

# **Karyotyping and Neurodevelopmental Follow-up of Intracytoplasmic Sperm Injection Children up to 4 Years of Age**

## **Thesis**

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# **دراسة الكروموسومات و متابعة النمو العصبى لأطفال الحقن المجهرى حتى عمر ٤ سنوات**

رسالة مقدمة من

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توطئة للحصول على  
درجة الدكتوراة فى طب الاطفال

تحت اشراف

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

"وَعَلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ وَكَانَ

فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا"

صدق الله العظيم

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# *DEDICATION*

*To My Dear Father*

*Prof. Dr. Selim Ismail Moustafa*

*Who*

*Live in my heart forever as a loving great father  
and  
gracious adviser*

*He will be remembered for his kindness & warmth  
radiated  
not only to his family but also extended to his students  
and friends all over the world*

*I owed him all the success and happiness in my entire life .*

*and*

*to My Mother*

*Who*

*Was always there for me with her support & love*

## **Abstract**

Intracytoplasmic sperm injection ( ICSI ) is now accepted as the treatment of choice for severe male infertility in many centers around the world . This study containing 80 cases and comparing them with 40 controls from the medical , genetic and neuro developmental point of view using the The Denver Developmental Screening Test (DDST), commonly known as the Denver Scale, Which is the most widely used test and has been standardized in 15 different countries for screening developmental problems in children.

**Keywords :** ICSI , Karyotyping , Denver Developmental Screening Test

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## LIST OF ABBREVIATIONS

<b>AAP</b>	American Academy of Pediatrics
<b>AB</b>	Abnormal
<b>ADHD</b>	Attention Deficit Hyperactivity Disorder
<b>ART</b>	Assisted Reproduction Technique
<b>ASRM</b>	American Society of Reproductive Medicine
<b>BLT</b>	Birth Length
<b>BSID - II</b>	Bayley Scales of Infant Development (2nd edition)
<b>BWT</b>	Birth Weight
<b>CA</b>	Congenital Anomaly
<b>CAT</b>	Cognitive Adaptive Test
<b>CBAVD</b>	Congenital Bilateral Absence of Vas Deference
<b>CLAMS</b>	Clinical Linguistic and Auditory Milestone Scale
<b>cm</b>	Centimeter
<b>CO<sub>2</sub></b>	Carbon dioxide
<b>COH</b>	Controlled Ovarian Hyperstimulation
<b>DDST</b>	Denver Developmental Screening Test
<b>DM</b>	Diabetes Mellitus
<b>DST</b>	Developmental Screening Test
<b>EEG</b>	Electroencephalogram
<b>ELBW</b>	Extremely Low Birth Weight
<b>ESHRE</b>	European Society for Human Reproduction and Embryology
<b>FSH</b>	Follicular Stimulating Hormone
<b>FT</b>	Full Term
<b>GA</b>	Gestational Age

<b>GIFT</b>	Gamete Intra Fallopian Transfer
<b>gm</b>	gram
<b>GnRH</b>	Gonadotropin Releasing Hormone
<b>GnRH - a</b>	Gonadotropin Releasing Hormone agonist
<b>GQ</b>	General Quotient
<b>hCG</b>	human Chorionic Gonadotropin
<b>HEPES</b>	Hydroxyl ethyl piperazine ethane sulfonic acid
<b>hMG</b>	human Menopausal Gonadotropin
<b>HT</b>	Height
<b>HTN</b>	Hypertension
<b>ICSI</b>	Intracytoplasmic Sperm Injection
<b>IQ</b>	Intelligence Quotient
<b>IVF</b>	In Vitro Fertilization
<b>Kg</b>	kilogram
<b>LAMI</b>	Low and Middle Income
<b>LBW</b>	Low Birth Weight
<b>LT</b>	Length
<b>MESA</b>	Microsurgical Epididymal Sperm Aspiration
<b>ml</b>	milliliter
<b>mm</b>	millimeter
<b>N</b>	Normal
<b>NBW</b>	Normal Birth Weight
<b>NC</b>	Naturally Conceived
<b>NICH</b>	National Institute of Child Health
<b>NICU</b>	Neonatal Intensive care unit
<b>PDD</b>	Pervasive Developmental Delay
<b>PHA</b>	Phytohemagglutinin M form

<b>PT</b>	Preterm
<b>PVP</b>	Poly-vinyl-pyrrolidone
<b>PZD</b>	Partial Zona Dissection
<b>RBCs</b>	Red blood cells
<b>\$</b>	American Dollar
<b>SC</b>	Spontaneously Conceived
<b>SD</b>	Standard Deviation
<b>SPSS</b>	Statistical Package for Social Science
<b>STEP</b>	Screening Test for Evaluating Preschoolers
<b>SUZI</b>	Subzonal Sperm Injection
<b>TESE</b>	Testicular Sperm Extraction
<b>TET</b>	Tubal Embryo Transfer
<b>UK</b>	United Kingdom
<b>USA</b>	United states of America
<b>VLBW</b>	Very Low Birth Weight
<b>wk</b>	week
<b>WPPSI-R</b>	Wechsler Preschool and Primary Scales of Intelligence-Revised
<b>WT</b>	Weight
<b>ZIFT</b>	Zygote Intra Fallopian Transfer

## **Introduction and Aim of the Work**

Intra cytoplasmic sperm injection ( ICSI ) is a successful treatment for severe male factor infertility , since the first description of a successful human pregnancy , the technique has been widely applied and more than 750 centers are now using the technique in Europe alone . In ICSI, a single sperm is injected directly into the vitellus of an oocyte in metaphase II. This procedure bypasses all natural sperm selection barriers. Concerns have been expressed about the use of ICSI. Theoretically the sperm used may carry genetic abnormalities or may have structural defects. There is also potential for chemical or mechanical damage to the oocyte and for the introduction of foreign material (*Sutcliffe et al.,2001* ) .

Concerns about possible adverse outcomes for children conceived using ICSI were highlighted in 1998 when one year old ICSI children were found to be at increased risk ( relative risk = 9.2 ) of delayed mental development compared with children conceived naturally or using IVF . As the findings were biologically plausible, it was considered important to reassess child development when a more accurate measure of long term cognitive ability could be obtained ( *Leslie et al.,2003* ) .

There are biologically plausible reasons why children conceived using ICSI may be at increased risk for delayed mental development. Several studies have concentrated on the evaluation of risks associated with ICSI. The publication of a few recent articles on the subject is providing an opportunity to reconsider the situation ( *Leslie ,2004* ) .

Generally , women conceiving via ICSI are older , more often primipara and present increased rates of uterine pathologies compared to women conceiving naturally . Further more , Assisted reproduction technique pregnancies are source of anxiety resulting in significant increased rates of caesarean section in addition to elective caesarean section as outcome of these pregnancies are considered precious babies . ICSI children present an increased risk of low birth weight often linked to multiple pregnancy but this is also true for singleton pregnancy ( *Wittermer et al.,2004* ) .

Major studies have not revealed a significantly increased rate of malformations in ICSI children. However, sporadic observations of errors in genomic imprinting or of rare tumors in children conceived by ICSI point to a need for increased vigilance of ICSI practices.

Based on the previous data it has been found that further studies of ICSI babies concerning medical , genetic and neurodevelopmental outcome are much needed as breakage of natural barriers in ICSI children during fertilization may have implications on their clinical outcomes .

The aim of this work is to study ICSI babies, singleton and twins and compare them with singleton naturally conceived children from the genetic and neuro developmental point of view.