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RESEARCH ARTICLE

Intervention-Associated Psychosocial and Serum Ferritin Changes Following a Nurse-Led Self-Management Education Programme with a Family-Support Component among Adolescents with Thalassaemia: A Non-Randomised Quasi-Experimental Study

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ABSTRACT

Introduction: Thalassaemia is a lifelong haematological disorder that requires lifelong blood transfusions and iron chelation therapy. During adolescence, developmental changes and psychosocial challenges often compromise treatment adherence, increasing the risk of iron overload and long-term complications. Grounded in the Middle Range Theory of Self- and Family Management of Chronic Illness, this study examined intervention-associated changes in psychosocial determinants and clinical outcomes following a self-management and family support component among adolescents with thalassaemia.

Methods: A non-randomised quasi-experimental pre–post design at the participant level, with a concurrent control group, was conducted among 96 adolescents with thalassaemia. Four eligible hospitals were selected using predefined institutional criteria and randomly allocated at the hospital level to the intervention or control condition; individual adolescents were not randomised (48 intervention; 48 control). The intervention group received an eight-week nurse-led self-management education programme with a family-support component delivered through standardised printed modules, direct education, and monitoring sheets, covering thalassaemia self-management, treatment-related practices, complication prevention, family support, and quality-of-life management, in addition to routine care. Family members were asked to reinforce adolescents' application of self-management behaviours at home, while the control group received routine services. No single primary outcome was prespecified; the study treated changes in knowledge, attitudes, treatment practices, perceived family support, health-related quality of life measured using PedsQL, and serum ferritin levels as co-outcomes.

Results: Compared with the control group, the intervention group demonstrated greater improvements in knowledge, attitudes, treatment practices, perceived family support, and health-related quality of life (all $p = 0.001$). The intervention group also showed a greater change in serum ferritin concentration than the control group (mean change: −2,323.69 ± 2,618.20 ng/mL vs. −682.15 ± 859.33 ng/mL; $p = 0.001$).

Conclusion: In this participant-level non-randomised quasi-experimental study, participation in a structured self-management education programme with a family-support component was associated with greater improvement in psychosocial outcomes and a larger reduction in serum ferritin compared with routine care. Although hospital sites were randomly allocated, individual adolescents were not randomised and the reported analyses did not account for hospital-level clustering; findings should therefore be interpreted as intervention-associated and may be affected by residual confounding. Further randomised or longitudinal studies are needed.

Keywords: Thalassaemia; Self-Management; Adolescents; Quality of Life; Ferritin

INTRODUCTION

Adolescents with thalassaemia face intertwined medical and psychosocial challenges that substantially influence health behaviours, treatment adherence, and long-term outcomes. Thalassaemia remains a globally distributed monogenic blood disorder requiring lifelong transfusion and iron chelation therapy, particularly among individuals with transfusion-dependent thalassaemia. Across regions, disease-related complications such as iron overload, infections, endocrine dysfunction, growth impairment, and organ damage continue to shape morbidity patterns, while quality-of-life impairments are widely reported in adolescent cohorts. In Southeast Asia and the Middle East, epidemiological reports highlight a persistent burden among adolescents who require frequent transfusions and sustained chelation therapy, with associated financial and systemic pressures on families and health systems (1). Studies conducted in Indonesia further corroborate the heavy lifelong burden borne by adolescents with thalassaemia and emphasise the need for psychosocial supports to complement biomedical management (2).

Adolescence represents a critical developmental stage characterised by identity formation, increasing autonomy, and evolving social roles. These developmental processes may intensify adherence challenges to lifelong therapies, including iron chelation, particularly in contexts marked by socioeconomic disparities and limited healthcare access (3,4). Complication profiles in adolescent and young adult cohorts demonstrate cumulative risk patterns, including infection, cholelithiasis, endocrinopathies, and metabolic disturbances that escalate with age and suboptimal iron control (1), as well as growth and developmental problems (5). Such clinical vulnerabilities intersect with psychosocial stressors, including anxiety, depression, and impaired school functioning, which collectively contribute to reduced health-related quality of life and increased healthcare utilisation during adolescence (6).

Despite advances in transfusion protocols and iron chelation therapies, adherence to treatment remains suboptimal among adolescents. Evidence indicates that approximately half of adolescent patients in certain settings report good adherence, while the remainder face financial, psychological, and systemic barriers that hinder consistent therapy. Poor adherence is directly associated with increased iron burden, organ iron deposition, endocrinopathies, infections, growth impairment, and diminished quality of life (1). While bone marrow transplantation offers a curative option for select patients, donor limitations and procedural risks render lifelong adherence to medical therapy essential for most adolescents. Therefore, strengthening adherence during adolescence is pivotal to safeguarding long-term survival and facilitating transition to adult care.

Conventional care models predominantly emphasise biomedical management, yet psychosocial determinants—including knowledge, attitudes, practices, family support, and resilience—play critical roles in shaping adherence behaviours and clinical outcomes. Previous thalassaemia interventions have addressed these determinants through partially overlapping but distinct approaches. A theory-based PRECEDE–PROCEED educational programme for adolescents improved awareness, attitudes, enabling and reinforcing factors, and health-promoting lifestyle, but it did not evaluate an integrated adolescent–family management pathway together with a clinical iron-burden biomarker (7). A family-centred empowerment programme involving adolescents and an active family member incorporated education, problem solving, family participation, and evaluation and improved self-efficacy, but its principal outcome was self-efficacy rather than a multidimensional set of behavioural, family, quality-of-life, and clinical outcomes. The SCOPE programme combined supportive and coping strategies, ongoing assessment, prevention of complications, and empowerment and evaluated health-related quality of life and health status in children with thalassaemia (8). In parallel, a systematic review of iron-chelation adherence among children and adolescents identified only a small number of adherence-focused intervention studies and substantial heterogeneity in intervention approaches and adherence measurement (9). Although health education can improve knowledge, knowledge alone does not consistently translate into sustained behavioural change or favourable clinical indicators (10). Taken together, previous studies support individual educational, adherence, self-management, and family-oriented components, but evidence remains limited regarding their integration within a theory-guided adolescent self-management programme with a family-support component that simultaneously evaluates proximal psychosocial outcomes and downstream clinical indicators (3,11).

Psychosocial burden among adolescents with thalassaemia is well documented. Elevated anxiety, stress, and depressive symptoms are frequently reported, often exceeding levels observed in healthy peers (5,12). Altered physical appearance due to chronic transfusions and skeletal changes may disrupt self-image and social participation, contributing to withdrawal and school disruption (5). Indonesian studies further identify hope as a protective psychosocial resource that positively correlates with quality of life and life satisfaction, highlighting the importance of culturally embedded resilience mechanisms. These findings suggest that psychosocial empowerment is not peripheral but central to adolescent adaptation and disease management.

