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## **Main Article**

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Dr Ohad Ronen, Department of Otolaryngology – Head and Neck Surgery, Galilee Medical Center, PO Box 21, Nahariya 2210001, Israel E-mail: ohadr@gmc.gov.il Assessment of seasonal pattern of idiopathic sudden sensorineural hearing loss: a retrospective cross-sectional study

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#### **Abstract**

**Background.** A seasonal trend of patients with idiopathic sudden sensorineural hearing loss may direct research into possible aetiology.

**Methods.** This study reviewed data from the medical records of patients who presented from 2004 to 2019 and who were diagnosed with new-onset idiopathic sudden sensorineural hearing loss. Seasonal pattern was assessed using chi-square and Rayleigh tests, and further confirmed by Monte Carlo simulation.

**Results.** The study included 740 patients with a mean age of 48.3 years and a median age of 49 years. There was no statistical evidence for a difference in the distribution of sensorineural hearing loss cases for the four seasons of each year or with the cumulative data. New-onset idiopathic sudden sensorineural hearing loss cases averaged around 11 per month; there was no statistical evidence for a seasonal difference, as determined either by the Rayleigh test or with Monte Carlo simulation.

**Conclusion.** There was no evidence to support the claim that idiopathic sudden sensorineural hearing loss incidence displays a seasonal pattern. More research is necessary to explore potential external factors such as climate or infection.

#### Introduction

Idiopathic sudden-onset sensorineural hearing loss (SNHL) is a medical emergency that continues to be poorly understood despite recognition in the literature since 1944. Idiopathic sudden-onset SNHL is most commonly defined as SNHL of 30 dB or greater over at least three contiguous audiometric frequencies occurring within a 72-hour period. The vast majority of cases are unilateral, and the estimated annual incidence is 20 per 100 000 persons. <sup>2</sup>

A cause for the hearing loss is identified in only up to 10 per cent of cases, yet 50 per cent of patients will improve spontaneously.<sup>3</sup> Insufficient knowledge of pathogenesis and the lack of a standard method for patient evaluation, in addition to a high spontaneous recovery rate, all complicate the study of idiopathic sudden-onset SNHL and the investigation of different treatment modalities. One possible pathogenesis is an external vector such as a virus or bacterium.<sup>4</sup> A seasonal distribution of the disease might support such a plausible cause, as some microbial infections also have a seasonal pattern.

This study was conducted to determine whether the occurrence of idiopathic sudden-onset SNHL varies throughout the year, with attention to the seasonal pattern. We hypothesised that the distribution of new patients with idiopathic sudden-onset SNHL varies throughout the year and displays a seasonal pattern.

## Materials and methods

# Study design

We carried out a retrospective cross-sectional study of all patients diagnosed with newonset idiopathic sudden-onset SNHL diagnosis admitted to our medical centre from 2004 to 2019. Data were retrieved from electronic medical records. Idiopathic sudden-onset SNHL was defined according to pure tone audiometry results as described in accepted guidelines.<sup>4</sup>

This seasonal distribution study was performed by dividing each year into four seasons: spring (March to May), summer (June to August), autumn (September to November) and winter (December to February), as in studies conducted in similar Mediterranean weather conditions.<sup>5</sup> We calculated the occurrence of new cases of idiopathic sudden-onset SNHL admitted to our medical centre over periods of months, seasons and years. Patients of all ages with idiopathic sudden-onset SNHL were included.

Our exclusion criteria were patients with: inadequate data; non-idiopathic sudden-onset SNHL; concurrent intracranial neoplasms; and those with a history of

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Table 1. Patients' demographics

