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**Systematic Review**

# Impact of subclinical hypothyroidism on infertility and other metabolic parameters in women with polycystic ovarian syndrome in South Asia

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## ABSTRACT

Polycystic ovary syndrome (PCOS), is a very common endocrine and metabolic disorder in premenopausal women that affects 1 in 10 women of childbearing age. According to recent studies, the prevalence of PCOS was found around 53%. Many studies showed that subclinical hypothyroidism (SCH) and PCOS share symptoms which can influence PCOS symptoms like infertility and hormonal changes. This systematic review aimed to evaluate the impact of SCH on infertility and other metabolic parameters in women with polycystic ovarian syndrome in South Asia. For this review work, after a literature search through PubMed, Cochrane, and Google Scholar, 5 relevant papers were identified for this systematic review. The publication time was limited to the most recent 10 years, from 2011 to 2022. This review considered quantitative research on PCOS and SCH and used evidence-based data to support the findings. Among the mentioned 5 studies, 3 were cross-sectional and 2 were case-control. The studies were conducted on 2 groups: the SCH-PCOS intervention group and the PCOS control group. For the quality assessment, Cochrane's software, review manager (RevMan) was used to eliminate duplicate studies and reduce bias. The systematic review was conducted on 1468 female patients and measured anthropometric parameters in both groups. Total cholesterol, body mass index (BMI), TSH, free testosterone levels, insulin resistance and menstrual irregularities were all higher in the SCH-PCOS group compared to the PCOS group, along with a $p<0.001$ for each of the parameters. Usually, SCH and PCOS share symptoms. In cholesterol, BMI, TSH, free testosterone levels, insulin resistance and menstrual irregularities there are significant correlations between SCH and PCOS. So, there are some potential impacts of SCH on infertility and other metabolic parameters in women with polycystic ovarian syndrome in South Asia.

**Keywords:** PCOS, SCH, Infertility, Metabolic parameters, South Asia

## INTRODUCTION

Polycystic ovarian syndrome (Group) is a cluster of symptoms caused by an imbalanced hormone level in women and girls of reproductive age.[1] It is a condition that affects more than 10% of women during the reproductive years of their life, making it the most frequent endocrine disorder.[2] More than 70% of anovulatory infertility is linked to PCOS (Escobar-Morreale, 2018). It is also a heterogeneous androgen-excess disorder with different degrees of metabolic dysfunctions.[3] Because of insulin resistance raises the risk factors of developing cardiovascular disease and is made worse by the prevalence of obesity, even though insulin resistance can also be found in women with PCOS who do not have an obesity-related weight issue.[4] On the other hand, abnormalities of the thyroid gland such as SCH are also common forms of endocrine gland illnesses found worldwide.[5] SCH is characterized by elevated thyroid-stimulating hormone levels despite normal free thyroxine levels.[6] An irregular supply of thyroid hormones in peripheral tissues can lead to metabolic abnormalities.[7] Thyroid dysfunction can also lead to a slight change in fertilization and endometrial receptivity, leading to infertility in women.[8] Overt hypothyroidism must be ruled out before diagnosing PCOS since it shares symptoms with PCOS, including irregular menstruation, oligo/anovulation, subfertility, miscarriage, and polycystic

