

ASSESSMENT OF OXIDATIVE STRESS VIA 8-ISO PROSTAGLANDIN F_{2α} (8-isoPGF_{2α}) IN FEMALES WITH INFERTILITY

*¹Kani, Y.A, ²Muhammad Y, ³Zainab I, ⁴Ahmed, A.Y.

^{*1}College of Medicine and Health Sciences, Federal University Dutse

²Department of Chemical Pathology, Rasheed Shekoni Teaching Hospital Dutse.

³Department of Hematology and Blood Bank, Rasheed Shekoni Teaching Hospital Dutse.

²Department of Chemical pathology, Usmanu Danfodiyo University Teaching Hospital Sokoto.

Corresponding Author's Email: yamunakani4@gmail.com

Abstract: The fact that hormonal imbalance leads to infertility has long been documented, evidence is also accumulating that oxidative stress plays a great role in female infertility. The present study comprises of 83 infertile women and 59 control subjects attending Rasheed Shekoni specialist hospital Dutse. All the analytes were analyzed using ELIZA technique. Serum levels of LH, FSH, PRL and 8-isopg F_{2α} of infertile subjects were statistically (p<0.005) higher than that of control of subjects. Conclusively, the infertility may be due to hormonal imbalance, oxidative stress or a combination of both factors.

Keywords: Infertility, Oxidative Stress, 8-isoPGF_{2α}, fertility hormones.

I. INTRODUCTION

Oxidative stress (OS) results when the generation of free radicals such as reactive oxygen species (ROS) or reactive nitrogen species (RNS) outweighs the capability of antioxidant system (Cindrova-Davies *et al.*, 2007; Al-Gubory 2010; Burton 2010). The imbalance between the prooxidant and antioxidant can lead to unfavorable environment for female biological system (Al-Gubory, 2010). Oxidative stress is associated with complications during pregnancy such as spontaneous abortion, recurrent pregnancy loss (RPL), pre-eclampsia, and intrauterine growth restriction (IUGR) (Webster, 2008). The role of ROS and antioxidant substances in the regulation of oocyte maturation, folliculogenesis, ovarian steroidogenesis and luteolysis has long been documented (Shiotani *et al.*, 1991; Behrman *et al.*, 2001; Sugino *et al.*, 2004). Determination of free radicals or their end products is complicated. Isoprostanes, derived from the non-enzymatic peroxidation of arachidonic acid are now considered to be reliable biomarkers and therefore assessment of bioactive 8-*isopg* F_{2α} levels offers a great opportunity to study oxidative stress-related diseases and inflammatory conditions (Murrow, *et al.*, 1990; Vacchiano and Tempel, 1994). Both Barrington *et al.*, (1996) and Vural *et al.*, (2000) reported that decreased antioxidant status increased risk of spontaneous abortion. Significant decrease of serum levels of ascorbic acid (vitamin C) and α-tocopherol (vitamin E) were observed among the women with recurrent abortion according to Vural *et al.*, (2000). OS has been reported to cause damage of cellular membrane, retard embryo development and induce cellular apoptosis (Rai and Regan, 2006; Stephenson and Kutteh, 2007). Assessment of Os proves to be important elements in the cases of infertility. Measurement of oxidative stress by various other methods lacks specificity and sensitivity, thus the current research reports the serum levels of 8-*iso* prostaglandin F_{2α} (8-*isopg* F_{2α}) of infertile women attending Rasheed Shekoni specialist Hospital.

II. METHODOLOGY

Study population: The current study comprises of 89 infertile women of age bracket 15-45 attending Rasheed Shekoni specialist Hospital Dutse and 59 apparently healthy age and sex-matched fertile subjects as controls.

Blood specimen Collection; Blood samples were collected by clean venopuncture into labeled plain test tubes, without undue pressure on either the arm or the plunger of the syringe. Four milliliters (4.0mls) of blood samples were collected by venopuncture and delivered into clean dry test tubes. The samples were allowed to clot at room temperature and centrifuged at 3000 rpm for 5 minutes to obtain the serum. The separated sera were transferred into sterile serum bottles and kept frozen at -20°C until used for the assay.

Biochemical determination: 8-isoPGF_{2α} determination was based on competitive enzyme-linked immunoassay (ELIZA).

