Journal of Young Pharmacists, 2024; 16(2):187-194.
https://www.jyoungpharm.org

Review Article

Exploring the Connection between Hypothyroidism and Polycystic Ovary Syndrome: A Comprehensive Review

Indrani Barman[1], Trishna Sharma[2], Nayan Talukdar[2,*]

[1]Program of Biochemistry, Faculty of Science, Assam down town University, Assam, INDIA.
[2]Program of Biotechnology, Faculty of Science, Assam down town University, Assam, INDIA.

ABSTRACT

Hypothyroidism and Polycystic Ovary Syndrome (PCOS) constitute prevalent endocrine conditions that have serious effects on the health of women. Hormonal dysregulation, ovarian dysfunction, and polycystic ovarian morphology are hallmarks of PCOS, whereas insufficient thyroid hormone production causes hypothyroidism. This study explores the complex interactions between hypothyroidism and PCOS, highlighting the urgent need for a thorough understanding of their coexistence. It is crucial to understand that PCOS and hypothyroidism frequently co-occur since they both involve similar metabolic and hormonal dysregulations. The complex interrelationship between these illnesses is further highlighted by genetic predispositions and epigenetic changes. Clinical manifestations and reproductive issues in afflicted people are mostly influenced by hormonal imbalances, insulin resistance, and metabolic abnormalities. It is crucial to use a multidisciplinary approach to patient treatment, collaborating with endocrinologists, gynaecologists, primary care doctors, nutritionists, and mental health specialists. This comprehensive approach takes into account not only the hormonal and metabolic components of PCOS and hypothyroidism but also the psychological well-being of persons dealing with these conditions. The importance of understanding and treating the interaction between PCOS and hypothyroidism in clinical practice is emphasized in this study. Improved results and a higher quality of life for afflicted people can result from early diagnosis and suitable care techniques. Future research initiatives on genetic, epigenetic, and metabolic issues also show potential for improving therapeutic and diagnostic approaches, eventually improving patient care. This review provides a comprehensive understanding of the challenges linked to PCOS and hypothyroidism, emphasizing the importance of a comprehensive treatment plan for improved outcomes.

Keywords: Polycystic Ovary Syndrome, PCOS, Hypothyroidism, Endocrine Disorders, Interplay, Hormonal Imbalances, Metabolic Dysregulation, Fertility, Reproductive Health.

Correspondence:
Dr. Nayan Talukdar
Associate Professor, Biotechnology, Faculty of Science, Assam Down Town University, Assam, INDIA.
Email: nayan.new16@gmail.com

Received: 06-01-2024;
Revised: 10-02-2024;
Accepted: 16-02-2024.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a complex endocrine condition marked by oligo-anovulation, hyperandrogenism, and polycystic ovarian morphology.[1] It is one of the most typical hormonal abnormalities in this community and affects between 5 and 10% of women of reproductive age. PCOS is known for its major metabolic component, which frequently shows up as insulin resistance, obesity, and dyslipidemia, in addition to its effects on reproduction. An elevated risk of type 2 diabetes and cardiovascular disease is brought on by these metabolic abnormalities.[1,2] Therefore, PCOS is a disorder that warrants serious clinical attention and has broad health consequences for women. As a result of inadequate thyroid hormone synthesis, hypothyroidism, on the other hand, can have a variety of systemic repercussions.[3] Cellular homeostasis, metabolism, and energy expenditure are all significantly regulated by thyroid hormones. Fatigue, weight gain, cognitive decline, and probable cardiovascular problems are a few signs of hypothyroidism.[3,4] Untreated hypothyroidism during pregnancy can also have a negative impact on foetal development, perhaps leading to long-term cognitive impairments in the progeny.[4]

The high prevalence rates and widespread effects of PCOS and hypothyroidism on several elements of well-being highlight the importance of these conditions for women's health. Globally, PCOS affects millions of women, placing a significant strain on healthcare infrastructure and quality of life.[2] Women are disproportionately more likely than males to have hypothyroidism, which is thought to affect up to 5% of the general population.[3] Beyond endocrine function, its effects on metabolic health, cardiovascular risk, and general well-being throughout the course of a woman's lifetime are also significant.

DOI: 10.5530/jyp.2024.16.25

Publishing Partner : EManuscript Tech. [www.emanuscript.in]

This in-depth examination explores the complex interplay between hypothyroidism and PCOS, recognizing the prevalence and variety of traits shared by both disorders. The stated objective of this study is to identify the underlying pathophysiological processes that closely connect hypothyroidism and PCOS by methodically investigating the clinical impact of both conditions and combining recent research findings. It also covers the many therapy approaches that might be used to address the intricate problems brought on by these common endocrine illnesses.

