

REVIEW ARTICLE

The Association of IL-6 and IL-10 Serum Levels with Childhood Febrile Seizure

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Abstract:

Background Febrile seizures (FS) that are also known as febrile..fits or febrile_ convulsions that happen in children between the ages_ of 6 months and 5 years) who* have a fever of more, than"38 degrees Celsius that is not related to an intracranial reason/ (e.g.,*an infection, head. injury, or epilepsy).

Objective- The purpose of the present study is to detect the Association of Inflammatory cytokines (IL-6, IL-10) serum levels with the onset of childhood febrile seizure.

Methods- A case-control study was managed using 40 patients with febrile seizures and 40 controls whose ages ranged from 5 months to 5 years) to determine the association of serum IL-6, and IL-10 levels with FS. The samples were collected from Al-Zahra Maternity and Pediatric Hospital and outpatient clinics for the period from

8 October 2022 to 5 February 2023 under the supervision of a specialist pediatrician.

Results- A case-control study of 40 patients with FS and 40 controls without FS revealed that the mean blood IL-6 and IL-10 levels in the patients group were significantly higher than in the control group.

Keywords: IL-6 serum, IL-10 serum, Febrile Seizure.

Introduction

Febrile seizures are also known -as febrile..fits or febrile convulsions[1] that occur in children between/the ages of 6 months and 5 years who have a fever of more, than"38 degrees Celsius (100,4 degrees Fahrenheit), that are not associated with intracranial reasons/(like an-infection, head.injury, or epilepsy) [2].

They are assorted as simple (often, lasting less than 15 minutes, occurring just once in 24 hours) or complex. (prolonged, more than one in 24 hours). More frequently than complex FS, simple FS makes up more than 70% of all FS. A subtype of complex FS named febrile status epilepticus (FSE) is described by protracted, ongoing, or intermittent seizures without awareness that progress to status epilepticus. FSE accounts for 5% of all FS [3]. FSs are the extreme..epidemic/neurologic; state..in children under five years/in, Western*Europe" and the United; States [4].

Every-racial/group can experience FSs, however,//Asian children are most likely<to" test them [5-10%* of -Indian /chil-

dren 'and =6-9% =of- Japanese' children] [5].

Studies on families and twins mentioned that genetics play an important effect in FS. About one-third of children with FSs have a family history of the condition[6] and the primary cause of fever in about 80% of febrile convulsions is a viral infection[7].

IL-6 is one of the pro-inflammatory cytokines that is involved in the production of acute-phase inflammation reactions like fever. While IL-10 is one of the anti-inflammatory cytokines that have a negative feedback impact on fever during which they are released. The degree of the fever depends on how well these two cytokine groups are balanced. The etiology of FSs is affected by complex interactions between the immune system, inflammatory processes, cytokine activation, and hereditary variables [8].

IL-6 is a pleiotropic pro-inflammatory cytokine that is released by T lymphocytes, macrophages, endothelial cells, and epithelial cells. It has a broad spectrum of biological functions In terms of regulating the immune system, hematopoiesis, inflamma-



tion, and neoplasia, A substantial association between IL-6 and fever has been found [9].

IL-10 can control the fever response during acute infections, resulting in inhibition of temperature raising and subsequently depress susceptibility to FS, as the antipyretic action of IL-10 has been suggested in humans and animals. As a result, the overproduction of IL-10 can be caused by environmental agents and genetic resistance factors together [10].

Complications of FS include the risk of future epilepsy in children, with complex FSs [11]. Rarely, FSs can lead to encephalopathy missense mutations in the sodium channel genes SCN1A and SCN2A may predispose children to severe FSs according to recent data [12].

2-The Methods and Materials

A case-control study was conducted based on 40 patients with FSs and 40 controls whose ages ranged from 5 months to 5 years to detect the association of serum IL-6, and IL-10 levels with FS.

Under the supervision of a specialist pediatrician, the samples were collected from Al-Zahra Maternity and Pediatric Hospital and outpatient clinics for the period from 8 October 2022 to 5 February 2023. The control group has been selected due to their regular calcium levels, normal complete blood counts, and general health. About 2 mL blood sample was collected from each group by sterile syringe under aseptic condition, the blood was placed into a gel tube to separate the serum. The blood was centrifuged at 3000 rpm for 5 minutes after being left at room temperature for around 30 minutes to allow for clotting. The serum is then collected in sterile Eppendorf tubes and kept frozen at -20 C to determine the level of IL-6 and IL-10 cytokines. In the current study the MELSIN kit has been used that uses a single-step, double-antibody sandwich enzyme-linked immunosorbent assay method to measure Interleukin-6, IL-10 in human serum. The interleukin concentration in the samples is calculated by comparing their O.D. to a standard curve after a wavelength of 450 nm is used to spectrophotometrically measure the colour change as shown in Figure-1

