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REVIEW ARTICLE

The Efficacy of Extended High-Frequency Audiometry in Early Detection of Noise-Induced Hearing Loss: A Systematic Review and Meta-Analysis

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ABSTRACT
Early detection of noise-induced hearing loss is important to prevent the extension of hearing loss to speech frequencies. This study was assessed the efficacy of high frequency audiometry for early detection of NIHL by a systematic review of literature and meta-analysis. A systematic literature search was performed in Medline, Scopus, ISI web of science, EMBASE, CINAHL, Health star, and Ovid databases. Mean difference between hearing threshold in conventional and high frequencies was considered as the effect size. Pooled and stratum-specific MD was estimated. The number of 23 and 11 systematic review and meta-analysis studies were entered respectively throughout 3031 articles which initially searched. Since mean difference was higher in exposed subjects than non-exposed ones in most hearing frequencies, therefore, the effect size was higher in high frequencies, though not statistically significant. High frequency audiometry cannot be considered as a method for early detection of NIHL.

KEYWORDS: *NIHL, pure-tone audiometry, high-frequency audiometry, conventional-frequency audiometry*

INTRODUCTION

Noise, as a physical hazard, is a common environmental and occupational exposure [1-2]. Many workers in various workplaces were exposed to noise; e.g. 28% of the workers in the European Union and more than 5.7 million workers in manufacturing industries in the US are exposed to hazardous noise [3-4].

Noise affects hair cells in the organ of Corti which are placed in the cochlea in a frequency-sensitive manner. The damage to hair cells may be due to metabolic, mechanical or vascular mechanisms [5-6]. This injury begins at the basal end of the organ of Corti where hair cells sensitive to high frequencies of hearing are placed [5,7-8]. Basal region of cochlea is more vascularized, so it is probably prone to the effect of vascular damage [9]. Exposure to noise may induce some health effects, especially noise-induced hearing loss (NIHL). This will mostly happen when noise level is higher than 85 dBA, the threshold limit value (TLV) for this physical exposure [10]. After presbycusis, NIHL is the most common acquired sensorineural hearing loss with a high prevalence [11-13]. Ten million workers in the US were estimated to suffer from this disorder [14].

NIHL is a permanent and irreversible, but preventable disorder which develops gradually during years [15-16]. The conventional frequencies

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most commonly affected by noise include 3, 4 and 6 KHz [5,17- 18], but the defect may extend to speech frequencies (i.e., 0.5, 1, 2, and 3KHz) as well, with possible functional problems [19-21]. A method for prevention of NIHL is early detection of disorder before onset of clinical disease, which can help to prevent the extension of hearing loss to speech frequencies [22]. Hearing conservation program of Occupational Safety and Health Association (OSHA) obligates the workers exposed to noise levels ≥ 85 dBA (8-hour time-weighted average) to be periodically screened for their hearing status. This screening program was usually applied to test the noise-exposed workers by pure-tone audiometry (PTA), measuring hearing thresholds at 0.5, 1, 2, 3, 4, 6 and 8 KHz frequencies, i.e. by conventional frequency audiometry (CFA), in routine occupational health evaluations [23].

Although there is not a consensus about the best screening method for early detection of NIHL, some methods other than CFA, such as otoacoustic emissions (OAEs) and high-frequency audiometry (HFA) have been proposed for detection of NIHL in an earlier stage [24-26].

Ultra-audiometric or extended high frequency (EHF) range of hearing test was introduced in the early 1960s as a method of assessing auditory system [27], and some studies assessed its validity and accuracy [28-29]. It was then assumed that some types of hearing loss (especially due to noise and ototoxic substances) may be identified by HFA, earlier than conventional audiometry, so it can be more sensitive to the effects of noise on hearing [13-30].

If it is proved that HFA is more sensitive than conventional audiometry to noise effects, it has value to perform HFA for the screening of noise-exposed workers, so clinical NIHL and its impact on normal function of the individuals could be prevented.

Most studies performed on this subject have cross-sectional or historical cohort designs. In the current study only one review which has assessed only 6 studies in this field and has failed to show that HFA can detect NIHL in an earlier stage than CFA was found [31].

This study was designed to assess the efficacy of HFA for early detection of NIHL comparing CFA by a systematic review of literature and meta-analysis.

MATERIALS AND METHODS

A systematic literature search was performed in Medline, Scopus, ISI web of science, EMBASE, CINAHL, Health star, and Ovid databases for available resources on “efficacy of HFA in early detection of NIHL”. The literature was searched from inception to30.6.2016.

Combination of MeSH and non-MeSH key words related to HFA(i.e. “high-frequency audiometry”, “high frequency audiometry", "HFA", "high-tone audiometry", and “high tone audiometry”), CFA (i.e. “pure-tone audiometry”, “pure tone audiometry", "PTA", "conventional audiometry", "conventional frequency audiometry", and "CFA"),NIHL (i.e. “noise-induced hearing loss", "noise induced hearing loss", "NIHL", "occupational hearing loss", "noise-induced hearing impairment", "noise induced hearing impairment", "noise-induced deafness", and "noise induced deafness") and early detection(i.e. “early detection”, "efficacy”, and "early diagnosis")were used to search selected databases.

