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Original Article

Retrospective Review of Iron Deficiency Profiles in Toddlers Presenting With Their First Febrile Seizure

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ABSTRACT

Background: Febrile seizures are common neurological events in early childhood, and iron deficiency has been proposed as a biologically plausible contributor to altered neuronal excitability because of its role in neurodevelopment, neurotransmitter synthesis, and cerebral energy metabolism. **Objective:** To determine whether iron deficiency profiles are associated with prolonged seizure duration among toddlers presenting with their first febrile seizure. **Methods:** This retrospective observational analytical study reviewed electronic medical records, archived laboratory reports, and paediatric emergency registers from tertiary care hospitals in Central Punjab for children aged 6–36 months presenting with first documented febrile seizure between January 2022 and December 2024. After exclusions, 132 eligible records were analyzed. Iron status was categorized as normal iron status, depleted iron stores, latent iron deficiency, or iron deficiency anemia using integrated hematological indices. Statistical analysis included descriptive statistics, chi-square testing, ANOVA, and binary logistic regression adjusted for age, sex, nutritional status, family history, and peak presenting temperature. **Results:** Depleted iron stores were identified in 42 children (31.8%), latent iron deficiency in 36 (27.3%), iron deficiency anemia in 29 (22.0%), and normal iron status in 25 (18.9%). Mean seizure duration increased progressively from 3.1 ± 1.2 minutes in children with normal iron status to 5.6 ± 2.0 minutes in those with iron deficiency anemia. Seizures lasting longer than five minutes increased from 12.0% to 48.3% across the same spectrum. Iron profile was significantly associated with prolonged seizure duration ($\chi^2 = 11.82$; $p = 0.008$), with latent iron deficiency (adjusted OR = 2.18; 95% CI: 1.04–4.55; $p = 0.038$) and iron deficiency anemia (adjusted OR = 2.94; 95% CI: 1.31–6.58; $p = 0.009$) independently associated with higher odds of prolonged seizure. **Conclusion:** Worsening iron deficiency profiles were significantly associated with prolonged first febrile seizure duration in toddlers, suggesting that latent and overt iron deficiency may represent clinically relevant markers of greater seizure severity during febrile illness. **Keywords:** Anemia, Iron-Deficiency; Child, Preschool; Ferritins; Febrile Seizures; Hematologic Tests; Infant; Risk Factors.

INTRODUCTION

Febrile seizures are the most common seizure events of early childhood and typically occur between six months and five years of age in association with fever, without evidence of intracranial infection, metabolic disturbance, or previous afebrile seizure disorder. Although most febrile seizures are benign and self-limiting, their abrupt onset frequently causes substantial parental distress and often results in emergency medical evaluation (1). The clinical challenge is not limited to diagnosing the seizure event

itself, but also to identifying modifiable biological vulnerabilities that may influence seizure expression, recurrence risk, or severity during febrile illness. Among toddlers, this issue is particularly relevant because the peak age for febrile seizures overlaps with a developmental period characterized by rapid brain growth, high nutritional demand, and increased susceptibility to micronutrient deficiencies (2).

The biological basis of febrile seizures is multifactorial and involves the interaction of developmental brain immaturity, genetic susceptibility, fever-mediated inflammatory responses, and transient changes in neuronal excitability. During infancy and toddlerhood, incomplete maturation of inhibitory neural pathways and relatively heightened excitatory neurotransmission may lower the seizure threshold. Fever may further intensify neuronal excitability through increased metabolic demand, altered ion-channel function, cytokine activation, and systemic inflammatory stress. However, many children experience febrile illnesses without seizures, suggesting that additional host-specific factors may modify seizure vulnerability. Nutritional and hematological factors have therefore received increasing attention, particularly iron deficiency, because iron is closely linked to neurodevelopmental integrity and neuronal stability (3,4).

