HEARING AND COCHLEAR FUNCTIONING IN POLYCYSTIC OVARIAN SYNDROME (PCOS)

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This Dissertation is submitted as part fullfillment for the Degree of Master of Science in Audiology University of Mysore, Mysore

MAY 2016

CERTIFICATE

This is to certify that this dissertation entitled **"Hearing and cochlear functioning in Polycystic ovarian syndrome (PCOS)"** is a bonafide work in part fulfilment for the degree of Master of sciences (Audiology) of the student (Registration No. 14AUD025). This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore
May, 2016

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DECLARATION

This is to certify that this dissertation entitled **"Hearing and cochlear functioning in polycystic ovarian syndrome (PCOS)"** is the result of my own study under the guidance of Ms. Chandni Jain, Lecturer in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysore and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

Mysore
May, 2016

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Dedicated to

My parents

My guide, Ms. Chandni Jain

&

My bestie, Ms. Latika Prabhu

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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.

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Chapter 1

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).

1.1. **Need for the study**

As reported earlier, PCOS is a condition with chronic anovulation, hyperandrogenism and the hormonal changes which can lead to cardiovascular diseases. The biochemical and hormonal changes in PCOS affects the intravascular blood flow and the vascular diseases and chronic inflammation may play an important role in pathogenesis of hearing impairment in PCOS.

Kucur et al., (2013) 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.

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

1.2. Aim of the Study

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.

1.3. Objectives of the Study

The objectives of the study were:

- To compare the hearing thresholds using conventional audiometry and EHFA in women with PCOS to those without PCOS.
- To compare the cochlear functioning in women with PCOS to those without PCOS using DPOAEs.

1.4. Hypothesis

The null hypothesis was assumed for the present study indicating:

1. There is no significant difference on conventional audiometry and EHFA among women with PCOS to those without PCOS.
2. There is no significant difference on DPOAEs among women with PCOS to those without PCOS.

Chapter 2

Review Of Literature

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder affecting 7% women in their reproductive age (Asuncion et al., 2000). It is a chronic condition beginning most commonly in adolescence. It causes anovulation and infertility in women of reproductive age and many other health risks are associated with it (Archer & Chang, 2004).

PCOS is defined as the presence of two of the following three features after the exclusion of other etiologies, (i) oligo- or anovulation (fewer than six menstrual periods in the preceding year), (ii) hyperandrogenism and/or biochemical signs of hyperandrogenism, and/or (iii) polycystic ovaries (Fauser, 2004). Among the above mentioned symptoms, hyperandrogenism is the major biological marker that affects hearing threshold (Talbott et al., 1995). Auditory abilities are affected in PCOS due to its features like insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations (Oghan & Coksuer, 2012).

The extended high frequency is more sensitive to vascular pathologies which leads to high frequency hearing loss in patients with PCOS (Oghan & Coksuer, 2012; Kucur et al., 2013). Thus, to know the hearing and cochlear functioning in patients with

PCOS, an extended high frequency audiometry and distortion product otoacousic emissions are needed, for the frequencies from 9000 Hz- 16000 Hz.

2.1. Hyperandrogenism and PCOS

Hyperandrogenism is the hallmark of the polycystic ovary syndrome (Rodin et al., 1994). All major diagnostic criteria for PCOS include hyperandrogenism as one of the diagnostic feature. Huang et al., (2010) evaluated 716 women with PCOS, and found that approximately three fourths of patients with PCOS diagnosed by the National Institute of Health (NIH), 1990, criteria had an evidence of hyperandrogenemia. They also reported that 60% of women demonstrated supranormal levels of free testosterone, which is the only most predictive assay

The excessive androgen is the mainl pathophysiological change and clinical expression of PCOS. Among the hypothesis for pathogenesis of PCOS, one hypothesis is that, the increase in ovarian androgen production is due to the excessive secretion of luteinizing hormone (LH) (Yen, 1980). Another hypothesis, says that, a key enzyme in androgen synthesis is P- 450 17-hydroxylase, dysregulation of this enzyme leads to hyperandrogenism and such secretions may be either dependent or independent of hypersecretion of LH (Barnes & Rosenfield, 1989). Stewart et al., (1990) revealed that a mechanism for gonadotropin-independent hyperandrogenism occur by an increase in corticotrophin secretion to maintain normal cortisol secretion, and as a consequence

there is also an increase in adrenal production of androgens . Other evidences suggests that the ovaries are the primary source of excess androgens in PCOS. The principal androgens secreted by testosterone and androstenedione, and the synthesis of both is increased in polycystic ovarian tissue in vitro (Axelrod & Goldzieher, 1962).