EPIDEMIOLOGY AND PREVALENCE

Understanding the epidemiology and incidence of PCOS and hypothyroidism is essential to understanding how they affect the health of women throughout the world. Due to the high prevalence of these two endocrine illnesses, they have attracted a lot of interest from researchers and medical experts worldwide. One of the most prevalent endocrine illnesses affecting people of reproductive age worldwide is polycystic ovary syndrome (PCOS). Different racial and geographic groupings have varying PCOS prevalence rates. According to estimates, 5-10% of sexually active women have PCOS.[5] This wide variety in incidence is related to differences in diagnostic standards, genetic predispositions, and lifestyle elements among various ethnicities. Another endocrine illness that is remarkably common around the world is hypothyroidism, which is characterized by inadequate thyroid hormone production. According to estimates, it affects up to 5% of the world's population, with women experiencing it more frequently.[4] The likelihood of having hypothyroidism tends to rise with age, and some areas-such as those with iodine deficiency-might have greater rates. PCOS and hypothyroidism both have a notable preference for female patients, which is an interesting trait. PCOS primarily affects people with female reproductive anatomy, underlining its enormous importance to women's health. Conceiving and sustaining pregnancies might be difficult due to hormonal imbalances and reproductive abnormalities that are a part of PCOS. Therefore, PCOS is a significant factor in female infertility. Beyond the reproductive years, the metabolic problems linked to PCOS, such as insulin resistance and obesity, have wider effects on women's health.[4-6] The prevalence of hypothyroidism is also greater in women. The autoimmune nature of some thyroid conditions, such as Hashimoto's thyroiditis, which is more often seen in women, is partly to blame for this gender gap. Thyroid function can also be impacted by hormonal changes brought on by the menstrual cycle and pregnancy. As a result, throughout their reproductive years, women are more vulnerable to thyroid disorders.[5]

PCOS and hypothyroidism are more common in women, which highlights the major influence they have on female health and well-being. It is critical for medical practitioners and researchers working to address the particular difficulties experienced by women with PCOS and hypothyroidism to be aware of the prevalence of both disorders.

CLINICAL PRESENTATION

Polycystic Ovary Syndrome (PCOS)

PCOS is a complicated endocrine illness that affects people who are genetically predisposed to becoming feminine. It is a difficult disorder to identify and effectively treat since it is characterized by a wide range of clinical characteristics (Figure 1) that span hormonal, reproductive, and metabolic domains.[5,6]

Hyperandrogenism

A defining characteristic of PCOS is hyperandrogenism, which is characterized by increased levels of androgens (male hormones) in people who were born with female gender preference. Clinical indications of this hormonal imbalance include hirsutism (excessive hair growth in androgen-sensitive regions), acne, and androgenic alopecia (hair thinning in a male-pattern distribution).

Ovulatory Dysfunction

PCOS frequently throws off a woman's typical menstrual cycle, which leads to erratic or nonexistent menstrual cycles. The lack of ovulation, or anovulation, is a typical feature. This causes irregular menstrual cycles, such as oligomenorrhea (rare menstruation) or amenorrhea (lack of menstruation).

Polycystic Ovarian Morphology

PCOS patients may have larger ovaries on ultrasound examination along with numerous tiny, immature follicles. It's important to remember that not all PCOS sufferers have this distinguishing finding.

Metabolic Aberrations

PCOS and metabolic issues are usually linked. These could include central obesity, dyslipidemia, insulin resistance, and decreased glucose tolerance. Because of this, people with PCOS are more likely to develop Type 2 diabetes and cardiovascular disease.

Reproductive Challenges

PCOS is a major contributor to infertility since it causes anovulation. Additionally, those who have PCOS may be more likely to experience pregnancy issues such as gestational diabetes and hypertensive diseases.

Hypothyroidism Manifestations

An array of systemic repercussions, including hypothyroidism, result from insufficient thyroid hormone production. There is an enormous variance in the degree of severity and plurality of the clinical symptoms.[6-8]

Tiredness and Weakness

Chronic weariness, weakness, and sluggishness are common symptoms of hypothyroidism. The impact of these symptoms on everyday living and quality of life can be severe.

Weight Gain and Fluid Retention

Hypothyroidism can cause weight gain, frequently as a result of a slowed metabolic rate. Furthermore, people could have fluid retention, which results in leading to swelling, especially in the face and extremities.

Cognitive Impairment

Hypothyroidism can impair cognitive function, which can result in issues with focus, memory, and processing speed.

Cold Intolerance

People who have hypothyroidism may be less tolerant of cold weather and may experience overheating even in temperate climates.

Dry Skin and Hair

Hypothyroidism can result in dry, brittle nails, coarse hair, and dry, dry skin.