STUDY SELECTION:

All original studies comparing hearing thresholds obtained by CFA and HFA, with sufficient data about exposure and outcome of interest were entered to the review. Non-English resources were checked for eligible studies if their references were available in English. Abstracts, editorials, case reports, ecologic studies, and review articles were excluded. After duplicates removal, titles and abstracts were evaluated by two independent reviewers (A.F. and A.H.M.). In the case of inconsistency between reviewers, the third reviewer (M.J.Z.S) assessed the eligibility criteria of the study. Studies with sufficient data (mean difference and standard deviation of hearing threshold between conventional and high frequencies) were also entered the meta-analysis. For studies that did not report a necessary data explicitly, but reported sufficient data in a graph. In current study the exact value using Web Plot Digitizer software Version.2.4 was extracted [32]. In addition, study-specific information such as study design, geographic location of the study, type of occupation, exposure source (e.g. recreational or occupational) were abstracted and the hearing frequencies which thresholds were measured in the study.

STATISTICAL ANALYSIS:

Mean difference between hearing threshold

(in dBA) in conventional frequencies (0.25 KHz to 8 KHz) and high frequencies (9 KHz to 20 KHz) was considered as the effect size. Mean difference standard deviation was calculated based on Cochrane handbook. Given known conceptual heterogeneity among studies, fixed effect model wasn't used to estimate a mean difference (MD); rather, uni-variable random effect analysis was used to assess the pooled effect size. Dersimonian and Laird random-effects models were used to estimate pooled and stratum-specific MD and 95% confidence intervals (CIs). Stratum-specific heterogeneity was assessed using the P-value for Cochrane's Q (where α=0.20 given the low power of this test) and quantified by I^2 statistic.

In addition, a random-effects meta-regression analysis was applied to assess the association among hearing threshold MD and type of noise exposure, age and working duration.

According to the results of heterogeneity tests, meta-regression was performed under random effects model.

RESULTS

having considered aforementioned search strategy 3031 articles initially searched, then 23 studies fulfilled the inclusion criteria and were included for final evaluation in the review [1, 2, 5, 8, 13, 17, 18, 19, 21, 22, 33, 24-26, 34-42] and 11 studies [1, 5, 8 ,13, 24-26, 34, 36, 37, 41] were included in meta-analysis (Figure 1).