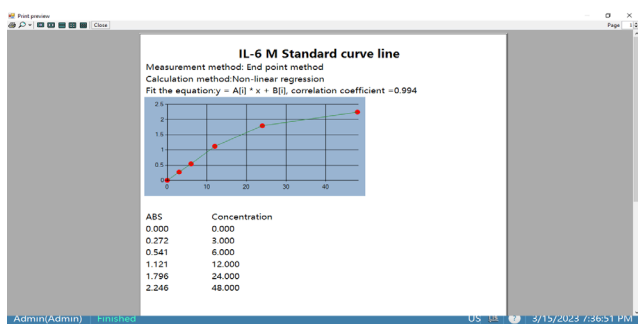


Figure-1: IL-6 standard curve line

3-Results

IL-6 and IL-10 serum concentrations in patient versus control group:

Table 1 presents the evaluation of serum levels of IL-6 in addition to IL-10 among the patients cluster and the control

cluster, the average IL-6 serum was also significantly advanced in the patients’ cluster in comparison with the control cluster, (p = 0.005). Additionally, the average serum IL-10 was found to be significantly advanced in the patients’ cluster in comparison with the control cluster, (p = 0.003).

Table 1: Comparison of the patients’ group and the control group’s serum concentrations of IL-6 and IL-10

Characteristic	Patients group n = 40	Control group n = 40	P
Serum IL-6			
Mean ±SD	4.91 ±1.16	4.06 ±1.44	0.005 I **
Range	1.01 -6.84	0.33 -6.06	
Serum IL-10			
Mean ±SD	83.61 ±21.16	68.88 ±21.18	0.003 I **
Range	13.09 -114	6.24 -96.64	

n: number of cases; SD: standard deviation; I: independent samples t-test; ***: significant at p ≤ 0.01

The relationship between serum IL-6 and serum IL-10 is shown in Figure 2, there was a significant positive correlation between them (r = 0.816, p<0.001).

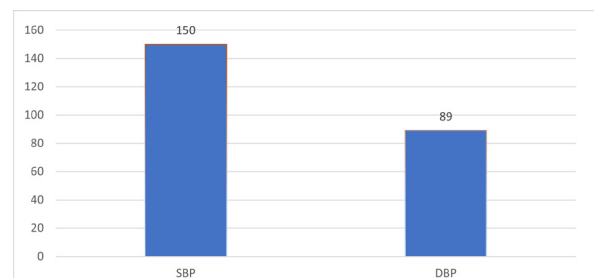


Figure 2: Scatter graph showing a correlation between serum IL-6 and serum IL-10

4-Discussion

In the current study, the Mean serum IL-6 was found significantly higher in the patients group in comparison with the control group, 4.91±1.16 versus 4.06±1.44, respectively (p=0.005). This increment of IL-6 serum concentration could be related to the function of such Pro-inflammatory cytokines that act as a key factor of the host response to infection induces fever, leukocytosis, and acute phase protein synthesis (13).

IL-6 also induces synthesis of Cyclooxygenase2 (COX2) as a result of endogenous pyrogens in cytokines which also cause the production of prostaglandinE2(PGE2) in perivascular cells and vascular endothelial cells in the brain. The blood-brain barrier (BBB) is breached by lipophilic PGE2, which then excites hypothalamic neurons(14).

The current result corresponds with the study by Azab et al which exposed significantly higher serum IL-6 levels in the FS group than in the FC and HC groups In the CFS group, serum and CSF IL-6 levels were significantly higher when compared with the SFS group (15). While Choi et al noted that serum IL-6 levels in FSs were raised 1.8-fold when compared with FCs, but it was not statistically significant (p = 0.07) (16)

Additionally, in the current study, the Mean serum IL-10 was found notably higher in the patients group in comparison with the control group, 83.61 ± 21.16 versus 68.88 ± 21.18 , respectively ($p = 0.003$). This result can reflect an anti-convulsive mechanistic effect of IL-10 in FSs or compensatory activation of the anti-inflammatory role of IL-10.

Three studies provided conflicting results as to the relationship between FS and IL-10., Straussberg et al. had shown increased lipopolysaccharide-induced IL-10 production by peripheral blood mononuclear cells from children with a history of FS(17).

In contrast, Virta et al. have reported that no difference in plasma IL-10 level was found between children with and without FS (18).

The present results together with other findings support the proconvulsant action of IL-6 in FSs and can reflect compensatory activation of the anti-inflammatory role or an anti-convulsive mechanistic effect of IL-10 in FSs, so there was a positive correlation between them.

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