



DNA REPAIR CAPABILITIES AMONG WOMEN WITH ENDOMETRIOSIS OR POLYCYSTIC OVARIAN SYNDROME

Medical Science

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ABSTRACT

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders, affecting approximately 5–10% of women in reproductive age with association between amenorrhea, hirsutism, obesity, etc. Prevalence of PCOS in India ranged from 3.7 to 22.5% depending on the population studied and the criteria used for diagnosis. Endometriosis is defined as the presence of endometrial glands and stroma like lesions outside of the uterus, which is also a risk factor which leads to recurrent pregnancy loss. Endometriosis affects 2.5-3.3% of women of reproductive age and is diagnosed in 20-68% of the women studied for infertility. The root cause behind Polycystic Ovarian Disease (PCOD), endometriosis and its related risk factors is not yet studied well. Hence the present study was undertaken to evaluate the association between DNA repair capabilities among women with endometriosis or PCOD. Sixty females were selected; among them forty individuals have PCOD and or endometriosis were selected as test subjects and twenty healthy women as control group. Mutagen induced chromosome sensitivity assay was performed for evaluating DNA repair mechanism in all the subjects. The mean b/c value of the test subjects was higher than the control group. Moreover, subjects with abnormal biochemical, physiological and endocrinological characters showed increased mean b/c value. There is a positive correlation observed between these risk factors with the mean b/c value.

KEYWORDS

DNA repair mechanism, Polycystic ovary syndrome, Endometriosis, Mutagen induced chromosome sensitivity assay

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders, affecting approximately 5–10% of women in reproductive age with association between amenorrhea, hirsutism, obesity and polycystic ovaries (Ndefo et al 2013). Polycystic Ovary Syndrome (PCOS) is a genetically complex endocrine disorder of women of uncertain aetiology and is a common cause of anovulatory infertility, menstrual dysfunction and hirsutism (Azziz 2003). PCOS appears to be associated with an increased risk of metabolic aberrations, including insulin resistance and hyperinsulinism, type 2 diabetes mellitus, dyslipidaemia, cardiovascular disease and endometrial carcinoma (Wild 2002).

Endometriosis is defined as the presence of endometrial glands and stroma like lesions outside of the uterus (Kao 2004). Endometriosis is associated with increased risks of auto-immune diseases and ovarian endometrioid and clear-cell cancers, as well as other cancers, including non-Hodgkin's lymphoma and melanoma (Giudice et al 2010). Endometriosis is an inflammatory disease associated with pelvic pain and infertility that is characterized by lesions of endometrial-like tissue outside of the uterus (Johnson and Hummelshoj 2013). Endometriosis affects 2.5-3.3% of women of reproductive age and is diagnosed in 20-68% of the women studied for infertility (Mishra et al 2015). The prevalence of endometriosis has been estimated as 176 million women worldwide (Adamson et al 2010). Women with endometriosis and PCOD are three times more likely to have recurrent pregnancy loss. The root cause behind PCOD and endometriosis and its related risk factors is not yet studied well. Hence the present study was undertaken to evaluate the DNA repair capability among women with endometriosis and PCOD.

MATERIALS AND METHODS:

Sixty female were selected in this study, among them forty subjects reported with PCOD or endometriosis were considered as test subjects and twenty healthy individuals as control group. Detailed family history and relevant information were recorded using proforma. Seven ml of venous blood was collected after 10-12 hours of fasting. 2 ml of blood was transferred aseptically to a sodium heparinised vacutainer. Mutagen induced chromosome sensitivity assay was performed as per the method of Hsu et al (1987) the rest amount of blood was transferred into a plain tube for the biochemical and hormonal evaluations. For chromosome sensitivity analysis the mean number of breaks/cell (b/c) were calculated. Relevant demographic, anthropometric, physiological, clinical characteristics were also recorded.

OBSERVATIONS AND RESULTS:

The observed mean b/c value of test and control subjects was 0.812 and 0.691 respectively. The mean b/c value of test subjects was found much higher than that of control subjects. The observed mean b/c value of test subjects with PCOD was 0.804 and for test subjects with endometriosis showed a mean b/c value of 0.84. Comparatively, an elevated DNA repair inefficiency was observed among test subjects with endometriosis than the subjects reported with PCOD. The age group above 35 years showed an increased mean b/c value of 0.844.

