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Overview of Febrile Seizures in Iranian Children and Related Factors: A 30-Year Review

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Abstract

Background: Febrile seizures (FS) are a common neurological disorder in children. This study aims to review the epidemiological and clinical characteristics associated with FS in Iranian children.

Materials and Methods: In this overview, a search for systematic reviews, reviews, or recent research was conducted across online databases, including Scopus, Web of Science, PubMed, and Google Scholar, up to October 2023. Two reviewers assessed the quality of eligible studies and managed the selection process.

Results: Febrile seizures are a prevalent condition among children, particularly those under five years old globally, affecting 2-5% of this age group. In Iran, studies indicate a moderate prevalence, with specific findings from Zahedan reporting a rate of 3.5% among children. Notably, the incidence of FS among Iranian children experiencing convulsions overall is as high as 47.9%. The age group most affected by FS in Iran is children aged 6 months to 5 years, with a peak incidence observed between 12 and 18 months. The overall recurrence rate of FS is 20.9% (95% CI: 12.3-29.5), with the majority classified as simple febrile seizures (69.3%), while complex febrile seizures account for about 25.3%. The main causes of FS in Iranian children include infectious causes (such as upper respiratory infections and shigellosis), non-infectious factors (including family history), demographic factors (age and gender), and other influences (such as fertility treatments and environmental factors).

Conclusion: The prevalence of febrile seizures among Iranian children remains significant, although recent studies suggest a decline compared to earlier decades. This variation in the prevalence of FS highlights the need for targeted public health strategies and further research to understand their causes and effects on pediatric healthcare.

Key Words: Children, Febrile Seizures, Iran, Prevalence.

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1- INTRODUCTION

Febrile seizures (FS) are convulsive events that occur in infants and children aged six months to five years, triggered by fever without any signs of central nervous system infection. They are the most prevalent neurological disorder within this age group, affecting approximately 2-12% of children (1-5). Febrile seizures are classified into two main categories: simple febrile seizures (SFS), and complex febrile seizures (CFS). Based on some evidence, SFS are typically brief, lasting less than 10 minutes, and do not recur within 24 hours (6). They occur in 2-5% of children aged 6-60 months, are generally self-limiting, and resolve without intervention (7-9). However, CFS are less common, accounting for about 18% of all febrile seizures. CFS is characterized by prolonged duration (greater than 15 minutes), and the potential for recurrence (10, 11). The International League Against Epilepsy (ILAE) has established specific criteria for defining seizure events in infants and children, particularly in relation to febrile seizures. According to their guidelines, seizure events in this demographic should be characterized by:

- **Fever**: The presence of an elevated body temperature, specifically above 38°C.
- **Absence of acute conditions**: There must be no evidence of acute electrolyte imbalances or central nervous system (CNS) infections.
- **History of febrile seizures**: The individual should not have a prior history of febrile seizures (12, 13).

As defined by the American Academy of Pediatrics (AAP), a febrile seizure occurs in conjunction with a fever of at least 100.4°F (38°C) without any central nervous system infection. These seizures typically manifest during the initial hours of a fever and are often brief, lasting less than five minutes; however, they can occasionally extend longer (14, 15). Previous studies indicate that the prevalence of febrile seizures varies across different regions of Iran. A study conducted in Zahedan found a prevalence of 3.5% among 600 children under seven years of age (12). In Tehran, the prevalence rates varied across different studies, with some reporting rates around 57% for specific age groups, indicating a higher incidence compared to Zahedan. A large-scale meta-analysis found that the prevalence of FS was approximately 47.9% compared to other childhood seizures, with significant geographical variation (central Iran: 40%, east: 59.4%, west: 57.5%) consistent with findings from other major urban areas (13). Additionally, a meta-analysis indicated a recurrence rate of about 20.9% among Iranian children (16).

