

All analyses were performed using SPSS software, version 22 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized using mean and standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. According to the distribution and characteristics of the variables, appropriate statistical tests were used to evaluate the associations between the study variables. Associations between categorical variables, including age group and sex with growth disorder, were assessed using categorical data analysis. Comparisons of serum ferritin levels between participants with and without growth disorder were performed using an appropriate two-group comparison method based on the distribution of the data. All statistical analyses were performed using two-sided tests, and a P-value of less than 0.05 was considered statistically significant.

3.Results

A total of 80 children with β-thalassemia major were included in the study. The mean age of the participants was 12.1 ± 3.4 years. Most participants were aged 11–15 years (n = 43, 53.8%), followed by those aged >15 years (n = 19, 23.8%) and 5–10 years (n = 18, 22.5%). Regarding sex, 30 participants (37.5%) were female and 50 (62.5%) were male (Table 1).

Table 1. Demographic characteristics of children with β-thalassemia major (n = 80)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	5–10	18	22.5
	11–15	43	53.8
	>15	19	23.8
	Mean ± SD	**12.1 ± 3.4**	—
Sex	Female	30	37.5
	Male	50	62.5
	Total	**80**	**100.0**

The distribution of height-for-age and weight-for-age percentiles is presented in Table 2. The mean height of the participants was 141.1 ± 16.1 cm. Overall, 63 children (78.7%) had a height-for-age below the 50th percentile, including 32 children (40.0%) with a height below the 5th percentile. The mean weight of the participants was 35.7 ± 11.7 kg. A total of 70 children (87.6%) had a weight-for-age below the 50th percentile, including 24 children (30.0%) with a weight below the 5th percentile.

Growth parameter	Percentile category	Frequency (n)	Percentage (%)
Height-for-age	<5th percentile	32	40.0
	5th–<10th percentile	9	11.2
	10th–<25th percentile	10	12.5
	25th–<50th percentile	12	15.0
	50th–<75th percentile	13	16.3
	75th–<90th percentile	4	5.0
	Total	80	100.0
	Mean height ± SD (cm)	141.1 ± 16.1	—
Weight-for-age	<5th percentile	24	30.0
	5th–<10th percentile	12	15.0
	10th–<25th percentile	19	23.8
	25th–<50th percentile	15	18.8
	50th–<75th percentile	8	10.0
	75th–<90th percentile	0	0.0
	90th–95th percentile	2	2.5
	Total	80	100.0
	Mean weight ± SD (kg)	35.7 ± 11.7	—

Table 3: presents the association of age group and sex with growth disorder among the studied children with transfusion-dependent β-thalassemia major. Growth disorder was observed in 4 of 18 children (22.2%) aged 5–10 years, 28 of 43 children (65.1%) aged 11–15 years, and 12 of 19 children (63.2%) aged >15 years. The association between age group and growth disorder was statistically significant (P = 0.006), indicating that growth disorder was more frequently observed among older age groups than among children

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aged 5–10 years. With regard to sex, growth disorder was observed in 14 of 30 females (46.7%) and 30 of 50 males (60.0%). However, the association between sex and growth disorder was not statistically significant (P = 0.246).

Table 3. Association of age group and sex with growth disorder among children with transfusion-dependent β-thalassemia major (n = 80)

Variable	Category	Growth Disorder, Yes n (%)	Growth Disorder, No n (%)	P-value
Age group (years)	5–10	4 (22.2)	14 (77.8)	**0.006**
	11–15	28 (65.1)	15 (34.9)	
	>15	12 (63.2)	7 (36.8)	
Sex	Female	14 (46.7)	16 (53.3)	**0.246**
	Male	30 (60.0)	20 (40.0)	

Footnote: Data are presented as frequency (percentage). P-values <0.05 were considered statistically significant.

Table 4 presents the distribution of serum ferritin levels among the studied children. Serum ferritin levels were <1,000 µg/L in 4 children (5.0%), between 1,000 and 2,500 µg/L in 20 children (25.0%), and >2,500 µg/L in 56 children (70.0%). Overall, 76 participants (95.0%) had serum ferritin levels of ≥1,000 µg/L. The overall mean serum ferritin concentration was 4,702.2 ± 3,934.2 µg/L.

Table 4. Distribution of serum ferritin levels among children with β-thalassemia major (n = 80)

Serum ferritin level (µg/L)	Frequency (n)	Percentage (%)
<1,000	4	5.0
1,000–2,500	20	25.0
>2,500	56	70.0
Total	**80**	**100.0**
Mean ± SD (µg/L)	**4,702.2 ± 3,934.2**	—

Children with growth disorder had a higher mean serum ferritin level (5,020.3 ± 4,870.1 µg/L) than those without growth disorder (4,313.5 ± 2,348.1 µg/L). However, the difference was not statistically significant (P = 0.551) (Table 5).

Table 5. Comparison of serum ferritin levels according to growth disorder status among children with β-thalassemia major

Growth disorder status	n	Mean serum ferritin (µg/L)	SD (µg/L)	P-value
Yes	44	5,020.3	4,870.1	0.551
No	36	4,313.5	2,348.1	

Footnote: Serum ferritin values are presented as mean ± standard deviation (SD). A P-value <0.05 was considered statistically significant.

