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Risk Factors Associated with First Episode of Simple Febrile Seizures in Children Aged 6 Months to 5 Years

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Abstract

Background: Febrile seizures are among the most common neurological events encountered in children between 6 months and 5 years of age. Although simple febrile seizures are generally benign, identification of factors associated with their first occurrence is important for recognizing susceptible children and providing appropriate counseling to parents. Various genetic, environmental, perinatal, and nutritional factors have been implicated in their occurrence.

Aim: To identify the risk factors associated with the first episode of simple febrile seizures in children aged 6 months to 5 years.

Materials and Methods: This observational cross-sectional study included 60 children aged 6 months to 5 years, comprising 30 children presenting with their first episode of simple febrile seizure (cases) and 30 febrile children without seizures (controls).

Detailed demographic and clinical histories were obtained. Potential risk factors including prematurity, prolonged NICU stay, neonatal problems, daycare attendance, family history of febrile and a febrile seizure, developmental milestones, and anthropometric parameters were assessed. Laboratory investigations included haemoglobin, serum iron, serum ferritin, total iron-binding capacity (TIBC), random blood sugar,

serum calcium, sodium, and potassium. Appropriate statistical analysis was performed to compare the two groups.

Results: The mean age was 37.07 ± 12.10 months among cases and 38.47 ± 13.58 months among controls. Daycare attendance was significantly more frequent among cases (43.3%) than controls (16.7%), with p = 0.02. A positive family history of febrile seizures was also significantly associated with cases (50.0%) compared with controls (26.7%), with p = 0.03.

Prematurity was more frequent among cases (36.7%) than controls (16.7%), although the association did not reach statistical significance (p = 0.08). Serum iron levels were lower among cases (52.1 ± 26.4 µg/dL) than controls (68.7 ± 27.9 µg/dL), but the difference was not statistically significant (p = 0.20). No significant differences were observed in developmental milestones, anthropometric parameters, haemoglobin, serum ferritin, TIBC, random blood sugar, serum calcium, or potassium. Serum sodium was slightly lower among cases but did not reach statistical significance (p = 0.07).

Conclusion: Daycare attendance and a positive family history of febrile seizures were significantly associated with the first episode of simple febrile seizures in children aged 6 months to 5 years. Prematurity, lower serum iron, and lower serum sodium showed possible associations but did not attain statistical significance. Recognition of these factors may facilitate identification of children at increased risk and enable appropriate parental counseling and clinical monitoring.

Keywords: Simple febrile seizure; Febrile seizures; Risk factors; Daycare attendance; Family history; Prematurity; Iron deficiency; Children.

Introduction

Febrile seizures are among the most common neurological disorders encountered in infancy and early childhood and are a frequent cause of seizure-related emergency visits in children[1]. They usually occur in association with fever in children without evidence of intracranial infection, metabolic disturbance, or a previous history of a febrile seizures.

Although generally benign and self-limiting, febrile seizures often cause considerable anxiety among parents regarding recurrence, epilepsy, and possible neurological consequences [2,3]. The American Academy of Pediatrics defines a febrile seizure as a seizure occurring in a febrile child between 6 and 60 months of age without intracranial infection, metabolic disturbance, or a previous history of a febrile seizure [4]. Febrile seizures are strongly age - dependent, with most episodes occurring during early childhood[3,5]. They affect approximately 2–5% of children in Western populations, although their prevalence varies geographically and among different ethnic groups [2,6,7]. Approximately one-third of affected children may experience recurrence after the first episode [3,8]. Febrile seizures are classified as simple or complex. A simple febrile seizure is generalized, lasts for less than 15 minutes, and does not recur within 24 hours during the same febrile illness [4,9]. In contrast, complex febrile seizures may have focal features, persist for 15 minutes or longer, or recur within 24 hours. Simple febrile seizures constitute the majority of cases and generally have an excellent neurological prognosis [9,10]. The pathogenesis of febrile seizures is multi factorial and involves an interaction between age - dependent neuronal susceptibility, fever, genetic pre disposition, inflammatory responses, and environmental factors[11].

The immature brain has greater neuronal excitability and a relatively lower seizure threshold. Fever and inflammatory cytokines, particularly interleukin - 1β, may further enhance neuronal excitability and precipitate seizures in susceptible children [12-14].

Genetic predisposition is an important risk factor for febrile seizures. Familial clustering and twin studies support a strong genetic contribution, and children with a positive family history of febrile seizures have an increased susceptibility [15]. Several genetic loci and abnormalities involving neuronal ion channels and neurotransmitter pathways have been implicated [15,16]. Although febrile seizures and epilepsy are distinct conditions, the subsequent risk of epilepsy may be greater in children with complex febrile seizures, developmental abnormalities, or a family history of epilepsy[8,17].

