DOI: https://doi.org/10.54393/pbmj.v4i2.157

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

Volume 4, Issue 2 (July-Dec 2021)

Systematic Review

Relation of Amenorrhea with Polycystic Ovarian Syndrome Below the age of Thirty-Five

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ARTICLE INFO

Keywords:
Polycystic ovarian syndrome, Amenorrhea, Hypothalamic amenorrhea, Oligo-amenorrhea

How to Cite:
Fazal, A. ., Khadija , S. ., Zafar, W., Sana, A., Shazadi, R. ., & Rasool , K. . (2021). Relation of Amenorrhea with Polycystic Ovarian Syndrome below the age of thirty five. *Pakistan BioMedicalJournal*, *4*(2). https://doi.org/10.54393/pbmj.v4i2.157

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ABSTRACT

1. Polycystic Ovarian Syndrome (PCOS) is a series of disorders which comprises anovulation, hyper-androgenism indications and polycystic ovaries. There are many causes of amenorrhea such as estrogen-deficient amenorrhea, estrogen-replete amenorrhea, exercise induced amenorrhea, stress induced, medication induced amenorrhea, eating disorders, anorexia nervosa, hypothalamic amenorrhea and PCOS **Objective:** To review the frequency of amenorrhea in patients with PCOS and to assess the complex relationship between the PCOS and amenorrhea **Methods:** Articles were reviewed from Google Scholar, Sci-Hub, and PubMed etc. Inclusion criteria was studies in which females presented with different gynecological complaints and PCOS **Results:** By reviewing previous studies, oligo-amenorrhea is much more common than amenorrhea in females diagnosed with PCOS in their reproductive age. Amenorrhea especially secondary amenorrhea is most common in teenagers and adolescents. PCOS is a common cause of secondary amenorrhea **Conclusions:** In previous studies, there are many patients with complaints of amenorrhea and diagnosed with PCOS but there are also some patients who came with other gynecological complaints and diagnosed with PCOS. So this also challenges somehow the Rotterdam criteria for PCOS.

INTRODUCTION

Vaginal bleeding absenteeism in women is called amenorrhea [1]. In pubescent; amenorrhea is split into primary amenorrhea as well as secondary amenorrhea. If a woman is of 16 years or above and also has absenteeism of vaginal bleeding or menstruation for approximately 4 years after commencement of secondary sexual features is known as primary amenorrhea [2].The female that has established consistent menstrual cycles and sometimes have amenorrhea of 3 or above months is entitled as secondary amenorrhea [3]. (PCOS) Polycystic ovarian syndrome is a series of disorders which comprises anovulation, hyperandrogenism indications and polycystic ovaries. In 35 percent to 50 percent cases, obesity is a common attribute [4]. In pubescent PCOS, mostly females presented with oligoamenorrhea, signs of acne and hirsutism or secondary amenorrhea [5]. With primary amenorrhea, women infrequently present with primary amenorrhea [6]. The percentage of girls with PCOS with presenting primary amenorrhea is wide-ranging from 1.4% to 14% [6-8]. This indicates that there is raise level of androgens and metabolic instabilities in adolescent age in their early stages of life [9]. However, menstrual irregularity is very common after menarche in initial two to three years. If prolonged amenorrhea then it is not normal sign, it might be linked with deficiency of estrogen in amenorrhea or repletion of estrogen in amenorrhea. Deficiency of estrogen in amenorrhea is related by low density of bone which can lead to increased bone fractures and replete-estrogen in amenorrhea can be the reason metrorrhagia or atypical uterine bleeding, later can lead to endometrial carcinoma. Hypothalamic-amenorrhea is the utmost predominant reason in amenorrhea, followed by PCOS. Exercise, stress, some medications, eating disorders, chronic illness and hyperprolactinemia are some of the etiologies of amenorrhea[3].

METHODS

Articles were reviewed from Google scholar, Sci-hub, PubMed etc. Literature with population of females having different gynecological complaints including PCOS was reviewed. PCOS is common cause of secondary amenorrhea but PCOS is more common in females with oligo-amenorrhea.

