

## The Effect of Simple Febrile Seizure on Attention Deficit Hyperactivity Disorder (ADHD) in Children

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### Abstract

#### Background

Febrile seizure is one of the most prevalent childhood convulsions. There are controversy about possible relation between febrile seizure and Attention Deficit Hyperactivity Disorder (ADHD). The aim of this study was to find the effect of simple febrile seizure on ADHD in children.

#### Materials and Methods

In a case-control study all children of 3-12 years old with febrile seizure referring Amir-Kabir hospital, Arak-Iran. Among these children, 103 of them with no corporeal or psychiatric disorders were compared to 103 children of the same age and gender admitted due to disease other than febrile seizure utilizing DSM-IV criteria for ADHD. Data were analyzed using SPSS 16.

#### Results

This study shows that the hyperactivity disorder in the same order were 34.3% and 16.7%, respectively, which also denotes a significant relation between simple febrile seizure and hyperactivity ( $P < 0.05$ ). The frequency of consanguineous marriages was 26.2% in parents of children with simple febrile seizure, and 9.7% in the control group ( $P < 0.05$ ).

#### Conclusion

A significant relationship observed between FS with HI and CT of ADHD among children. In addition, hyperactivity has a significant relation with febrile seizure in male gender, making further investigation in these children prudent for early diagnosis and management.

**Key Words:** ADHD, Children, Febrile seizure.

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## 1- INTRODUCTION

Febrile seizure (FS) is the most common type of type of childhood convulsion that occurred in 2% to 5% of children (1-4). The most common age at onset is 14-18 months and usually the children experience the FS between 3 months and 5 years of age (1, 3, 5). Incidence of febrile seizure before 9 months and after 5 years of age suggests underlying neurological abnormality and could be as a results of comorbidity with other disease yet in adults(6). FS is inherently a benign process and the cumulative incidence of febrile seizures is estimated higher in Asian countries than the US and Western Europe countries and varied since 2-5% in US to 9% in Japan, and 14% in India(7). Recurrence of febrile seizure is about 30%, but epilepsy has only been reported in 2% of cases. Studies have shown that fever leads to seizure by reducing brain threshold (1, 7, 8). Positive familial background has been reported in 25% to 40% of cases (3, 9). Febrile seizure is the focus of local infection cannot be detected and it is divided into two groups of simple and complex seizures(2, 7).

Attention deficit hyperactivity disorder (ADHD) are among the most controversial childhood disorders, and lead to referrals to child psychiatrists and consultants more than any other single disorder (10-13). Moreover, ADHD is one of the most prevalent psychiatric disorders among children(14) and its prevalence in Iran estimated as 4.1% for attention deficit(AD), 4.7% for hyperactive impulsive (HI), 1.7% for combined type (CT)(15). This disorder profoundly affects lives of thousands of children and their families, and has improper developmental symptoms (attention deficit, hyperactivity, and impulsivity) (13, 15, 16). Several studies with controversies in result conducted about the ADHD and seizure (4-12). Risk factors of ADHD could be age, gender, and neuropsychological

factors such as seizure and familial factors including proper relationship with family, and parental response to their behavior (8, 14, 17). In addition key risk factors include low education of caregivers, reduced family support and low confidence of parents in children's capabilities are related to increased risk of behavioral disorders in children (18, 19). It is suggested that ADHD is a risk factor for FS(20).

Therefore, children with seizures had greater internal and external behavioral disorders compared to healthy children (5). Moreover, children with a history of seizure showed greater levels of behavioral disorders, attention deficit disorders, hyperactivity, lack of concentration and attention-seeking and somatic complaints (12, 13). Thus, given controversy in studies regarding the absence evidence for relationship in FS and ADHD, the current study aimed to assess the effect of FS on occurrence of ADHD disorders including AD, HI and CT among children aged less than 12 years.

