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## Estimation of IL-1 $\beta$ and TNF Concentration in Children Suffering from Febrile Convulsion

JWAN A. ALI<sup>1\*</sup>, ZAYTOON A.R. AL-KAJAJI<sup>2</sup> AND ADNAN H. AL-JOTHERY<sup>3</sup>

<sup>1\*</sup>*University of Babylon, Collage of Medicine, Microbiology Department, Iraq.*

<sup>2</sup>*University of Babylon, Collage of Medicine, Microbiology Department, Iraq.*

<sup>3</sup>*University of Babylon, Collage of Medicine - pediatric Department, Iraq.*

<sup>1\*</sup>*Jwanalhamawandi@gmail.com*

### Abstract.

A total of (150) blood samples were taken from children who suffering from febrile convulsion, during the period from April (2019) to October (2019), who admitted to Babel Hospital, Al-Noor Hospital and Al-Imam Al-Sadiq Center, at age range from six month to five years old. out of (150) blood samples, (50) samples of children who suffering from febrile convulsion fit as group one [31 male (62%) and 19 female (38%)], (50) samples of children who suffering from fever without fit as group two [34 male (68%) and 16 female (32%)] and (50) samples of control case (healthy children) as group three [male 36 (72%) and 14 female (28%)]. Interleukin-1 $\beta$  and tumor necrotic factor (TNF) were studied, it was found that, there were a high important variances in the results of IL-1 $\beta$  in patients with fever and fit (P= 0.001) when compared to those with fever without fit and control. About TNF, there were no important variance among the study groups (P= 0.057).

**Aim of Study.** To determine the concentration of IL-1 $\beta$  and TNF in Children Suffering from Febrile Convulsion.

**Keywords.** Febrile Convulsion, Human Herpes Virus-6, Fit with Fever, IL-1 $\beta$  and TNF.

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## INTRODUCTION

Febrile seizure (FS) is considered the utmost popular of disease spastic through infancy and childhood young. Febrile seizure have been known via the Academy American of Pediatrics (AAP) as a seizure, that happen among of 6 months of the ages, and in febrile children at 5 years don't suffer of infection intracranial, in history of afebrile seizure or abnormality of the metabolic, [1]. One utmost significant parameter, that show a part in the technique of febrile seizures, is cytokines. They are mediators immunological having several diseases immunological and illness infectious. Studies appear favorable part to understood the part of cytokines pro-inflammatory of the pathogenesis for convulsions febrile [2]. The dispersal of febrile seizures differs among 2% and 5% at 6 months of children aged from to 5 years. It decrease after 4 years of age and little denounce after 7 years. chance about 15 -70% next a single offense of febrile seizures to improve another one [3,4]. TNF and IL-1 $\beta$  are considered the utmost significant. They have indirect and direct affects on neurons and neurotransmitters, that concealed through stress and fever in children [5]. The IL-1 cytokine family consists of IL-1 alpha (IL-1 $\alpha$ ), IL-1 beta. (IL-1 $\beta$ ), and IL-1 receptor antagonist (IL-1RA), wholly of which bind the IL-1 receptor (IL-1R). IL-1 $\beta$  is utmost secreted but IL-1 $\alpha$  is predominantly membrane-bound. IL-1 $\beta$  is extra closely associated to IL-1R.A than it is to IL-1 $\alpha$  [6]. Proinflammatory and anti-inflammatory cytokines play a pivotal role in the regulation of febrile response during infections. Among these cytokines, interleukin-1 (IL-1) is defined as the first endogenous pyrogen, because it was originally discovered with function of inducing fever in experimental models and humans [7]. TNF level in the cerebrospinal fluid was considerably elevated in patients for febrile seizures through the acute phase paralleled with the levels in the controller group. A variance among the cerebrospinal fluid and serum tumor necrosis factor- $\alpha$  levels in children with febrile seizures and the group control [8]. The aim of the study to compared levels serum of cytokines, particularly TNF and IL-4, in patients for febrile seizures and controls. Also compared the relationships among levels of cytokine for these factors between groups [9].