In a study, urinary excretion of hormone metabolities for 24 hours, in 65 women with PCOS, Rodin et al., (1994) found that the adrenal secretion of cortisol and androgens were elevated in women with PCOS, due to the dysregulation of 11β-hydroxysteroid dehydrogenase. The primary defect of chronic adrenal hyperandrogenemia and subsequent ovarian changes in PCOS could be due to increased metabolic clearance of cortisol

In women with PCOS, hyperandrogenism is clinically manifested by hirsutism (abnormal growth of hair on a woman's face and body), acne (a skin condition that occurs when hair follicles plug with oil and dead skin cells) and androgen alopecia (male pattern of hair loss that is thinning of hair on the crown) and it contributes to chronic anovulation and menstrual dysfunction. B The elevated circulating levels of serum total or unbound testosterone, androstenedione and an increased free androgen index (FAI) establish hyperandrogenism bichemically. (Georgopoulos et al., 2009).

2.2. Cardiovascular diseases and PCOS

Several metabolic alterations are associated with PCOS that could increase the risk of cardiovascular diseases (CVD). Early signs of vascular damage and increased CVD risk are commonly associated with PCOS (Orio et al., 2006). The increased CVD risk profile in individuals with PCOS has a multifactorial origin and it does notresult only from metabolic abnormalities (Luque-Ramirez et al., 2007). Along with other risk factors, insulin resistance, chronic inflammation and obesity are also involved (Legro, 2003). The carotid intima-media thickness (IMT) is increased in young women with PCOS when compared to women with no hyperandrogenism (Orio et al., 2006). Increased carotid IMT could also be due to hyperinsulinemia (Folsom et al., 1994). Luque- Ramirez et al, (2007) reported that there is only minor influence of insulin resistance on carotid IMT.

Hyperandrogenism, which is the central pathogenesis of PCOS, is the major factor for increased carotid IMT (Wu & Eckardstein., 2003). The biochemical and hormonal changes affects the intravascular blood flow (Atalay et al., 2005). Insulin resistance, hyperandrogenemia, and dyslipidemia are likely the major risk factors for the occurrence of cardiovascular disease in PCOS (Talbott et al., 1995).

Assessment of preclinical vascular disease have revealed that the increasedpredisposition to atherosclerosis in middle-aged PCOS patients with greater

carotid intima–media thickness (Orio et al., 2004) and more prevalent coronary artery calcium (Christian et al., 2003), compared with healthy controls. Both the elevated androgen levels and insulin resistance (Rajala et al., 2002) are associated with precocious atheroscelrosis, (Allan et al., 1997; Pignoli et al., 1986) which is due to IMT of the common carotid artery.

Conway et al., (1992) determined the risk factors for coronary artery disease in lean and obese women with PCOS. They reported, the obese women with PCOS were found to have higher systolic blood pressure, serum triglyceride and plasma glucose concentration than lean women with PCOS and controls. The lean women with PCOS were found to be hyperinsulinaemic and have reduced serum high density lipoprotein (HDL) and HDL_2 concentrations compared to women with normal ovaries. Thus, there results supports the evidence that hyperinsulinaemic women with PCOS have an increased risk of developing cardiovascular disease.

Wild et al., (2000) evaluated a long term follow up retrospective study which revealed, women with PCOS had higher levels of several cardiovascular risk factors, such as, diabetes, hypertension, hypercholesterolaemia, hypertriglyceridaemia and increased waist:hip ratio (WHR).

Polak et al., (2000) showed that, in case of hyperinsulinemia, ophthalmic artery blood flow velocity increases. In humans, altered insulin signaling is implicated in reduced glucose availability to insulin-sensitive cells, which further leads to vasoconstriction and endothelial damage (Oghan & Coksuer, 2012).

2.3. PCOS and Hearing loss

In individuals with PCOS, as mentioned earlier, hyperandrogenism is the major biochemical marker that could affect hearing thresholds. Biochemical and hormonal variations seen in this condition, affects the inner ear which, further leads to abnormal hearing thresholds.

Oghan & Coksuer (2012) evaluated the hearing thresholds between 250 Hz and 8000 Hz using audiometric measurements in young women with PCOS and compared it with controls. They also reported the contribution of the hyperandrogenemic and metabolic phenotype that exists in these individuals. The results of the data revealed no statistically significant difference between the two groups for low frequencies (250 Hz – 2000 Hz) air conduction thresholds. However, there was a statistically significant difference observed between two groups for high frequencies (4000 Hz – 8000 Hz) air conduction thresholds. Also, there was no statistically significant difference seen between the two groups in tympanometric values. The findings of the study suggests that, individuals diagnosed with PCOS should be advised audiologic evaluation especially in high frequency.

