

# Hearing loss among adults with sickle cell disease in an endemic region: a prospective case-control study

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Ann Saudi Med 2016; 36(2): 135-138

DOI: 10.5144/0256-4947.2016.135

**BACKGROUND:** Sickle cell disease (SCD) is a common disease in the Eastern province of Saudi Arabia. One of the underreported complications of sickle cell disease is sensorineural hearing loss (SNHL).

**OBJECTIVES:** The aim of this study was to estimate the prevalence of SNHL in patients with sickle cell disease by comparison with a control group from hematological diseases, and to consider the possible options that might minimize the occurrence of SNHL.

**DESIGN:** Prospective case-control study.

**SETTING:** Outpatient clinics in the Eastern province over a 9-month duration from July 2014 to March 2015.

**PATIENTS AND METHODS:** Cases were selected consecutively and controls were matched for age and sex. Means for pure tone audiometry measurements and hearing thresholds were compared.

**MAIN OUTCOME MEASURE(S):** SNHL in patients with sickle cell disease.

**RESULTS:** Nine patients (22.5%) had hearing loss using pure tone audiometry. The mean of pure tone averages in the patient group was 21.1 on the right side and 21.5 on the left side, while the control group average was 15.4 on the right side and 15.2 on the left side. Comparison of the means of the hearing thresholds on each side for both groups showed statistically significant differences in all frequencies.

**CONCLUSIONS:** Hearing loss is a common complication in patients with SCD. Annual hearing assessment is highly recommended to discover this complication as early as possible.

**LIMITATIONS:** Relatively small sample size. The study was in a single outpatient clinic. Recall bias in the number of hospital admissions in the last ten years.

Sickle cell disease (SCD) is an autosomal recessive genetic disorder that results from replacement of glutamic acid by valine at position number 6 in the beta-globin chain. It affects mainly people from Sub-Saharan Africa, South and Central America, Cuba, Saudi Arabia, India and Mediterranean countries.<sup>1</sup> It was first described by Herrick in 1910.<sup>2</sup> In Saudi Arabia, the prevalence of SCD is highest in the Eastern province where it reaches 2.6% (vs. around 0.2% for African-Americans), and for the carrier state in the same province it is approximately 21%.<sup>3-6</sup> SCD was first recognized in Saudi Arabia during a survey of the employees of the Arabian American Oil Company (ARAMCO) in the Eastern province in the 1960s.<sup>7</sup>

Normal red blood cells (RBCs) are pliable and oval in shape, which contributes to their smooth flow through

vessels. In contrast, when red blood cells in patients with SCD are exposed to any stress like dehydration, deoxygenation, cold temperature or blood infections, they become hard and sickle in shape. This change significantly hinders their smooth flow through small vessels, which may lead to obstruction, ischemia and end-organ hypoxia. This is manifested clinically in what is called vaso-occlusive crisis, which may affect different systems of the body. One of the most vulnerable systems in the body to hypoxia is the nervous system, as it has poor tolerance to low oxygen levels.

SCD has diverse complications. One of these, which is related to the nervous system, is sensorineural hearing loss (SNHL). The reported incidence of this complication in previous studies varies between 8% in Nigeria to 60% in Ghana.<sup>8</sup> In this study, the prevalence of

SNHL was estimated among patients with SCD in the Eastern province of Saudi Arabia, and compared with a matched group of controls. The possible mechanisms by which hearing loss may happen in these patients is discussed in an attempt to suggest possible methods to prevent its occurrence and hinder its progress once it has happened.