Various perinatal factors**,** including prematurity and neonatal complications, have also been investigated as possible risk factors[18,19]. Premature infants may experience altered neurological maturation and greater exposure to neonatal illnesses, metabolic abnormalities, infections, and intensive care. Similarly, prolonged NICU stay may reflect significant neonatal morbidity that could potentially influence neurological susceptibility later in childhood.

Environmental factors may also contribute to febrile seizure occurrence. Day care attendance increases children's exposure to respiratory and gastrointestinal infections because of close contact with other children [20]. Consequently, day care attendees may experience more frequent febrile illnesses, potentially increasing the opportunity for febrile seizures to occur in susceptible children [20,21].

Iron deficiency has received particular attention as a possible risk factor. Iron is essential for normal neurological development, neurotransmitter metabolism, myelination, and neuronal energy metabolism[22]. Deficiency during early childhood may alter neuronal excitability and potentially reduce the seizure threshold [23]. Several studies have reported lower haemoglobin, serum iron, or serum ferritin levels among children with febrile seizures [23-25], while systematic reviews have suggested a possible association between iron deficiency anaemia and febrile seizures [26]. However, findings remain inconsistent across different populations. Electrolytes such as sodium and calcium are also important in maintaining normal neuronal activity. Significant electrolyte disturbances can themselves precipitate seizures [27]. Mild reductions in serum sodium have been reported in children with febrile seizures and have also been investigated in relation to seizure recurrence [28]. Evaluation of a child presenting with a first simple febrile seizure should primarily focus on identifying the cause of fever and excluding central nervous system infection or other serious underlying disorders [4,29]. A detailed history regarding seizure characteristics, fever, developmental milestones, perinatal events, day care exposure, and family history of febrile or a febrile seizure is essential. Routine EEG, neuro imaging, or extensive investigations are generally unnecessary in a neurologically healthy child with a typical simple febrile seizure, while lumbar puncture should be considered when intracranial infection is clinically suspected [4,29,30]. Despite their generally favourable prognosis, febrile seizures remain a major source of parental anxiety. Identification of factors associated with the first episode of simple febrile seizure may help recognize susceptible children and facilitate

appropriate parental counselling. Therefore, the present study was undertaken to evaluate the association of prematurity, prolonged NICU stay, day care attendance, family history of febrile and a febrile seizure in first-degree relatives, and iron deficiency with the first episode of simple febrile seizures among children aged 6 months to 5 years**.**

Materials and Methods

Study Design and Study Population

The present study was an case control study conducted among children aged 6 months to 5 years presenting to a tertiary care hospital. The study was undertaken to identify various risk factors associated with **the** first episode of simple febrile seizures**.** A total of 60 children were included and divided equally into two groups. The case group comprised 30 children presenting with their first episode of simple febrile seizure, while the control group comprised 30 children presenting with fever without seizures.

Clinical Assessment

A detailed history was obtained from the parents or caregivers of all participants. Demographic information, including age and gender, was recorded. Particular attention was given to potential risk factors such as prematurity, prolonged NICU stay, neonatal problems, day care attendance, family history of febrile seizures, family history of a febrile seizures in first-degree relatives, and iron deficiency. The clinical presentation of the child was documented, including fever and seizure - associated manifestations. Developmental milestones were assessed under gross motor, fine motor, social, and linguistic domains.

Physical Examination

All participants underwent a detailed general physical and systemic examination. Anthropometric parameters, including height, weight, and head circumference, were recorded. Vital parameters such as heart rate**,** systolic and diastolic blood pressure, respiratory rate**,** and body temperature were also documented.

Results

Table 1: Distribution of Study Population According to Study Groups.

Group	Number	Percentage
Simple Febrile Seizure (Cases)	30	50%
Febrile without Seizure (Controls)	30	50%
Total	60	100%

The study population consisted of a total of 60 participants, equally divided between the two groups. Among them, 30 participants (50%) were categorized under the simple febrile seizure group (cases), while the remaining 30 participants (50%) were included in the fever without seizure group (controls). This equal distribution ensured comparability between the groups.

Table 2: Socio-Demographic Profile of Study Participants.

Variables	Cases (n=30)	Controls(n=30)
Age (months)	37.07±12.10	38.47±13.58
Gender		
Male	16(53.3%)	18(60.0%)
Female	14(46.7%)	12(40.0%)

The mean age of participants in the case group was 37.07±12.10 months, while in the control group it was 38.47±13.58 months, indicating comparable age distribution. In terms of gender, males constituted 53.3% (16 participants) in the case group and 60.0% (18 participants) in the control group, whereas females accounted for 46.7% (14 participants) in cases and 40.0% (12 participants) in controls.

Table 3: Comparison of Perinatal Risk Factors Between Cases and Controls.