2.3.1. Extended high frequency audiometry in PCOS

Measurement of hearing in the frequency range from 8000 Hz – 20,000 Hz is called Extended high frequency audiometry (Osterhammel, 1980). Clinically, EHFA is valued because of its extreme sensitivity in the early detection of cochlear pathology. Since the pathlogical process tends to starts in the more basal-high frequency region, it is more sensitive test for detection of hearing loss.

Kucur et al., (2013) measured hearing thresholds in subjects with PCOS, for low frequencies (250 Hz-2000 Hz), high frequencies (4000 Hz-8000 Hz) and extended high frequencies (9000 Hz-20000 Hz). Although the hearing thresholds of groups were similar at frequencies from 250 Hz to 4000 Hz, significant hearing loss was observed for frequencies 8000 Hz, 10000 Hz, 12000 Hz, and 14000 Hz in PCOS group compared to controls. 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 EHFA are more efficient in detecting early hearing loss compared to pure tone audiometry in PCOS.

2.3.2. Otoacoustic emissions in PCOS

The cochlear functioning can be determined by measuring otoacoustic emissions (OAE), since it originates from outer hair cells. OAEs can be used to monitor medial olivocochlear (MOC) effects on the cochlear amplifier. Medial olivocochlear system

activation can be achieved through acoustic stimulation. This reflex can be activated with ipsilateral and/or contralateral acoustic stimuli.

Eren et al., (2013) evaluated the effects of hyperandrogenism on otoacoustic emission levels. Distortion product otoacoustic emissions (DPOAE) and transient evoked otoacoustic emissions (TEOAE) were recorded in the frequency range from 500 Hz – 8000 Hz and 1000 Hz – 4000 Hz, respectively. The results revealed no statistically significant difference in OAEs between the PCOS group and the control group. It was concluded that hyperandrogenism does not influence otoacoustic emission level. However, no difference on DPOAE measures could be because vascular diseases are more sensitive to extended high frequency range (9000 Hz-20000 Hz), rather than the conventional DPOAE frequency range (500 Hz - 8000Hz).

Thus, from the above studies, it can be concluded that hearing thresholds are affected in individuals with PCOS. Biochemical and hormonal variations, majorly hyperandrogenism affects the intravascular blood flow and cardiovascular diseases like insulin resistance which affects the hearing in women with PCOS.

Chapter 3

Method

The present study aimed to study the hearing and cochlear functioning through extended high frequency audiometry and distortion product otoacoustic emissions in women with polycystic ovarian syndrome. In order to investigate the same, the following method was used.

3.1. Research design

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

3.2. 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).

3.3. Participant selection criteria

The inclusion criteria for the ***Group- I***

- 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
- No other otologic or neurologic complaints

The inclusion criteria for ***Group- II***

- Healthy women with normal menstrual cycle
- No evidence of hyperandrogenism
- Normal ovarian morphology on ultrasonography
- No other otologic or neurologic complaints

The exclusion criteria for ***Group-I*** and ***Group- II*** comprised of, participants with

- Otologic and neurologic diseases-chronic tinnitus, middle ear pathologies such as tympanic membrane perforations, chronic otosclerosis and any other infectious middle ear diseases, neurological diseases that could affect hearing such as intra and extra axial tumors, demyelinating lesions and polyneuropathies were excluded.
- History of otologic surgery
- Hearing loss
- Endocrine diseases such as diabetes, androgen secreting tumors and thyroid dysfunctions were excluded from the study

- Hypertension
- Family history of hearing loss
- History of acoustic trauma
- Exposure to ototoxic drugs
- Occupational noise exposure
- Autoimmune diseases
- History of smoking and alcohol consumption
- Intake of any other medications which could alter the sex hormones were also excluded from the study
- 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.

3.4. Instrumentation

- Otoscope was used to visualize the ear canal and to rule out any contraindications for audiological evaluation.

- A calibrated clinical audiometer, Inventis Piano plus VRA model with TDH-39 head phones for conventional air conduction audiometry and the bone vibrator Radio ear B-71 model was used for conventional bone conduction audiometry. The same audiometer with Sennheiser HDA 200 headphone was used for the extended high frequency audiometry (EHFA).
- A calibrated Grason stadler Incorporation, GSI- Tympstar, middle ear analyzer was used to rule out middle ear pathologies.
- A calibrated DP-2000 Starkey was used to record DPOAEs.

3.5. Test environment

The tests was carried out in an air conditioned, sound treated room with the ambient noise levels within permissible limits (ANSI S3.1; 1991). Conventional and high frequency audiometry were carried out in a double room settings, whereas, DPOAE and immitance evaluations were done in a single room situations.

