

## Hearing and Auditory Working Memory in Women with Polycystic Ovarian Syndrome (PCOS)

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### Abstract

**Objectives:** The present study assessed the hearing and auditory working memory in women with polycystic ovarian syndrome (PCOS).

**Study Design:** Standard group comparison.

**Materials and Methods:** A total of 20 female participants were included in the study and were divided into two groups. Group-1 included ten women diagnosed with PCOS, under ultrasound examination and hyperandrogenism was confirmed through hormonal analysis. Group-2 included ten healthy women, with no evidence of hyperandrogenism and normal menstrual cycles. Routine pure tone audiometry was done in the frequency range of 250 Hz to 8000 Hz and extended high frequency hearing thresholds from 9000 Hz to 16,000 Hz, was also obtained. Auditory working memory was assessed through digit span and digit sequencing tasks.

**Results:** The results revealed that the extended high frequency audiometry threshold was significantly poorer for PCOS group compared to the normal group for 9000 Hz ( $F_{1, 34}=9.444, p<0.05$ ), 10000 Hz ( $F_{1, 34}=6.120, p<0.05$ ), 11200 Hz ( $F_{1, 34}=9.211, p<0.05$ ), 12500 Hz ( $F_{1, 34}=12.651, p<0.05$ ), 14000 Hz ( $F_{1, 34}=41.342, p<0.05$ ), 16000 Hz ( $F_{1, 34}=12.230, p<0.05$ ). Comparison across various auditory working memory tasks showed that the PCOS group performed significantly poorer on backward digit task ( $Z=-1.996, p<0.05$ ), ascending digit task ( $Z=-1.989, p<0.05$ ) and descending digit task ( $Z=-3.198, p<0.01$ ).

**Conclusion:** These findings suggest that the high frequency sensitivity and working memory is affected in subjects with PCOS compared to the normal group. The study highlights the importance of early identification of hearing loss in PCOS group and the importance of auditory working memory screening in women with PCOS.

**Keywords:** High frequency; PCOS; Working memory; Hyperandrogenism

### Introduction

Polycystic ovarian syndrome (PCOS), otherwise called hyperandrogenic anovulation or Stein-Leventhal syndrome is a heterogeneous endocrine disorder affecting 5-10% of reproductive age women [1]. The disease is characterized by oligo-amenorrhea, hyperandrogenism and polycystic ovaries. It is a chronic condition beginning most commonly in adolescence and includes a wide spectrum of clinical signs and symptoms. There are three different diagnostic classifications proposed to define this syndrome. The National Institute of Health (NIH) proposed the first criteria in 1990, which stated that simultaneous presence of hyperandrogenism and menstrual dysfunction should be used to diagnose PCOS [2].

Later in 2003, in Revised Diagnostic criteria of PCOS, the presence of polycystic ovarian morphology detected by transvaginal ultrasonography was added to diagnose PCOS [3]. Finally, the Androgen Excess Society (2006) gave a new diagnostic criteria which required the presence of clinical or biochemical hyperandrogenism, oligovulation and/or anovulation and/or Polycystic ovary (PCO) and exclusion of other entities that could cause PCOS [4]. In all the above

mentioned signs and symptoms, hyperandrogenism is the major biological marker to diagnose PCOS and it can affect hearing also.

In a study by Ciccone et al., [5] they reported that the anteroposterior diameter of the infrarenal abdominal aorta is higher in women with polycystic ovary syndrome. Twenty nine women with PCOS and twenty six healthy women were included in the study. The intima media thickness of the common carotid arteries and common femoral arteries and the anteroposterior diameter of the infrarenal abdominal aorta were measured using ultrasound. The results revealed that, the women with PCOS had higher levels of luteinizing hormone, follicle-stimulating hormone, follicle stimulating hormone, total testosterone, increased fasting insulin, and lower sex hormone binding globulin compared to that of control women. It was also noted that, women with PCOS had a higher anteroposterior diameter than control women. This shows that atherosclerotic change starts early in women with PCOS.

Studies have shown that auditory abilities are affected in PCOS due to its features like insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations. In humans, altered insulin signaling is implicated in reduced glucose availability to insulin-sensitive cells, vasoconstriction and endothelial damage [1]. Within endothelial damage diseases, the high frequency

hearing is mostly affected in early stages of PCOS [6]. Also, in young patients with PCOS, the carotid intima-media thickness (IMT) is increased compared with non-hyperandrogenic women [1]. Carotid (IMT) is used as the structural subclinical marker for atherosclerosis and cardio vascular diseases (CVD). Studies have shown that biochemical and hormonal changes can affect intravascular blood flow in PCOS and sensorineural hearing loss can occur due to these vascular pathologies [1]. Vascular occlusions can occur in the arteries or arterioles, which supply oxygen to inner ear. This can result in hearing loss in patients with PCOS. However, hearing in low and mid frequencies might recover, if the blood supply returns to normal [7].