Family dynamics constitute another foundational determinant of adolescent health behaviour. High levels of family support are associated with proactive decision-making regarding carrier screening and premarital planning, illustrating the broader preventive implications of familial engagement. The caregiver–adolescent dyad is central to chronic disease management, as caregiver involvement can enhance monitoring, reinforce treatment routines, and support problem-solving processes (13). Theoretical frameworks of middle-range self-care emphasise self-care maintenance, monitoring, and management as interconnected processes that benefit from structured caregiver contribution and self-efficacy enhancement (13). However, explicit theory-guided applications tailored to adolescents with thalassaemia remain limited, indicating a need for structured development of integrated self-management and family-support models.

Empirical evidence further indicates that psychosocial variables interact with clinical biomarkers in complex ways. Treatment adherence was not directly assessed in the present study. Adherence is generally associated with lower ferritin levels, yet knowledge and positive attitudes do not uniformly translate into favourable biomarker profiles (3,11). Ferritin, while widely

used as a proxy for iron overload, may not fully capture organ-specific iron deposition or endocrine complications, underscoring the importance of comprehensive outcome evaluation (1). Consequently, interventions that strengthen psychosocial capacities, family engagement, and adherence behaviours may exert both direct and indirect effects on biological outcomes, bridging psychosocial and biomedical domains.

Taken together, the research gap is not the absence of educational, self-management, adherence, or self-management education programme with a family-support component in thalassaemia, but the limited evidence on their integration and on the simultaneous assessment of outcomes across the proposed self- and family-management pathway. Multidimensional care models that incorporate developmentally appropriate self-management education and family support are required to address the intertwined medical and psychosocial challenges faced during adolescence. The present study aims to examine intervention-associated differences in knowledge, attitudes, practices, perceived family support, health-related quality of life, and serum ferritin levels among adolescents with thalassaemia. By integrating the Middle Range Theory of Self- and Family Management of Chronic Illness with a context-adapted family-support component, this study tests an established theoretical pathway in an Indonesian hospital-based adolescent thalassaemia context rather than proposing a new self-management theory. Its contribution lies primarily in the contextual integration of established self-management and family-support elements and in evaluating proximal psychosocial outcomes, a distal patient-reported outcome, and a downstream clinical indicator within the same eight-week programme. This positioning defines the study as a contextual and integrative contribution while avoiding claims of a previously untested causal mechanism.

METHODS

This study examined an integrated educational intervention combining adolescent self-management and structured family support in relation to psychosocial and clinical outcomes among adolescents with thalassaemia. The methodological approach was informed by existing literature on quasi-experimental designs for chronic disease education, validated measurement strategies in adolescent thalassaemia research, and identified gaps in theory-guided, family-inclusive intervention (3,11,14–16).

Study Design

A non-randomised quasi-experimental pre–post design at the participant level with a concurrent control group was employed. Four eligible hospitals were selected according to predefined institutional criteria and randomly allocated at the hospital level to the intervention or control condition; individual adolescents were recruited within participating hospitals and were not individually randomised (14,15). Both groups were assessed at baseline (pre-test) and after the eight-week intervention period (post-test), enabling within-group and between-group comparisons. Because individual adolescents were not randomised and key hospital-allocation details were unavailable in the retained materials, the design supported assessment of intervention-associated changes rather than definitive causal effects.

The study was conducted in four hospitals selected according to predefined institutional criteria. Eligible hospitals were required to have at least a Type B classification, full accreditation (*Paripurna*), thalassaemia services, a haematology subspecialist, and an on-site blood bank. After identifying hospitals that met these criteria, four hospitals were selected as study sites. The hospitals were then randomly allocated to the intervention or control condition. Thus, random allocation was performed at the hospital level rather than at the individual participant level. The retained materials do not report the number of hospitals assigned to each condition, the randomisation sequence method, the role of the person who performed hospital allocation, or whether that person had access to baseline outcome information. Adolescents with thalassaemia were eligible to participate if they were aged 15–18 years, could read, write, and communicate in Indonesian, understood the study and agreed to participate, and were registered at one of the participating hospitals, as verified through hospital medical records. Adolescents were excluded if they had other disease complications, had undergone splenectomy, or experienced deterioration in their health condition during the study that prevented participation. Consequently, the precise contribution of the allocation process to selection bias cannot be reconstructed from the retained dataset. The study documentation referred to matching or comparability procedures based on age, sex, educational level, duration of illness, and baseline clinical-psychosocial characteristics; however, the retained dataset does not contain individual matched-pair identifiers, matching tolerances, frequency-matching strata, or records of unmatched participants. The analyses therefore treated the intervention and control groups as independent groups rather than as matched pairs, and the manuscript does not interpret the procedure as individual pair matching. Potential contamination was considered because participants were treated within the same regional health system. To reduce contamination, intervention and control activities were separated by content and timing: structured modules and nurse-led education sessions were delivered only to the intervention group during the study period, control participants received routine care without access to the structured modules during data collection, and the same intervention was offered to the control group only after completion of post-test assessment. Baseline comparisons were used descriptively to characterise observed group differences and were not considered evidence of statistical equivalence. Nevertheless, residual confounding could not be excluded because unmeasured factors, such as disease severity, prior adherence patterns, socioeconomic conditions, caregiver capacity, medication access, and healthcare-use patterns, may have differed between groups in this non-randomised design.

Population and Sample

Participants were adolescents diagnosed with thalassaemia who were receiving routine transfusion and chelation therapy in participating thalassaemia services. A total of 96 adolescents were included in the retained analysis dataset and allocated

into two groups: an intervention group (n=48) and a control group (n=48). Inclusion criteria were confirmed diagnosis of thalassaemia, age 15–18 years, ability to read, write, and communicate in Indonesian, registration as a patient at the study hospitals, understanding of the study information, and willingness to participate after parental or legal guardian consent and adolescent assent had been obtained. Exclusion criteria included a documented category of “other disease complications,” previous splenectomy, severe cognitive impairment, acute medical instability, or health deterioration that would preclude participation in education sessions or follow-up measurement. The retained analysis dataset does not specify which diagnoses or clinical thresholds constituted “other disease complications,” who made each clinical exclusion determination, or the number excluded under each individual criterion. These details therefore cannot be reconstructed from the analysis file and represent a limitation in assessing external validity.

This study used a total sampling approach, in which adolescents with thalassaemia who were registered and routinely received care at four hospitals providing thalassaemia services in Bekasi Regency and Bekasi City were screened based on the study eligibility criteria. Recruitment began with coordination between the researcher and participating hospitals to identify potential respondents from medical records. After screening, adolescents and parents or legal guardians received study information and completed consent or assent procedures. Participants and their parents or legal guardians were informed that participation was voluntary, that data would be kept confidential and de-identified, and that adolescents could withdraw from the study at any time without affecting their routine care. The retained participant-level analysis dataset contains 96 enrolled adolescents, all of whom have baseline and post-test records and were included in the reported analyses. However, the dataset does not contain the original recruitment dates, hospital-specific numbers screened or enrolled, screening logs documenting reasons for ineligibility, or source records permitting independent verification of the number of refusals. Accordingly, the manuscript reports the participant flow that can be verified from the retained dataset rather than inferring undocumented screening events. Because participants were drawn from adolescents receiving care in participating hospitals, selection bias related to service attendance and referral patterns may still remain.