Constipation

Reduced gastrointestinal motility due to slowed metabolism might result in constipation.

Menstrual Irregularities

In women, hypothyroidism can cause menstrual disorders, such as severe or protracted menstrual flow.

The clinical presentation can be particularly difficult when PCOS and hypothyroidism co-occur. Both diagnosis and treatment may be complicated by symptoms that coexist with one another. For instance, PCOS and hypothyroidism patients may experience more severe cases of the two disorders' common symptoms, such as fatigue and weight gain. Additionally, hypothyroidism may make metabolic abnormalities, such as insulin resistance, worse, which may affect the course and seriousness of metabolic problems associated with PCOS.[6,7]

PATHOPHYSIOLOGICAL MECHANISMS

PCOS is characterized by a disruption in hormone signaling. Hyperandrogenism results from reduced levels of Sex Hormone-Binding Globulin (SHBG), increased levels of Luteinizing Hormone (LH), and Insulin-like Growth Factor-1 (IGF-1). As a result, the ovaries and adrenal glands produce more androgen.[5] Insufficient thyroid hormone production is the cause of hypothyroidism. In an effort to make up for the low thyroid hormone levels, this causes high levels of Thyroid-Stimulating Hormone (TSH). Thyroid hormone insufficiency is exacerbated by the fact that free Thyroxine (T4) and Triiodothyronine (T3) levels are lower.[8] PCOS and hypothyroidism may have synergistic effects on hormone dysregulation when they co-occur. The hypothalamic-pituitary-ovarian axis can be upset by hypothyroidism, which may exacerbate the hormonal abnormalities associated with PCOS. Furthermore, PCOS might

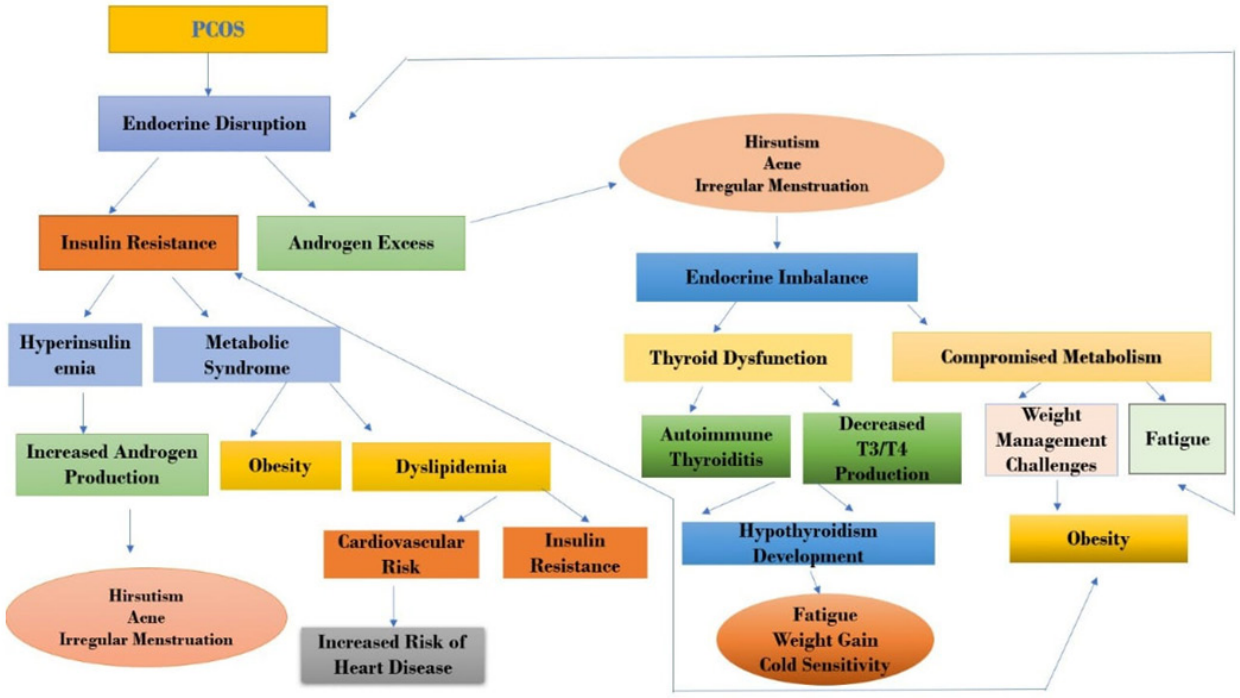

Figure 1: This chart explains how PCOS, with its hormonal imbalances can potential impacts on metabolism, can increase the risk of hypothyroidism.

have high androgen levels due to insulin resistance, which is prevalent in both diseases.[9] These interactions might provide a more complicated hormonal profile, which would make diagnosis and therapy more challenging.

