ORIGINAL ARTICLE

Levels and Trends of Fecundity Hormones in Adolescence

RABAIL JAVED[1], FARKHANDA GHAFOOR[2], ASMA MUNIR[3], ATIYA MAHBOOB[4], MUHAMMAD ASIM[5]
[1]Research Officer NHRC (PMRC), Shaikh Zayed Medical Complex, [2]Senior Research Officer NHRC (PMRC), Shaikh Zayed Medical Complex, [3]Demonstrator, Department of Haematology, Shaikh Zayed Medical Complex, [4]Professor and Head of Dermatology Dept, Shaikh Zayed Medical Complex, [5]Statistician NHRC (PMRC), Shaikh Zayed Medical Complex, Lahore,
Correspondence: NHRC 2nd Floor Federal Post Graduate Medical Institute, Sheikh Zayed Medical Complex, Lahore. Mobile: 009-23214312913, Email: rabailjaveed@hotmail.com

ABSTRACT
Objective: To find the trends of fertility hormone profile among teenagers.
Study design: Retrospective analytical study.
Method: Recorded data in NHRC lab (year 2006- 2011) was statistically analyzed for different fertility hormones including leutinizing hormone (LH), follicular stimulating hormone (FSH), prolactin, testosterone, progesterone and cortisol, in teenager boys and girls (13-19 years).
Results: Out of 218 registered cases, 30 were males and 188 were females. An increase in cases of polycystic ovaries (PCO) was seen in 2007, 2010 and 2011. Hirsutism and infertility cases were high in year 2010 and 2011.
Conclusion: Disturbances of fecundity hormones can lead to an increase in infertility and obesity in both sexes and diseases as PCO and hirsutism in females. The causes of this increase should be seriously looked into and further elucidated by detailed and large scale study.

Keywords: Fecundity hormones. Infertility. Obesity. PCO. Hirsutism.

INTRODUCTION
Adolescent years are the most significant years of life when a boy develops into a man and girl into a woman. It is a period during which the body attains adult secondary sexual characteristics and reproducing capability. [1] Hormones are the key operators which not only help in physical development but also bring substantial impact on mental development during this transitory phase. [2] The onset of puberty depends upon fertility hormones reactivity [1] which influence countless biological processes across the adolescence, to cause permanent tissue-specific alterations in anatomy and physiology [2]. The subsequent hormonal changes regulate mental process, mood, growth, prenatal development, metabolism and tissue function[2]. A normal functioning of hormone brings normal physical and psychological health and healthy puberty. Age considered as adolescent in Asian countries is between 13 to 19 years.

In a number of studies it has been illustrated that girls of puberty age suffer from menses associated health problems such as premenstrual symptoms, acne, hirsutism, obesity, menstrual pain, and irregular menstrual cycles [3, 4]. The major cause of these problems is indeed hormonal imbalance which can also result into health issues as polycystic ovarian syndrome (PCOS) and primary or secondary infertility. [2] Similarly hormonal imbalance in boys can lead to fertility and puberty health problems such as erectile dysfunction, micro penis, late puberty and hair loss.[1]

Typically LH, FSH, prolactin, testosterone, progesterone and cortisol are considered as puberty hormones. LH and FSH levels are determined for diagnosis of oligomenorhea, PCOS (in girls), primary and secondary disorders involving the hypothalamus, pituitary glands or gonads in both sexes. Progesterone is measured in determining fertility in girls [5, 6]. Testosterone hormone has a fundamental role in adolescents. As in girls high levels of this hormone might result in hirutism. Whereas in adolescent boys this hormone is not only important for sexual characteristics, but also in shaping the personality, libido, pitch of voice, body shape, emotional and physical strength and sexual performance [7].

Prolactin chiefly causes breast enlargement and milk production in pregnancy. Higher levels of prolactin in teenagers can cause hypogonadism. The most important symptom of hyperprolactinemia in adolescent is

amenorrhea/oligmenorrhea, breast enlargement, galactorrhea, decreased libido, erectile dysfunction, failure to enter or progress through puberty, high risk of benign breast tumors and reduced bone density. Increased levels of prolactin can be because of prolactinomas that account for 40% of all pituitary tumors [8].

