

# **Protein S100b Serum Level as an Indicator of Intraventricular Hemorrhage in Preterm Infants**

**Thesis**

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# قياس نسبة البروتين إس 100 في مصل الدم كمؤشر لحدوث النزيف الدماغي البطني في الأطفال المبتسرين

رسالة

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## **List of Abbreviations**

CBC : Complete blood count

CBF	: Cerebral blood flow
CNS	: Central nervous system
CP	: Cerebral palsy
CRP	: C-reactive protein
CSF	: Cerebrospinal fluid
CT	: Computerized tomography
CUS	: Cranial ultrasound
EIA	: Enzyme immunoassay
G	: Grade
GA	: Gestational age
GM	: Germinal matrix
GMH	: Germinal matrix hemorrhage
GM-IVH	: Germinal matrix-intraventricular hemorrhage
HIE	: Hypoxic ischemic encephalopathy
HRP	: Horseradish peroxidase
HS	: Highly significant
IUGR	: Intrauterine growth retardation
IVH	: Intraventricular hemorrhage
LP	: Lumbar puncture
MAb	: Anti-S100 BB monoclonal antibody
Min	: Minute
MRI	: Magnetic resonance imaging
NEC	: Necrotizing enterocolitis
NS	: Non significant

**List of Abbreviations      - I -      (Cont.)**

PHH	: Post hemorrhagic hydrocephalus
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PT	: Prterm
PVI	: Periventricular Infarction
PVL	: Periventricular leukomalacia
RAGE	: Advanced glycation end product
RDS	: Respiratory distress syndrome
S	: Significant
S100	: S100 protein
U/S	: Ultrasonography
V	: Vein
VLBW	: Very low birth weight
VP	: Ventriculo-peritoneal

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## الملخص العربي

يعتبر نزيف بطين المخ من أهم أسباب الإعاقة العصبية الحركية والمعرفية في الأطفال المبتسرين، مما يؤدي إلى ارتفاع نسبة الوفاة والإعاقة بين الأطفال حديثي الولادة.

وحيث أن تحديد نسبة هذه الإصابة العصبية مبكراً يعتبر مشكلة شائعة في طب حديثي الولادة، فإن هذه الدراسة هدفت إلى قياس نسبة بروتين اس 100 في الدم كمؤشر لقياس حجم نزيف بطين المخ في الأطفال المبتسرين وكدليل على درجة الإصابة العصبية.

وقد أجريت هذه الدراسة على مجموعة من الأطفال في وحدة العناية المركزة لحديثي الولادة بمستشفى الجلاء للولادة.

وشملت الدراسة 30 طفلاً مبتسراً يتراوح العمر الجيني لهم ما بين 28-34 أسبوعاً وكان وزنهم عند الولادة ما بين 800-1700 جرام، وقد تم تقسيمهم إلى 3 مجموعات:-

**المجموعة الأولى:** وتشمل خمسة أطفال مبتسرين معتلين ولا يعانون من نزيف في بطين المخ.

**المجموعة الثانية:** وتشمل 15 طفلاً مبتسراً مصاباً بنزيف بطين المخ.

**المجموعة الثالثة :** وتشمل 10 أطفال مبتسرين طبيعيين كمجموعة ضابطة.

وقد تم أخذ التاريخ المرضي المفصل للأحداث ما قبل الولادة، أثناءها وما بعدها وذلك لجميع الأطفال.

كما تم فحص الأطفال حديثي الولادة فحصاً إكلينيكياً دقيقاً شاملاً الفحص العصبي، وعمل تحاليل معملية تشمل صورة الدم، عامل البروتين سي التفاعلي، غازات بالدم الشرياني، وكذلك عمل أشعة عادية على الصدر لتحديد درجة صعوبة التنفس وعدم اكتمال الرئة. وقد تم قياس نسبة بروتين اس 100 في الدم لجميع الأطفال خلال 48 ساعة من العمر باستخدام تقنية الكيموليمونيسنت، عمل أشعة

تليفزيونية على الدماغ لتحديد وجود نزيف في بطين المخ ودرجته. كذلك وقد تم إعادة الفحص العصبي الإكلينيكي بعد 7 أيام من عمر الطفل.

أظهرت نتائج الدراسة ارتفاعاً ذا دلالة إحصائية في مستوى بروتين اس 100 في دم الأطفال المصابين بنزيف بطين المخ مقارنة بباقي الأطفال المرضى والأصحاء، وقد كانت نسبة الزيادة ملحوظة بدرجة أكبر في حالات درجات النزيف الشديدة (الدرجات الثالثة والرابعة).