Metabolic Dysfunctions

Insulin resistance is a key component of Polycystic Ovary Syndrome (PCOS). It results in decreased glucose absorption in peripheral tissues as a result of defective insulin signaling. Due to compensatory hyperinsulinemia, which worsens androgen production and fuels metabolic abnormalities such as central obesity, dyslipidemia, and reduced glucose tolerance, leads to metabolic abnormalities.[6,9] This condition can result in a decreased metabolic rate, which may result in weight gain and fluid retention. Subclinical hypothyroidism may affect glucose homeostasis and lipid metabolism in addition to overt hypothyroidism, which is linked to weight gain.[8] The specific metabolic dysfunctions of PCOS and hypothyroidism may get worse when they coexist. A more severe metabolic disruption, including an increased risk of type 2 diabetes and cardiovascular disease, may result from the cumulative effects of insulin resistance from PCOS and the changed metabolic rate in hypothyroidism.

Inflammation and Immune Response

PCOS is characterized by a chronic low-grade inflammatory response, as seen by elevated levels of pro-inflammatory markers such as Interleukin-6 (IL-6) and C-Reactive Protein (CRP). The detected inflammation has a complex relationship with insulin resistance and plays a role in the development or aggravation of metabolic disorders.[10] Dysregulation of the immune system is correlated with thyroid dysfunction, notably autoimmune thyroiditis (Hashimoto's thyroiditis). Thyroid hormone production is decreased as a result of thyroid gland inflammation. In hypothyroidism, systemic inflammatory indicators may also be increased.[3] Interactions between inflammatory processes may occur when both diseases are present. It is possible that the inflammatory conditions PCOS and autoimmune-related hypothyroidism might worsen one another. The difficulty of their co-occurrence may be a result of shared pathways between immunological dysregulation and inflammation.[9,10]

The interaction of hormonal imbalance, metabolic dysfunction, and inflammation is complicated when PCOS and hypothyroidism co-occur. For the best possible diagnosis and treatment plans for afflicted people, it is essential to comprehend the complex pathophysiological mechanisms underlying these illnesses.

GENETIC AND EPIGENETIC INFLUENCES ON PCOS AND HYPOTHYROIDISM

The complicated endocrine illnesses Polycystic Ovary Syndrome (PCOS) and hypothyroidism have a serious negative effect on the health and quality of life of those who are affected. Even though these diseases have distinctive clinical signs, new evidence points to the critical roles that genetic and epigenetic variables play in their development. To fully understand PCOS and hypothyroidism's complicated aetiology and advance focused therapy strategies, it is essential to comprehend the genetic foundations and epigenetic alterations connected to these conditions. The genetic component of PCOS is well known. Identical twin studies have shown a greater concordance rate for PCOS compared to non-identical twin studies, demonstrating a significant genetic contribution.[11] Multiple genetic loci linked to PCOS have been found by Genome-Wide Association Studies (GWAS), involving genes involved in insulin signaling, ovarian function, and hormonal control.[12,13] In a manner similar to hyperthyroidism, also demonstrates a hereditary propensity, particularly in cases of autoimmune thyroid illnesses like Hashimoto's thyroiditis. Underscoring the genetic component of autoimmune thyroid disorders, certain Human Leukocyte Antigen (HLA) alleles have been linked to vulnerability.[14] The onset of hypothyroidism has also been linked to changes in genes involved in the manufacture and function of thyroid hormones.[15] The co-occurrence of PCOS and hypothyroidism may be caused by hereditary variables that emerging evidence shows may be shared. It has been suggested that PCOS and hypothyroidism are both caused by genetic variations linked to insulin resistance, such as those affecting the insulin receptor and signaling pathways.[11] Additionally, PCOS-related genes shown to be involved in ovarian and hormonal control may potentially affect thyroid and hormone production. The reported co-occurrence of PCOS and hypothyroidism in certain people may be caused by these shared genetic susceptibilities.[15]

Epigenetic modifications, such as DNA methylation, histone modifications, and non-coding RNA control, have a big impact on how genes are expressed and how cells work. Epigenetic modifications have attracted interest as possible disease pathogenesis mediators in both PCOS and hypothyroidism**.** In PCOS patients, epigenetic alterations, notably DNA methylation patterns, have been found in the genes that control insulin signaling, steroidogenesis, and hormonal regulation. The hormonal dysregulation and metabolic abnormalities that characterized PCOS may be a result of these epigenetic alterations.[16,17] Epigenetic changes may potentially contribute to the development of hypothyroidism. Histone modifications and DNA methylation patterns in thyroid-related genes can affect thyroid hormone production and function.[18] The autoimmune component of hypothyroidism may also be influenced by epigenetic changes in immune-related genes.[19] For the complex mechanisms behind PCOS and hypothyroidism to be fully understood, it is essential to comprehend how genetic predispositions and epigenetic changes interact. Furthermore, it shows promise for the creation of focused therapies meant to modify these parameters and enhance clinical outcomes for people with these complicated endocrine illnesses.

