A Clinical Study of Effect of Hyperpyrexia on Otoacoustic Emissions in Children

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Received: 16 November 2017 / Accepted: 10 April 2018 / Published online: 26 April 2018
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Abstract Various degrees of sensory neural hearing loss can be seen in the progression of some hereditary periodic fever syndromes. Otoacoustic emission testing can help to establish the inner ear involvement at an early period of a periodic fever with a risk of hearing loss (Abdul Kadir et al. in *J Int Adv Otol* 9(2.79):08–11, 2014). Sensorineural hearing loss is the common most complication of bacterial meningitis in childhood (Richardson in *Pediatrics* 102(6):1364–1368, 1998). When present from birth, or acquired in the pre-school years, hearing loss of any degree, even mild hearing loss, interferes with speech and language development. In addition to obvious communication deficits, the consequences of hearing loss in children and adults include psychosocial problems, such as frustration, irritability, anxiety, the tendency to withdraw from social interactions, and even depression (Dhar and Hall in *Otoacoustic emissions: principles, procedures, and protocols*, Plural Publishing, San Diego, 2011). OAE are acoustic signals emitted from cochlea to the middle ear and into the external ear where they are recorded. Evoked OAE are undetectable when deafness is above 30–35 dB Sound pressure level (Biswas in *Clinical audio-vestibulometry for otologists and neurologists*, Bhalani Publishing House, Mumbai, 1995). OAEs permit early detection of inner ear abnormalities associated with a wide variety of diseases and disorders, including Alport syndrome etc. With early detection, the serious consequences of hearing loss can sometimes be prevented. With proper identification and diagnosis of hearing impairment, timely and effective

management for the same can be taken. Data for this study was collected from children (5–14 years) attending the Department of Otorhinolaryngology and Paediatrics Out-patient departments in P.E.S.I.M.S.R, Kuppam. Among the study population 43 (57.3%) were male and 32 (42.7%) were females showing the slight male preponderance. study was done on children with temperature > 1000 F, children with temperature were screened with OAE, and OAE was recorded in same children once fever has subsided and results were compared. This is a new study where we compared same group of children with fever and once fever has subsided. In most other studies, study group was compared to the healthy control group. In our study, children with fever having abnormal FDP values at f1 were 9, they reverted back to base line once fever has subsided. This shows that there is no much damage to inner ear at lower frequencies. Almost 47 abnormal FDP values at f2 reverted back to normal. At higher frequencies (f3 and f4), there is no much change in abnormal FDPs with fever and after fever has subsided, this shows that there is more damage to inner ear at higher frequencies. This study demonstrated that hyperpyrexia causes hearing loss in children with fever probably due to cochlear involvement. We conclude that OAE can be used as a screening tool in detecting hearing loss among children because the technique is simple, reproducible, not expensive, not time consuming also effectively narrows down the children with high chances of hearing loss thereby effectively improves the chances of early diagnosis and hence children can be rehabilitated early, making a marked change in their future.

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Keywords Hyperpyrexia · Otoacoustic emission · Sensorineural hearing loss · Frequency distortion products · Auditory brainstem response · Distortion-product noise floor (SNR)

Introduction

Various degrees of sensory neural hearing loss can be seen in the progression of some hereditary periodic fever syndromes. Otoacoustic emission testing can help to establish the inner ear involvement at an early period of a periodic fever with a risk of hearing loss [1]. Sensorineural hearing loss is the common most complication of bacterial meningitis in childhood [2]. When present from birth, or acquired in the pre-school years, hearing loss of any degree, even mild hearing loss, interferes with speech and language development. In addition to obvious communication deficits, the consequences of hearing loss in children and adults include psychosocial problems, such as frustration, irritability, anxiety, the tendency to withdraw from social interactions, and even depression [3].

OAE are acoustic signals emitted from cochlea to the middle ear and into the external ear where they are recorded. Evoked OAE are undetectable when deafness is above 30–35 dB Sound pressure level [4]. OAEs permit early detection of inner ear abnormalities associated with a wide variety of diseases and disorders, including Alport syndrome etc. With early detection, the serious consequences of hearing loss can sometimes be prevented.

With proper identification and diagnosis of hearing impairment, timely and effective management for the same can be taken.

Aims and Objectives of the Study

1. To analyse the otoacoustic emissions in patients with hyperpyrexia in the age group of 5–14 years.
2. To evaluate the inner ear involvement in children with hyperpyrexia by testing otoacoustic emission in children so that proper precautions can be taken to prevent early onset of hearing loss.

Methodology

Source of Data

Data for this study was collected from children (5–14 years) attending the Department of Otorhinolaryngology and Paediatrics Out-patient departments in P.E.S.I.M.S.R. Kuppam, Chittoor district, Andhra Pradesh between November 2014 and June 2016.

This study was approved by ethical committee of our college.

Type of Study

Prospective cohort study.

Inclusion Criteria

Children (age group of 5–14 yrs) with hyperpyrexia with temperature > 100 F.

