GHRELIN LEVEL IN CONSTITUTIONAL DELAYED PUBERTY

Thesis
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List of Abbreviations

- **GnRH** – Gonadotrophin Releasing Hormone
- **SD** – Standard Deviation
- **CDGP** – Constitutional Delayed Growth and Puberty
- **CDGM** – Constitutional Delayed Growth and Maturation
- **LH** – Leutinizing Hormone
- **FSH** – Follicle Stimulating Hormone
- **HCG** – Human Chorionographic Hormone
- **IGF-1** – Insulin Growth Factor
- **IDDM** – Insulin Dependant Diabetes Mellitus
- **CRH** – Corticotrophic Hormone
- **SBP** – Systolic Blood Pressure
- **DBP** – Diastolic Blood Pressure
- **C-AMP** – Cyclic Adenosine Monophosphate
- **TSH** – Thyroid Stimulating Hormone
- **GHSR** – Growth Hormone Secretagogue Receptor
- **ISS** – Idiopathic Short Stature
- **NPY** – Neuropeptide Y
- **ACTH** – Adrenocorticotrophic Hormone
- **ERK** – External Activated Receptor Kinase
- **MAPK** – Mitogen Activated Protein Kinase
- **PKC** – Protein Kinase C
- **IGHD** – Isolated Growth Hormone Deficiency
- **IP3** – Inositol triphosphate
- **T4** – Thyroxin
- **Ca** – Calcium
- **GH** – Growth Hormone
- **mRNA** – Messenger Ribonucleic Acid
- **LHRH** – Leutinizing Hormone Releasing Hormone
- **HPG** – Hypothalamo-Pituitary-Gonadal axis
- **BMI** – Body Mass Index
- **Hb** – Hemoglobin
- **Plt** – Platelet count
- **TLC** – Total Leucocytic count
- **ESR** – Erythrocyte Sedimentation Rate
- **TNF** – Tumour Necrosis Factor

- **IL** – Interleukin
- **FBG** – Fasting Blood Glucose
- **N** – Number
- **NS** – Non-significant
- **Sig** – Significant
- **HS** – Highly significant
- **X^2 -** Pearson Chi Square
- **R** – Pearson Correlation Coefficient
- **HCL** – Hydrochloride
- **AChE** – Acetyl Choline Esterase
- **EIA** – Enzyme Immunometric Assay
- **CBC** – Complete Blood Count
- **MPH** – Mid-parental Height
- **EDS** – Ethylene Dimethane Sulfonate
- **RT-PCR** – Reverse Transcriptase Polymerase Chain Reaction
- **SCF** – Stem Cell Factor
- **ELISA**
- **EDTA**
- **HUVEC** – Human Umbilical Vein Endolthelial Cells
- **NO** – Nitric Oxide
- **PI3** – Phosphoinositide 3 Kinase
- **HEX** – Hexaghrelin
- **VDCC** – Voltage Dependant Calcium Channels
- **ATP** – Adenosine Triphosphate
- **ADP** – Adenosine Diphosphate
- **KATP** – ATP sensitive potassium channel
- **GOAT** – Ghrelin O Acyltransferase
- **DHEA** – Dihydroepiandrosterone
- **DHEAS** – Dihydroepiandrosterone Sulphate
- **SHBG** – Sex Hormone Binding Globulin
- **POMC** – Propiomelanocortin
- **GABA** – Gamma Amino Butyric Acid
- **KAL** – Kallman
- **CAH** – Congenital Adrenal Hyperplasia
- **AgRP** – Agouti Related Peptide
- **BMD** – Bone Mineral Density
- **PSA** – Prostate Specific Antigen

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Introduction

Puberty is the result of increasing gonadotropin releasing hormone (GnRH) release by the hypothalamus followed by a complex sequence of endocrine changes with functioning of negative and positive feedbacks and associated with the development of sex characteristics, a growth spurt and reproductive competence **(Van de Waal,2004**)

There is wide variation in the onset of puberty .According to the national center for health statistics, the upper 95th percentile in the United States for age for boys 14 years (i.e an increase in testicular size being first sign) and for girls is 12 years (breast development being the first sign). **(Bhasin, 2007**)

It is considered to be delayed if the initial signs of sexual maturation do not appear by an age that is 2.5 SD beyond the mean for healthy boys or girls (**Bhasin, 2007**)

Delayed Puberty result from inadequate gonadal steroid secretion which, in turn, is most often caused by a defective secretion of GnRH from the hypothalamus resulting in low gonadotropin secretion, the key functional defect in patients with constitutional delay. **(Francois and William, 2007)**

Delayed puberty can, however, also be caused by variety of hypothalamic, pituitary and gonadal disorders **(Francois and William, 2007)**

Impaired secretion of hypothalamic gonadotropin –releasing hormone is generally the underlying cause of secondary hypogonadism. It can be functional in origin (as constitutional delay of puberty, chronic illness, excessive exercise, and malnutrition) or related to associated pathology (as with hypothalamic and pituitary tumors, especially craniopharyngioma) or genetic (idiopathic hypogonadotropic hypogonadism kallmann syndrome**) (Raivio et al, 2007)**

Recently published studies indicate that ghrelin and leptin play a role in puberty initiation and progress. They have been implicated in regulation of GnRH secretion, with ghrelin having inhibitory, and leptin having facilitatory effects. It has been hypothesized that elevated ghrelin

and reduced leptin concentrations could be implicated in altering the tempo of puberty in adolescents with CDGP. **(El-Eshmawy et al, 2010)**

Ghrelin is a 28-amino acid peptide produced in a variety of human tissues; however the major source of circulating ghrelin is the stomach **(Kangawa et al, 1999)**

Expression of ghrelin has been demonstrated in mature Leydig cells of rat and human testis, as well as in steroidogenically active luteal and interstitial hilus cells of the ovary. Gonadal expression of acylated-ghrelin receptors was also shown in Sertoli and Leydig cells of the testis and in follicular, luteal, surface epithelial and interstitial hilus cells of the ovary. **(Fernandez-Fernandez et al, 2007)**

Ghrelin can inhibit GnRH pulse activity in ovariectomized adult monkey **(Vulliemoz et al, 2004)**

Ghrelin inhibits LH secretion *in vivo* in the pre-pubertal males as well as gonadectomized male and female rats, whereas FSH remained unaffected **(Fernandez-Fernandez et al, 2004)**

Aim of the Work

To evaluate ghrelin hormone levels among adolescent boys with constitutional delayed puberty and their relation with reproductive hormones including LH, FSH and Testosterone.

Review of Literature