International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Jahan N et al. Int J Reprod Contracept Obstet Gynecol. 2023 Aug;12(8):2337-2342
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20232269

Original Research Article

Association of kisspeptin in patients with poly cystic ovarian syndrome

Nishat Jahan[1]*, Jesmine Banu[2], Kazi Fahim Mahmud[3], Shakeela Ishrat[2], Farzana Deeba[4], Nurjahan Begum[4], Shaheen Ara Anwary[5], Sumaiya Akter[6], Shirin Jahan[7]

[1]Medical Officer, Nabinagar Upazilla Health Complex, Brahmanbaria, Bangladesh
[2]Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[3]Medical Officer, Department of Cardiology, Comilla Medical College Hospital, Cumilla, Bangladesh
[4]Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[5]Department of Reproductive Endocrinology and Infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh
[6]Medical Officer, Kurmitola General Hospital, Dhaka, Bangladesh
[7]Maternal and Child Health and Training Institute, Azimpur, Dhaka, Bangladesh

Received: 13 June 2023
Accepted: 05 July 2023

***Correspondence:**
Dr. Nishat Jahan,
E-mail: drnishatjahan158@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Poly cystic ovarian syndrome (PCOS) is a complex multifactorial disorder, affecting millions of women worldwide. Kisspeptin, a hypothalamic peptide encoded by the KISS1 gene, is widely reported as a key factor in the regulation of luteinizing hormone (LH)/follicular stimulating hormone (FSH) secretion, which may be potentially involved with the development of PCOS. The aim of the study was to estimate the serum kisspeptin level in PCOS patients and evaluate the association of kisspeptin with other biochemical, and hormonal parameters in women with PCOS.
Methods: This case-control study was conducted at the department of reproductive endocrinology and infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from August 2020 to July 2021. A total of 90 patients between age 18-30 years were enrolled in this study. Data was collected on variables of interest by using the structured questionnaire designed for interview, observation, clinical examination, and biochemical investigation of the patients and analyzed by using the t-test, non-parametric test (Mann-Whitney U test) and chi-square test as appropriate.
Results: We found no significant difference between PCOS & control group, but acanthosis nigricans (AN), waist hip (W:H) ratio were statistically significant in PCOS group. We found serum LH (11.98±6.29 mIU/ml), LH: FSH (1.71±0.92), AMH (10.09±3.8 ng/ml), fasting insulin (26.53±28.34 µU/ml), ovarian volume (16.91±4.57), was significantly higher in PCOS patients. Kisspeptin value in PCOS patients was 85.92±56.59 pg/ml and control group was 63.74±43.16 pg/ml. In the PCOS group, there was a positive correlation between kisspeptin and LH, AMH, and ovarian volume.
Conclusions: Serum kisspeptin levels were similar in women with or without PCOS but positively correlated with ovarian volume, serum LH and AMH in PCOS patients.

Keywords: Fasting insulin, Kisspeptin, LH, Polycystic ovary syndrome

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a common endocrine and metabolic disorder, which is characterized by chronic anovulation, polycystic ovaries and hyperandrogenism, affecting 5-22% of women of reproductive age group and accounts for approximately 75% of anovulatory infertility disorders.[1-3] According to

The European Society for Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (2003), The syndrome is now defined as the presence of any two of the following three criteria: polycystic ovaries, oligo/anovulation, clinical and/or biochemical evidence of hyperandrogenism.[4,5] Though the etiopathogenesis of PCOS remains to be unclear, the hypothalamic-pituitary gonadal axis has been proposed to be involved with disturbances in gonadotrophin secretion, increased luteinizing hormone (LH) levels and perturbed LH/follicle-stimulating hormone (FSH) ratios.[6] Women with PCOS are at greater risk to develop metabolic dysfunction, type 2 DM, cardiovascular diseases and endometrial cancer, having a serious impact on reproduction and quality of life.[7]

Kisspeptin, a novel peptide, is encoded by kiss-1 gene. Kiss-1 gene is located in chromosome 1q32. Expression of kisspeptin gene and it's receptor was shown in hypothalamus, arcuate nucleus, periventricular nucleus, infundibular nucleus.[8] Kisspeptin initially synthesized as 145 amino acid polypeptide in length and after cleaving it becomes active shorter lengths. Their nomenclature represents the number of amino acids: kisspeptin- 54, 14, 13 and 10 and all are biologically active. Kisspeptin- 54 is the most abundant circulating isoform in human consisting of 54 amino acids which was derived first from the human placenta in 2001.[8] Kisspeptin action is started by a trans-membrane G-protein coupled receptor, named GPR54 and its ligand was observed first in cancer studies. When kisspeptin binds to the receptor GPR54, phospholipase C activates and intracellular calcium level increase. This action has direct or indirect effects on reproductive and neuroendocrine system.[9]