Iron is essential not only for hemoglobin synthesis and oxygen transport but also for several neurobiological processes relevant to seizure threshold, including myelination, mitochondrial energy metabolism, neurotransmitter synthesis, and synaptic function. Iron-dependent pathways contribute to the regulation of dopamine, serotonin, and gamma-aminobutyric acid activity, each of which has a role in maintaining the balance between excitatory and inhibitory neuronal signaling. In early childhood, iron depletion may therefore affect cerebral oxygen delivery, neuronal metabolism, and inhibitory neurotransmission at a time when the brain is still undergoing rapid synaptogenesis and myelination. These mechanisms provide a biologically plausible explanation for why iron deficiency may be associated with febrile seizure characteristics, particularly prolonged seizure duration during acute febrile stress (5).

Iron deficiency is common among toddlers because of rapid growth, increased physiological iron requirements, inadequate dietary intake, prolonged milk-dominant feeding patterns, and variable nutritional access. Importantly, iron deficiency develops along a continuum, beginning with depleted iron stores, progressing to latent iron deficiency, and ultimately resulting in overt iron deficiency anemia. This staged progression is clinically important because neurological vulnerability may arise before anemia becomes apparent on routine clinical assessment. Reliance on hemoglobin alone may therefore underestimate the potential relevance of earlier iron depletion, whereas integrated profiles incorporating ferritin, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width, and transferrin saturation may better capture the biological spectrum of iron deficiency (6,7).

Previous studies examining the relationship between iron deficiency and febrile seizures have produced inconsistent findings. Some investigations have reported lower hemoglobin, serum ferritin, and mean corpuscular volume among children with febrile seizures compared with febrile controls, supporting a possible association between iron deficiency and seizure susceptibility. Other studies have not demonstrated a significant association, and some have suggested that differences in ferritin interpretation during acute illness, population characteristics, definitions of iron deficiency, and study design may partly explain the conflicting results. A further limitation of the available literature is that many studies evaluate isolated hematological markers rather than clinically meaningful iron deficiency profiles, making it difficult to determine whether progressive iron depletion is associated with more severe febrile seizure presentation (8,9).

In the present study context, the most appropriate knowledge gap is not whether iron deficiency predicts the occurrence of a first febrile seizure in the general febrile toddler population, because the available dataset includes only children who presented with first febrile seizure and does not include a febrile non-seizure comparison group. Rather, the key gap is whether different stages of iron deficiency are associated with clinically relevant seizure characteristics among toddlers experiencing their first febrile

seizure. This distinction is important because it aligns the research question with the retrospective observational design and avoids overstating causal or predictive inference. Evaluating iron deficiency profiles within this cohort may still provide clinically useful evidence by identifying whether worsening hematological status corresponds to greater seizure severity, particularly seizure duration exceeding five minutes (10).

The present retrospective analytical study was therefore designed according to a PICO framework in which the population comprised toddlers aged 6–36 months presenting with their first documented febrile seizure, the exposure was iron deficiency profile classified as depleted iron stores, latent iron deficiency, or overt iron deficiency anemia, the comparator was normal iron status, and the principal clinical outcome was prolonged febrile seizure duration. By examining integrated hematological indices rather than isolated laboratory values, the study aimed to clarify whether progressive iron depletion is associated with more severe first febrile seizure presentation. The objective of this study was to determine whether iron deficiency profiles are independently associated with prolonged seizure duration among toddlers presenting with their first febrile seizure after adjustment for relevant clinical confounders, including age, sex, nutritional status, family history, and fever severity (11).

MATERIALS AND METHODS

This retrospective observational analytical study was conducted to evaluate the association between iron deficiency profiles and prolonged seizure duration among toddlers presenting with their first documented febrile seizure. The study used routinely recorded clinical and laboratory data obtained from electronic medical records, archived laboratory reports, and paediatric emergency department admission registers. A retrospective design was selected because it allowed assessment of real-world clinical presentations and hematological profiles without altering patient management, while enabling inclusion of consecutively documented cases over a defined review period. Medical records from 1 January 2022 to 31 December 2024 were reviewed, and data extraction, verification, coding, cleaning, and statistical analysis were completed between May 2025 and December 2025.