Febrile seizures in Iranian children present a complex landscape characterized by varying prevalence rates and associated factors. While ongoing research continues to clarify these aspects, there remains a critical need for consolidated studies that can streamline findings and enhance clinical practices. By synthesizing existing data, future research can facilitate the development of improved health policies aimed at effectively managing this common pediatric condition. This study aimed to review the epidemiological and clinical characteristics of febrile seizures in Iranian children, focusing on prevalence, recurrence rates, demographic trends, and underlying triggers. By synthesizing existing data, future research can facilitate the development of improved health policies aimed at effectively managing this common pediatric condition.

2- MATERIALS AND METHODS

This overview encompasses all reviews, systematic reviews, and meta-

analyses, along with current original research written in Persian or English that report on febrile seizures and their associated factors among Iranian children. We searched the electronic databases of Scopus, EMBASE, Web of Science, PubMed, CIVILICA, SID, CINAHL, and the Google Scholar search engine for articles available in full text with no time restrictions up to October 10, 2023. Two independent researchers conducted the search process, with a supervisor resolving any discrepancies. The search terms included "fever," "febrile seizure," "febrile convulsions," "pediatrics," "children," "prevalence," "clinical features," and "Iran," utilizing the Boolean operators 'AND' and 'OR.'

The methodological quality of each systematic review was evaluated using the Assessment of Multiple Systematic Reviews (AMSTAR-2) instrument. AMSTAR-2 is a critical appraisal tool specifically designed to assess the methodological quality of systematic reviews (SRs) and meta-analyses (MAs) of healthcare interventions. This tool includes a total of 16 items, with seven items identified as essential for evaluating high-quality reviews. Each item is answered with “yes,” “partial yes,” “no,” or “no meta-analysis conducted.” Studies are categorized based on the number of “yes” answers they receive:

- **High quality:** Studies with ≥13 “yes” answers,
- **Moderate quality:** Studies with 9–12 “yes” answers,
- **Low quality:** Studies with 5–8 “yes” answers, and
- **Critically low quality:** Studies with ≤4 “yes” answers (17-19).

In addition, the quality of the original articles was evaluated using the modified STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist. This checklist consists of 11 items, with each item worth one point. Final scores range from zero to 11, categorizing studies into three quality levels: high quality (8-11), average quality (4-7), and poor quality (0-3) based on their scores (20).

Approval from a research ethics committee was not necessary, as the study analyzed only publicly available articles. The research adhered to ethical standards by respecting copyright laws and ensuring transparency in methods and sources.

3- RESULTS

A total of eight relevant studies were selected for analysis. The systematic review and meta-analysis cover the years from 1996 to 2012, while the original studies provide insights up to 2020. All articles included in the selection were assessed as moderate to high quality. Based on the review of existing literature, the incidence ranges from 3.5% to 47.9%, depending on the population and methodology. The main characteristics and quality assessments of the included articles are summarized in **Table 1** and in the following sections:

3-1. Overview of Systematic Reviews and Meta-Analyses (1996-2014)

1. A systematic review and meta-analysis conducted in 2013, which included 21 studies, aimed to assess the frequency of febrile seizure recurrence and evaluate its associated risk factors in Iran. The results indicated that the overall recurrence rate of febrile seizures was 20.9% (95% CI: 12.3-29.5). Simple febrile seizures accounted for 69.3% of cases (95% CI: 59.5-79.0), while complex febrile seizures represented 25.3% (95% CI: 19.6-31.0). Additionally, 28.8% of children with febrile seizures had a positive family history, with a 95% confidence interval ranging from 19.3% to 38.4% (21).