4. Discussion

This study was conducted to assess height and weight parameters among children with thalassemia major. The findings indicated that 55% of the patients exhibited growth indices below the 50th percentile, whereas, in a healthy population, approximately 45% of individuals are expected to fall within the 50th to 95th percentiles. Similarly, Khalili et al. reported that more than 90% of patients with beta-thalassemia major had growth measurements below the 50th percentile (38). In the present study, 40% of the patients had a height below the 5th percentile. Consistent with these results, Noori and Berberi, in a study conducted in Zahedan, reported that 47 out of 157 affected girls and 59 out of 167 affected boys had heights below the 5th percentile (39). Numerous studies worldwide have identified short stature as a common complication among patients with beta-thalassemia major. Regarding weight, 30% of the patients in the current study were below the 5th percentile. Kamali et al. also demonstrated that the mean weight of girls and boys with thalassemia was below the standard growth curves, with the disparity becoming more pronounced with increasing age. This difference reached its peak at 14 years of age in girls and at 16–17 years of age in boys (40). The findings of Noori and Berberi further corroborated these results, as all patients were reported to have weights below the 3rd percentile (39). A study in Tehran found that short stature, defined as height below the 3rd percentile, was present in 39.3% of patients (41). Wu et al. investigated growth retardation in patients with beta-thalassemia major and reported that 50% of the 29 studied patients exhibited physical growth failure (42). In a study by Mohammadi et al. evaluating growth indices in 456 patients, 43% had height below the 5th percentile, 4.6% were between the 5th and 10th percentiles, 10% had hypoparathyroidism, 76% of girls over 13 years of age and 96.6% of boys over 14 years of age were diagnosed with hypogonadism (43). The Turkish Hemoglobinopathy Committee found short stature in about 40% of their patients (44), while a study from China reported growth failure in 52% of cases (45).

In our study, growth disorders appeared more often in boys than in girls at first glance. But once we ran the stats, the difference wasn't significant. This suggests sex probably isn't an independent factor driving growth impairment here. Age, on the other hand, showed a clear link. Growth problems became much

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more common as the children got older. That makes sense biologically—chronic anemia and all the built-up effects of the disease slowly take a toll on growth year after year. We saw a particularly sharp rise in growth failure after age 12. This hints that starting treatment early and keeping it consistent might help push back the worst effects until later in the second decade of life (46, 47). There are some noticeable differences when we compare our results to studies from other places. For example, a European study found growth failure in only 12% of boys and 15% of girls over eight years old (48). In contrast, a study in Hong Kong reported much higher rates—62% in boys and 75% in girls older than 12 (49). These variations could come from differences in treatment protocols, access to chelation, nutrition, or even how growth was measured across studies.

Shiva et al. found that more than 50% of patients older than 10 years had short stature, compared with only 10% among those younger than 10 years (50). A longitudinal study by Mohammad et al. assessed growth trends in Iranian children and adolescents aged 2–18 years over approximately one decade. The results indicated that the median height and weight of Iranian boys and girls up to the age of 15 were generally below the 20th percentile of the US National Center for Health Statistics (NCHS) standards. Between the ages of 15 and 18, height and weight increased to the 20th and 25th percentiles, respectively, with only girls' weight reaching the 35th percentile at 14 years of age (51).

Normal serum ferritin levels range from 15 to 300 µg/L in healthy adult males and 12 to 150 µg/L in females (52). Since iron accumulated through repeated blood transfusions cannot be excreted physiologically, iron chelation therapy, particularly with desferrioxamine, is essential. Daily subcutaneous administration of desferrioxamine every 8–10 hours is effective in achieving a negative iron balance (53).

At the Ahvaz Thalassemia Research Center, they found suboptimal ferritin levels among 80% of patients (54)—a result that's quite similar to that observed in our study, where nearly 70% had elevated ferritin. Iron imbalance, whether too low or too high, can clearly impair growth. Low iron impairs hemoglobin production and oxygen delivery to cells, while excess iron accumulates and damages organs, potentially further impairing growth. Ferritin, as the main storage form of iron, indirectly helps growth by making sure there's enough iron for hemoglobin and tissue oxygenation (55). But in this study—and in line with several others—we didn't find any significant link between plasma ferritin levels and short stature. This reinforces that growth failure in thalassemia is multifactorial, not just driven by iron storage alone (56). That said, some studies do report a direct connection. For example, Hamidah et al. saw significantly higher ferritin in short-statured patients (56). On the other hand, Gulati et al. found no link between short stature, growth hormone deficiency, and ferritin (45). Shamshir Saz et al. also reported no real difference in ferritin between short and non-short patients (41). Gobar-Hinde et al. saw no relationship either (58). In a large study from Shiraz by Karamifar et al. on 1,100 patients with beta-thalassemia major, they noted hypoparathyroidism in seven patients who had seizures from calcium deficiency—all with ferritin over 2000 ng/mL. They stressed keeping ferritin below 1500 ng/mL and using proper deferoxamine dosing to cut down on endocrine complications (59). A study from Israel similarly showed that high ferritin during puberty raises the risk of hypogonadism, and elevated levels in early childhood predict shorter final adult height (58). Overall, growth failure in thalassemia is complicated and comes from many directions. Chronic anemia, iron overload, and higher calorie needs from ineffective erythropoiesis are major players. Other contributors include poor nutrition, deferoxamine side effects, deficiencies in zinc or folic acid, hypersplenism, delayed puberty, hypogonadism, chronic liver issues, hypothyroidism, hypoparathyroidism, and growth hormone deficiency (60).