ovaries.[9] SCH may have many PCOS-related reproductive symptoms.[10] PCOS and SCH exhibit metabolic symptoms despite different etiopathogenesis.[11] PCOS may have hereditary and environmental causes.[12] Oligo-ovulation and hyperandrogenism are the only criteria for PCOS.[13] As a result of the ethnicity of people around the world, PCOS is said to be significantly more prevalent in South Asian countries such as Bangladesh, India, and Pakistan than it is in Caucasians.[14] Several studies have found that South Asian women, in comparison to Caucasian women, are at a higher risk of developing metabolic issues and insulin resistance owing to PCOS.[15] The lack of effective norms and policies, as well as education and treatment options, contributes to serious public health issues, especially among women, and may help explain why this phenomenon is more common in South Asian countries.[16] However, there is currently a dearth of data for doctors to use in understanding the link between SCH and PCOS, as well as how to treat infertility and metabolic abnormalities.[17] Multiple trials have shown SCH has an effect, although minimal, on metabolic markers and the infertility of PCOS women.[18] PCOS has been linked to several other conditions as well. In South Asia, around 55-75% of women with PCOS (Group) also have insulin resistance, which can lead to cardiovascular illnesses, metabolic syndromes, and infertility.[19] Insulin resistance is the root cause of several health issues, including hyperandrogenism, hirsutism, menstrual abnormalities, and infertility due to anovulation.[20] A few studies found that a woman with PCOS with a stimulating thyroid hormone (Tashi Dendup) level higher than 2.5 mIU/l had a more elevated insulin resistance index, BMI, and fasting insulin concentration.[21] In PCOS patients, the presence of hypothyroidism was associated with a significant increase in the severity of insulin resistance and obesity.[15] In women who have PCOS, there is a correlation between thyroid function and insulin resistance, and this correlation can be seen regardless of age or BMI.[22] As a result, a problem with the thyroid must be one of the conditions ruled out before a woman's PCOS diagnosis can be made, even though there is active controversy regarding SCH's influence on PCOS.[23] However, there is evidence from both research and pathophysiology to suggest that SCH may affect PCOS-related symptoms such as metabolic and ovulation problems.[10] In contrast, when someone has primary hypothyroidism, overall thyrotropin-releasing hormone (TRH) levels rise, which causes their TSH and prolactin levels to increase.[10] Prolactin (PRL) affects the polycystic structure of the ovary.[14] PRL inhibits ovulation, which also alters the proportion of follicle-stimulating hormone (FSH) to luteinizing hormone (LH), two hormones that contribute to an increase in the production of the hormone dehydroepiandrosterone by the adrenal gland.[24] The ultimate sign of hypothyroidism is an enhanced TSH spill-over action on FSH receptors and increased collagen deposition over the ovaries.[13] In 2017, PCOS was recognized as a worldwide disease burden because women of reproductive age (15-44) in approximately 194 nations worldwide are affected by the condition.[25] Regarding this topic, there are no systematic reviews that have been conducted in South Asia. Therefore, the outcome of this research will contribute to addressing the informational gap. This systematic review will enable the healthcare ministry and health professionals to know the facts about SCH and PCOS, and it will encourage them to undertake additional studies to figure out the actual pathology and correlations between SCH and PCOS.

## METHODOLOGY

The purpose of the method section was to explain how further studies were conducted. It would provide an overview of the research aim and objectives, provide an answer to the question of research, establish chosen studies, eligibility criteria, assess risk, provide data extraction and analysis and bias, and evaluate the quality.

### *Research question and objectives*

In a quantitative systematic review, having a research question that has been well-structured is essential.[26] A research question that helps to find out the gap in knowledge by using the PICO format, where P refers to people, I represent the intervention, C stands for the comparison, and O is for the outcome of the study.[27] PCOS and other thyroid illnesses, such as SCH, are more common in South Asian women and are known to cause metabolic problems and exacerbate infertility. Several studies' results were combined to come to this conclusion.[8] The research question for this systematic review was- 'Is SCH in any relation to PCOS? How does SCH impact infertility and metabolic parameters of PCOS women?' Because of this, the population was made up of female patients who were suffering from PCOS. The intervention was the SCH, which influences the metabolic parameters of those patients as well as their infertility. The outcome of the investigation was analyzed whether or not there was a connection between the two disorders by calculating the percentage of patients who have both SCH and PCOS. A research hypothesis was developed from the research question. Through empirical investigation, the research hypothesis primarily elaborates on the connections between the dependent variables and the independent factors.[28] As a result, the factors that have been discussed in this systematic review were changes in metabolic hormonal markers and infertility of PCOS women with SCH (independent variables), as well as the outcome correlations between SCH and PCOS women in South Asia (dependent variables).[29] However, for this systematic review, the null and alternative hypotheses mostly described the categories.

### *Search strategy*

For this review, the researcher searched an electronic database using potential outcomes and phrases along with selected keywords. This search was well-constructed, organized, and detailed. It was also reliable. The keywords that were used in the research are combined in a search