2. A meta-analysis conducted in 2013, which included 21 studies, aimed to provide reliable information about recurrent febrile seizures in Iranian children with febrile seizures. The results indicated that the pooled recurrence rate of FS in Iranian children was 20.9% (95% CI: 12.3-29.5). The incidence of febrile seizures was notably higher in children under 2 years of age (55.8%) compared to those aged 2 to 6 years (44.2%). Simple febrile seizures occurred in 69.3% (95% CI: 59.5-79.0) of cases, while complex febrile seizures accounted for 25.3% (95% CI: 19.6-31.0). Recurrence rates varied by region, with estimates of 25%, 20.8%, and 27.1% reported in central, eastern, and western Iran, respectively. Additionally, a positive family history of febrile seizures was noted in approximately 28.8% (95% CI: 19.3-38.4) of the cases (22).

3. A meta-regression analysis conducted in 2014, which included 21 studies, aimed to provide insights into the epidemiological and clinical characteristics as well as risk factors associated with febrile seizures among Iranian children. The findings revealed that the overall pooled prevalence rate of FS was 47.9% (95% CI: 38.8–59.9%). Among the identified causes, recent upper respiratory infections were the most significant, accounting for 42.3% of cases (95% CI: 37.2%–47.4%). Gastroenteritis was responsible for 21.5% of FS cases (95% CI: 13.6%–29.4%), while otitis media contributed to 15.2% of occurrences (95% CI: 9.8%–20.7%) (23).

4. A systematic review conducted in 2014, which included 28 studies, aimed to identify the influential factors associated with the first febrile seizure among Iranian children. The results indicated that 25-40% of children with febrile seizures had a family history of the condition. The highest incidence of febrile seizures occurred in children aged 6 months to 5 years, peaking around 12 to 18 months. The review highlights that multiple factors contribute to febrile seizures, including trace elements (such as iron and zinc), perinatal complications, a family history of epilepsy, and body temperature during fever episodes (24).

3-2. Overview of Original Research in Iran (2014-2023)

1. A retrospective study conducted in Kerman, Iran, aimed to determine the causes of seizures in children admitted to local hospitals in 2017. The study involved 250 hospitalized children diagnosed with seizures. The results revealed that febrile seizures were the most common cause, accounting for 44% of cases. Contributing factors to febrile seizures included various infections with the following prevalence rates: upper respiratory infections at 43.6%, gastroenteritis at 15.7%, shigellosis at 10.5%, urinary infections at 9.9%, pneumonia at 8.1%, unidentified fevers at 7.8%, otitis media at 3%, and dental abscesses at 1.4% (25).

2. A cross-sectional study aimed to investigate the prevalence of febrile seizures in 600 children under 7 years old in Zahedan, southeast Iran, in 2014. The study found a prevalence of 3.5% for febrile seizures among these children, with no significant differences observed based on age or gender. Among the children with a history of febrile seizures, 9.5% had a positive family history of seizures. Most seizures occurred before one year of age (61.9%), while the remaining occurred after one year in eight patients (38.1%) (11).

3-3. Risk Factors Associated with Fertility Treatments

3-3-1. Maternal Fertility Treatments and the Risk of Febrile Seizures in Children:

1. A cohort study aimed to investigate the association between fertility treatments and the risk of febrile seizures in children born to sub-fertile couples. This study

included over a million live-born children in Denmark from 1996 to 2012 and found that children conceived via any fertility treatment had an 11% increased risk of experiencing febrile seizures compared to naturally conceived children, with a hazard ratio (HR) of 1.11 (95% CI: 1.06-1.16). Children conceived through specific fertility treatments, such as in vitro fertilization (IVF), and intracytoplasmic sperm injection (ICSI), showed even higher risks, with HRs of 1.15 (95% CI: 1.05-1.25) and 1.20 (95% CI: 1.10-1.32), respectively (1). These findings suggest that children conceived through assisted reproductive technologies may face slightly elevated risks of febrile seizures in comparison to their naturally conceived counterparts (26).