The study was carried out in the paediatric emergency and inpatient departments of tertiary care hospitals in Central Punjab, Pakistan. These centres receive a high volume of paediatric emergency presentations and maintain structured electronic and laboratory records, allowing retrieval of demographic, clinical, seizure-related, and hematological data relevant to the study objective. The source population comprised children aged 6–36 months who presented during the review period with a first-time febrile seizure. This age range was selected because it corresponds to the peak developmental period for febrile seizures and overlaps with a period of increased physiological iron requirement during early childhood.

Eligible records were identified through consecutive screening of paediatric emergency and inpatient registers. Children were included if they were aged 6–36 months, had a first documented febrile seizure diagnosed by a consultant paediatrician or emergency consultant, had a recorded body temperature of at least 38°C at presentation or within the preceding 24 hours, had complete clinical documentation of the febrile illness and seizure episode, and had available hematological investigations including hemoglobin concentration, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width, serum ferritin, and transferrin saturation where documented. Records were excluded if there was any previous history of afebrile seizures or recurrent febrile seizures, diagnosed epilepsy, suspected or confirmed central nervous system infection, metabolic or electrolyte abnormality capable of precipitating seizure activity, chronic neurological disorder, known hematological disease such as thalassemia, blood transfusion within the preceding three months, ongoing iron supplementation, incomplete hematological data, or inconsistent seizure documentation.

A minimum sample size of 132 children was calculated using an expected prevalence of iron deficiency markers of 35%, a 95% confidence level, and 8% absolute precision. To maintain representativeness and

reduce selection bias, all consecutively eligible cases during the review period were screened rather than selecting cases by convenience sampling. A total of 147 records were initially assessed, and after exclusion of records with incomplete hematological profiles, previous recurrent febrile seizures, neurological comorbidities, or inconsistent seizure documentation, 132 eligible records were included in the final analytical dataset.

Data were collected using a structured data abstraction proforma developed for uniform extraction from hospital electronic databases and laboratory information systems. Record retrieval and data extraction were performed independently by two trained paediatric research reviewers. Extracted data were compared for consistency, and discrepancies were resolved by rechecking source records and reaching consensus before final coding. The proforma captured demographic variables including age in months and sex; clinical variables including presenting temperature, type of febrile illness, seizure duration in minutes, family history of febrile seizures, and documented nutritional risk indicators; and hematological variables including hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width, serum ferritin, serum iron, total iron-binding capacity, and transferrin saturation where available.

The primary exposure variable was iron deficiency profile. Iron status was categorized using integrated hematological interpretation into normal iron status, depleted iron stores without anemia, latent iron deficiency, and overt iron deficiency anemia. Classification was based on age-adjusted hemoglobin indices and iron parameters, with serum ferritin interpreted alongside available inflammatory information because ferritin may rise during acute febrile or inflammatory illness. Depleted iron stores were defined as reduced iron storage markers without anemia; latent iron deficiency was defined as biochemical iron deficiency with evolving red cell index changes but without overt anemia; and overt iron deficiency anemia was defined as iron deficiency accompanied by reduced hemoglobin concentration and compatible red cell indices. Normal iron status was assigned when hematological and iron indices were within expected age-adjusted ranges.

The primary outcome variable was prolonged first febrile seizure duration, defined as seizure duration exceeding five minutes during the index febrile seizure presentation. Seizure duration was abstracted from emergency records, physician notes, or caregiver-reported duration documented at presentation. Febrile seizure was defined as a seizure occurring in association with fever, without evidence of intracranial infection, structural neurological pathology, metabolic disturbance, or previous unprovoked seizure activity. Additional seizure-related and clinical variables included mean seizure duration, peak temperature above 39°C, type of febrile illness, family history of febrile seizure, and nutritional risk status.