Exclusion Criteria

1. Children with pathologic finding at the otologic examination
2. Children with history of recurrent otitis media
3. Children with history of using proven ototoxic drugs
4. Children having abnormal tympanometry finding
5. Children with any other pathology in external, middle and inner ear
6. Children whose guardians are not giving consent to the study are excluded.

Method of Collection of Data

1. Children who presented to outpatient departments of ENT and Pediatrics in PESIMSR from November 2014 to June 2016 with hyperpyrexia were examined and OAE test was conducted.
2. Temperature was recorded in the axillary region during episode of hyperpyrexia and follow up period.
3. Measurements of DPOAE were carried out in all subjects while the subjects were seated in the sound proof test room. This test was performed by 'Intel-ligent hearing systems'.
4. DPOAEs were measured at four different frequencies ranging from 1000 to 4000 Hz. By calculating the difference between distortion products and the noise floor for two standard deviations, the signal to noise ratio for each frequency was determined.
5. Patients were advised to review after pyrexia has subsided and once again OAE test was conducted, results noted and tabulated. The two results compared and analyzed.

Observation and Results

In the present study a total of 75 children presenting with hyperpyrexia to Outpatient departments of ENT and Paediatrics at PESIMSR from November 2014 to June 2016 were included (Table 1).

In the present study total of 75 patients i.e. 42.7% were female and 57.3% were male (Table 2).

Table 1 Gender distribution

Sl. no.	Gender	Number	Percentage (%)
1	Female	32	42.7
2	Male	43	57.3

Table 2 Temperatures ranges

S. no.	Temperature range	Total children	Males	Females
1	100–100.9 F	25	12	13
2	101–101.9 F	26	16	10
3	> 102 F	24	15	9

Table 3 Frequencies tested

Sl. no.	Frequency (kHz)	
1	f1	1
2	f2	1.5
3	f3	2
4	f4	4

In the present study temperature ranged from 100 to 103 F. 25 children had 100–100.9 F, 26 children had 101–101.9 F, 24 children had 102–103 F (Table 3).

In present study distortion products were measured at 4 frequencies.

Table 4 shows FDP in children at f1 frequency with fever. Abnormal FDP in 75 right ears were 5 and in 75 left ears were 4.

Table 5 shows FDP in children at f1 frequency after fever has subsided. Abnormal FDP in 75 right ears was 1 and in 75 left ears were 3.

Abnormal FDP at f2 in 75 right ears were 24 and in 75 left ears were 23 with fever (Table 6).

Abnormal FDP at f2 frequency in 75 right ears were 3 and in 75 left ears were 4 after fever has subsided (Table 7).

Abnormal FDP at f3 frequency in 75 right ears were 26 and in 75 left ears were 29 with fever (Table 8).

Table 4 FDP in children at f1 frequency with fever

Ear	FDP	Male	%	Female	%
Right	Abnormal	4	9.3	1	3.1
	Normal	39	90.7	31	96.9
	Excellent	0		0	
Left	Abnormal	3	6.9	1	3.1
	Normal	40	93.1	31	96.9
	Excellent	0		0	

Table 5 FDP in children at f1 frequency after fever has subsided

Ear	FDP	Male	%	Female	%
Right	Abnormal	1	2.3	0	0
	Normal	42	97.7	32	100
	Excellent	0		0	
Left	Abnormal	2	4.65	1	3.1
	Normal	41	95.35	31	96.9
	Excellent	0		0	

Table 6 FDP in children at f2 with fever

Ear	FDP	Male	%	Female	%
Right	Abnormal	13	30.2	11	34.4
	Normal	30	69.8	21	66.6
	Excellent	0		0	
Left	Abnormal	14	32.5	9	28.1
	Normal	29	67.5	23	71.9
	Excellent	0		0	

Table 7 FDP in children at f2 frequency after fever has subsided

Ear	FDP	Male	%	Female	%
RIGHT	Abnormal	3	6.9	0	0
	Normal	40	93.1	32	100
	Excellent	0		0	
LEFT	Abnormal	2	4.65	2	6.3
	Normal	41	95.35	30	93.7
	Excellent	0		0	

Abnormal FDP at f3 frequency in 75 right ears were 23 and in 75 left ears were 23, which show there was no much decrease after the fever has subsided (Table 9).

Abnormal FDP at f4 frequency with fever in 75 right ears were 29 and in 75 left ears were 29 (Table 10).

Abnormal FDP at f4 frequency after fever has subsided in 75 right ears were 30 and in 75 left ears were 29, which shows there was no much difference in FDP at f4 in study group during fever and in follow up (Table 11).

The above table shows over all comparison of abnormal FDP in the study group with fever and in follow up (Tables 12, 13).

At f1 frequency, SNR:

1. in right ears was found to be bad in 2 (2.6%) 1 was male and 1 was female,
2. in left ears was found to be bad in 2 (2.6%) children, 1 was male and 1 was female.

