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Comparison between the Serum Levels of Tissue Matrix Metalloproteinase Inhibitor-1 and Serum Glucose Level in Patient with Traumatic Brain Injury

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Abstract

Traumatic brains injury (TBI) it an acquired defect which inhibits brain functions resulting in a complete or partial brain cell dysfunction. One of most commons cause of traumatic brain injuries is car accidents recognized to be one of the more significant severe factors for the increase of mortality and morbidity and the second most common cause is to fall from height .The most frequent ages for brain injury are the Middle Ages. Tissue inhibitor of metalloproteinases-1 (TIMP-1) is the one of the top induced genes in the injured nerve and PNS injury repair or pain effects remain mostly so we analyze TIMP-1 to determined and available features in the damaged PNS. The Brain has a continuous require for energy that is get by oxidative metabolism of oxygen and glucose so inadequate supply of oxygen or glucose causes cognitive dysfunction and dependent on the duration and severity there will be a progressive deterioration from coma to persistent brain damage and finally death. Samples were taken from 40 infected people and 40 healthy people, and the L-temp-1b enzyme was measured by an ELISA technique, and high blood sugar was measured by a spectrophotometer for the same people, where an elevation was observed serum glucose was also higher in patients than controls (7.96±1.78 mmol/L versus 5.26±1.28 mmol/L) with highly significant difference, Mean serum concentration of TIMP-1 inn patients was 25.06±7.59 ng/ml (range 16.5-44.6 ng/ml) compared with 5.88±2.14 ng/ml (range 2.4-9.7 ng/ml) in controls with highly significant difference. So can use

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the TIMP-1 as a marker elevated in traumatic brain injury and glucose level is one of parameter that associated with mortality in patient with traumatic brain injury.

Keywords: serum, Tissue matrix metalloproteinase inhibitor-1, serum glucose, traumatic brain injury

Introduction

Traumatic brains injury (TBI) it an acquired defect which inhibits brain functions resulting to complete or partial brain cell defects and this disorder is not congenital and refers to the dysfunction of one of the functions of the brain. TBI are the cause of deaths for many traumatized peoples as well as a major source of disability for people between the ages of 20-40 years (Haddad, et al,.2012) . Traumatic brain injury leads to acute or damaging head injury that interrupts the normal brain function that causing altered perception and memory changes in mood and major changes in sensory and motor in many patients. Neuroimaging is typical for determining severity early on after injury Determination of altered consciousness or lack of consciousness to Determination of the existence of post traumatic amnesia and evaluation of the Glasgow Coma Scale score has been the gold standard in trauma patient neuroscience evaluation since Teasdale and Jennett established it in 1974(Scott, etal,.2015). Glasgow Coma Scales (GCS) it import ants components of a primary surveys are obtains an accurates GCS has becomes the standards for quantitative calculation TBI magnitude and the neurological state of a patient's base on three components: muscle control, verbalizations and openness of the eye. (Graham , et al ,. 2016).The TBI is categorizes into three group mild's TBI (GCS: 13–15) moderates TBI (GCS: 9–12) and severest TBI (GCS: 3–8). (Salim, et al,. 2018) . Mild Traumatic brain injury GCS 13 to 15 most cranial trauma injuries fall into this category Patients are responsive and may be confused and they can speak and understand order. (Zollman ,et al ,.2016)

Moderate Traumatic Brain Injury GCS (9-12) these patients are normally drowsy and acquired but not comatose and They will have their eyes open to detect uncomfortable sensations They are at high risk of health decline and require monitoring (Zollman ,et al ,.2016)

Severe traumatic brain injury is GCS (3 to 8) these patients are acquired for comatose do not follow orders and can show of important feature and They have severe defective

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physiological and metabolic brain and are at high risk of secondary brain damage and degradation (Zollman,etal,.2016).

Matrix metalloproteinases (MMPs) are a family of proteinases which have the role of remodeling in the extracellular matrix (ECM) and are regulated by matrix metalloproteinase (TIMP) tissue inhibitors .MMPs play a role in numerous physiological processes such as morphogenesis tissue remodeling menstrual cycle and cell growth and in numerous pathological processes such as atherosclerosis and inflammation in invasion of tumors and brain ischemia. (Lorente, et al ,.2019).

Tissue inhibitors of metalloproteinases TIMP-1 make up a class of secreted glycoprotein and TIMPs inhibit MMPs' proteolytic activities by forming close noncovalent complexes with TIMPs being two-domain proteins bound by three disulfide bonds and three disulfides every site and could be that TIMPs bind MMPs at a ratio of 1:1 such that when the expression of TIMPs matches that of MMPs in equilibrium and the MMP is therefore hindered by TIMP binding to its catalytic domain. This TIMP and MMP equilibrium disturbance impacts CNS ECM-to-cell and cell-to cells signaling (Wright,etal,.2016).

