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Original research paper

Biochemical and endocrinological aspects of female infertility: Descriptive comparative study

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Abstract

Infertility is a disease of the reproductive system and its treatment can affect all aspects of people's lives, which can cause various psychological-emotional disorders or consequences including frustration, hopelessness, depression, guilt, anxiety and feelings of worthlessness in life. In order to evaluate Biochemical and endocrinological aspects of female infertility, a test-control study was designed. For the study 150 clinically diagnosed infertile female subjects and 150 age matched healthy females with one or more children were involved in the study as control. Level of uric acid concentration was comparatively higher among test group (5.5mg/dL) than the control subjects (4.4mg/dL) ($p<0.005$). The inflammatory marker (hsCRP) demonstrated a very high concentration among the test subjects than the control group (1.0±0.59) ($p<0.005$). It was evident that, study group expressed an FSH concentration of 30±10 and control with a FSH level of 12.8±6.00 ($p=<0.005$).

Keywords: Biochemical, endocrinological aspects, female infertility

Introduction

"Infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse" [World Health Organization (WHO), (2020)]. Meanwhile the WHO's epidemiologic definition of infertility as "women of reproductive age at risk of becoming pregnant who report unsuccessfully trying for a pregnancy for more than two years" (WHO 2006) [1].
Cwikel *et al*. (2004) and Hämmerli *et al.* [2] (2009) reported that, "infertility is not a disease, it and its treatment can affect all aspects of people's lives, which can cause various psychological-emotional disorders or consequences including frustration, hopelessness, depression, guilt, anxiety and feelings of worthlessness in life". Studies done by Inhorn and Birenbaum-Carmeli and Greil *et al*. suggested that, "the infertility-related complexities and life experiences are highly influenced by the socio-cultural context in which the infertile person lives, so any comprehensive study on the subject with disregard to this context is pointless" [3].

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Parikh *et al*. (2012) [4] suggested in study that, "infertility shares some common pathways with Cardiovascular Diseases (CVDs)". Parikh *et al.* (2012) add on that, "Hypertension, thyroid dysfunction, diabetes, endocrinological factors and lifestyle related problems (obesity) are all known to be associated with CVD". Bevc *et al*. (2008) mentioned that, "CVD is the one of the most common causes of morbidity and mortality in the world and atherosclerosis is known to be the main reason for increased cardiovascular risk. Moreover, it is widely known that inflammation plays an important role in atherosclerosis" [5].
In 2017, Zegers-Hochschild *et al.* [6] mentioned in a study that, "infertility is further categorized as primary or secondary. The primary infertile female is a woman who has never been diagnosed with a clinical pregnancy and meets the criteria of being classified as having infertility". Vander and Wyns (2018) [7] illustrated that, "secondary female infertility applies to a woman unable to establish a clinical pregnancy but who has previously been diagnosed with a clinical pregnancy".
Hart (2016) suggested that, "the most powerful negative predictive factor of fertility is increasing women's age at conception, other factors including lifestyle and environmental factors are believed to play an increasing role". Study by Vander and Wyns mentioned that, "factors influencing fertility will be presented as gender specific or not". Mascarenhas *et al*. reported that, "there are 48.5 million couples are suffering with infertility worldwide" [8].

Methodology

A case-control study layout was adopted for the present study to identify and evaluate Biochemical and endocrinological aspects of female infertility. The test subjects were referred from various infertility clinics were chosen for the study. Demographic, physiological and lifestyle features were noted using Proforma. Venous blood samples were collected and used to measure CBMN assay, mutagen sensitivity analysis, hormonal assay and biochemical assay. Observations and outcomes were analyzed using the SPSS statistical software.
For the study 150 clinically diagnosed infertile female subjects and 150 age matched healthy females with one or more children were involved in the study as control.

Inclusion criteria

1. **Patients:** Clinically proven patients with infertility by a Gynecologist were included in the study.
2. **Controls:** Subjects without history of infertility, dyslipidemia, hypertension, diabetes, renal disease or other cardio vascular disease were not included as Controls.

Exclusion criteria

1. Neither the patients nor the controls should be suffering from any acute or chronic illness, cancer or on prolonged medication are excluded.
2. Subjects above the age of 45 and below the age of 18 are excluded.