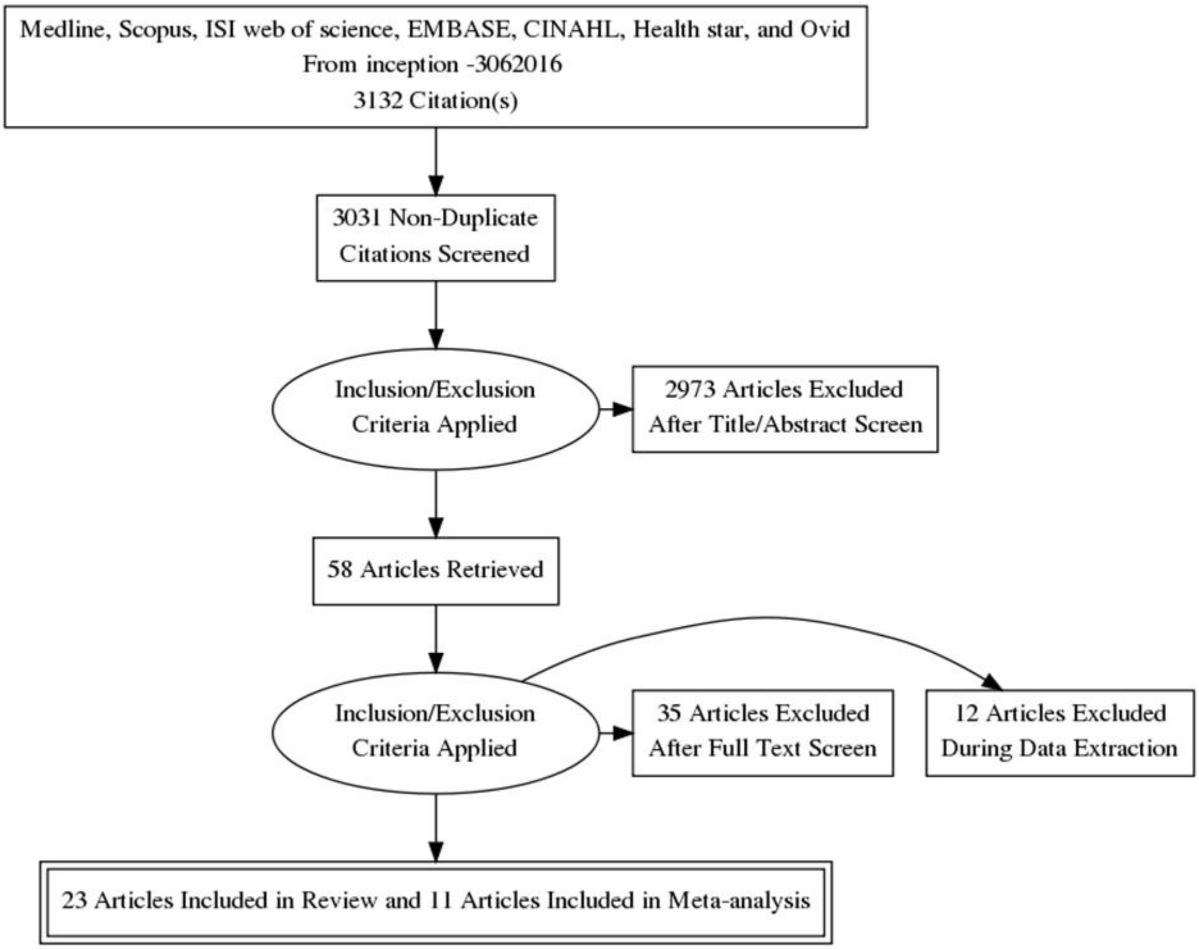

Figure 1. Flowchart of study selection for review and meta-analysis.

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Methodology of the studies:

All the included studies were retrospective with cross-sectional or historical cohort designs and compared CFA (frequencies between 0.25 and 8 KHz) and HFA (frequencies between 9 and 20 KHz) for measuring hearing thresholds and detection of NIHL (Table 1). All studies were performed in adults exposed to continuous noise, though with different noise intensities. All studies were selected occupational noise-exposed subjects, except for three studies which were assessed recreational noise exposure, and exposure to music. All studies were assessed permanent threshold shift (PTS).

Routine conventional frequencies (0.25, 0.5, 1, 2, 3, 4, 6, and 8 KHz) were tested in all studies, except for Korres et al. and Wang et al. in which 3 and 6 KHz frequencies were not assessed; but there was more diversity in high frequencies which were tested. The only high frequency which was assessed in all studies was 12 (12.5) KHz followed by 14 KHz. Most studies assessed both ears concurrently, but eight studies provided the data for each ear separately [1, 2, 5, 24, 25, 26, 37, 38, 41].

The effect of age on HFA was considered in few studies. Ahmed et al., da Rocha et al., Lopes et al., Schwarz et al., and Somma et al. considered age as a confounding factor for NIHL and performed subgroup analysis in different age groups. Goncalvez et al., 2015 controlled the effect of age on hearing for aerial tone hearing thresholds of 0.5 to 8 KHz, using I.S.O 1999 criteria; and Riga et al. performed subgroup analysis according to work history (years of employment). The methodologic characteristics of the studies have presented in Table 1.

Noise exposure and audiometric evaluations information have shown in Table 2. In order to find the effect of noise on HFA, da Rocha et al.,Le Prell et al., and Sliwinskaet al. selected noise-exposed subjects with normal CFA, and Ahmed et al. separately analyzed a group of noise-exposed workers with normal CFA.

Mean difference (MD) between high and low frequencies was higher in exposed subjects than non-exposed ones in most hearing frequencies, though with a high level of heterogeneity between different studies (Table 3)

Table 1. Methodology characteristics of the studies*

First author (date)	Design	Number of cases		Gender	Age range (Mean), y	Work Experience, y	Inclusion Criteria	Exclusion Criteria
		Exp.	Nexp.					
Osterhammel (1979)	NR	28	-	M	30-59 (45.09)	NR	NR	NR
Fausti (1981)	NR	22	30	NR	20-29 (25)	NR	Age: 20-29 y	CHL, ototoxicity
Hallmo (1994)	Cross-sectional	167	-	M	18-59 (NM)	NR	NR	hearing loss due to heredity, previous ear disease, ototoxicily or injury
Ahmed (2001)	Cross-sectional	184	52	M	18-49 (28.4)	NR	NR	CHL
Sliwinska (2002)	NR	17	12	M	21-35 (26.3±4)	0.5-5	Normal ENT examinations, no ear disease	NR
Schwarze (2005)	Cross-sectional	482	-	M/F	32-69 (57.5)	NR	NR	CHL, suspected Menière, suspected retro cochlear defects, sudden deafness
Schmuziger (2007)	Cross-sectional Cohort	16	-	M/F	27-49 (35.5±6.8)	17±8	Non-professional musician, work experience> 5 ys	acoustic trauma, occupational noise exp., CHL, ototoxicity, familial hearing loss
Singh (2008)	Cross-sectional	20	50	M/F	13-65 (39)	NR	NR	NR
Wang (2008)	Cross-sectional	36	20	M	26-41 (32.8)	NR	NR	NR
Somma (2008)	Cross-sectional	186	98	M	21-60 (39.8)	NR	Work experience> 1 y	CHL, familial hearing-related diseases, ototoxic drug use, firing guns, abnormal orthoscopic examination
Korres (2008)	NR	139	32	M/F	24-54 (41.9±9.4)	11.8±6.9	Age < 55 years	active or previous ear infections, hx of head injury, aminoglycoside medication or exp.to other sources of noise, family hx of hearing loss
Riga (2010)	Prospective	151	-	M	24-55 (41.9±9)	11.8 ±6.9	Age<55 y	previous or active ear infections, hx of head injury, intake of ototoxic drugs or exposure to other sources of noise, family hx of hearing loss, hx of neurological disorders, Ménière disease