3.6. Test procedure

The testing was done in the following steps:

- Case history
- Otoscopic examination
- Immittance evaluation
- Conventional audiometry

- Extended high frequency audiometry
- Recording of DPOAEs

3.6.1. Case history

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.

3.6.2. Otoscopic Examination

Otoscopic examination was done to inspect the external ear and tympanic membrane. Participants with normal external ear and healthy tympanic membrane were included in the study.

3.6.3. Immittance Evaluation

Immittance evaluation was carried out with low probe tone frequency of 226 Hz. Ipsilateral and contralateral acoustic reflexes were measured for frequencies 500 Hz, 1000 Hz, 2000 Hz and 4000 Hz and reflex decay test for 500 Hz and 1000 Hz in both ipsilateral and contralateral side was administered to rule out middle ear pathology, retrocochlear pathology and neural adaptation.

3.6.4. Conventional Audiometry

Participants were seated comfortably in the patient room and the following instructions were given to the them. “Raise your finger whenever you hear the sound. Pay attention and respond even for the faintest sound you hear”. 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.

3.6.5. Extended High Frequency Audiometry

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.

3.6.6. Recording of DPOAEs

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 f_2, 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 L_1 = 65 dB SPL, L_2 = 55 dB SPL. The response parameters to consider DPOAE as present included DP amplitude and SNR. The protocol of DPOAE is summarized in Table 3.1.

Table 3.1: *Protocol for recording DPOAE*

Parameters	*Values*
Primary stimuli	F1<F2; F1:F2=1.2
Level of primaries	L1=65dB SPL ; L2= 55 dB SPL
Emissions recorded at	2f1-f2
Test Frequencies	500Hz-16000 Hz
Number of sweeps	260 sweeps
Number of points per octave	2 points per octave

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.

3.7. Statistical analysis

The data of the present study was tabulated and statistically analyzed using the Statistical Package for Social Sciences (SPSS, version 20.0) software. Descritive statistics was used to estimate the mean and standard deviation of the test parameters. The hearing thresholds and the DPOAE between the two groups was compared using Mann Whitney U test.

Chapter 4

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. The results of all the measures are presented under the following headings :

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

4.2. Comparison of DPOAE across Group 1 and 2

4.2.1. DPOAE amplitude across Group 1 and 2

4.2.2. DPOAE SNR across Group 1 and 2

4.1. 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 is shown in Table 4.1.

Table 4.1: *Mean, Median and SD of hearing thresholds in Group 1*

		Group 1		
Frequency (Hz)	Ear	Mean	Median	SD
250	*Right*	4.66	5.00	3.51
	Left	4.00	5.00	3.87
500	*Right*	5.33	5.00	3.51
	Left	6.66	5.00	3.08
1000	*Right*	4.00	5.00	2.07
	Left	5.66	5.00	3.71
2000	*Right*	5.66	5.00	4.16
	Left	5.66	5.00	3.19
4000	*Right*	5.00	5.00	3.27
	Left	5.66	5.00	3.71
8000	*Right*	14.00	15.00	2.07
	Left	5.66	5.00	4.95
9000	*Right*	7.33	5.00	5.30
	Left	7.66	5.00	5.30
10000	*Right*	7.66	10.00	3.19
	Left	9.66	10.00	4.41
11200	*Right*	10.33	10.00	4.41
	Left	8.66	10.00	5.81
12500	*Right*	10.33	10.00	4.41
	Left	8.66	10.00	2.96
14000	*Right*	12.00	10.00	3.16
	Left	12.66	10.00	4.57
16000	*Right*	13.66	15.00	3.51
	Left	15.33	15.00	7.66

The mean, median and the one standard deviation of the hearing thresholds for frequencies ranging from 250 Hz to 16000 Hz for Group 2 is shown in Table 4.2.

Table 4.2: *Mean, Median and SD of hearing thresholds in Group 2*

Group 2				
Frequency (Hz)	Ear	Mean	Median	SD
250	*Right*	2.33	0.00	3.19
	Left	3.33	5.00	2.43
500	*Right*	3.33	5.00	4.08
	Left	4.33	5.00	3.71
1000	*Right*	6.66	5.00	3.08
	Left	5.33	5.00	3.51
2000	*Right*	4.33	5.00	3.19
	Left	4.33	5.00	3.19
4000	*Right*	4.33	5.00	3.19
	Left	1.66	0.00	4.49
8000	*Right*	8.00	5.00	3.68
	Left	5.00	5.00	4.22
9000	*Right*	2.66	5.00	2.58
	Left	2.33	0.00	2.58
10000	*Right*	3.33	5.00	2.43
	Left	6.33	5.00	3.51
11200	*Right*	3.00	5.00	3.16
	Left	5.00	5.00	3.27
12500	*Right*	3.00	5.00	3.16
	Left	5.33	5.00	3.99
14000	*Right*	3.66	5.00	2.96
	Left	6.00	5.00	3.38
16000	*Right*	7.66	10.00	2.58
	Left	9.66	10.00	3.99

It can be noted from both Table 4.1 and 4.2 that the mean thresholds for Group 1 is 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 4.3.