Comparison of variables using t-test for FBS, TC, FSH, LH and Progesterone among test and control subjects was performed. It was observed that biochemical variables such as FBS and TC showed a statistically significant difference between test and control subjects with a p-value less than 0.05. Similarly, it was also observed that the t-test value for endocrinological parameters such as FSH, LH and progesterone showed statistically significant increase among test subjects when compared to the control subjects ($p < 0.05$) (Table 1). The test subject who resides in urban area also showed an increased mean b/c value of 0.828. Moreover, an elevated mean b/c value was observed among test subjects with sedentary type of occupation and subjects without regular exercise. The women who had delayed menarche (age >13 years) and subjects with irregular menstrual periods showed a higher mean b/c value. The test subjects reported with obesity showed an increased mean b/c value (0.837) when compared to subject without obesity.

Table – 1 Distribution Of Mean B/c Value According To Biochemical And Endocrinological Parameters

| Variables | Category | Number | Mean b/c value |
|----------------------|----------|--------|----------------|
| FBS (mg/dL) | ≤110 | 23 | 0.785 |
| | >110 | 17 | 0.849 |
| TC (mg/dL) | ≤200 | 24 | 0.794 |
| | >200 | 16 | 0.839 |
| FSH (mIU/L) | ≤21.5 | 10 | 0.7518 |
| | >21.5 | 30 | 0.8324 |
| LH (IU/L) | <12.5 | 15 | 0.7677 |
| | ≥12.5 | 25 | 0.8389 |
| Progesterone (ng/mL) | ≤20 | 21 | 0.8331 |
| | >20 | 19 | 0.7891 |

DISCUSSION:

Polycystic ovary syndrome (PCOS) is the most common cause of

female infertility due to anovulation and it affects approximately 6–10% of reproductive-aged women (Baillargeon et al 2008). Moreover, PCOS is associated with significant reproductive, endocrine, metabolic and cardiovascular, morbidity (Solomon 1999). In the present study 40 subjects who were suffering from PCOD or endometriosis were selected as test subjects among them 77% of study subjects reported with PCOD and remaining 23% have endometriosis.

Endometriosis affects 10–15% of women in their childbearing age. Most of the patients are in 18–25 age range (Gao et al 2006). Polycystic ovary syndrome (PCOS) is the most frequent endocrinopathy in women, affecting up to 10% of those in reproductive age (Carmina 2012). In the present study, the test subjects were selected from the age range of 18 to 45 years. Out of 40 test subjects, 19 individuals with age ≤ 36 years, they showed a highest mean b/c value.

Stouffs et al (2019) estimated that, “25% to 50% of women with endometriosis are infertile and that 25% to 30% of all infertile women have endometriotic lesions as the only identifiable cause for infertility”. According to Barbosa et al (2009) it was noted that, “endometriosis can also be found in 16% of fertile women”. In the current study test subject with a family history of infertility and sub infertility showed an increased mean b/c value were reported.

Reports by Cunha-Filho et al (2001) and Trinder and Cahill (2002), it was mentioned that, “endometriosis is associated with alterations in the hypothalamus-hypophysis-ovary axis, with alterations resulting thereof in the concentrations of hormones FSH, LH, estradiol and progesterone in serum, peritoneal fluid and follicular fluid of women with endometriosis”. In the present study it was observed that, test subject with FSH level $>21.5\text{mIU/L}$ showed higher mean b/c value than with $\leq 21.5\text{mIU/L}$. Similarly, individuals with LH level $>12.5\text{IU/L}$ showed increased mean b/c value than the subjects with LH concentration $\leq 12.5\text{IU/L}$.

In 2015, Bareh et al reported that, “total cholesterol, triglycerides and LDL cholesterol levels were statistically higher in the endometriosis group compared with the control group”. Legro et al (2001) mentioned that, “dyslipidaemia is very common in PCOS patients and present with different patterns, including low levels of high-density lipoprotein cholesterol (HDL-C), increased values of triglycerides and total and low-density lipoprotein cholesterol (LDL-C), as well as altered LDL quality”. In the current study, the test subjects with elevated FBS, total cholesterol, LH and FSH showed an increased mean b/c value when compared to the rest. Whereas, test subject with progesterone level $\leq 20\text{ng/mL}$ and $>20\text{ng/mL}$ showed a mean b/c value of 0.8331 and 0.7891 respectively. It clearly indicates that, test subjects with lower progesterone concentration showed increased mean b/c value.

CONCLUSION:

In short, majority of the test subjects with PCOD or endometriosis showed an abnormal biochemical and hormonal parameters. Moreover, subjects with abnormal biochemical, physiological and endocrinological characters showed an increased mean b/c value also. There is a positive correlation observed between, these risk factors with the mean b/c value. Lifestyle modifications and proper dietary management will help to decrease the overweight and obesity, and thereby it would be able to reduce the further complications among subjects with PCOD or endometriosis.