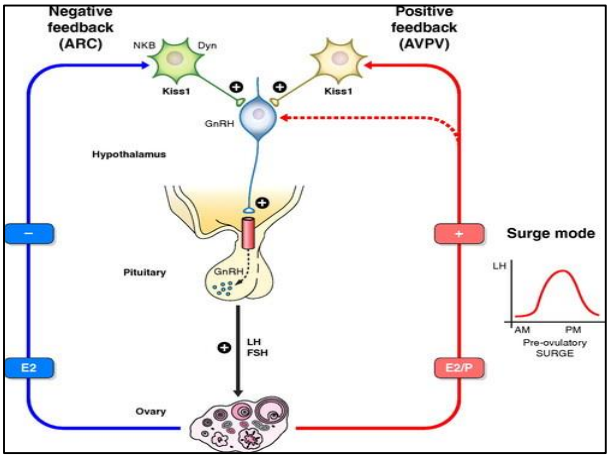

Figure 1: Mechanism of action of Kisspeptin.[10]

Kisspeptin stimulates to release gonadotrophin-releasing hormone (GnRH) via GPR54 receptor present on the GnRH neurons and participates in the maintenance of hypothalamo-pituitary -gonadal (HPG) axis and it is also affected by ovarian steroid negative feedback (Figure 1).[11]

Kisspeptin has been proposed to be important in reproduction that includes brain sex differentiation, gonadotrophin secretion, puberty onset and is also known to regulate LH secretion during the promotion of ovulation and metabolic regulation of fertility.[12] It is found in many studies that kisspeptin is altered or high in PCOS patients. However, the association of kisspeptin with PCOS remains poorly understood and the data available on the circulatory kiss-1 levels in PCOS have been inconsistent.[6,11-16] Due to the complex relationship between the neuropeptide kisspeptin and the hypothalamic-pituitary-gonadal axis, the present study was planned to measure the kisspeptin levels in women with PCOS to analyze the correlation between kisspeptin and PCOS-related hormonal and metabolic changes.

METHODS

This case-control study was conducted at the department of reproductive endocrinology and infertility, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from August 2020 to July 2021. A total of 90 patients between age 18-30 years were enrolled in this study. Subjects were divided equally into 2 groups, 45 PCOS patients considered as case and 45 normally menstruating healthy women considered as control. Other causes of hyperandrogenism, e.g. CAH, Cushing syndrome, virilizing ovarian tumor, hyperprolactinemia and thyroid disorder, hypogonadotrophic hypogonadism, patient taking OCP, antiandrogens or any other medications that can influence carbohydrate metabolism, liver disease, renal disease were excluded from the study.

Data was collected on variables of interest by using the structured questionnaire designed for interview, observation, clinical examination, and biochemical investigation of the patients. After the anthropometric measurement and physical examination, on menstrual days 2-3, overnight fasting venous blood samples were taken from all participants for serum kisspeptin, AMH, LH, FSH, fasting insulin and ovarian volume measurement by transvaginal sonography (TVS). The serum kisspeptin was measured using Sandwich-enzyme linked immunosorbent assay (ELISA) kit from Elabscience Biotechnology Inc. USA. For every subject a separate data sheet was used.

Statistical analyses of the results were obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22). Data was analyzed by using the t-test, non-parametric test (Mann-Whitney U test) and chi-square test as appropriate. Spearman's correlation co-efficient was calculated to evaluate the relationship between two groups. P value <0.05 was considered statistically significant throughout the study.

The study was approved by Ethical Review Committee of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

RESULTS

Majority 23 (51.2%) of the patients incorporated in this study belonged to age of 18-25 years in both PCOS group and control. The mean age was 23.2±3.1 years in PCOS patients and 24.48±3.47 in control. Three fourth 34 (75.6%) patients were housewife in case and 31 (68.9%) in control. The differences were not statistically significant (p>0.05) between two groups (Table 1).