III. RESULTS

Table 1: Average Serum levels of 8-*isopg* F_{2α} and some fertility hormones among infertile and control fertile subjects

Parameters	LH(mIU/ml)	FSH(mIU/ml)	PRL(ng/ml)	PROG()	8- <i>isopg</i> F _{2α} (Pg/mL)
Infertile (n=83)	7.2±0.69	8.0±0.86	19.9±3.73	6.7±6.22	932.8±224
Control (n=59)	4.5±0.5	5.2±6.4	8.3±0.7	6.1±1.0	359.1±60.3

n=number of subjects; LH=Lieutenizing hormone; FSH=Follicle stimulating hormone; PRL=Prolactin; PROG=Progesterone;

Table 2: Serum levels of 8-*isopg* F_{2α} (Pg/mL) among infertile women with respect to age groups

Parameters	8- <i>isopg</i> F _{2α} (Pg/mL)
Age (yrs)	
15-24 (n=21)	899±240
25-34 (n=42)	902±232
35-44 (n=12)	895±255
44 and above (n=8)	920±222

n=Number of infertile subjects; yrs=years

IV. DISCUSSION

The problem of infertility in women may be due to obstruction of fallopian tube, uterine problems, hormonal imbalance, stress, obesity, other infections associated with reproductive system etc (Roupa *et al.*, 2009). Strong correlation between hormonal imbalance and infertility was documented among infertile women (Scott *et al.*, 1989; Ban *et al.*, 2013). According to the results obtained from this study serum levels of FSH, LH and Prolactin were significantly higher (p<0.005) in infertile women compared to the control subjects. This is in accordance with the findings of with Ban *et al.*, (2013) and Aroma *et al.*, (2014). FSH and LH play significant role in the development of follicles and oestrogen production. The present study revealed an increased prolactin levels in infertile women compared to control subjects, it is similarly reported by Parijatham and Saikumar (2014), Goswami *et al.*, (2009) and Kumkum *et al.*, (2006). Hyperprolactinemia among the infertile subjects shown in the current study may be responsible for the infertility, due to instrumental function of Prolactin in development and regulation of lactation and this may lead to amenorrhea, unexpected lactation, hypoestrogenism and lack of ovulation.

Serum levels of 8-*isopg* F_{2α} among the infertile women were significantly (p<0.005) higher than the control subjects. The increase may be due overproduction of free radicals leading to lipid peroxidation and consequent elevation of 8-*isopg* F_{2α}. Infertile women with 44 years and above have highest concentration of 8-*isopg* F_{2α} compared to other age groups, this may be due to aging and other factors.

V. CONCLUSION

In conclusion, serum FSH, LH, Prolactin and ISOPs were statistically higher in infertile women compared to control subjects and that infertility may be due to a combination of hormonal imbalance and oxidative stress.

VI. RECOMMENDATION

It is therefore recommended that infertile women should be routinely given antioxidants while being treated for infertility of hormonal aetiology.

ACKNOWLEDGEMENT

The authors are grateful to Rasheed Shekoni specialist Hospital Dutse and Albarka Clinics Dutse for samples provision and conducive working environments.

