STUDY ON IMMUNOHISTOCHEMISTRY OF UMBILICAL CORD WITH HISTOLOGICAL CHANGES AND NEONATAL REPERCUSSIONS IN INTRAUTERINE GROWTH RESTRICTION

A THESIS

Submitted by

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In partial fulfilment for the award of the degree

Of

DOCTOR OF PHILOSOPHY

Under the Supervision of

Dr. G. SUMATHY, M.Sc., Ph.D.,

DEPARTMENT OF ANATOMY

FACULTY OF MEDICINE

BHARATH INSTITUTE OF HIGHER EDUCATION AND RESEARCH

CHENNAI -600 073

AUGUST 2023

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ACKNOWLEDGEMENT

First and foremost, I am thankful to the almighty for giving me knowledge, ability, opportunity and strength to complete this thesis.

I would like to acknowledge my warmest thanks to the following members of Bharath Institute of Higher Education and Research: Vice-Chancellor- **Prof. K. Vijaya Bhaskar Raju**, Registrar- **Dr.S. Bhuminathan**, Controller of Examination- **Dr. R.M.Suresh** and former Research Dean- **Dr. M. Prem Jaya Kumar (late)** and present R & D Dean **Dr .A. P Naveenchandran** for giving me an opportunity to register and complete my Ph.D. I am thankful to Ph.D. section staff **Dr. M. Sriram** and **Mrs. Shanthi** for their support.

I would also like to thank my Doctoral Committee members- **Dr. N.Venkata Lakshmi, Dr. M.Karthik Ganesh** and **Dr.S. Jaya Kumari** for their valuable comments and suggestions, which helped to shape and refine this thesis.

I am deeply indebted to my supervisor, **Dr. Sumathy Govindarajan** for the continuous support of my Ph.D study and research, for her patience, motivation, enthusiasm, and immense knowledge. Her guidance helped me in all the time of research and writing of this thesis. I could not have imagined having a better advisor and mentor for my Ph.D study. Words fall short to express her unconditional and unlimited support in my thesis.

I could not have undertaken this journey without following faculty of KIMS, Koppal: **Dr. Vijayanadh Itagi,** Director; **Dr. Channabasanagouda**, Professor and HOD, Department of Anatomy I also extend my thanks to **Dr. Vijayashree**, Assoc Prof of Pathology.

I would like to express my deepest gratitude to **Dr. B. H. Narayani**, Professor of OBG for moral support, encouraging and standing with me to carry out research in the department by giving valuable inputs. I thank **Dr. Surekha S M**, Assoc. Prof of OBG for constantly clarifying my doubts whenever I ask and suggestions during the course of my research.

This endeavor would have been possible without contributions of **Dr. Stheevan**, Pathologist who helped us in procuring the marker kits and explaining the whole IHC procedures. We extremely appreciate the welcome of Palamur Biosciences Private Limited, Mahbubnagar for their support in this research.

I am extremely grateful to **Dr. Manjula K** and **Dr. Chetana B** and their friends, my students who helped me a lot during the pandemic in data and sample collection.

I must express my very profound gratitude to my school friends who made me to reach this position in my tough times. I would like to acknowledge the immense contribution of my fellow research scholar **Dr**. **Upendhar Reddy P** who builds the courage each day to complete work in time. I also thank **Mr. Bhaskar K**, Asst. Prof who helped us in statistical work. I thank **Mr. I Gnana Chandu** who helped us in alignment of data.

I owe this thesis to my parents **Mr. Ch. Ramulu** and **Mrs. Bhagyam** for showing faith in me and liberty to choose what I desired.

Special thanks to my sisters **Mrs. I. Nirmala**, **Mrs. P. Rajini**, **Mrs. N. Sailaja** and my brother **Mr. Ch. Hari Babu**, brother in laws -**Mr. I. Koteswara Rao, Mr. P. Subba Rao, Mr .N. Thrivendra Babu** and sister-in-law, **Mrs. Ch. Jyothi** who always stood by me and provided strength in pursuing this work.

It's my fortune to acknowledge the support of my uncle & aunt **Mr .B. Prasad** and **Mrs. Suvartha**.

I would like to express my gratitude to **Mr. A L P Devananda Babu** & **Deva Swarna Kumari**, my in-laws for their continuous support and valuable prayers.

My earnest thanks to **Mr. Marciano Wrightman** and **Mrs. Divya Wrightman** for their encouragement and moral support.