The sample size was determined based on the accessible population of adolescents with thalassaemia in the Greater Bekasi area. No a priori sample-size calculation based on a single prespecified primary outcome was documented. The original analysis treated knowledge, attitudes, practices, perceived family support, quality of life, and serum ferritin as multiple study outcomes rather than identifying one prospectively specified primary outcome. Because the accessible population was limited, 96 participants were included and allocated equally into the intervention and control groups with a 1:1 ratio, resulting in 48 participants in each group. As a post hoc indication of statistical precision, 48 participants per group would provide approximately 80% power for a two-sided independent comparison to detect a standardised between-group difference of about 0.58 at $\alpha = 0.05$ under conventional parametric assumptions. This calculation is descriptive only, does not account for multiplicity or non-normal outcomes, and is not a substitute for prospective power determination. The absence of an a priori primary-outcome-based calculation should therefore be considered when interpreting the findings.

Research Location

The study was conducted in four hospitals providing thalassaemia services in Bekasi Regency and Bekasi City, Indonesia, from October to November 2025. Hospital names were omitted from the anonymised manuscript to maintain blinded peer review.

Instruments and Outcome Measures

The knowledge, attitudes, and practices (KAP) questionnaire was developed by the researchers based on the Indonesian Ministry of Health's guidance on thalassaemia management and a pocketbook for adolescents with thalassaemia. The questionnaire items underwent expert review before validity and reliability testing. Pilot testing was conducted with 30 respondents who were not included in the intervention or control groups. Item validity was assessed using product–moment correlations, with a critical r value of 0.361. All items had calculated r values greater than the critical value and were therefore considered valid according to this item-level criterion. Reliability testing yielded a Cronbach's alpha coefficient of 0.960 for the tested item set, exceeding the prespecified threshold of 0.60. However, separate reliability coefficients for the knowledge, attitudes, and practices scales were not available. Because the knowledge items used dichotomous true/false responses, a scale-specific Kuder–Richardson Formula 20 (KR-20) coefficient would be appropriate; however, this coefficient was not available in the retained study documentation. Therefore, the reported alpha coefficient should be interpreted as an overall estimate for the tested item set rather than evidence of the reliability of each individual KAP scale.

Family support was measured using an adolescent-reported Family Support Scale capturing emotional, informational, instrumental, physical, and practical dimensions of caregiver involvement. The scale consisted of 20 items with four response options, reflecting the extent of support perceived by the adolescent in managing thalassaemia. Items were summed to form a total score; the instrument comprised 20 four-point items, corresponding to a possible total range of 20–80 when scored 1–4 per item. The main findings indicate that thalassaemia affects the daily lives, education, employment, and social relationships of both patients and caregivers (18). Because use of the FSS in the Indonesian context was limited, the instrument was translated into Indonesian with assistance from the Language Institute of Universitas Nasional and contextually adapted for adolescent respondents. Item-level validity of the Indonesian-translated FSS was examined using product-moment correlations, with all corrected item correlations exceeding 0.30. The overall Cronbach’s alpha was 0.949, indicating high internal consistency for the tested FSS item set. However, the available documentation did not identify a more specific version designation, permissible item-level missing-data rules, or confirm whether the reported Cronbach’s alpha was calculated specifically in the 96-participant analysis sample. Therefore, these findings provide evidence of acceptable item

correlations and overall internal consistency for the tested instrument but should not be interpreted as establishing comprehensive psychometric validation of the FSS in the present study sample. In addition, because family support was reported by adolescents, the resulting scores represent perceived family support rather than independently verified caregiver behaviour.

Health-related quality of life was assessed using the Pediatric Quality of Life Inventory (PedsQL), completed by the adolescents. The instrument assesses physical, emotional, social, and school functioning. In the present study, the reported total scores were transformed to a 0–100 scale, with higher scores indicating better health-related quality of life, according to the scoring approach documented in the study records. However, the exact PedsQL version and module administered, the corresponding Indonesian validation source, and the applicable version-specific missing-item rules could not be verified from the available study documentation. The documentation also did not establish whether internal consistency was calculated in the main study sample of 96 participants. Accordingly, the reported results are interpreted on the basis of the available total scores and are not presented as evidence of version-specific validation or reliability in the study sample. Domain-specific changes were not analysed or inferred because separate scores for physical, emotional, social, and school functioning were not available for analysis.

Serum ferritin levels were obtained from routine laboratory assessments recorded in the hospital medical records and used as a clinical biomarker related to body iron burden. Ferritin is commonly used in thalassaemia research as an indicator of iron burden, although it may not fully capture organ-specific iron deposition and can vary with acute-phase responses and clinical management (3,16). Serum ferritin concentrations were obtained from routine hospital records at the pre-intervention and post-intervention assessments. However, the available study documentation did not permit verification of the ferritin assay manufacturer or analytical platform, the exact sampling window, or the timing of blood sampling relative to transfusion. The procedures used to identify acute infection or inflammation at the time of sampling could also not be established. In addition, information on iron chelator type, dose, administration regimen, and any treatment changes during the follow-up period could not be recovered from the available study records. These limitations were considered when interpreting changes in serum ferritin, which are reported as intervention-associated changes in serum ferritin concentration rather than as definitive evidence of a reduction in iron overload.

Data Collection Procedures

Baseline data were collected prior to intervention implementation. Participants completed psychosocial questionnaires, and ferritin values were recorded from clinical laboratory results. Following the eight-week intervention period, the same instruments were re-administered to both groups. Participants and intervention nurses could not be blinded to group allocation because the intervention involved active education. The retained documentation does not establish whether questionnaire administrators, ferritin-data extractors, outcome assessors, or statistical analysts were blinded, or whether the same personnel both delivered the intervention and collected post-test outcomes. This incomplete blinding information is relevant particularly to the self-reported outcomes and is treated as a potential source of measurement bias. The final analysis population comprised the 96 participants with intervention-group identifiers and recorded baseline and post-test outcome data in the retained analysis dataset. No participant-level loss between the recorded baseline and post-test datasets was identified. However, the retained materials do not document prespecified rules for handling item-level questionnaire missingness, ferritin measurements obtained outside an intended assessment window, protocol deviations, or incomplete intervention exposure. Consequently, the available dataset supports reporting of participant-level completeness but does not permit confirmation that every measurement was obtained strictly within all intended protocol conditions.