بل إن نسبة بروتين اس 100 كانت أعلى في الأطفال الذين توفوا خلال الأسبوع الأول عندهم في الأطفال الناجيين.

على الرغم من أن نسبة بروتين إس 100 لم تتأثر بعوامل مثل وزن الطفل وعمره الجنيني، إلا أنه كان هناك علاقة عكسية بين بروتين إس 100 ونتيجة أبحار في الدقيقة الأولى والخامسة من عمر الطفل.

كما كانت هناك علاقة اضطرابية بين مستويات بروتين إس 100 في دم الأطفال ودرجة نزيف بطين المخ وكذلك درجة نضوج الرئة والذين احتاجوا لجهاز تنفس صناعي مقارنة بالأطفال المولودين بدرجة أعلى في اكتمال الرئة والذين لم يحتاجوا لهذا النوع من العلاج.

وفي النهاية نستطيع أن نستنتج أن بروتين إس 100 يعتبر مؤشراً دقيقاً لدرجة الإصابة العصبية في الأطفال المصابين بنزيف بطين المخ.

## INTRODUCTION

Intraventricular hemorrhage, a common problem associated with prematurity, is accompanied by high morbidity and mortality rates (*Linder et al., 2003*). It is currently difficult to diagnose it during the first 72 hours of life, despite accurate postnatal monitoring (*Volpe, 1995*).

Early and accurate evaluation of the severity of brain damage remains one of the most difficult problems in the neonatal care units. To date, neuro-radiological evaluation together with cerebral blood flow studies are the most readily available methods. However, a biochemical index of brain injury would be a highly desirable diagnostic tool for augmenting the reliability of prediction of neurologic sequelae (*Garcia et al., 2000*).

Recently, S100b protein has been reported as a biochemical index of neuronal damage (*Stroick et al., 2006*).

It is a member of the calcium-binding proteins and constitutes a major component of the cytosol predominantly of glial cells which was studied by *Persson et al., (1987) and Sindis et al., (1984)* as a marker of cell damage of human central nervous system. It has also been shown to be a reliable tool to monitor brain distress in preterm infants (*Gazzolo et al., 1999*).

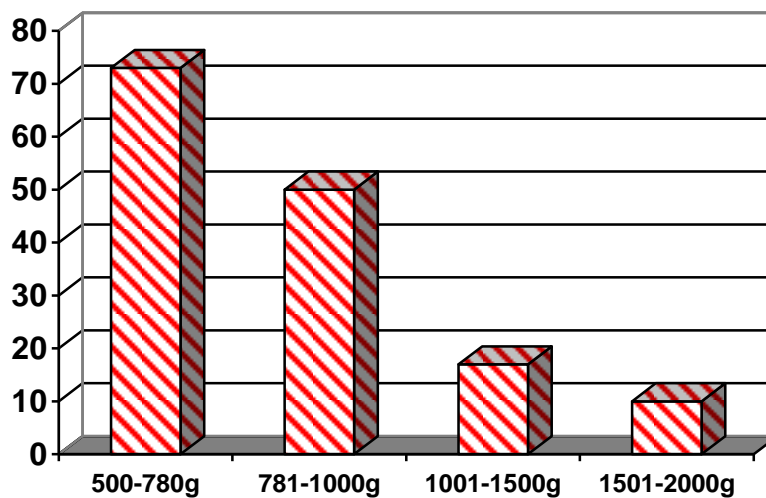
## **Aim of the Work**

The aim of this work is to investigate whether S100 protein is a useful mean of evaluating perinatal brain distress in preterm infants, which ultimately leads to intraventricular hemorrhage, through its assessment in sera of preterms with intraventricular hemorrhage versus those without.

## Intraventricular Hemorrhage of The Premature Infant

Intraventricular hemorrhage (IVH), also called germinal matrix-intraventricular hemorrhage (GM-IVH) is the most common variety of neonatal intraventricular hemorrhage and is characteristic of the preterm (PT) infant (*Ronald and Hill, 2003*).

The magnitude of the problem of IVH in the preterm infant relates to the relatively high and unchanging incidence of the prematurity, the relatively high survival rates of preterm infants, and the relatively high incidence of IVH. In parallel with the large number of PT births, there has been a continual decline in mortality rates. Approximately 85% of infants between 700-1500 gm birth weights survive the neonatal period (*Dokoupilova and Paluka, 2003*).



**Fig. (1):** Incidence of IVH as a function of birth weight of 210 infants admitted to a university based NICU. Numbers at top bars are percentage values. The overall incidence of IVH was 29% (*Perlman et al., 1993*)