Potential sources of bias were addressed at multiple stages of the study process. Selection bias was reduced through consecutive inclusion of all records meeting predefined eligibility criteria within the review period. Information bias was minimized by using standardized clinical documentation, laboratory results generated through accredited hospital laboratories, and duplicate independent data extraction. Misclassification bias was reduced by applying predefined clinical criteria for first febrile seizure and integrated hematological criteria for iron status classification.

Confounding was addressed by collecting clinically relevant covariates, including age, sex, nutritional status, family history of febrile seizure, and peak presenting temperature, and incorporating these variables into adjusted regression analysis.

Data were entered, coded, cleaned, and analyzed using SPSS version 26.0. Continuous variables were summarized as means and standard deviations, while categorical variables were summarized as frequencies and percentages. Distribution of iron deficiency profiles was described across the full cohort. Mean hematological parameters and seizure duration were compared across iron profile categories using one-way analysis of variance for multiple-group comparisons. Categorical associations between

iron profile categories and prolonged seizure duration were assessed using the chi-square test. Binary logistic regression analysis was performed to evaluate whether iron deficiency profiles were independently associated with seizure duration exceeding five minutes after adjustment for age, sex, nutritional status, family history of febrile seizure, and peak presenting temperature. Normal iron status was treated as the reference category for regression comparisons. Adjusted odds ratios with 95% confidence intervals were reported, and statistical significance was set at $p \leq 0.05$.

Missing data were handled according to their relevance to study eligibility and analysis. Records with missing core hematological parameters or ambiguous seizure documentation were excluded before final dataset construction. For isolated missing non-critical covariates, pairwise exclusion was applied during relevant analyses to preserve available information without compromising the primary exposure and outcome assessment.

Data integrity was maintained through duplicate abstraction, source-record verification, coded variable entry, range checks for continuous variables, consistency checks for categorical coding, and reconciliation of discrepancies before final statistical analysis.

Patient confidentiality was maintained throughout all stages of data handling. Records were anonymized at the time of extraction using coded identifiers, and no personally identifiable information was retained in the analytical dataset. As the study involved retrospective review of existing clinical records and no direct patient contact, all analyses were conducted using anonymized secondary clinical data within secure institutional data-handling procedures.

RESULTS

A total of 147 records of toddlers presenting with seizure-related complaints during the review period were screened. Fifteen records were excluded, including 8 with incomplete hematological profiles, 4 with previous recurrent febrile seizures, 2 with neurological comorbidities, and 1 with inconsistent seizure-onset documentation.

The final analytical cohort included 132 toddlers aged 7–36 months. The mean age was 20.8 ± 6.9 months, with the largest proportion in the 13–24-month age group. Male children accounted for 74 cases (56.1%), while 58 (43.9%) were female. The mean presenting temperature was 39.0 ± 0.6°C, family history of febrile seizure was documented in 28 children (21.2%), and nutritional risk indicators were recorded in 44 children (33.3%).

Table 1. Screening Flow and Baseline Characteristics of the Study Population (n = 132)

Variable	Frequency / Value
Records initially screened	147
Records excluded	15
Incomplete hematological profile	8
Previous recurrent febrile seizures	4
Neurological comorbidity	2
Inconsistent seizure-onset documentation	1
Final analyzed cohort	132
Age, months, mean ± SD	20.8 ± 6.9
Age range, months	7–36
6–12 months	23 (17.4%)
13–24 months	61 (46.2%)
25–36 months	48 (36.4%)
Male sex	74 (56.1%)
Female sex	58 (43.9%)
Presenting temperature, °C, mean ± SD	39.0 ± 0.6
Family history of febrile seizure	28 (21.2%)
Documented nutritional risk indicators	44 (33.3%)

The cohort showed a heterogeneous distribution of iron status. Depleted iron stores without anemia were the most frequent profile, observed in 42 children (31.8%), followed by latent iron deficiency in 36 (27.3%) and overt iron deficiency anemia in 29 (22.0%). Normal iron status was present in 25 children

(18.9%). Overall, 107 of 132 children (81.1%) had some degree of iron depletion or deficiency, while 65 children (49.3%) had either latent iron deficiency or overt iron deficiency anemia.