## METHODS AND MATERIALS

### *Patients and clinical specimens*

A total of (150) blood samples were taken from children who suffering from febrile convulsion, during the period from April 2019 to October 2019, who admitted Babel Hospital, Al-Noor Hospital and Al- Imam Al-Sadiq Center, at age range from six month to five years old. Any child aged from 6-60 months developed fit with fever with normal S. Na, S.Ca (ionized fraction). Four ml of blood samples were collected, and divided in to three groups 50 samples of children who suffering from febrile conversion fit, 50 samples of children who suffering from fever without fit and 50 samples as control case (healthy children). These samples were collected according to diagnosis of seiner doctors. Each blood samples were divided into two tubes (2ml putted in EDTA tube, to

obtain of holly blood, and 2ml putted in gully tube to obtain serum). All samples were stored in freezing at (-20C°) until used.

#### *Control groups*

Control group 1: Child matched age and sex with fever without fit.

Control group 2: Child matched age and sex without fever and fit.

#### *Exclusion criteria*

1. Age less than 6 months and more 60 months.
2. Any child with known case of epilepsy.
3. Any child with neurodevelopmental delay (CP).
4. Any child with explainable cause of FS (meningitis).
5. Any child with abnormal S.b Na, S.Ca (ionized fraction).

#### *Human IL-1 $\beta$ and TNF ELISA Kit*

Human IL-1 $\beta$  and TNF ELISA Kit wear utilized in this study for quantitative estimation for IL-1 $\beta$  and TNF concentration in fit, fever patients and healthy control serum samples and done according to company instruction (Elabscience/ China) as following procedure: Wholly kit samples and reagents at room temperature.

1. **Sample Add:** preparing 100 $\mu$ L of all the Standard, Sample, Blank, was additional in carefully chosen E.L.I.S.A plate wells. It is additional with diluent Sample. After that incubated at 37C for 90 mint.
2. **Wash:** Wholly plate wells and washing and aspirated, repeated the method for 3time The washing completed via filling each well for Washing Buffer (approximately 350 $\mu$ L) utilizing a squirt flask.
3. **HRP Conjugate: solution** 100 $\mu$ L of H.R.P additional for each well and covered of the sealer plate. And then incubated at 37°Cfor 30 mint.
4. **Wash:** The washing method was repeated of5 times as conducted in three step.
5. **Substrate:** preparation the stock Solution90 $\mu$ L additional to each well and covered for a new sealer Plate, after that incubated at 37°C of 15 mint.
6. **Stop:** Stop Solution of 50 $\mu$ L additional to each well. Then, the color turns to yellow immediately.
7. **OD Measurement:** Estimation (OD value) of each well at once, utilized a microplate reader set at 450 nm.

#### **RESULTS AND DISCUSSION**

A total of (150) blood samples were taken from children who suffering from febrile convulsion, during the period from April (2019) to October (2019), who admitted to Babel Hospital, Al-Noor Hospital and Al- Imam Al-Sadiq Center, at age range from six month to five years old. Out of (150) blood samples were taken from children, and divided in to three groups, at age range from six months to five years old. From (150) blood samples, (50) samples of children who suffering from febrile convulsion fit as group one [31 male (62%) and 19