## 2- MATERIALS AND METHODS

### 2-1. Study design and population

In this case control study, the study population consisted of all 3-12 year-old children, attending Amir-Kabir Hospital in Arak city- Iran, during August 2011 and June 2012, with diagnosis of simple febrile seizure. According to sampling calculation, 103 children who were 3-12 year-old selected as case group. In addition, 103 children with similar age and gender of cases that admitted to the infectious clinic of Amir-Kabir Hospital without simple febrile seizure selected by simple random sampling as control group.

### 2-2. Methods

In two groups, required data including patients' history, checklist prepared from Kaplan book based on DSM-IV, and demographic details of all patients were completed. Necessary coordination was

made with project psychiatrist to ensure patients met ADHD criteria according to the checklist. The psychiatrist was present in the psychiatry clinic of hospital and reassessed all the probable children who diagnosed as ADHD by checklist.

The ADHD checklist is a screening test for behavioral symptoms for children disorders such as ADHD. The ADHD symptoms contained 18 items including nine for ADHD-AD, and nine for ADHD-HI; all of the items are used for ADHD-CT. This scale scoring, 0 for "never/sometimes" and 1 for "often/almost always". The total score for each dimension varied between 0 to 9 and children with total score > 6 in inattention dimension labeled as AD. Moreover, if score >6 obtained in hyperactive impulsive dimension, that child detect as HI and if in two dimensions the score calculated more than 6, he/she is affected to CT of ADHD(21). This scale is validated in Iranian studies (15, 22) and psychometric properties of ADHD scale is enough.

### 2-3. Inclusion criteria

The cases suffering from simple febrile seizure that diagnosed by the pediatrician and based on clinical guidelines entered to the study. Including criteria for cases were without history of physical or mental diseases such as depression, anxiety, schizophrenia, or congenital diseases. Patients not qualifying for febrile seizure definition such as children with focal seizures, frequent seizures (more than once) in 24 hours, duration of seizure longer than 15 minutes, and possible central nervous system (CNS) diseases such as meningitis, encephalitis, and possible epilepsy (given previous frequent seizures) were excluded from the study.

Informed consent was taken from all participants in two groups. Moreover, parents or guardians of patients were able to withdraw their children from the study at any stage.

### 2-4. Data analyses

In this descriptive-analytical study, statistical tables and figures as well as t-test and Chi square were used for comparison of mean in the independent groups and comparison of ratios. Collected data were analyzed using SPSS-16 software and  $P < 0.05$  was determined significant.

## 3- RESULTS

According to sample size calculations, 206 children including 103 cases with FS and 103 controls entered in the study. The boy/girl ratio was 1.7 and 76 (36.9%) was girls and 130(63.1%) were boys. **Table.1** presents distribution of frequency and relative frequency of attention deficit/hyperactivity, impulsivity disorders, and combination of these in study groups according to gender. The ratio of ADHD in cases and control was statistically significant and estimated as 62(60.2%) vs. 44(42.7%) respectively ( $P=0.024$ ).

Moreover, the overall percent of AD was 4.9% in control group vs. 0 in cases that was not significant. The prevalence of HI in cases and control groups was 30.1% and 18.4% and it was statistically significant ( $P=0.03$ ). Moreover, the CT of ADHD in cases and controls was 30.1% and 19.4%, respectively ( $P=0.01$ ). The results showed that 6.1% of the control group had attention deficit. Moreover, 34.3% of male children with simple febrile seizure and 16.7% from the control group had hyperactivity/impulsivity disorder. In addition, 34.3% of male children with simple febrile seizure and 18.2% from the control group had combined disorders. The prevalence of hyperactivity/impulsivity disorders was statistically significant in the two groups. Conversely, 2.7% of the control group had attention deficit. Moreover, 23.1% of female children with simple febrile seizure and 21.6% from the control group had hyperactivity/impulsivity disorder. In

addition, 21.3% of female children with simple febrile seizure and 21.6% from the control group had combined disorders. There was no significant difference in the prevalence of hyperactivity/impulsivity disorders in the two groups ( $P>0.05$ ). **Table.2** shows a significant difference in the mean age of mothers in the two groups.

