

Comparing the frequency of polycystic ovary syndrome in women with and without epilepsy

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders; the impact of epilepsy and antiepileptic drugs influences the function of hypothalamic–pituitary–gonadal axis and dysfunction of the endocrine system and reproductive hormones in women with epilepsy. This study was carried out with an aim of determining and comparing the frequency and intensity of the complications of the hirsutism in women with and without epilepsy in Tehran in 2016–2017. **Materials and Methods:** This is a cross-sectional-comparative study which was carried out on 338 women of 18–35-year-old women with and without epilepsy who were selected by continuous sampling method. Data were collected and analyzed by Chi-square statistical test. The quantity of *P* was considered to be 0.05 as the level of significance. **Results:** The results of this study indicated that there was a statistically significant difference between the two groups with and without epilepsy in terms of the frequency of some of the clinical symptoms of the PCOS and affected by it. The results of this study showed that a higher percentage of women with epilepsy were affected PCOS. In the group of epileptic patients, some of the clinical symptoms of PCOS such as hirsutism, acanthosis nigricans, disordered menstruation, and amenorrhea were higher which as a result led to an increase in the frequency of PCOS. **Conclusion:** As a result, epilepsy can lead to an increase in the frequency of PCOS and some other clinical symptoms.

Keywords: Acanthosis nigricans, amenorrhea, epilepsy, hirsutism, polycystic ovary syndrome

Introduction

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in women within fertility age. A mixture of factors including hyperandrogenism (i.e., either clinical or chemical), chronic anovulation, and polycystic ovaries are among the features of this syndrome. The relation between PCOS and epilepsy was discovered in 1984 by Herzog *et al.* Epilepsy is a phenomenon which is due to the abnormal discharge of brain cells by which 1/1 million women in the female fertility age are affected and its prevalence in Iran in 2014–2015 was estimated by 0.5% to 1%.^[1–4] Several studies have concluded that the hypothalamic–pituitary–gonadal axis function and epilepsy

with changes in endocrine and hormonal disorders can cause reproductive fertility is a spectrum of disorders. The researchers showed that many women with epilepsy, production, and release of hormones such as luteinizing hormone (LH), follicle-stimulating hormone (FSH), gonadotropin-releasing hormone (GnRH), estradiol, testosterone, dehydroepiandrosterone sulfate, and prolactin and testosterone changes; in finally, it may be hormonal disorders origin for the incidence of clinical symptoms such as amenorrhea hypothalamic, PCOS, and hyperprolactinemia. Dispersion of the epileptic discharges toward hypothalamus brings an increase in GnRH secretion frequency, and as a result, an increase in LH hormone (i.e., a specific yellow material) and the ratio of LH/FSH and the development of nongrowing follicle in the presence of aromatase deficiency in follicles which is responsible for changing androgens to estrogens lead to the incidence of an increase in menstrual disorders, fertility disorders,

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overweight, insulin resistance, acne, hirsutism, and acanthosis nigricans (AN). Among women whom are affected by epilepsy, the incidence of ovary syndrome is more prevalent than women whom are unaffected by it.^[4,5,6,8,9] PCOS occurs in 10%–25% of women whom are affected by epilepsy.^[10-12] Furthermore, the prevalence of this syndrome in women whom are affected by idiopathic generalized epilepsy is reported by 15% all over the world.^[13] Noting the high-level prevalence of epilepsy in female fertility age and its after effects and the significance of making women more aware of it and perform a comprehensive management of women who are affected by epilepsy including counseling on fertility disorders, promotion, and preservation of the reproductive health and by noting that there is not any definite frequency of PCOS and its clinical symptoms in women with epilepsy in Iran and few studies have been carried out in this field. The present study was carried out with an aim of comparing the frequency of PCOS in women with and without epilepsy in the city of Tehran.