strategy for a systematic review.[30] To acquire the numerical data needed for this review, several databases' publications and articles were searched using keywords taken from the research questions that were provided as the search strategy. To broaden and increase the depth of the search, the Boolean operators AND, and OR were implemented throughout the process.[31] The eligibility criteria were the most essential stage in the process of conducting a systematic review. That also provided the review's foundation. There was a predetermined set of guidelines or eligibility criteria that determined which studies were included and which were not. That clarified the meaning of the qualifying requirements of the study, which not only reduced the amount of ambiguity but also helped to keep a strategic distance from any potential bias throughout the process of selecting the studies. The PICO framework, which stands for the population, intervention, comparative, and outcome of the study, was used to establish the criteria.[32] The reviewers used certain criteria to determine whether or not an article should be included in this review. First, the framework of the review was reduced to quantitative research, which means that cross-sectional studies, case-control studies, and observational studies carried out in the 12 years encompassing from 2010 to 2022 were taken into consideration. It was carried out to achieve the goal of the study and provide numerical statistics supported by adequate documentation. Therefore, a randomized controlled trial and a cross-sectional study will be ideal for providing an answer to the research topic.[33] On the other hand, non-randomized studies, also known as NRS, are not advised for use in the field of healthcare research; for this reason, they were not included in the criteria for study acceptance. Noted that employing NRS for systematic reviews has the risk of bias.[34] Following that, patients who had PCOS with symptoms and who also had SCH were included in the research. Consequently, research that had not been chosen to meet the review's inclusion criteria was not considered for inclusion. In addition, the studies that were conducted before 2010 were not chosen since the reviewer placed restrictions on the research. In addition, the research that included PCOS patients but did not discuss SCH-related consequences was excluded. Before dealing with research, a vital step that must be taken is to take ethical considerations into account.[35] This study was a combination of primary research and a systematic review, all of the ethical concerns, most particularly autonomy, have previously been considered. The researcher obtained ethical approval from the ethics board committee at the university of Chester. The university made the Endnote 20 program available to us to prevent any unnecessary replication of previous research.[36] The researcher utilized RevMan 5.4.1 collaboration by Cochrane to eliminate the possibility of bias and to evaluate the study's potential dangers. In addition, the PRISMA20 flow diagram has been implemented so that all of the research can be included in this review appropriately.[37] Diagram of PRISMA20, which concentrates on the process of assessing systematic reviews. Data collection, processing, and analysis have all been carried out methodically using various online search engines according to the flow diagram. The researcher searched for correlations between PCOS and SCH as well as with other thyroid disorders in the databases PubMed, CINHAL, and Cochrane.[38] This was done before searching for eligible publications. This was done to carry out this systematic review. First and initially, the primary goal of the researcher was to locate the paper that had already been published and provide answers to the research-specific issues. Some of the papers did not provide answers to the research-specific queries. In addition, a few of the papers failed to provide an adequate number of studies addressing the two issues. After using electronic search engines to find relevant publications, the investigator should follow the PRISMA flow chart to collect data and evidence from them that can be recognized.[39] Because these systematic review questions were concerned with matters concerning health, a variety of databases, including PubMed, Cochrane, and CINHAL, were searched. In addition, electronic search engines such as Google Scholar have been used to look for appropriate documentation.[40] The portal for the university library included access to PubMed, as well as Cochrane and CINHAL. To locate the applicable studies utilizing Boolean operators results in database research that is both more comprehensive and detailed.[41] The researcher looked over all of the recent studies that have come out in the last ten years, from 2011 to 2022. For this investigation, the English language was chosen, and full-text articles were favored. After searching, a total of 27 papers were discovered, 24 of which were in PubMed, and 3 in Cochrane. All of the studies were uploaded into the EndNote software library so that duplicates of studies could be identified and removed. When duplicates were removed, there was only 18 total research. Researchers chose papers that were supported by electronic databases for this systematic review. After that, the studies were imported into Endnote software to remove any instances of duplication.[42] The population that was investigated in this research consists of South Asian women who suffer from PCOS and PCOS in association with SCH. Currently, PCOS is the most prevalent endocrine condition in the world. South Asian women, particularly those in Bangladesh, India, and Pakistan, are the ones who are suffering the most from it. The patients from these nations are being considered as part of the search pattern because of this reason.[27] A pathway refers to a group of patients who have been exposed to a disease or risk behavior or another prognostic factor. An intervention, variable, or interest might be considered an interest group. As a result, the intervention of this study in SCH has brought about a worsened outcome for PCOS patients, such as an increase in PCOS symptoms.[42] After excluding duplicate studies, the total number of studies dropped from 46 to 18. The researcher then applied the inclusion criteria to make the database studies with full texts more specific, and they removed 10 studies as a result. Following that, two other studies were disqualified based on the criteria for exclusion. In conclusion, considering the available time frame and the fact that there was no outcome found in any of the 3 trials and left 5 studies for review. As a result, the

five papers have been submitted for consideration in the systematic review; of these, three were cross-sectional studies, while the other two were case-control studies. They are depicted in the PRISMA flow diagram figure that can be found below.