TIMP-1 and -2 have been reported to be substantially improved in eccentric muscle damage sustained by exercise (Kim , et al ,. 2016)

Tissue inhibitor of metalloproteinase-1 (TIMP-1) is a protein implicated in the control of inflammation in a number of autoimmune diseases (Eisner, et al ,. 2017).

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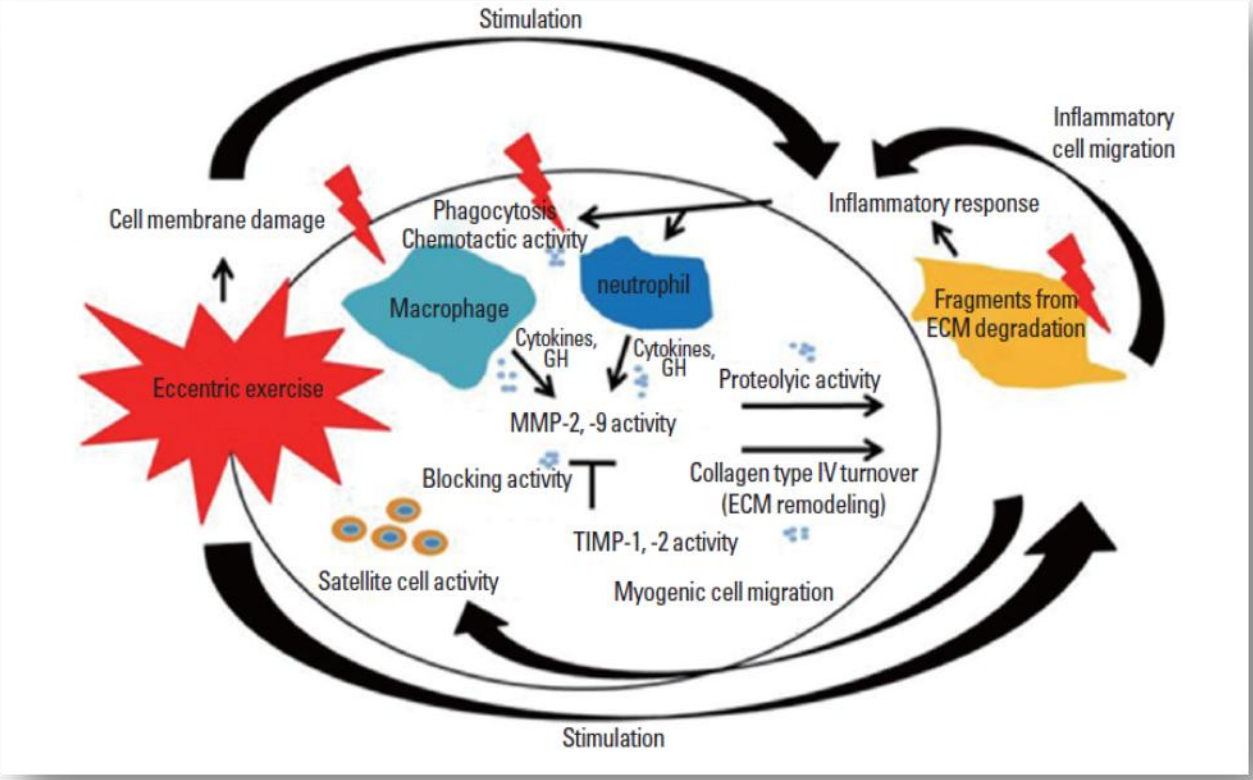

Figure1-1: TIMP responses after eccentric exercise (ECM) extracellular matrix and (GH) growth hormone (MMP) matrix metalloproteinase (TIMP) tissue inhibitor of metalloproteinase. (Wright , et al ,. 2016).

TIMP-1 concentrations were slightly higher in older patients at 72 h after poly trauma in Many clinical trials have recently verified the essential function of both tissue injury and acute inflammation proteins as caused by several inflammatory conditions such as serious trauma or sepsis and burn and severe TBI. . High levels of TIMP-1 were associated with 90-day death and the high levels of TIMP-1 are correlated with higher mortality rates after traumatic brain injury a prognostic biomarker in TBI patients. The TIMP-1 tends to be an indication of the degree of pathological immune activation and is correlated as bad outcome in these cases (Braunstein ,etal,.2020).

Glucose is the main substrate used by the brain under normal conditions glycogen and high-energy phosphate compounds such as phosphocreatine and adenosine phosphates only support neuronal functions for 1–3 min (Rostami,etal,.2014).