da Rocha (2010)	Cross-sectional cohort	47	33	M	30-49 (NR)	NR	NR	NR
Mehrparvar (2011)	Historical cohort	120	120	M	NM (33.64±5.22)	10.72±5.01	Age<50y	hx of acoustic trauma, CHL, exp. to ototoxic substances or drugs
Ottoni (2012)	Cross-sectional cohort	347	-	M	NR	NR	≥ 1 year employment, age range: 19 - 65 y	Occupational noise exp., working directly with chemicals; using ototoxic drugs, hx of high frequency acoustic trauma
Lopes (2012)	Cross-sectional	108	-	M/F	17-59 (35.59)	NR	professionals in dentistry with ≥ 2 years of experience	hx of diseases e.g. mumps, HTN, diabetes, meningitis, HIV, syphilis, and other conditions that can compromise hearing and/or pre-existing hearing impairment
Goncalvez (2013)	Historical cohort	50	44	M	21-51 (34.9±7.8)	1-29 (14.2± 7.7)	NR	compromised middle ear
Le Prell (2013)	Cross-sectional	87	-	M/F	18-29 (21.6)	NR	Normal PTA and tympanometry	CHL
Sulaiman (2014)	NR	35	35	M/F	NM (22.8±2.3)	NR	Age: 18–30 y, using PLDs coupled with headphones ≥ 1 year, listening to a PLD ≥ 1 h/day	Hx of ear disease, ototoxicity, occupational noise exp.
Mehrparvar (2014)	Cross-sectional	142	121	M	NR (35±6.33)	10.76±5.52	Age<50	Hx of acoustic trauma, exp. to ototoxic substances or consuming ototoxic drugs, and smoking
Lüders (2014)	Retrospective cohort	42	42	M/F	18-58 (26)	NR	Being a music student	conductive and/or sensorineural hearing disorders not associated with noise exp.
Macca (2014)	NM	113	148	M/F	19-86 (39.88±9.99)	0.5-47 17.62±10.85	NR	NR
Gonçalves (2015)	Historical cohort	40	40	M/F	23-61 (40.55±9.87)	1-39 (16.32±9.67)	NR	CHL

* Abbreviations: NR: not reported; Exp: Exposed; Nexp: Non-exposed; CHL: conductive hearing loss; Hx: history

Table 2. Information about noise exposure and audiometric evaluations and findings of the studies*

First author	Job/ Industry	Noise level (dBA)	Noise abstinence (h)	Audiometer		Headphone		Audiometric frequencies (KHz)		Findings
				CFA	HFA	CFA	HFA	CFA	HFA	
Osterhammel	NR	NR	NR	Madsen OB-70	NR	NR	NR	0.25, 0.5, 1, 2, 4, 8	12, 14, 16, 18, 20	It is of value to use HFA before exposing young persons to noisy work
Fausti	Military veterans	NR	NR	Grason-Stadler 1701	General Radio 1312	TDH 49	Koss HV/1A	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20	HFA holds promise for better early detection, description,and differentiation of NIHL
Hallmo	Military personnel and civilians	NR	NR	Madsen OB70	Interacoustics ASlOHF	TDH39	Koss HV/lA	NR	10, 12, 14, 16, 18	EHF thresholds are of the same order of magnitude for all age groups in the more severe grades of CF NIHL. The younger age groups maintain an EHF threshold superiority in the lesser grades of CF NIHL
Ahmed	Steel pipes, Air conditioner	>85	14	Grason-Stadler GSI 16	Interacoustic AS10HF	TDH-50P	Koss HV	0.25, 0.5, 1, 2, 4, 8	10, 12, 14, 16, 18	HFA is an early indicator of NIHL and is more reliable than CFA (4 KHz hearing loss) especially at early stages
Sliwinska	Metal	85-92	48	Interacoustic AC40	Interacoustic AC40	TDH39	Koss HV-PRO	0.125, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	Hearing thresholds at HFA was higher than conventional frequencies in both noise exposed and non-exposed individuals
Schwarze	NR	NR	NR	NR	NR	NR	NR	0.125, 0.25, 0.5, 1, 1.5, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	This study do not indicate that a loss of hearing capacity at HFA may give relevant information for a possible risk of developing NHIL in conventional audiometry
Schmuziger	Non-professional Musicians	NR	36	Audiocare	NR	Sennheiser HDA 200	NR	0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14	HFA does not seem advantageous as a means of the early detection of noise-induced hearing loss
Singh	Various	NR	NR	Interacoustic AC40	Interacoustic AC40	TDH39	Koss HV	0.5, 1, 2, 4, 6, 8	10, 12, 14, 16, 18, 20	HFA is useful in detecting early NIHL especially in young subjects
Wang	Military pilots	NR	NR	Madsen OB922	Madsen OB922	NR	NR	0.25, 0.5, 1, 2, 4, 8	10, 12.5	HFA, along with some other variables may be objective indicators of early NIHL. 4 KHz is more sensitive than HFA for early detection of NIHL.
Somma	Cement workers	>85	18	Amplaid A319	Amplaid A319	TDH-49	Sennheiser HDA200	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16, 18	EHFA may represent a useful tool for the detection of early sub-clinical changes of NIHL in the workplace, mainly in young workers (<40)