This retrospective study intended to assess all the above mentioned hormones in adolescent girls and boys based on data collected from national health research complex (NHRC), It provided trends in levels of fertility hormone during 2006-2011. By this the prevalence and association of specific diseases caused by hormonal imbalance have been assessed which may help in their early diagnosis and better management.

MATERIALS AND METHODS

This was a retrospective study conducted in NHRC, Shaikh Zayed Medical Complex, Lahore. Hormone profile (LH, FSH, Prolactin, Testosterone, Progesterone and Cortisol) of 218 teenage boys and girls (13-19 years) available in records of NHRC laboratory from year 2006- 2011 were reviewed. Patients with incomplete records were excluded.

Age, sex and lab results of analytes such as LH, FSH, prolactin, testosterone, progesterone cortisol and expected clinical diagnosis were recorded for the given period. The tests were conducted by NHRC laboratory where LH and FSH were measured using Immunometric Assay kits from Biocheck (USA). The calibration range of LH and FSH assays was upto 200mIU/ml with an analytical sensitivity of 1.0 mIU/ml and 2.5mIU/ml respectively. Enzyme Linked Immunosorbant Assay (ELISA) was used for the analysis of cortisol using kit of Novatec (Germany) with a calibration range of 500ng/ml and sensitivity of 2.24ng/ml. Testosterone, prolactin and progesterone were analyzed by ELISA method using kit of Biocheck (USA). The calibration range of these analytes was 18ng/ml, 3200mIU/ml and 25ng/ml respectively with a minimum sensitivity up to 0.05 ng/ml, 2.0mIU/ml and 0.05ng/ml respectively.

The sample handling and temperature conditions were strictly monitored for all procedures keeping them in accordance to manufacturer instructions. Assay precision was maintained by using routinely calibrated micro/multichannel pipettes from Gilson and washing steps were performed with automatic plate washer. For diagnostic assurance of results, all investigations were carried out with 5-6 standards points each time a batch was placed with 2 quality control pools. The results of all the tests were analyzed by using micro plate reader and MANTA software.

The clinical diagnoses were recorded from laboratory request forms. The interpretation of results was done under guidance of a gynecologist and dermatologist. The frequencies of recorded fertility hormones levels were clinically interpreted in accordance with their high, low or normal values. For females disturbed LH: FSH ratio inferred PCO, amenorrhea and infertility. Disturbed testosterone and progesterone levels inferred PCO and hirsutism while prolactin high or low levels were clinically interpreted as hyper/hypo prolactenemia, brain tumor and obesity related problems. Abnormal levels of cortisol presented as mood disturbances, depression, aggression and anxiety in teenagers. In males high levels of LH, FSH and progesterone were interpreted as puberty issues and very high levels, impotency. The abnormal levels of prolactin and cortisol had similar interpretation in males as in females. Raised testosterone level inferred aggressive behavior in males while its low level was interpreted as puberty related disorders and fertility problems.

Data analysis was done by using SPSS version 16.0. The data for age and gender for study period was presented as frequency and percentages. p- value <0.05 was considered significant. For quantitative variables t test and ANOVA were applied.

RESULTS

Out of 218 cases in the age group 13-19 years, 30 were males and 188 were females with mean age 16.7±1.7 and 17.2±1.7 years respectively (Table I).

Maximum LH: FSH ratio, high testosterone and prolactin levels among females were recorded in 2007, 2010 and 2011 respectively. The change in levels of prolactin and cortisol was insignificant ($p = 1.2$). (Table II).