At f1 and f2 Frequency- abnormal SNR were reverted back to base line once fever has subsided, at f3 and f4-

Table 8 FDP at f3 with fever

Ear	FDP	Male	%	Female	%
Right	Abnormal	14	32.6	12	37.5
	Normal	29	67.4	20	62.5
	Excellent	0		0	
Left	Abnormal	17	39.5	12	37.5
	Normal	26	60.5	20	62.5
	Excellent	0		0	

Table 9 FDP in children at f3 frequency after fever has subsided

Ear	FDP	Male	%	Female	%
Right	Abnormal	13	30.2	10	31.2
	Normal	30	69.8	22	68.8
	Excellent	0		0	
Left	Abnormal	14	32.5	9	28.1
	Normal	29	67.5	23	71.9
	Excellent	0		0	

Table 10 FDP AT f4 with fever

Ear	FDP	Male	%	Female	%
Right	Abnormal	18	41.9	11	34.4
	Normal	25	58.1	21	65.6
	Excellent	0		0	
Left	Abnormal	17	39.5	12	37.5
	Normal	26	60.5	20	62.5
	Excellent	0		0	

Table 11 FDP in children at: f4 frequency after fever has subsided

Ear	FDP	Male	%	Female	%
Right	Abnormal	18	41.8	12	37.5
	Normal	25	58.2	20	62.5
	Excellent	0		0	
Left	Abnormal	17	39.5	12	37.5
	Normal	26	60.5	20	62.5
	Excellent	0		0	

abnormal SNR were not reverted to base line. (SNR = DISTORTION PRODUCT – NOISE FLOOR.)

In the present study, among 75 children in the age group 5–14 years, in fever at f1 frequency FDPs in

1. right ears were found to be abnormal in 5 (6.6%) 4 were male and 1 was female,
2. left ears were found to be abnormal in 4 (5.3%); 3 were male and 1 was female, and

Table 12 Comparison of abnormal FDP between children with fever and without fever at all frequencies

Frequency	With fever	After fever has subsided
f1	9	4
f2	47	7
f3	55	46
f4	58	59

Table 13 Comparison of abnormal SNR with fever and after fever has subsided

Frequency	With fever	After fever has subsided
f1	4	0
f2	9	5
f3	35	33
f4	59	59

after fever has subsided abnormal FDPs at f1 frequency FDPs in

1. right ears was found to be 1 (1.3%) 1 was male,
2. left ears were 3 (4%) among them 2 were male and 1 was female.

In children with fever average FDP at f1 in right ears was 3.11 and average FDP after fever has subsided in right ear was 4.51 (P value < 0.001) which shows significant difference (Tables 14, 15).

The average FDP at f1 in left ears was 3.03 and average FDP after fever has subsided in left ears was 4.03 ($P < 0.001$) which shows significant difference.

Table 14 Normative data for frequency distortion products (FDP)

FDP	Range
Abnormal	– 15–0
Normal	0–8
Excellent	8–15

Table 15 Normative data for SNR

SNR	Range
Bad	6 or < 6 dB
Fair	7–10 dB
Good	11–20 dB
Excellent	20–28 dB
Out standing	> 29 dB

Table 16 Comparison of average FDP with and after fever has subsided at f1

Ear	FDP with fever	FDP after fever has subsided	<i>P</i> value
Right ears	3.11	4.51	< 0.001
Left ears	3.03	4.03	0.000

In present study at f1 frequency all abnormal DPOAE and SNR in children with fever returned to normal levels when fever subsided (Tables 16, 17, 18).

In a study by Abdulkadir et al. [1], on 49 children in the age group of 6–16 years, at f1 average FDP was 2.5 in children with fever and 9.4 in control group with *P* value < 0.01. Average SNR at f1 was 1.5 in children with fever and 7.1 in control group with *P* value < 0.01.

In a study by Lordoglu et al. [5], on 50 children in the age group of 4–18 years, at f1 frequency average DPOAE was 4.05 with fever and 7.2 after fever has subsided. Average SNR at f1 frequency was 9.85 with fever and 13.65 after fever has subsided.

At f2, FDPs in

1. right ears were found to be abnormal in 24 (32%), 13 were male and 11 were female.
2. left ears were found to be abnormal in 23 (30.6%), 14 were male and 9 were female.

After fever has subsided, abnormal FDPs at f2 in

1. right ears was found to be 3 (4%) who were all male.