Table 1: Distributions of the study patients by demographic profile (n=90).

Demographic profile	Case (n=45)		Control (n=45)		P value
	n	%	n	%	
Age in years					
18-25	23	51.2	23	51.2	
26-30	11	24.4	17	37.8	
Mean±SD	23.2±3.1		24.48±3.47		[a]0.068[ns]
Educational status					
SSC	12	26.6	6	13.3	
HSC	16	35.6	14	31.1	
Higher education	7	15.6	16	35.6	[b]0.221[ns]
Class V	9	20.0	8	17.8	
Illiterate	1	2.2	1	2.2	
Occupation					
Student	9	20	13	28.9	
Housewife	34	75.6	31	68.9	
Service	2	4.4	0	0	[b]0.276[ns]
Others	0	0	1	2.2	

ns= not significant, [a]p value reached from Unpaired t-test, [b]p value reached from Chi-square test

Almost two third 27 (60.0%) patients had primary infertility in case and 28 (62.2%) in control. The difference between two groups was not statistically significant (p=0.828) (Figure 2).

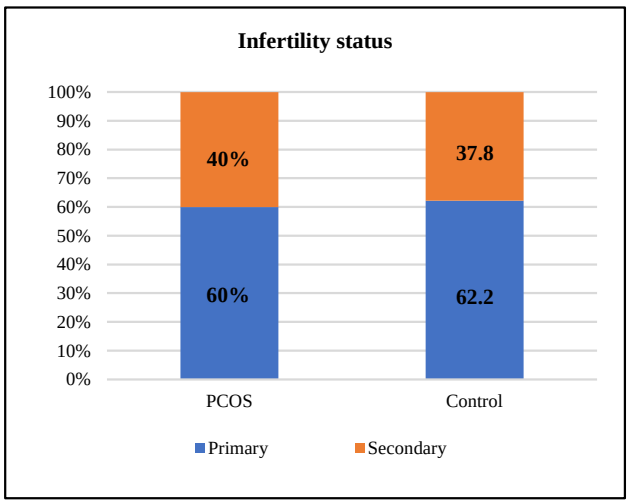

Figure 2: Infertility status between study population.

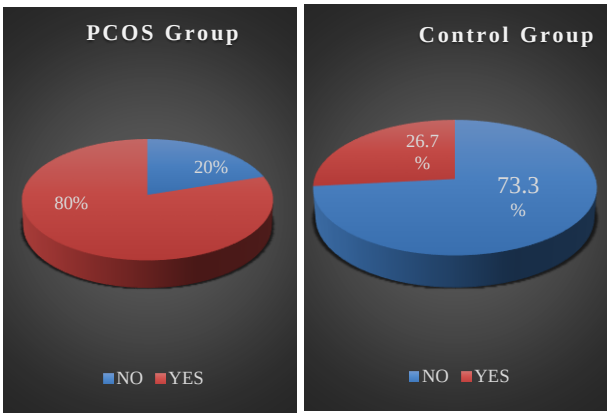

Figure 3: Frequency of acanthosis nigricans in study population.

Majority (80.0%) of the patients had acanthosis nigricans in the PCOS group and (26.7%) in control. The difference between two groups was statistically significant (p=0.001) (Figure 3).

Table 2: Distributions of the study patients by clinical characteristics (n=90).

Characteristics	Case (n=45)	Control (n=45)	P value
BMI (kg/m^2)	26.09±2.38	25.9±2.53	[b]0.714[ns]
Waist/hip ratio	0.86±0.04	0.79±0.05	[b]0.001[s]
Serum LH (mIU/ml)	11.98±6.29	4.57±1.61	[a]0.001
Serum FSH (mIU/ml)	5.52±1.85	6.42±1.78	[a]0.021
LH:FSH	1.71±0.92	0.77±0.44	[a]0.001
AMH (ng/ml)	10.09±3.8	3.57±0.77	[a]0.001
Ovarian volume cm^3	16.91±4.57	8.62±2.19	[b]0.001[s]
Fasting insulin (µU/ml)	26.53±28.34	12.99±5.74	[a]0.002

s=significant, ns= not significant; [a]p value reached from Chi-square test; [b]p value reached from Unpaired t-test