According to results presented in **Table.3**, the frequency of familial marriages was 26.2% in parents of children with simple febrile seizure, and 9.7% in the control group ( $P=0.025$ ). Based on the completed questionnaire, none of the patients had any family history of psychiatric diseases in their parents or siblings.

**Table1:** Frequency and percentile distribution according to gender and ADHD subtypes (attention deficit, hyperactivity - impulsivity, and combined) in group with and without simple febrile seizure

| Disorder        |       | Combined       |                  | Hyperactivity - Impulsivity |                  | Attention Deficit |                  |
|-----------------|-------|----------------|------------------|-----------------------------|------------------|-------------------|------------------|
|                 |       | Cases<br>N (%) | Control<br>N (%) | Cases<br>N (%)              | Control<br>N (%) | Cases<br>N (%)    | Control<br>N (%) |
| Female          | Yes   | 9(23.1)        | 8(21.6)          | 9(23.1)                     | 8(21.6)          | 0                 | 1(2.7)           |
|                 | No    | 30(76.9)       | 29(78.4)         | 30(76.9)                    | 29(78.4)         | 39(100)           | 36(93.3)         |
|                 | Total | 39(100)        | 37(100)          | 39(100)                     | 37(100)          | 39(100)           | 37(100)          |
| P- value        |       | P=0.05         |                  | P=0.05                      |                  | P=0.4             |                  |
| Male            | Yes   | 22(34.3)       | 12(18.2)         | 22(34.3)                    | 11(16.7)         | 0                 | 4(6.1)           |
|                 | No    | 42(65.6)       | 54(81.8)         | 42(65.6)                    | 55(83.3)         | 64(100)           | 62(93.3)         |
|                 | Total | 64(100)        | 66(100)          | 64(100)                     | 66(100)          | 64(100)           | 66(100)          |
| P- value        |       | P=0.046        |                  | P=0.017                     |                  | P=0.06            |                  |
| Female and Male | Yes   | 31(30.1)       | 20(19.4)         | 31(30.1)                    | 19(18.4)         | 0                 | 5(4.9)           |
|                 | No    | 72(69.9)       | 83(80.6)         | 72(69.9)                    | 84(81.6)         | 103 (100)         | 98(95.1)         |
|                 | Total | 103(100)       | 103 (100)        | 103(100)                    | 103 (100)        | 103 (100)         | 103 (100)        |
| P- value        |       | P=0.01         |                  | P=0.03                      |                  | P=0.05            |                  |

**Table 2:** The comparison of age, maternal age, birth weight between groups with and without simple febrile seizure in children

| Variables           | Case<br>Mean± SD | Control<br>Mean± SD | P- value |
|---------------------|------------------|---------------------|----------|
| Age (month )        | 61.55(22.6)      | 61.75(22.5)         | 0.951    |
| Maternal age (year) | 23.81(3.7)       | 24.9(4.4)           | 0.046    |
| Birth weight (gram) | 3052.7(386)      | 3039(536)           | 0.847    |

**Table 3:** The relationship between family history and familial marriage with attention deficit and hyperactivity in both groups with and without simple febrile seizure in children

| Variables         | Responsible | Case<br>Mean± SD | Control<br>Mean± SD | P- value |
|-------------------|-------------|------------------|---------------------|----------|
| Family history    | Yes         | 1(1)             | 0(0)                | 0.78     |
|                   | No          | 102(99)          | 103(100)            |          |
| Familial marriage | Yes         | 27(26.2)         | 10(9.7)             | 0.025    |
|                   | No          | 76(73.8)         | 93(90.3)            |          |