Variables	Cases(n=30)	Controls(n=30)	p-value
Gestational Age			
Preterm	11(36.7%)	5(16.7%)	0.08
Term	19(63.3%)	25(83.3%)	
Prolonged NICU Stay			
Present	9(30.0%)	11(36.7%)	0.58
Absent	21(70.0%)	19(63.3%)	
Neonatal Problems			
Jaundice	5(16.7%)	5(16.7%)	0.79
TTNB (Transient Tachypnea)	3(10.0%)	0(0.0%)	
Me conium-stained liquor	6(20.0%)	5(16.7%)	
Respiratory Distress	0(0.0%)	1(3.3%)	
Growing Preterm	0(0.0%)	1(3.3%)	
Total Present	14(46.7%)	12(40.0%)	

Preterm birth was observed in 36.7% of cases compared to16.7 % of controls, while term births were seen in 63.3% and 83.3%respectively (p =0.08). Prolonged NICU stay was present in 30.0% of cases and 36.7% of controls (p = 0.58). Neonatal problems were reported in 43.3% of cases and 40.0% of controls, with jaundice being the most common in both groups (16.7% each). Other conditions included transient Tachypnea (10.0% in cases), me conium-stained liquor (20.0% in cases and 16.7% in controls), and isolated cases of respiratory distress and growing preterm in controls. No statistically significant differences were observed.

Table 4: Distribution of Chief Complaints Among Study Groups.

Chief Complaint	Cases(n=30)	Controls(n=30)	Total(n=60)
Fever	30(100%)	30(100%)	60(100%)
Clenching of teeth	20(66.7%)	0(0.0%)	20(33.3%)
Uncontrolled body movements	30(100%)	0(0.0%)	30(50.0%)
Frothing from mouth	12(40.0%)	0(0.0%)	12(20.0%)

Fever was present in all participants (100%) in both groups. Clenching of teeth was reported in 66.7% of cases but absent in controls. Uncontrolled body movements were observed in all cases (100%) and none of the controls, while frothing from the mouth was present in 40.0% of cases and absent in controls. These findings highlight seizure-specific symptoms exclusively in the case group.

Table 5: History of Present Illness Among Study Groups.

Variable	Cases(n=30)	Controls(n=30)	p-value
Daycare Attendance			
Present	13(43.3%)	5(16.7%)	0.02
Absent	17(56.7%)	25(83.3%)	
Family History (Febrile Seizures)			
Present	15(50.0%)	8(26.7%)	0.03
Absent	15(50.0%)	22(73.3%)	
Family History (A febrile Seizures)			
Present	5(16.7%)	6(20.0%)	0.74
Absent	25(83.3%)	24(80.0%)	

Table 6: Comparison of Developmental Milestones between Cases and Controls.

Developmental Domain	Cases(n=30)	Controls(n=30)
Gross Motor		
Normal	30(100%)	30(100%)
Delayed	0(0.0%)	0(0.0%)
Fine Motor		
Normal	30(100%)	30(100%)
Delayed	0(0.0%)	0(0.0%)
Social		
Normal	30(100%)	30(100%)
Delayed	0(0.0%)	0(0.0%)
Linguistic		
Normal	30(100%)	30(100%)
Delayed	0(0.0%)	0(0.0%)

Developmental milestones were normal in both groups across all domains. No delays were observed in gross motor, fine motor, social, or linguistic development. All participants in both groups demonstrated normal developmental milestones, indicating no significant differences between the groups.

Table 7: Anthropometric Profile of Study Participants

Parameter	Cases(n=30) Mean±SD	Controls(n=30) Mean±SD	p-value
Height(cm)	94.9±8.5	93.5±7.8	0.52
Weight(kg)	13.7±3.1	13.9±3.5	0.81
Head Circumference (cm)	50.1±1.8	49.6±1.6	0.27

The mean height was 94.9 ± 8.5 cm in cases and 93.5 ± 7.8 cm in controls (p = 0.52). Mean weight was 13.7 ± 3.1 kg in cases and 13.9±3.5 kg in controls (p=0.81). Head circumference was 50.1 ± 1.8 cm in cases and 49.6 ± 1.6 cm in controls (p = 0.27). No statistically significant differences were observed in anthropometric parameters.

Table 8: Comparison of Vital Parameters Between Study Groups.

Parameter	Cases (n = 30) Mean ± SD	Controls (n = 30)Mean ± SD	p-value
Heart Rate (per minute)	114.7 ± 10.8	130.9 ± 15.2	<0.001
Blood Pressure (mmHg)			
SBP	94.3 ± 4.5	94.1 ± 2.8	0.84
DBP	60.6 ± 4.2	59.8 ± 6.8	0.59
Respiratory Rate (per minute)	25.6 ± 2.8	28.7 ± 6.4	0.02
Temperature (°F)	101.6 ± 0.9	101.8 ± 1.0	0.42

The mean heart rate was lower in cases (114.7 ± 10.8/min) compared to controls (130.9 ± 15.2/min). Systolic blood pressure was comparable between cases (94.3 ± 4.5 mmHg) and controls(94.1±2.8mmHg), while diastolic blood pressure was 60.6±4.2mm Hg in cases and59.8±6.8 mm Hg in controls.