Study Limitations

When looking at these results, there are a few important limitations to keep in mind.

Because this was a cross-sectional study, we can only spot associations at one moment in time—we can't prove that one thing actually causes another, like whether poor growth is directly caused by high ferritin or other factors. The sample size was fairly small (80 children), and all came from just one city (Jiroft). That means the findings might not apply as well to kids in other parts of Iran or different countries where demographics, income levels, or access to care look quite different. We mainly relied on basic anthropometric measurements (height and weight) and serum ferritin levels to assess growth. We didn't include other key things that can affect growth, such as hormone function tests, detailed nutrition assessments, pubertal stage evaluation, checks for micronutrient deficiencies (like zinc or vitamin D), or more accurate ways to measure iron overload (like liver or heart MRI). Those missing pieces could have given a fuller picture. Finally, since the data came from medical records, there could be some information bias—records aren't always complete, measurements might vary depending on who took them or when, and some details could have been missed or recorded inconsistently. All of this means

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we should interpret the results carefully. It also points to the need for future studies to use larger, more diverse samples, follow children over time (longitudinal design), and include a wider range of assessments to get a clearer understanding of what really drives growth problems in thalassemia. In addition, the use of NCHS growth references rather than more contemporary international references, such as WHO growth standards and references, may affect comparisons with studies using different growth reference populations.

5. Conclusion

Growth impairment represents a major and clinically significant challenge for children with β-thalassemia major in Jiroft—being much more common and severe than expected among healthy children of the same age. Most of these children fall well below normal ranges for both height and weight, demonstrating how deeply and persistently the disease affects their physical development over time. The pattern becomes noticeably worse as they get older, with the most pronounced impairments appearing in late childhood and especially during adolescence. This can be explained biologically by the long-term effects of chronic anemia, repeated transfusions, progressive iron overload, and the gradual development of endocrine complications, which cumulatively exert a heavier toll over the years. These results further emphasize how important it is to identify growth impairment early, start treatment promptly, and maintain close follow-up from a young age. Doing so can help delay or lessen the most severe effects on growth.

Although we observed growth disorders more frequently in boys, the difference was not statistically significant. This suggests that gender itself may not be a major determinant; rather, shared disease-related factors, such as anemia and iron overload, may affect boys and girls in a similar manner.

We also found elevated serum ferritin levels in almost everyone, but there was no clear association between higher ferritin levels and greater growth impairment. This further highlights the multifactorial nature of growth failure in thalassemia, as a single marker such as ferritin cannot fully account for growth impairment. Other factors, including nutrition, endocrine dysfunction, chelation therapy-related effects, and other factors, are clearly involved. Ultimately, these findings underscore the importance of a broader, team-based approach to caring for these children. Growth monitoring should not be limited to controlling hemoglobin or iron levels. It should also include regular assessment of nutrition, endocrine function, including pubertal development and hormonal status, and personalized treatment plans tailored to each child. Only with such integrated care can we hope to prevent or minimize long-term growth impairment and promote the best possible overall health and quality of life for these children.

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Ethical Considerations and Compliance with Ethical Guidelines

All procedures were carried out in accordance with the ethical standards set by the institutional and national research committees, as well as the 1975 Helsinki Declaration and its subsequent amendments, or comparable ethical standards. Prior to commencing the study, approval was obtained from the dissertation committee, followed by permission from the ethics committee of the university's vice-chancellor for research and technology. A formal letter of introduction was secured from the medical school, granting the researcher authorization to initiate the project. The ethics approval code assigned to this study was IR.JMU.REC.1402.088.

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Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

Authors' contributions

R.R., E.A., and N.H. came up with the original concept, planned the project, carried out the experiments, and composed the manuscript.

AI Using Declaration

In the preparation of this manuscript, the authors used ChatGPT (OpenAI) strictly as a language-polishing tool to improve grammar, sentence structure, and readability. The core research, ideas, data, analysis, and scientific reasoning are entirely the authors' original work. The AI was not used to generate any part of the research content, conclusions, or data interpretations. The authors take full responsibility for the integrity and originality of the scholarly content presented herein. This manuscript was conceived, researched, analyzed, and drafted by the human authors. AI assistance was limited to post-drafting language enhancement, and all AI-influenced sections have been carefully reviewed, revised, and finalized by the authors to ensure alignment with their intended

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meaning and academic standards.

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