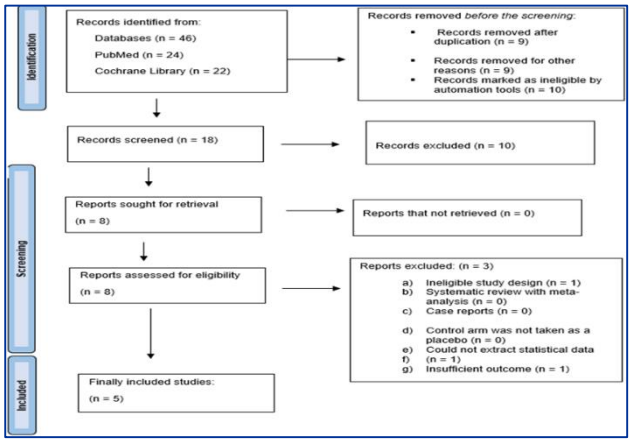


**Figure 1: PRISMA flow chart of study selection.**

***Quality assessment***

The systematic review and the research are both improved by the quality evaluation tools, making them more specific and comprehensive.[44] The researcher chose to conduct this review using the Newcastle-Ottawa Scale (NOS) quality evaluation methods because the studies under consideration are non-randomized.[45] The researcher selected three cross-sectional studies and two case-control studies. Researchers evaluate the studies based on a total of eight criteria that are divided into three distinct categories employing NOS.[46] The categories are titled "selection," "comparability," and "exposure," respectively. Every category has certain requirements denoted with stars. Individual evaluations of the research that are of very high quality are rewarded with stars.[47] Although it has been selected as the gold standard for this evaluation by the Cochrane review for the study's interventions, The quality of nonrandomized research may be determined using this tool due to its comprehensive evaluation.[14] In this review, for quality assessment, Newcastle-Ottawa-scale was used.

**Table 1: Newcastle-Ottawa-scale for quality assessment.**

| First author (Year) → | | (Deepak Raj, 2021)[48] | (Kamrul-Hasan et al, 2020)[14] | (Fatima et al, 2020)[11] | (Sinha et al, 2013)[49] | (Ganie et al, 2011)[50] |
|---|---|---|---|---|---|---|
| **NOS quality assessment** | Selection | □□□ | □□□ | □□ | □□□ | □□ |
| | Comparability | □ | □ | □ | □ | □ |
| | Outcome | □□ | □ | □□□ | □□□ | □□ |

***Data analysis and extraction***

The procedure of extracting and analyzing the data is the most fundamental part of a systematic review. It is necessary to perform the data extraction as well as analysis to prove the primary research, answer the questions raised by the research, and the provide researchers with the evidence.

The data that were extracted include names of authors, the years study was conducted, the sample sizes of the studies, types of studies, nations, intervention, and the control group.

**Table 2: Baseline characteristics of included studies.**

| Authors/ year | Country | Study design | Diagnostic criteria | Sample size | Intervention (SCH with PCOS) | Comparison (Group) |
|---|---|---|---|---|---|---|
| **(Raj, 2021)[48]** | Pakistan | Case-control | Rotterdam criteria | 400 | 200 | 200 |
| **(Kamrul-Hasan et al, 2020)[14]** | Bangladesh | Cross-sectional | Rotterdam criteria | 465 | 50 | 415 |
| **(Fatima et al 2020)[11]** | Pakistan | Cross-sectional | Rotterdam criteria | 90 | 31 | 59 |
| **(Ganie et al, 2011)[50]** | India | Case-control | NIH | 353 | 62 | 291 |
| **(Sinha et al, 2013)[49]** | India | Cross-sectional | Rotterdam criteria | 160 | 80 | 80 |

## OBSERVATIONS

Data that was extracted and the results that were obtained from the parameters of the investigations that were conducted on the intervention group as well as the control group were separately disseminated showed in the below Table 3.

**Table 3: Outcome with parameters.**

| Authors | TSH | BMI | TC | Testosterone | Outcome |
|---|---|---|---|---|---|
| **(Raj, 2021)[48]** | Here, I=5.01±1.02 C=3.42±0.76 | Here, I=25.12±2.51 C=22.51±2.01 | Here, I=×, C=× | Here, I=33.51±25.11 C=31.29±27.44 | In this study, each parameter shows high markers in the Intervention group. PCOS and SCH can cause clinical, biochemical, and metabolic abnormalities that affect fertility and pregnancy. |
| **(Kamrul-Hasan et al, 2020)[14]** | I=7.38, C=1.32 | I=27.39±4.93 C=26.53±5.14 | I=173.54±31.33 C=171.54±34.21 | I=16.0, C=19.8 | In this study, each parameter shows high markers in the Intervention group. So, SCH has an impact on PCOS symptoms. |
| **(Fatima et al 2020)[11]** | I=3.9±1.09 C=1.8±0.38 | I=32.5±3.75 C=25.7±3.27 | I=183.64±32.34 C=180.89±33.29 | I=87.2±33.11 C=84.9±36.57 | Here, the study shows SCH group has a significant effect on PCOS. Hence this means SCH has a relation with PCOS. |
| **(Ganie et al, 2011)[50]** | I=7.13±1.28 C=2.51±1.21 | I=25.3±4.7 C=25.3±4.1 | I=4.62±0.92 C=4.45±0.86 | I=×, C=× | In this study, TSH shows high in the intervention group which means SCH has some effect on PCOS and shows the other parameters higher in the intervention group. |
| **Sinha et al, 2013)[49]** | I=4.547±2.66 C=2.67±3.11 | I=24.68±3.07 C=23.55±3.02 | I=×, C=× | I=23.33±7.836 C=15.68±6.28 | Here, study shows higher parameters in intervention group which means that SCH and PCOS have relationships and impact on their parameters. |