Normal Ranges: LH in follicular phase: 2.0-18.0mIU/ml, FSH in follicular phase: 2.0-10.0mIU/ml, Prolactin: 65-666 mIU/ml, Progesterone in follicular phase: 0.6-1.26 ng/ml, Cortisol (morning): 138-625 nmol/L, Testosterone: 0.2-0.8 ng/ml

In males the frequency of hormones such as LH and FSH was maximum in 2006. Testosterone was normal in all teenagers. Levels of

progesterone and cortisol remained nearly unchanged between 2006- 2011. (Table III)

Table I: Age & sex distribution of study population during 2006-2011 (n=218)

		Male			**Female**		
YEAR	Total N	n (%)	Mean Age(yrs)	SD	n (%)	Mean Age(yrs)	SD
2006	38	9(23.6)	16.6	1.4	29(76.3)	17.2	1.4
2007	39	4(10.3)	16.0	1.7	35(89.7)	16.7	1.6
2008	24	4(16.6)	16.7	1.5	20(83.3)	17.7	1.3
2009	27	3(11.1)	17.7	1.5	24(88.8)	17.0	1.8
2010	48	5(10.4)	17.5	0.7	43(89.5)	17.3	1.9
2011	42	5(11.9)	16.0	4.2	37(88.1)	17.3	1.7
Total	218	30(13.7)	16.7	1.7	188(86.2)	17.2	1.7

Table II: Frequency chart of fertility hormone profile in females

Year	**LH: FSH**			**Testosterone**			**Progesterone**			**Cortisol**			**Prolactin**		
	*H	*L	*N	H	L	N	H	L	N	H	L	N	H	L	N
2006	15	3	2	-	1	-	-	-	-	-	-	-	5	8	-
2007	20	3	2	2	1	-	1	-	-	-	-	-	2	22	1
2008	10	5	1	4	1	-	1	-	-	-	2	1	-	8	1
2009	15	14	2	4	1	1	1	-	-	-	1	-	4	10	-
2010	15	15	4	17	-	-	-	-	-	-	-	-	1	24	-
2011	17	4	8	6	3	-	2	-	-	-	-	-	2	14	1
Total	92	44	19	33	7	1	5	-	-	-	3	1	14	86	3

*N= Normal, *L= Low ,* H= High

Table III: Frequency chart of fertility hormone profile in males
N= Normal, L= Low , *H= High
Normal ranges: LH: 2.0-18.0mIU/ml, FSH: 1.0-11.0mIU/ml, Prolactin: 73-356mIU/ml,

Year	LH			FSH			Testosterone			Progesterone			Cortisol			Prolactin		
	*H	*L	*N	H	L	N	H	L	N	H	L	N	H	L	N	H	L	N
2006	-	3	3	2	3	1	-	-	5	-	1	-	-	1	-	1	3	-
2007	1	2	-	1	3	-	-	1	-	-	-	-	-	-	-	-	1	-
2008	1	-	1	1	-	-	-	1	2	1	1	-	-	-	1	-	3	-
2009	1	1	-	-	2	-	-	1	-	-	-	-	-	-	-	1	1	-
2010	-	3	1	-	1	1	-	3	-	-	-	-	-	-	-	1	1	-
2011	-	1	-	1	2	-	-	3	1	-	-	-	1	-	-	1	1	-
Total	3	10	5	5	11	2	-	9	8	1	2	-	1	1	1	4	10	-

Cortisol (morning): 138-625 nmol/L, Testosterone: 3-10 ng/ml, Progesterone : 0.13-1.26 ng/ml

The clinical interpretations of recorded data revealed that the percentage of cases with PCO were almost equivalent in years 2006 and 2010 with a certain decline at year 2008 and 2009 and a significant (p=0.04) increase during 2007 and 2011. The number of cases with hirsutism increased over time and was maximum in the year 2010. (Figure I)

The percentage of cases with infertility increased in both sexes with no case in 2006, 2008 and 2009 while it was 8.9% and 7.7% in 2010 and 2011. Similarly the percentage of normal cases which were on an increase from year 2006 to 2009 decreased to around 36% in the year 2010 and 2011. (Figure II)