Respiratory rate was slightly lower in cases (25.6± 2.8/min) than controls (28.7±6.4/min). Mean temperature was similar in both groups (101.6°F in cases and 101.8°F in controls).

Table 9: General Physical Examination Findings Among Study Groups.

Clinical Finding	Cases (n = 30)	Controls (n = 30)	p-value
Pallor	15 (50.0%)	11 (36.7%)	0.43
Lymphadenopathy	5 (16.7%)	2 (6.7%)	0.42
Icterus	0 (0.0%)	0 (0.0%)	1.00
Cyanosis	0 (0.0%)	0 (0.0%)	1.00

Pallor was observed in 50.0% of cases and 36.7% of controls. Lymphadenopathy was noted in 16.7 % of cases and 6.7 % of controls. No cases of icterus or cyanosis were reported in either group.

Table 10: Comparison of Central Nervous System Examination Findings Between Study Groups

CNS Parameter	Cases (n = 30)	Controls (n = 30)	p-value
Level of Consciousness			0.01
Alert	23 (76.7%)	30 (100%)	
Drowsy	7 (23.3%)	0 (0%)	
Cranial Nerves			1.00
Normal	30 (100%)	30 (100%)	
Abnormal	0	0	
Motor Examination			1.00
Normal	30 (100%)	30 (100%)	
Abnormal	0	0	
Reflexes (Superficial)			1.00
Normal	30 (100%)	30 (100%)	
Abnormal	0	0	
Reflexes (Deep)			1.00
Normal	30 (100%)	30 (100%)	
Abnormal	0	0	
Signs of Meningeal Irritation			1.00
Present	0	0	
Absent	30 (100%)	30 (100%)	

Table 11: Comparison of Iron Profile and Random Blood Sugar Between Study Groups.

Parameter	Cases (n = 30) Mean ± SD	Controls (n = 30) Mean ± SD	p-value
Haemoglobin(g/dL)	10.6 ± 1.5	10.9 ± 1.7	0.46
Serum Iron(µg/dL)	52.1 ± 26.4	68.7 ± 27.9	0.20
Serum Ferritin (ng/mL)	27.5 ± 16.8	29.8 ± 17.9	0.59
TIBC(µg/dL)	340.8 ± 61.5	338.9 ± 73.2	0.91
Random Blood Sugar (mg/dL)	107.4 ± 23.1	112.6 ± 24.8	0.41

Most participants in the case group were alert (76.7%), while 23.3%were drowsy.

All controls (100%) were alert. Cranial nerve examination, motor system, and reflexes (both superficial and deep) were normal in all participants across both groups. No signs of meningeal irritation were observed in any participant.

Table11: Comparison of Iron Profile and Random Blood Sugar Between Study Groups.

Parameter	Cases(n=30) Mean±SD	Controls(n=30) Mean±SD	p-value
Haemoglobin(g/dL)	10.6±1.5	10.9±1.7	0.46

Serum Iron(µg/dL)	52.1±26.4	68.7±27.9	0.20
Serum Ferritin (ng/mL)	27.5±16.8	29.8±17.9	0.59
TIBC(µg/dL)	340.8±61.5	338.9±73.2	0.91
Random Blood Sugar (mg/dL)	107.4±23.1	112.6±24.8	0.41

Mean hemoglobin levels were 10.6 ± 1.5g/ dL incases and 10.9±1.7g/dL in controls (p= 0.46). Serum iron levels were lower in cases (52.1±26.4µg/dL) compared to controls (68.7 ±27.9µg/dL), though not statistically significant (p=0.20). Serum Ferr it in, TIBC, and random blood sugar levels were comparable between groups, with no significant differences observed.

Table 12: Comparison of Serum Electrolytes Between Study Groups

Parameter	Cases (n=30) Mean ± SD	Controls (n=30) Mean ± SD	p-value
Serum Calcium (mg/dL)	9.53±0.57	9.57±0.63	0.78
Serum Sodium (mEq/L)	136.3±2.1	138.6±5.8	0.07
Serum Potassium (mEq/L)	4.05±0.49	4.22±0.52	0.19

Serum calcium levels were similar in both groups (9.53±0.57mg/dL in cases and 9.57± 0.63 mg/dL in controls; p = 0.78). Serum sodium was slightly lower in cases (136.3 ± 2.1 mEq/L) compared to controls (138.6 ± 5.8 mEq/L), approaching statistical significance (p = 0.07). Serum potassium levels were comparable between cases (4.05 ± 0.49 mEq/L) and controls (4.22 ± 0.52 mEq/L) (p = 0.19).