TBI has been associated with increased blood glucose levels so the Hyperglycemia has been associated with poor outcome and increased mortality and There are several

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mechanisms by which hyperglycemia are induced after TBI have already reported that patients with severe TBI had significantly higher serum glucose levels compared to patients with mild TBI Patients with a serum glucose level greater than 151mgdl it will may be develop coagulopathy which is associated with increased morbidity and mortality (Alexiou, etal,2019).

Material and methods

Study subjects

Study design is Case Control study , the goal of study are demonstrate possibility of using this enzyme Evaluate of serum TIMP-1in assessing the severity of head injuries and Glucose level in patient with TBI.

Methods: The study was executed during the term from April 2020 to September 2020.Serum was collected from Al-Imameen Al-Kadhimin Medical City Hospital and Neurosurgical Teaching Hospital in Baghdad. This Study Included 40 Patients (Male and Female) with Traumatic Brain Injury and 40 healthy people. Seven ml of bloods are takes from each Patients and control subjects.

Exclusion criteria:

*The exclusion criteria were representing as follow:

- 1-Patients with psychiatric illnesses
- 2-Patients with seizures.
- 3-CNS infection.
- 4-Patients were dead on arrival to ICU.

Sample collection:-

- Seven ml of blood was taken from each Patients and control subject.
- Serum will be separated after blood clotting and centrifuged at 2000rpm for 10 min and divided into small aliquots for analysis.
- The basal levels of serum blood glucose and TIMP-1.

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And use the to measure marker was different away according the substance that

Kits biochemical	Supplied Company
Human TIMP-1 ELISA Kit	Ray Biotech
Glucose	Analyticon

Results

Demographic Characteristics of the Study Population

The mean age of the patients was 40.37± 16.52 years (range 18-80 years) which did not differ significantly from that of controls (mean 35.0± 13.31years, range 18-70 years). However, females were more common among controls (60%) than patients (37.5%) with a significant difference

Variables	TBI(n=40)	Controls(n=40)	p-value
Glucose (mmol/L) Mean±SD Range	7.96±1.78 4.0-11.0	5.26±1.28 3.5-10.1	<0.001
TIMP-1(ng/ml) Mean±SD Range	25.06±7.59 ng/ml 16.5-44.6 ng/ml	5.88±2.14 ng/ml 2.4-9.7 ng/ml	p< 0.001

Serum Concentration of Tissue Inhibitor of Metalloproteinases-1

Mean serum concentration of TIMP-1 inn patients was 25.06±7.59 ng/ml (range 16.5-44.6 ng/ml) compared with 5.88±2.14 ng/ml (range 2.4-9.7 ng/ml) in controls with highly significant difference (Figure 1-2).

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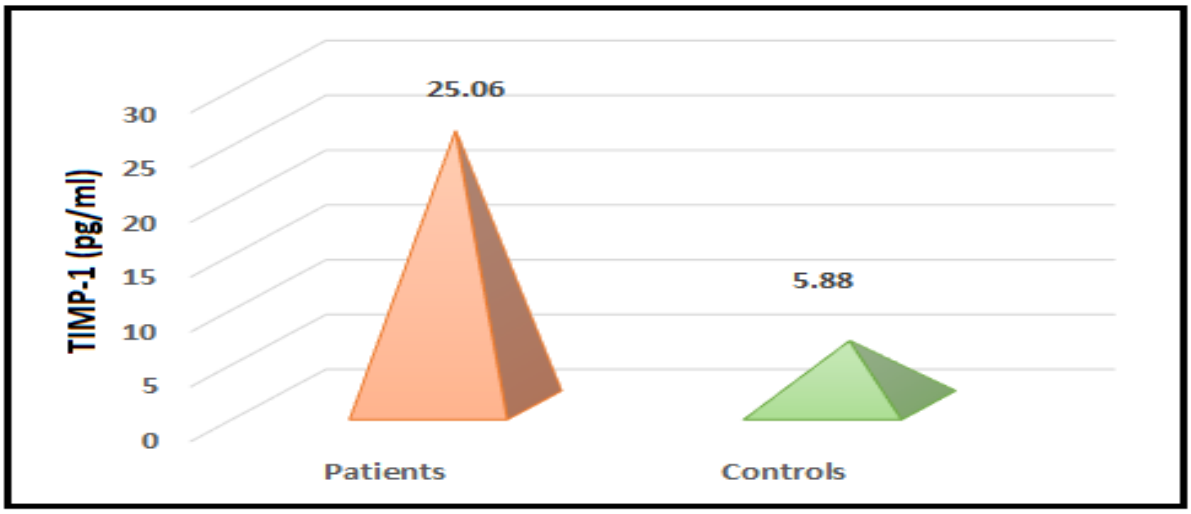

Figure 1-2: Mean serum concentration of Tissue Inhibitor of metalloproteinase-1 in patients and controls

Serum glucose was also higher inpatients than controls (7.96±1.78 mmol/L versus 5.26±1.28 mmol/L) with highly significant difference. .