RESULTS

By reviewing previous studies, oligo-amenorrhea was observed to be much more common than amenorrhea in

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females diagnosed with PCOS in their reproductive age. Amenorrhea especially secondary amenorrhea is most common in teenagers and adolescents. According to previous results a lot of patients have oligo/secondary amenorrhea but few have typical symptoms of PCOS, this challenges the Rotterdam criteria for PCOS.

YEAR	AUTHORS	RESULTS/CONCLUSION
1990	National Institute of Health	Standards of PCOS are hyper -androgenism, oligo or anovulation for definite diagnosis
2003	Rotterdam criteria	Required 2 of 3 features for the diagnosis of PCOS (hyper-androgenism, oligo/ anovulation or polycystic ovaries on ultrasound.
2006	Rauh MJ , Nichols JF, Jl M, Lawson MJ	23.5 percent had menstrual abnormalities.
2007	Wiksten Almstomer M, Inden Hirschberg	58% girls were diagnosed with secondary amenorrheaand 42% with oligo - amenorrhea and ultrasound features were in 17 % with secondary and 22% with oligo -amenorrhea
2009	Razi M, Dadgistar H, Aleyasin A	In Iran, mean age of 13 -37, 71% females had oligo - amenorrhea/amenorrhea and in those 11% had PCOS.
2010	Teeda H , D eeks A , Moran L	Secondary amenorrhea can happen in 3 -5 percent of females in their pubescent age. The 2 common sourcesare polycystic -ovary - syndrome in 2-13 percent.
2012	Rausch ME, Lee TT	Polycystic ovaries can develop in the United States in women who are screened for other gynecologic conditions. The evidences put forward that 23 percent of women of reproduction age have polycystic ovaries. O nly five-ten percent of these females have typical indications of PCOS like asamenorrhea, infertility, overweight or histrutism
2017	Kaplan JR , Gordon CM , Ackerman KE, Berga SL	Fundamental characteristic of PCOS is polycystic -ovarian - morphology (PCOM), present in 80-88 percent, but PCOM is frequently established in slightly overweight females, 20-30 percent and even further in FHA about 30 - 45percent, so its incidence might be accidental
2021	Patel C , Phylactou SA	Maximum eighty to ninety percent females with oligo - amenorrhea have PCOS, as corresponding to only forty percent of females with amenorrhea. Thus, amenorrhea is probably to secondary with FHA and oligo -amenorrhea by PCOS

Table 1: Literature review for Poly Cystic Ovarian Syndrome

DISCUSSION

Polycystic Ovarian syndrome is an endocrine disorder that may affect 5 to 10% of 18-25 years old females world-wide [10]. Although considered by hyper-androgenism, prolonged oligo- amenorrhea or anovulation & polycystic ovaries appreciated on ultrasound, the conditions for finding is under consideration. Evidence required by National Institutes of Health in 1990, standards of PCOS is hyper-androgenism, oligo or anovulation for definite diagnosis and in 2003; the Rotterdam criteria required 2 of 3 features for the diagnosis of PCOS [11]. So there are no formal standards for diagnosis of PCOS in pubescent age. PCOS is tremendously diverse in presentations which mirror the dissimilar pathologies initiating the disorder. The source of PCOS is indistinct but then again appears with combination of disorders such as resistance of insulin and hypersensitive ovaries and adrenal glands. The characteristic attribute is resistance of insulin and enhancement in insulin, which is not dependent of obesity [12]. Resistance of insulin furthermore gives the impression to be particular of tissue; the adrenal gland and ovary remain exceptionally insulin subtle, while the muscles of skeleton are unaffected. In a pubescent who has repletion of estrogen, extended amenorrhea caused by anovulation prompts to hyper-plasia of endometrium. Underneath the impact of uncontested estrogen encouragement, endometrium thickens, overtakes the blood source and initiates the flaking unevenly, prominent to Abnormal/atypical Uterine Bleeding (AUB). Metrorrhagia is the utmost related reason of uterine abnormal bleeding in youths. Menstruation bleeding is typically pain-less. It can be minor and continued, but it can as well extreme, causing serious shock or anemia [3].