Year	Gender*		Age (years) <sup>†</sup>	
	Male (n (%))	Female ( <i>n</i> (%))	Mean (SD)	Median (range)
2004–2005	20 (46.5)	23 (53.5)	49.7 (14.8)	50.0 (18-81)
2005–2006	25 (55.6)	20 (44.4)	49.2 (16.5)	49.0 (18-80)
2006–2007	33 (50.8)	32 (49.2)	46.3 (15.4)	47.0 (16–78)
2007–2008	37 (55.2)	30 (44.8)	48.9 (17.7)	49.0 (10-84)
2008–2009	29 (55.8)	23 (44.2)	51.9 (18.0)	51.0 (9-99)
2009–2010	30 (58.8)	21 (41.2)	48.0 (18.3)	50.0 (11-87)
2010-2011	26 (56.5)	20 (43.5)	46.6 (15.1)	49.0 (14–74)
2011–2012	22 (51.2)	21 (48.8)	48.5 (17.8)	45.5 (11–83)
2012–2013	22 (59.5)	15 (40.5)	49.9 (19.8)	50.0 (11-86)
2013–2014	31 (54.4)	26 (45.6)	46.2 (17.1)	46.0 (16-76)
2014–2015	28 (62.2)	17 (37.8)	46.4 (17.0)	46.0 (18-83)
2015–2016	24 (58.5)	17 (41.5)	53.5 (17.3)	54.0 (14-82)
2016–2017	21 (55.3)	17 (44.7)	46.5 (19.1)	45.0 (15-82)
2017–2018	28 (53.8)	24 (46.2)	44.5 (15.3)	43.0 (14–90)
2018–2019	36 (62.1)	22 (37.9)	49.3 (17.6)	47.0 (15–84)
Total	412 (55.7)	328 (44.3)	48.3 (17.1)	49 (9–99)

\*No significant statistical difference in gender was found between the studied years (chi-square test, two-sided p = 0.718). <sup>1</sup>No significant statistical difference in age was found between the studied years (Kruskal-Wallis test, p = 0.533). SD = standard deviation

Ménière's disease, previous ear procedures, chemotherapy or radiotherapy to the head or neck, intercurrent ear infection, or barotrauma to the ear.

The data collected with each sample included: date of admission, demographics (age, gender), co-morbidities, recent fever or acute febrile illness, hearing examination, and time from hearing insult to treatment.

## Statistical analysis

Continuous data were presented as mean, median and range values. The two-sided chi-square test and Kruskal-Wallis test were used to examine differences in patients' gender and age distributions across the studied years, as there was non-normality of the age variable. The seasonal pattern was examined with: the one-sample chi-square test (if expected distribution (degrees of freedom) was 4 or lower), which assesses for any deviation from uniform distribution; the circular mean, which specifically assesses for seasonality (a cyclical average); and the Rayleigh test, which examines whether there is no sample mean direction. The new-onset idiopathic sudden-onset SNHL distribution is not around a cyclical average but, rather, varies throughout the year. According to the Rayleigh test's assumption, more than 8 observations are required, but as the basic data were grouped, we further confirmed our results by the Rayleigh test and Monte Carlo simulation method based on 10 000 random cases.

The analysis was performed using the following software: IBM® SPSS® Statistics version 27.0, R Studio version 4.1.0 and Matlab version 9.11.

### Ethical approval

This study protocol was reviewed and approved by the Galilee Medical Center Helsinki Committee (approval number:

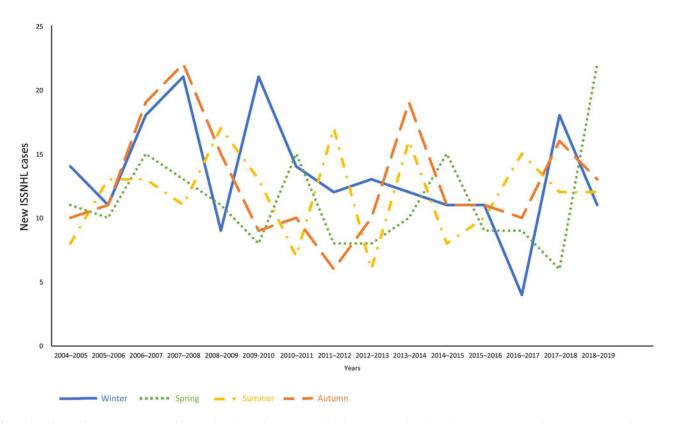
NHR006514). The study was granted an exemption from requiring written informed consent by the same committee.

### **Results**

Between 2004 and 2019, 740 patients were admitted to our hospital with a primary diagnosis of idiopathic sudden-onset SNHL. All patients underwent an audiogram, were seen by an otolaryngologist and were treated according to accepted guidelines.<sup>4</sup> The study population had a mean age of 48.3 years and a median age of 49 years; 56 per cent of the patients were male. There was no statistical evidence for a difference in gender or age between the studied years (gender, two-sided chi-square test p = 0.718; age, Kruskal–Wallis test p = 0.533) (Table 1).

New cases of idiopathic sudden-onset SNHL throughout the investigated years were grouped into months, seasons and years. When we compared the number of new idiopathic sudden-onset SNHL cases among the years for each season separately, we did not find statistical evidence for a difference in dispersion for the four seasons (chi-square test results: winter p = 0.079, spring p = 0.114, summer p = 0.396 and autumn p = 0.085; Figure 1). There was also no statistical evidence for a difference in the numbers of new idiopathic sudden-onset SNHL cases distributed between the seasons within the studied years (Figure 1).