TIMP-1 had a positive significant correlation with each of glucose (r= 0.429, p= 0.006) mild group showed significantly higher glucose concentration (9.72±2.12 mmol/L) than either moderate group (7.87±1.09 mmol/L) or severe group (7.95±1.78 mmol/L

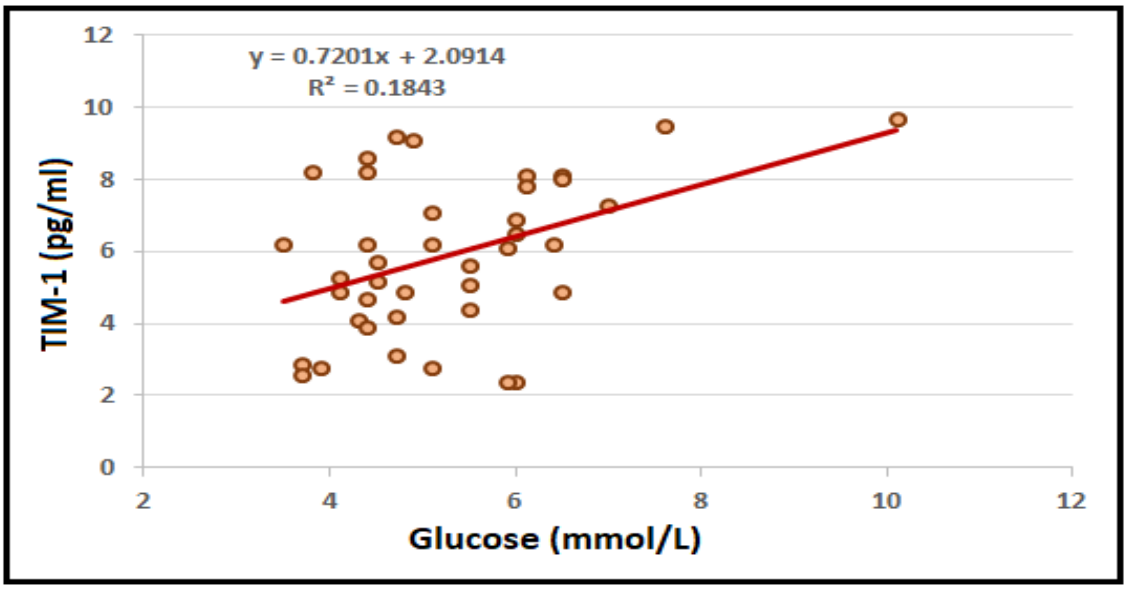

Figure (1-3) regression line between glucose concentration and TIMP-1 concentration

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Discussion

The cause of this injury and its rise is due to crashes and cases of falling from high altitudes, which have been found in Iraq in a large way, particularly motorcycle accidents and traffic accidents. That appear age is another important factor that greatly affects morbidity and mortality rates and that head injuries are not restricted to a specific age and This agrees with a study that confirms that age has a significant effect on mortality(Rafiq,et al,.2013) and In our result the serum glucose was also higher inpatients than controls (7.96±1.78 mmol/L versus 5.26±1.28 mmol/L) with highly significant difference. During the examination of patients with head injuries samples collected found that high blood sugar during the period of injury. This study agrees (Alexiou,etal,.2019) that show the Increased blood glucose levels can be found after TBI and Stress response has been suggested as a mechanism of hyperglycemia after TBI by the induction of catecholamine's that in turn leads to a decrease in insulin secretion the Systemic inflammatory response syndrome (SIRS) has been frequently found after TBI. In our study we find elevated levels of the enzyme TIMP-1 in the take data that this increase was compatible with this study (Lorente,etal,.2014) the TIMP-1 levels could play a role in pathophysiology of TBI It is possible that increased serum TIMP-1 levels in non-survivors TBI patients is not the cause of death in TBI patients but only a biomarker associated mortality serum TIMP-1 levels were associated with TBI mortality and could be used as a prognostic biomarker of mortality in TBI patients.(Lorente,etal,.2014).

The increase of this enzyme has a significant relationship in head trauma diseases and this corresponds to the study Circulating levels of some biomarkers TIMP-1 fragmented and related to inflammation and coagulation and oxidation and apoptosis have been recently associated with mortality in patients with TBI and These biomarkers that could help in the prognostic classification of the patients could open new research lines in the treatment of patients with TBI (Lorente,etal,.2015).

Conclusions

High concentration of enzyme TIMP-1 level with patient of traumatic brain injury rather than control patient. High concentrations of glucose level in patient with traumatic brain injury

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