Table 2. Distribution of Iron Deficiency Profiles

Iron Profile Category	Frequency, n	Percentage, %
Normal iron status	25	18.9
Depleted iron stores without anemia	42	31.8
Latent iron deficiency	36	27.3
Iron deficiency anemia	29	22.0
Any abnormal iron profile	107	81.1
Latent deficiency or iron deficiency anemia	65	49.3

Hematological indices showed a graded deterioration across iron-profile categories. Mean hemoglobin was highest in children with normal iron status at 12.3 ± 0.5 g/dL and lowest in those with iron deficiency anemia at 9.8 ± 0.7 g/dL. Children with latent iron deficiency had an intermediate mean hemoglobin of 11.4 ± 0.6 g/dL. Serum ferritin also declined progressively, from 34.7 ± 6.8 ng/mL in the normal iron-status group to 9.6 ± 2.1 ng/mL in the iron deficiency anemia group. Across the iron-profile categories, hemoglobin, ferritin, and mean corpuscular volume differed significantly, with ANOVA p-values below 0.001 for each comparison.

Table 3. Hematological Profile Across Iron Status Categories

Hematological Variable	Normal Iron Status	Latent Iron Deficiency	Iron Deficiency Anemia	Test Statistic	p-value
Hemoglobin, g/dL, mean ± SD	12.3 ± 0.5	11.4 ± 0.6	9.8 ± 0.7	F = 16.85	<0.001
Serum ferritin, ng/mL, mean ± SD	34.7 ± 6.8	—	9.6 ± 2.1	F = 19.41	<0.001
Mean corpuscular volume comparison	—	—	—	F = 13.27	<0.001

Seizure characteristics demonstrated a clear gradient across worsening iron-profile categories. Mean seizure duration increased from 3.1 ± 1.2 minutes in children with normal iron status to 4.0 ± 1.5 minutes in those with depleted stores, 4.8 ± 1.7 minutes in latent deficiency, and 5.6 ± 2.0 minutes in iron deficiency anemia.

The proportion of seizures lasting longer than five minutes rose from 3 of 25 children (12.0%) in the normal group to 9 of 42 (21.4%) in the depleted-store group, 12 of 36 (33.3%) in the latent-deficiency group, and 14 of 29 (48.3%) in the iron deficiency anemia group. The association between iron profile and seizure duration greater than five minutes was statistically significant ($\chi^2 = 11.82$, $p = 0.008$). Peak temperature above 39°C also increased numerically across categories, from 44.0% in normal iron status to 58.6% in iron deficiency anemia.

Table 4. Febrile Seizure Characteristics Across Iron Profile Groups

Clinical Variable	Normal Iron Status (n = 25)	Depleted Stores (n = 42)	Latent Deficiency (n = 36)	Iron Deficiency Anemia (n = 29)	Test Statistic	p-value
Mean seizure duration, minutes, mean ± SD	3.1 ± 1.2	4.0 ± 1.5	4.8 ± 1.7	5.6 ± 2.0	—	—
Seizure duration >5 minutes	3 (12.0%)	9 (21.4%)	12 (33.3%)	14 (48.3%)	$\chi^2 = 11.82$	0.008
Peak temperature >39°C	11 (44.0%)	20 (47.6%)	18 (50.0%)	17 (58.6%)	—	—

Crude odds estimates derived from the group counts showed an increasing likelihood of seizure duration greater than five minutes across the iron-deficiency spectrum. Compared with children with normal iron status, the crude odds ratio was 2.00 for depleted iron stores, 3.67 for latent iron deficiency, and 6.84 for iron deficiency anemia.

After adjustment for age, sex, family history, nutritional status, and peak presenting temperature, latent iron deficiency remained significantly associated with prolonged seizure duration (adjusted OR = 2.18; 95% CI: 1.04–4.55; p = 0.038), and iron deficiency anemia showed the strongest independent association

(adjusted OR = 2.94; 95% CI: 1.31–6.58; p = 0.009). Depleted iron stores showed elevated but non-significant adjusted odds (adjusted OR = 1.47; 95% CI: 0.69–3.12; p = 0.287).