Table 13: Distribution of Special Investigations Among Study Groups

Investigation	Cases(n=30)	Controls(n=30)
EEG		
Not Indicated	30(100%)	30(100%)
Abnormal	0	0
CSF Analysis		
Not Indicated	30(100%)	30(100%)
Abnormal	0	0
Neuro imaging		
Not Indicated	30(100%)	30(100%)
Abnormal	0	0

Figure 1: Bar graph representing comparison of CSF analysis between cases and controls

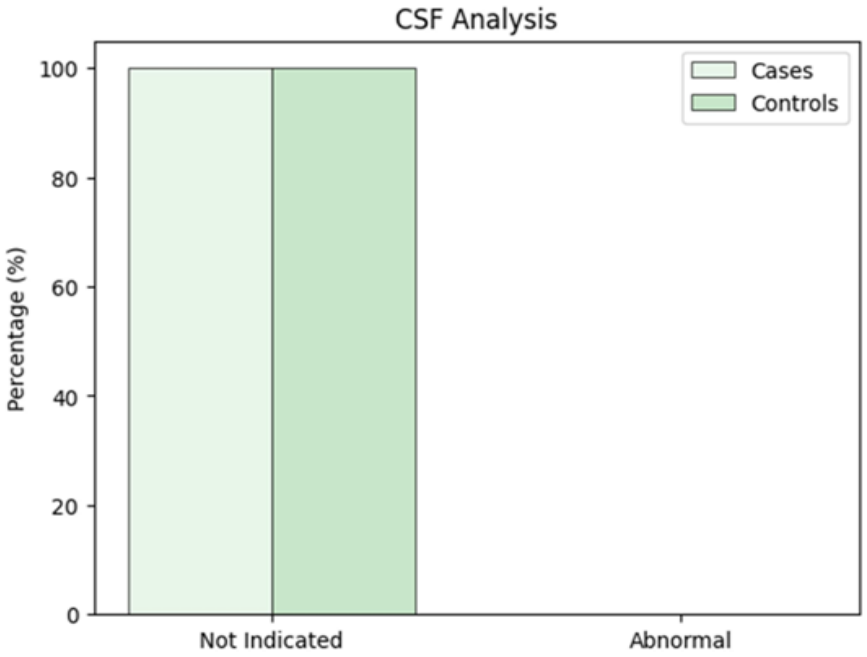
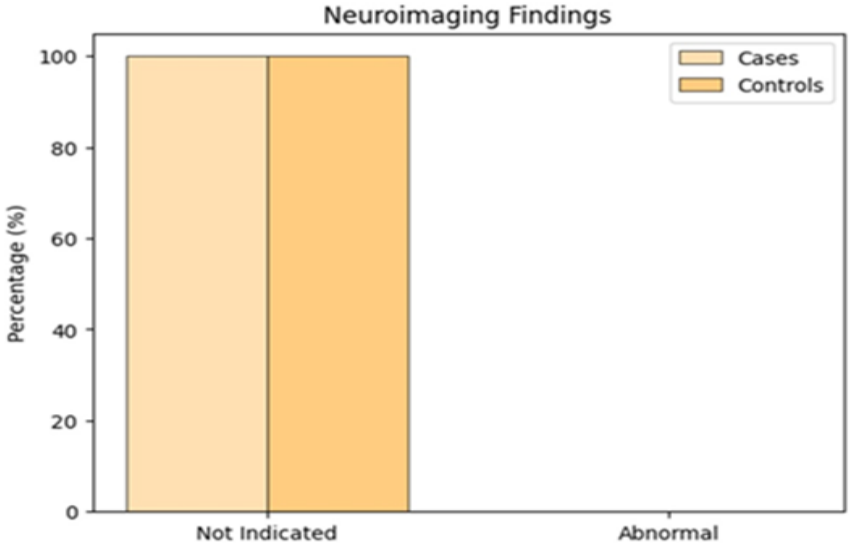


Figure 2: Bar graph representing comparison of neuro imaging findings between cases and controls.



Special investigations including EEG, CSF analysis, and neuro imaging were not indicated in any of the participants in either group. No abnormal findings were reported in any of these investigations.

Discussion

Febrile seizures are among the most common seizure disorders encountered during early childhood. Although simple febrile seizures generally have a favourable prognosis, identification of factors predisposing a child to the first episode is clinically important. The present study evaluated various demographic, perinatal, environmental, familial, developmental, anthropometric, and biochemical factors associated with the first episode of simple febrile seizures among children aged 6 months to 5 years. The present study included 60 children**,** comprising 30 cases with the first episode of simple febrile seizure and 30 febrile controls without seizures**.** The principal findings demonstrated that day care

attendance and a positive family history of febrile seizures were significantly associated with the occurrence of simple febrile seizures. Prematurity was more frequent among cases, while serum iron and serum sodium levels were comparatively lower among cases; however, these differences did not reach statistical significance. Other evaluated parameters, including prolonged NICU stay, family history of a febrile seizures, developmental milestones, anthropometric measurements, and most biochemical parameters, did not demonstrate significant associations.