Kucur et al., [6] determined the hearing thresholds on subjects with PCOS, for low frequencies (250 Hz-2000 Hz), high frequencies (4000 Hz-8000 Hz) and extended high frequencies (9000 Hz-20000 Hz) and compared it with control group. Results revealed that there was no significant difference in hearing threshold, in frequencies from 250 Hz to 4000 Hz, whereas statistically significant difference was observed in frequencies from 8000 Hz-20000 Hz. Thus, authors concluded that, it is important to evaluate the presence of hearing loss by using audiometric measurements in young women with PCOS, especially in extended high frequency range. High Frequency Audiometry (HFA) and Extended High Frequency Audiometry (EHFA) are more efficient in detecting early hearing loss compared to pure tone audiometry.

Scicchitano et al., [8] reported that women with PCOS have higher risk of cardiovascular diseases, which is related to metabolic dysfunction, peculiar hormonal pattern, hyper androgenism, insulin resistance, dyslipidemia and inflammatory state. Cincona et al., [9] evaluated cardiovascular risk factors and pre-clinical atherosclerosis in subjects affected with Idiopathic Sudden Sensorineural Hearing Loss (ISSHL) and reported that ISSHL seemed to be associated with vascular endothelial dysfunction and an increased cardiovascular risk.

There are also evidences that report male and female differ in their cognitive profiles due to differences in the levels of testosterone and estrogen between the sexes [10,11]. In women with PCOS, cognitive functioning may be affected as a result of hyperandrogenism and hyperestrogenism [12]. Testosterone and estrogen provides alterations in cognitive performance observed in PCOS. Since, PCOS is associated with abnormalities in hormonal levels other than testosterone and estrogen, hormones like follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone and prolactin are also responsible for the effects of PCOS on cognition. Studies have also reported that women with endocrine disorder associated with increased levels of free testosterone have an influence on cognitive functioning, and showed significantly worse performance on tests of verbal fluency, verbal memory, manual dexterity and visuospatial working memory.

Schattman and Sherwin [13] investigated the cognitive profile of women with elevated free testosterone levels due to PCOS. They studied twenty-nine women with PCOS and twenty-two healthy women served as control. The participants were assessed with cognitive test questionnaire visuospatial tasks, verbal tasks and perceptual and motor tasks. The results revealed that PCOS group had lower scores on verbal fluency and other sub measures. There was no significant group difference on tests of attention, which suggested that there was a specificity of negative influence of high free testosterone levels on verbal fluency, verbal learning memory and manual dexterity.

The working memory processes includes temporal storage and manipulation of information and it needs multiple processes of

cognition such as language, perceptual speed, verbal and visual memory, and planning [14]. Studies have also reported that menstrual cycle pattern dependent  $E_2$  levels relate to working memory [15,16], but it was not clear that whether changes in androgen level will affect working processes as well [17-19]. The present study aimed to evaluate the hearing and cognition in cases with polycystic ovarian syndrome using conventional audiometry, extended high frequency audiometry and auditory working memory tasks.

## Materials and Method

### Participants

The study included 20 participants in the age range of 18-25 years, who were divided into two groups. Group-1 included ten women diagnosed with PCOS, under ultrasound examination and hyperandrogenism was confirmed through hormonal analysis. Group-2 included ten healthy women, with no evidence of hyperandrogenism and normal menstrual cycles. Informed consent was taken from all the participants of the study. The participant's selection criteria ensured that both Group-1 and Group-2, had no otologic, neurological diseases, endocrine diseases such as diabetes, androgen secreting tumours and thyroid dysfunctions, hypertension, exposure to ototoxic drugs, noise exposure, autoimmune diseases, intake of any medications which could alter the sex hormones and pregnant women were excluded from the study.

The health of Group 1 and the Group 2 participants was determined on the basis of medical history (history of menstrual cycle, otologic history, blood pressure level), blood chemistry including glucose and insulin level and hormone profile (LH, FSH, Estradiol (E2), testosterone total and free (total-T and free- T)), prolactin level and pelvic ultrasound. Body mass index (BMI) was calculated based on weight in kilogram and height in meter. The participants selected for the study primarily had hyperandrogenism that is elevated total and free testosterone with irregular menstrual cycle. The ultrasonography of the participants revealed polycystic ovaries.

### Procedure

A detailed case history of the participants was documented. The ear was examined with otoscope to visualize the ear canal and to rule out any contraindications for audiological evaluation. Further, routine audiological evaluation was carried out to ensure the normal hearing and normal middle ear functioning. The modified Hughson-Westlake procedure was used to track the hearing thresholds of the subjects across the audiometric octave frequencies from 250 Hz to 8000 Hz.

