Hearing and Cochlear Functioning in Polycystic Ovarian Syndrome (Pcos)

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Abstract

Polycystic ovarian syndrome (PCOS), is a heterogeneous endocrine disorder, characterized by oligo-amenorrhea, hyperandrogenism and polycystic ovaries. The auditory abilities are affected in PCOS due to its features like insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations, which leads to high frequency hearing loss in early stages of PCOS. Since the vascular diseases and endothelial dysfunction plays an important role in pathogenesis of hearing impairment in PCOS, it is important to determine cochlear functioning in patients with PCOS. The study aimed at determining the hearing and cochlear functioning in cases with PCOS using conventional and extended high frequency audiometry (EHFA) and distortion product otoacoustic emissions (DPOAE). Two group of participants in the age range of 18-25 years were included in the study. Group-1 included 15 women diagnosed with PCOS and Group-2 included 15 healthy women, with no evidence of PCOS. Conventional audiometry was carried out in the frequency range of 250 Hz-8000 Hz and EHFA was done from 9000 Hz-16000 Hz. DPOAEs were also recorded from 500 Hz -16000 Hz. Results showed that there was no significant difference in the thresholds between both the groups for conventional audiometry from 250 Hz-8000 Hz ($p > 0.05$). But, the EHFA threshold was significantly poorer for PCOS group than the control group. Results of DPOAE showed no statistically significant difference ($p > 0.05$) at all the frequencies between the PCOS and control group. The study highlights the importance of early identification of hearing loss in the PCOS group, through extended high frequency screening'

Key words: *Reliability, contralateral inhibition, otoacoustic emissions*

Introduction

Polycystic ovarian syndrome (PCOS), otherwise called hyperandrogenic anovulation or Stein-Leventhal syndrome is a heterogeneous endocrine disorder (Oghan & Coksuer, 2012) affecting 5-10% of reproductive age women. The disease is characterized by oligo-amenorrhea, hyperandrogenism and polycystic ovaries. It is a chronic condition beginning most commonly in adolescence.

PCOS 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 (Artini et al., 2010).

Later in 2003, in a Revised Diagnostic criteria of PCOS, the presence of polycystic ovarian morphology detected by transvaginal ultrasonography was added to diagnose PCOS (Fauser, 2004). 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 (Azziz et al., 2006). In all the above mentioned signs and symptoms, hyperandrogenism is the major biological marker to diagnose PCOS and it can affect hearing also.

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 (Oghan & Coksuer, 2012). Within endothelial damage diseases, the high frequency hearing is mostly affected in early stages of PCOS (Kucur et al., 2013). Also, in young patients with PCOS, the carotid intima-media thickness (IMT) is increased compared with non-hyperandrogenic women (Oghan & Coksuer, 2012). 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 (Oghan & Coksuer, 2012) and sensorineural hearing loss can occur due to these vascular pathologies. 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 may be able to recover, if the blood supply returns to normal (Asakuma & Shida, 2001).

High frequencies are sensitive to the effects of vascular diseases, and vascular pathologies which could be a cause of high frequency hearing loss in patients with PCOS. These vascular pathologies could be due to insulin resistance, hyperandrogenism, elevated serum CRP as an inflammatory marker and dyslipidemia (Kucur et al., 2013 ; Oghan & Coksuer, 2012). Especially, extended high frequency is more sensitive to the effects of vascular diseases (Kucur et al., 2013).

Eren et al., (2013) evaluated the effects of hyperandrogenism on otoacoustic emission levels.

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Distortion product otoacoustic emissions (DPOAEs) and transient evoked otoacoustic emissions (TEOAEs) were recorded in the frequency range from 500 Hz-8000 Hz and 1000 Hz-4000 Hz, respectively. The results revealed no statistically significant difference between the PCOS group and the control group. They concluded that hyperandrogenism does not influence otoacoustic emission level. However, no difference in DPOAE measures could be because vascular diseases are more sensitive to extended high frequency (9000 Hz-20000 Hz), rather than the conventional DPOAE frequency range (500 Hz-8000 Hz). Since extended high frequencies are more sensitive to vascular pathologies, and conventional audiometry measures hearing from 500 Hz- 8000 Hz, an extended high frequency audiometry is needed to measure the hearing thresholds in patients with polycystic ovarian syndrome. Thus, it is important to determine cochlear functioning in patients with PCOS using EHFA and DPOAE for the high frequency range.