Table 4.3: Z values of hearing thresholds across groups for right and left ear

	Right		Left	
Frequency(Hz)	**|Z|**	**Significance**	**|Z|**	**Significance**
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. Thus, the null hypothesis was rejected for this objective.

4.2. Comparison of DPOAE across Group 1 and 2

Figure 4:1(a) and 4:1(b) represents the DP-gram of one participant of Group 1 for frequencies ranging from 500 Hz – 6000 Hz and 8000 Hz – 16000 Hz respectively.

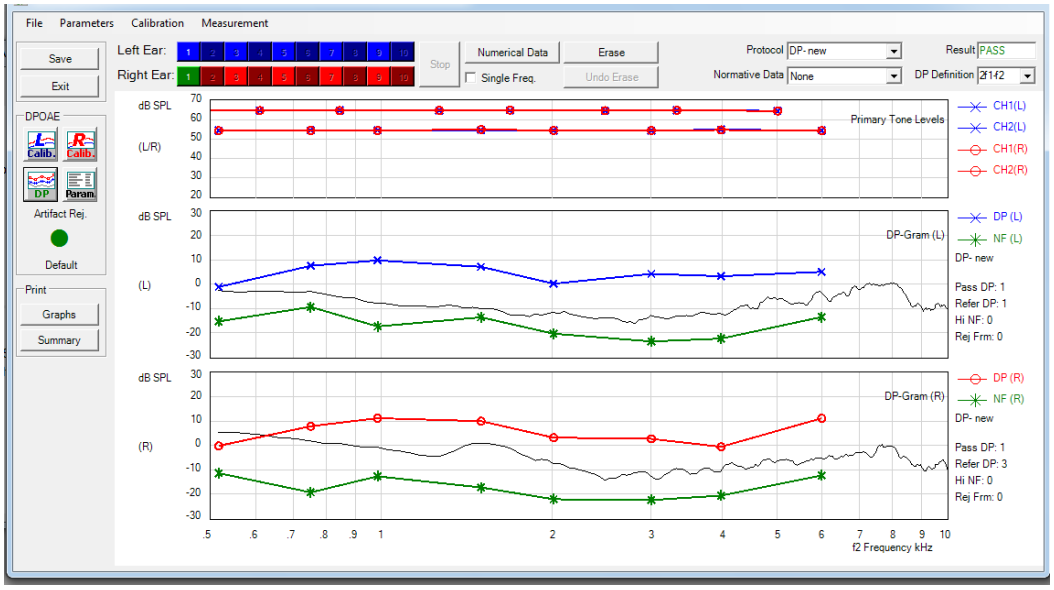

Figure 4:1:(a) *Representation of DP-gram for frequencies ranging from 500 Hz-6000 Hz of one participant in Group 1*

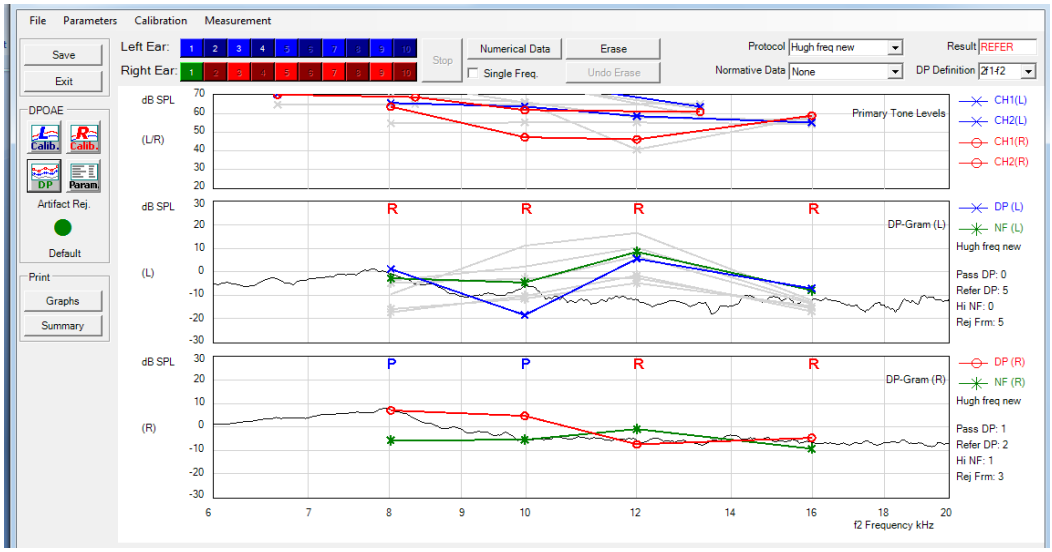

Figure 4:1:(b) *Representation of DP-gram for frequencies ranging from 8000 Hz-16000 Hz of one participant in Group 1*

