

SIGNIFICANCE OF SERUM INHIBIN IN FEMALE INFERTILITY Muhammad Tayyab, Sarnia Samiullah*, Allah Ditta and Ghazala Jaffery

Postgraduate Medical Institute, Lahore and "Institute of Public Health, Lahore

Background: Serum inhibin, a glycoprotein hormone is secreted from granulosa cells in females and has been shown to suppress secretions of FSH from pituitary. **Methods:** A total of 45 women, 30 infertile subjects and 15 age matched fertile controls were included in this study. Blood samples from each subject were collected during follicular and luteal phases separately and were tested for serum inhibin levels using an enzyme linked immunosorbent assay (ELISA). **Results:** Serum inhibin concentration of infertile subjects during follicular phase was 35.5 ± 22.94 pg/ml and luteal phase was 32.4 ± 24.2 pg/ml. Whereas serum inhibin level in follicular phase was 10.39 ± 2.03 pg/ml and luteal phase was 12.78 ± 6.86 pg/ml of the fertile subjects. Serum inhibin was significantly raised in the infertile subjects as compared to the fertile subjects ($P < 0.05$). However, serum inhibin concentration during the follicular and luteal phases of the infertile subjects was not significantly different ($P > 0.05$). **Conclusion:** It is thus concluded that increased serum inhibin level may be treated as sensitive and early index of declining ovarian function

INTRODUCTION

The existence of inhibin has been postulated as early as 1932.¹ However, it has taken almost 53 years for the concept of inhibin to become a reality.² Inhibin is a glycoprotein hormone produced by the testis and ovary and is believed to have an important role in the physiological regulation of pituitary FSH secretion.

Infertility is a disease entity which has been recognized for centuries but to-date remains a dilemma for the clinicians from the diagnostic point of view.⁶ Flomional causes of female infertility are most accessible to the diagnosis and therefore, most amenable to treatment. Most of the studies on endocrine aspects of infertility have mainly focused on hormones other than inhibin. The role of inhibin, a hormone of ovarian origin remains to be elaborated from the infertility point of view.⁷

Several attempts have been made to investigate the role of inhibin in various phases of menstrual cycle, in pregnancy and in certain ovarian diseases. The first such report was about inhibin as a marker of granulosa cell tumors of the ovary and it was noted that inhibin increases in active neoplasm of granulosa cell and also in cases of residual disease and recurrent disease.

In view of the controversial reports on the role of serum inhibin in various disorders related to infertility this study on infertile females in reproductive age is conducted to ascertain the diagnostic importance of inhibin.

MATERIALS AND METHODS

Thirty infertile women between 18-35 years of age were included in this study from Sir Ganga Ram Hospital, Lahore. Fifteen age-matched subjects with proven fertility were included as controls. Blood samples, were drawn on day 7 and 21st day of menstrual cycle between 8-10 AM in disposable syringe. Serum was separated and assayed for inhibin through an enzyme linked immunosorbent assay (ELISA) using serotic KIT from Germany.

RESULTS

The mean \pm SD levels of inhibin in infertile subjects were 35.5 ± 22.94 and 32.4 ± 24.2 pg/ml respectively on the 7th day (follicular phase) and 21st day (luteal phase) (Table-1).

In the fertile subjects the mean \pm SD serum inhibin levels were 10.39 ± 2.03 and 12.78 ± 6.86 pg/ml in the follicular and luteal phases (Figure-1). The serum inhibin levels of infertile subjects in follicular phase were found to be significantly raised as compared to the fertile subjects ($P < 0.05$). Similarly, serum inhibin levels of infertile subjects in luteal phase were significantly raised ($P < 0.05$) as compared to fertile subjects.

Table-1: Comparison of serum inhibin concentrations in follicular and luteal phases of menstrual cycle in infertile and fertile subjects (Mean \pm SD Range values in parentheses)

Subjects	Inhibin (pg/ml)	
	Follicular phase (7 th day)	Luteal phase (21 st day)
Infertile n=30	35.5 ± 22.94 (12.56-58.44)	32.4 ± 24.2 (8.20-56.60)
Fertile n=15	10.39 ± 2.03 (0.46-4.32)	12.78 ± 6.86 <5 92-19.64
Statistical analysis Infertile vs Fertile Key	Significant $p < 0.05$	Significant $p < 0.051$

S = Significant ($p < 0.05$).