The present study aimed to evaluate the hearing and cochlear functioning in cases with polycystic ovarian syndrome using conventional audiometry and extended high frequency audiometry and distortion product otoacoustic emissions.

Method

Research design

The standard group comparison was used to fulfill the aim of the present study.

Participants

Two groups of participants in the age range of 18-25 years were taken. Group 1 included 15 participants (Mean age: 21.6 years, SD: 1.61) with polycystic ovarian syndrome (PCOS group) and Group 2 included 15 participants (Mean age: 21.4 years, SD: 1.57) with no history of PCOS (Control group).

Participant selection criteria

The inclusion criteria for the Group- I, included, oligo and /or anovulation - infrequent or irregular ovulation / absence of ovulation, hyperandrogenism (excessive levels of androgen in the body) / biochemical signs of hyperandrogenism, polycystic ovaries on ultra sound examination and no other otologic or neurologic complaints. The inclusion criteria for Group- II , included, healthy women with normal menstrual cycle, no evidence of hyperandrogenism ,normal ovarian morphology on ultrasonography and no other otologic or neurologic complaints.

The health of participants of both the groups 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.

Test procedure

A detailed case history was taken to collect information about the demographic details and to rule out the presence of any significant history and any other otologic complaints, in the Group-1 and 2. The modified Hughson-Westlake procedure was used to track the hearing thresholds of the subjects across the audiometric frequencies 250 Hz to 8000 Hz. The bone conduction thresholds were obtained from 250 Hz to 4000 Hz. The above steps were carried out in order to ensure that the subjects met the specified selection criteria of normal hearing sensitivity and the thresholds for these frequencies were also compared between both the groups. The hearing thresholds of the participants for frequencies 9000 Hz, 10000 Hz, 11200 Hz, 12500 Hz, 14000 Hz and 16000 Hz were obtained using the same procedure as mentioned for conventional audiometry. For DPOAE recording, the participants were asked to sit comfortably and were instructed to relax and minimize extraneous movements during the test. An appropriate probe tip was inserted gently into the ear canal. The DP-gram menu was selected in the Starkey OAE instrument and check fit routine was carried out to ensure whether the best fit is achieved. After all these preliminaries, the actual test was carried out. Primary signals f1 and f2, with f2/f1 = 1.2 was used. The testing was done with test frequencies ranging from 500 Hz to 16000 Hz with a frequency resolution of two points per octave was used. Two level chosen were L1 = 65 dB SPL, L2 = 55 dB SPL. The response parameters to consider DPOAE as present included DP amplitude and SNR.

After the recording of DPOAEs, the difference between the level of emissions and the level of noise floor (S/N value) was noted at 85% replicability.

Results

The aim of the present study was to evaluate the hearing and cochlear functioning in polycystic ovarian syndrome (PCOS). Extended high frequency audiometry (EHFA) and distortion product otoacoustic emissions (DPOAEs) were measured for Group- I (PCOS) and Group- II (controls). The data was statistically analyzed using Statistical Package for Social Sciences (SPSS, version 20.0). To assess whether the data fits into the normal distribution, test of normality was done using the Shapiro- Willk's test. Result showed that the data for conventional audiometry, EHFA and DPOAE did not follow the normal distribution ($p<0.05$). Hence, further data was analysed using non parametric tests.

Comparison of hearing thresholds for conventional audiometry and EHFA across Group 1 and 2

The mean, median and the one standard deviation (SD) of the hearing thresholds for frequencies ranging from 250 Hz to 16000 Hz for Group 1 and 2 is shown in Table 1.