Figure 4:2(a) and 4:2(b) represents the DP-gram of one participant of Group 2 for frequencies ranging from 500 Hz – 6000 Hz and 8000 Hz – 16000 Hz respectively.

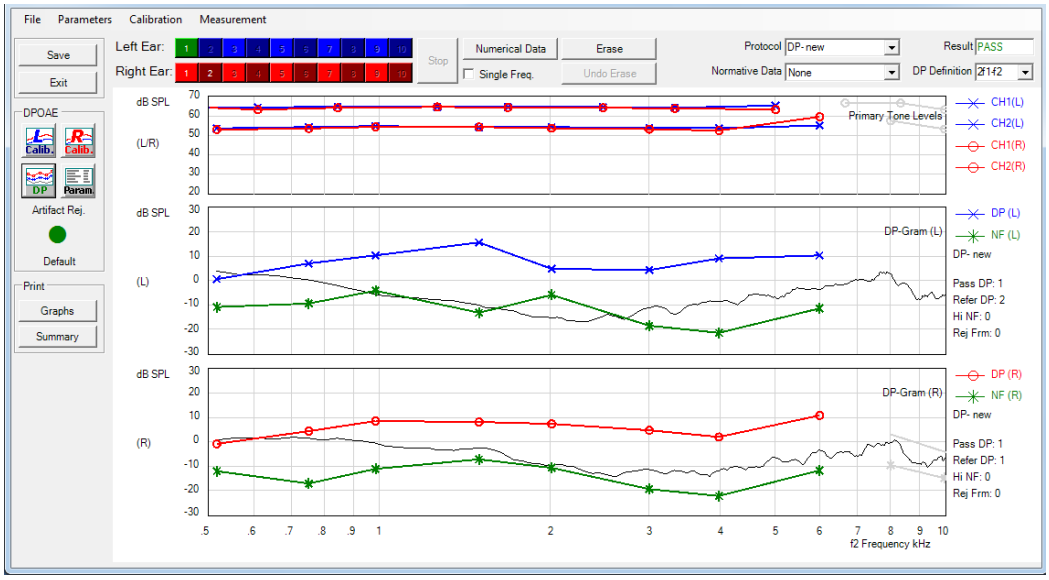

Figure 4:2:(a) *Representation of DP-gram for frequencies ranging from 500 Hz-6000 Hz of one participant in Group 2*

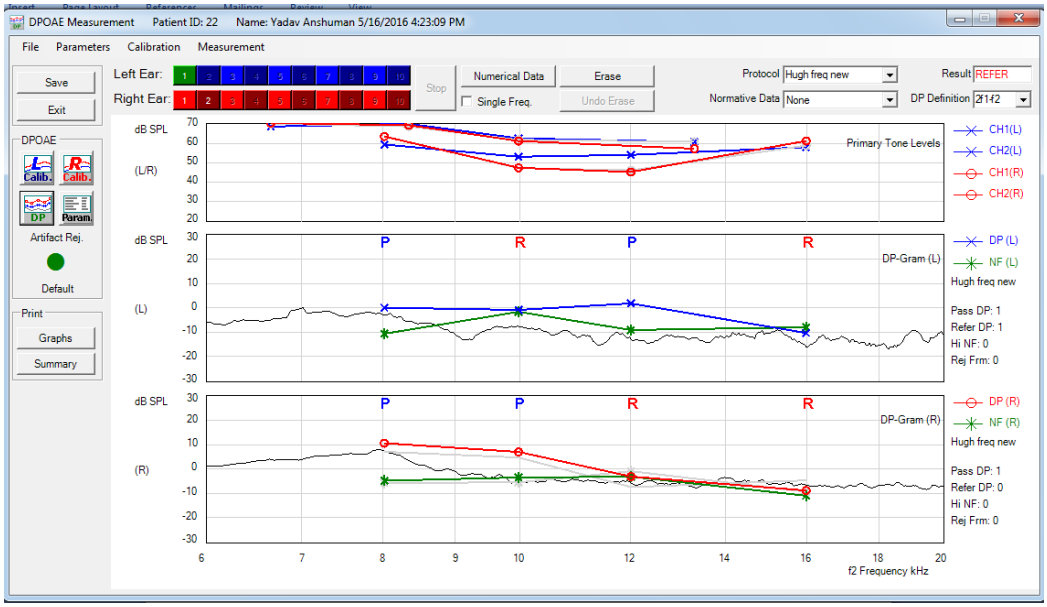

Figure 4:2:(b) *Representation of DP-gram for frequencies ranging from 8000 Hz-16000 Hz of one participant in Group 2*