The intervention was a structured self-management education programme with a family-support component delivered to adolescents with thalassaemia in the intervention group for eight weeks, in addition to routine hospital care. The intervention was implemented using standardised printed modules covering thalassaemia self-management, treatment adherence, daily care practices, prevention of complications, family support, and quality-of-life improvement. Education sessions were conducted according to the module sequence during the eight weeks and were facilitated by trained nurses from the thalassaemia care units. Nurse facilitators received three days of training, followed by practice, mentoring, and competency assessment using a self-management education checklist before implementation. The educational media included printed modules, direct nurse-led education, and monitoring sheets. The programme remained adolescent-directed: the modules, nurse-led education, and self-management monitoring activities were delivered to adolescents, while family members were asked to reinforce, rather than replace, adolescents' own self-management activities at home. The documented family role primarily involved encouragement and practical reinforcement of treatment-related and daily-care behaviours introduced through the adolescent programme. Although the family-support outcome measure assessed emotional, informational, instrumental, physical, and practical dimensions of support, the available intervention documentation did not identify these dimensions as separate family-training modules and did not document a distinct family-only curriculum, specified family-session dose, or independent assessment of changes in family behaviour. Accordingly, the family element is described as a family-support component rather than as a fully structured self-management education programme with a family-support component. This approach was intended to preserve adolescent autonomy by keeping self-management responsibilities centred on the adolescent while positioning family members as supporters of the adolescent's implementation of those behaviours. Intervention fidelity was supported through standardised modules, trained facilitators, competency testing, mentoring, and nurse-completed monitoring sheets, and checklist-guided delivery. Session attendance, module completion, checklist implementation, and monitoring-sheet compliance were monitored as part of implementation; however, quantitative fidelity data, including attendance percentages, module completion rates, checklist compliance rates, and monitoring-sheet

completion rates, were not available in the anonymised analysis dataset. The absence of quantitative fidelity indicators is acknowledged as a methodological limitation. The control group received routine thalassaemia care only during the study period without access to the structured modules, nurse-led self-management education, monitoring materials, or programme-specific instruction for family reinforcement at home and was offered the same intervention after completion of post-test data collection.

Data Analysis

Data analysis followed the pre–post structure of the participant-level non-randomised quasi-experimental design (14,15). Data processing included editing, coding, processing, and cleaning to ensure completeness, accuracy, and consistency before analysis using SPSS version 29.0. The reported analyses were conducted at the individual-participant level; no cluster-adjusted model or cluster-robust standard errors were documented in the retained analysis materials. Descriptive statistics were used to summarise demographic characteristics and baseline measures. Categorical variables, such as sex and education level, were presented as frequencies and percentages, while numerical variables, such as age, duration of illness, and outcome scores, were presented as means and standard deviations or as medians with minimum–maximum values, according to data distribution.

Normality testing was performed before hypothesis testing to determine the appropriate parametric or non-parametric statistical procedures. Since the main outcome variables—knowledge, attitudes, practices, perceived family support, quality of life, and serum ferritin levels—were numerical, data distribution was assessed using the skewness and kurtosis ratio, with values between −2 and +2 considered normally distributed. The distribution was also examined using the Shapiro–Wilk test, with a p value > 0.05 indicating normal distribution. The retained manuscript materials identify which outcomes were subsequently treated as parametric or non-parametric but do not provide the exact Shapiro–Wilk statistics or skewness/kurtosis values for each outcome; therefore, these diagnostic values cannot be reconstructed from the manuscript alone. For normally distributed outcomes, such as family support and quality of life, paired t-tests were used to analyse within-group changes from pre-test to post-test, and independent t-tests were used to compare mean differences between the intervention and control groups. For outcomes that did not meet the normality assumption, including knowledge, attitudes, practices, and ferritin levels, Wilcoxon signed-rank tests were used for within-group comparisons, while Mann–Whitney U tests were used for between-group comparisons. Because ferritin was treated as non-normally distributed, rank-based inference was used; mean ± SD values were retained only as descriptive summaries and should not be interpreted as an adjusted parametric treatment effect.

No single primary outcome or primary estimand was prospectively documented in the retained study materials. Knowledge, attitudes, treatment practices, perceived family support, health-related quality of life, and serum ferritin were therefore analysed as multiple co-outcomes. Between-group differences were examined using the observed pre-test and post-test values and the corresponding change scores. Statistical tests were selected according to the distribution and measurement characteristics of each outcome. No baseline-adjusted regression models were used as the principal analysis, and no adjusted intervention-versus-control estimates were derived.

Because individual adolescents were not randomised and the reported analyses did not account for hospital-level clustering, between-group differences were interpreted cautiously. Although baseline characteristics were compared descriptively, the absence of statistically significant baseline differences was not considered evidence of baseline equivalence. Accordingly, the observed differences in change scores were interpreted as intervention-associated differences rather than definitive causal effects. Within-group pre–post changes were also interpreted descriptively and were not considered evidence of intervention efficacy in isolation. No multiplicity-adjustment procedure was documented; therefore, individual p values were interpreted cautiously, and the multiple-outcome analysis was considered exploratory rather than confirmatory testing of six independent primary hypotheses (3,11).

No correlation analysis was performed or retained in the final analysis. Accordingly, no statistical association between psychosocial outcomes and serum ferritin concentration was estimated. Knowledge, attitudes, treatment practices, perceived family support, health-related quality of life, and serum ferritin were analysed as separate co-outcomes, and the results were interpreted independently rather than as components of a tested psychosocial–biological pathway.

Ethical Approval

This study received ethical approval from the Komite Etik Penelitian Kesehatan, Fakultas Ilmu Kesehatan, Universitas Nasional, Indonesia (approval no. 104/eKEPK/FIKES/2025; issued 2 October 2025). Institutional research permission was also obtained before data collection. Participation was voluntary, study aims and procedures were explained before data collection, and written informed consent from parents or legal guardians and adolescent assent were obtained in accordance with the approved protocol. All participants were informed that they had the right to withdraw from the study at any time without consequences for their routine care. Participant confidentiality was maintained by using coded data, limiting access to research data, and reporting findings in aggregate form without identifying individual adolescents or families. No prospective public trial registration or separate statistical analysis plan was identified in the retained study materials. The study protocol submitted for ethical approval described the study procedures; however, no registry name, registration number, registration date, or separately archived statistical analysis plan was available in the retained records. This lack of documented prospective registration and a separate statistical analysis plan is acknowledged as a limitation when assessing selective-reporting risk. The data supporting the findings of this study are not publicly available because they contain participant-level information that requires protection of confidentiality. De-identified data may be made available by the corresponding author

upon reasonable request, subject to ethical requirements, applicable data-protection regulations, and approval of the proposed data use. Access is not guaranteed and will depend on the feasibility of sharing the requested data without compromising participant confidentiality.