Table 1: Mean, Median and SD of hearing thresholds in Group 1 and Group 2

		Group 1			Group 2		
Frequency (Hz)	Ear	Mean	Median	SD	Mean	Median	SD
250	*Right*	4.66	5.00	3.51	2.33	0.00	3.19
	Left	4.00	5.00	3.87	3.33	5.00	2.43
500	*Right*	5.33	5.00	3.51	3.33	5.00	4.08
	Left	6.66	5.00	3.08	4.33	5.00	3.71
1000	*Right*	4.00	5.00	2.07	6.66	5.00	3.08
	Left	5.66	5.00	3.71	5.33	5.00	3.51
2000	*Right*	5.66	5.00	4.16	4.33	5.00	3.19
	Left	5.66	5.00	3.19	4.33	5.00	3.19
4000	*Right*	5.00	5.00	3.27	4.33	5.00	3.19
	Left	5.66	5.00	3.71	1.66	0.00	4.49
8000	*Right*	14.00	15.00	2.07	8.00	5.00	3.68
	Left	5.66	5.00	4.95	5.00	5.00	4.22
9000	*Right*	7.33	5.00	5.30	2.66	5.00	2.58
	Left	7.66	5.00	5.30	2.33	0.00	2.58
10000	*Right*	7.66	10.00	3.19	3.33	5.00	2.43
	Left	9.66	10.00	4.41	6.33	5.00	3.51
11200	*Right*	10.33	10.00	4.41	3.00	5.00	3.16
	Left	8.66	10.00	5.81	5.00	5.00	3.27
12500	*Right*	10.33	10.00	4.41	3.00	5.00	3.16
	Left	8.66	10.00	2.96	5.33	5.00	3.99
14000	*Right*	12.00	10.00	3.16	3.66	5.00	2.96
	Left	12.66	10.00	4.57	6.00	5.00	3.38
16000	*Right*	13.66	15.00	3.51	7.66	10.00	2.58
	Left	15.33	15.00	7.66	9.66	10.00	3.99

It can be noted from Table 1 that the mean thresholds for Group 1 are higher than Group 2 for all the frequencies. Further, whether there was any statistical difference in hearing thresholds across groups for each frequency Mann Whitney U test was done for both right and left ear and the results are depicted in Table 2.

Table 2: Z values of hearing thresholds across groups for right and left ear

	Right		**Left**	
Freq. (Hz)	**|Z|**	**Sig.**	**|Z|**	**Sig.**
250	1.860	0.063	0.729	0.466
500	1.835	0.067	1.764	0.078
1000	2.539	0.011*	0.166	0.868
2000	0.857	0.391	1.053	0.292
4000	0.568	0.570	2.446	0.014*
8000	3.888	0.000*	0.359	0.720
9000	2.566	0.010*	3.077	0.002*
10000	3.392	0.001*	2.168	0.030*
11200	3.803	0.000*	2.026	0.043*
12500	3.803	0.000*	3.803	0.024*
14000	4.457	0.000*	4.457	0.000*
16000	3.927	0.000*	3.927	0.017*

Note : * indicates $p<0.05$

It is evident from the above table that there is no statistical difference in the thresholds of both the groups for the frequencies 250 Hz, 500 Hz, 2000 Hz, 4000 Hz ($p>0.05$) in the right ear. In the left ear, there was no statistical difference in thresholds for the frequencies 250 Hz, 500 Hz, 1000 Hz, 2000 Hz, 8000 Hz ($p>0.05$). However, the extended high frequency audiometry thresholds for frequencies 9000 Hz to 16,000 Hz showed statistically significantly difference between the groups ($p< 0.05$) for both ears.

Comparison of DPOAE across Group 1 and 2

The mean DPOAE amplitude and SNR along with one standard deviation for Group 1 and Group 2 is shown in Table 3. From the Table 3, it can be noted that the mean DPOAE amplitude for frequencies ranging from 750 Hz to 6000 Hz is better than other frequencies, for both right and left ears. It can also be noted that in Group 2 the mean SNR for frequencies from 500 Hz - 8000 Hz are higher than other frequencies in both the ears. In Group 1 the mean SNR of frequencies 500 Hz, 750 Hz and 1500 Hz - 8000 Hz are higher than the other frequencies in both the ears.