4.2.1. DPOAE amplitude across Group 1 and 2

The mean DPOAE amplitude along with one standard deviation for Group 1 and Group 2 is shown in Table 4.4 and Table 4.5 respevtively. From the Table 4.4 and Table 4.5 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.

Tabel 4.4: *Mean and SD of DPOAE amplitude across frequencies for Group 1*

Group 1			
Frequency (Hz)	Ear	Mean	SD
500	*Right*	-9.18	5.97
	Left	-9.36	6.38
750	*Right*	-3.81	7.12
	Left	-1.99	8.16
1000	*Right*	-4.466	10.57
	Left	-3.52	10.29
1500	*Right*	1.45	6.62
	Left	4.59	6.82
2000	*Right*	-1.42	3.01
	Left	-3.79	8.99
3000	*Right*	-1.09	6.2
	Left	-1.4	8.07
4000	*Right*	-0.66	5.02
	Left	-2.64	7.12
6000	*Right*	0.12	4.95
	Left	-0.13	7.03
8000	*Right*	-8.53	9.97
	Left	-3.88	6.20
9000	*Right*	-12.98	4.96
	Left	-12.87	5.76
12000	*Right*	-2.16	8.20
	Left	-1.64	7.68
16000	*Right*	-14.56	6.36
	Left	-3.09	8.91

Table 4.5: *Mean and SD of DPOAE amplitude across frequencies in Group 2*

		Group 2	
Frequency (Hz)	Ear	Mean	SD
500	*Right*	-7.82	4.40
	Left	-9.46	6.28
750	*Right*	-1.41	7.95
	Left	-0.27	7.07
1000	*Right*	1.28	10.50
	Left	4.54	7.39
1500	*Right*	-1.95	8.57
	Left	0.58	7.01
2000	*Right*	0.9	5.15
	Left	2.76	5.48
3000	*Right*	-1.59	8.21
	Left	1.76	4.58
4000	*Right*	2.88	4.18
	Left	2.24	4.05
6000	*Right*	-2.3	6.03
	Left	0	6.3
8000	*Right*	-4.67	5.02
	Left	-4.72	6.23
9000	*Right*	-12.22	5.60
	Left	-10.28	8.14
12000	*Right*	-5.41	9.72
	Left	-6.93	7.91
16000	*Right*	-10.92	6.60
	Left	1.29	5.59

To compare the DPOAE amplitude across groups for both the ears Mann Whitney U test was carried out. Table 4.6 showed that there was no statistically significant difference between groups for frequencies ranging from 500 Hz – 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

Table 4.6: *Z values for DPOAE amplitude across groups for right and left ear*

	Right		Left	
Frequency (Hz)	**|Z|**	**Significance**	**|Z|**	**Significance**
500 Hz	1.03	0.30	0.47	0.63
750 Hz	0.97	0.32	0.66	0.50
1000 Hz	1.37	0.17	2.09	0.03*
1500 Hz	1.10	0.27	1.09	0.27
2000 Hz	1.49	0.13	2.53	0.01*
3000 Hz	0.22	0.81	1.22	0.22
4000 Hz	1.77	0.08	2.17	0.02*
6000 Hz	1.05	0.29	0.06	0.95
8000 Hz	1.26	0.20	0.60	0.54
9000 Hz	0.04	0.96	0.33	0.74
12000 Hz	1.12	0.26	1.76	0.07
16000 Hz	0.93	0.35	0.31	0.75

*Note : * indicates $p<0.05$*

4.2.2. DPOAE SNR across Group 1 and 2

The Table 4.7 and Table 4.8 shows the mean and SD of DPOAE SNR for Group 1 and Group 2, respectively. It can 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 4.7: *Mean and SD of DPOAE SNR for Group 1*