RESULTS

Participant Flow

The retained analysis dataset contained 96 adolescents with recorded group assignments: 48 in the intervention group and 48 in the control group. All 96 participants had recorded baseline and post-test assessments, and no participant-level loss between these recorded assessments was identified. Because recruitment dates, hospital-specific screening and enrolment counts, screening logs, reasons for ineligibility, and source records documenting refusals were unavailable, the numbers originally screened, eligible, excluded before enrolment, or declining participation could not be independently verified and are therefore not reported. Consequently, all 96 participants completed baseline and post-test assessments and were included in the final analysis (48 intervention and 48 control).

Intervention Fidelity

Procedures intended to support intervention fidelity included standardised modules, a fixed eight-week session sequence, trained nurse facilitators, competency assessment using a self-management education checklist, mentoring, and nurse-completed monitoring sheets. Session attendance, module completion, checklist implementation, and monitoring-sheet completion were monitored, but the available manuscript dataset did not include quantitative fidelity rates. Therefore, the achieved intervention dose and adherence to planned delivery could not be quantified. Fidelity is consequently described in terms of the procedures used to support standardised delivery rather than as verified implementation performance, and no unsupported quantitative fidelity indicators are reported.

Baseline Characteristics of Participants

Participant characteristics are presented in Table 1.

Table 1. Baseline Characteristics of Participants in the Intervention and Control Groups (n = 96)

Features	Intervention Group					Control Group					p
	n	%	Mean ±SD	Median	Min-Max	n	%	Mean±SD	Median	Min-Max	
Gender											**1.000[b]**
Male	26	54.2				25	52.1				
Female	22	45.8				23	47.9				
Education											**0.828[c]**
junior high school	16	33.3				14	29.2				
senior high school	32	66.7				34	70.8				
Duration of illness											**1.000[c]**
< 10 years	2	4.2				3	6.3				
≥ 10 years	46	95.8				45	93.8				
Age (year)			16.31±1.15	16.00	15-18			16.38±1.10	16.00	15-18	**0.787[a]**

[a]Independent t-test; [b]Continuity correction; [c]Fisher's exact test

Forty-eight participants were allocated to the intervention group and forty-eight to the control group. Baseline demographic and clinical characteristics were examined descriptively before implementation of the self-management and family-support education model. These comparisons were used to characterise observed baseline differences and were not interpreted as establishing statistical equivalence.

As presented in Table 1, the distribution of gender was descriptively similar between groups. In the intervention group, 26 participants (54.2%) were male and 22 (45.8%) were female, while the control group included 25 males (52.1%) and 23 females (47.9%). Statistical testing showed no significant difference in gender distribution between groups (p = 1.000). Educational level showed a similar descriptive distribution: 16 participants (33.3%) in the intervention group and 14 (29.2%) in the control group were enrolled in junior high school (SMP), whereas 32 (66.7%) and 34 (70.8%), respectively, were enrolled in senior high school (SMA), with no significant difference observed (p = 0.828).

Regarding duration of illness, the majority of adolescents in both groups had been living with thalassaemia for more than ten years. In the intervention group, 46 participants (95.8%) had illness duration exceeding ten years, compared with 45 participants (93.8%) in the control group. Only a small proportion in each group had illness duration under ten years (4.2% vs. 6.3%), and the difference was not statistically significant (p = 1.000). Mean age was also similar between groups, with 16.31 ± 1.15 years in the intervention group and 16.38 ± 1.10 years in the control group (p = 0.787). These findings indicate that no statistically significant between-group differences were observed in the reported baseline demographic variables.

Intervention-Associated Changes in Knowledge, Attitudes, and Practices

The results of within-group and between-group statistical analyses are presented in Tables 2–4. For all outcomes, delta was defined consistently as post-test minus pre-test (Δ = post − pre); positive values therefore indicate an increase and negative values indicate a decrease.

Table 2. Knowledge Scores Before and After the Intervention (n = 96)

Knowledge Score	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	5.00±1.76	5.00	1-9	5.17±1.79	5.00	1-8	0.623[a]
Post-test	9.46±1.36	10.00	6-12	5.27±1.78	5.00	5-9	0.001[a]
p	0.001 [b]			0.315[b]			
Delta score	4.46±2.25	5.00	1-9	0.10±0.69	0.00	(-2) -(1)	0.001[a]

[a]Mann–Whitney, [b]Wilcoxon

Table 3. Attitude Scores Before and After the Intervention (n = 96)

Attitude Score	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	19.98±3.09	20.00	15-25	20.35±3.12	20.50	15-25	0.546[a]
Post-test	39.31±5.27	40.50	25-48	20.33±2.99	21.00	15-25	0.001[a]
P	0.001[b]			0.942[b]			
Delta score	19.33±5.93	20.00	4-30	-0.02±0.63	0.00	(-3)-(1)	0.001[a]

[a]Mann–Whitney, [b]Wilcoxon

Table 4. Thalassaemia Treatment Practice Scores Before and After the Intervention (n = 96)

Practice Score	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	30.69±5.33	30.00	22-43	30.19±5.23	30.00	22-43	0.659[a]
Post-test	39.77±3.64	40.00	28-46	30.13±4.46	30.50	23-40	0.001[a]
p	0.001[b]			0.886[b]			
Delta score	9.08±4.82	9.00	2-21	-0.06±2.30	0.00	(-9)-(9)	0.001[a]

[a]Mann–Whitney, [b]Wilcoxon

The self-management and family support education model was associated with substantial improvements in knowledge, attitudes, and treatment-related practices among adolescents in the intervention group.

Knowledge scores increased markedly following the eight-week intervention. In the intervention group, the mean knowledge score improved from 5.00 ± 1.76 at pre-test to 9.46 ± 1.36 at post-test (p = 0.001). The mean change (delta) was 4.46 ± 2.25, representing a 4.46-point mean increase on the 0–12 knowledge scale; no threshold for clinically meaningful change was prespecified or applied. In contrast, the control group showed minimal change, from 5.17 ± 1.79 to 5.27 ± 1.78, with a non-significant within-group difference (p = 0.315) and a negligible delta of 0.10 ± 0.69. Between-group comparison of change scores demonstrated a statistically significant difference (p = 0.001), supporting an intervention-associated improvement in disease knowledge.

Attitude scores exhibited an even more pronounced shift. In the intervention group, mean attitude scores increased from 19.98 ± 3.09 at baseline to 39.31 ± 5.27 post-intervention (p = 0.001), with a mean increase of 19.33 ± 5.93. Conversely, the control group demonstrated no meaningful change (20.35 ± 3.12 to 20.33 ± 2.99; p = 0.942), and the delta score was −0.02 ± 0.63. The between-group difference in change was statistically significant (p = 0.001), indicating that the intervention was associated with more favourable attitudes toward thalassaemia management.