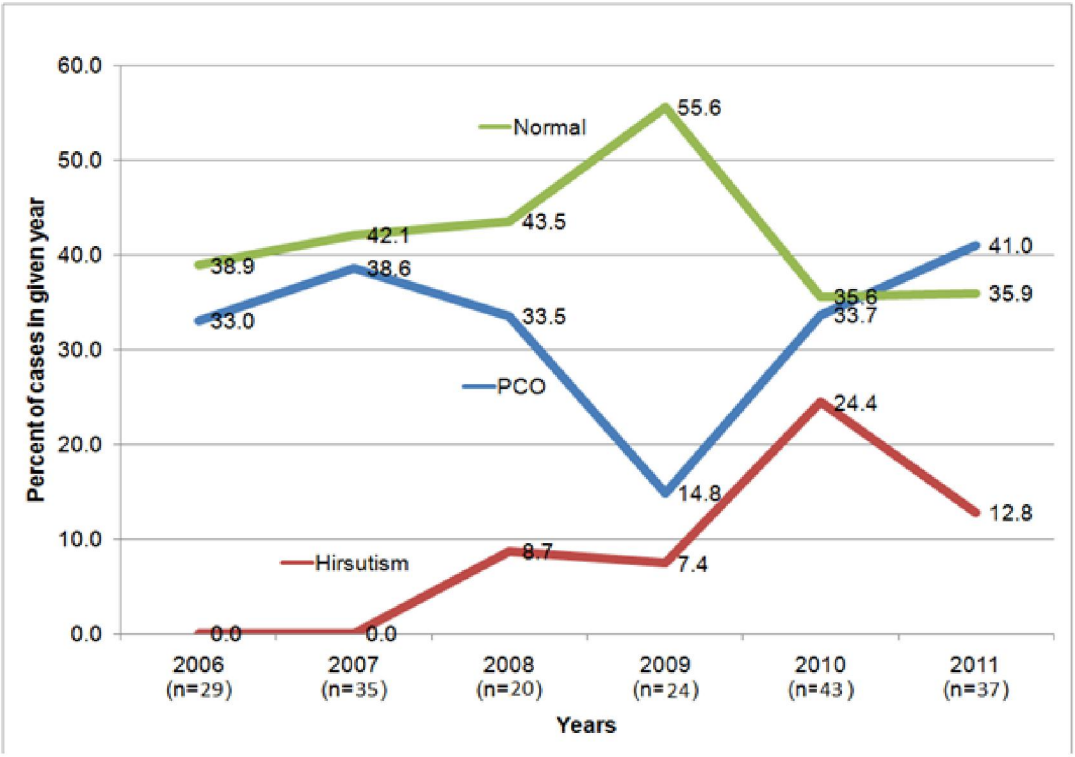
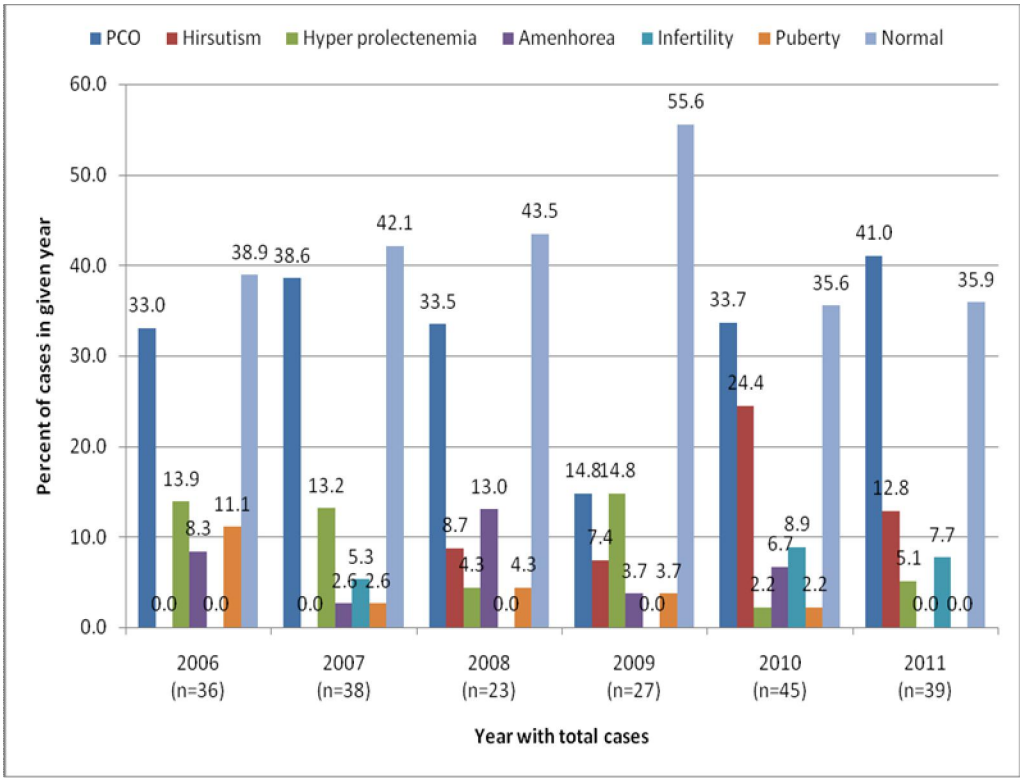


