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Review

Paediatric Sudden Sensorineural Hearing Loss: Pooled Analysis and Systematic Review

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Sudden sensorineural hearing loss (SSNHL) is defined as hearing loss of ≥30 dB in one or both ears, developing within 3 days, affecting ≥3 contiguous frequencies. It is rare in children, but if untreated can cause significant morbidity. During the critical developmental period, it may cause lifelong social, behavioral, and mental sequelae. Currently, little guidance exists on prognosis and management within a pediatric population. A systematic literature review of pediatric SSNHL on PubMed, EMBASE, and the Cochrane CENTRAL database was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations. A total of 620 papers met the Medical Subject Headings criteria, of which 14 met analysis criteria—13 were level 4 and 1 was level 2b evidence. A population of 732 individuals was analyzed. Most reported cases of pediatric SSNHL were idiopathic. Other etiologies included viral infection, trauma, ototoxic drugs, and structural abnormalities. Recovery was defined as any improvement in hearing after the initial loss, from "slight" to "complete." Recovery ranged from 20% to 100%, with a pooled rate of 56%. Systemic steroids were the mainstay of treatment, although salvage intratympanic steroid therapy had a role after the failure of systemic steroids. Children with bilateral SSNHL had poorer outcomes than those with unilateral loss, with 29% showing improvement. Two studies reported outcomes with no treatment, for which recovery rate was 7%. This analysis of SSNHL shows that 61% of children with unilateral and 29% of children with bilateral SSNHL demonstrate some recovery, a worse prognosis than adults. Multiple treatment regimens exist, although comparison is challenging owing to inconsistently reported improvement parameters.

KEYWORDS: Child, ear, hearing loss, sudden, hearing loss, sensorineural, steroids

INTRODUCTION

Although sudden sensorineural hearing loss (SSNHL) in children is rare with only 20–30 cases per 100,000 children per year [1], if left untreated, it can lead to lifelong mental [2], social [3], and behavioral [4] sequelae affecting both the children and those close to them. Much has been written about SSNHL, but the majority of existing treatment guidelines are based on the treatment of adults [5] whose hearing loss may have differing etiologies than those of children [6].

SSNHL is usually defined as a hearing loss of ≥30 dB, in either or both ears, developing within 3 days and within 3 contiguous frequencies [7].

This study aimed to review the literature on pediatric SSNHL and evaluate the current evidence on the etiology, treatment options, and prognosis of children presenting with SSNHL. A pooled analysis of the current documented audiological outcomes in the literature was performed in an attempt to practically guide clinicians encountering this problem when counseling affected patients and their families.

MATERIALS AND METHODS

The PubMed, EMBASE (Ovid), and Cochrane CENTRAL databases were searched on July 7, 2019, for studies examining SSNHL in children. Search terms included "sudden sensorineural hearing loss," "SSNHL" (MeSH), and "paediatric/pediatric/children" from January 1, 1999 to December 31, 2019. Only articles in English language were investigated. For the purposes of this paper, "children" were

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Table 1. Studies analyzed in this review

No.	Authors	Year of publication	Number of children	Mean age (years)	Bilateral cases	Audiological criteria used for improvement
1	Tarshish et al. [20]	2013	17	11.41	7	Not defined
2	Pitaro et al. [13]	2016	19	14	1	Complete/partial/none
3	Dedhia et al. [21]	2016	20	11.25	8	Unspecified improvement
4	Chen et al. [9]	2018	101	10.4	28	Siegel's audiological criteria
5	Ha et al. [8]	2019	42	14.5	0	Siegel's audiological criteria
6	Kim et al. [14]	2018	67	14	0	Siegel's audiological criteria
7	Inci et al. [17]	2011	43	11.14	7	Hearing threshold gain
8	Kizilay et al. [18]	2016	14	10.1	2	Complete/partial/none
9	Övet et al. [19]	2016	49	14.35	0	Mean PTA improvement and complete/partial/none
10	Wu et al. [10]	2018	25	10.4	10	Siegel's audiological criteria/mean PTA improvement/word recognition score gain
11	Na et al. [15]	2014	87	12.5	7	Siegel's audiological criteria
12	Li et al. [11]	2016	136	11.7	15	Modified Siegel's audiological criteria
13	Qian et al. [12]	2018	75	15.74	3	Modified Siegel's audiological criteria
14	Chung et al. [16]	2015	37	14.3	0	Siegel's audiological criteria
	All patients		732	12.56	88	

No.: number; PTA: Pure tone audiogram.