Age and Gender Distribution

The mean age of children presenting with simple febrile seizures was 37.07 ± 12.10 months, compared with 38.47 ± 13.58 months among febrile controls. Thus, both groups were comparable with respect to age. This age distribution falls within the well-established period of susceptibility to febrile seizures, which predominantly occur between 6 months and 5 years of age [1-4].

The increased susceptibility of younger children to febrile seizures has been attributed to developmental characteristics of the immature brain. During early childhood, neuronal networks demonstrate increased excitability, while inhibitory mechanisms are still undergoing maturation. Fever and inflammatory mediators may further reduce the seizure threshold in genetically susceptible children [5,6].

A slight male predominance was observed in both groups. Among cases, 53.3% were males and 46.7% were females, while among controls, 60.0% were males and 40.0% were females. Previous studies have also reported a mild male predominance among children with febrile seizures, although gender is generally not considered a major independent determinant of febrile seizure occurrence [1,7].

Prematurity

Prematurity was observed in 36.7% of cases compared with 16.7% of controls. Although the proportion was more than twice as high among cases, the association did not attain conventional statistical significance (p=0.08). This finding suggests that prematurity may have a possible contributory role in susceptibility to febrile seizures, but the present study did not establish it as a statistically significant independent risk factor. Vestergaard et al. evaluated several prenatal and perinatal determinants of febrile seizures and demonstrated that factors surrounding pregnancy and birth may influence subsequent susceptibility to febrile convulsions [18].

Premature infants may experience alterations in neurological maturation and are more frequently exposed to neonatal illnesses, metabolic disturbances, respiratory problems, infections, and intensive care. Such factors may potentially influence subsequent neuronal excitability. However, the absence of statistical significance in the present study indicates that larger studies would be required to clarify the relationship between prematurity and the first episode of simple febrile seizure.

Prolonged NICU Stay and Neonatal Problems

A history of prolonged NICU stay was present in 30.0% of cases and 36.7% of controls, and the difference was not statistically significant (p=0.58). Similarly, neonatal problems were reported in 43.3% of cases and 40.0% of controls (p=0.79). The neonatal problems documented included jaundice, transient Tachypnea of the newborn, me conium-stained liquor, respiratory distress, and problems associated with prematurity. The relatively similar frequency of these conditions between the two groups suggests that, in the present population, neonatal

morbidity and NICU admission were not independently associated with the first occurrence of simple febrile seizures.

These findings are important because a history of NICU admission may initially raise concern regarding neurological vulnerability. However, the present results suggest that prolonged NICU stay by itself may not necessarily predispose a child to simple febrile seizures in the absence of significant neurological injury or developmental abnormalities.

Clinical Presentation

Fever was present in 100% of both cases and controls, which was expected because the study specifically compared children with febrile seizures with febrile children without seizures. Among cases, uncontrolled body movements were reported in all children, clenching of teeth in 66.7%, and frothing from the mouth in 40.0%. These manifestations were absent among controls and represented clinical features accompanying the seizure episode.

The presence of fever in both groups is particularly relevant to the study design because it allows potential risk factors for seizure occurrence to be evaluated among children experiencing a febrile illness, rather than simply comparing febrile children with healthy children.

Daycare Attendance

One of the most important findings of the present study was the significant association between day care attendance and simple febrile seizures. Day care attendance was reported in 43.3% of cases compared with only 16.7% of controls, and the difference was statistically significant (p=0.02).

Children attending day care are exposed to close contact with other young children and may consequently experience a higher frequency of respiratory and gastrointestinal infections [9,10]. Since febrile illnesses represent the immediate setting in which febrile seizures occur, repeated exposure to infectious illnesses may increase the frequency of febrile episodes and thereby increase opportunities for a febrile seizure to occur in a susceptible child.

However, day-care attendance should not necessarily be inter preted as a direct biological cause of febrile seizures. Rather, it may represent an environmental factor associated with greater exposure to infectious agents and febrile illnesses. Genetic susceptibility and age-dependent neuronal excitability are likely to determine which children ultimately experience seizures during these illnesses. The statistically significant association observed in the present study therefore highlights the potential importance of environmental exposure in addition to intrinsic susceptibility.

Family History of Febrile Seizures

A positive family history of febrile seizures emerged as another significant finding. It was present in 50.0% of cases compared with 26.7% of controls, with a statistically significant difference (p=0.03).

This finding supports the well-established role of genetic susceptibility in febrile seizures. Familial aggregation has been repeatedly demonstrated, and children with affected first-degree relatives have an increased susceptibility to febrile seizures[11,12]. Genetic studies have suggested considerable heterogeneity in febrile seizure susceptibility. Multiple genetic loci and genes involved in neuronal ion channels and neurotransmission have been implicated, indicating that the genetic basis is complex rather than attributable to a single abnormality [11].

