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Serum level of IL-1 β in patients with ischemic stroke

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ABSTRACT

Background and purpose-IL-1 β is a key inflammatory mediator driving the host response to infection, injury, and disease. It is produced by numerous cell types, including the brain parenchyma. Its levels are elevated as a result of increased production from inflammatory cells, glia and neurons and it is associated with exacerbation of injury in stroke. Conversely, it may be beneficial in protecting the brain from ischemia and it activates astrocytes which upon activation, they are considered to be the main source of antioxidant defense in the brain following ischemia. The aim of the study was to compare the levels of IL-1 β in Sudanese patients with ischemic stroke and normal control subjects. Methodology-Thirty-five patients with ischemic stroke and 81 apparently healthy subjects were included in the study. Sera were collected from them in the morning and IL-1 β was estimated using ELISA technique. Unpaired T-test (at the level of 0.05) was used to assess the significant difference in the means of the studied variables in the different groups. Results-The mean level of IL-1 β (pg/ml) was significantly higher in patients with stroke compared with that of the control group (23.52 \pm 59.44 vs 9.86 \pm 7.41, p <0.001). Conclusion-IL-1 β , as a pro-inflammatory cytokine, in the combination with other risk factors for stroke might have a both positive and negative effect on the development and pathogenesis of the stroke and its severity. The major risk factors are old age, hypertension, diabetes mellitus, dyslipidemia, and obesity.

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1. Introduction

A stroke is a medical emergency and can cause permanent neurological damage, complications, and death[1] due to disturbance in the blood supply to the brain that is caused by ischemia commonly resulted from an arterial obstruction by a thrombus or embolus or a hemorrhage^[2,3].

Evidence is emerging that inflammation plays a key role in the pathophysiology of ischemic stroke^[4].

Within hours after the onset of focal cerebral ischaemia peripheral leukocytes adhere to the cerebral endothelium, cross the vessel wall and invade the damaged parenchyma^[5]. At the

same time astrocytes and microglia become activated. These cellular events depend on the secretion of inflammatory mediators which are produced by neural and glial cells in response to an ischaemic insult. Once activated in the site of injury, inflammatory cells start to secrete a large variety of cytotoxic agents such as cytokines and chemokines^[6].

IL-1 β is a key inflammatory mediator driving the host response to infection, injury, and disease. During disease, IL-1 β -driven inflammation has often disastrous consequences, and thus represents a therapeutic target^[7]. IL-1 β is the best characterised of the 11 IL-1 family members. It is produced by numerous cell types, including the brain parenchyma, although the majority of studies focus on its production by cells of the innate immune system, such as monocytes and macrophages. It is produced in response to 'pathogen-associated molecular patterns' (PAMPs), or 'damage-AMPs' (DAMPs) as an inactive 31-kDa precursor, called pro-IL-1 β .

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PAMPs and DAMPs function through pattern recognition receptors (PRRs) on macrophage membranes to regulate pathways that control gene expression^[8,9].

Ischaemic stroke could be defined as a cardiovascular disease that affects blood vessels that supply the brain with blood. The usual cause for stroke is atherosclerotic damage of blood vessel. Bursting of blood vessels, formation of a local thrombosis and release of a blood clot, can lead to the blockade of cerebral blood flow. The necrosis of the brain tissue behind that rupture or blockage leads to the neurological deficit[10].

During the past several years a number of studies have been conducted to identify the genetic factors involved in ischemic stroke. However, the results obtained are not consistent[11].

Cytokines in the CNS originate not only from the immune cells of the brain, but also from astrocytes and neurons[12]. The action of cytokines in this tissue is via cytokine receptors on the glial cells and neuronal cells. As a direct consequence of the ionic imbalances and free calcium accumulation, there is a release of free fatty acids and other pro-inflammatory lipid metabolites associated with ischemic injury. These agents promote the release of pro-inflammatory cytokines.

The aim of the study was to compare the levels of IL-1β in Sudanese patients with ischemic stroke and normal control subjects.

Patients and methodology:

Hospital-based case-control study was carried out in the period April 2010 - October 2012 and included 35 patients with cerebrovascular accident (stroke) and 81 apparently healthy subjects. The study was conducted in Khartoum state - Sudan. Samples were collected from three hospitals, namely Alshaab teaching hospital, Ahmad Gasim teaching hospital and El-Mawada hospital. The study had received an ethical approval from the Ethical Review Committee at Al-Neelain University, Faculty of Medicine and Health Sciences; Research Council-Institute Review Board. Written informed consents were obtained from the studied subjects after explaining the aims and protocol of the study.

Venous blood samples (10-12

3. Results:

The study included 35 stroke patients, 14 female (40%) and 21 male (60%). Data results are summarized in tables 1.

