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Anusha Singh

Contents

Abbreviations

%	Percentage
µg	Microgram
µm	Micrometer
µl	Micro litre
°C	Degree Celsius
3β-HSD	Three beta hydroxyl steroid dehydrogenase
aa	Amino acid
ANOVA	One way of analysis of variance
Adipo R1	Adiponectin Receptor 1
BSA	Bovine serum albumin
CL	Corpus luteum
DAB	Diaminobenzedine
DHEA	Dehydroepiandrosterone
DMEM	Dulbecco Modified Eagle's Medium
E2	17- β estradiol
ECL	Enhanced Chemilumunscence
ERK	Extracellular signal-regulated kinase
EDTA	Ethylenediamine tetra acetic acid
ELISA	Enzyme-linked immunosorbent assay
g	Gram
GC	Granulosa cells
GPR54	G- protein coupled receptor 54
GnRH	Gonadotropin Releasing Hormone
HA	Hyperandrogenism
HI	Hyperinsulinemia
H_2O_2	Hydrogen peroxide
HRP	Horseradish peroxidase
IR	Insulin Receptor
IgG	immunoglobulin
kDa	Kilo Dalton
KP	Kisspeptin
LH	Lutenizing hormone
LH-R	Lutenizing Hormone receptor
mg	Milligram
ml	Millilitre

mm	Millimetre
ng	Nanogram
PBS	Phosphate buffered saline
PCNA	Proliferating cell nuclear antigen
PCOS	Polycystic ovary syndrome
pg	Pico gram
PMSF	Phenylmethylsulphonyl fluoride
PVDF	Polyvinylidene fluoride
rpm	Revolutions per minute
S.E.	Standard Error
SDS	Sodium Dodecyl sulphate
StAR	Steroidogenic Acute Regulatory protein
T	Testosterone
TC	Theca cells
WAT	White Adipose Tissue

Preface

The polycystic ovary syndrome (PCOS) is one of the leading causes of infertility due to anovulation in women. It affects upto 10% women of reproductive age and over 75% of all cases of anovulatory infertility. It is multifactorial disorder characterized by chronic anovulation, hyperandrogenism (HA), hyperinsulinemia (HI), insulin resistance (IR), polycystic ovary and recurrent miscarriage. About half of women with PCOS are obese. The mechanism of anovulation is uncertain, but there is evidence of incomplete development of antral follicle, which might be due to abnormal interaction of insulin and luteinizing hormone (LH) on granulosa cells. Decreased fertility in PCOS may also be due to changed levels of gonadotropin- releasing hormone, gonadotropins, HA and HI. Despite the prevalence of PCOS worldwide, a clear understanding of the aetiology, pathophysiology and treatment of this syndrome remains inconclusive. The heterogeneous pathophysiology of PCOS results in a number of constraints for its management. If PCOS is not corrected, it may lead to other serious consequences such as Type II diabetes mellitus, cardio-vascular diseases, ovarian and endometrial cancer, depression etc. Thus, PCOS is a major issue for women's health with ramifications well beyond the reproductive age.

HA is considered as a core feature of PCOS since it can be induced by treatment with large dose of androgen. About 70-80% of women with HA are diagnosed with PCOS. HA is also the major factor behind most clinical manifestation of PCOS. Insulin resistance followed by HI is regarded as the second most important factor responsible for development of HA and other PCOS-like features. Besides HA and abnormal insulin secretion and action, defects in neuro-endocrine regulation lead to hyperpulsatility of GnRH secretion and obesity related metabolic dysfunctions. These are the two important factors responsible for manifestation of PCOS. Because the primary cause of PCOS is not yet precisely known, treatment is mainly directed to the symptoms of the disorder. Currently, reversing HA and IR or inducing ovulation in women with PCOS constitute the fundamental approach for the management of PCOS. Although the drugs such as anti-androgen-spironolactone; insulin sensitizers-metformin and ovulation inducer-clomiphene citrate are often being used to induce ovulation and pregnancy in PCOS, but effective treatment to manage PCOS is still a challenge. The obesity factor and neuro-

endocrine/hypothalamic regulator are relatively understudied factors that may play important role in the development and manifestation of the PCOS.

Therefore, in the present study the obesity factor, adiponectin and hypothalamic factor, kisspeptin, are selected to evaluate their role in development of PCOS-like features in the mouse. The information obtained through studies on mouse-model may help in developing suitable therapeutics for PCOS treatment in humans. Further, it is thought out to examine the physiological role of adiponectin and kisspeptin in the ovary of cyclic mice. In order to confirm the pathophysiological role of adiponectin and kisspeptin in women with PCOS, a preliminary study is also performed in the ovaries of normal and PCOS women.

The study incorporated in this thesis is broadly divided into three sections. **Section-I** describes the role of obesity factor, adiponectin on ovarian activities of normal and PCOS-induced mice. This section is divided into two chapters. **Chapter 1** incorporates the effects of adiponectin on ovarian activities of normal mice. **Chapter 2** describes the effect of adiponectin on ovarian activities in PCOS mice. This chapter is subdivided into part 2.1 and 2.2 describing the effect of adiponectin on ovarian activities in PCOS-induced mice *in vitro* (Part 2.1) and *in vivo* (Part 2.2). **Section-II** incorporates the studies demonstrating the role of hypothalamic factor, kisspeptin on ovarian activities of normal and PCOS-induced mice. This section is also divided into two chapters. **Chapter 3** deals the effects of kisspeptin on ovarian activities of normal mice. **Chapter 4** describes the effect of kisspeptin on ovarian activities of PCOS-induced mice. **Section-III** includes **Chapter 5** which incorporates the comparative studies demonstrating the immunolocalization of GnRH, GnRH-R, Kisspeptin and Adiponectin on the ovary of normal and PCOS women.