Korres	Food industry	92-93	24	Amplaid A321	Amplaid A321	TDH-49	Sennheiser HDA200	0.25, 0.5, 1, 2, 4, 8	10, 12.5, 14, 16, 18, 20	EHF audiometry is a useful adjunct to conventional audiometry in the audiological assessment of subjects exposed to occupational noise, but there is greater variability in the results compared with conventional audiometry
Riga	Food processing	90-110	NR	Amplaid A321	Amplaid A321	TDH-49	Sennheiser HDA200	0.25, 0.5, 1, 2, 4, 8	10, 11.2, 12.5, 14, 16, 18	EHF audiometry is able to identify the first deleterious effects of occupational noise exposure, much earlier than conventional audiometry
da Rocha	Military firefighters	NR	14	Interacousti c AC40	Interacoustic AC40	TDH39P	Koss HV/PRO	-	9, 10, 11.2, 12.5, 14, 16	Study data reinforce the importance of studying high frequencies, even with normal conventional audiometry in the early detection of NIHL
Mehrparvar	Textile	>85	16	Interacousti c AC40	Interacoustic AC40	TDH39	Koss R80	0.25, 0.5, 1, 2, 3, 4, 6, 8	10, 12, 14, 16	HFA is more sensitive to detect NIHL than conventional audiometry
Ottoni	stone, wood, metal and cement	>85	14	Interacousti c AD40	Interacoustic AD40	TDH39	Koss HIPRO	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 12, 14, 16	The use of HFA yielded an early detection of hearing damage
Lopes	Dentistry	NR	NR	Siemens SD50	Siemens SD50	HDA200	HDA200	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	HFA has greater sensitivity for the early detection of hearing problems
Goncalvez	Military musicians	91-96.3	14	Interacousti c AC40	Interacoustic AC40	TDH39	Koss HVPRO	0.5, 1, 2, 3, 4, 6, 8	9, 10, 11, 12.5, 14, 16	Exposure to music causes hearing loss both in CFA and HFA with higher thresholds in HFA than CFA in individuals older than 30 years old
Le Prell	College students	NR	48	Grason-Stadler GSI 61	Grason-Stadler GSI 61	EAR 3A	Sennheiser HAD 200	0.25, 0.5, 1, 2, 3, 4, 6, 8	10, 12.5, 14, 16	Utility of EHF threshold for monitoring “pre-clinical” changes in auditory function remains unclear
Sulaiman	PLDs users	NR	24	Siemens, SD28HF	NR	NR	Sennheiser HDA200	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	HFA can show hearing loss in an early stage compared to conventional audiometry in PLD users
Mehrparvar	Tile workers	91.97	16	Interacousti c AC40	Interacoustic AC40	TDH39	Koss R80	0.25, 0.5, 1, 2, 3, 4, 6, 8	10, 12, 14, 16	HFA is a useful method for early diagnosis of NIHL compared to conventional audiometry
Lüders	Music students	NR	14	Madsen Itera II	Madsen Itera II	TDH 39P	Sennheiser HDA200	0.25, 0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	Sporadic high-frequency threshold assessment can be useful in early detection of hearing loss in musicians
Macca	Textile, metal, cement, building	NR	16	Labat Audiopack	Labat Audiopack	NR	Sennheiser HD 500	2, 3, 4, 6, 8	9, 10, 11, 12, 13, 14, 15, 16, 17, 18	HFA could be useful in the early diagnosis of NIHL particularly in young subjects
Gonçalves	Dentists	NR	14	Madsen Itera II	Madsen Itera II	NR	Sennheiser HD 200	0.5, 1, 2, 3, 4, 6, 8	9, 10, 11.2, 12.5, 14, 16	There is no significant difference between hearing thresholds at high and conventional frequencies

* NR: not reported; CF: conventional frequency; HFA: High-frequency audiometry; NIHL: Noise-induced hearing loss

Table 3. Heterogeneity of results in the studies in selected conventional and high frequencies.*