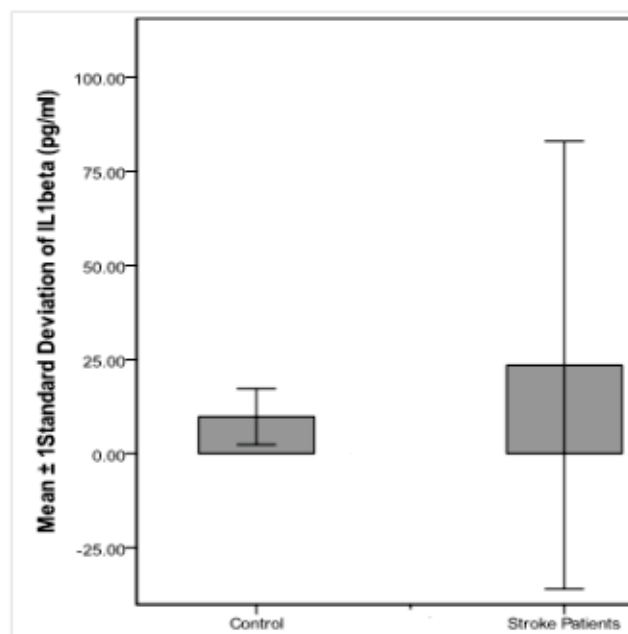
The mean level of IL-1β (pg/ml) was significantly higher in patients with stroke (figure 1) compared with that of the control group (23.52±59.44 vs 9.86±7.41, p <0.001).

Table 1: Results of the control group and patients with stroke.

	Control Group (N = 81) (M±SD)	Atherosclerotic Patients with stroke (N = 35) (M±SD)	P Value
Age (years)	50.37±12.56	50.37±12.56	0.000*
Weight (Kg)	72.68±18.02	72.68±18.02	0.185
Height (Cm)	170.33±13.64	170.33±13.64	0.001*
Body Mass Index	26.63±20.51	26.63±20.51	0.247
Systolic Blood Pressure	120.37±7.15	120.37±7.15	0.002*
Diastolic Blood Pressure	78.79±5.23	78.79±5.23	0.534
Mean Arterial Blood Pressure	92.65±5.21	92.65±5.21	0.017*
Random Blood Glucose Level (mg/dl)	86.58±3.92	86.58±3.92	0.000*
Triglyceride Level (mg/dl)	93.09±30.69	93.09±30.69	0.629
Cholesterol Level (mg/dl)	140.39±24.54	140.39±24.54	0.779
HDL Level (mg/dl)	33.86±6.52	33.86±6.52	0.780
LDL Level (mg/dl)	87.91±25.12	87.91±25.12	0.652
IL-1β (pg/ml)	9.86±7.41	9.86±7.41	0.000*

*Significance at level 0.05

Figure 1: IL-1β means' levels in the studied groups



4. Discussion:

Although cytokines are detected in the brain and cerebrospinal fluid (CSF) of patients with acute ischaemic stroke, the relevance of measurements in the peripheral circulation is uncertain[13-15].

Our results revealed that the mean level of IL-1 β (pg/ml) is significantly higher in patients with stroke comparing with the control group (23.52 \pm 59.44 vs 9.86 \pm 7.41, p <0.001). This may give some indication about the role of IL-1 β in the pathogenesis of stroke.

There is a balance between pro- and anti-inflammatory cytokines in a normal physiological state. This balance is lost after stroke[16]. Following acute ischemic stroke, it seems reasonable to hypothesise that cytokines measured in the plasma arise from cells associated with inflammatory activity in the brain, but this is not certain[15].

Previous studies have demonstrated that following brain insult cytokine levels are elevated as a result of increased production from inflammatory cells, glia and neurons[17,18]. Of which, IL-1 β had been associated with exacerbation of injury in stroke[19]. Conversely, some other study indicated that modestly increased levels of IL-1 β may be beneficial in protecting the brain from ischemia[20] and IL-1 β activates astrocytes which upon activation, they are considered to be the main source of antioxidant defense in the brain following ischemic reperfusion and are less vulnerable to injury from reactive oxygen species than neurons[20,21]. This is fortified by other studies showed that inflammatory cytokines like IL-1 α , IL-1 β , IL-6 and TNF α provide neuroprotection from the toxic influx of calcium, so called excitotoxicity, that is a major contributor to neuronal death induced by stroke[22]. Moreover Boutin et al (2001) showed that simultaneous deletion of both IL-1 β and IL-1 genes caused a marked reduction of ischemic brain damage[23]. Thus, it seemed that the pro-inflammatory cytokines, of which IL-1 β , in the combination with other risk factors for stroke might have a both positive and negative effect on the development and pathogenesis of the stroke and its severity. The major risk factors are old age, hypertension, diabetes mellitus, dyslipidemia, and obesity.

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