### Extended High Frequency Audiometry (EHFA)

The hearing thresholds of the participants for frequencies 9000 Hz, 10000 Hz, 11200 Hz, 12500 Hz, 14000 Hz and 16000 Hz was also estimated using Modified Hughson and Westlake procedure in a two-channel Inventis Piano Plus VRA model.

### Auditory working memory tasks

The auditory working memory was assessed through digit span task and digit sequencing tasks. Auditory digit span included forward and backward digit span test and auditory digit sequencing tasks included ascending and descending digit test. These tests were administered

using “Auditory cognitive training module” [20] and the brief description of each test is given below.

In digit span task, participants were instructed to listen to the digits and arrange them in same order in forward digit task and in reverse order in backward digit task. In digit sequencing measure they were asked to rearrange the digits in increasing order in ascending digit task and to rearrange the digit in decreasing order in descending digit task. The test item started with four digits and went up to ten digits. Adaptive staircase procedure was used to assess the minimum number of digits that the participants can sequence. Stimuli consisted of English digits from one to nine.

## Results

The results of conventional audiometry, extended high frequency audiometry and auditory working memory are discussed separately.

### Comparison of hearing threshold across both the groups

Figure 1 shows the mean and standard deviation (SD) of pure tone thresholds for group 1 and 2. From the Figure 1 it is evident that PCOS group had poorer thresholds compared to that of control group. Further the comparison of hearing thresholds between both the groups was done using ANOVA (Analysis of variance). The hearing thresholds between right and left ear showed no significant difference and thus for further analysis the scores of both the ears were combined for both the groups. The pure tone thresholds for both extended high frequency as well as conventional pure tone audiometry were compared. Results revealed that there was no significant difference in the thresholds of both the groups for conventional audiometry from 250 to 8000 Hz ( $p > 0.05$ ). However, the extended high frequency audiometry threshold was significantly poorer for PCOS group compared to the control group for 9000 Hz ( $F_{1, 34} = 9.444, p < 0.05$ ), 10000 Hz ( $F_{1, 34} = 6.120, p < 0.05$ ), 11200 Hz ( $F_{1, 34} = 9.211, p < 0.05$ ), 12500 Hz ( $F_{1, 34} = 12.651, p < 0.05$ ), 14000 Hz ( $F_{1, 34} = 41.342, p < 0.05$ ), 16000 Hz ( $F_{1, 34} = 12.230, p < 0.05$ ).

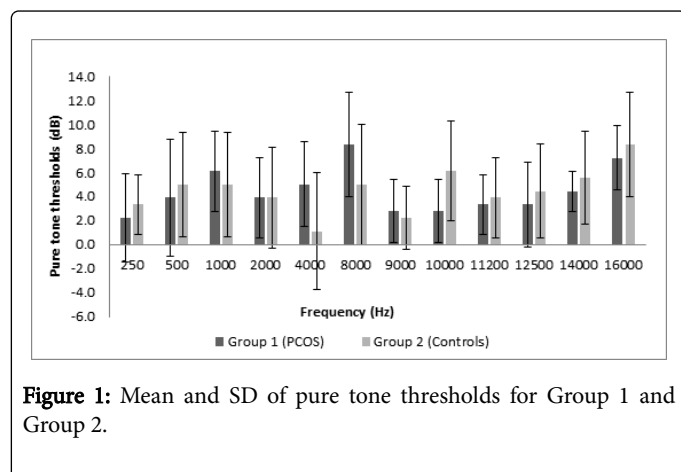


Figure 1: Mean and SD of pure tone thresholds for Group 1 and Group 2.

### Comparison of auditory working memory results across both the groups

Figure 2 shows the mean and standard deviation of various working memory tasks for group 1 and 2. It can be seen from the figure that PCOS group performed poorer in all the task compared to that of control group. The auditory working memory results for digit span and

digit sequencing was compared using Mann Whitney U test. The results showed that there was no difference in the forward digit task for both the groups ( $Z = -0.494, p > 0.05$ ). However, the backward digit task ( $Z = -1.996, p < 0.05$ ), ascending digit task ( $Z = -1.989, p < 0.05$ ) and descending digit task ( $Z = -3.198, p < 0.01$ ) showed significant difference between both the groups.