CLINICAL IMPLICATIONS

Polycystic Ovary Syndrome (PCOS) is one of the main factors preventing women from getting pregnant. Having a baby naturally might be difficult for people with PCOS due to hormonal abnormalities and ovulatory dysfunction. In order to help women get pregnant, Assisted Reproductive Technologies (ART) are frequently used, such as *in vitro* Fertilization (IVF) or ovulation induction.[2,5,6] An increased likelihood of multiple pregnancies may accompany these treatments, though. PCOS sufferers also have a higher risk of pregnancy problems such as gestational diabetes and hypertensive diseases.[20] Hypothyroidism, particularly when inadequately treated, can have a detrimental influence on fertility. The menstrual cycle can be thrown off, and ovulation can be compromised by low thyroid hormone levels. People with hypothyroidism who want to get pregnant need to have thyroid hormone replacement medication. Optimal thyroid function is ensured by proper management, which lowers the chance of ovulatory dysfunction and enhances the success of fertility treatments.[21]

METABOLIC HEALTH AND CARDIOVASCULAR RISK

Insulin Resistance and Metabolic Disorders

Insulin resistance and metabolic disorders are linked to both hypothyroidism and PCOS. There may be an additional impact when both diseases coexist, worsening insulin resistance and raising the risk of glucose intolerance and type 2 diabetes. Additionally, the development of metabolic syndrome, which is characterized by a concentration of cardiovascular risk factors, might be facilitated by the presence of central obesity, a characteristic shared by both illnesses.[5,8]

Cardiovascular Health

Having PCOS and hypothyroidism together may result in a higher risk profile for cardiovascular disease. A part of the metabolic syndrome, which is linked to an increased risk of cardiovascular disease, involves central obesity, dyslipidemia, and insulin resistance. A change in lipid profiles and an elevated risk of atherosclerosis can result from hypothyroidism if it is untreated or inadequately managed.[8,22]

Interventions and Management

A multidisciplinary approach is required for the effective therapy of patients with PCOS and hypothyroidism. It could contain:

Hormone Replacement Therapy (HRT)

The use of synthetic thyroid hormones for hypothyroidism to restore normal thyroid function and enhance reproductive results.[4]

Lifestyle changes

Applying food and exercise therapies to enhance insulin sensitivity and metabolic parameters in both scenarios.[2,5]

Pharmacological Interventions

To treat certain PCOS or hypothyroidism-related symptoms or problems, medication may occasionally be administered.[6,22]

The co-existence of PCOS and hypothyroidism poses special difficulties for those trying to get pregnant and emphasizes the value of comprehensive, multidisciplinary therapy. Healthcare professionals may considerably enhance the reproductive and general health outcomes for people with these complicated endocrine diseases by treating hormone imbalances, improving metabolic health, and reducing cardiovascular risk factors.

DIAGNOSTIC CHALLENGES

Polycystic Ovary Syndrome (PCOS) manifests a significant diagnostic difficulty due to its wide range of clinical symptoms. The Rotterdam criteria comprise a widely used diagnostic paradigm that includes polycystic ovarian morphology, hyperandrogenism, and ovulatory dysfunction. However, it's possible that certain PCOS presentations may not be covered by these criteria, which might result in underdiagnosis.[5,6] Further confounding the diagnosis when both illnesses occur is the fact that PCOS symptoms, such as irregular menstrual periods, can also be hypothyroidism symptoms. Hypothyroidism, especially in its subclinical form, can be difficult to diagnose. The diagnosis may be difficult to make since clinical symptoms may be modest and test results may fall within the normal reference range.[3] Additionally, hypothyroidism symptoms like fatigue and weight gain might be confused for typical PCOS symptoms, which could delay getting the right therapy.