The mean BMI was 26.09±2.38 kg/m^2 in PCOS patients and 25.9±2.53 kg/m^2 in control. The difference was not statistically significant (p>0.05) between two groups. The mean waist/hip circumference ratio was 0.86±0.04 in PCOS group and 0.79±0.05 in control. The mean ovarian volume was 16.91±4.57 cm^3 in PCOS group and 8.62±2.19 cm^3 in control. The differences of waist/hip circumference ratio and ovarian volume were statistically significant (p<0.05) between two groups. The mean serum LH was 11.98±6.29 mIU/ml in PCOS group and 4.57±1.61 mIU/ml in control. The mean serum FSH was 5.52±1.85 mIU/ml in PCOS group and 6.42±1.78 mIU/ml in control. The mean LH:FSH was 1.71±0.92 in PCOS group and 0.77±0.44 in control. The mean anti-mullerian hormone (AMH) was 10.09±3.8 ng/ml in PCOS group and

3.57±0.77 ng/ml in control. The mean fasting insulin was 26.53±28.34 µU/ml in case and 12.99±5.74 µU/ml in control. The differences of serum LH, FSH, LH:FSH, AMH and fasting insulin were statistically significant (p<0.05) between two groups (Table 2).

Table 3: Distributions of the study patients by kisspeptin (n=90).

Kisspeptin (pg/ml)	Case (n=45)	Control (n=45)	p value
Mean±SD	85.92±56.59	63.74±43.16	0.059^{ns}
Range (min, max)	2.48, 220	0.37, 152.7	

c

Table 3 shows the distributions of the study patients by kisspeptin. The mean kisspeptin was 85.92±56.59 pg/ml in PCOS patients and 63.74±43.16 pg/ml in control. The difference was not statistically significant (p>0.05) between two groups.

Table 4: Spearman's correlation of kisspeptin with other parameters in PCOS group.

Variables	Spearman's rho	P value
Age (year)	0.039	0.801^{ns}
BMI (kg/m^2)	-0.123	0.42^{ns}
WHR	-0.020	0.898^{ns}
Serum FSH	0.019	0.902^{ns}
Mean ovarian volume	0.338	0.023^{s}
Serum LH	0.419	0.004^{s}
Anti-Mulleran hormone	0.379	0.010^{s}
Fasting insulin	0.092	0.547^{ns}

s= significant, ns=not significant

The correlation analyses of kisspeptin and other parameters were performed in women with PCOS. The kisspeptin level was positively correlated with serum AMH, LH, mean ovarian volume (Table 4).

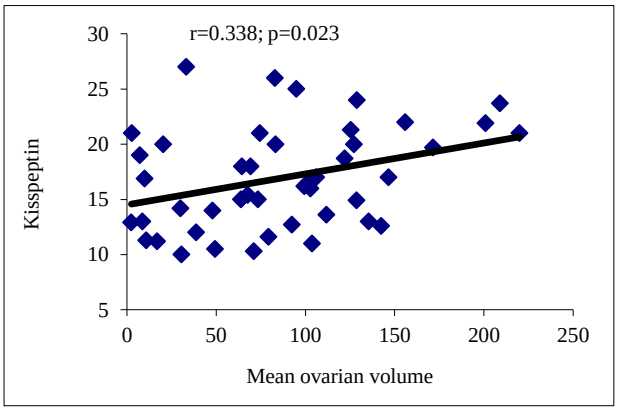

Figure 4: Scatter diagram showing positive Spearman's significant correlation (r=0.338; p=0.023) between kisspeptin with mean ovarian volume.

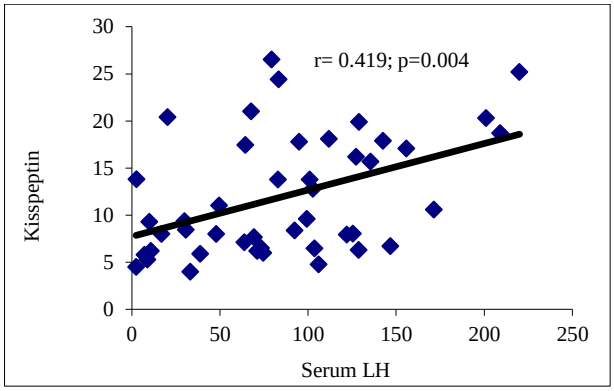

Figure 5: Scatter diagram showing positive Spearman's significant correlation (r=0.419; p=0.004) between kisspeptin with serum LH.