The high proportion of positive family history among cases in the present study reinforces the importance of

obtaining a detailed family history when evaluating a child with a first febrile seizure. It may also assist clinicians in counselling parents regarding familial susceptibility.

Family History of A febrile Seizures

A family history of a febrile seizures was present in 16.7% of cases and 20.0% of controls, with no significant association (p=0.74).

Thus, unlike family history of febrile seizures, family history of a febrile seizures was not associated with the first episode of simple febrile seizure in the present study. This distinction is noteworthy because febrile seizure susceptibility and epilepsy are related but clinically distinct phenomena. Although certain genetic epilepsy syndromes may include fever-sensitive seizures, most children experiencing simple febrile seizures do not subsequently develop epilepsy [13,14].

Developmental Milestones

Developmental assessment demonstrated that all children in both groups had normal gross motor, fine motor, social, and linguistic milestones. No developmental delay was identified.

This finding is consistent with the clinical characteristics expected in simple febrile seizures. Simple febrile seizures generally occur in neurologically healthy children and are not usually associated with pre-existing neurodevelopmental abnormalities [2,3].

Normal neurological development in all cases also supports the clinical classification of the seizure episodes as simple febrile seizures rather than seizures occurring secondary to underlying neurological disease.

Anthropometric Parameters

There were no significant differences in anthropometric parameters between the groups. Mean height was 94.9 ± 8.5 cm among cases and 93.5 ± 7.8 cm among controls (p=0.52). Mean weight was 13.7 ± 3.1 kg and 13.9 ± 3.5 kg, respectively **(**p=0.81), while mean head circumference was 50.1 ± 1.8 cm among cases and 49.6 ± 1.6 cm among controls (p=0.27).

These observations indicate that general physical growth was comparable between children with simple febrile seizures and febrile controls. Therefore, differences in overall growth status did not appear to explain seizure susceptibility in the present study.

General and Neurological Examination

Pallor was observed in 50.0% of cases compared with 36.7% of controls, while lymphadenopathy was observed in 16.7% and 6.7%, respectively. No icterus or cyanosis was detected.

The greater frequency of pallor among cases is of interest because iron deficiency was one of the risk factors specifically evaluated in the study. However, laboratory parameters of iron status did not demonstrate statistically significant differences, and therefore pallor alone cannot be considered evidence of an association between iron deficiency and febrile seizures.

On neurological examination, 76.7% of cases were alert while 23.3% were drowsy, whereas all controls were alert. The transient drowsiness among some cases could reflect the postictal state following the seizure.

Importantly, cranial nerve examination, motor examination, superficial reflexes, and deep tendon reflexes were normal in all children, and no signs of meningeal irritation were detected. These findings are compatible with the diagnosis of simple febrile seizures and provide reassurance against an obvious underlying focal neurological disorder or meningeal involvement.

Iron Status and Febrile Seizures

Iron deficiency has been extensively investigated as a potential risk factor for febrile seizures because iron

plays an important role in neurological development, neurotransmitter metabolism, myelination, and cellular energy metabolism [15].

In the present study, mean haemoglobin was 10.6 ± 1.5 g/dL among cases compared with 10.9 ± 1.7 g/dL among controls, and the difference was not statistically significant (p=0.46).

Mean serum iron was lower among cases (52.1 ± 26.4 µg/dL) compared with controls (68.7 ± 27.9 µg/dL). Although this numerical difference was notable, it was not statistically significant (p=0.20).

Similarly, serum ferritin was 27.5 ± 16.8 ng/mL among cases and 29.8 ± 17.9 ng/mL among controls (p=0.59), while TIBC was 340.8 ± 61.5 µg/dL and 338.9 ± 73.2 µg/dL, respectively (p=0.91)**.**

Previous studies have produced variable findings regarding iron deficiency and febrile seizures. Daoud et al. reported an association between iron status and the first febrile seizure [24]. Annegers JF al. also reported an association between iron deficiency and febrile seizures in childhood [17]. Vestergaard M, Basso O, suggested that iron deficiency may represent a risk factor for first febrile seizure [18].

A systematic review and meta-analysis by Habibian et al. further suggested an association between iron deficiency anaemia and febrile convulsions[26]. However, differences in definitions of iron deficiency, age distribution, nutritional background, inflammatory status, and laboratory cut-off values may explain variations between studies.

The present study therefore demonstrated a trend toward lower serum iron among cases, but the absence of statistical significance prevents a definitive conclusion that iron deficiency was a risk factor in this population.

Random Blood Sugar

Mean random blood sugar was 107.4 ± 23.1 mg/dL in cases and 112.6 ± 24.8 mg/dL in controls, with no statistically significant difference (p=0.41).

This finding indicates that blood glucose levels were comparable between the groups and that significant abnormalities in random blood glucose did not contribute to the observed seizure episodes.