Group 1			
Frequency (Hz)	**Ear**	**Mean**	**SD**
500	*Right*	6.93	7.68
	Left	8.77	6.77
750	*Right*	9.88	10.74
	Left	10.94	11.35
1000	*Right*	3.01	10.78
	Left	-1.1	12.08
1500	*Right*	10.64	10.09
	Left	10.84	11.08
2000	*Right*	17.57	4.84
	Left	13.52	9.31
3000	*Right*	18.63	6.48
	Left	17.51	7.47
4000	*Right*	20.42	6.26
	Left	17.24	6.6
6000	*Right*	14.54	5.15
	Left	14.86	5.67
8000	*Right*	6.34	7.32
	Left	5.54	8.18
9000	*Right*	-1.28	5.2
	Left	0.36	6.46
12000	*Right*	3.49	6.22
	Left	4.27	5.55
16000	*Right*	-3	5.91
	Left	3.09	8.91

Table 4.8: *Mean and SD of the DPOAE SNR for Group 2*

Group 2			
Frequency (Hz)	**Ear**	**Mean**	**SD**
500	*Right*	7.51	6.91
	Left	6.1	9.85
750	*Right*	13.81	7.03
	Left	16.53	8
1000	*Right*	11.61	12.49
	Left	8.24	13.56
1500	*Right*	15.86	8.81
	Left	16.86	7.88
2000	*Right*	20.36	6.68
	Left	20.45	7.95
3000	*Right*	15.88	7.62
	Left	19.45	5.48
4000	*Right*	22.48	7.41
	Left	20.52	14.31
6000	*Right*	17	6.93
	Left	16.56	7.76
8000	*Right*	8.9	4.19
	Left	8.87	4.34
9000	*Right*	2.23	4.53
	Left	2.56	4.52
12000	*Right*	2.09	6.44
	Left	3.32	6.03
16000	*Right*	3.72	5.94
	Left	1.29	5.59

To compare the DPOAE SNR across groups fo both the ears Mann Whitney U test was carried out. The results are shown in Table 4.9 and it can be noted that there was statistically 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. Thus, the null hypothesis was accepted for this objective.

Table 4.9: *Z values of DPOAE SNR across groups for right and left ear*

	Right		Left	
Frequency (Hz)	**|Z|**	**Significance**	**|Z|**	**Significance**
500 Hz	0.27	0.78	1.37	0.16
750 Hz	1.07	0.28	1.47	0.14
1000 Hz	2.03	0.04*	2.05	0.04*
1500 Hz	1.45	0.14	1.55	0.12
2000 Hz	0.85	0.39	1.99	0.04*
3000 Hz	1.32	0.18	0.74	0.45
4000 Hz	0.78	0.43	1.92	0.05
6000 Hz	0.78	0.43	0.76	0.44
8000 Hz	1.10	0.27	0.85	0.39
9000 Hz	1.37	0.17	0.62	0.53
12000 Hz	0.47	0.63	0.22	0.82
16000 Hz	2.51	0.01*	0.31	0.75

*Note : * indicates $p<0.05$*

Chapter 5

Discussion

The aim of the present study was to evaluate the hearing thresholds using EHFA in cases with PCOS, and to determine the cochlear functioning in cases with PCOS using DPOAE. The results are discussed under the following headings.

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

5.2. Comparison of DPOAE across Group 1 and 2

5.1. 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 were 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.

5.2. 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 differ 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.

Chapter 6

Summary and Conclusion

Polycystic ovarian syndrome (PCOS) is a characterized by oligo-amenorrhea, hyperandrogenism and polycystic ovaries. It's a chronic condition begins most commonly in adolesecence. The auditory abilities are affected in PCOS due to its features such as insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical variations, like hyperandrogenism which affects the intravascular blood flow. The diseases with endothelial damage further affects the high frequency hearing in early stages of PCOS. Thus, it is needed to evaluate hearing in women with PCOS. In the present study the hearing and cochlear functioning was evaluated in cases with polycystic ovarian syndrome using extended high frequency audiometry and distortion product otoacoustic emissions. Hearing thresholds in the frequency range from 250 Hz to 16000 Hz was measured and DPOAE was recorded in the frequency range of 500 Hz to 16000 Hz in women with PCOS and in control group. Fifteen participants in the age range of 18 to 25 years were taken in both the groups. The salient results obtained in the present study are as follows:

- The EHFA (8000 Hz – 16000 Hz) showed statistically significant difference in individuals with PCOS compared to the control group.
- The DPOAE amplitude and SNR did not show any statistically significant difference between individuals with PCOS and control group.

The significant difference seen in EHFA can be attributed to the features of PCOS like insulin resistance, endothelial damage, cardiovascular problems, hormonal and biochemical changes, like hyperandrogensim which affects the intravascular blood flow. The DPOAE results suggests that hyperandrogenism does not seem to influence otoacoustic emission levels.

Implications of the Study

- The study highlights the importance of androgen hormone on hearing.
- The study highlights 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.

Future Directions

- 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 are progressive.
- If the underlying factors are revealed, it might be possible to prevent progression of hearing impairment in these individuals.

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