Similarly, treatment practice scores improved substantially in the intervention group. Baseline practice scores increased from 30.69 ± 5.33 to 39.77 ± 3.64 (p = 0.001), with a mean delta of 9.08 ± 4.82. The control group showed no significant change (30.19 ± 5.23 to 30.13 ± 4.46; p = 0.886), and the mean delta was −0.06 ± 2.30. Between-group comparison confirmed a statistically significant difference in change scores (p = 0.001). These findings indicate that the education model may be associated with improved self-management behaviours alongside knowledge and attitudinal gains.

Intervention-Associated Changes in Family Support and Quality of Life

The results of within-group and between-group statistical analyses are presented in Tables 5 and 6.

Table 5. Family Support Scores Before and After the Intervention (n = 96)

Family Support Score	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	38.42±3.23	38.00	30-46	38.48±3.13	38.50	32-46	0.924[a]
Post-test	71.38±3.64	71.00	64-78	38.54±3.02	38.50	32-46	0.001[a]
p	0.001[b]			0.444[b]			
Delta score	32.96±3.74	33.50	23-41	0.06±0.56	0.00	(-3)-(1)	0.001[a]

[a]Independent t-test, [b]Dependent t-test, [c]Mann–Whitney

Table 6. Quality of Life Scores Before and After the Intervention (n = 96)

Quality of Life Score	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	44.83±10.14	44.00	25-63	42.69±8.94	42.00	24-59	0.275[a]
Post-test	77.23±4.50	78.00	66-84	42.48±9.04	42.00	20-59	0.001[a]
p	0.001[b]			0.096[b]			
Delta score	32.40±7.37	33.00	20-56	-0.21±0.84	0.00	(-4)-(1)	0.001[a]

[a]Independent t-test, [b]Dependent t-test, [c]Mann–Whitney

The intervention was also associated with significant improvements in self-reported perceived family support and health-related quality of life. Perceived family support scores in the intervention group increased from 38.42 ± 3.23 at baseline to 71.38 ± 3.64 post-intervention (p = 0.001), representing a mean increase of 32.96 ± 3.74. In contrast, the control group exhibited virtually no change (38.48 ± 3.13 to 38.54 ± 3.02; p = 0.444), with a delta of only 0.06 ± 0.56. The between-group difference in change was statistically significant (p = 0.001). Because family support was reported by the adolescents themselves, this change represents an increase in perceived support rather than independently verified change in family behaviour. No caregiver-reported, observational, or other independent measure of family behaviour was obtained. Given the unblinded intervention, expectancy effects, social-desirability bias, and measurement reactivity may have contributed to the magnitude of the reported change and should be considered when interpreting this result.

The PedsQL total score improved significantly in the intervention group. Mean scores increased from 44.83 ± 10.14 at pre-test to 77.23 ± 4.50 at post-test (p = 0.001), with a mean delta of 32.40 ± 7.37. In the control group, the total score remained relatively stable (42.69 ± 8.94 to 42.48 ± 9.04; p = 0.096), and the mean delta was −0.21 ± 0.84. Between-group comparison demonstrated a statistically significant difference in change scores (p = 0.001). The observed 32.40-point mean increase describes the magnitude of change in the overall PedsQL score. Domain-specific scores for physical, emotional, social, and school functioning were not presented in the current analysis; therefore, the findings should not be interpreted as demonstrating improvement in any specific PedsQL domain, including school participation or social functioning. No prespecified version-specific minimal clinically important difference was applied in this study, and the magnitude is therefore reported descriptively rather than assigned clinical significance.

Serum Ferritin Levels

Intervention-Associated Changes in Serum Ferritin Levels. The results of within-group and between-group statistical analyses are presented in Table 7.

Table 7. Serum Ferritin Levels Before and After the Intervention (n = 96)

Serum Ferritin	Intervention Group (n=48)			Control Group (n=48)			p
	Mean±SD	Median	Min-Max	Mean±SD	Median	Min-Max	
Pre-test	7297.98± 4185.39	6109.5	2112-23363	7578.48± 3718.35	6693.5	2974-16824	0.459[a]
Post-test	4974.29± 3102.90	4187.5	1179-15831	6896.33± 3935.22	5957.5	2278-16890	0.001[a]
P	0.001[b]			0.001[b]			
Delta score	-2323.69± 2618.20	-1360	(-10552)-(-11)	-682.15± 859.33	-736	(-3100)-(1095)	0.001[a]

[a]Mann–Whitney, [b]Wilcoxon

Serum ferritin levels were analysed to assess intervention-associated biomarker changes in iron overload. At baseline, mean ferritin levels were 7,297.98 ± 4,185.39 ng/mL in the intervention group and 7,578.48 ± 3,718.35 ng/mL in the control group, with no significant difference (p = 0.459).

Following the intervention, ferritin levels in the intervention group decreased significantly to 4,974.29 ± 3,102.90 ng/mL (p = 0.001). The mean reduction (delta) was −2,323.69 ± 2,618.20 ng/mL. In contrast, the control group exhibited a smaller decrease from 7,578.48 ± 3,718.35 to 6,896.33 ± 3,935.22 ng/mL (p = 0.001), with a mean reduction of −682.15 ± 859.33 ng/mL. Between-group comparison of change scores showed a statistically significant difference (p = 0.001), indicating that the intervention was associated with a greater decrease in serum ferritin concentration. This finding should be interpreted specifically as an intervention-associated difference in serum ferritin concentration rather than as evidence of reduced body iron burden or organ iron deposition. The assay platform, timing of ferritin measurement relative to transfusion, screening for acute infection or inflammation, chelator type and regimen, and treatment changes during follow-up were not documented; therefore, stronger biological attribution cannot be established from these data.

DISCUSSION

The present study suggests that participation in a self-management programme with a family-support component was associated with improvements in psychosocial outcomes and a change in serum ferritin concentration among adolescents with thalassaemia. The programme was primarily directed at adolescents, while family members provided reinforcement of self-management behaviours at home. These findings are consistent with literature suggesting that psychosocial factors, self-management behaviours, and supportive family contexts may be relevant to treatment-related behaviours and quality of life

in adolescents with chronic conditions. Improvements in knowledge, attitudes, self-management practices, and perceived family support may contribute to more effective disease-management behaviours; however, these pathways were not directly tested in the present study. Similarly, the observed change in serum ferritin should be interpreted as an intervention-associated change in serum ferritin concentration rather than as verified evidence of reduced body or organ iron burden (3,11,17,20).