Table 17 Comparison of average DPOAE at 1 kHz (f1) with other studies

	In present study	Abdul kadir et al.	Lordoglu et al.
DPOAE			
Patient group	3.06	2.5	4.05
Follow up/control	4.26	9.4	7.2
<i>P</i> value	< 0.001	< 0.01	0.586
SNR			
Patient group	8.86	1.5	9.85
Follow up/control	8.9	7.1	13.65
<i>P</i> value	0.585	< 0.01	0.421

Table 18 Comparison of average FDP with and after fever has subsided at f2

Ear	FDP with fever	FDP after fever has subsided	<i>P</i> value
Right	2.21	3.40	< 0.01
Left	2.11	3.09	< 0.001

Table 19 Comparison of average DPOAE and SNR at 1.5 kHz (f2) with other studies

	In present study	Abdul kadir et al.	Lordoglu et al.
DPOAE			
Patient group	2.1	6.1	6.15
Follow up/control	3.2	15.3	6.95
<i>P</i> value	< 0.001	< 0.001	< 0.05
SNR			
Patient group	8	11	17.05
Follow up/control	8.5	14.8	17.45
<i>P</i> value	< 0.06	< 0.01	< 0.01

Table 20 Comparison of average FDP with and after fever has subsided at f3

Ear	FDP with fever	FDP after fever has subsided	<i>P</i> value
RIGHT	2	2.03	< 0.05
LEFT	1.48	1.59	< 0.05

2. left ears were 4 (5.3%) children among them 2 were male and 2 were female.

At f2 frequency, SNR in

1. right ears was found to be bad in 5 (6.6%), 3 were male and 2 were female,
2. left ears was found to be bad in 4 (5.4%) children, among bad SNRs 3 were male and 1 was female.

In children with fever, average FDP at f2 frequency in right ears was 2.21 and average FDP after fever has subsided in right ears was 3.40 (*P* value < 0.01).

The average FDP with fever at f2 frequency in left ears was 2.11 and average FDP after fever has subsided in left ears was 3.09 (*P* value < 0.001) showing a statistically significant difference (Tables 19, 20, 21, 22, 23, 24, 25, 26, 27).

In present study, average DPOAE at 1 kHz improved in children after fever has subsided, which is similar to study by Lordoglu et al. [5] where they examined DPOAE in patient group with fever and in follow up period.

Abdul kadir et al. [1] found that at f2 average FDP was 6.1 in children with fever and 15.3 in children without fever and average SNR at f2 was 11 in children with fever and 14.8 in children without fever.

Lordoglu et al. [5] found that at f2 frequency DPOAE was 6.15 with fever and 6.95 after fever has subsided, SNR at f2 frequency was 17.05 with fever and 17.45 after fever has subsided.

Table 21 Comparison of average DPOAE at 2 kHz (f3) with other studies

	In present study	Abdul kadir et al.	Lordoglu et al.
DPOAE			
Patient group	1.74	4.1	9
Follow up/control	1.8	12.15	9.85
P value	< 0.05	< 0.001	< 0.003
SNR			
Patient group	7.2	12.2	15.75
Follow up/control	7.25	18.5	18.05
P value	< 0.003	< 0.001	< 0.004

Table 22 Comparison of average FDP with and after has subsided at f4

Ear	FDP with fever	FDP after fever has subsided	P value
Right	1.08	1.12	< 0.04
Left	1.03	1.00	< 0.03

Table 23 Comparison of average DPOAE at 4 kHz (f4) with other studies

	In present study	Abdul kadir et al.	Lordoglu et al.
DPOAE			
Patient group	1.05	7	12.5
Followup/control	1.06	13.2	10.7
P value	< 0.04	< 0.01	< 0.002
SNR			
Patient group	6.72	12.5	24.5
Followup/control	6.78	19	24.8
P value	< 0.01	< 0.01	< 0.002

Table 24 Comparison of abnormal DPOAE between three groups based on temperature

Frequency (kHz)	Group1 (100–100.9 F)	Group 2 (101–101.9 F)	Group 3 (> 102 F)
1	0	2	7
1.5	2	15	30
2	9	20	26
4	7	17	34

In study by Abdul kadir et al. [1] who examined DPOAE in children with fever and compared them with healthy control group, DPOAE was decreased in patient group

Table 25 Comparison of DPOAE in study by Lordoglu et al. between mild, moderate and severs groups based on severity scores

Frequency (kHz)	Mild FMF (3–5)	Moderate FMF (6–8)	Severe FMF (9 or > 9)
1	4.05	8.2	3.3
1.4	6.15	8.05	4.75
2	9	11.2	3.7
2.8	7.4	9	2.65
4	12.5	11.9	5.7

Table 26 Comparison of abnormal DPOAE with fever and after fever has subsided at f1,f2,f3 and f4

	With fever	After fever has subsided
F1	9	4
F2	47	7
F3	55	46
F4	58	59

Table 27 Comparison of abnormal SNR with fever and after fever has subsided

Frequency	With fever	After fever has subsided
f1	4	0
f2	9	5
f3	35	33
f4	59	59

compared to control group which proved that there is some relation to damage to inner ear with temperature.

In present study, at f2 all abnormal DPOAE and SNR in children with fever returned to normal levels when fever subsided.

Koybası et al. [6] found increased hearing thresholds, including high frequencies (8000, 10,000, 12,500, and 16,000 Hz) in HFA, and showed decreased distortion products and signal–noise ratios for FMF children, including frequencies (1400–4000 Hz) in the otoacoustic emission evaluation.

In present study, at f3 frequency FDPs in:

1. Right ears were found to be abnormal in 26 (34.6%) 14 were male and 12 were female.
2. Left ears were found to be abnormal in 29 (38.6%) 17 were male and 12 were female.