Figure I: Trends of females towards PCO and hirsutism during 2006-2011.



*Diseases as PCO, Hirsutism and Amenorhea only refer to females and their year wise trend.

Figure II: Trends of fertility associated diseases in male and female teenagers during 2006-2011

DISCUSSION

Teenage is a stressful time as the body and mind is passing through many changes. The hormones in the body not only allow procreating, but they also alter physical appearance and behavior. Hormonal imbalance occurs when hormonal secretions in the body are disrupted, which often leads to depression, anxiety, headaches and other problems [1].

This study was conducted on a retrospective data between years 2006-2011. The results showed a high frequency of teenage females getting tested for their puberty hormones than males. The reason behind this can be ethnic discrimination in the developing countries or that the females are affected more with physical and psychological hormone imbalance than males during adolescence. [9,10]

PCOS is a serious problem caused by hormonal imbalance. It increases risk of infertility, endometrial cancer and gestational complications. It has also been highly related with obesity, hirsutism, metabolic syndrome, type 2 diabetes mellitus and hypertension [11]. Several studies in American and European countries using NIH criteria have estimated an increase in the prevalence of PCO, hirsutism and infertility between 4-8% in their population [12-18]. In this study it was noticed that ratio of LH:FSH (1:1) increased upto 3:1 or 2:1 in the recent years (2010 and 2011). This increase in PCOS and hirsutism can be due to change in lifestyle of adolescents, as in last few years teenagers are more interested in eating junk/fast food than constraining to healthy diet. [19]

High levels of prolactin, testosterone which were noticed in this study can be a major cause of infertility and obesity in both sexes and its related diseases as PCO and hirsutism in females. The levels of these hormones can be increased or decreased due to many physiological and environmental factors including abdominal diseases, lead and other toxins present in surrounding environment, excessive radiographies, lack of healthy diet and exercise and use of drugs. [20] Unfortunately our teenagers are prone to all these risk factors which have escalated within a few recent years. [20] A recent study reported that placing laptops on the laps can decrease testosterone levels and cause male infertility. [21] More over stress agents as examinations or dating can also result in hormonal imbalance such as of cortisol and progesterone resulting in manic depression and puberty issue in adolescents. [21]

In this study the recorded data is limited. There is an urgent need of a larger population based study to justify the hormonal imbalances in adolescence.

CONCLUSION

Disturbances of fecundity hormones can lead to an increase in infertility and obesity in both sexes and related diseases as PCO and hirsutism in females. The causes of this increase should be seriously looked into and further elucidated by detailed and stratified sample size study.