Table 3: Mean and SD of DPOAE amplitude and SNR across frequencies in Group 1and Group 2

		Group 1			Group 2				
Freq (Hz)	**Ear**	**Mean DP amp**	**SD**	**SNR**	**SD**	**Mean**	**SD**	**SNR**	**SD**
500	*Right*	-9.18	5.97	6.93	7.68	-7.8	4.40	7.51	6.91
	Left	-9.36	6.38	8.77	6.77	-9.4	6.28	6.1	9.85
750	*Right*	-3.81	7.12	9.88	10.74	-1.4	7.95	13.81	7.03
	Left	-1.99	8.16	10.94	11.35	-0.3	7.07	16.53	8
1000	*Right*	-4.46	10.5	3.01	10.78	1.28	10.50	11.61	12.49
	Left	-3.52	10.2	-1.1	12.08	4.54	7.39	8.24	13.56
1500	*Right*	1.45	6.62	10.64	10.09	-1.9	8.57	15.86	8.81
	Left	4.59	6.82	10.84	11.08	0.58	7.01	16.86	7.88
2000	*Right*	-1.42	3.01	17.57	4.84	0.9	5.15	20.36	6.68
	Left	-3.79	8.99	13.52	9.31	2.76	5.48	20.45	7.95
3000	*Right*	-1.09	6.2	18.63	6.48	-1.6	8.21	15.88	7.62
	Left	-1.4	8.07	17.51	7.47	1.7	4.58	19.45	5.48
4000	*Right*	-0.66	5.02	20.42	6.26	2.88	4.18	22.48	7.41
	Left	-2.64	7.12	17.24	6.6	2.24	4.05	20.52	14.31
6000	*Right*	0.12	4.95	14.54	5.15	-2.3	6.03	17	6.93
	Left	-0.13	7.03	14.86	5.67	0	6.3	16.56	7.76
8000	*Right*	-8.53	9.97	6.34	7.32	-4.6	5.02	8.9	4.19
	Left	-3.88	6.20	5.54	8.18	-4.7	6.23	8.87	4.34
9000	*Right*	-12.9	4.96	-1.28	5.2	-12	5.60	2.23	4.53
	Left	-12.8	5.76	0.36	6.46	-10	8.14	2.56	4.52
12000	*Right*	-2.16	8.20	3.49	6.22	-5.4	9.72	2.09	6.44
	Left	-1.64	7.68	4.27	5.55	-6.9	7.91	3.32	6.03
16000	*Right*	-14.5	6.36	-3	5.91	-11	6.60	3.72	5.94
	Left	-3.09	8.91	3.09	8.91	1.29	5.59	1.29	5.59

To compare the DPOAE amplitude and SNR across groups for both the ears Mann Whitney U test was carried out. Table 4 shows that there was no statistically significant difference in DP amplitude between groups for frequencies ranging from 500 Hz to 16000 Hz in the right ear. However, in the left ear, frequencies 1000 Hz, 2000 Hz and 4000 Hz showed statistically significant difference between the groups. It can also be noted that there was statistically significant difference between the groups only for 1000 Hz and 16,000 Hz in the right ear. In the left ear, DPOAE SNR of only 1000 Hz and 2000 Hz showed statistically significant difference.

Table 4: Z values for DPOAE amplitude and SNR across groups for right and left ear

	DP amplitude				SNR			
	Right		**Left**		**Right**		**Left**	
Frequency (Hz)	**|Z|**	**Sig.**	**|Z|**	**Sig.**	**|Z|**	**Sig.**	**|Z|**	**Sig.**
500 Hz	1.03	0.30	0.47	0.63	0.27	0.78	1.37	0.16
750 Hz	0.97	0.32	0.66	0.50	1.07	0.28	1.47	0.14
1000 Hz	1.37	0.17	2.09	0.03*	2.03	0.04*	2.05	0.04*
1500 Hz	1.10	0.27	1.09	0.27	1.45	0.14	1.55	0.12
2000 Hz	1.49	0.13	2.53	0.01*	0.85	0.39	1.99	0.04*
3000 Hz	0.22	0.81	1.22	0.22	1.32	0.18	0.74	0.45
4000 Hz	1.77	0.08	2.17	0.02*	0.78	0.43	1.92	0.05
6000 Hz	1.05	0.29	0.06	0.95	0.78	0.43	0.76	0.44
8000 Hz	1.26	0.20	0.60	0.54	1.10	0.27	0.85	0.39
9000 Hz	0.04	0.96	0.33	0.74	1.37	0.17	0.62	0.53
12000 Hz	1.12	0.26	1.76	0.07	0.47	0.63	0.22	0.82
16000 Hz	0.93	0.35	0.31	0.75	2.51	0.01*	0.31	0.75

Note : * indicates $p<0.05$

Discussion

Comparison of the hearing thresholds using conventional audiometry and EHFA across Group 1 and 2

In the current study, statistically significant difference in hearing thresholds between Group 1 and Group 2 was observed for frequencies ranging from 9000 Hz-16000 Hz. There was no statistical significant difference in hearing thresholds across both the groups for conventional audiometric frequency range i.e., 250 Hz-8000 Hz.