3-3-2. Febrile Seizures in Children of Infertile Couples:

1. A secondary study was conducted to explore the relationship between fertility treatments and the incidence of febrile seizures in children born to sub-fertile couples. The findings, derived from an analysis of data from the Danish National Birth Cohort, which included 83,194 live singleton births, indicated that children of sub-fertile couples who underwent hormonal treatment faced a 37% increased risk of experiencing febrile seizures. The research demonstrated that while children of sub-fertile couples generally did not exhibit an increased risk for febrile seizures, those who received hormonal therapy showed a significant rise in risk, with an incidence rate ratio (IRR) of 1.37 (95% CI: 1.14–1.66) compared to children conceived without the aid of infertility treatments (27).

Tabale-1: The general characteristics of included studies (n=8).

Author, Publication year, (Reference)	Study Design	Time	Sample size	Number of studies	Target group	Prevalence	Quality assessment of studies
Veisani et al., 2013, (21)	Systematic review and meta-analysis	Up Feb 2012	4,599 FS children	21	Iranian children	The overall recurrence rate of febrile seizures was 20.9% (95% confidence interval: 12.3–29.5).	*Moderate Quality
Veisani et al., 2013, (22)	Systematic review and meta-analysis	1997-2009	4,599 FS children	21	Iranian children	The recurrent rate of FS in children was found to be 20.9%. Simple FS occurred in 69.3% of cases, while complex FS accounted for 25.3%.	*Moderate Quality
Delpisheh et al., 2014, (23)	Meta-regression analysis	1997-2009	4,599 FS children	21	Iranian children	The overall pooled prevalence rate of FS was found to be 47.9%.	*Moderate Quality
Nasehi et al., 2014, (21)	Systematic review	Up to 2012	--	28	Iranian children	The highest incidence of FS occurs in children aged 6 months to 5 years, with a peak around 12 to 18 months.	*Moderate Quality
Ghaedamini. et al., 2023, (25)	Retrospective study	2017	250	1	Iranian children	Febrile seizures were the most common cause of seizures in the study, accounting for 44% of cases.	**Moderate Quality
Miri Aliabadi et al., 2019, (11)	Cross-sectional study	2014	600	1	Iranian children	The study found a 3.5% prevalence of FS among children, with no significant differences based on age or gender.	**Moderate Quality

Guleria et al., 2020, (26)	Cohort study	1996-2012	1,065,901	1	Danish children	The study found that children conceived through any fertility treatment had an 11% increased risk of experiencing fetal loss (FS), with a hazard ratio (HR) of 1.11 compared to those conceived naturally.	**High Quality
Sun et al., 2007, (27)	Secondary study	1997-2003	83,194	1	Danish children	The study found that children of subfertile couples who underwent hormonal treatment faced a 37% increased risk of experiencing FS.	**High Quality

*Based on the AMSTAR-2 instrument (17) and ** the STROBE checklist (20), FS: Febrile seizures.

4- DISCUSSION

This overview aimed to review the epidemiological and clinical characteristics of febrile seizures in Iranian children. The results indicate that the incidence of febrile seizures (FS) in children ranges from 3.5% to 47.9%, depending on the population studied and the methodology used. The highest incidence of FS occurs in children aged 6 months to 5 years, peaking around 12 to 18 months. The overall recurrence rate of FS is 20.9%, with a significant 69.3% classified as simple FS. Understanding the epidemiology, risk factors, and management strategies for FS is crucial for effective treatment and parental reassurance.

4-1. Prevalence Rate of Febrile Seizures in Iranian Children

In a meta-regression analysis, the prevalence of febrile seizures among Iranian children was reported to be approximately 47.9%, indicating that nearly half of all childhood convulsions in this population are associated with FS (23). Over the past decade, research has highlighted significant regional variations in the prevalence of FS across Iran. For instance, specific populations have reported an incidence as low as 3.5% in Zahedan, while other areas exhibit much higher rates, reaching up to 44% among children aged 1 month to 16 years (11, 26).