The substantial gains observed in knowledge, attitudes, and treatment practices are consistent with evidence that structured education can strengthen adolescents' cognitive and motivational readiness for disease management. Prior studies have shown that education improves disease-specific knowledge, yet knowledge alone rarely produces sustained behavioural change unless accompanied by skills training, problem-solving strategies, and motivational reinforcement (11,17,21). The present findings support this broader understanding: improvements in attitudes and practices paralleled knowledge gains, suggesting that the intervention may have extended beyond information transfer to behavioural activation. This is consistent with evidence from chronic disease self-management literature, where integrated educational models incorporating routine planning, reminders, and coping strategies have been associated with better outcomes compared with didactic approaches alone (22). The family-support component may have contributed to these psychosocial changes, although its independent effect was not evaluated (23). The marked improvement in perceived family support observed in this study echoes cross-cultural evidence indicating that caregiver engagement is associated with stronger adherence-related behaviours and adolescents' sense of security and shared responsibility. In Indonesian cohorts, family context and psychosocial resources such as hope have been shown to moderate quality-of-life outcomes among adolescents with thalassaemia (5). In the present intervention, the documented family role consisted of encouraging and practically reinforcing adolescents' application of self-management behaviours at home, rather than participation in a separately structured family-centred curriculum. Accordingly, the observed increase should be interpreted as an increase in adolescents' perceived family support and not as evidence of caregiver session participation, improved caregiver self-efficacy, or enhanced caregiver coordination of treatment routines. Family reinforcement may nevertheless provide a supportive context for adolescent self-management, although caregiver-level effects were not measured (24).

The observed improvement in health-related quality of life further suggests a potential psychosocial benefit of the integrated model. Quality-of-life gains are consistent with previous studies using instruments such as PedsQL and TranQOL, which have reported that structured psychosocial and family-inclusive interventions are associated with improvements in physical, emotional, social, and school functioning domains in adolescents with chronic illness (5). However, only the total PedsQL score was analysed in the present study; domain-specific scores for physical, emotional, social, and school functioning were not reported. Therefore, the observed change should be interpreted as an improvement in overall health-related quality of life without attributing the improvement to any specific PedsQL domain. The overall PedsQL change may reflect a broader perceived quality-of-life benefit associated with adolescent-centred self-management education and its family-support component, although the specific domains contributing to this change cannot be determined from the available analysis (10).

The concurrent improvements in psychosocial outcomes and the change in serum ferritin concentration provide a basis for considering a possible relationship between self-management processes and biological outcomes. One hypothesis is that improvements in knowledge, attitudes, and self-management practices may, over time, be accompanied by changes in treatment-related behaviours and biological indicators. However, this pathway was not directly examined in the present study. Chelation adherence, caregiver-level behaviours, and other treatment-related factors were not comprehensively measured; therefore, the observed change in serum ferritin cannot be attributed to adherence or caregiver behaviour. The findings should consequently be interpreted as concurrent intervention-associated changes rather than evidence of a psychosocial-to-adherence-to-ferritin mechanism. Longitudinal studies incorporating objective measures of chelation adherence, caregiver behaviours, and repeated biological assessments are needed to test whether such a pathway exists (9,25).

A possible, but untested, pathway is that improvements in knowledge and attitudes could strengthen adolescents' understanding of regular treatment, while family support could facilitate organisation and reinforcement of daily self-management routines (26,27). If such changes improved chelation adherence, they could potentially influence ferritin trajectories. However, neither chelation adherence nor mediation was measured, so this sequence remains a theoretical hypothesis rather than a mechanism demonstrated by the present study. It is also important to acknowledge that ferritin is influenced by inflammatory states and infection and may not fully capture organ-specific iron deposition (16,28,29). Thus, the observed reduction in serum ferritin should be interpreted as a short-term biomarker change rather than direct evidence of reduced tissue iron burden or organ protection. Future studies incorporating direct adherence measures, transfusion and chelation data, inflammatory markers, and imaging-based iron assessment would be required to test the proposed pathway more rigorously (30,31).

Socioeconomic and health-system factors may also moderate these outcomes. Evidence from multiple contexts demonstrates that economic stability, medication access, and satisfaction with healthcare services are associated with adherence behaviours and biomarker outcomes (3). In resource-constrained settings, education alone may be insufficient to achieve ferritin reduction without concurrent structural supports. The present intervention's integration within routine care may have mitigated some access-related barriers, suggesting that successful psychosocial programmes should ideally be embedded within supportive health systems.

The present findings provide a preliminary rationale for further evaluation of theory-informed adolescent self-management programmes with family-support components, but they do not by themselves establish a basis for routine service or policy implementation. Before integration into standard thalassaemia care pathways can be recommended, implementation studies should examine feasibility, acceptability to adolescents and families, intervention costs and resource requirements,

sustainability, workforce capacity, and equitable access across different hospital and socioeconomic settings (3). If subsequent effectiveness and implementation research supports such integration, potential service components could include structured educational materials, appropriately trained providers, and mechanisms for family support. Similarly, standardised outcome assessment—including psychosocial measures, direct adherence measures, quality of life, and appropriately interpreted clinical iron indicators—could be evaluated in future multicentre studies to improve comparability and evidence synthesis (11,16,17).

Clinically, multidisciplinary teams are important for delivering integrated interventions effectively. Haematologists, nurses, psychologists, and social workers can collaboratively address adherence barriers, caregiver burden, and emotional distress, thereby supporting the psychosocial-biomedical linkage. Embedding routine psychosocial screening for anxiety, depression, and caregiver strain within thalassaemia clinics can identify modifiable factors that may attenuate adherence and quality-of-life improvements (12). Moreover, incorporating structured feedback on adherence and biomarker trends may motivate sustained engagement and facilitate individualised problem-solving.

Despite its strengths, the interpretation of these findings should consider methodological limitations inherent in the quasi-experimental design. Although hospitals were randomly allocated to the intervention or control condition, individual adolescents were not randomised; the retained materials do not document the randomisation sequence method, the allocator's role or access to baseline information, or the number of hospitals assigned to each condition. In addition, the reported analyses were conducted at the individual-participant level without documented adjustment for hospital-level clustering. Although no statistically significant baseline differences were observed in the measured characteristics, these findings do not establish baseline equivalence and cannot exclude systematic differences between groups. Residual confounding therefore remains possible, including from unmeasured factors such as disease severity, prior treatment adherence, socioeconomic circumstances, caregiver capacity, medication access, and patterns of healthcare use. Future randomised or stepped-wedge trials with longitudinal follow-up, including follow-up through transition to adult care, would strengthen causal inference and help determine the sustainability of changes in psychosocial outcomes and serum ferritin concentration (14,15). The possibility that improvements in psychosocial self-management processes may be related over time to treatment adherence and subsequent biological outcomes remains an untested hypothesis. Future studies incorporating direct measures of adherence, caregiver-level behaviours, and repeated biological assessments could examine these potential pathways more rigorously.

The contribution of this study lies in its contextual integration of adolescent self-management education with a family-support component within thalassaemia care. Rather than establishing a family-centred intervention or a causal multidimensional model, the study provides preliminary evidence of concurrent changes across psychosocial outcomes and serum ferritin concentration following participation in the programme. The findings extend the existing discussion of adolescent self-management by illustrating how family support can be incorporated as a contextual component alongside adolescent-directed self-management education. However, because individual adolescents were not randomised, the reported analysis did not account for hospital-level clustering, and residual confounding remained possible, and did not include a direct measure of treatment adherence or caregiver-level behaviour, the observed findings should not be interpreted as evidence of a causal psychosocial–biomedical pathway or of improved tissue iron status. Future longitudinal and randomised studies should test whether changes in self-management processes are associated with subsequent changes in objective adherence and biological outcomes.