In hospital practice, PCOS are utmost predominant reasons of amenorrhea in Younger females. In few cases, teenage girls are thought to have secondary amenorrhea subordinate to the HPO axis can come later of having PCOS [3].In a study of 203 teenage girls for menstrual diseases who had previously been referred to Swedish youth clinic. The most common cause was hypo- thalamic suppression of HPO-axis and PCOS stood the second highest. Maximum often, 68% were diagnosed with an eating disorder representing with PCOS & amenorrhea was recognized in 55 percent of persons representing with oligo-amenorrhea [13].

As more and more women are involved in athletic activity, additional study is happening on the possessions of athletic actions during menstruation [15]. Syndrome in the initial of 1990s, Triad of Female Athlete (Random Menstruation, disorderly eating food and osteoporosis or osteo- penia). Inform doctors and trainers of the relationship between these 3 situations. While the occurrence of menstrual abnormalities diverse among for many sports are frequently very excessive, impact on 12 to 79 percent of sportspersons [16]. In the current study, university sportspersons, 23.5 percent had menstrual abnormalities [14]. In Iran, a study was conducted on female athletes, power of training sport or BMI were not threat aspects. About one/sixth of the athletes with amenorrhea/ oligo-amenorrhea were diagnosed with PCOS. Another strong point of this study is, it presents the occurrence of PCOS in women athletes, which has not been evaluated in past [17]. Around 50 percent of patients who are consuming anti-psychotic tablets will eventually come with menstrual disturbances and 12 percent will present with amenorrhea [18].Hypothalamic-amenorrhea is the utmost predominant reason of amenorrhea in the teenage group, have lower LH levels, Follicular-Stimulating-Hormone & estrogen levels with saved Luteinizing-Hormone and Follicular Stimulating Hormone reactions to Gn-RH .After menstruation in initial two to three years, ignorance of the HPO-axis can be source of Amenorrhea, but long secondary amenorrhea, HPO axis not fully development is not as

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common as it used to be. The utmost common reasons of hypothalamic Amenorrhea in people who are after menarche after 2-3 years have eating syndromes, extreme exercise, medication as well as anxiety [19]. Exercise, stress, some medications, eating disorders, chronic illness and hyperprolactinemia are some of the etiologies of amenorrhea [3].

Secondary amenorrhea can happen in 3–5 percent of females in their pubescent age. The 2 common sources are PCOS in 2–13 percent and FHA 1–2 percent [20]. A diagnostic challenge is often found in females with menstrual disorders, for whom PCOS are the utmost probable, various diagnoses. For instance, a fundamental characteristic of PCOS is polycystic-ovarian-morphology (PCOM), present in 80-88 percent, but PCOM is frequently established in slightly overweight females. Thus, even the clinician with specialized knowledge in women with oligo / amenorrhea may face the uncertainty of diagnosis, although it is difficult to completely avoid the possibility of misclassification [21]. Maximum eighty to ninety percent females with oligo-amenorrhea have PCOS, as corresponding to only forty percent of females with amenorrhea. Thus, amenorrhea is probably to secondary with FHA and oligo-amenorrhea by PCOS [22]. Polycystic ovaries can develop in the United States in women who are screened for other gynecologic conditions. The evidences put forward that 23 percent of women of reproduction age have polycystic ovaries. Nevertheless, only five-ten percent of these females have typical indications of PCOS like as amenorrhea, infertility, overweight or histrutism [23].