(Here, I=Intervention, C=Comparison)

Following the collection of data from several studies, the researcher discovered that the results of all of the studies indicated that there was a connection between SCH and PCOS. Furthermore, the results of every study indicate that there was a significant effect of the SCH group on PCOS metabolic parameters, which is responsible for further infertility when compared to the group of patients who only had PCOS. For this systematic review, there was a dearth of research conducted in South Asia on the links between SCH and PCOS and the impact SCH has on the development of PCOS. Until now, academics have only uncovered several studies dealing with this issue as it relates to South Asian countries. Researchers in Bangladesh, Pakistan, and India only found five articles with credible evidence. Out of the five studies, one was done in Bangladesh, two in Pakistan, and the other two in India. The study's author attempted to track down related research from other South Asian countries but was unsuccessful. In addition to examining the correlation between SCH and PCOS, the selected studies also examined the impact of both disorders on metabolic hormonal indicators. All results showed first-hand information regarding the treatment. Before moving on to the discussion of the overall result of all five studies being considered, the results of each of the five studies themselves are evaluated first. The first study was a case-control study that was carried out in Pakistan in a hospital that provided tertiary care. The purpose of the study was to identify the prevalence of SCH in women who had polycystic ovarian syndrome (Group). They recruited a total of four hundred young women between the ages of 18 and 30 to participate in the study.[48] Of these, two hundred of the females had PCOS, while another two hundred of the females had PCOS in conjunction with SCH. They were experiencing symptoms that were associated with PCOS. Following their participation, the participant's responses to a questionnaire and their BMI measurements were recorded. TSH, FT4, and FT3 levels, in addition to free testosterone levels, were measured on these individuals so that metabolic hormonal factors could be evaluated. On the other hand, the outcome support when alternative theories were found on the altering of metabolic parameters is more prevalent in the group of SCH patients who also have PCOS. The researcher compared the two groups' mean ages as well as their mean heights and discovered that BMI (25.12 2.51 kg/m$^2$) in the PCOS with SCH group and (22.51 2.01 kg/m$^2$) in the PCOS group, as well as the p-value (0.0001), were significantly different from one another.[48] Therefore, the BMI of participants who had SCH in the PCOS group was considerably higher than the BMI of participants in the PCOS group. They also discovered substantially higher levels of TSH in the intervention group in comparison to patients who solely had PCOS (5.01 1.02 mIU/L vs. 3.42 0.76 mIU/L; p=0.0000). After the investigation, mentioned in their study that obesity and insulin resistance also play an essential role in the mechanism of SCH and PCOS. They struggle when their BMI is high. It was discovered that the

