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

Thesis
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by

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

" وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا "

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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 contaning 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

AAP	American Academy of Pediatrics
AB	Abnormal
ADHD	Attention Deficit Hyperactivity Disorder
ART	Assisted Reproduction Technique
ASRM	American Society of Reproductive Medicine
BLT	Birth Length
BSID - II	Bayley Scales of Infant Development (2nd edition)
BWT	Birth Weight
CA	Congenital Anomaly
CAT	Cognitive Adaptive Test
CBAVD	Congenital Bilateral Absence of Vas Deference
CLAMS	Clinical Linguistic and Auditory Milestone Scale
cm	Centimeter
CO_2	Carbon dioxide
COH	Controlled Ovarian Hyperstimulation
DDST	Denver Developmental Screening Test
DM	Diabetes Mellitus
DST	Developmental Screening Test
EEG	Electroencephalogram
ELBW	Extremely Low Birth Weight
ESHRE	European Society for Human Reproduction and Embryology
FSH	Follicular Stimulating Hormone
FT	Full Term
GA	Gestational Age

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

PT	Preterm
PVP	Poly-vinyl-pyrrolidine
PZD	Partial Zona Dissection
RBCs	Red blood cells
$	American Dollar
SC	Spontenously Conceived
SD	Standard Deviation
SPSS	Statistical Package for Social Science
STEP	Screening Test for Evaluating Preschoolers
SUZI	Subzonal Sperm Injection
TESE	Testicular Sperm Extraction
TET	Tubal Embryo Transfer
UK	United Kingdom
USA	United states of America
VLBW	Very Low Birth Weight
wk	week
WPPSI-R	Wechsler Preschool and Primary Scales of Intelligence-Revised
WT	Weight
ZIFT	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 Π. 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 (***Sutecliffe etal.,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 etal.,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 ***(Wittemer etal.,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.