Table 5. Association Between Iron Deficiency Profiles and Prolonged Febrile Seizure Duration (>5 Minutes)

Iron Profile Category	Prolonged Seizure, n/N (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	p-value
Normal iron status	3/25 (12.0%)	Reference	Reference	—
Depleted iron stores without anemia	9/42 (21.4%)	2.00 (0.49–8.22)	1.47 (0.69–3.12)	0.287
Latent iron deficiency	12/36 (33.3%)	3.67 (0.91–14.74)	2.18 (1.04–4.55)	0.038
Iron deficiency anemia	14/29 (48.3%)	6.84 (1.67–28.01)	2.94 (1.31–6.58)	0.009
Overall iron profile vs seizure duration >5 minutes	—	—	$\chi^2 = 11.82$	0.008

Overall, the results demonstrated a stepwise relationship between worsening iron deficiency profile and prolonged febrile seizure duration. Children with iron deficiency anemia had the longest mean seizure duration at 5.6 ± 2.0 minutes and the highest frequency of seizures exceeding five minutes at 48.3%, compared with 3.1 ± 1.2 minutes and 12.0% among children with normal iron status. Latent iron deficiency also showed clinically relevant elevation in prolonged seizure frequency at 33.3%, with a significant adjusted association after controlling for demographic and clinical confounders. These findings indicate that both latent and overt iron deficiency were associated with more severe first febrile seizure presentation, with the strongest effect observed in children with iron deficiency anemia.

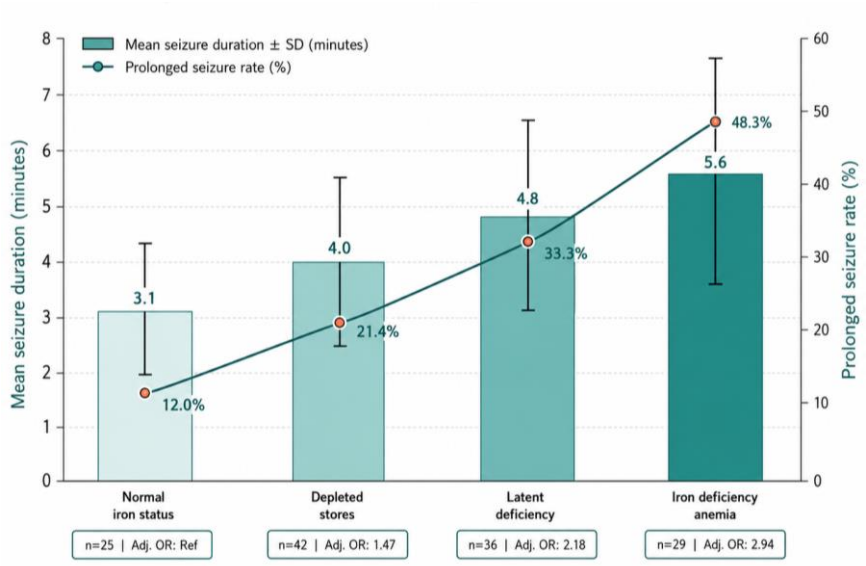

Figure 1. Severity Gradient Across Iron Deficiency Profiles in Toddlers With First Febrile Seizure

The figure demonstrates a progressive increase in febrile seizure severity across worsening iron deficiency profiles. Mean seizure duration increased from 3.1 ± 1.2 minutes in children with normal iron status to 4.0 ± 1.5 minutes in those with depleted iron stores, 4.8 ± 1.7 minutes in latent iron deficiency, and 5.6 ± 2.0 minutes in iron deficiency anemia. The proportion of seizures lasting longer than five minutes followed a similar upward pattern, rising from 12.0% to 21.4%, 33.3%, and 48.3% across the same categories. Adjusted odds ratios also increased across the deficiency spectrum, with the highest adjusted odds observed in children with iron deficiency anemia, indicating a clinically meaningful gradient between worsening iron status and prolonged first febrile seizure presentation.