Interpretation of Key Findings

The intervention was associated with greater improvements in knowledge, attitudes, treatment practices, perceived family support, and overall health-related quality of life, together with a greater change in serum ferritin concentration compared with routine care. These findings indicate concurrent changes across multiple psychosocial outcomes and serum ferritin concentration following participation in the self-management education programme with a family-support component. However, the study did not include a retained correlation analysis; therefore, no statistical association between psychosocial outcomes and serum ferritin concentration can be inferred. Similarly, the findings do not establish that improvements in psychosocial outcomes resulted in changes in treatment adherence or serum ferritin concentration. The observed findings should therefore be interpreted as intervention-associated changes across separate outcomes rather than evidence of a demonstrated psychosocial–biological pathway.

Comparison with Previous Studies

Compared with previous studies of self-management and educational interventions in adolescents with thalassaemia, the present study provides contextual evidence on the implementation of a nurse-led self-management education programme with a family-support component (11). The intervention was associated with greater improvements in knowledge, attitudes, treatment practices, perceived family support, and overall health-related quality of life, together with a greater change in serum ferritin concentration compared with routine care (3,17). These findings are broadly consistent with previous research indicating that educational and self-management approaches may influence psychosocial outcomes among adolescents with thalassaemia (3,28). However, the present study did not evaluate a structured family-centred intervention, and the family component was limited to family support for adolescents' self-management behaviours at home. In addition, no prespecified threshold for clinically meaningful ferritin change was established, and treatment adherence, caregiver-level behaviours, and a psychosocial–biological pathway were not directly assessed (5,12). Therefore, the findings should be interpreted as concurrent intervention-associated changes across multiple psychosocial outcomes and serum ferritin concentration rather

than evidence of a family-centred effect (16), clinically meaningful improvement in iron overload, an adherence-mediated mechanism, or a demonstrated association between psychosocial and biological outcomes (18).

Limitations and Cautions

Several limitations should be considered when interpreting the results of this study. First, although hospitals were randomly allocated to study condition, individual adolescents were not randomised and the reported analyses did not account for hospital-level clustering, introducing the possibility of selection bias, cluster-related dependence, and residual confounding despite baseline comparisons of measured characteristics (12,18). Although baseline analyses showed no statistically significant differences in the reported characteristics, these tests do not establish equivalence between participant groups and cannot exclude imbalance in unmeasured or imperfectly measured factors. In addition, the intervention was implemented across multiple hospitals, and potential differences in routine care, service delivery, medication access, or other hospital-level characteristics were not modelled; these factors may have influenced the observed between-group differences. Therefore, the observed differences should be interpreted as intervention-associated changes rather than definitive causal effects. Second, participants and intervention nurses could not be blinded, and the principal psychosocial outcomes—including knowledge, attitudes, treatment practices, perceived family support, and health-related quality of life—were based on participant self-report. Expectancy or Hawthorne effects, social-desirability bias, and measurement reactivity may therefore have contributed to the magnitude of the observed self-reported changes, particularly given the very large increases in several outcomes. In addition, version-specific or scale-specific reliability and validation information could not be fully confirmed for the KAP measures, Family Support Scale, and PedsQL version used in the retained study materials. Although these measures were used to assess the intended psychosocial constructs, incomplete instrument-specific psychometric documentation limits confidence in interpreting the magnitude of the observed score changes. Accordingly, the large self-reported changes should be interpreted as observed changes in study scores rather than definitive evidence of equivalently large changes in the underlying psychosocial constructs. Third, chelation adherence was not directly measured. Consequently, the study cannot determine whether adherence changed during the intervention or whether adherence mediated the association between psychosocial changes and serum ferritin change. Fourth, quantitative intervention-fidelity indicators, including attendance, module completion, checklist compliance, and monitoring-sheet completion rates, were unavailable. This limits assessment of the intervention dose actually received and the consistency with which the programme was delivered across participants and settings. Fifth, the relatively short eight-week intervention and follow-up period limits the ability to assess the sustainability of behavioural changes and the stability of ferritin reduction in the long term, while the literature suggests that iron overload control and complications are cumulative and require ongoing monitoring (20). Sixth, serum ferritin was the sole biological indicator, although this parameter can be influenced by inflammatory conditions and may not fully reflect organ-specific iron deposition or endocrine risk (21). The biological interpretation of the observed ferritin change is therefore uncertain because ferritin may also vary with acute infection or inflammation, transfusion-related factors, chelator type, dose and regimen, and treatment changes during follow-up. These factors were not incorporated into the present analysis as explanatory variables. Accordingly, the short-term decline in ferritin should not be interpreted as direct evidence of improved tissue iron burden or organ-level iron control.

Recommendations for Future Research

Further research should use more robust experimental designs, such as randomised controlled trials, stepped-wedge designs, or longitudinal approaches, to strengthen causal inferences and assess the sustainability of intervention-associated changes through transition to adult services. Future evaluation should include adherence measures, iron-overload indicators such as MRI-based organ iron assessment where feasible, and complete quantitative fidelity indicators. Studies with multicentre coverage and diverse health-system settings are also important to increase the generalisability of the findings.

CONCLUSION

This participant-level non-randomised quasi-experimental study showed that participation in a theory-guided self-management education programme with a family-support component was associated, over eight weeks, with greater between-group improvements in knowledge, attitudes, self-management practices, perceived family support, and health-related quality of life, as well as a larger reduction in serum ferritin levels than routine care among adolescents with thalassaemia. These findings describe concurrent short-term psychosocial and serum ferritin changes; they do not establish that family support improved chelation adherence or that the intervention caused the observed change in serum ferritin concentration, because adherence and the proposed psychosocial-to-clinical pathway were not directly measured. However, although hospitals were randomly allocated, individual adolescents were not randomised and the reported analyses did not account for hospital-level clustering; the results should therefore be interpreted as intervention-associated changes rather than definitive causal effects, and residual confounding cannot be excluded. The findings are therefore most directly applicable to adolescents receiving thalassaemia care within the participating hospital services and comparable clinical settings. Longer-term randomised studies with direct adherence measures and more comprehensive iron-status assessment are needed before broader clinical or service-level conclusions can be drawn.

DECLARATIONS

Author contributions: MES, MIK, and FM: Conceptualization; Methodology; Investigation; Formal analysis; Writing – original draft; Writing – review & editing. S: Conceptualization; Investigation; Formal analysis; Writing – review & editing. All authors critically reviewed and approved the final manuscript.

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