I express my deep sense of gratitude to my spouse **Mrs**. **Ch. Navya**, for her love, understanding, tremendous moral support and joy to me. It makes me happy to express my love to little angel, **Ch**. **Adwitha**, my daughter who joined in mid-way of my journey into research and always brought a smile and made each day better than the best.

SUDHAKARA BABU CHELLI

ABSTRACT:

Background:

Umbilical cord is of fetal origin and disturbance of blood flow through them would affect fetal growth. IUGR is a clinical disorder when the estimated fetal weight is below 10th percentile. It is classified into symmetrical, asymmetrical and mixed types. IUGR is an outcome caused by several risk factors, mainly maternal, placental, fetal, genetic, and other unknown factors. Intrauterine fetal death and fetal growth restriction are caused by hyper and moderate coiling of umbilical cord. Reduced artery and vein wall-to-lumen ratio has been observed in pathological groups such as preeclampsia, fetal growth restriction, fetal distress, gestational diabetes, oligohydramnios, and chronic hypertension.

Methodology

This study was carried out on 100 samples after taking ethical clearance from the institute. After delivery, umbilical cord was cut and fixed in formalin and processed for histomorphometry, histopathology, Masson's trichrome and immunohistochemistry. Morphometric analysis was carried out by using Leica LAS V4.12 software. Histopathology and immunohistochemistry interpretation was carried out with help of two pathologists who were unaware of this study. We used Leica/DM 1000-Microscope to view the slides in our study.

Summary

VEGF is an angiogenic factor and its immunoreactivity was less in IUGR when compared to normal. Endoglin is an anti-angiogenic factor its immunoreactivity was more in IUGR than the normal cord. It suggests that anti-angiogenic activity of endoglin interfere with vasculogenesis and inhibits the expression of VEGF. NSE expression was more in IUGR when compared to normal and GFAP expression was mild in IUGR while it was nil in normal cord. These markers indicate the injury of brain in IUGR neonates. Higher cephalization index was observed in IUGR shows brain injury. Neonatal weight, CAN score are less in IUGR which confirms the undernutrition.

NICU admission, fetal distress, still birth amount of liquor was more in IUGR when compared to normal and showed statistical significance in our study. All the histological parameters were less in cases when compared to normal. This might be the reason for reduced size of vessels and diminished blood flow to fetus. Only venous dilatation and Whartons jelly oedema was observed in IUGR cords. No significance was observed when immunomarker are correlated to histomorphometry and histopathology. Endoglin showed significant negative correlation with cephalization index.

Keywords: umbilical cord, intrauterine growth restriction, immunohistochemistry, CAN score, cephalization index, brain injury

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ABBREVATIONS

8OHdG - 8hydroxy 2`deoxyguanosine

Ab - antibody

AC - abdominal circumference

Ag - antigen

B.Wt - Birth weight

BI - Brain injury

BMI - Body Mass Index

CAN - Clinical Assessment of Nutrition

CC- Chest circumference

cfDNA - Cell free DNA

CI - Cephalization index

CNS - central nervous system

Conc - Concentration

ECF- Extra cellular fluid

FGR - Fetal growth restriction

FM - Fetal malnutrition

FW - Fetal weight

GD - Gestational diabetes

GF - Growth factor

GFAP- Glial fibrillary acidic protein

GH - Growth hormone

HC - Head circumference

HIF1 α - Hypoxia inducing factor 1α

HTN- Hypertension

IGF - Insulin like growth factor

IHC - Immunohistochemistry

IUD - Intrauterine death

IUFD - Intrauterine fetal death

IUGR - Intrauterine growth restriction

IVH - Intraventricular hemorrhage

MAC - Midarm circumference

MMP2 - Matrix metalloproteinase2

MSCs - Mesenchymal stem cell

NEC - Necrotizing enterocolitis

NICU - Neonatal intensive care unit

NIM - Neuronal injury marker

NSE - Neuron specific enolase

PE - Preeclampsia

PI - Ponderal index

PLCT - Placenta

PLGF – Placental growth factor

PT - Preterm

Ref1 - Redox factor 1

sEGFR - Soluble epidermal growth factor receptor

sEng - sEndoglin

sFlt1 - soluble fms like tyrosine kinase1

SMC - Smooth muscle cell

UA - Umbilical artery

UC - Umbilical cord

UPVP - Uteroplacental vascular pathology

USG - Ultrasonography

UV - Umbilical vein

VEGF - Vascular endothelial growth factor.

WJ - Wharton's jelly

Wt - Weight