#### 4- DISCUSSION

The results of study showed a significant relationship between FS and ADHD in children. This association is observed in another study by Hesdorffer et al. study (20). Moreover, the hyperactivity disorder was more prevalent in male children with simple FS compared to children without FS. This finding suggests a relationship between simple FS and hyperactivity in boys. However, the ADHD prevalence in boys was higher than the girls. In other studies in Iran (15) and other places(19), the hyperactivity estimated higher than in boys. In addition, boy gender is one of the known risk factors for hyperactivity disorder (3, 10, 22). Nevertheless, no significant difference was found in the prevalence of hyperactivity between female children with simple febrile seizure and control group. Based on our results FS was not related to AD disorder in both gender. Nevertheless, HI disorder, showed greater increase in male children with simple FS compared to the control group, while in female children the increase was not significant. In a study conducted at the University of Indiana in the U.S. (2009) on 282 with IQ > 70 and the present study showed that hyperactivity risk was greater in boys with simple febrile seizure, which concurs with the conducted study (23).

Another case control study on 332, 6-14 year-old children with first seizure and 225 healthy children, greater sleep disorders including timing of sleep and sleepiness during daytime observed in children with seizures (9). In the present study, hyperactivity disorder was greater in male children with simple febrile seizure, which agrees with the above study. In addition, another study on 229 children with first seizure showed that these children affected to greater internal and external behavioral disorders including neuropsychological and behavioral functions, especially practical function predict behavioral

outcomes 3 years after the onset of seizure, compared to healthy children (23). Moreover, first seizure in 6-14 year-old children was related to increased risk of neuropsychological disorder, which is in line with the present study. These results were similar to other study that conducted by Austin et al. on 300 6-14 children with first seizures and 196 healthy children. That study showed children with first seizure showed greater behavioral disorders over 3-year follow-up(18). Based on our results and other studies, FS is associated with behavioral and cognitive disorders, even in the absence of structural brain damage (24). It is demonstrated that children with febrile seizures experience the greater behavioral disorders than the control group (1, 3, 8). Moreover, based on our results, a greater risk of hyperactivity disorders was shown in boys with simple febrile seizure while this increased risk did not observe for attention deficit, which was different to Chang et al. studies (25, 26) . In the present study, the risk of hyperactivity/attention deficit disorder was greater in boys with simple febrile seizures, and gender had no effect on febrile seizure, which agrees with the Hesdorffer et al. and Stafstrom studies (20, 27). Moreover, in the present study, hyperactivity in boys with simple febrile seizure showed higher increase compared to the control group, which is in line with the Dunn et al. study (24). Higher prevalence of simple febrile seizure observed in our study among children with a history of familial marriages compared to children without such a history. In addition, incidence of ADHD disorder in children with FS estimated 2.5 times greater than normal children. However, based on the other studies the first seizure is associated with greater behavioral disorders such as ADHD. Although, our results could be in a same line, but since the age of onset, the seizure did not obtain in our data, this item is as our limitation of work (20).

#### 4-1. Limitations of the study

However, due to the design of current study, it is suggested that the effect of FS evaluated on the ADHD in a follow-up study.

#### 5. CONCLUSION

According to the present study results, there was a significant relationship between FS with HI and CT of ADHD among children. Nevertheless, FS is not related to AD disorder. Moreover, male hyperactivity was related to simple febrile seizure. Thus, preventive diagnosis in terms of likelihood of hyperactivity, and early and preventive actions should be performed in male children with simple febrile seizure.

#### 6- CONTRIBUTION OF AUTHORS

**SB:** Contributions to the conception and design of the research; drafting of the manuscript and final approval of the manuscript

**PY:** Contributions to the conception and design of the research; analysis and interpretation of data; final approval of the manuscript

**SAS:** Contributions to the acquisition and analysis of data; drafting of the manuscript and final approval of the manuscript

**ES:** Contributions to the conception and design of the research analysis; interpretation of data; final approval of the manuscript

**AM:** Contributions to the conception and design of the research; interpretation of data; final approval of the manuscript.

**7- CONFLICT OF INTEREST:** None.

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