Similar results are reported in the previous literature (Kucur et al., 2013; Oghan and Coksuer., 2012). Oghan and Coksuer (2012) reported high frequency (4000 Hz-8000 Hz) hearing loss in PCOS patients. Similarly, Kucur et al., (2013) 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 (Kucur et al., 2013; Oghan and Coksuer., 2012). Oghan and Coksuer., (2012) observed that altered insulin signalling 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 (Kucur et al., 2013).

PCOS is characterized by several metabolic alterations that could further increase the cardiovascular diseases (CVD) (Orio et al., 2006). 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 (Luque-Ramirez et al., 2007). The biochemical and hormonal changes can affect intravascular blood flow in PCOS and sensorineural hearing loss occur due to these vascular pathologies (Oghan & Coksuer., 2012).

Asakuma and Shida., (2001) 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. Hearing in low and mid frequencies may able to recover, if the blood supply returns to normal.

Comparison of DPOAE across Group 1 and 2

In the present study, distortion product otoacoustic emission levels showed no statistically significant difference ($p < 0.05$) across groups at all the frequencies in DPOAE amplitude , except the frequencies like 1000 Hz, 2000 Hz and 4000 Hz in the left ear and in DPOAE SNR, except the frequencies like 1000 Hz and 16000 Hz in the right ear and 1000 Hz and 2000 Hz in the left ear. Similar results have been reported in the literature (Eren et al., 2013). Eren et al., (2013) reported that there is no effect of hyperandrogenism on otoacoustic emission levels, in the conventional audiometric frequency range (500 Hz- 8000 Hz). So they concluded that, hyperandrogenism did not seem to influence otoacousic emission levels. However, in the present study no difference was observed even at high frequencies.

In the present study the DPOAE amplitude showed variablitlity and had poor amplitude at higher frequencies for both the groups. This can be explained based on the generation of standing waves. Whitehead et al., (1995) reported that interference between in-going and reflected stimulus waves results in standing waves. While measuring DPOAEs, the ear-canal standing waves complicate the calibration of stimulus SPLs

above about 3000 Hz, because stimulus SPLs near the eardrum differs from those at the DPOAE-mesurement probe. This variability of the stimulus levels at the eardrum is one among the factors contributing to DPOAE-amplitude variability.

Other factors includes, transmission of the stimuli through the middle ear to the cochlea, DPOAE generation by the cochlea, and transmission of the DPOAE through the middle ear and and ear canal to the DPOAE probe. The factors also includes, probe placement, which influences the termination impedance of the transmission of DPOAEs to the probe. Dreisbach and Siegel (2001) observed technical distortions which become more likely only above about 8000 Hz, where the notches are usually sharper than at lower frequencies. Zebian et al., (2011) reported that above 8000 Hz, ambiguous DPOAE levels were observed for intermediate and shallow insertion depths. High DPOAE levels, which are not typical of human ears, may be helpful in suspecting technical distortions.

Thus, in the current study, no difference between both the groups in DPOAE results could be attributed to the fact that DPOAE amplitude was not good even for control group. Factors like standing waves, technical distortions and variation in probe position in the ear canal can explain the variability in DPOAE amplitude at high frequencies. Moreover the results of DPOAE amplitude and SNR did show significant difference between the groups for few low frequency signals. This could be because the data was collected on small sample. If tested on larger population, low frequencies DPOAE might show significance at other frequencies too.

Conclusion

The study highlights the importance of androgen hormone on hearing and early identification of hearing loss in the PCOS group, through extended high frequency screening.. The results of the study, can be taken as preliminary findings, to design a future study with larger population. Also, the mechanism behind hearing impairment in PCOS has to be investigated to know whether the impairment of EHFA in these individuals is progressive. If the underlying factors are revealed, it might be possible to prevent progression of hearing impairment in these individuals.

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