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STUDY OF CD ٣٤ AMONG SMALL FOR GESTATIONAL AGE FULL TERM NEONATES

Thesis

Submitted for Partial Fulfilment
of Master Degree in **Paediatrics**

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بسم الله الرحمن الرحيم
وَأَنْزَلَ اللهُ
عَلَيْكَ الْكِتَابَ
والْحِكْمَةَ
وَعَلَّمَكَ مَا لَمْ
تَكُنْ تَعْلَمُ
وَكَانَ فَضْلُ
اللهِ عَلَيْكَ
عَظِيمًا
صدق الله العظيم
سورة النساء آية
(١١٣)

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Walid Elkobrosy

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LIST OF ABBREVIATIONS

Abbrev.	Full term
AC	Abdominal circumference
AGA	Appropriate for gestational age
AGM	aorta-gonad-mesonephros
ALDH^{br}	Aldehyde dehydrogenase bright
ALL	Acute lymphoblastic leukemia
BFU-E:	Burst forming unit – erythroid.
BM	Bone marrow
CADUCEUS	Cardiosphere-Derived Autologous Stem Cells to Reverse Ventricular Dysfunction
CB	Cord blood
CBC	Complete blood count
CD٣٤	Cluster of differentiation ٣٤
CFC	coloney forming cells
CFU – GM:	Colony forming unit - granulocyte-macrophage
CFU-E	Colony forming unit, erythrocyte.
CFU-GEMM:	Colony forming unit, granulocyte-erythrocyte-macrophage-megakaryocyte.
CMV	Cytomegalovirus
CRP	C- reactive protein
CRU / SRC:	Competitive repopulating unit /NOD/SCID mouse repopulating cell.
CS	Caesarean section
EDTA	Ethylene-diamine-tetra-acetic acid
EFW	Estimated fetal weight
EPCs	Endothelial progenitor cells
ES	Embryonic system
F/A ratio	Femure to abdomen contour ratio
FABPs	Fatty acid binding proteins
FGR	Fetal growth restriction
GA	Gestational age
GIT	Gastro intestinal track
GLUT١	Glucose transporter ١
GVHD	Graft versus host disease
HC	Head circumference
HLA	Human leucocytic antigen
HPP-CFC:	High proliferating potential - colony forming cell.
HSCs	Hematopoietic stem cells
HT	Length
HTN	Hypertension
HUCB	Human umbilical cord blood
I/T ratio	Immature / total neutrophils ratio
ISHAGE	International society for cellular therapy
IUD	intra uterine death
IUGR	Intrauterine growth restriction
kDa	Kilodalton , ١٠٠٠ unified atomic mass units

LIST OF ABBREVIATIONS (Cont...)

Abbrev.	Full term
LTC-IC/ CAFC:	Long-term culture-initating cell / cobblestone area-forming cell.
MNCs	Mononuclear cell count
NICU	Neonatal intensive care unite
NVD	Normal vaginal delivary
PE	Preeclampsia
PRECISE	A Randomized Clinical Trial of Adipose-Derived Stem Cells in Treatment of Nonrevascularizable Ischemic Myocardium
PT	Preterm
SCIPIO	Cardiac Stem Cell Infusion in Patients With Ischemic Cardiomyopathy
SD	Standard deviation
SFH	Symphyseal fundal height
SGA	Small for gestational age
TCD	Transverse cerebellar diameter
TNC	total nucleated cells
TORCH	Toxoplasmosis, Rubella, Cytomegalovirus, Herpes simplex type ٢.
U/S	Ultra sound
UCB	Umbilical cord blood
UTI	Urinary tract infection
WT	Weight

INTRODUCTION

Small for gestational age (SGA) is an infant whose weight is lower than population norms or lower than a predetermined cuttoff weight. SGA infant are defined as having a birth weight below the ١٠th percentile for gestational age or >٢ standard deviation below the mean for gestational age ***(Kinzler et al., ٢٠٠٧).***

Intrauterine growth restriction (IUGR): refers to a condition with decrease in fetal growth rate that prevents an infant from obtaining his or her complete growth potential and achieves its genetically determined potential size ***(Banister et al., ٢٠١١).***