4-2. Recurrence Rates of FS in Iran

The recurrence rate of febrile seizures in Iranian children is approximately 20.9%, with a notably higher incidence observed in males and younger children. This statistic is derived from a systematic review and meta-analysis that included data from 21 studies, encompassing a total of 4,599 children with febrile seizures across various regions in Iran (16).

4-3. Types of Febrile Seizures

Most cases in Iranian studies have been classified as simple febrile seizures, accounting for approximately 69.3% of cases. Complex seizures constitute the remaining 25.3% (21, 22). The majority of seizures are generalized (28).

4-4. Prevalence Rates by Region

The prevalence of febrile seizures among children in Iran demonstrates significant regional variation, influenced by factors such as demographics and local health conditions.

- **Zahedan**: A study reported a prevalence of 3.5% among 600 children, indicating a moderate incidence in this southeastern city (11).
- **Tehran**: In Tehran, prevalence rates varied across different studies, with some reporting rates around 57% for specific age groups, highlighting a

higher incidence compared to Zahedan (22).

- **Bandar Abbas**: Research indicated a prevalence of 60%, reflecting a significant occurrence of FS in this southern port city (22).
- **Isfahan**: Similar to Tehran, Isfahan has reported prevalence rates of about 60%, indicating a considerable number of cases (22).
- **Kerman**: Research indicates a prevalence of approximately 59%, emphasizing the impact of this condition in this central region (22).
- **Yazd**: In Yazd, the prevalence of febrile seizures is notably high, with studies indicating that 65% of infants and 30% of children older than one year have recurrences of FS (29). Another study shows prevalence rates ranging from 59% to 63%, suggesting a notable incidence among children in Yazd (23).

Overall, the prevalence of FS varies significantly across Iran, with Bandar Abbas, Yazd, and Isfahan exhibiting the highest rates. These findings emphasize the need for targeted health interventions and further research to understand the underlying causes and epidemiological patterns of FS in different regions of the country.

4-5. Main Causes of Febrile Seizures in Iranian Children

Febrile seizures are a common concern among children in Iran. The primary causes of these seizures can be categorized into infectious and non-infectious factors:

4-5-1. Infectious Causes:

- **Upper Respiratory Infections (URIs):** Upper respiratory infections are the leading cause of febrile seizures, accounting for approximately 42.3% to 43.6% of cases. These infections often lead to fever, which can trigger seizures in susceptible children (23, 26).
- **Gastroenteritis:** Gastroenteritis is another significant contributor, with prevalence rates around 15.7% to 21.5%. This condition can cause fever and dehydration, both of which are risk factors for febrile seizures (23, 25, 30).
- **Shigellosis:** Shigellosis is noted in about 10.5% of cases, particularly among children in developing regions where such infections are more prevalent (25).
- **Urinary Tract Infections (UTIs):** Urinary tract infections account for approximately 9.9% of febrile seizure cases, contributing to the febrile state that can lead to seizures (25).
- **Pneumonia:** Pneumonia is responsible for about 8.1% of cases, highlighting the impact of respiratory illnesses on the incidence of febrile seizures (25).
- **Unidentified Fever:** A notable percentage (approximately 7.8%) of febrile seizures occur without a clearly identifiable cause at the time of diagnosis (25).
- **Other Infections:** Various other infections, such as otitis media (ear infections) and dental abscesses, contribute smaller percentages; otitis accounts for about 3%, and dental issues for about 1.4% (25).

The high incidence of childhood infections leading to complications such as febrile seizures underscores the urgent need for effective public health measures. These measures are critical for managing childhood illnesses and ensuring better health outcomes in pediatric populations (31, 32).

4-5-2. Non-Infectious Factors:

- **Family History**: A positive family history of FS was reported in 28.8%

(95% CI: 19.3–38.4) of cases, while other reviews indicate that this figure ranges from 25% to 40%. This suggests a significant genetic component in the manifestation of these conditions (21, 28, 33).