Therapeutic Approaches

Polycystic Ovary Syndrome (PCOS) treatment focuses on the hormonal, reproductive, and metabolic components of the disease. The improvement of metabolic parameters and insulin sensitivity depends heavily on lifestyle changes, such as dietary adjustments and frequent exercise. In order to treat certain symptoms like hirsutism and irregular menstruation, hormonal therapies like combination oral contraceptives or anti-androgen drugs may also be administered. Ovulation induction treatments or assisted reproductive methods can be used by people who want to become pregnant.[1,6,8] Thyroid hormone replacement therapy, often using synthetic Thyroxine (T4), is the mainstay of treatment for hypothyroidism. In order to relieve symptoms and avoid consequences, it is important to get thyroid hormone levels back to normal. To ensure normal thyroid hormone levels, it is crucial to closely monitor thyroid function through routine blood testing.[3,21]

Importance of a Multidisciplinary Approach

The successful management of the complex interactions between hypothyroidism and Polycystic Ovary Syndrome (PCOS) requires a thorough and interdisciplinary approach. The complex interplay between these two endocrine diseases calls for a comprehensive and planned approach that incorporates several medical specialties.[3-8,20]

Gynaecologists and endocrinologists

Both the diagnosis and treatment of PCOS and hypothyroidism depend heavily on these professionals. They are in charge of managing hormonal therapies, fertility procedures, and thyroid hormone replacement.

Registered nutritionists and dietitians

Dietary changes and weight control techniques are essential elements of therapy due to the metabolic consequences of both illnesses. These experts can offer specialized dietary advice.

Primary care Physicians

They are essential in the early evaluation, diagnosis, and coordination of therapy. They keep track of cardiovascular risk factors as well as general health, and they make sure that the right referrals to experts are made.

Mental health professionals

Since infertility can have a negative influence on mental health, offering holistic care may depend heavily on mental health support.

Reproductive endocrinologists and infertility specialists

For those who want to become pregnant, these professionals have knowledge of ovulation induction treatments and assisted reproductive methods.

PCOS and hypothyroidism patients can receive thorough, individualized care that tackles the particular difficulties posed by these complicated endocrine conditions by working with a multidisciplinary team. Together with specialized medical knowledge, this team approach guarantees that patients receive the necessary emotional and psychological assistance to help them deal with the difficulties of having hypothyroidism and PCOS, eventually leading to improved quality of life and overall well-being.

FUTURE PERSPECTIVES AND RESEARCH DIRECTIONS

Recent developments in genomic research offer the potential to elucidate the nuanced genetic underpinnings of PCOS and hypothyroidism, opening the door to personalized treatment approaches.[9,11] DNA methylation patterns, histone modifications, and non-coding RNA regulation can all be used to better understand the molecular mechanisms behind these disorders.[14,15] Additionally, studies on the gut-endocrine axis and microbiome are being done, with a particular emphasis on how the gut microbiota influences metabolic health and hormone regulation. This field might lead to the development of novel medicines like probiotics or dietary modifications.[19,20] Concerning autoimmune thyroid issues in particular, research into immune dysregulation and autoimmune disease is becoming more and more significant. Immunological pathways and immunomodulatory therapies may lead to the development of novel therapeutic strategies for the treatment of hypothyroidism in affected patients.[12,17] Researchers may be able to identify specialized therapies and diagnostic tools for these complicated endocrine diseases by utilizing new fields like metabolic profiling and metabolomics.[23,24]

A subsequent investigation on PCOS and hypothyroidism should concentrate on their natural histories, trials, interdisciplinary treatment approaches, patient-centered outcomes research, medical technology, and global health inequities.[25,26] Early intervention strategies can be informed by natural history and longitudinal research, and trials of treatments can promote evidence-based care.[27,28] Multidisciplinary care models including endocrinologists, gynaecologists, family practitioners, dietitians, and mental health specialists can enhance patient results.[5,3] Patients with PCOS and hypothyroidism should participate in studies that focus on patient-reported outcomes, quality of life and shared decision-making.[2,26] Wearables, smartphone apps, and telemedicine are just a few examples of digital health and health technology treatments that can increase accessibility and patient engagement in care.[29,30] Addressing global health disparities and ensuring fair access to high-quality care is crucial to ensure fair access to high-quality care.[31-35] The scientific community can progress our understanding of PCOS and hypothyroidism by focusing on these study areas, which will eventually improve outcomes for people with these complex endocrine illnesses by improving diagnostic precision, developing more individualized treatment plans, and other benefits.

Future directions for study in three critical areas pertain to Polycystic Ovarian Syndrome (PCOS). From the outset, breaking the vicious cycle that is inherent in PCOS pathophysiology may be possible by understanding the complex interactions between reproductive dysfunction and metabolic problems, especially the ones that link hyperandrogenism and insulin resistance. To gain a complete understanding, it is important to investigate environmental variables, including the effects of pregnancy and lactation on the follicular microenvironment and lifestyle. Second, investigating the high heritability of PCOS further necessitates novel strategies, such as going beyond the limits of existing Genome-Wide Association Studies (GWAS) to investigate gene-environment interactions. Furthermore, the discovery of biomarkers that can be used to identify people who

are at risk early on presents a revolutionary opportunity that will allow for focused interventions and a paradigm change away from symptom-centric approaches and toward lifelong management techniques. Along with improving our understanding of PCOS, these research paths hope to spark the creation of better treatments and preventative strategies, which will ultimately usher in a new age of individualized and comprehensive care for PCOS patients.[36]