A random dispersion of idiopathic sudden-onset SNHL new cases was revealed when we combined all years together (chi-square test p = 0.398; Rayleigh test p = 0.2703; Table 2). For all years combined, the average number of new cases per season were 13.3, 11.3, 11.9 and 12.8 in the winter, spring, summer and autumn, respectively. In addition, no evidence was found for a difference in idiopathic sudden-onset SNHL new cases between months, based on the cumulative data for all studied years combined (Rayleigh test p = 0.3895; Figure 2).



**Fig. 1.** Idiopathic sudden-onset sensorineural hearing loss (ISSNHL) occurrence divided into seasons throughout the years 2004–2019. There was no statistical evidence for a difference in dispersion of cases for the four seasons across the studied years (chi-square test results: winter p = 0.079, spring p = 0.114, summer p = 0.396 and autumn p = 0.085).

Table 2. Dispersal of new seasonal idiopathic sudden SNHL cases over time

Year	Average idiop	Average idiopathic sudden SNHL cases per season (n)				Rayleigh test <i>p</i> -value
	Winter	Spring	Summer	Autumn		
2004–2005	14	11	8	10	0.6580	0.4254
2005–2006	11	10	13	11	0.9520	0.8959
2006–2007	18	15	13	19	0.7190	0.5322
2007–2008	21	13	11	22	0.1420	0.0671
2008–2009	9	11	17	15	0.3910	0.2147
2009–2010	21	8	13	9	0.0420	0.2796
2010-2011	14	15	7	10	0.3480	0.2520
2011–2012	12	8	17	6	0.0900	0.5121
2012–2013	13	8	6	10	0.4260	0.2401
2013-2014	12	10	16	19	0.3430	0.1824
2014–2015	11	15	8	11	0.5560	0.5763
2015–2016	11	9	10	11	0.9850	0.8864
2016–2017	4	9	15	10	0.0950	0.0393
2017–2018	18	6	12	16	0.0960	0.0731
2018–2019	11	22	12	13	0.1580	0.2432
Total	200	170	178	192	0.3980	0.2703

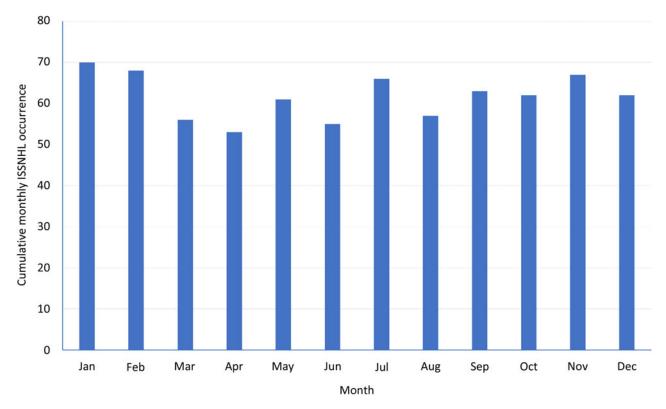
SNHL = sensorineural hearing loss

The monthly distribution of new cases varied slightly within the years examined, yet there was no statistical evidence for a difference through the months as indicated by the Rayleigh test and confirmed by the Monte Carlo simulation for each separate year and for all studied years combined (Table 3).

## **Discussion**

In most cases of idiopathic sudden-onset SNHL, the aetiology remains idiopathic.<sup>4</sup> Quality of life is dramatically low in those who fail to recover from idiopathic sudden-onset SNHL.<sup>6</sup> Therefore, it is of great importance to find the aetiology and

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**Fig. 2.** Cumulative monthly idiopathic sudden-onset sensorineural hearing loss (ISSNHL) occurrence in the years 2004–2019. There was no statistical evidence for a difference in distribution between months (Rayleigh test, *p* = 0.3895).