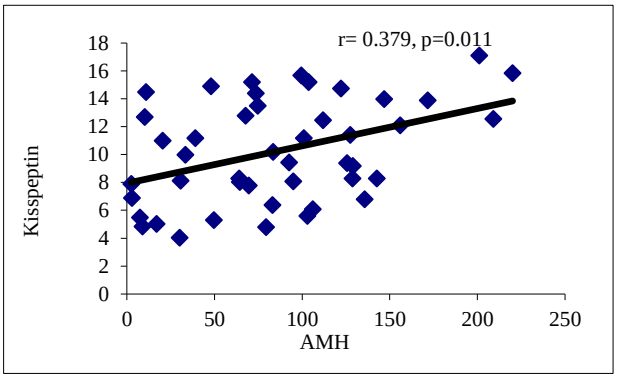

Figure 6: Scatter diagram showing positive Spearman's significant correlation (r=0.379; p=0.011) between kisspeptin with AMH.

DISCUSSION

In this study, the mean age was 23.2±3.1 years in PCOS group and 24.48±3.47 in control group. This finding was consistent with a previous study done by Emekci et al where the mean age was 23.99±4.63 years in PCOS group and 24.43±4.39 years in control.[16]

Our study observed, mean BMI was 26.09±2.38 kg/m^2 in PCOS patients and 25.9±2.53 kg/m^2 in control which was not statistically significant (p>0.05). Although BMI in higher in PCOS group than control, there was no impact of BMI on the serum kisspeptin levels in both groups. Ibrahim et al study found that the mean BMI was 26.05±3.76 kg/m^2 in infertile PCOS women and 25.93±3.7 kg/m^2 in control, which was similar to our study.[17] However, it was observed by Panidis et al that woman with PCOS and a BMI<25 kg/m^2 showed higher serum kisspeptin levels than those with a BMI>25 kg/m^2.[6]

We found that the mean waist/hip circumference ratio was 0.86±0.04 in patients with PCOS and 0.79±0.05 in control which was significant (p<0.05). Similarly, Daghestani et al study found the mean Waist-Hip ratio was 0.84±0.07 in PCOS and 0.77±0.06 in control (p=0.0001).[14] Abdominal

obesity, compared to general obesity, is of utmost importance in predicting women with PCOS.[16]

In this current study, it was observed that majority 80.0% patients had acanthosis nigricans in case and 26.7% in control. Acanthosis nigricans status was significantly ($p<0.05$) more common in patients with PCOS.

Mean serum FSH and mean serum LH was 5.52±1.85 mIU/ml and 11.98±6.29 mIU/ml in PCOS group and 6.42±1.78 mIU/ml and 4.57±1.61 mIU/ml in control group respectively. The mean LH:FSH was 1.71±0.92 in PCOS and 0.77±0.44 in control. The mean serum FSH, LH and LH:FSH were significantly ($p<0.05$) higher in PCOS patients. Similarly, in another study Daghestani et al observed that mean serum FSH, LH and LH:FSH were significantly higher in PCOS patients with compared to control group.[14] It was well established that PCOS has a complex multi factorial etiology and was associated with increased secretion of LH, normal or low level of FSH, and an increased ratio of LH-FSH.[18,19] Risvanli et al suggested that kisspeptin increased the luteinizing hormone (LH) concentration via GnRH and that the LH concentration was higher in women with PCOS.[20] We also found that, Serum LH was significantly correlated with the level of kisspeptin($r=0.419$, $p=0.004$) which was consistent.[16]

We observed that mean anti-Mullerian hormone was significantly ($p<0.05$) higher in patients with PCOS (10.09±3.8 ng/ml versus 3.57±0.77 ng/ml). Several other studies findings resembled with this observation.[21,22] AMH was positively correlated with kisspeptin ($r=0.379$, $p=0.010$) which was similar with Mut et al.[21]

In recent years, the KISS1 gene has been addressed as one of the crucial regulators in controlling the function and maturation of the reproductive system.[23] The role of kisspeptin (a major product of KISS1 gene) has been well identified in puberty, ovulation, brain sex differentiation, and fertility, with an essential regulatory function in the normal release of hypothalamic GnRH and consequently in LH secretion.[24,25] The pathophysiological mechanism of PCOS is also reflected in the inappropriate GnRH/LH secretion.[26,27]