DISCUSSION

The hormonal aspects of infertility have received particular impetus in the past few decades. The hormonal disorders have not only provided valuable insight in to the pathogenesis but also to their generalized effects⁹ in the present study, the serum inhibin in the infertile subjects during follicular phase was significantly higher ($P < 0.05$) than the serum inhibin concentration in the fertile subjects during the same phase. Similarly, in the luteal phase of the infertile subjects, the serum inhibin concentration was significantly higher ($P < 0.05$) than the fertile subjects. The present work is supported by the study conducted by Yohkaichiya *et al*, who reported a rise in serum inhibin levels during follicular phase of menstrual

cycle in infertile subjects, considered as an indication of ovulation failure.¹⁰

Buckler *et al*, reported that elevated serum inhibin level may be involved in producing the discordant gonadotrophin secretions.¹¹ These findings are similar to the present results where the serum inhibin level of infertile subjects was significantly higher than the controls.

The findings of Hughes *et al*, also supported the present conclusions that increased serum inhibin levels may be treated as a sensitive and early index of declining ovarian function.¹² In the present findings also the infertile subjects had a raised serum inhibin level as compared to the fertile subjects.

It is thus concluded that as serum inhibin levels are markedly raised in both the follicular and luteal phases of menstrual cycle of infertile subjects who otherwise have no other abnormality. It is likely that serum inhibin contributes towards ovarian dysfunction which in turn is responsible for infertility.¹³ Furthermore, serum inhibin response can be closely related with a number of follicles which are stimulated to develop (in vitro fertilization).

Further long term studies of serum inhibin in larger patients samples using manipulative methods may be helpful to further elucidate the role of serum inhibin in female infertility.

REFERENCES

1. McBullagh DR. Dual endocrine activity of the ovary. *Science* 1932;76:19
2. Robertson DM, Foulds IM, Leiersha L. et al. Isolation of inhibin from bovine follicular fluid. *Biophys Res Commun* 1985; 126(1):220-26
3. Cotran RS, Kumar V, Collins T (eds). In *Robbins Pathologic Basis of Disease Ed 6 Philadelphia/WB Saunders Co* 1999 1076-77
4. McLachlan R.I, Robertson DM, Dekretser DM, Burger MB. Inhibin a nonsteroidal regulator of pituitary follicle stimulating hormone. *Bailliers Clin Endocrinol Metab* 1987.1(1):89-112
5. Weinbauer B, Bartlett JM, Hingscheidt T, Tsonis CB, Dekretser DM, Nicschlag F. Evidence for a major role of inhibin in the feedback control of FSH in the female rat, *J Reprod Fertil* 1989; 85(2):355-62.
6. Wren BG. Infertility and contraception in Wren BG (ed) *Handbook of Obstetrics and Gynaecology*. 2nd Ed London: Chapman and Hall. 1985:268.
7. Kuku SF, Akinyanju PA, Djiefo JO. Serum levels of gonadotropins, progesterone in infertile female. *Africans Int J Fertility* 1987; 32:393-98.
8. Lappohn RE, Burger HG, Bourn J, Bougah M, Kraus M. Inhibin as a marker for granulosa cell tumour. *Acta Obstet Gynaecol Scand* 1992, 155:61-65.
9. Christiansen C, Rus BJ. Five years with continuous combined estrogen/progesterone therapy. Effects on calcium metabolism, lipoproteins and bleeding pattern. *Br J Obstet Gynaecol* 1990; 97:1087-92.
10. Yohkaichiya T, Fukava T, Hoshiaki H, Yajima A, DeKretser DM. Inhibin: A new circulating marker of hydatidiform mole. *BMJ* 1989; 298(24): 1684-86.
11. I. I. Buckler HM, Robertson WR, Sun JG, Morris ID. Immunoreactive inhibin levels during ovarian stimulation may predict granulosa cell maturity. *Clin Endocrinol Oxf* 1992.37(6) 552-57.
12. Hughes EB, Robertson DM, Handelsman DJ et al. Inhibin and estradiol responses to ovarian hyper stimulation. Effects of age and predictive value for in vitro fertilization outcome. *J Clin Endocrinol Metab* 1990; 70:358-64.
13. Mayne PD (ed). In: *Clinical Chemistry in Diagnosis and Treatment*. Glasgow/ELST, 1994:132-155