female (38%)], (50) samples of children who suffering from fever without fit as group two [34 male (68%) and 16 female (32%)] and (50) samples of control case (healthy children) as group three [male 36 (72%) and 14 female (28%), as shown in Figure (1).The results of present study were in agreement with results obtained by [10] who found that from (300) children were collected, 150(50%) suffering from febrile convulsion fit, 75(25%) samples of children who suffering from fever without fit and 75(25%) samples as control. Shibeeb and Altufaily, [11] found that, highly significant differences in residence that taken from children who suffering from febrile convulsion ( $p=0.001$ ). A study of [12] found that, wholly 6–month- 6-year-old children for the diagnosis of febrile convulsion, (81.8%) for the children had febrile seizure. Febrile seizure is the utmost communal kind of convulsive disorder and one of the utmost prevalent reason of emergency hospital admission in children [14].Interleukin-1 $\beta$  and tumor necrotic factor (TNF) were studied, it was found that, there were a high important variances in the results of IL-1 $\beta$  in patients with fever and fit ( $P= 0.001$ ) when compared to those with fever without fit and control. About TNF, there were no important difference among the study groups ( $P= 0.057$ ), as shown in Table (1). The results were agreement in IL-1 $\beta$  with results obtained by [13] who found that, the conc. of serum IL.-1 $\beta$  in the febrile convulsion patients and groups control was highly significant ( $P=0.001$ ). While in agreement with results of concentrations of TNF in febrile convulsion, patients and groups control, they was important variances among the case groups in TNF levels. Though, the levels of TNF didn't alteration considerably among the 3 groups. This study concluded that IL-1 $\beta$  was a possible parameter influencing the pathogenesis of febrile seizure. Interlaukin-1beta (IL-1 $\beta$ ) and tumor necrosis agent alpha (TNF) are the main cytokines [14], and it reported, raised produce of IL.-1 $\beta$  is included in the pathogenesis of febrile seizures. In contrast, [15] recommended IL.-1 $\beta$  don'ts how any parts in the pathogenesis of febrile seizures.

**Table 1. Differences in the concentration of interleukin-1 $\beta$  and tumor necrotic factor between the studied patients and control groups**

Parameter (mean $\pm$ SE)	Group 1 N=50	Group 2 N=50	Group 3 N=50	P-value
IL-1 $\beta$ pg/mL Concentration	46.48 $\pm$ 1.24 <sup>#</sup>	40.84 $\pm$ 1.13 <sup>#</sup>	41.75 $\pm$ 0.89	0.001 <sup>**</sup>
TNF pg/mL Concentration	47.79 $\pm$ 0.95	50.05 $\pm$ 1.05	51.21 $\pm$ 1.04	0.057

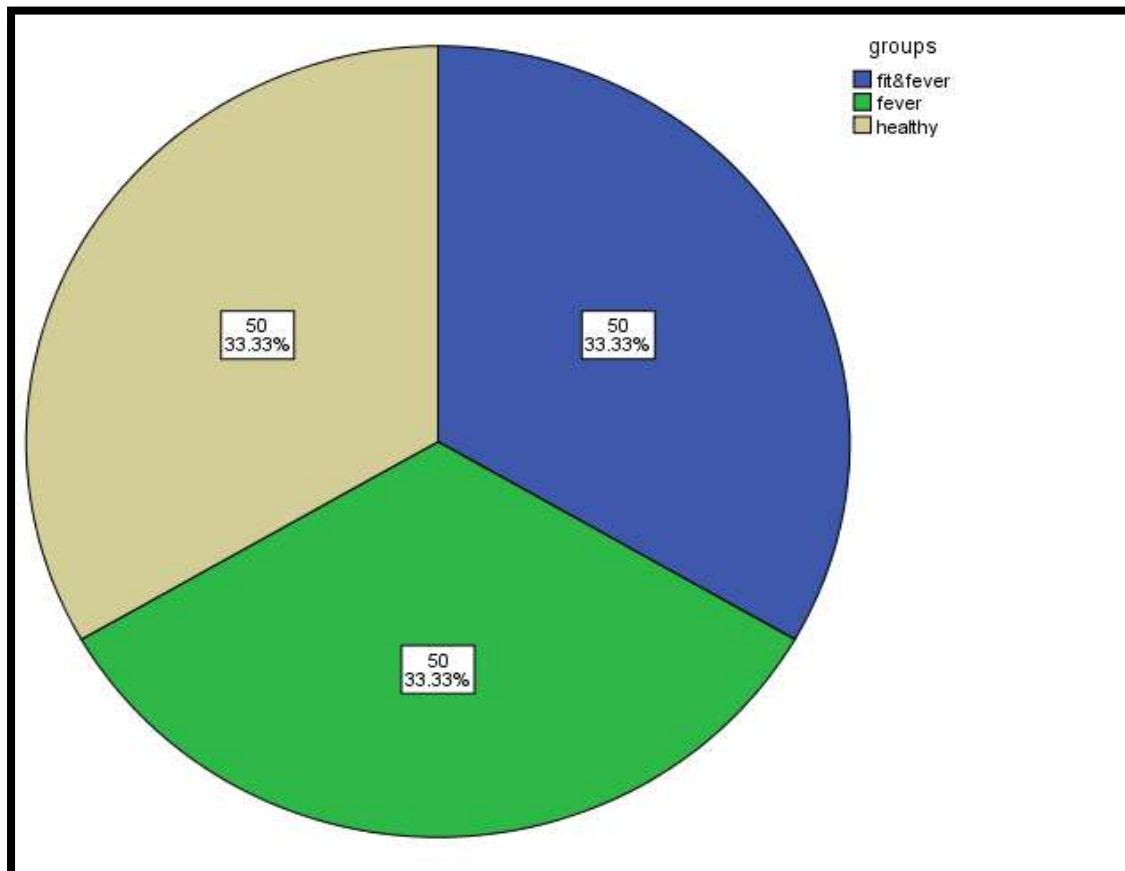
**\*\* P value is of highly statistical significant**