However, clear evidence for the role of KISS1/kisspeptin expression in the mechanism of PCOS pathogenesis is still not obtained. In this current study it was observed that the mean kisspeptin was 85.92±56.59 pg/ml in PCOS and 63.74±43.16 pg/ml in control. The mean kisspeptin was higher in PCOS patients compared with controls but the difference was not statistically significant ($p>0.05$) between two groups. This finding was in consistent with some other studies Mut et al, Emekci et al, Albalawi et al, Nyagolova et al while contrary finding was also observed in some other studies.[12,13,15-17,21]

Mean ovarian volume was 16.91±4.57 cm^3 in case and 8.62±2.19 cm^3 in control which was significant ($p<0.05$) in PCOS patients. Similarly, Rashad et al study observed that the mean ovarian volume was 7.85±3.84 cm^3 in PCOS and 5.17±0.88 cm^3 in control and which was statistically significant ($p<0.05$).[28] Mean ovarian volume was positively correlated with serum kisspeptin level in this study ($r=0.338$, $p=0.023$).

In this present study it was observed that the mean fasting insulin was 26.53±28.34 μU/ml in case and 12.99±5.74 μU/ml in control. The mean fasting insulin was significantly ($p<0.05$) higher in PCOS patients. Mut et al study observed that the mean Fasting insulin was 12.40±8.44 mU/ml in PCOS and 8.37±4.40 mU/ml in control.[21] In another study Emekci et al study found the mean fasting insulin was 14.13±11.09 μU/ml in PCOS and 7.68±7.16 μU/ml in control, which are comparable with the current study.[16]

Our study was a single-centre study. We took a small sample size due to our short study period. After evaluating those patients, we did not follow up with them for a long period and have not known other possible interference that may happen in the long term with these patients.

CONCLUSION

In summary, present findings showed that women with PCOS had slightly increased level of serum kisspeptin in comparison to women without PCOS, which was not statistically significant. The level of Kisspeptin was positively correlated with mean ovarian volume, LH and AMH. Further large-scale studies should be done to assess whether kisspeptin is associated with PCOS and obtain the cut-off level of kisspeptin in healthy population.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Tsilchorozidou T, Overton C, Conway GS. The pathophysiology of polycystic ovary syndrome. Clin Endocrinol. 2004;60(1):1-7.
2. Rutkowska AZ, Diamanti-Kandarakis E. Polycystic ovary syndrome and environmental toxins. Fertil Steril. 2016;106(4):948-58.
3. Shi Y, Zhao H, Shi Y, Cao Y, Yang D, Li Z, et al. Genome-wide association study identifies eight new risk loci for polycystic ovary syndrome. Nat Genet. 2012;44(9):1020-5.
4. Orio Jr F, Palomba S, Cascella T, Milan G, Mioni R, Pagano C, et al. Adiponectin levels in women with polycystic ovary syndrome. J Clin Endocrinol Metab. 2003;88(6):2619-23.
5. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-7.