DISCUSSION

The present retrospective analytical study demonstrated a graded association between worsening iron deficiency profiles and prolonged first febrile seizure duration among toddlers aged 6–36 months. The most clinically relevant finding was the progressive rise in mean seizure duration and in the proportion of seizures lasting longer than five minutes across the iron-status spectrum. Children with normal iron status had the shortest mean seizure duration, whereas those with iron deficiency anemia had the longest

duration and the highest proportion of prolonged seizures. This pattern was further supported by adjusted regression analysis, in which latent iron deficiency and overt iron deficiency anemia remained significantly associated with prolonged seizure duration after accounting for age, sex, nutritional status, family history of febrile seizure, and peak presenting temperature. These findings suggest that iron depletion may have clinical relevance beyond anemia alone and may be associated with more severe seizure expression during febrile illness in early childhood (12).

The observed gradient is biologically plausible because iron has essential roles in neurodevelopment, oxygen transport, mitochondrial energy metabolism, myelination, and neurotransmitter regulation. In the developing brain, iron-dependent enzymatic pathways contribute to dopamine, serotonin, and gamma-aminobutyric acid synthesis, which are closely involved in maintaining the balance between neuronal excitation and inhibition. When iron stores decline, especially during a period of rapid brain growth and high metabolic demand, impaired inhibitory neurotransmission and reduced neuronal energy efficiency may lower the threshold for sustained seizure activity during fever. Febrile illness itself increases neuronal excitability through inflammatory cytokine release, altered ion-channel function, and increased metabolic stress; therefore, iron-deficient toddlers may have reduced physiological reserve when exposed to the additional excitatory burden of fever (13).

An important contribution of this study is the distinction between different stages of iron depletion rather than reliance on anemia alone. The findings showed that latent iron deficiency was also significantly associated with prolonged seizure duration, indicating that clinically relevant neurological vulnerability may emerge before overt iron deficiency anemia becomes apparent. This is particularly meaningful in paediatric practice because hemoglobin concentration alone may fail to identify children with depleted iron stores or evolving iron-restricted erythropoiesis. The progressive decline in ferritin and hematological indices across categories supports the concept that iron deficiency should be interpreted as a spectrum, where earlier biochemical abnormalities may still carry functional consequences for the developing nervous system (14).

The results are consistent with several previous clinical observations reporting lower hemoglobin, reduced ferritin, and altered red-cell indices among children presenting with febrile seizures. Studies supporting this association have suggested that iron deficiency may contribute to reduced seizure threshold through impaired neurotransmitter synthesis, altered cerebral oxygenation, and reduced cellular energy production. The present findings extend this literature by focusing not only on the presence of iron deficiency but also on the severity pattern across defined iron-profile categories. The stepwise increase in prolonged seizure frequency from normal iron status to overt iron deficiency anemia strengthens the argument that integrated hematological profiling may provide more clinically informative insight than isolated laboratory markers (15).

At the same time, the findings should be interpreted within the context of a literature base that remains heterogeneous. Some investigations have reported no significant relationship between iron deficiency and febrile seizures, while others have proposed that acute inflammatory states, population differences, nutritional background, and variable diagnostic thresholds may explain conflicting results. Ferritin is especially challenging in febrile children because it functions as an acute-phase reactant and may be transiently elevated during infection or inflammation. This may obscure underlying iron depletion if inflammatory status is not considered. By evaluating broader iron profiles rather than ferritin alone, the present study reduces some of this interpretive limitation, although the retrospective nature of available laboratory data still constrains precise biological interpretation (16).