## PATIENTS AND METHODS

In this prospective case-control study we selected cases and controls from the outpatient clinics at King Faisal University, Eastern Province, Saudi Arabia, over 9 months from July 2014 to March 2015. Ethical approval for the research was granted by the institutional review board at the College of Medicine. The control group was a convenience sample matched for age and sex, but were free from hematological diseases. All patients were diagnosed as having SCD by electrophoresis, and all the controls were confirmed to be free of SCD by electrophoresis. Exclusion criteria included the following: history of ear operation, history of using ototoxic medications, history of meningitis, history of mumps or measles, history of noise exposure, positive ear discharge from history or by clinical examination, or positive tympanic membrane perforation. A detailed history, clinical examination and audiological assessment (which included pure tone audiogram and tympanogram) were done for all subjects by the ENT physician and audiologist. Further information about the medical history of each patient was gathered from the patient's medical file.

Pure tone audiometry was done with the standard settings for all the subjects (160 ears) for the frequencies of 250Hz, 500Hz, 1000Hz, 2000Hz, 4000Hz and 8000Hz. The pure tone audiograms were categorized into three categories: normal, positive for conductive hearing loss (CHL) or positive for SNHL. The degree of hearing loss was classified according to the pure tone average into mild (26-40 decibels), moderate (41-55 decibels), severe (56-90 decibels) or profound (more than 90 decibels) hearing loss. A subject was considered to have hearing loss when the pure tone average (the average of the thresholds on 500Hz, 1000Hz, 2000Hz) was more than 25 decibels for either the right or the left ear.

Statistical analysis were performed by IBM SPSS version 22 (<https://goo.gl/G0S4LT>). The Mann-Whitney U test was used to compare the two groups. A *P* value <.05 was considered statistically significant.

## RESULTS

Forty patients and 40 matching controls were enrolled

in the study. In the patient group, the male to female ratio was 1.9:1, the age range was from 20 to 45 years (mean [standard deviation] was 31.7 [6.5]). In the control group, the male to female ratio was 1.9:1; the age range was from 20 to 44 years (mean [standard deviation] was 29.2 [6.6]). The pure tone audiogram results from the patient group showed that 9 patients (22.5%) had hearing loss, with a pure tone average between 25 and 40 decibels. Six (15%) had bilateral hearing loss, and three patients (7.5%) had unilateral hearing loss (**Table 1**). The type of hearing loss was SNHL in all patients. In the control group, results were normal in all subjects (i.e. all subjects were free of hearing loss). There was no significant sex or side preponderance among patients with hearing loss.

The mean of pure tone averages for all subjects in the patient group was 21.1 on the right side and 21.5 on the left side. For the control group, it was 15.4 on the right side and 15.2 on the left side. The difference between controls and patients was statistically significant for both sides. The mean of pure tone averages for the subjects in the patient group after exclusion of those who had SNHL (9 patients) was 18.5 on the right side and 18.2 on the left side. When this was compared to the control group, the difference was statistically significant for both sides. The tympanometry results for all subjects in both groups were normal (type A).

A comparison of means of the hearing thresholds on each side in each group showed statistically significant differences in the means for all frequencies (**Table 2**). Although only 5 patients (12.5%) in the patient group had a positive complaint of hearing loss that was described by the patient as being mild and nondisabling. Patients with hearing loss had a higher average number of hospital admissions/year in the last 10 years before the study (**Table 3**).

## DISCUSSION

Sickle cell disease is a significant clinical, social and economic burden in Saudi Arabia. Pre-marital testing for SCD had been mandatory for the last 10 years in Saudi Arabia, with the hope of reducing the incidence. SCD has several complications that may affect different body systems. One of the underreported complications is SNHL.<sup>9</sup> It is more likely to occur in older patients with SCD who have suffered more vaso-occlusive crises.<sup>9,10</sup> A previous study in the same region showed a significant association between the SNHL and the onset of the first vaso-occlusive crisis at six years of age or less.<sup>11</sup>

Hearing loss associated with SCD may occur both in children and adults. It can be unilateral or bilateral,

**Table 1.** Results of pure tone audiograms in patients and controls.

Group	Number of subjects	Subjects with hearing loss* (%)	Bilateral hearing loss (%)	Unilateral hearing loss (%)	Mean of pure tone averages** (right side)	Mean of pure tone averages** (left side)
SCD group	40	9 (22.5)	6 (15)	3 (7.5)	21.1	21.5
Control group	40	0	0	0	15.4	15.2

\*Sensorineural hearing loss; \*\*P value <.05.