CONCLUSION

This in-depth review addressed the complex interplay between PCOS and hypothyroidism, two common endocrine conditions that have a major negative influence on the health of women. Insights into the co-occurrence of these disorders and their underlying pathophysiological processes have been revealed by synthesising recent research in numerous significant ways. The study emphasizes how complex genetic and epigenetic interactions contribute to the development of PCOS and hypothyroidism. It draws attention to the hormonal imbalances and metabolic disorders linked to both illnesses, notably insulin resistance. In order to address the specific reproductive issues that the co-occurrence of both disorders poses, a multidisciplinary strategy is required. To provide complete, patient-centered treatment, endocrinologists, gynaecologists, primary care doctors, nutritionists, and mental health providers must work together. It's essential to comprehend the intricate hormonal interactions to create remedies that are tailored to each afflicted person's unique requirements. The relationship between PCOS and hypothyroidism is crucial in clinical practice, as timely diagnosis and management strategies can improve outcomes and quality of life. A holistic approach to patient care is essential, considering hormonal imbalances, metabolic disturbances, and psychosocial and emotional well-being. Further research into the genetic, epigenetic, and metabolic underpinnings of these conditions is necessary, along with longitudinal studies and patient-centered outcomes research to refine diagnostic and therapeutic strategies.

In conclusion, this review highlights the complex interactions between PCOS and hypothyroidism, emphasizing the necessity for a thorough and team-based approach to therapy. Healthcare professionals may dramatically improve the well-being of people with PCOS and hypothyroidism by recognizing the intricacies of both disorders and treating them as a unit.

ACKNOWLEDGEMENT

The authors would like to thank the management of Assam down town University for significant cooperation in providing the necessary facilities and requirements.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

PCOS: Polycystic Ovary Syndrome; **SHBG:** Sex hormone-binding globulin; **LH:** Luteinizing hormone; **IGF:** Insulin-like growth factor-1; **TSH:** Thyroid-stimulating hormone; **T4:** Thyroxine; **T3:** Triiodothyronine; **IL-6:** Interleukin-6; **CRP:** C-reactive protein; **GWAS:** Genome-wide association studies; **HLA:** Human leukocyte antigen; **ART:** Assisted reproductive technologies; **IVF:** *In vitro* fertilization; **HRT:** Hormone replacement therapy.

REFERENCES

1. Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, *et al.* Polycystic ovary syndrome. Nature reviews Disease primers. 2016;2(1):1-8.
2. 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 medicine. 2010;8(1):1-0.
3. Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet. 2017;390(10101):1550-62.
4. Vanderpump MP, Tunbrldge WM, French J, Appleton D, Bates D, Clark F, *et al.* The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. Clinical endocrinology. 1995;43(1):55-68.
5. Azziz R. New insights into the genetics of polycystic ovary syndrome. Nature Reviews Endocrinology. 2016;12(2):74-5.
6. Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. Clinical epidemiology. 2013;18:1-3.
7. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nature Reviews Endocrinology. 2018;14(5):270-84.
8. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, Okosieme OE. Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology. 2018;14(5):301-16.
9. Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. Journal of human reproductive sciences. 2020;13(4):261.
10. Ganie MA, Vasudevan V, Wani IA, Baba MS, Arif T, Rashid A. Epidemiology, pathogenesis, genetics & management of polycystic ovary syndrome in India. The Indian journal of medical research. 2019;150(4):333.
11. Sadeghi HM, Adeli I, Calina D, Docea AO, Mousavi T, Daniali M, *et al.* Polycystic ovary syndrome: a comprehensive review of pathogenesis, management, and drug repurposing. International journal of molecular sciences. 2022;23(2):583.
12. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. Journal of the Endocrine Society. 2019;3(8):1545-73.
13. Azumah R, Hummitzsch K, Anderson RA, Rodgers RJ. Genes in loci genetically associated with polycystic ovary syndrome are dynamically expressed in human fetal gonadal, metabolic and brain tissues. Frontiers in Endocrinology. 2023 ;14:1149473.
14. Day F, Karaderi T, Jones MR, Meun C, He C, Drong A, *et al.* Large-scale genome-wide meta-analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnosis criteria. PLoS genetics. 2018;14(12):e1007813.
15. Tomer Y, Davies TF. Searching for the autoimmune thyroid disease susceptibility genes: from gene mapping to gene function. Endocrine reviews. 2003;24(5):694-717.
16. Panicker V. Genetics of thyroid function and disease. The Clinical Biochemist Reviews. 2011;32(4):165.
17. Humphreys KL, Moore SR, Davis EG, MacIsaac JL, Lin DT, Kobor MS, *et al.* DNA methylation of HPA-axis genes and the onset of major depressive disorder in adolescent girls: a prospective analysis. Translational psychiatry. 2019;9(1):245.
18. Ray RP, Padhi M, Jena S, Patnaik R, Rattan R, Nayak AK. Study of association of global deoxyribonucleic acid methylation in women with polycystic ovary syndrome. Journal of Human Reproductive Sciences. 2022;15(3):233.
19. Hannoush ZC, Weiss RE. Defects of thyroid hormone synthesis and action. Endocrinology and Metabolism Clinics. 2017;46(2):375-88.
20. Teixeira PD, Dos Santos PB, Pazos-Moura CC. The role of thyroid hormone in metabolism and metabolic syndrome. Therapeutic advances in endocrinology and metabolism. 2020;11:2042018820917869.
21. Boomsma CM, Eijkemans MJ, Hughes EG, Visser GH, Fauser BC, Macklon NS. A meta-analysis of pregnancy outcomes in women with polycystic ovary syndrome. Human reproduction update. 2006;12(6):673-83.
22. Krassas GE. Thyroid disease and female reproduction. Fertility and sterility. 2000;74(6):1063-70.