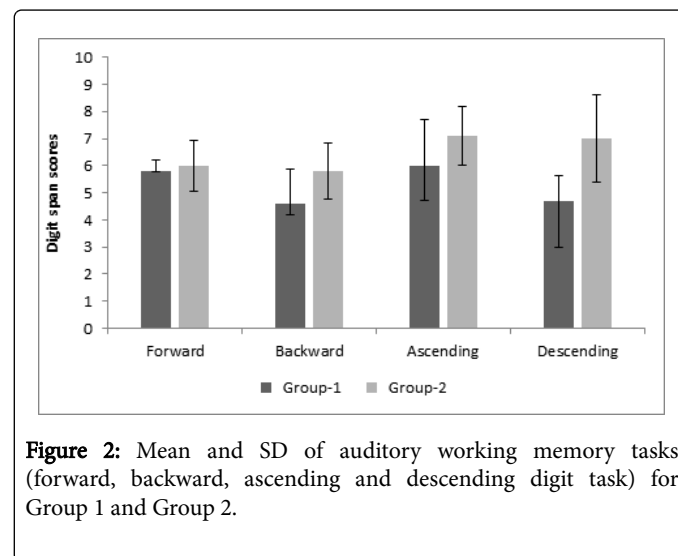


Figure 2: Mean and SD of auditory working memory tasks (forward, backward, ascending and descending digit task) for Group 1 and Group 2.

## Discussion

The aim of the present study was to evaluate the hearing thresholds and cognition in PCOS group and to compare it with control group. Results showed that PCOS group had poorer threshold for higher frequencies compared to the control group. Similar results are reported in the literature [6,18]. Oghan and Coksuer [1] reported high frequency (4000 Hz-8000 Hz) hearing loss in PCOS patients. Similarly, Kucur et al., [6] found that the hearing thresholds of PCOS group was higher at extended high frequencies from 8000 Hz, 10000 Hz, 12000 Hz, and 14000 Hz compared to controls.

The affected auditory abilities in PCOS in the current study could be explained based on feature like insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations [1,6]. Oghan and Coksuer [1] observed that altered insulin signaling is implicated in reduced glucose availability to insulin-sensitive cells, vasoconstriction and endothelial damage. Endothelial damage further leads to high frequency hearing loss which is mostly affected in early stages of PCOS [6].

PCOS is characterized by several metabolic alterations that could further increase the cardiovascular diseases (CVD) [21]. In young women with PCOS, the carotid intima-media thickness is increased compared to non-hyperandrogenic women. The increased risk of cardiovascular profile in cases with PCOS is of multifactorial origin and does not result from any specific metabolic abnormality [22]. The biochemical and hormonal changes can affect intravascular blood flow in PCOS and sensorineural hearing loss occur due to these vascular pathologies [1]. Asakuma and Shida [7] reported that vascular occlusions can occur in the arteries or arterioles, which supply oxygen to inner ear and has been discussed as the reason for hearing loss in patients with PCOS. However, hearing in low and mid frequencies might recover, if the blood supply returns to normal.

The results of auditory working memory tasks revealed that there was statistically significant difference in backward digit span, ascending digit sequencing and descending digit sequencing task between both the groups. The forward digit span did not show a difference between both the groups. This could be because forward digit span is a simple span task and backward digit span, ascending digit sequencing; descending digit sequencing are complex tasks. Studies have also shown that memory processes involved in forward digit and backward digit is different [23]. Forward digit test is a task of short-term auditory memory, sequencing, and simple verbal expression [24], whereas backward digit is more sensitive test for working memory [25,24]. In the present study, The difference in various measures of working memory could be attributed to the hormonal differences between both the groups. The impaired performance could be because of hyperandrogenism, testosterone and estrogen levels in women with PCOS [26-28]. Besides testosterone and estrogen, the follicle stimulating hormone (FSH), luteinizing hormone (LH), progesterone and prolactin is also altered in women with PCOS. Individually or combined effects of these hormones could be responsible for the poor working memory in PCOS. In a study by Barnard et al., [12] they compared the cognitive abilities of 221 women with PCOS (with and without anti androgenic treatment) with 442 controls on an internet based study. Results showed that PCOS group had significantly longer reaction time on an attention control task, higher number of errors in a word recognition task and a slower reaction time during a spatial location test. Schattmann and Sherwin [13] investigated cognition in women with PCOS with high T levels and found that the performance was significantly worse on female-favoring tasks such as verbal fluency, verbal memory, manual dexterity, and visuospatial working memory than control women, but they did not show enhanced performance on male-favored tasks. The results of the study suggest that androgens compromise performance on female-favoring tasks in women with PCOS.

Thus, from the findings of the present study, it may be hypothesized that hyperandrogenism, insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations affects the auditory abilities and working memory in women with PCOS. The study highlights the importance of androgen hormone on hearing and also the importance of early identification of hearing loss in the PCOS group, through extended high frequency screening. Further, the study delivers the importance of counseling, regular monitoring and follow up of the subjects with PCOS, to provide appropriate rehabilitation.

However the study has few limitations such as small sample size. The results of the study can be taken as preliminary findings, to design a future study with larger population. The mechanism behind hearing impairment in PCOS has to be investigated to know whether the impairment of EHFA in these individuals is progressive. Further, if the underlying factors are revealed, it might be possible to prevent progression of hearing impairment in these individuals.

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