Materials and Methods

This study is a cross-sectional, comparative one which was performed in two groups of women with and without epilepsy between 13 to 35 years of age in the city of Tehran in the year 2016–2017. This study was performed through continuous sampling. Women with epilepsy were selected from among women who were under the auspices of the Iranian Epilepsy Association and the women unaffected by epilepsy from among women who referred to the hygiene and treatment centers which were affiliated to Iran University of Medical Sciences and the patients’ attendants. Criteria for entering the study included passage of 2 years from the occurrence of the menarche in the subjects, not suffering from any other debilitating, chronic, psychosomatic diseases except for epilepsy, lack of addiction and not taking any sedative or neuropsychiatric drugs, being affected by idiopathic generalized epilepsy, not being affected endometrial diseases, and not taking valproate sodium medicine. The criteria for exiting the study included not answering at least 25% of the questionnaire items. In case of having the arrival factors, a testimonial was filled out by subjects under study. Then, a personal attribute questionnaire was filled out by the researcher including age, economic status, marital status, having any child, educational level, economic and employment status, and a number of lists about the clinical symptoms of PCOS which included questions about menstruation cycles, hirsutism, acne, skin oiliness, infertility, AN, and a sonography test related to polycystic ovaries which was completed by a researcher for the subjects under study. In this study, data were analyzed after being collected by means of the statistical software of SPSS 21 (Chicago, IL, USA) and the statistical test of Chi-square and by considering $P < 0.05$ as the level of significance.

Results

Three hundred and thirty-eight women within the age range of 18–35 years old were studied under the two groups of affected

and unaffected ones by epilepsy [Table 1]. Comparing the frequency of personal qualifications of the women participating in the present study in two groups of with and without epilepsy in the city of Tehran from 2016-2017. The results of this study indicated that there was a statistically significant difference between the two groups with and without epilepsy in terms of the frequency of PCOS [Table 2]. The two groups with and without epilepsy were statistically significant in terms of affection by clinical symptoms of PCOS such as hirsutism, AN, disordered menstruation, and amenorrhea [Table 3] ($P < 0.05$). However, there was no meaningful difference in terms of affection by other clinical symptoms such as acne, skin oiliness, infertility, and overweight.

Discussion

The present study intends to determine and compare the frequency of PCOS in women with and without epilepsy in the

Table 1: Frequency and percentage of demographics in women with and without epilepsy participated in the study, Tehran, 2017

| Demographic | Groups, frequency (%) | | P |
|------------------------|--------------------------|-----------------------|-------|
| | Without epilepsy (n=169) | With epilepsy (n=169) | |
| Age (year) | | | |
| <20 | 9 (5.3) | 7 (4.1) | 3.00 |
| 20-25 | 46 (2.27) | 20 (1.34) | |
| 25-30 | 51 (30.1) | 50 (29.6) | |
| 30 | 63 (37.4) | 78 (46.2) | |
| The mean (SD) | 27.9 (5.1) | 29.46 (4.8) | |
| Marital status | | | |
| Single | 101 (59.7) | 117 (69.2) | 0.069 |
| Married | 68 (40.3) | 52 (30.8) | |
| Having children | | | |
| Yes | 49 (29) | 39 (23) | 0.215 |
| No | 120 (71) | 130 (77) | |
| Job | | | |
| Employee | 24 (14.2) | 26 (3.15) | 0.296 |
| Housewife | 56 (33.1) | 68 (40.3) | |
| Collegiate | 89 (52.7) | 75 (44.4) | |
| The economic situation | | | |
| Desired | 13 (8) | 14 (3.8) | 0.928 |
| Moderate | 139 (82) | 137 (78.7) | |
| Undesirable | 17 (10) | 18 (13) | |

SD: Standard deviation

Table 2: Frequency and percentage of polycystic ovary syndrome in women with and without epilepsy participated in the study, Tehran, 2017

| Polycystic ovary syndrome | Groups, frequency (%) | | Test results |
|---------------------------|-----------------------|---------------|------------------|
| | Without epilepsy | With epilepsy | |
| Affected | 25 (14.8) | 85 (53.2) | $P < 0.001$ |
| Unaffected | 144 (85.2) | 84 (49.7) | $\chi^2 = 48.51$ |
| Total | 169 (100) | 169 (100) | |