Results

Table 1: Comparison study-FBS concentration among study and control subjects

FBS	Mean	SD(±)	p
Study Subjects	101	23.2	<0.005
Control Subjects	95.5	10.4	

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Table 2: Comparison study-total cholesterol concentration among study and control subjects

Total Cholesterol	Mean	SD (±)	p
Study Subjects	220	30.0	<0.005
Control Subjects	180	21.1	

Table 3: Comparison study-uric acid concentration among study and control subjects

Uric Acid	Mean	SD (±)	p
Study Subjects	5.5	1.25	<0.005
Control Subjects	4.4	1.00	

Table 4: Comparison study of hSCRP concentration

hSCRP	Mean	SD (±)	p
Study Subjects	3.0	0.70	<0.005
Control Subjects	1.2	0.59	

Table 5: Comparison study of TSH concentration among study and control subjects

TSH	Mean	SD (±)	p
Study Subjects	5.0	2.00	<0.005
Control Subjects	2.5	1.3	

Table 6: Comparison study of FSH concentration between study and control subjects

FSH	Mean	SD (±)	p
Study Subjects	30	10	<0.005
Control Subjects	12.8	6.0	

Table 7: Comparison study of LH level between study and control subjects

LH	Mean	SD (±)	p
Study Subjects	30.7	11.5	<0.005
Control Subjects	15	5.0	

Table 8: Comparison study of progesterone level among study and control subjects

Progesterone	Mean	SD(±)	p
Study Subjects	6.0	4.99	<0.005
Control Subjects	12.1	4.00	

Table 9: Comparison study of estradiol level between study and control subjects

Estradiol	Mean	SD	p
Study Subjects	90	29.8	<0.005
Control Subjects	115	41.12	

Table 10: Comparison of prolactin level among study and control subjects

PRL	Mean	SD	p
Study Subjects	36.10	8.54	<0.005
Control Subjects	13.34	5.20	

Table 11: Comparison of MDA level among study and control subjects

MDA	Mean	SD	p
Study Subjects	2.99	1.70	<0.005
Control Subjects	1.46	0.89	

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Table 12: Comparison of MCBMNF among study and control subjects

mCBMNF	Mean	SD	p
Study Subjects	13.00	1.25	<0.005
Control Subjects	9.00	0.75	

Table 13: Comparison of mean b/c value among study and control subjects

Mean b/c value	Mean	SD	P
Study Subjects	0.890	0.058	<0.005
Control Subjects	0.599	0.054	

Discussion

In 2014, Sirmans and Pate reported that, "the complex coordination of hormones that affects the reproductive cycle in women can be modified by certain conditions that cause altered ovulation. Polycystic ovary syndrome (PCOS) is the most common endocrine disorder of reproductive-aged women that affects 5% to 10% of women ages 15 to 44 years in the United States" [9]. Later, Bergh *et al*. (2016) pointed out that, "risk factors for PCOS in adults include type 1 and type 2 diabetes and gestational diabetes. Insulin resistance affects 50% to 70% of women with PCOS, which can lead to comorbidities including metabolic syndrome, hypertension, dyslipidemia, glucose intolerance, and diabetes" [10].

According to Sirmans and Pate (2014), "polycystic ovary syndrome (PCOS) has a cardiovascular effect that includes increased coronary artery calcium scores and increased carotid intima-media thickness. Additionally, women with PCOS are at increased risk of mental health disorders including depression, anxiety, bipolar disorder and binge eating disorder". Deyhoul *et al*. in 2017 reported that, "there are many hormonal disorders that cause infertility. Hypothyroidism, hyperprolactinemia (high male hormone levels) and luteal phase defect (low progesterone) are a few examples of these disorders. Hormonal disorders are a major cause of infertility in women. The inability of women at ovulation and regulation of hormone levels leads to too high or too low production of hormones" [9].

According to Meneses and Holland (2014) [11], "these hormonal disorders are characterized with symptoms such as irregular menstrual cycles, excessive bleeding, or very little bleeding, pelvic and abdominal cramps, absence of menstruation or long menstruation and excessive weight loss or weight gain". Deyhoul *et al*. (2017) mentioned that, "these following factors may cause hormonal disorders: gland problems such as thyroid gland, pituitary gland and hypothalamus gland problems. These preliminary glands are responsible for the production of sex hormones. Birth control pills, stress and some diseases such as hypothyroidism affect these glands. If any of these glands encounter any problem, a disorder can prevent from the full process of ovulation, and thereby, pregnancy will become difficult" [12].

In study done by Meneses and Holland (2014) it was pointed out that, "some treatments can cause hormonal disorders. Targeted cancer therapies can cause anatomical and hormonal changes which negatively affect the breast cancer patient's sexual potential. There are large differences in the evidence-based interdisciplinary treatment and management of breast cancer young patients who are treated and are fertile now and there are concerns about pregnancy after cancer treatment" [11].