presence of SCH in a PCOS patient raised the chance of metabolic abnormalities as well as infertility in women; however, they could not offer sufficient data on this topic. However, it was shown that the intervention group had significantly greater levels of testosterone (33.51 25.11 compared to 31.29 27.44). There was ultimately only a minimal amount of data available, but the statistics back up the alternative hypothesis. The results demonstrated links between SCH and PCOS, as well as their effects on metabolic hormonal markers and infertility. In the second study for the outcome analysis, which was a cross-sectional study, the research was carried out in Bangladesh. The research found a total of four hundred sixty-five female patients, all of whom were diagnosed with either PCOS simply or PCOS in addition to SCH. They were given out to a total of four hundred fifteen female patients diagnosed with PCOS and an additional fifty female patients diagnosed with SCH along with PCOS. The Rotterdam criteria were utilized to arrive at a diagnosis for each of them. All the patients were measured with anthropometric measurements and also analyzed by different markers. In patients who were married, they also performed a transvaginal ultrasound, and in patients who were not married, they performed a transabdominal ultrasound. Researchers have employed SPSS version 23.0 to measure the variables, which were then reported as the mean along with the standard deviation (SD), and the median was presented for normal distributions. The statistical analysis was done with this software. They used the students' t-test, the Chi-square test, and the Mann-Whitney U test to compare the variables of the two different groups. The conclusion reaches by the study shows that the alternative hypothesis is correct. They identified increased markers in practically every marker in a study in SCH with the PCOS group. Patients with SCH who had stronger anti-TPO antibodies made up more than 10.8 percent of the total. On the other side, the TSH cut-off value was significantly higher in the SCH group with PCOS than it was in the PCOS group, coming in at 7.38 (5.74-9.81) when compared to 1.32 (0.83-2.15).[14] It was discovered that the BMI of those with SCH who also had PCOS was significantly higher than that of those with PCOS alone (27.39±4.93 vs. 26.53±5.14). They also discovered that patients who had SCH with PCOS shared so many clinical abnormalities, such as menstrual irregularities, spontaneous abortion, infertility, obesity, and also metabolic parameter abnormalities, where they discovered that total cholesterol was higher in the intervention group (SCH with PCOS) than in the control (Group) group (173.54±31.33 vs 171.54±34.21). Furthermore, indicated triglyceride levels (TG) which also higher in the intervention group (53.14±56.09 vs 143.12±53.92).[14] After the findings of the statistical analysis showed that PCOS and SCH are connected with common conditions with undesirable effects such as abnormal menstruation and infertility, they made the discovery. Although the existence of SCH in PCOS also has an impact on the increased risk of metabolic diseases. In the group of women with PCOS and SCH, they also found a higher frequency of acne and hirsutism. Additionally, they discovered that patients with PCOS who had SCH had higher systolic and diastolic blood pressures. As a result, the alternate hypothesis gives legitimacy to the study because it shows through analysis that SCH had a significant influence on PCOS at a larger and more significant level. Karachi, Pakistan appointed as the location for the third study, which was carried out between June 2019 and December 2019. Researchers have examined a total of ninety women, all of whom met the criteria for PCOS according to the Rotterdam criteria. From these, they selected women and divided them into two groups: the patients who had simply PCOS, which included fifty-nine women, and the women who had been diagnosed with SCH along with PCOS, which included thirty-one women.[11] In this study, two groups are compared using statistical analysis based on mean age, BMI, fasting insulin, and evaluation of metabolic markers. They used version 20 of the SPSS statistical package for the analysis. They determined the standard deviation, also known as SD, as well as the median and the mean for the numerical variables. In addition, the Mann-Whitney test was carried out to compare the two groups. Spearman's correlation was the method that was used for the analysis of correlation. Following the completion of the investigation, the researchers uncovered numerical data indicating changes in both groups. It was discovered that people with SCH and PCOS had a higher BMI than patients who only had PCOS (32.5±3.75 vs 25.7±3.27).[11] They found a significant correlation between TSH and intervention SCH and PCOS with clinical, hormonal, and metabolic parameters, including weight (p=0.001), BMI (p=0.001), and insulin (p=0.001). Additionally, they found a significant correlation between TSH and insulin (p=0.001). They also discovered that women with PCOS who had SCH had higher levels of total cholesterol compared to those in another group, which was (180.89±33.29). In comparison to the PCOS group, the TSH levels in the SCH group with PCOS were significantly higher (3.9±1.09) than in the PCOS group (1.8±0.38).[11] As a result, the numerical data provided evidence in favor of the alternative hypothesis and demonstrated a significantly higher incidence of connections between SCH and PCOS. The next investigation was a case-control study that was carried out in India. It included a total of three hundred fifty-three patients who had PCOS along with accompanying symptoms, and they were diagnosed based on the criteria established by the National Institutes of Health. There was a total of patients, of which sixty-two patients were diagnosed with both SCH and PCOS and two hundred ninety-one patients were diagnosed with PCOS alone. SPSS was utilized for the data analysis portion of the investigation.[50] The study found a variety of alterations in the parameters, the majority of which resulted in an increase in SCH among women with PCOS who were in the intervention group. According to the study's findings, the TSH levels in the intervention group were significantly higher than those in the other group (7.13±1.2 vs. 2.51±1.2). They also looked at BMI, which showed that the intervention group had a significantly higher BMI