After fever has subsided, abnormal FDPs at f3 frequency in

1. Right ears were found to be 23 (30.6%) 13 were male, 10 were female.

- Left ears were 23 (30.6%), among them 14 were male and 9 were female.

At f3 frequency, SNR in

- right ears was found to be bad in 20 (26.6%) 15 were male and 5 were female.
- left ears was found to be bad in 15 (20%) children.

Among bad SNRs 12 were male and 3 were female.

In children with fever, average FDP at f3 frequency in right ears was 2 and average FDP after fever has subsided was 2.03 (P value < 0.005).

In children with fever, the average FDP at f3 frequency in left ears was 1.48 and average FDP after fever has subsided was 1.59 ($P < 0.005$) which shows no significant difference.

In present study at f3 abnormal DPOAE are 55 with fever and 50 after fever has subsided, this shows there is no change in abnormal DPOAE even after temperature returned to normal which might indicate permanent damage to outer hair cells due to increased body temperature.

Abdul kadir et al. [1] found that at f3 average FDP was 4.1 in children with fever and 12.15 in children without fever, average SNR at f3 was 12.2 in children with fever and 18.5 in children without fever.

Lordoglu et al. [5] found that at f3 frequency DPOAE was 9 with fever and 9.85 after fever has subsided. SNR at f3 frequency was 15.75 with fever and 18.05 after fever has subsided.

In present study, at f4 frequency FDPs in

- Right ears were found to be abnormal in 29 (38.6%) 18 were male and 11 were female.
- Left ears were found to be abnormal in 29 (38.6%) 17 were male and 12 were female.

After fever has subsided, abnormal FDPs at f4 in

- Right ears were found to be 30 (40%) 18 were male and 12 were female.
- Left ears were abnormal in 29 (38.6%) children among them 18 were male and 12 were female.

At f4 frequency, SNR in

- Right ears was found to be bad in 30 (40%) 19 were male and 11 were female,
- Left ears were found to be bad in 29 (38.6%) children, 18 were male and 11 were female.

In children with fever, average FDP at f4 frequency in right ears was 1.08 and average FDP after fever has subsided was 1.12 ($P < 0.04$).

The average FDP at f4 frequency in left ears was 1.03 and average FDP after fever has subsided was 1.00 (< 0.003) which shows no significant difference.

In present study, at f4 abnormal DPOAE were 58 with fever and 56 after fever has subsided and abnormal SNR were 59 with fever and 59 after fever has subsided, this shows there is no change in abnormal DPOAE and SNR even after temperature returned to normal which might indicate permanent damage to outer hair cells due to increased body temperature.

Abdulkadir et al. [1] found that at f4 average FDP was 7 in children with fever and 13.2 in children without fever; Average SNR at f3 was 12.5 in children with fever and 19 in children without fever.

Lordoglu et al. [5] found that at f4 frequency DPOAE was 12.5 with fever and 10.75 after fever has subsided; SNR at f3 frequency was 24.5 with fever and 24.85 after fever has subsided.

In our study, DPOAE test results were grouped into 3 based on temperature range

- In 25 children at temperature range 100–100.9 F abnormal FDPs in both ears were noted in 2 cases at f2, 9 at f3, 7 at f4 and after temperature returned to normal, abnormal FDP's were noted in only 4 cases at f3 and 7 at f4.
- In 26 children at temperature range 101–101.9 F abnormal FDP's in both ears were found to be 2 at f1, 15 at f2, 20 at f3 and 17 at f4; after fever has subsided abnormal FDP's were 17 at f3 and 17 at f4.
- In 24 children at temperature range > 102 F abnormal FDP's in both ears were found to be 7 at f1, 30 at f2, 26 at f3, 34 at f4 and after fever has subsided abnormal FDP's were 4 at f1, 7 at f2, 25 at f3 and 35 at f4.

Abnormal DPOAE were more at higher temperatures when compared to lower temperatures which shows that there is more damage to inner ear at higher temperatures.

Lordoglu et al. [5] compared DPOAE test results at different frequencies with the disease severity scores. There were statistically significant differences between the patient severity scores at 1.4 and 2.8 kHz frequency. This shows DPOAEs decreased with increasing severity of disease. Mild, moderate and severe FMF patients were divided based on the disease severity scoring system developed by Pras et al. [7]. SNR ratio results at different frequencies were also compared with the disease severity scores. There were no statistically significant differences between the SNR results and the patient severity scores. There were no significant differences between the patient and the control group in respect to age and gender distribution.

DPOAE at f1 and f2 reverted to normal after fever has subsided. At f3 and f4 abnormal DPOAE did not revert, this show at higher frequencies damage to cochlea is more with temperature.

In present study, bad SNRs are more at frequencies f3 and f4, at f1 and f2 abnormal SNRs are less and they were reverted back to normal after fever has subsided. This shows that at higher frequencies damage to the cochlea was present.