Table 3. Dispersal of new idiopathic sudden SNHL cases over time

Year     Rayleigh test p-value     Monte Carlo simulation p-value       2004–2005     0.6019     0.6020       2005–2006     0.9570     0.9572       2006–2007     0.9675     0.9707       2007–2008     0.0779     0.0757       2008–2009     0.4329     0.4336       2009–2010     0.2982     0.2975       2010–2011     0.1705     0.1698       2011–2012     0.8832     0.8821       2012–2013     0.4032     0.4114       2013–2014     0.2233     0.2211       2014–2015     0.8998     0.9006       2015–2016     0.6795     0.6813       2016–2017     0.1095     0.1082	•	·	
2005-2006   0.9570   0.9572     2006-2007   0.9675   0.9707     2007-2008   0.0779   0.0757     2008-2009   0.4329   0.4336     2009-2010   0.2982   0.2975     2010-2011   0.1705   0.1698     2011-2012   0.8832   0.8821     2012-2013   0.4032   0.4114     2013-2014   0.2233   0.2211     2014-2015   0.8998   0.9006     2015-2016   0.6795   0.6813	Year		Monte Carlo simulation <i>p</i> -value
2006-2007   0.9675   0.9707     2007-2008   0.0779   0.0757     2008-2009   0.4329   0.4336     2009-2010   0.2982   0.2975     2010-2011   0.1705   0.1698     2011-2012   0.8832   0.8821     2012-2013   0.4032   0.4114     2013-2014   0.2233   0.2211     2014-2015   0.8998   0.9006     2015-2016   0.6795   0.6813	2004–2005	0.6019	0.6020
2007-2008   0.0779   0.0757     2008-2009   0.4329   0.4336     2009-2010   0.2982   0.2975     2010-2011   0.1705   0.1698     2011-2012   0.8832   0.8821     2012-2013   0.4032   0.4114     2013-2014   0.2233   0.2211     2014-2015   0.8998   0.9006     2015-2016   0.6795   0.6813	2005–2006	0.9570	0.9572
2008-2009   0.4329   0.4336     2009-2010   0.2982   0.2975     2010-2011   0.1705   0.1698     2011-2012   0.8832   0.8821     2012-2013   0.4032   0.4114     2013-2014   0.2233   0.2211     2014-2015   0.8998   0.9006     2015-2016   0.6795   0.6813	2006–2007	0.9675	0.9707
2009-2010 0.2982 0.2975   2010-2011 0.1705 0.1698   2011-2012 0.8832 0.8821   2012-2013 0.4032 0.4114   2013-2014 0.2233 0.2211   2014-2015 0.8998 0.9006   2015-2016 0.6795 0.6813	2007–2008	0.0779	0.0757
2010-2011 0.1705 0.1698   2011-2012 0.8832 0.8821   2012-2013 0.4032 0.4114   2013-2014 0.2233 0.2211   2014-2015 0.8998 0.9006   2015-2016 0.6795 0.6813	2008–2009	0.4329	0.4336
2011–2012 0.8832 0.8821   2012–2013 0.4032 0.4114   2013–2014 0.2233 0.2211   2014–2015 0.8998 0.9006   2015–2016 0.6795 0.6813	2009–2010	0.2982	0.2975
2012-2013   0.4032   0.4114     2013-2014   0.2233   0.2211     2014-2015   0.8998   0.9006     2015-2016   0.6795   0.6813	2010-2011	0.1705	0.1698
2013-2014 0.2233 0.2211   2014-2015 0.8998 0.9006   2015-2016 0.6795 0.6813	2011–2012	0.8832	0.8821
2014-2015 0.8998 0.9006   2015-2016 0.6795 0.6813	2012–2013	0.4032	0.4114
2015–2016 0.6795 0.6813	2013-2014	0.2233	0.2211
	2014–2015	0.8998	0.9006
2016–2017 0.1095 0.1082	2015–2016	0.6795	0.6813
	2016–2017	0.1095	0.1082
2017–2018 0.0584 0.0570	2017–2018	0.0584	0.0570
2018-2019 0.2283 0.2343	2018–2019	0.2283	0.2343
Total 0.3895 0.3836	Total	0.3895	0.3836

A chi-square test was performed when possible, and similar results to the Rayleigh test were achieved. The Monte Carlo simulation was conducted on 10 000 random cases. SNHL = sensorineural hearing loss

improve its treatment. Because some pathogens, especially viruses, display seasonal distribution, we investigated a cohort of 740 patients over 15 years in one climate zone with Mediterranean weather conditions. We failed to demonstrate statistical evidence for uneven seasonal or monthly distribution in each year, and in the cumulative time span of months, seasons and years. Our findings do not support a seasonal

external factor, such as climate or infection, as a possible aetiological factor.