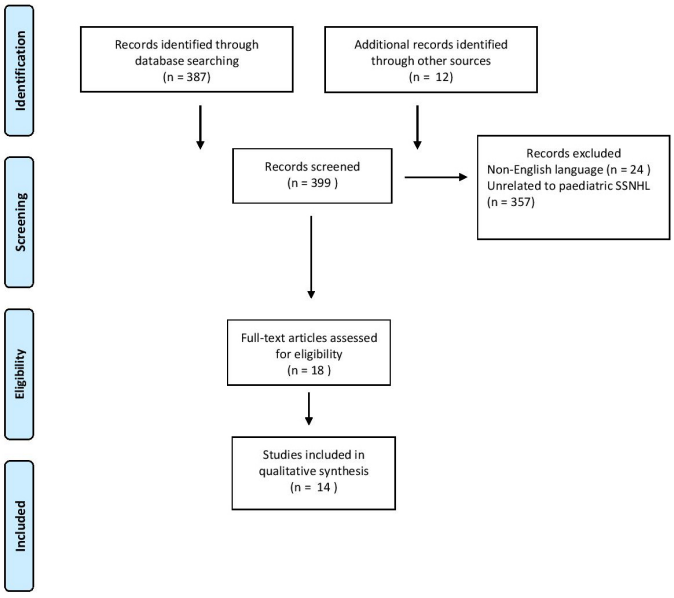

Figure 1. PRISMA 2009 Flow Diagram.

defined as individuals aged less than 18 years.

The articles were assessed by 2 reviewers independently for inclusion according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Figure 1). The references and citation links of these articles were hand-searched to identify further articles of relevance.

A total of 620 papers met the appropriate Medical Subject Headings criteria, of which 14 met inclusion criteria for further analysis. Of the 14 papers, 13 were level 4 evidence (retrospective records reviews) and 1 was level 2b evidence (prospective cohort study). A patient population of 732 individuals was analyzed.

RESULTS

Table 1 lists the 14 papers analyzed in this study. A total population of 732 children were analyzed. The condition occurred bilaterally in 88 patients. The mean age of all the patients with SSNHL was 12.56 years.

A total of 13 of these papers were retrospective records reviews (level 4 evidence), and 1 [8] was a prospective cohort study (level 2b evidence). No randomized controlled trials were undertaken in this age group. The papers differed considerably in terms of methods, scope of investigation, and reporting of results. Therefore, a meta-analysis was not performed owing to the degree of heterogeneity.

Papers analyzed originated from China [9–12], Israel [13], South Korea [8,14–16], Sweden [11], Turkey [17–19], and the United States of America [20,21].

Definition of SSNHL

SSNHL is defined by the American Academy of Otolaryngology-Head and Neck Surgery (AAOHNS) as a hearing loss of ≥30 dB in one or both ears, developing within 3 days, affecting at least 3 contiguous frequencies. It can affect one or both ears [22]. A total of 11 papers analyzed used this definition, although 3 [12,15,16] did not specify the timescale of symptoms required.