Frequency (KHz)	Group	N	Studies	MD	95%CI	I^2 (%)	P
18 and 3	Nexp	339	8, 13, 43	24.50	14.94 – 34.12	99.6	<0.001
	Exp	277		19.83	15.07 – 24.59	97.7	<0.001
	Total	616		20.75	16.50 – 25.02	99.2	<0.001
18 and 4	Nexp	845	5, 8, 13, 36, 43	40.31	28.19 – 52.44	99.4	<0.001
	Exp	418		35.05	24.73 – 45.31	99.8	<0.001
	Total	1263		37.24	29.39 – 45.08	99.7	<0.001
18 and 6	Nexp	528	8, 13, 43	20.93	10.85 - 31.00	99.4	<0.001
	Exp	190		15.00	9.13 – 20.88	97.9	<0.001
	Total	718		16.50	11.43 – 21.58	99.1	<0.001
16 and 3	Nexp	1453	1, 8, 13, 27, 28, 29, 38, 39, 43	18.85	18.24 – 30.50	98.3	<0.001
	Exp	1212		24.37	15.07 - 22.51	99.58	<0.001
	Total	2665		20.93	17.17 – 24.69	99.44	<0.001
16 and 4	Nexp	1731	1, 5, 8, 13, 27, 29, 36, 38, 39, 42, 43	23.21	18.06 – 28.37	98.53	<0.001
	Exp	1276		25.00	19.47 – 30.53	99.41	<0.001
	Total	3007		20.04	20.27 - 27.81	99.27	<0.001
16 and 6	Nexp	1453	1, 8, 13, 27, 29, 38, 39, 42, 43	15.92	10.85 – 20.99	97.97	<0.001
	Exp	1212		19.69	12.75 – 26.63	97.89	<0.001
	Total	2665		17.23	13.14 – 21.33	98.35	<0.001
14 and 3	Nexp	1453	1, 8, 13, 27, 29, 38, 39, 42, 43	13.80	9.72 – 17.88	98.2	<0.001
	Exp	1212		15.80	12.96 – 18.65	98.0	<0.001
	Total	2665		15.15	12.81 - 17.48	98.1	<0.001
14 and 4	Nexp	1731	1, 5, 8, 13, 27, 29, 36, 38, 39, 42, 43	15.21	11.1 – 19.33	97.92	<0.001
	Exp	1276		16.31	13.31 – 19.30	98.08	<0.001
	Total	3007		15.91	13.51 – 18.35	98.34	<0.001
14 and 6	Nexp	1453	1, 8, 13, 27, 29, 38, 39, 42, 43	10.94	6.76 - 15.13	97.69	<0.001
	Exp	1212		11.28	8.07 – 14.48	97.95	<0.001
	Total	2665		11.15	8.61 - 13.70	98.16	<0.001

* N: total number of cases considering subgroup analysis; MD: Mean difference; CI: confidence interval; Nexp: non-exposed, Exp: exposed

Meta-analysis:

Meta-analysis on 11 studies was conducted for three selected high frequencies (14, 16 and 18 KHz) paired with three most important conventional frequencies including 3, 4 and 6 KHz totally led to 9 separate comparisons. Data from five studies with missing data about SD or other relevant measure of dispersion were also excluded from meta-analysis. A sub-group analysis regarding age was also performed for all studies (Table 4).

Table 4. The results of sub-group analysis in different frequency pairs based on exposure pattern and age group of studies.

Frequency pair	Exposure	Age group	Studies	N	MD (95% CI)	p- value
18 vs 3	Yes	<30	13, 43	45	13.43 (0.39; 26.48)	0.480
	Yes	>30	13, 43	209	18.73 (11.96; 25.49)	
	No	<30	8, 13, 43	83	31.51 (-5.2; 68.22)	0.657
	No	>30	13, 43	112	22.82 (11.54; 34.1)	
18 vs 4	Yes	<30	13, 36, 43	68	51.54 (3.49; 99.59)	0.183
	Yes	>30	5, 13, 43	268	18.68 (13.04; 24.32)	
	No	<30	8, 13, 36, 43	156	58.3 (24.24; 92.36)	0.106
	No	>30	5, 13, 43	390	29.02 (19.05; 38.99)	
18 vs 6	Yes	<30	13, 43	50	11.69 (-5.75; 29.13)	0.976
	Yes	>30	13, 43	204	11.4 (2.97; 19.83)	
	No	<30	8, 13, 43	83	29.24 (-5.97; 64.45)	0.572
	No	>30	13, 43	112	18.55 (6.82; 30.29)	
16 vs 3	Yes	<30	13, 28, 38, 39, 43	462	20.5 (8.43; 32.58)	0.631
	Yes	>30	1, 13, 27, 29, 43	828	17.33 (12.68; 21.98)	
	No	<30	8, 13, 38, 39, 43	321	18.63 (9.04; 28.22)	0.953
	No	>30	1, 13, 27, 29, 42, 43	762	18.98 (12.52; 25.43)	
16 vs 4	Yes	<30	13, 28, 36, 38, 39, 43	480	25.58 (14.01; 37.14)	0.086
	Yes	>30	1, 5, 13, 27, 29, 43	892	14.87 (10.9; 18.83)	
	No	<30	8, 13, 36, 38, 39, 43	394	26.94 (15.9; 37.99)	0.305
	No	>30	1, 5, 13, 27, 29, 42, 43	1040	20.3 (14.09; 26.52)	
16 vs 6	Yes	<30	13, 28, 38, 39, 43	462	17.56 (4.46; 30.66)	0.447
	Yes	>30	1, 13, 27, 29, 43	828	12.13 (7.19; 17.08)	
	No	<30	8, 13, 38, 39, 43	321	16.79 (5.89; 27.69)	0.798
	No	>30	1, 13, 27, 29, 42, 43	762	15.16 (9.07; 21.25)	
14 vs 3	Yes	<30	13, 28, 38, 39, 43	433	11.66 (7.53; 15.78)	0.194
	Yes	>30	1, 13, 19, 27, 29, 43	844	16.9 (10.15; 23.65)	
	No	<30	8, 13, 38, 39, 43	321	12.68 (6.27; 19.09)	0.661
	No	>30	1, 13, 27, 29, 42, 43	762	14.72 (8.25; 21.19)	
14 vs 4	Yes	<30	13, 28, 36, 38, 39, 43	480	13.63 (7.16; 20.1)	0.611
	Yes	>30	1, 5, 13, 19, 27, 29, 43	908	13.63 (7.16; 20.1)	
	No	<30	8, 13, 36, 38, 39, 43	394	16.9 (10.03; 23.77)	0.509
	No	>30	1, 5, 13, 27, 29, 42, 43	1040	13.83 (7.87; 19.79)	
14 vs 6	Yes	<30	13, 28, 38, 39, 43	462	8.7 (3.34; 14.05)	0.480
	Yes	>30	1, 13, 19, 27, 29, 43	844	11.62 (5.54; 17.69)	
	No	<30	8, 39, 43	321	4.82 (4.04; 5.59)	0.988
	No	>30	1, 13, 27, 29, 42, 43	762	1.98 (1.03; 2.93)	

