UMBILICAL CORD GHRELIN IN PRETERM AND TERM NEWBORNS AND ITS RELATION TO SOME METABOLIC HORMONES AND ANTHROPOMETRIC MEASUREMENTS

THESIS

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List of Abbreviation

- GH: growth hormone.
- GHS: growth hormone secretagogue.
- GHRP: growth hormone releasing peptide.
- GHS-R1a: growth hormone secretagogue receptor 1a.
- GHRH: growth hormone releasing hormone.
- GH-IGF-1 axis: growth hormone –insulin growth factor 1 axis.
- GLP-1: glycoprotein 1.
- IGF-I: insulin growth factor 1.
- STAT: signal transducers and activators of transcription 1.
- EAE:
- SCN: suprachiasmatic nucleus.

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INTRODUCTION

Ghrelin and Leptin are newly discovered metabolic hormones that play an important role in the regulation of appetite, carbohydrate, lipid metabolism and energy balance of the human body **(Ng et al., 2005).**

Ghrelin is a 28-amino acid peptide secreted by the fundus of the stomach, the hypothalamus and the placenta in rats and humans. Ghrelin stimulates GH secretion and has orexigenic effects and also increases adiposity by decreasing fat utilization **(Farquhar et al., 2003)**.

In adult humans, plasma ghrelin increases and decreases to a nadir 90 min after the meal, suggesting that it plays a physiological role in meal initiation **(Cummings et al., 2001).** Ghrelin is closely associated with glucose metabolism and body mass. It induces hyperglycemia and decreases plasma insulin concentration. Conversely, hyperglycemia and insulin (in absence of hypoglycemia) decrease plasma ghrelin **(Farquhar et al., 2003)**.

Leptin is single chain proteohormone secreted by white adipocytes and acts on leptin receptor of the hypothalamus to suppress the appetite and stimulates energy expenditure **(Kojima et al., 1999).**

Recent evidence suggests that both ghrelin and leptin follows a similar diurnal pattern and may interact in providing important adiposity signals from the periphery to the central nervous system **(Traebert et al., 2002).**

Previous studies on leptin in preterm infants demonstrated a significant temporal relationship between

increase in circulating leptin levels and rapid accumulation of body fat mass, especially during the latter half of the third trimester **(Ng et al., 2005).**

Whether ghrelin follows the same pattern of increase as Leptin with increasing gestational age is unknown**.** So, we will discuss that in our study.

Aim of the Work

This study aims to investigate plasma ghrelin concentration at birth, the relationship of ghrelin with metabolic hormones including Leptin and insulin and its association with anthropometric parameters, in appropriately grown preterm and term newborns.

Fetal Growth

Growth is the process of increasing size (body dimensions) over a period of time ***(Lubchenco and Koops, 1987)***. Normal fetal growth depends on genetically predetermined growth potential that can be predicted from parental characteristics. This growth potential is further modulated by fetal, placental, maternal and external factors ***(Bascha and Wiener, 2004)***.

Fetal Development

- **Embryonic period**

The human embryonic period represents the first 8 weeks of intrauterine life. The first week of human development begins with fertilization followed by early cell division forming the blastocyst. This is then followed by a series of cell divisions without cytoplasmic growth. At the end of the first week and into the second week the implantation occurs.

By the second week rapid growth/differentiation of the extraembryonic tissue (trophoblast) occur. The cavity within the blastocyst and the inner cell mass that forms the embryo begin early differentiation. During the third week trophoblast cells continue to invade uterine wall in the process of early placentation (villi formation). Also axial process formation (notochord), mesoderm differentiation (somites, heart, vascular) ectoderm differentiation (neuralation), the embryonic disc begins to fold,on the embryo surface sensory placodes and limb buds appear. This period of organogensis is usually extended to cover until 8 weeks of development. Folding of the embryo continues and the earliest functioning organ is the heart. Other systems such as the circulatory, digestive, urogenital and nervous system begin to all take shape ***(Hill, 2007)***.

During WK 4-8, lateral folding of the embryonic plate, followed by growth at the cranial and caudal ends and the budding of arms and legs, produces a human like shape. Precursors of skeletal muscles and vertebrae (somites) appear, along with the branchial arches. By the end of WK 8, the rudiments of all major organ systems have developed ***(Needlman, 2004)***.

Table (1): Stages of fetal growth

Week	*Developmental Events*
1	**Fertilization and implantation; beginning of embryonic period**
2	**Endoderm and ectoderm appear(bilaminar embryo)**
3	**First missed menstrual period; mesoderm appears (trilaminar embryo); somites begin to form.**
4	**Neural folds fuse; folding of embryo into human-like shape; arm and leg buds appear; crown-rump length 4-5 mm**
5	**Lens placodes, primitive mouth, digital rays on hands**
6	**Primitive nose, philtrum, primary palate; crown-rum length 21-23 mm**
7	**Eyelids begin**
8	**Ovaries and testes distinguishable**
9	**Fetal period begins; crown-rump length 5 cm; weight 9 g**
10	**External genitals distinguishable**
20	**Usual lower limit of viability; weight 460 g; length 19 cm**
25	**Third trimester begins; weight 900g; length 25 cm**
28	**Eyes open; fetus turns head down; weight 1,300 g**
38	**Term**

(Needlman et al., 2004)