Diagnosis of SSNHL

Children can present a diagnostic challenge when compared with

Table 2. Treatments used and associated outcomes

Authors	Main etiology of SSNHL	Treatment	Number of patients	Number of patients showing any improvement (%)
Tarshish et al. [20]	Viral of unknown type – 71 %	Systemic steroid alone	8	3 (38) + 1 (13) unknown
		Systemic steroid + antibiotic/antiviral	5	2 (40)
		Antibiotic/antiviral alone	1	Unknown
		None	2	0 (0)
		Unknown	1	0 (0)
		Overall	17	5 (29) + 2 (12) unknown
Pitaro et al. [13]	Idiopathic – 74 %	IV steroid alone	3	3 (100)
		Oral steroid alone	8	4 (50)
		IV + intratympanic steroid salvage	6	4 (67)
		Oral + intratympanic steroid salvage	2	1 (50)
		Overall	19	12 (63)
Dedhia et al. [21]	Idiopathic – 30 %	Oral steroid alone	6	2 (33)
		Oral + intratympanic steroid salvage	2	2 (100)
		None	12	1 (8)
		Overall	20	5 (20)
Chen et al. [9]	Idiopathic – 72 %	Systemic steroid + mecobalamine	101	31 (31)
		Overall	101	31 (31)
Ha et al. [8]	Not reported	Oral steroid alone	20	17 (85)
		Oral + intratympanic steroid	22	18 (82)
		Overall	42	35 (83)
Kim et al. [14]	Not reported	Systemic steroid alone	50	30 (60)
		Systemic + intratympanic steroid salvage	17	7 (41)
		Overall	67	37 (55)
Inci et al. [17]	Idiopathic – 64 %	Systemic steroid + hyperbaric oxygen	43	24.5† (57)
		Overall	43	24.5† (57)
Kizilay et al. [18]	Idiopathic – 79 %	Systemic steroid	14	3 (21)
		Overall	14	3 (21)
Övet et al. [19]	Idiopathic – 100 %	Systemic steroid alone	23	15 (65)
		Systemic + intratympanic steroid	26	22 (85)
		Overall	49	37 (76)
Wu et al. [10]	Idiopathic – 80 %	Systemic steroid, ATP, mecobalamin	25	25 (100)
		Overall	25	25 (100)
Na et al. [15]	Not reported	Systemic steroid	87	63 (72)
		Overall	87	63 (72)
Li et al. [11]	Idiopathic – 63 %	*	136	55.5† (38)
		Overall	136	55.5† (38)
Qian et al. [12]	Idiopathic – 57 %	Systemic steroid, dipyridamole, alprostadil ± batroxobin Systemic steroid, dipyridamole, alprostadil + intratympanic steroid salvage ± batroxobin	48 21	39 (81) 13 (62)

Table 2. Treatments used and associated outcomes (Continued)

Authors	Main etiology of SSNHL	Treatment	Number of patients	Number of patients showing any improvement (%)
		Systemic steroid, dipyridamole, alprostadil + postauricular steroid salvage ± batroxobin	3	0 (0)
		Systemic steroid, dipyridamole, alprostadil + intratympanic and postauricular steroid salvage ± batroxobin	3	1 (33)
		Overall	75	53 (71)
Chung et al. [16]	Idiopathic – percentage not reported	Systemic steroid + plasma volume expansion	37	22 (59)
		Overall	37	22 (59)
All patients	(Where available) Idiopathic – 67 %		732	408 (56)

SSNHL: sudden sensorineural hearing loss; IV: intravenous; ATP: adenosine triphosphate.
*Li et al. [11] describe a variety of treatments used, including steroid, low-salt diet, vasodilators, fibrinolytics, plasma volume expansion, diuretics, antivirals, anti-inflammatories, and hyperbaric oxygen. However, they do not record the proportion of patients receiving each treatment.
†0.5 patients indicates a patient with bilateral SSNHL, who had hearing recovery in one ear only.