Discussion

Abdulkadir et al. [1] in their study “Inner Ear Involvement in Children with Familial Mediterranean Fever” demonstrated that FMF disease may cause hearing loss in children. Various degrees of sensorineural hearing loss (SNHL) can be seen in the progression of some hereditary periodic fever syndromes (HPFS), and FMF is the most common disease of HPFS [13]. Children with familial Mediterranean fever showed decreased distortion products and decreased signal noise ratios in the tested frequencies from 1 to 4 kHz which was attributed to cochlear involvement.

Richardson et al. [2], in their study, “Otoacoustic emissions as a screening test for hearing impairment in children recovering from acute bacterial meningitis” demonstrated the efficacy of OAEs as a screening test for hearing impairment in children with acute bacterial meningitis. Hearing tests were performed in children before discharge from the hospital in an attempt to identify and avoid delays in the diagnosis of postmeningitic hearing loss. Children with bacterial meningitis were recruited from 21 centres, before discharge from the hospital, all patients underwent a thorough audiological assessment consisting of TEOAE, auditory brain stem responses (ABRs), otoscopy, and tympanometry. The results of OAE screening were compared with the ABR threshold. They concluded that OAE screening in children recovering from meningitis was found to be feasible and effective. Inpatient OAE screening helps in early diagnosis of post meningitic hearing loss and prompt auditory rehabilitation.

Lordoglu et al. [5] In their study “Evaluation of cochlear functions in children with Familial Mediterranean Fever” evaluated the cochlear functions in patients with Familial Mediterranean Fever in relation to the disease severity score [15] and treatment duration. They concluded that FMF affects cochlear functions particularly at high frequencies. 50 patients (4–18 years) who had been followed-up with the diagnosis of FMF and regularly receiving appropriate colchicine treatment and 39 healthy controls were included in the study. All the patients and controls evaluated showed that there is improvement in DPOAE in follow up period.

Koybasi et al. [6], in their study “Cochlear involvement in Familial Mediterranean Fever” assessed the cochlear functions in children with FMF and also investigated the

correlation between the hearing levels and some clinical features of FMF including the duration of the disease, age at onset, genetic analysis and colchicine use. Thirty-four children with FMF and 27 age matched children were included in the study. Audiological results of the two groups were compared and correlation between the audiological status and clinical parameters of the disease like the duration of disease, age at onset, mutations and colchicine treatment were studied. This study showed increased hearing thresholds at higher frequencies in FMF children in audiometry together with decreased distortion products and signal–noise ratios demonstrated by DPOAE testing.

Seifert et al. [8] in their study, “The influence of body temperature on transient evoked otoacoustic emission” concluded that there was a clear influence of body temperature on the amplitudes and reproducibilities of the TEOAEs. In their study they concluded the relationship of temperature and amplitude or reproducibility of otoacoustic emissions, during the cooling phase was significantly different from that during rewarming. Their results suggest a hysteresis in the relationship between the amplitude of TEOAE and temperature [13].

Ferber-Viart et al. [9] studied the influence of hyperthermia on cochlear micromechanical properties in humans. They investigated the effect of body temperature on OAEs. The reduction in OAE found in hyperthermia suggests that temperature-dependent mechanisms are involved in the generation of TEOAEs.

Cevik et al. [10] in their study “Determination of hearing levels in patients with Familial Mediterranean Fever” aimed to investigate hearing levels and cochlear functions by using DPOAE and High Frequency Audiometry (250–20,000 Hz) in pediatric patients with FMF. In children with FMF, Pure tone audiometry values, hearing values obtained at all frequencies from 250 to 20,000 Hz, and Distortion product Otoacoustic Emissions levels were within normal range.

Schmutzhard et al. [11] demonstrated that severe malaria in children leads to a significant impairment of TEOAE. Their study analyses OAEs in patients with severe malaria up to the age of 10 years. They included 144 patients with severe malaria and 108 control children. The present study shows 40% of children have involvement of the inner ear early in severe malaria. The severe non-cerebral and cerebral malaria may lead to a significant impairment of the inner ear function in the acute stage of the disease. Through the course of disease there was further impairment of the OAE in the cerebral malaria group. Cerebral malaria is known to influence the blood–brain barrier. Similar disturbance of the blood labyrinth barrier has been observed in an animal model of cerebral malaria.

Foust et al. [12] in their study “Using Otoacoustic Emissions to Screen Young Children for Hearing Loss in

Primary Care Settings” found that OAE screening was an effective method to identify young children with permanent hearing loss in primary care settings. Their study examines the efficacy of integrating OAE hearing screening into services routinely provided in health care settings. Subjects included were 846 children who were screened during routine visits to their primary care providers using a DPOAE instrument. The results of this study reinforce the importance of hearing screening during early childhood to identify children with post neonatal permanent hearing loss as well as providing further screening and diagnostic services to infants who were not screened at birth or who did not pass the newborn screening and were subsequently lost to follow-up.