compared to the PCOS alone group (25.3±4.7 vs. 25.3±4.1).[50] In the SCH group, the total cholesterol was greater (4.62±0.92 vs. 4.45±0.86) while it was lower (4.45±0.86) in the PCOS group. In addition, the study evaluated the severity of menstrual abnormalities with acne and hirsutism in individuals diagnosed with SCH who also had PCOS to patients diagnosed with PCOS alone. In terms of the levels of the hormones LH, FSH, and testosterone, there was not a visible difference between the two groups. The findings, however, add credibility to the alternative hypothesis that SCH has some influence on PCOS. The last research was a cross-sectional study that was carried out in India. It included a total of one hundred sixty female patients who had PCOS and were given a diagnosis based on the Rotterdam criteria. The research was accomplished between the years 2010 and 2012. There was a total of one hundred sixty individuals, of which eighty had SCH with PCOS and eighty just had PCOS. During the study, several clinical metabolic and hormonal parameters have, among other things, been compared. Following the completion of the statistical analysis, it was determined that the intervention group had a BMI that was significantly higher than the control group's BMI (24.68±3.07 vs 23.55±3.02).[49] While the BMI was high, the thyroid stimulating hormone (Tashi Dendup) levels of patients with SCH with PCOS were significantly higher than those of patients with PCOS (4.547±2.66 vs 2.67±3.11), where the p-value was significantly lower (0.001). When compared to patients who only had PCOS, those who also had SCH had a significantly higher level of free testosterone (23.33±7.836 vs 15.68±6.28). On the other hand, they found that the levels of anti-TPO antibodies were greater in patients with PCOS who were in the SCH group (28.037±9.138), but the levels in the comparison group were (25.72±8.27).[49] Therefore, the results of the study showed that the SCH group had a higher prevalence of obesity compared to the control group. The conclusion that SCH does affect PCOS was supported by the findings of the study in a significant way. As a result, the alternative hypothesis for a more fruitful conclusion in the search for a link between SCH and PCOS.

## DISCUSSION

For this quantitative systematic review, evidence of the impact of SCH on PCOS and PCOS-related symptoms such as clinical, metabolic, and hormonal has been gathered and extracted using the methods described above by data extraction and analysis, and results have also been taken into consideration. Within this thorough overview, the result, together with the outcome and hypothesis, has been emphasized in the upper area. This chapter is going to compare the results with various ideas that have been proposed previously.

### *Summary of the results*

The researchers doing this systematic review selected the five papers that were discussed in the previous section under the heading "Results." Although this systematic review was performed on South Asian women who had PCOS and its linked symptoms and complications with women who already had SCH and PCOS.[5] After receiving a large number of inquiries for this review, which was carried out in Bangladesh, Pakistan, and India, the researcher decided to undertake three cross-sectional studies and two case-control studies. There were additional countries in South Asia, but the researchers were unable to discover any papers that adequately characterized the issue and provided relevant data. The five investigations were each divided into two groups and carried out in a separate tertiary care institution to be compared to one another. The amount of time spent on each study was comparable. Each study presented a description and analysis of the data regarding clinical, metabolic, and hormonal characteristics. For the statistical analysis of the review, the research team employed SPSS version 23.0. The numerical and normal distribution data were provided as mean standard deviation (SD), the categorical data were presented as percentages, and the normal distribution data were displayed as the median. In each study, they also conducted the students' t-test, the Chi-square test, and the Mann-Whitney U test to compare the two variables in each of the two groups. A $p>0.005$ was taken into consideration to indicate statistically significant results.[48] The researcher found confirmation of the validity of the findings after conducting all five inquiries. All studies that compared SCH with PCOS intervention groups to a control group (Group) reported significant differences in the intervention groups' indicators. Also found that the groups who received the intervention had significant reductions in clinical symptoms such as obesity, menstrual irregularities, and infertility. Those with SCH and PCOS are more likely to have and have higher levels of metabolic markers like total cholesterol (TC), hormonal markers like luteinizing hormone (LH), follicle-stimulating hormone (FSH), and free testosterone, and clinical characteristics including monthly irregularities. Raj et al reported significantly elevated levels of BMI and thyroid-stimulating hormone (Tashi Dendup) in patients with SCH and PCOS.[48] Although every study produced a p value that was less than 0.001, which indicates that the investigations all rejected the null hypothesis. After the researcher determined the answer, they looked at the alternative hypothesis again and verified it with definite, numerical, and clear statistics. Following an analysis of five separate research, the primary conclusions drawn from the evaluation pointed to a connection between SCH and PCOS. In every study, the characteristics of PCOS were shown to affect the individuals who had PCOS. The increased values also demonstrated that SCH affected PCOS patients by causing metabolic and hormonal alterations, which in turn affected the fertility of South Asian women. As a result, the research questions raised were addressed by this review through the provision of solid data and evidence, all of which are detailed in the results section. The fact that every single study had a p value that was less than 0.001 indicated that the alternative hypothesis was confirmed by this systematic review and