The strongest MD was observed for pooled estimate of 14 KHZ vs. 4 KHz (15.91, CI: 13.51-18.35). A huge amount of heterogeneity was observed in pooled estimate which was not changed after subgroup analysis based on exposure pattern and age group. MDs in most of comparisons in this frequency pair were significantly higher than zero in favor of high frequency. However, some subgroups in selected studies in exposed subjects and controls had MDs that were not significantly different from zero. The pooled effect size in random effects model for exposed and non-exposed subjects was less than 2 dB which were not statistically significant. No similar pattern was found for observed effect size after subgroup analysis based on age in different exposure groups. Difference between two age subgroups in 14 KHz vs. 6 KHz comparison was in its lowest value among other three frequencies (0.1 and 0.3 dB for non-exposed and exposed subjects, respectively). In 14 KHz vs. 6 KHz and 14 KHz vs. 4 KHz comparisons also in some studies, there were some MDs in favor of conventional frequencies which were in contrast with other findings

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16 KHz vs. 3, 4 and 6 KHz:

Generally, all pooled MDs were in favor of high frequency. In some studies, calculated MDs were not significantly different from zero. However, there was no consistency between different frequency pairs in term of superiority of exposed to non-exposed groups MD or vice versa. Totally 10 studies were entered into final analysis for 16 KHz vs. 3 KHz. Computed MD for studies in exposed subjects was higher than the value in non-exposed subjects (24.37 vs.18.85), but the difference was not significant. Subgroup analysis based on age in exposed subjects showed that MDs for below 30 years group were consistently from 3 to 10 dB higher than calculated one for above 30 years group. However, the difference was not statistically significant.

18 KHz vs. 3,4 and 6 KHz:

The pooled effect size in each frequency pair was significantly in favor of 18 KHz findings (positive MD). However, calculated MDs in some subgroups in Macca et al. were not significantly different from zero. Calculated MDs for non-exposed groups in all comparison pairs for 18 KHz were higher than MDs for exposed subjects. The largest effect size was for exposed group in 18 KHz vs. 4 KHz frequency pair (40.31, CI: 28.19-52.44); However, the differences were not statistically significant. Huge amount of heterogeneity was observed in estimates even after subgroup analysis based on exposure pattern and age group. Sensitivity analysis showed that study by Fausti et al. had the most different and strongest effect size (5 dB change in pooled MD). The heterogeneity remained high even after removal of Fausti et al. study from analysis. Subgroup analysis based on age showed higher MD in favor of high frequency for age group >30 y in all frequency combinations except for exposed group in 18 KHz vs. 3 KHz. However, the differences were not statistically significant.

DISCUSSION:

NIHL as a common occupational disease may pose an important social and economic burden on the individual and the society. Timely detection of the effect of noise on hearing, i.e. before involvement of speech frequencies, is of utmost importance. HFA as a test for evaluation of hearing status at frequencies higher than conventional frequencies which has been proposed as a means for early detection of hearing loss due to noise.

It is said that HFA is time-consuming and probably sensitive to some technical errors [18- 35]. It is probably due to physical interactions in the ear canal that may lead to a high inter and intra-individual variability (18, 34); so it was assumed that it is difficult to recommend normative thresholds in HFA range [5-18]. Newer devices seem to have overcome this problem [34-43, and now it is said that hearing thresholds at frequencies higher than 8KHz are reliable to hearing thresholds test, especially for monitoring serial changes in the thresholds [34]. Although, now most problems with HFA has been overcome, one major problem still exist which is the lack of an international standard providing normal thresholds in HFA. It is probably due to the high inter-individual variability [5,18-44], although high intra-individual test-retest reliability is obtained now [34]; in addition, the effect of age is also important which may intervene with the effect of noise in HFA to a higher amount than CFA [18].

In this review, 23 articles which compared CFA and HFA for detection of NIHL were assessed. The studies were performed from 1979 till 2016 in different noise-exposed populations, mostly among workers in different industries. The noise exposure status was different in the aforementioned studies regarding the intensity of noise, duration of exposure and frequency spectrum of the noise; so the populations studied were completely heterogeneous regarding noise exposure. The studied populations were different regarding age as well; totally the individuals between 17 to 86 years old were assessed, but in most studies individuals were between 20 and 50 years old.