SGA infants have birth weights below the ١٠th percentile for the population's birth weight–gestational age relationship. SGA infants include constitutionally small infants growing at their potential and infants with IUGR. SGA/IUGR is a result of poor maternal environment, intrinsic fetal abnormalities, congenital infections, or fetal malnutrition ***(Baschat, ٢٠٠٧).***

Intrinsic fetal abnormalities causing SGA/ IUGR (often termed primordial short stature) include Russell-Silver, Seckel, Noonan, Bloom, and Cockayne syndromes, and progeria. Many children with mild SGA/IUGR and no intrinsic fetal abnormalities exhibit catch-up growth during the first ٣ years ***(Baschat, ٢٠٠٧).***

However, ١٥–٢٠٪ remains short throughout life, particularly those whose growth restriction in utero occurred over several months rather than just the last ٢–٣ months of gestation. Catch-up growth may also be inadequate in preterm SGA/IUGR infants with poor postnatal nutrition. Children who do not show catch-up growth may have normal growth velocity, but they will follow a lower height percentile than expected for the family. In contrast to children with constitutional growth delay, those with SGA/IUGR have skeletal maturation that corresponds to chronologic age or is only mildly delayed ***(Baschat, ٢٠٠٧).***

One of the most important goals of effective antenatal care is the detection of the fetus at risk from suboptimal growth. Fetuses identified during pregnancy as being small for gestational age (SGA) comprise a heterogeneous group in regard to aetiology, management and prognosis ***(Resnik, ٢٠٠٤).***

Stem cell therapy has proven of clear benefit in a diverse range of diseases. Research tries to find the best source for these cells ***(Rookmaaker, ٢٠٠٣).***

Ethical, political, and biological issues limit the embryonic stem (ES) cell therapies. This mandates the use of non-ES cell therapies to solve this problem. Stem cell sources should be easily available in large numbers as in the bone

marrow, adipose tissue, and umbilical cord blood ***(Verfaillie, ٢٠٠٠).***

Human umbilical cord blood (HUCB) has been established as a source for hematopoeitic stem cell transplantations since the first transplantation was performed in ١٩٨٨. Cord blood collection is easier and safer. The naive nature of newborn's immune system is one of its major advantages. This allows HUCB transplantations with less restriction of the HLA system, and with fewer encountered graft versus host disease (GVHD). HUCB is the major source for hematopoeitic stem cell transplantation in hematological and oncologic diseases ***(Goldstein, ٢٠٠٧).***

HUCB is a rich available source for hematopoeitic and mesenchymal stem cells, which are alternative sources for bone marrow transplantation. They have high number of early and committed hematopoietic progenitor cells ***(Gluckman, ١٩٩٧).***

Thus, CB stem cells can be used to treat a wide variety of diseases including cardiovascular, hepatic, ophthalmic, orthopedic, neurological, and endocrine diseases ***(Harris, ٢٠٠٧).***

Clinical results and research on cord blood transplantation are promising. HUCB stem cells are proved to promote skin wound/lesion repair and myocardial repair after infarction ***(Valbonesi, ٢٠٠٤).***

In neural repair, studies concluded the reparative power of stem cells in brain and spinal cord injuries, and neurodegenerative diseases ***(Iwanami, ٢٠٠٥).***

The expression or absence of specific cell surface antigens is used to characterize the hematopoietic progenitor/ stem cells. It is widely accepted that the cell surface glycoprotein CD٣٤ (type I transmembrane protein) is expressed on the majority of hematopoietic stem cells. CD^{34^+} may be involved in cell–cell adhesion by promoting adhesion of hematopoietic cells to the stromal layer of bone marrow ***(Healy, ١٩٩٥).***

Previous studies involved CD^{34^+} expression in full term and preterm newborns; however its relation to IUGR is still under research.

AIM OF THE WORK

The aim of this work is to evaluate cord blood hemopoietic progenitor stem cell $(CD^{٣٤})^{+ve}$ cells in small for gestational age full term neonates and to study its relationship with factors associated with intrauterine growth restriction (IUGR).