According to Shahini *et al*. (2013), "MS is a very common disease in Western countries and includes multiple endocrine disturbances, such as overweight, altered levels of hepatocytolysis, arterial hypertension, obesity, dyslipidemia, and IR. MSi samaj or social health problem, particularlyin developed nations such as the United States but also in Europe, with a prevalence of 20 and 30%, respectively" [13].

Study done by Silvestris *et al*. in 2019 reported that, "several factors have been implicated and primarily include the hypercaloric diet in association with deregulated dietary habits,

sedentary lifestyles, increased age and augmented BMI. MS is also suspected to play a definite role in carcinogenesis, particularly in the gastrointestinal tract" [14].
Studies done by Iñiguez *et al*. (2008) and Livshits and Seidman *et al*. (2009) had demonstrated that, "females with MS, inadequate metabolic control and primary or secondary amenorrhea show low levels of LH and FSH, associated with a lack of residual insulin secretion".
Vujkovic *et al*. (2010) [15] reported that, "abnormalities of GnRH pulse generator, as well as a decrease in numbers and amplitude of LH pulses in patients with diabetes and amenorrhea compared to patients with normal menstrual cycles. On the other hand, IR, hyperinsulinemia and related metabolic abnormalities in MS may exert a role in the progress of the PCOS". According to Hammiche *et al*. (2011), "all therapeutic approaches used for the correction of insulin homeostasis in obese and MS patients, such as Thiazolidinedione's, Metformin, lifestyle modification for weight reduction or bariatric surgery have been proven to produce restoring effects on ovulation and hyperandrogenemia" [16].

Conclusion

FBS, total cholesterol, uric acid, hsCRP, TSH, FSH, LH, progesterone, estradiol, prolactin, MDA, mCBMNF and mean b/c value showed a statistical significance difference among study and control.

References

1. World Health Organization. Reproductive health indicators: guidelines for their generation, interpretation and analysis for global monitoring. World Health Organization, 2006.
2. Cwikel J, Gidron Y, Sheiner E. Psychological interactions with infertility among women. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2004;117(2):126-131.
3. Inhorn MC, Birenbaum-Carmeli D. Assisted reproductive technologies and culture change. Annual Review of Anthropology. 2008;37:177-196.
4. Parikh NI, Cnattingius S, Mittleman MA, Ludvigsson JF, Ingelsson E. Subfertility and risk of later life maternal cardiovascular disease. Human reproduction. 2012;27(2):568-575.
5. Bevc S, Šabić S, Hojs R. Atherosclerosis in hemodialysis patients-the role of microinflammation. Renal failure. 2008;30(10):1012-1016.
6. Zegers-Hochschild F, Adamson GD, De Mouzon J, Ishihara O, Mansour R, Nygren K, *et al.*, The international committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary on ART terminology. Human reproduction. 2009;24(11):2683-2687.
7. Vander Borght M, Wyns C. Fertility and infertility: Definition and epidemiology. Clinical biochemistry. 2018;62:2-10.
8. Hart RJ. Physiological aspects of female fertility: role of the environment, modern lifestyle and genetics. Physiological reviews. 2016;96(3):873-909.
9. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clinical epidemiology. 2014;6:1.
10. Bergh CM, Moore M, Gundell C. Evidence-based management of infertility in women with polycystic ovary syndrome. Journal of Obstetric, Gynecologic & Neonatal Nursing. 2016;45(1):111-122.
11. Meneses K, Holland AC. Current evidence supporting fertility and pregnancy among young survivors of breast cancer. Journal of Obstetric, Gynecologic & Neonatal Nursing.

2014;43(3):374-381.
12. Deyhoul N, Mohamaddoost T, Hosseini M. Infertility-related risk factors: a systematic review. Int. J Womens Health Reprod Sci.2017;5(1):24-29.
13. Shahini N, Shahini I, Marjani A. Prevalence of metabolic syndrome in Turkmen ethnic groups in Gorgan. Journal of clinical and diagnostic research: JCDR. 2013;7(9):18-49.
14. Silvestris E, Lovero D, Palmirotta R. Nutrition and female fertility: an interdependent correlation. Frontiers in endocrinology, 2019, 10.
15. Vujkovic M, De Vries JH, Lindemans J, Macklon NS, Van der Spek PJ, Steegers EA, *et al.* The preconception Mediterranean dietary pattern in couples undergoing *in vitro* fertilization/intracytoplasmic sperm injection treatment increases the chance of pregnancy. Fertility and sterility. 2010;94(6):2096-2101.
16. Hammoud A, Carrell DT, Meikle AW, Xin Y, Hunt SC, Adams TD, *et al.* An aromatase polymorphism modulates the relationship between weight and estradiol levels in obese men. Fertility and sterility. 2010;94(5):1734-1738.