- **Other Factors**: Several additional factors, including the duration of breastfeeding and body temperature during fever, are likely contributors (23, 34). Furthermore, cesarean delivery has been identified as a risk factor, with children born via cesarean section exhibiting higher odds of experiencing febrile seizures (35).

4-5-3. Demographic Factors:

- **Age:** The highest incidence of febrile seizures occurs in children aged 6 months to 5 years, peaking around the age of two (22, 24, 28).
- **Gender:** Some evidence suggests that gender may play a role in febrile seizures, indicating that boys are more frequently affected than girls (28-30, 34).

4-5-4. Other Contributing Factors:

- **Electrolyte Imbalances**: Electrolyte Imbalances: Electrolyte imbalances can significantly affect neurological function, particularly in relation to seizures. While not a direct cause, disturbances in essential electrolytes such as sodium, calcium, potassium, and selenium can increase the risk of seizures, especially during febrile episodes (16, 36). Evidence suggests that hypokalemia (low potassium levels) is a potential risk factor for febrile seizures, indicating that nutritional status may play a role in seizure susceptibility (37).
- **Environmental Factors**: Urban residency has been linked to higher incidences of febrile seizures, possibly due to increased exposure to infections prevalent in densely populated areas. Other studies have shown that seasonal variations significantly influence the incidence of FS. In Iranian children, increased occurrences are observed during the autumn months. This trend aligns with findings from other studies that demonstrate a higher frequency of FS during winter, which is attributed to the prevalence of febrile illnesses and infections during this season, particularly respiratory infections that peak in the colder months (38-40).
- **Fertility treatments:** Children conceived through various fertility treatments exhibit a modestly elevated risk of fetal syndrome (FS) (26). Furthermore, children born to infertile couples who underwent hormone therapy—whether or not accompanied by intrauterine insemination—also face an increased risk of FS (27).

Understanding these causes is crucial for developing preventive measures and improving health outcomes for children in Iran who are susceptible to febrile seizures.

4-6. Prevalence Rate of FS among Children Worldwide

Febrile seizures (FS) are a prevalent condition among children globally, particularly affecting those under five years of age, with approximately 2-5% of this age group impacted (41-43). In specific regions, such as Japan and Guam, studies have indicated that the prevalence rates for FS can reach 8% to 14% (42). The peak incidence occurs between 12 and 18 months of age (44). These seizures, typically triggered by fever, are influenced by a combination of genetic and environmental factors, including viral infections and vaccinations. Understanding these factors is crucial for clinicians when assessing and managing affected children (45).

Recent studies reveal that the prevalence of FS among Iranian children is moderate,

with specific findings from Zahedan indicating a rate of 3.5% (11). This aligns with global data, where FS prevalence typically ranges from 2% to 5% in children under five years; however, some studies report higher rates in certain populations (41-43). Notably, the incidence of FS among children experiencing convulsions can be as high as 47.9%, highlighting a significant public health concern (23).

5- CONCLUSION

Febrile seizures are a common neurological disorder in children, with varying incidences and characteristics observed in Iranian children compared to global data. This review indicates that the prevalence of FS in Iranian children is high but has decreased compared to previous decades. The literature shows a moderate prevalence of FS, with approximately 3.5% of children in Zahedan affected, while the overall incidence of childhood convulsions is significantly higher at 47.9%. The highest incidence of FS is found in children aged 6 months to 5 years, peaking around 12 to 18 months.

The overall recurrence rate of FS is 20.9%, with the majority classified as simple febrile seizures (69.3%), while complex febrile seizures account for about 25.3%. The main causes of FS in Iranian children include infections (such as upper respiratory infections and shigellosis), non-infectious factors (including family history), demographic factors (age and gender), and other influences (such as fertility treatments and environmental factors). The variation in the prevalence of FS across different regions in Iran underscores the need for targeted public health strategies and further research to understand the underlying causes and implications for pediatric health care.

6- CONFLICT OF INTEREST: None.

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