**# significant group by post hoc tests for one- way ANOVA**

**Group1= fever with fit, Group2= fever without fit, Group 3= healthy control, IL1 $\beta$ =interleukin 1B, TNF=tumor necrotic factor, pg/ml=picogram/milliliter, SE= standard errors.**

IL-1 $\beta$  and TNF level in febrile seizure patients through the acute phase of the illness was considerably greater than this in controls [16]. Yet, TNF levels, IL-1 $\beta$  levels was not considerably several among the case and groups control as data[17]. Though numerous study has executed on the identification for parameter make happen febrile seizures in children, the actual reason for illness have no discovered [18-22]. Thus significant part of IL.-

IL-1 $\beta$  and TNF is indirect and direct modulating affects on a neurotoxic and neurons neurotransmitters release through inflammation [23]. in the study concluded the IL-1 $\beta$  is the probable parameter impact the pathogenesis of seizures febrile. other study appeared that inducement of leukocytes via double stranded RNA resulted in a greatly production of IL-1 $\beta$  in the patients febrile seizure [24].Chou et al., [15] appeared energizing of peripheral blood mononuclear cells through liposaccharide in children of febrile seizures lead to raised product of IL-1 $\beta$  in the children as comparative to the in control. other study of [25] appeared a important attachment among IL-1 $\beta$  and febrile seizures. Choy et al., [26] that recommended IL-1 $\beta$  is a estimation agent in the improvement of febrile seizures. A study via [27,28]. Therefore, the reaction of IL-1 $\beta$ , and another inflammatory cytokines too from large importance in the generation of FS [22].When children was infected, IL-1, that is well famous as the inducer of fever, rise and the levels of IL-1 and TNF raised. These cytokines are possible to be included in synaptic plasticity, neural transmission, and Ca<sup>2+</sup> signaling [29]. IL-1 $\beta$  rise contained by one h. then seizure, reaches its level most in 4–12 hrs. Next seizure, and returns to its usual level next 24 hrs. Therefore, IL-1 $\beta$  is better measured contained by 12 hrs.[30]. The measurement of IL-1 $\beta$  is so problematic because IL-1 $\beta$  binds to great proteins like alpha 2- macroglobulin and complements. It have appeared of pro inflammatory cytokines razed then bacterial infections and viral[16].



**Figure 3-1. Frequency distribution of the studied groups**

## CONCLUSION

Interleukin-1 $\beta$  and tumor necrotic factor (TNF) were studied, it was found that, there were a high important variances in the results of IL-1 $\beta$  in patients with fever and fit (P= 0.001) when compared to those with fever without fit and control. About TNF, there were no important variance among the study groups (P= 0.057).

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