23. Osibogun O, Ogunmoroti O, Michos ED. Polycystic ovary syndrome and cardiometabolic risk: Opportunities for cardiovascular disease prevention. Trends in cardiovascular medicine. 2020;30(7):399-404.
24. Moran LJ, Norman RJ, Teede HJ. Metabolic risk in PCOS: phenotype and adiposity impact. Trends in Endocrinology & Metabolism. 2015;26(3):136-43.
25. Toulis KA, Goulis DG, Mintziori G, Kintiraki E, Eukarpidis E, Mouratoglou SA, *et al.* Meta-analysis of cardiovascular disease risk markers in women with polycystic ovary syndrome. Human reproduction update. 2011;17(6):741-60.
26. Couto Alves A, Valcarcel B, Mäkinen VP, Morin-Papunen L, Sebert S, Kangas AJ, *et al.* Metabolic profiling of polycystic ovary syndrome reveals interactions with abdominal obesity. International Journal of Obesity. 2017;41(9):1331-40.
27. Rudnicka E, Suchta K, Grymowicz M, Calik-Ksepka A, Smolarczyk K, Duszewska AM, *et al.* Chronic low grade inflammation in pathogenesis of PCOS. International journal of molecular sciences. 2021;22(7):3789.
28. Patel S. Polycystic ovary syndrome (PCOS), an inflammatory, systemic, lifestyle endocrinopathy. The Journal of steroid biochemistry and molecular biology. 2018;182:27-36.
29. Yildiz BO, Bozdag G, Yapici Z, Esinler I, Yarali H. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Human reproduction. 2012;27(10):3067-73.
30. Deswal R, Narwal V, Dang A, Pundir CS. The prevalence of polycystic ovary syndrome: a brief systematic review. Journal of human reproductive sciences. 2020;13(4):261.
31. Bednarz K, Kowalczyk K, Cwynar M, Czapla D, Czarkowski W, Kmita D, *et al.* The role of glp-1 receptor agonists in insulin resistance with concomitant obesity treatment in polycystic ovary syndrome. International Journal of Molecular Sciences. 2022;23(8):4334.
32. Sharma RK, Patel S, Gallant JN, Esianor BI, Duffus S, Wang H, *et al.* Racial, ethnic, and socioeconomic disparities in the presentation and management of pediatric thyroid cancer. International Journal of Pediatric Otorhinolaryngology. 2022;162:111331.
33. Zhao HH, Wilhelm SM. Pediatric thyroid cancer: Socioeconomic disparities and their impact on access to care. Surgery. 2023.
34. Vahratian A, Smith YR, Dorman M, Flynn HA. Longitudinal depressive symptoms and state anxiety among women using assisted reproductive technology. Fertility and sterility. 2011;95(3):1192-4.
35. Hull MG. Epidemiology of infertility and polycystic ovarian disease: endocrinological and demographic studies. Gynecological endocrinology. 1987;1(3):235-45.
36. Harada M. Pathophysiology of polycystic ovary syndrome revisited: Current understanding and perspectives regarding future research. Reproductive Medicine and Biology. 2022;21(1):e12487.

Cite this article: Barman I, Sharma T, Talukdar N. Exploring the Connection between Hypothyroidism and Polycystic Ovary Syndrome: A Comprehensive Review. J Young Pharm. 2024;16(2):187-94.