REFERENCES:

- [1] Adamson, G.D., Kennedy, S. and Hummelshoj, L., 2010. Creating solutions in endometriosis: global collaboration through the World Endometriosis Research Foundation.
- [2] Azziz R., 2003. The evaluation and management of hirsutism. *Obstet Gynecol* 101:995–1007.
- [3] Baillargeon, J.P., Nestler, J.E., Ostlund, R.E., Apridonidze, T. and Diamanti-Kandarakis, E., 2008. Greek hyperinsulinemic women, with or without polycystic ovary syndrome, display altered inositols metabolism. *Human Reproduction*, 23(6), pp.1439-1446.
- [4] Barbosa, C.P., Souza, A.M.B.D., Bianco, B., Christofolini, D., Bach, F.A.M. and Lima, G.R.D., 2009. Frequency of endometriotic lesions in peritoneum samples from asymptomatic fertile women and correlation with CA125 values. *Sao Paulo Medical Journal*, 127(6), pp.342-345.
- [5] Bareh, G.M., Robinson, R.D. and Schenken, R.S., 2015. Endometriosis and Lipid Concentration: Do We Have to Screen Patients for Hyperlipidemia? [349]. *Obstetrics & Gynecology*, 125, p.110S.
- [6] Carmina, E., 2012. PCOS: metabolic impact and long-term management. *Minerva ginecologica*, 64(6), pp.501-505.
- [7] Cunha-Filho, J.S.L.D., Gross, J.L., Lemos, N.A., Brandelli, A., Castillos, M. and Passos, E.P., 2001. Hyperprolactinemia and luteal insufficiency in infertile patients with mild and minimal endometriosis. *Hormone and Metabolic Research*, 33(04), pp.216-220.
- [8] Gao, X., Outley, J., Botteman, M., Spalding, J., Simon, J.A. and Pashos, C.L., 2006. Economic burden of endometriosis. *Fertility and sterility*, 86(6), pp.1561-1572.
- [9] Giudice, L.C., Swiersz, L.M. and Burney, R.O., 2010. Endometriosis *Endocrinology*.
- [10] Hsu, T.C., 1987. Genetic predisposition to cancer with special reference to mutagen sensitivity. *In vitro cellular & developmental biology*, 23(9), pp.591-603.
- [11] Johnson, N.P., Hummelshoj, L., World Endometriosis Society Montpellier Consortium, Abrao, M.S., Adamson, G.D., Allaire, C., Amelung, V., Andersson, E., Becker, C., Birna Ardal, K.B. and Bush, D., 2013. Consensus on current management of endometriosis. *Human reproduction*, 28(6), pp.1552-1568.
- [12] Kao, L.G.L., 2004. Article Title Endometriosis. *Lancet*, 364, pp.1789-1799.
- [13] Legro, R.S., Kunselman, A.R. and Dunaif, A., 2001. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. *The American journal of medicine*, 111(8), pp.607-613.
- [14] Mishra, V.V., Gaddagi, R.A., Aggarwal, R., Choudhary, S., Sharma, U. and Patel, U., 2015. Prevalence; characteristics and management of endometriosis amongst infertile women: a one year retrospective study. *Journal of clinical and diagnostic research: JCDR*, 9(6), p.QC01.
- [15] Ndefo, U.A., Eaton, A. and Green, M.R., 2013. Polycystic ovary syndrome: a review of treatment options with a focus on pharmacological approaches. *Pharmacy and therapeutics*, 38(6), p.336.
- [16] Solomon, C.G., 1999. The epidemiology of polycystic ovary syndrome: prevalence and associated disease risks. *Endocrinology and metabolism clinics of North America*, 28(2), pp.247-263.
- [17] Stouffs, K., Daelemans, S., Santos-Ribeiro, S., Seneca, S., Gheldof, A., Gürbüz, A.S., De Vos, M., Tournaye, H. and Blockeel, C., 2019. Rare genetic variants potentially involved in ovarian hyperstimulation syndrome. *Journal of assisted reproduction and genetics*, 36(3), pp.491-497.
- [18] Trinder, J. and Cahill, D.J., 2002. Endometriosis and infertility: the debate continues. *Human Fertility*, 5(sup1), pp.S21-S27.
- [19] Wild R.A., 2002. Long-term health consequences of PCOS. *Hum Reprod Update* 8:231-241.