

Association of single nucleotide polymorphism in the promoter region of the Inhibin α gene with infertility in Pakistani males

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Madam, infertility is a worldwide problem. World Health Organization (WHO) defines infertility as a reproductive system disorder, resulting in failure to attain pregnancy after a regular unprotected sexual intercourse for 12 months or more.¹ It is further defined as, one couple out of six is suffering from infertility, the rate is equally distributed between males and females.^{2,3} For male fertility the gold standard is the quality of semen. Therefore, on the basis of poor quality of semen three major types of infertility as, oligozoospermia, asthenozoospermia, and teratozoospermia are reported.⁴ Other causes include: unfavourable environment for spermatogenesis, hormones regulation and gene mutations.¹ Infertility with unknown causes is termed as idiopathic infertility.²

About 30% of male infertility cases reported as genetic mutations in male gonads.⁴ Major focus of studies is on the genes expressing high mutation rates, like AZoospermia Factor (AZF) gene located on Y chromosome.⁵ However, three inhibin genes INHA, INHBB, and INHBA located on chromosome 2 (2q33-36, 2cen-q13) and chromosome 7(7p15-p13) respectively,⁴ are known to express in Sertoli cells of testis by producing their protein product "inhibin", an endocrine feedback regulator of pituitary follicle stimulating hormone (FSH) (Figure). Thereby, through their protein product inhibin

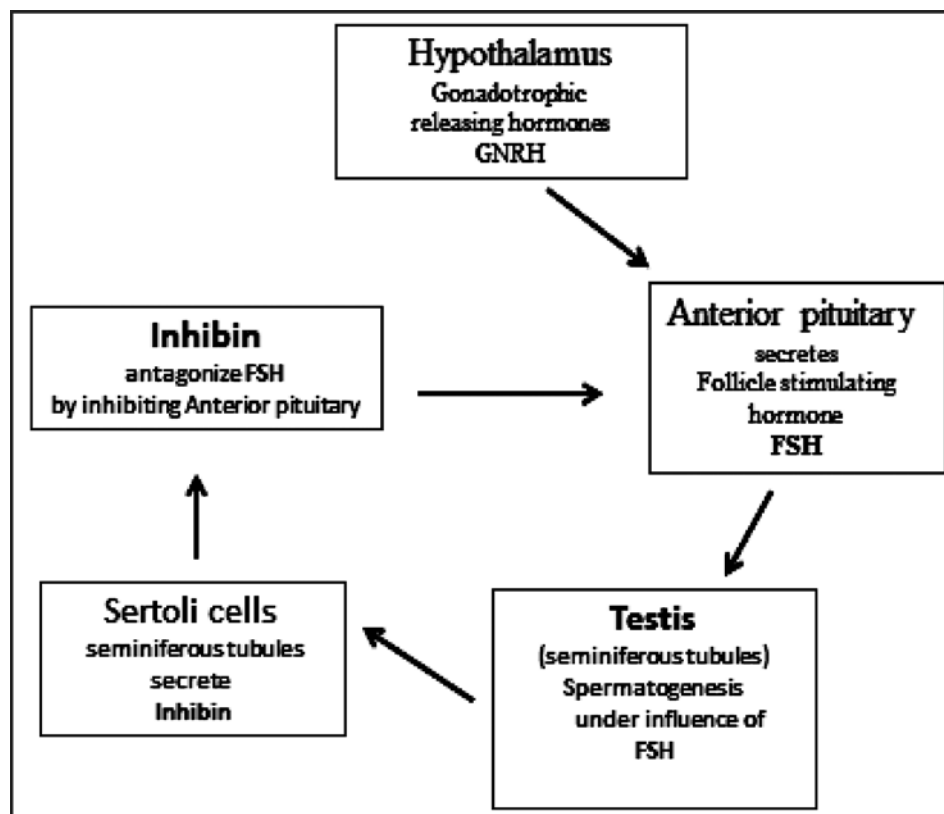


Figure: Depiction of endocrine feedback role of hormone inhibin on FSH regulating the process of spermatogenesis.

the inhibin genes (INHA) influencing the process of the spermatogenesis, hence play a significant role in maintaining male fertility or reproductive health.⁴

Inhibin is a glycoprotein composed of an 18 kDa α -subunit linked by disulfide bonding to a 14 kDa β A subunit (inhibin A) or β B-subunit (inhibin B).⁴ Both of the subunits inhibin A and B are known to present in immature germ cells the spermatogonia and developing germ cells including spermatocytes and spermatids.⁴ Strong link is revealed between serum inhibin B and spermatozoa concentration, disturbing this link can lead to azoospermia or primary testicular failure.⁴ Lots of work on hormonal assays has been carried out to prove the association of serum inhibin with male fertility. But little literature is available regarding the genes responsible for

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encoding inhibin. Even, only few studies have shown a link between male infertility and INHA gene polymorphism (124A>G;16C>T).⁴ Therefore, more studies should be carried out to confirm association between INHA gene mutations and male infertility.

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