The instruments (audiometer and earphone) used for CFA and HFA also were different in the studies which can be considered as another measure of heterogeneity.

Totally, mean hearing thresholds at HF was higher than CF in both exposed and non-exposed subjects when pooling the data of all studies; although the difference was higher in exposed than non-exposed participants in most hearing frequencies, but considering the high heterogeneity of the studies, a statistically significant difference could not be achieved.

Overall, 15 studies have concluded that high frequencies of hearing are affected earlier than conventional frequencies and have proposed HFA as a more sensitive method for detection of noise effect on hearing thresholds [2, 5, 8, 13, 17, 19, 22, 24, 26, 34, 36-39, 41, 42], and six studies didn't find any difference between CFA and HFA regarding the detection of NIHL [1, 18, 21, 33, 25, 35, 40].

The studies with positive results were performed on 1966 noise-exposed and 773 non-exposed individuals, but negative studies assessed 845 noise-exposed and only 72 non-exposed individuals. From six studies with negative results, three assessed musicians, so the noise exposure was not as high as occupational settings; although Le Prell et al. found that for those with higher exposures among musicians, the HFA thresholds were higher than CFA; but most studies with positive results were performed in occupational groups, although with different noise exposures.

There are some possible mechanisms that predispose higher frequencies to the effects of noise more than lower frequencies; shape of the cochlea and its pattern of vascularization are two most important explanations [17], so theoretically high frequencies are more vulnerable to the effect of noise.

It was documented that age affects hearing thresholds especially after 40 years old and this effect increases by increasing the frequency, so it is more obvious in higher frequencies, i.e.18 KHz is more severely affected by age than 16 KHz and so on [34-45]. Age and noise interact simultaneously affect hearing [25], and may have an additive effect [41].

In most studies, standard deviation from mean of hearing thresholds was higher in HFA than CFA [34] which shows a higher inter-individual variability. Consequently it is a weak point of HFA. Macca et al. found that due to the effect of age on hearing thresholds especially in EHF region, HFA can be an early indicator of NIHL only in the age below 30 years old [41]. Ahmad et al. and Goncalvez et al. assessed HFA in noise-exposed workers with normal CFA and found abnormal thresholds in HFA [34-40]. Goncalvez et al. and Macca et al. reached to similar results that in ages more than 30 years, HFA cannot be reliably used as an early indicator of noise effect [40-41]. In the present study, subgroup analysis according to age showed that MD between high and conventional frequencies is higher in exposed group than non-exposed one, but due to the high heterogeneity this difference was not statistically significant.

Other factors may affect HFA as well, such as gender, type of the earphone and its positioning [9- 46]. It is said that hearing thresholds in women are lower than men and are less affected by increasing age [46]. Ten studies in this review were assessed both males and females concurrently which is probably another reason for heterogeneity of data [2, 5, 18, 19, 25, 35, 36, 37, 40, 41].

Da Rocha et al. concluded that HFA is influenced by noise earlier than CFA [10]. Silva et al. found HFA as a more sensitive method to detect threshold increases than CFA, although generally not due to noise alone [46].

Korres et al. concluded that HFA can be used besides CFA for detection of NIHL and can provide additional information, but it cannot be used as a substitute for it due to its high variability [5].

Le prell et al. presented a possible explanation for increased thresholds in HFA than CFA and it is the higher variability of EHF thresholds which may reflect the effect of noise. They concluded that HFA is more sensitive to the effect of noise only for who are exposed to a high level of noise [25], but recreational noise exposure does not affect HFA in healthy young adults [25]. It should be noticed that they assessed recreational music users which are not probably exposed to noise levels as high as is produced in industrial settings or even among professional musicians.

Riga et al. found that in the workers with few years of work experience, CFA cannot show the effect of noise, but EHF in this group of workers is relatively sensitive to the effect of noise, so it may be more sensitive than CFA for identification of the first effects of noise on hearing much earlier than CFA [22]. Singh et al. and Somma et al. also found that EHF is efficacious for screening of noise effects on hearing in young age groups, mostly due to the probable effect of age in older age groups [13-19].

Meta-regression of the studies showed a difference between CF and HF thresholds both in exposed and non-exposed subjects, though the difference was not statistically significant. It is probably due to the high heterogeneity of the studies. Sources of heterogeneity can be summarized as: different level of noise exposure (intensity and duration), noise spectrum, age, gender, and instruments used for threshold testing.

All the studies in this review, due to their methodology (mostly cross-sectional) suffer from inherent limitations of these studies. In order to conclude that HFA is more sensitive to the effect of noise than CFA and can detect NIHL earlier than CFA, longitudinal studies are needed.

CONCLUSION:

It can be concluded from the studies of this review that there was a higher MD between HF and CF thresholds in exposed groups than non-exposed ones in most hearing frequencies and this difference was more prominent in younger ages (<30y), but the difference even in age subgroup analysis was not statistically significant. So it cannot be concluded from the results of this review than HFA can detect NIHL earlier than CFA.

CONFLICT OF INTEREST

There is no conflict of interest for any of the authors.

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