Chi-square test showed that polycystic ovary syndrome in the two groups were significantly different

Table 3: Frequency and percentage of clinical symptoms of polycystic ovary syndrome in women with and without epilepsy participated in the study, Tehran, 2017

| Polycystic ovary syndrome | Groups, frequency (%) | | Test results |
|---------------------------|-----------------------|---------------|------------------|
| | Without epilepsy | With epilepsy | |
| Hirsutism | | | |
| Affected | 31 (18/3) | 71 (42) | $P < 0.001$ |
| Unaffected | 138 (81/3) | 98 (58) | $\chi^2 = 22.46$ |
| Acanthosis nigricans | | | |
| Affected | 7 (4) | 13 (22) | $P = 0.004$ |
| Unaffected | 162 (69) | 147 (87) | $\chi^2 = 8.48$ |
| Amenorrhea | | | |
| Affected | 36 (21) | 60 (35) | $P = 0.004$ |
| Unaffected | 133 (79) | 109 (65) | $\chi^2 = 8.38$ |
| Irregular menstruation | | | |
| Affected | 13 (7.23) | 59 (73.2) | $P < 0.001$ |
| Unaffected | 146 (2.86) | 40 (69.8) | $\chi^2 = 36.1$ |

Chi-square test showed that hirsutism, acanthosis nigricans, amenorrhea, Irregular menstruation in the two groups were significantly different

city of Tehran in the year 2016–2017. Findings of the study indicated that the frequency of PCOS in women with epilepsy was higher. Noting the results of the current study, 52.3% of the epilepsy sufferers and 18.3% of unaffected subjects by epilepsy were affected by PCOS. Paying attention to endocrine disorders was one of the key considerations in the epileptic patients.

Betts *et al.* in the year 2003 carried out a comparative study on the function of ovary in the two groups of epileptic patients who take a type of antiepileptic drug and another group of epileptic patients who do not take epileptic drugs and came to this conclusion that PCOS in the group of epileptic patients increases and this increase of frequency in the group of epileptic patients who do not take antiepileptic drugs in comparison with the group who take a specific antiepileptic drug is more and its results were compatible with the present study.^[14] Pennell *et al.* in the year 2009 performed a study with an aim of scrutinizing the hormonal level in epileptic patients and came to the conclusion that production and the release of LH and FSH hormones, GnRHs, estradiol, progesterone, prolactin, testosterone, and dehydroepiandrosterone sulfate change in epileptic patients which is itself an origin of the incidence of disorders in endocrine glands such as PCOS.^[15] In a case study which was performed by Bauer and Cooper-Mahkorn in the year 2006 with an aim of the study, the incidence and frequency of fertility disorders such as PCOS, infertility, and disorders in menstruation cycles, the influence of epilepsy and also taking antiepileptic drugs on fertility disorders were illustrated.^[16] Furthermore, Herzog *et al.* and Bilo *et al.*, who studied the disorders in the endocrine glands came to this conclusion that in epileptic women, the PCOS was more prevalent which was compatible with the results of the current study.^[8,16] It seems that, in women, some of the clinical symptoms of the PCOS and affected by it had a higher frequency. For instance, in the current study, hirsutism in several areas of the body, AN, and menstrual disorders such as amenorrhea and disordered menstruation in epileptic patients

had higher frequency. Probable mechanisms of epilepsy involve the influence of epilepsy and antiepileptic drugs on the brain centers for endocrine glands sexual hormones and their binding proteins. It seems that epilepsy by influencing the function of hypothalamic–pituitary–gonadal axis and changing the frequency of secretions in these hormones' glands such as GnRH, LH, and FSH, and as a result, the occurrence of hyperandrogenism sets the stage for the occurrence of clinical symptoms of PCOS and affection by it in epileptic patients.^[13,17] This subject is observed more prevalent in some of the symptoms of PCOS. For instance, hirsutism may increase be due to hormonal changes such as hyperprolactinemia, hyperandrogenism, and resistance to insulin. On the other hand, one of the probable reasons for an increase in the frequency of disorders in endocrine glands may be due to excessive stress or over stress and social stresses in epileptic patients.