**Table 2.** Comparison of the means of hearing thresholds.

Freq. (Hz)	Controls (n=40)		Patients (n=40)		P value	
	Right ear	Left ear	Right ear	Left ear	Right ear	Left ear
250 Hz	13.6	12.1	18.9	19.8	<.001	<.001
500 Hz	14	13.8	20	21.3	<.001	<.001
1 KHz	16	15.8	21.8	21.1	.005	.012
2 KHz	16.3	16.2	21.6	22.1	.011	.007
4 KHz	17.5	18.4	23.3	24.4	.006	.005
8 KHz	18	18.5	22.9	24.3	.026	.013

Comparison of same ear between cases and controls.

mild or severe, transient or permanent and its onset can be sudden or progressive. More often it is due to inner ear pathology (SNHL) than to external ear or middle ear complications (CHL).<sup>12</sup>

Because of longer life expectancy, the incidence of the SNHL among patients with SCD has become more apparent as other previously milder complications became more severe and common.<sup>12</sup>

The hypothesized mechanisms of the SNHL in patients with SCD include impairment of oxygen supply (secondary to deformed RBCs), which results in hypoxia to the cochlea, peripheral and central auditory pathways,<sup>8</sup> sluggish blood flow to the cochlea due to sickling of the red blood cells,<sup>10</sup> and compression of the auditory canal and auditory nerve by the hyperactive bone marrow in the petrous part of the temporal bone.<sup>8,10,13</sup> Another possible mechanism of hearing loss in SCD patient is increased susceptibility to bacterial meningitis, as the immune function of these patients is affected.<sup>14</sup>

In this study, although only 5 patients (12.5%) complained clinically of hearing loss among adults with SCD, 9 patients (22.5%) were diagnosed with hearing loss. Furthermore, the difference in the means of the hearing thresholds between the patients and the controls on all frequencies was statistically significant. These findings reflect the significance of this complica-

**Table 3.** Average number of hospital admissions/year for the last 10 years among patient group.

Group	Average number of hospital admissions/year for the last 10 years*
Patient with hearing loss	3.5
Patient without hearing loss	1.5

\*P value <.05

tion wherein the hidden nature of it usually manifests subclinically, and indicates the importance of screening for and intervention if possible to hinder progress.

The comparison between the means of hearing thresholds between the patients and controls showed no statistically significant differences at all frequency. Similar findings were shown in previous studies.<sup>2,15</sup> The average number of hospital admissions per year for the last 10 years in the patients was significantly greater than the controls. Patients with more hospital admissions due to vaso-occlusive crises had SNHL. This indicates that the hearing level is affected by the chronic course of the disease. Consequently, good control of the disease will reduce the incidence of this complication.

The limitations of this study include the relatively

small sample size; the study was conducted in a single outpatient clinics, and there was possibly some recall bias for the number of hospital admissions for the last 10 years.

We recommend that all patients with SCD undergo hearing tests annually, starting at the age of 6 years. This will be very helpful as baseline data to prevent the progression of the hearing loss (e.g. to avoid other risk factors for hearing loss, control of the general status of the disease) and to provide early management (e.g. hearing aids or cochlear implant). It is also

important to avoid other risk factors for SNHL in SCD patients (e.g. noise exposure and the use of ototoxic medications).

In conclusion, SCD is a common disease in Saudi Arabia. One of the under-reported complications of SCD is the SNHL. This complication has become more common with increased life expectancy. Annual hearing tests are recommended for these patients, starting at age of 6 years, to discover this complication as early as possible, to prevent its progression and to provide for early management.

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