Vasconcelos et al. [13] in their study “Transient evoked otoacoustic emissions and distortion product in school children” compared the results of suspected hearing loss, through the examination of TEOAE and by DPOAE using data from audiometric exams; and observed which of the procedures of EOAE better respond to school children triage. Audiometry and acoustic impedance were performed on the children who presented alterations at any point during the TEOAE and/or DPEOAE exams. They did a statistical comparison between the examinations that failed only the TEOAE and DPOAE with the results from audiometric examinations; they did not find any significant difference.

Neely et al. [14] in their study “Distortion-product otoacoustic emission input output characteristics in normal-hearing and hearing-impaired human ears” observed characteristics of DPOAE input/output functions are consistent with the loss of cochlear compression that is typically associated with mild-to-moderate hearing loss. They proved that DPOAE will alter in cochlear involvement.

Angeli et al. [15] in their study “Comparative study between school performance of first grade children and suppression of otoacoustic transient emission” studied the auditory function and most specifically that of auditory communication in children. This study aims at checking the lack of OAE inhibition on the right ear by a contralateral stimulus, which can be used as screening tool or when the physician suspects of auditory processing dysfunction seen when children between 6 and 12 years of age under perform at school.

Keogh et al. [16] in their study “Distortion-Product Otoacoustic Emissions in Schoolchildren: Effects of Ear Asymmetry, Handedness, and Gender”—examined effects of ear asymmetry, handedness, and gender on DPOAEs obtained from schoolchildren. The results revealed a small but significant difference in SNR between ears, with right ears showing a higher mean SNR than left ears at 1.9, 3.0, 3.8, and 6.0 kHz. At these frequencies, the difference in mean SNR between ears was less than 1 dB. A significant

gender effect was also found. Girls exhibited a higher SNR than boys at 3.8, 4.8, and 6.0 kHz. They concluded that the reasons for the ear asymmetry effect in DPOAEs are, as yet, unclear. It is possible that the slightly poorer hearing sensitivity in the left than in the right ear could result in an ear asymmetry effect.

Botelho et al. [17] in their study “Prevalence of hearing impairment in children”—underlined the importance of early audiological testing. This study describes the prevalence of hearing loss and the features of children born in a tertiary reference hospital and monitored in an outpatient clinic for patients discharged from that hospital. The population and healthcare professionals involved in childcare should be made aware of the impact of hearing loss; this could result in increased adhesion to neonatal screening programs.

Christensen et al. [18] in their study “A pass/refer criterion for screening newborns using DPOAEs” established a pass/refer criterion for OAEs. When screening infants or children for hearing loss using OAEs, they established a single pass/refer criterion that minimized referrals of babies with normal hearing (false positives), yet maximized the likelihood that babies with actual hearing loss will be identified (test sensitivity). They used OAEs and SNR to derive pass or refer criterion.

Borin and Cruz [19] in their study “Study of distortion-product otoacoustic emissions during hypothermia in humans” evaluated the function of cochlear outer hair-cells under the influence of extra-corporeal circulation and moderate hypothermia during cardiac surgery. DPOAE were registered before surgery, immediately after general anesthesia induction, during extra-corporeal circulation with moderate hypothermia and after the surgical procedure. Comparison of response-amplitudes before and after surgery and before and after general anesthesia initiation did not demonstrate statistical difference. Comparison of amplitudes before and after extra-corporeal circulation with moderate hypothermia demonstrated a statistically significant decrease in responses amplitudes during hypothermia. In this study they concluded that the amplitudes of DPOAE decreased during moderate hypothermia induced during extra-corporeal circulation.

Patel et al. [20] demonstrated that OAEs can be used as a neonatal screening tool as well as for the evaluation of a suspected paediatric population to help diagnose childhood hearing impairment at a very early stage, allowing for the 18 rehabilitation of the child within the critical period for speech and language development.

Aydin et al. [21] investigated the influence of extreme hypothermia on DPOAE. DPOAE measurements were performed preoperatively, several times intraoperatively, and postoperatively. They found that inner ear functions diminished with the degree of hypothermia and returned to

normal with warming. They concluded that hypothermia causes a transient loss of inner ear functions.

VeUILlet et al. [22] investigated the influence of hypothermia on TEOAEs in humans and concluded that the motile properties of outer hair cells (OHCs), that are related to TEOAEs, are temperature-sensitive.

O'Brien [23] in their study "Temperature dependency of the frequency and level of a spontaneous otoacoustic emission during fever" found that there was clear evidence of inverse relationship between temperature and both the frequency and level of the emission. The occurrence of fever was due to simple urinary tract infection and was considered to be without ototoxic implication; there was no associated worsening of pure tone threshold nor change in measurements of middle ear function. Temperature measurement was obtained with a thermometer measuring infra-red radiation from the ear-drum, indicative of body core temperature.