Furthermore, it may be that a change in hormones such as prolactin, androgens, estrogen, and progesterone set the stage for an increase in the occurrence of menstrual disorders in epileptic patients. For instance, epilepsy may increase the serum level of sex hormone binding globulin (SHBG) and this increase can lead to a decrease in the bioactivity of estradiol and a decrease in the ratio of SHBG/estradiol and as a result leads to menstrual disorders.^[18]

Menstrual disorders such as amenorrhea and disordered menstruation are among the clinical symptoms of PCOS which its frequency was higher in the group of epileptic patients. Herzog *et al.* in the year 2003 performed a study with an aim of the study, the menstrual disorders and reproductive hormones in the two groups of epileptic and nonepileptic patients and came to this conclusion that a disorder in endocrine glands, disorder in reproductive glands, and as a result, menstrual disorders in the group of epileptic patients in comparison with the control group are more prevalent.^[5] In a study by Herzog and Serret-montoya *et al.* who studied the menstrual disorders in epileptic women; in epileptic women, the menstrual disorders including disordered menstruation and amenorrhea were more prevalent which were compatible with the present study.^[19,20]

A study by Herzog *et al.* titled as study the sexual hormones and the menstrual disorders in 132 women from 18 to 35 years old were performed which were compatible with the present study in terms of age range.^[5,20]

Furthermore, in the present study, there was a significant statistical difference between hirsutism and AN ($P < 0.05$). Epilepsy by influencing the hypothalamic–pituitary–gonadal axis and changing various glands such as androgens, prolactin, and also an increase in resistance to insulin can lead to an increase in the frequency of hirsutism in epileptic patients. Furthermore, stress is one of the probable reasons for an increase in the frequency of hirsutism in epileptic patients.

In a study by Ayyagari *et al.* in the year 2012,^[7] which was performed with an aim of studying the PCOS, overweight, and

thyroidal disorders in sixty women with epilepsy, they concluded that disorders in endocrine glands during fertility such as PCOS and hyperprolactinemia increase in epileptic women which is a basis for the occurrence of menstrual disorders, galactorrhea, and hirsutism in these persons. Furthermore, Bauer *et al.* (1992) studied on prolactin serum in epileptic patients. Results indicated that, in these patients, the occurrence of hyperprolactinemia increases and can lead to hirsutism.^[21] In a study by Bauer *et al.*, it was recommended for hirsutism to be attended in epileptic women which was compatible with the present study.

The frequency of AN in the epileptic women was also higher which was due to higher levels of the occurrence of PCOS, resistance to insulin, and a change in the endocrine glands in these persons.^[11] Furthermore, an increase in the frequency of AN in the epileptic women can be due to a higher level of occurrence of PCOS in these persons. The second purpose of our study was to determine the frequency of emotional disorders such as anxiety and stress. There was a meaningful relation between emotional disorders and epilepsy. As a result in epileptic women, stress and anxiety had higher frequency. Since this study was performed in Tehran in order for us to be able to generalize the results to the whole persons in the research population or universe, it is recommended that a similar study be performed throughout the state and with a higher statistical universe.

Conclusion

PCOS in the epileptic patients from 18 to 35 years old in the city of Tehran had a relatively higher frequency. Furthermore, in the group of epileptic patients, some of the clinical symptoms of PCOS such as hirsutism, AN, disordered menstruation, and amenorrhea were higher which as a result led to an increase in the frequency of PCOS. However, in the two groups under study, the frequency of other clinical symptoms such as acne, skin oiliness, infertility, and overweight was meaningfully different. As a result, epilepsy can lead to an increase in the frequency of PCOS and some other clinical symptoms.

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Conflicts of interest

There are no conflicts of interest.

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