Other studies have also attempted to investigate the aetiology of idiopathic sudden-onset SNHL with emphasis on seasonality. In 2002, Danielides *et al.*<sup>5</sup> examined 82 cases of idiopathic sudden-onset SNHL investigating the seasonal distribution of idiopathic sudden-onset SNHL and evaluating the influence of meteorological parameters. The results of their study, which took place in Greece, could not prove a statistically significant effect of weather conditions on the frequency of idiopathic sudden-onset SNHL. Our medical centre is situated in proximity to Greece and shares a similar Mediterranean climate. However, our study had a larger sample size and spanned more than a decade. Our medical centre covers a population of roughly 600 000 patients along the hills and shores of the Mediterranean Sea, so the current results might preclude generalisability to other climate areas.

In 2006, Wu *et al.*, in Taiwan, investigated the relations between monthly idiopathic sudden-onset SNHL incidence rates and weather conditions such as temperature, humidity, rainfall and so on.<sup>7</sup> Like Danielides *et al.*,<sup>5</sup> they found no statistical evidence for a link between idiopathic sudden-onset SNHL and weather conditions throughout the year. A statistically significant trend in seasonal variation was found, with the highest incidence rates occurring in autumn (August to October in Taiwan).<sup>7</sup> In nearby South Korea, a large-scale study over a period of five years similarly found that most patients with idiopathic sudden-onset SNHL were diagnosed in October, with the fewest diagnosed in January.<sup>8</sup>

A study from the USA, published in 2010, using the same statistical analysis as was used in the current study, suggested that idiopathic sudden-onset SNHL incidence does not display uneven distribution throughout the year; however, they conducted their study over a period of only three years, on fewer than 100 patients.<sup>9</sup>

Viruses might be a possible aetiology for a disease that has a seasonal pattern of presentation. It was suggested that a recent Epstein–Barr virus or cytomegalovirus infection might be a cause for idiopathic sudden-onset SNHL in children. Other viruses associated with idiopathic sudden-onset SNHL are human immunosuppression virus, herpes simplex virus, varicella zoster virus and mumps. We did not have relevant data on patients' viral infections; however, because some of these viral diseases have a seasonal presentation, our results do not support such an aetiology. 12–14

## Study strengths

Our study was conducted on 740 patients spanning 15 years in one climate zone. The additional analysis based on seasons rather than months diminishes minor climate changes that might occur in separate months. The size of the ENT service was stable throughout the investigated period, thus precluding it as a possible confounding factor.

#### Study limitations

We did not have exact weather information for those weeks in which the patients were referred to the hospital, so we could not analyse whether regional climate changes played a possible aetiological role. Because of the retrospective nature of the study, we could not prove causality, and did not have any ancillary tests supporting a possible vector causing idiopathic sudden-onset SNHL that might be linked to the weather. We did not have enough data to control for confounding factors such as a recent upper respiratory infection or other infectious aetiology that preceded the idiopathic sudden-onset SNHL. Our findings are limited to seasons in the Mediterranean area and might not be generalisable to other regions worldwide.

- Idiopathic sudden sensorineural hearing loss (SNHL) is a medical emergency with unknown aetiology
- Seasonal distribution of the disease might support an external vector as a possible pathogenesis
- This study investigated whether new-onset SNHL incidence follows a seasonal pattern
- This retrospective study showed that 740 cases over 15 years were spread evenly between seasons and months
- These findings do not provide evidence of a seasonal factor related to sudden SNHL pathogenesis in a Mediterranean-climate country

Other possible idiopathic sudden-onset SNHL aetiologies, and related systemic risk factors such as diabetes mellitus and hypertension, were not controlled for as confounding factors in the analysis because of the retrospective nature of this study.

As stated above, our medical centre covers around 600 000 people. As idiopathic sudden-onset SNHL has an estimated yearly rate of 20 per 100 000 population, we should have seen an annual rate of 120 idiopathic sudden-onset SNHL patients. However, 740 cases diagnosed in 15 years is equivalent to an annual rate of only about 50 patients. This difference might be explained by the fact that many idiopathic sudden-onset SNHL cases were not included in our cohort

as they were treated and followed up in community clinics, causing a possible bias in the study.

#### **Conclusion**

We did not find enough evidence to support the claim that idiopathic sudden-onset SNHL occurrence displays a seasonal pattern. However, this study was not designed to investigate a pathogenesis for this idiopathic disease. The findings presented here do not support an external aetiology that has a seasonal pattern related to the occurrence of idiopathic sudden-onset SNHL. Further studies should explore possible aetiologies for idiopathic sudden-onset SNHL.

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Competing interests. None declared

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