REFERENCES

- [1] Al-Gubory KH, Fowler PA, Garrel C. The roles of cellular reactive oxygen species, oxidative stress and antioxidants in pregnancy outcomes. *Int J Biochem Cell Biol*, 42:1634–1650, 2010
- [2] Aroma Solomon Odiba, Parker Elijah Joshua, Chimere Young Ukegbu and Iruoghene Onosakponome. Evaluation of the quantitative expression and correlation between follicle stimulating hormone (FSH) and Luteinizing hormone (LH) during follicular phase in primary infertile women of reproductive age. *IOSR JDMS*.13(1): 60-5, 2014.
- [3] Ban Mousa Rashid, tayfoor Jalil Mahmoud and Beston F. Nore. Hormonal study of primary infertile women. *Journal of Zankou Sulaimani-Part A (IJS-A)*;15(2): 137-43, 2013.
- [4] Barrington JW, Lindsay P, James D, et al. Selenium deficiency and miscarriage: a possible link? *Br J Obstet Gynaecol*;103:130–132, 1996.
- [5] Behrman HR, Kodaman PH, Preston SL, Gao S. Oxidative stress and the ovary. *J Soc Gynecol Investig*, 8, S40–S42, 2001.
- [6] Burton GJ, Hempstock J, Jauniaux E. Oxygen, early embryonic metabolism and free radical-mediated embryopathies. *Reprod Biomed Online*.; 6: 84-96, 2003.
- [7] Burton GJ, Jauniaux E: Oxidative Stress. *Best Pract Res Clin Obstet Gynaecol*, 25:287–299, 2010.
- [8] Choudhury SD and Goswami A. Hyperprolactinemia and reproductive disorders--a profile from north east. *J Assoc Physicians India*.;3(9): 617–8, 1995.
- [9] Cindrova-Davies T, Yung HW, Johns J, Spasic-Boskovic O, Korolchuk S, Jauniaux E, Burton GJ, Charnock-Jones DS: Oxidative stress, gene expression, and protein changes induced in the human placenta during labor. *Am J Pathol* 171:1168–1179, 2007.
- [10] Goswami B, Patel S, Chatterjee M, Koner BC and Saxena A. Correlation of Prolactin and Thyroid Hormone Concentration with Menstrual Patterns in Infertile Women. *J Reprod Infertil*.; 10(3): 207-12, 2009.
- [11] Jauniaux E, Watson AL, Hempstock J, Bao YP, JN, Skepper JN, Burton GJ. Onset of maternal arterial blood flow and placental oxidative stress. A possible factor in human early pregnancy failure. *Am J Pathol*.; 157: 2111-2122, 2000.
- [12] Kumkum A, Jasmine K, Shweta G and Pal Ajeshwar N. Hyperprolactinemia and its correlation with hypothyroidism in infertile women. *J Obstet Gynecol India* ;56(1): 68–71, 2006.
- [13] Morrow, J. D. Hill, K. E. Burk, R. F. et al. A series of prostaglandin F₂-like compounds are produced in vivo in humans by a non-cyclooxygenase, free radical-catalyzed mechanism. *Proceedings of the National Academy of Sciences of the United States of America* 87 9383-9387, 1990.

- [14] Parijatham S Saikumar P. Serum levels of Follicle Stimulating Hormone, Luteinizing Hormone and Prolactin in Primary female infertility in rural population. *Research Journal of pharmaceutical, Biological and Chemical sciences.*;5 (2): 1155-8, 2014.
- [15] Rai R, Regan L. Recurrent miscarriage. *Lancet.*; 368: 601-611, 2006.
- [16] Roupa Z, Polikandrioti M, Sotiropoulou P, Faros E, Koulouri A and Wozniak G. Causes of infertility in women at reproductive age, *Health Science J.*;3: 80-7, 2009.
- [17] Scott MG, Ladenson JH, Green ED. and Gast MJ. Hormonal evaluation of female infertility and reproductive disorders. *Clin Chem. Apr*;35(4): 620-9, 1989.
- [18] Shiotani M, Noda Y, Narimoto K, Imai K, Mori T, Fujimoto K, Ogawa K. Immunohistochemical localization of superoxide dismutase in the human ovary. *Hum Reprod*, 6, 1349–1353, 1991.
- [19] Stephenson M, Kutteh W. Evaluation and management of recurrent early pregnancy loss. *ClinObstet Gynecol.*; 50: 132-145, 2007.
- [20] Sugino N, Karube-Harada A, Taketani T, Sakata A, Nakamura Y. Withdrawal of ovarian steroids stimulates prostaglandin F₂α production through nuclear factor-kappaB activation via oxygen radicals in human endometrial stromal cells: potential relevance to menstruation. *J Reprod Dev*, 50, 215–225, 2004.
- [21] Vacchiano C. A. and Tempel.G. E. Role of nonenzymatically generated prostanoid, 8-iso-PGF₂α, in pulmonary oxygen toxicity. *Journal of Applied Physiology* 77 2912-2917, 1994.
- [22] Vural P, Akgul C, Yildirim A, Canbaz M. Antioxidant defence in recurrent abortion. *ClinChimActa*; 295:169–177, 2000.
- [23] Webster RP, Roberts VH, Myatt L: Protein nitration in placenta – functional significance. *Placenta*, 29:985–994, 2008.