REFERENCES

1. Dunkel L, Quinton R. Transition in endocrinology: induction of puberty. *Eur J Endocrinol*. 2014;170(6):229-39.
2. Nugent BM, Tobet SA, Lara HE, Lucion AB, Wilson ME, S Recabarren SE et al. Hormonal Programming Across the Lifespan. *Horm Metab Res.* 2012; 44(8): 577–86.
3. Perkin C. Holistic help. Effect of Stress. [Internet]. 2012. [cited 2014 Dec 3]. Available from http://www.holistichelp.net/effects-of-stress.html
4. Kauppila A, Martikainen H, Puistola U, Reinilä M, Rönnberg L. "Hypoprolactinemia and ovarian function". *Fertil Steril*. 1988;49 (3): 437–41.
5. Schwärzler P, Untergasser G, Hermann M, Dirnhofer S, Abendstein B, Berger P. "Prolactin gene expression and prolactin protein in premenopausal and postmenopausal human ovaries". *Fertil Steril*. 1997;68 (4): 696–701.
6. Corona G, Mannucci E, Jannini EA, Lotti F, Ricca V, Monami M, Boddi V, Bandini E, Balercia G, Forti G, Maggi M. "Hypoprolactinemia: a new clinical syndrome in patients with sexual dysfunction". *J Sex Med*. 2009;6 (5): 1457–66.
7. Gonzales GF, Velasquez G, Garcia-Hjarles M . "Hypoprolactinemia as related to seminal quality and serum testosterone". *Arch Androl*. 1989;23 (3): 259–65.
8. Snyder PJ. Clinical manifestations and evaluation of hyperprolactinemia. In: Cooper DS, Martin KA eds. Uptodate 2014. Available from: http://www.uptodate.com.
9. Perkin C. No-hype holistic health solutions. [Internet]. 2012. [cited 2014 Dec 3] Available

from http://www.holistichelp.net/hormone-imbalance.html
10. Centre of Disease and control prevention. [Internet]. 2013. [cited 2014 Nov 28]. Available from http://www.cdc.gov/reproductivehealth/infertility/.
11. Hacker Neville F. Hacker and Moore's essentials of Obstetrics and Gynecology: 5th ed. China: Elsevier; 2012.
12. Diamanti-Kandarakis E, Kouli CR, Bergiele AT, Filandra FA, Tsianateli TC, Spina GG, Zapanti ED, Bartzis MI. A survey of the polycystic ovary syndrome in the Greek island of Lesbos: hormonal and metabolic profile. J Clin Endocrinol Metab. 1999;11:4006–11.
13. Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. J Clin Endocrinol Metab. 1998;83(9):3078–82.
14. Asuncion M, Calvo RM, San Millan JL, Sancho J, Avila S, Escobar-Morreale HF. A prospective study of the prevalence of the polycystic ovary syndrome in unselected Caucasian women from Spain. J Clin Endocrinol Metab. 2000;11:2434–38. doi: 10.1210/jc.85.7.2434.
15. March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod. 2010;11:544–51.
16. Lindholm A, Andersson L, Eliasson M, Bixo M, Sundström-Poromaa I. Prevalence of symptoms associated with polycystic ovary syndrome. Int J Gynaecol Obstet. 2008;102(1):39–43.
17. Chen X, Yang D, Mo Y, Li L, Chen Y, Huang Y. Prevalence of polycystic ovary syndrome in unselected women from southern China. Eur J Obstet Gynecol Reprod Biol. 2008;139(1):59–64.
18. Kumarapeli V, Seneviratne Rde A, Wijeyaratne CN, Yapa RM, Dodampahala SH. A simple screening approach for assessing community prevalence and phenotype of polycystic ovary syndrome in a semiurban population in Sri Lanka. Am J Epidemiol. 2008;168(3):321–8.
19. Ravn P, Haugen AG, Glintborg D. Overweight in polycystic ovary syndrome. An update on evidence based advice on diet, exercise and metformin use for weight loss. Minerva Endocrinol. 2013;38(1):59-76.
20. http://www.stanford.edu/class/siw198q/websites/reprotech/New Ways of Making Babies/Causefem.htm
21. Hitti M. Laptop Computers May Affect Male Fertility. WebMD Health News. [Internet] 2004. [cited November 2014]. Available from http://www.webmd.com/infertility-and-reproduction/news/20041208/ laptop-computers-may-affect-male-fertility.