CONCLUSIONS

By reviewing previous articles, it is observed that there are different causes of amenorrhea like estrogen-deficient amenorrhea, estrogen-replete amenorrhea, exercise induced amenorrhea, stress induced, medication induced amenorrhea, eating disorders, anorexia nervosa, hypothalamic amenorrhea and PCOS. Well there is a very complex relationship between amenorrhea and PCOS, as PCOS are the utmost predominant reasons of amenorrhea in Younger females. In some studies, women who came for other gynecological complains are found with polycystic ovaries and few are found with classical symptoms of PCOS. So, all the previous studies challenge the Rotterdam criteria for PCOS.

REFERENCES

[1] Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea. Fertil Steril. 2004 Sep;82 Suppl 1:S33-9. doi: 10.1016/j.fertnstert.2004.07.001. doi.org/10.1016/j.fertnstert.2004.07.001

[2] Rosenfield RL, Ghai K, Ehrmann DA, Barnes RB. Diagnosis of the polycystic ovary syndrome in adolescence: comparison of adolescent and adult hyperandrogenism. J Pediatr Endocrinol Metab. 2000;13Suppl5:12859. https://pubmed.ncbi.nlm.nih.gov/11117671/

[3] Golden NH, Carlson JL. The pathophysiology of amenorrhea in the adolescent. Ann N Y Acad Sci. 2008;1135:163-78. doi: 10.1196/annals.1429.014. PMID: 18574222.doi.org/10.1196/annals.1429.014

[4] Buggs C, Rosenfield RL. Polycystic ovary syndrome in adolescence. Endocrinol Metab Clin North Am. 2005 Sep;34(3):677-705, x. doi: 10.1016/j.ecl.2005.04.005. PMID: 16085166 doi.org/10.1016/j.ecl.2005.04.005

[5] Franks S. Adult polycystic ovary syndrome begins in childhood. Best Pract Res Clin Endocrinol Metab. 2002 Jun;16(2):263-72. doi: 10.1053/beem.2002.0203. doi.org/10.1053/beem.2002.0203

[6] Dramusic V, Goh VH, Rajan U, Wong YC, Ratnam SS. Clinical, endocrinologic, and ultrasonographic features of polycystic ovary syndrome in Singaporean adolescents. J Pediatr Adolesc Gynecol. 1997 Aug;10(3):125-32. doi: 10.1016/s1083-3188(97)70072-x.doi.org/10.1016/S1083-3188(97)70072-X

[7] Franks S. Polycystic ovary syndrome. N Engl J Med. 1995 Sep 28;333(13):853-61. doi: 10.1056/NEJM199509283331307. Erratum in: N Engl J Med 1995 Nov 23;333(21):1435 doi.org/10.1056/NEJM199509283331307

[8] Obhrai M, Lynch SS, Holder G, Jackson R, Tang L, Butt WR. Hormonal studies on women with polycystic ovaries diagnosed by ultrasound. Clin Endocrinol (Oxf). 1990 Apr;32(4):467-74. doi: 10.1111/j.1365-2265.1990.tb00887.x. doi.org/10.1111/j.1365-2265.1990.tb00887.x

[9] Rashid, Fahmida, Sufia Khanam, Anowara Begum, and Moshammat Zebunnessa. "Primary Amenorrhea in a Teenage Girl with Polycystic Ovarian Syndrome." Bangladesh J 1, no. 1 (2021): 63-66. https://www.researchgate.net/publication/350173537_Bangladesh_Journal_of_Fertility_Sterility_BJFS_Primary_Amenorrhea_in_a_Teenage_Girl_with_Polycystic_Ovarian_Syndrome

[10] Driscoll DA. Polycystic ovary syndrome in adolescence. Ann N Y Acad Sci. 2003 Nov;997:49-55. doi:10.1196/annals.1290.006.doi.org/10.1196/annals.1290.006

[11] Michelmore KF, Balen AH, Dunger DB, Vessey MP. Polycystic ovaries and associated clinical and biochemical features in young women. Clin

DOI: https://doi.org/10.54393/pbmj.v4i2.157

Endocrinol (Oxf). 1999 Dec;51(6):779- 86. doi: 10.1046/j.1365-2265.1999.00886.x. doi.org/10.1046/j.1365-2265.1999.00886.x