rejected the null hypothesis. This indicates that there are correlations between the two variables. In the past, several other nations, including the United States of America, Europe, and China, have also carried out a systematic review to investigate the correlations between SCH and PCOS as well as the effect of SCH on the characteristics of PCOS. After analyzing the results, they discovered that SCH and PCOS have a significant relationship with one another. In which they compared several anthropometric and metabolic metrics. In the SCH-PCOS group, all of the parameters exhibited greater values, and the p-value was significantly lower than 0.001. Whereas Bedaiwy et al discovered that patients with SCH-PCOS had high levels of fasting plasma glucose (FPG) (OR 3.01; CI: 1.12-8.07. p=0.03) and that the intervention group had reduced insulin sensitivity.[51] This quantitative systematic review likewise exhibited the same results and conclusions as the previous study, which demonstrated that SCH and PCOS are connected and showed that the intervention group had higher metrics. This systematic review also included the p value, which was less than 0.001.

### *Certainty of evidence*

The level of reliability associated with the evidence is referred to as the "certainty" of the evidence.[52] Following the grade methodology, the degree of certainty associated with the evidence has been categorized into the following four levels: very low, low, moderate, and high.[53] This observational systematic review only provides a moderate amount of assurance at this early stage. Because every study that has been conducted has produced a reaction including an intervention and has also shown comparable results. The intervention SCH and their association have been measured in the selected studies with p values, CI values, and consistency with the true effect, which makes the certainty of this review moderate. This systematic review has a severe effect on certainty because this review has a moderate effect on certainty. Due to the irregularity and indirect nature of the studies, the conclusions of the study may only have a moderate degree of certainty at most.

### *Overall completeness and acceptance of evidence of review*

The authors of this quantitative systematic review conducted an extensive search and ultimately opted to include only five studies in their analysis. All the research was conducted in countries with a low to moderate GDP. There were five studies done as part of randomized controlled trials where individuals with PCOS and patients who also suffered from SCH were recruited to take part in the studies. A small sample size of participants from a specific area was used in the study. Therefore, the study's interpretation may factor into or be affected by the external validity.[54] Furthermore, trial investigations were carried out in a short amount of time, which may have influenced the outcomes of the research, and this might also affect the conclusions drawn from this analysis.

### *Limitations*

A major flaw of the study is that it was conducted by a single researcher who was responsible for the entire systematic review. There was only one reviewer because the evaluation was for a master's degree in public health at the school. As a result, the review needs to be carried out by a team of two different researchers to meet the criteria set by the Cochrane collaboration. For this reason, it was acknowledged that there was a possibility for bias due to this restriction of the study. On the other hand, while this study was conducted in the countries of South Asia, there was not enough research or data that included all of the countries that make up South Asia. The researcher was only able to find data and papers about South Asian women from Bangladesh, Pakistan, and India; nevertheless, these countries do not represent the condition of all South Asian women. In addition, each of the studies that were used in this analysis was conducted in a single hospital, therefore the findings cannot be generalized to the entire nation. Due to the short time duration that was considered in the investigation, this was considered to be a weakness of the study because it had the potential to affect the findings of the inquiry. In addition, every previous study that was carried out was either of the cross-sectional or case-control varieties. There was no randomized control trial conducted, which eliminates one potential source of bias. On the other hand, the overall population for the two groups was similarly limited in all of the studies, which meant that they did not reflect the entire community of women and might also have an effect on the outcome.

## CONCLUSION

In summation, the findings of this comprehensive research indicated that polycystic ovarian syndrome (Group) and SCH shared the majority of the same metabolic, hormonal, and clinical characteristics. However, several factors revealed inequalities in the features they displayed. Both groups' anthropometric measurements likewise proposed and produced varied findings, demonstrating that the two groups are indeed different. On the other hand, the purpose of this review was to investigate the effect of SCH on PCOS (Group) as well as metabolic hormonal markers and infertility. As a result, after researching to obtain reliable data and solid scientific proof supporting the outcome and reviewed five studies that were conducted over the past decade. This finding will be useful for policymakers in the South Asian country in terms of both long-term illness management and policymaking, and the creation of recommendations for treating this disease, which can help prevent additional complications. Furthermore, this opens the door for further research to be done. The recommendation for future research is that a meta-analysis should be carried out in South Asia. This will result in more accurate outcomes. Additionally, it is highly suggested that the studies should be carried out in the form of randomized clinical trials and should be carried out at multiple centers.

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