Serum Calcium

Mean serum calcium was 9.53 ± 0.57 mg/dL among cases and 9.57 ± 0.63 mg/dL among controls, with no statistically significant difference (p=0.78).

Calcium plays a fundamental role in neuronal excitability, and significant hypocalcaemia can itself provoke seizures[20].

However, comparable calcium concentrations in the two groups indicate that calcium disturbance was not associated with the simple febrile seizures observed in this study.

Serum Sodium

Mean serum sodium was 136.3 ± 2.1 mEq/L in cases compared with 138.6 ± 5.8 mEq/L in controls. Serum sodium was therefore numerically lower among cases, and the p-value of **0.07** approached but did not reach statistical significance.

Previous investigations have evaluated the relationship between serum sodium and febrile seizures, particularly the possibility that relatively lower concentrations may be associated with recurrence during the same febrile illness [21].

The present finding suggests a possible trend toward lower serum sodium among children with febrile seizures. Nevertheless, because the difference was not statistically significant, serum sodium cannot be

considered an established risk factor based on the present data.

Serum Potassium

Mean serum potassium was 4.05 ± 0.49 mEq/L among cases and 4.22 ± 0.52 mEq/L among controls, with no statistically significant difference **(**p=0.19). Therefore, serum potassium levels were essentially comparable between the groups and did not appear to contribute significantly to seizure occurrence.

Role of Special Neurological Investigations

EEG, CSF examination, and neuro imaging were not indicated in any participant in either study group. This observation is consistent with the general approach to a neurologically healthy child with a typical simple febrile seizure. The American Academy of Pediatrics recommends that routine EEG, neuro imaging, and extensive investigations are generally unnecessary in children presenting with a simple febrile seizure when clinical evaluation does not suggest an intracranial infection or another neurological disorder [22].

The absence of signs of meningeal irritation, focal neurological abnormalities, or persistent neurological deficits in the present cases further supports this conservative investigative approach.

Overall Interpretation of Findings

The present study demonstrates that the occurrence of the first episode of simple febrile seizures is likely influenced by a combination of familial and environmental factors rather than by a single clinical or biochemical abnormality. Among all variables evaluated, day care attendance and a positive family history of febrile seizures emerged as statistically significant factors. Day care attendance may reflect greater exposure to infectious illnesses and consequently more frequent febrile episodes, whereas a positive family history supports an underlying genetic predisposition.

Prematurity was substantially more frequent among cases than controls, although the association did not reach statistical significance. Similarly, serum iron and serum sodium were lower among cases, but these findings remained statistically non-significant. These trends may nevertheless warrant further evaluation in studies with larger sample sizes.

The lack of significant differences in developmental milestones, anthropometric measurements, prolonged NICU stay, family history of a febrile seizures, serum calcium, potassium, haemoglobin, ferritin, and TIBC suggests that these parameters were not major determinants of the first simple febrile seizure within the present study population.

Overall, the findings emphasize the importance of obtaining a detailed family and environmental history when assessing children presenting with their first febrile seizure. Recognition of relevant risk factors can assist clinicians in counselling parents, reducing unnecessary anxiety, and explaining the generally favourable nature of simple febrile seizures.

The results should, however, be interpreted in the context of the relatively small sample of 60 children. Larger prospective and multicentric studies would be useful to further clarify the contribution of prematurity, iron status, serum sodium, daycare exposure, and familial susceptibility to the development of the first episode of simple febrile seizures.

Conclusion

The present study evaluated the risk factors associated with the first episode of simple febrile seizures in children aged 6 months to 5 years. Among the various demographic, perinatal, environmental, familial,

developmental, and biochemical factors assessed, day-care attendance and a positive family history of febrile seizures were found to be significantly associated with the occurrence of simple febrile seizures. Prematurity was more frequently observed among children with febrile seizures, while serum iron and serum sodium levels were comparatively lower in cases than in controls; however, these differences did not reach statistical significance.

Prolonged NICU stay, neonatal problems, family history of a febrile seizure, developmental milestones, anthropometric parameters, and other laboratory parameters showed no significant association with the first episode of simple febrile seizures. The findings highlight the importance of obtaining a detailed family and environmental history when evaluating a child presenting with a first febrile seizure. Identification of susceptible children and appropriate counselling of parents regarding the generally benign nature of simple febrile seizures may help reduce parental anxiety and facilitate appropriate clinical management.

Further studies with larger sample sizes and multicentric populations are recommended to clarify the possible contribution of prematurity, iron deficiency, electrolyte variations, and other potential risk factors to the occurrence of febrile seizures in children.

Limitations

1. The small sample size of 60 participants may limit the generalizability of the findings.
2. Being a single - centre observational study, the results may not represent children from different geographical and socioeconomic populations.
3. Some potential risk factors showed trends but did not reach statistical significance; larger multicentric studies are required to confirm these associations.

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