[12] Dunaif A, Finegood DT. Beta-cell dysfunction independent of obesity and glucose intolerance in the polycystic ovary syndrome. J Clin Endocrinol Metab.1996Mar;81(3):9427.doi:10.1210/jcem.81.3.8772555.doi.org/10.1210/jcem.81.3.8772555

[13] Wiksten-Almströmer M, Hirschberg AL, Hagenfeldt K. Menstrual disorders and associated factors among adolescent girls visiting a youth clinic. Acta Obstet Gynecol Scand. 2007;86(1):65-72. doi: 10.1080/00016340601034970. doi.org/10.1080/00016340601034970

[14] Nichols JF, Rauh MJ, Lawson MJ, Ji M, Barkai HS. Prevalence of the female athlete triad syndrome among high school athletes. Arch Pediatr Adolesc Med. 2006 Feb;160(2):137-42. doi: 10.1001/archpedi.160.2.137. doi.org/10.1001/archpedi.160.2.137

[15] Frisch RE, Gotz-Welbergen AV, McArthur JW, Albright T, Witschi J, Bullen B, Birnholz J, Reed RB, Hermann H. Delayed menarche and amenorrhea of college athletes in relation to age of onset of training. JAMA. 1981 Oct 2;246(14):1559-63. doi.org/10.1001/jama.246.14.1559

[16] Warren MP, Perlroth NE. The effects of intense exercise on the female reproductive system. J Endocrinol. 2001 Jul;170(1):3-11. doi: 10.1677/joe.0.1700003.doi.org/10.1677/joe.0.1700003

[17] Dadgostar H, Razi M, Aleyasin A, Alenabi T, Dahaghin S. The relation between athletic sports and prevalence of amenorrhea and oligomenorrhea in Iranian female athletes. Sports Med Arthrosc Rehabil Ther Technol. 2009 Jul 30;1(1):16. doi: 10.1186/1758-2555-1-16. 32598.doi.org/10.1186/1758-2555-1-16

[18] Thangavelu K, Geetanjali S. Menstrual disturbance and galactorrhea in people taking conventional antipsychotic medications. Exp Clin Psychopharmacol. 2006 Nov;14(4):459-60. doi: 10.1037/1064-1297.14.4.459. doi.org/10.1037/1064-1297.14.4.459

[19] Phylactou M, Clarke SA, Patel B, Baggaley C, Jayasena CN, Kelsey TW, Comninos AN, Dhillo WS, Abbara A. Clinical and biochemical discriminants between functional hypothalamic amenorrhoea (FHA) and polycystic ovary syndrome (PCOS). Clin Endocrinol (Oxf). 2021 Aug;95(2):239-252. doi: 10.1111/cen.14402.doi.org/10.1111/cen.14402

[20] Gordon CM, Ackerman KE, Berga SL, Kaplan JR, Mastorakos G, Misra M, Murad MH, Santoro NF, Warren MP. Functional Hypothalamic Amenorrhea: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2017 May 1;102(5):1413-1439. doi: 10.1210/jc.2017-00131.doi.org/10.1210/jc.2017-00131

[21] Teede H, Deeks A, Moran L. Polycystic ovary syndrome: a complex condition with psychological, reproductive and metabolic manifestations that impacts on health across the lifespan. BMC Med. 2010 Jun30;8:41.doi:10.1186/17417015841.doi.org/10.1186/1741-7015-8-41

[22] Lakhani K, Seifalian AM, Atiomo WU, Hardiman P. Polycystic ovaries. Br J Radiol. 2002 Jan;75(889):9-16. doi: 10.1259/bjr.75.889.750009. PMID: 11806952. doi.org/10.1259/bjr.75.889.750009

[23] Lee TT, Rausch ME. Polycystic ovarian syndrome: role of imaging in diagnosis. Radiographics. 2012 Oct;32(6):1643-57. doi: 10.1148/rg.326125503. doi.org/10.1148/rg.326125503