The clinical implications of these findings are relevant for paediatric emergency and outpatient care. In toddlers presenting with first febrile seizure, the presence of latent or overt iron deficiency may help identify a subgroup with greater likelihood of prolonged seizure duration. This does not establish that iron deficiency causes febrile seizures or independently predicts seizure occurrence in the general febrile toddler population, but it does support closer clinical attention to iron status among children with first

febrile seizure, particularly when nutritional risk indicators are present. Early recognition of iron depletion may also have broader neurodevelopmental value, as iron deficiency in infancy and toddlerhood has been associated with adverse effects on cognitive, behavioral, and motor development beyond seizure-related outcomes (13).

The study has several methodological strengths. Consecutive inclusion of eligible cases over a defined three-year review period reduced selection bias and improved the representativeness of the clinical sample. Restricting the cohort to first febrile seizure presentations minimized confounding from recurrent febrile seizures, established epilepsy, chronic neurological disease, and prior seizure-related management. The use of structured data abstraction, independent review by trained paediatric research reviewers, and exclusion of records with incomplete hematological or ambiguous seizure documentation strengthened internal consistency. Adjustment for relevant clinical confounders, including age, sex, nutritional status, family history, and fever severity, further improved the interpretability of the observed association between iron profiles and prolonged seizure duration (14).

Several limitations should also be acknowledged. The retrospective design depended on the completeness and accuracy of existing clinical records, including caregiver-reported seizure duration, which may be vulnerable to recall imprecision during emergency presentations. The absence of a febrile non-seizure control group limits inference regarding whether iron deficiency increases the risk of developing a first febrile seizure; the findings are more appropriately interpreted as evidence of association with seizure duration among children who already presented with a first febrile seizure. Ferritin interpretation may also have been affected by acute febrile or inflammatory illness, even when interpreted alongside available clinical information. In addition, the study was conducted in tertiary care hospitals in Central Punjab, which may limit generalizability to rural settings, primary-care populations, or regions with different nutritional and healthcare profiles (17).

Future research should build on these findings through prospective multicentre cohort designs that include both febrile seizure cases and febrile controls without seizures. Such designs would allow clearer distinction between factors associated with seizure occurrence and factors associated with seizure severity. Serial measurement of iron indices before, during, and after febrile illness would help clarify the influence of acute inflammation on ferritin and other iron markers. Incorporating inflammatory biomarkers, dietary assessment, anthropometry, and neurodevelopmental follow-up may also help define whether iron deficiency contributes to a broader vulnerability phenotype in early childhood. Interventional studies evaluating whether correction of latent iron deficiency reduces prolonged febrile seizure presentation or improves broader neurological outcomes would provide clinically actionable evidence (18).

Overall, the findings indicate that worsening iron deficiency profiles are associated with progressively more severe first febrile seizure presentation in toddlers, particularly as reflected by seizure duration exceeding five minutes. The association observed for latent iron deficiency is especially important because it suggests that subtle iron depletion may have neurological relevance before the development of overt anemia. While causal inference remains limited by the retrospective design and lack of a febrile non-seizure comparator group, the study supports the clinical value of considering iron status as part of the broader evaluation of toddlers presenting with first febrile seizure.

CONCLUSION

This retrospective analytical study demonstrated that worsening iron deficiency profiles were associated with progressively more severe first febrile seizure presentation among toddlers aged 6–36 months. Children with latent iron deficiency and overt iron deficiency anemia showed higher mean seizure duration and greater frequency of seizures lasting longer than five minutes compared with children who had normal iron status, with the strongest association observed in the iron deficiency anemia group. These findings indicate that iron depletion may have clinical relevance beyond overt anemia and that

earlier stages of deficiency may also be linked with neurological vulnerability during febrile illness. Although the retrospective design does not establish causality or determine the risk of developing a first febrile seizure, the observed gradient supports the importance of considering iron status in toddlers presenting with first febrile seizure, particularly when nutritional risk indicators are present. Further prospective studies with febrile non-seizure controls are needed to clarify temporal relationships, validate these associations, and determine whether early correction of iron deficiency can reduce prolonged febrile seizure presentation.

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