6. Panidis D, Rousso D, Koliakos G, Kourtis A, Katsikis I, Farmakiotis D, et al. Plasma metastin levels are negatively correlated with insulin resistance and free androgens in women with polycystic ovary syndrome. Fertil Steril. 2006;85(6):1778-83.
7. Wild RA, Carmina E, Diamanti-Kandarakis E, Dokras A, Escobar-Morreale HF, Futterweit W, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab. 2010;95(5):2038-49.
8. Kotani M, Detheux M, Vandenbogaerde A, Communi D, Vanderwinden JM, Le Poul E, et al. The metastasis suppressor gene KiSS-1 encodes kisspeptins, the natural ligands of the orphan G protein-coupled receptor GPR54. J Biol Chem. 2001;276(37):34631-6.
9. Pinilla L, Aguilar E, Dieguez C, Millar RP, Tena-Sempere M. Kisspeptins and reproduction: physiological roles and regulatory mechanisms. Physiol Rev. 2012;92(3):1235-316.
10. Tena-Sempere M. Kisspeptin signalling in the brain: recent developments and future challenges. Mol Cell Endocrinol. 2010;314(2):164-9.
11. Kaya C, Alay İ, Babayeva G, Gedikbaşı A, Ertaş Kaya S, Ekin M, et al. Serum kisspeptin levels in unexplained infertility, polycystic ovary syndrome, and male factor infertility. Gynecol Endocrinol. 2019;35(3):228-32.
12. Gorkem U, Togrul C, Arslan E, Sargin Oruc A, Buyukkayaci Duman N. Is there a role for kisspeptin in pathogenesis of polycystic ovary syndrome? Gynecol Endocrinol. 2018;34(2):157-60.
13. Albalawi FS, Daghestani MH, Daghestani MH, Eldali A, Warsy AS. rs4889 polymorphism in KISS1 gene, its effect on polycystic ovary syndrome development and anthropometric and hormonal parameters in Saudi women. J Biomed Sci. 2018;25(1):1-6.
14. Daghestani MH, Daghestani MH, Daghistani M, Ambreen K, Albalawi FS, AlNeghery LM, et al. Influence of KISS1 gene polymorphisms on the risk of polycystic ovary syndrome and its associated variables, in Saudi women. BMC Endocr Disord. 2020;20(1):1-0.
15. Nyagolova PV, Mitkov MD, Orbetzova MM, Terzieva DD. Kisspeptin and galanin-like peptide (GALP) levels in women with polycystic ovary syndrome. Int J Pharm Med Res. 2016;4:6-12.
16. Emekci Ozay O, Ozay AC, Acar B, Cagliyan E, Seçil M, Küme T. Role of kisspeptin in polycystic ovary syndrome (PCOS). Gynecol Endocrinol. 2016;32(9):718-22.
17. Ibrahim RO, Omer SH, Fattah CN. The correlation between hormonal disturbance in PCOS women and serum level of kisspeptin. Int J Endocrinol. 2020;2020.
18. Balen AH. Hypersecretion of luteinizing hormone and the polycystic ovary syndrome. Hum Reprod. 1993;8(suppl_2):123-8.
19. de la Llata ES, Moraga-Sánchez MR, Romeu-Sarrió A, Carmona-Ruiz IO. LH-FSH ratio and polycystic ovary syndrome: a forgotten test? Ginecol Obstet México. 2016;84(02):84-94.
20. Risvanli A, Ocal H, Timurkaan N, Ipek P, Seker I, Karabulut B. Expression of the anti-Mullerian hormone, kisspeptin 1, and kisspeptin 1 receptor in polycystic ovary syndrome and controlled ovarian stimulation rat models. Bosnian J Basic Med Sci. 2020;20(1):37.
21. Mut A, Erel CT, İnan D, Öner YÖ. Serum kisspeptin levels correlated with anti-mullerian hormone levels in women with and without polycystic ovarian syndrome. Gynecol Endocrinol. 2021;37(5):462-6.
22. Varikasuvu SR, Prasad VS, Vamshika VC, Satyanarayana MV, Panga JR. Circulatory metastin/kisspeptin-1 in polycystic ovary syndrome: a systematic review and meta-analysis with diagnostic test accuracy. Reprod Biomed Online. 2019;39(4):685-97.
23. Cao Y, Li Z, Jiang W, Ling Y, Kuang H. Reproductive functions of kisspeptin/KISS1R systems in the periphery. Reprod Biol Endocrinol. 2019;17(1):1-9.
24. Trevisan CM, Montagna E, de Oliveira R, Christofolini DM, Barbosa CP, Crandall KA, et al. Kisspeptin/GPR54 system: what do we know about its role in human reproduction? Cell Physiol Biochem. 2018;49(4):1259-76.
25. Hu KL, Zhao H, Chang HM, Yu Y, Qiao J. Kisspeptin/kisspeptin receptor system in the ovary. Front Endocrinol. 2018;8:365.
26. Rosenfield RL, Ehrmann DA. The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocr Rev. 2016;37(5):467-520.
27. Coutinho EA, Kauffman AS. The role of the brain in the pathogenesis and physiology of polycystic ovary syndrome (PCOS). Med Sci. 2019;7(8):84.
28. Rashad NM, Ateya MA, Saraya YS, Elnagar WM, Helal KF, Lashin ME, et al. Association of miRNA-320 expression level and its target gene endothelin-1 with the susceptibility and clinical features of polycystic ovary syndrome. J Ovarian Res. 2019;12(1):1-0.

Cite this article as: Jahan N, Banu J, Mahmud KF, Ishrat S, Deeba F, Begum N, et al. Association of kisspeptin in patients with poly cystic ovarian syndrome. Int J Reprod Contracept Obstet Gynecol 2023;12:2337-42.