Poornima et al. [24] in their study "Hearing evaluation for neonates with hyperbilirubinemia using otoacoustic emission and brain stem auditory evoked response" showed that by detecting the hearing loss in time with screening methods we can ensure normal language development by appropriate intervention like hearing aids and infant stimulation. It is important to identify and evaluate the jaundice early to prevent complications like bilirubin encephalopathy leading to hearing loss. They used otoacoustic emission and brain stem auditory evoked response and the results will be analyzed to look for the effectiveness of using otoacoustic emission for mass screening.

Santos-Sacchi and Huang [25] studied the temperature dependence of outer hair cell motility-related gating current and capacitance under whole-cell voltage clamp. Temperature change caused a shift of these voltage-dependent functions along the voltage axis. They concluded that such temperature-dependent effects on the outer hair cells may mediate known temperature effects on in vivo cochlear physiology.

In the mammalian cochlea, motile properties of outer hair cells may contribute to sharp tuning and amplification. Length changes of isolated outer hair cells in response to various physical and chemical stimuli have therefore been investigated by many laboratories. Alteration of temperature changes the length of outer hair cells of the guinea pig cochlea as much as $0.22 \mu\text{m}/^\circ\text{C}$. Length changes in response to alterations of temperature are similar to length changes in response to other physical and chemical stimuli. [26]

Avan et al. [27] in their study found that Distortion product otoacoustic emissions emitted by the cochlea at 2 f1–f2 in response to pairs of pure tones at f1 and f2 (DPOAE) form a class of otoacoustic emissions and as such, are viewed as a reliable tool for screening outer hair cell (OHC) dysfunctions on a pass/fail basis.

Paul [28] in their study conducted in a tertiary care hospital in Cochin compared hearing loss incidence between high risk and well babies using OAE as screening tool which showed 21(1%) babies with hearing loss out of 2031 in high risk group and 8 (0.09%) babies with hearing loss out of 8134 in well babies.

OAE screening is used widely in newborn hearing screening programs, it holds great promise in screening infants and children for permanent hearing loss because it is:

- a. Objective and independent of child's behaviour;
- b. Painless;
- c. Portable, reliable and efficient;
- d. Simple to administer with an appropriate protocol [29].

In our study 75 children satisfying the inclusion criteria were screened using OAE. Mean age of the study population was 8.4 years. Out of the 75 children studied 43(57.3%) were male and 32(42.7%) were females which is similar to the study conducted by Lordoglu et al. [5] with male predominance and mean age of patient was 11.1 years. While analyzing the study population, they were grouped based on temperature range into:

- a. Group 1(100–100.9 F).
- b. Group 2(101–101.9 F).
- c. Group 3(> 102 F).

Group 1 includes 25 children, Group 2 includes 26 children, Group 3 includes 24 children. The age group of children in this study was 5–14 years. Mean temperature of children in study group was 101.4 F. Mean temperature in the study group was 98.0 F after fever subsided.

In this study, oto-acoustic emissions of 75 children were examined with hyperpyrexia and after temperature returned to normal, FDP were tabulated at f1, f2, f3 and f4. The FDP and SNR values were tabulated based on the pass or refer criterion by Christensen et al. [18].

Conclusion

Hearing impairment in children across the world constitutes a particularly serious obstacle to their optimal development and education, including language acquisition. Deaf and hearing-impaired children often experience delayed development of speech, language and cognitive skills, which may result in slow learning and difficulty progressing in school. Many studies worldwide showed the involvement of inner ear in hyperpyrexia (Malaria, FMF, Bacterial Meningitis etc.).

The diagnosis of hearing loss early in the life allows the opportunity to begin early intervention services for families

with disabled children. Otoacoustic emissions are the most sensitive tests for screening although it may have to be combined with other tests for complete diagnosis [30].

Brainstem Evoked Response Audiometry (BERA), though highly reliable, requires high technical expertise, which is more expensive as opposed to OAE. Also BERA makes use of a cumbersome machine whilst the OAE screener is a portable machine.

In our study, children with hyperpyrexia were screened using for OAE and compared with results of OAE in same children after fever had subsided. Among 150 ears in 75 children OAE results at 4 frequencies were compared with OAE results once fever had subsided. Abnormal DPOAE were more in children with fever at higher frequencies f3 and f4 when compared with lower frequencies.

The results show that there is relation between temperature and inner ear functions, which might be due to cochlear involvement.

In a similar study OAE in children having FMF with the control group, they observed OAE in children with fever are lower when compared with control group. They concluded that this might be due to cochlear involvement.

Use of OAE to test for hearing loss is less time consuming, simple procedure, cost effective and its sensitivity and specificity in detecting hearing loss is around 85–100 and 78.2–95% as quoted by different studies.

The screening procedure should be streamlined and can be used to test children with fever thereby an attempt to diagnose hearing loss in children without any risk factors can be made. As the procedure is not cumbersome health care professionals can be easily trained about the procedure, also it is less time consuming. Thereby, large number of population can be screened. Use of OAE to screen the children helps to diagnose hearing loss early and helps to rehabilitate the child early, making a marked improvement in the literary, social, academic and most of all self confidence in their future.

Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interests, financial or otherwise.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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