Table 3. Outcomes after each treatment option

Treatment	Number of patients	Number of patients showing any audiological improvement (%)
Steroid (all)	580	350 (60)
Systemic steroid alone	219	140 (64)
Systemic steroid + intratympanic steroid (all)	99	68 (69)
Systemic steroid + intratympanic steroid salvage	51	28 (55)
Systemic steroid + intratympanic steroid (not salvage)	48	40 (83)
Systemic steroid + mecobalamine	101	31 (31)
Systemic steroid + hyperbaric oxygen	43	23 (53)
Systemic steroid + ATP + mecobalamin	25	25 (100)
Systemic steroid + postauricular steroid salvage	3	0 (0)
Systemic steroid + postauricular + intratympanic steroid salvage	3	1 (33)
Systemic steroid + plasma volume expansion	37	22 (59)
No treatment	14	1 (7)

ATP: adenosine triphosphate.

adults because audiometry requires a degree of co-operation that some children may struggle to provide. However, to diagnose sensorineural hearing loss, formal testing is required. In addition to a focused history and examination, methods used in the papers analyzed included conventional audiometry, visual reinforcement audiometry, play audiometry, and auditory brainstem response testing [20], which could be done under sedation or general anesthetic if required. Tympanometry helps to differentiate between conductive and sensorineural hearing loss if there is a diagnostic doubt.

The World Health Organization (WHO) grades hearing loss as "mild" (21–40 dB), "moderate" (41–60 dB), "severe" (61–80 dB), and "profound" (81 dB) [23]. As such, the AAOHNS definition (≥30 dB) is comparable with "moderate" to "profound" hearing loss as defined by WHO, as well as some "mild" hearing loss.

Patient Workup

The possible etiologies of SSNHL in children are multitudinous and varied, and as such the options for investigation, beyond history and examination, of these children described in the papers analyzed are similarly numerous.

A myriad of blood tests was suggested by the papers analyzed. Full blood count, erythrocyte sedimentation rate, and C-reactive protein [14] can point toward acute inflammation or infection [13]. Urea and electrolytes [14] can point toward chronic kidney disease, which is associated with SSNHL in adults [24]. Liver function tests may suggest a diagnosis of hepatitis, a disease that can present as sudden hearing loss [7]. Anti-nuclear antibody, rheumatoid factor [14], and immunoglobulin levels [11] can point toward autoimmune or rheumatological disease, also associated with SSNHL in adults [25]. Thyroid dysfunction (both hypo and hyperthyroidism) can cause SSNHL [7], and thus, thyroid function tests can be beneficial [14]. One paper [17] suggested analyzing the patients' blood lipid profiles, although the relationship between hyperlipidemia and SSNHL is disputed [26]. Coagulopathy may cause damage to the micro-circulation in the ear, leading to SSNHL in adults [7], and fibrinogen levels have been shown to be a prognostic indicator for these individuals [27]; therefore, a coagulation profile and homocysteine levels [11] may be of benefit.

Acute infection with Epstein-Barr virus (EBV), herpes simplex virus (HSV), rubella, mumps [28], syphilis [7], hepatitis B or C [29], and Lyme disease [30] can cause sudden hearing loss, and thus, EBV, HSV, rubella,

Table 4. A comparison of unilateral and bilateral sudden sensorineural hearing loss

Authors	Number of unilateral cases	Number of patients showing any improvement (%)	Number of bilateral cases	Number of patients showing any improvement (%)
Tarshish et al. [20]	10	3 (30) + 1 (10) unknown	7	2 (29) + 1 (14) unknown
Pitaro et al. [13]	18	12 (67)	1	0 (0)
Dedhia et al. [21]	12	Not reported	8	Not reported
Chen et al. [9]	73	48 (66)	28	11 (39)
Ha et al. [8]	42	35 (83)	0	NA
Kim et al. [14]	67	37 (55)	0	NA
Inci et al. [17]	36	22 (61)	7	2.5 (36)
Kizilary et al. [18]	12	3 (25)	2	0 (0)
Övet et al. [19]	49	37 (76)	0	NA
Wu et al. [10]	15	Not reported	10	Not reported
Na et al. [15]	80	Not reported	7	Not reported
Li et al. [11]	121	54 (45)	15	1.5 (10)
Qian et al. [12]	72	52 (72)	3	1 (33)
Chung et al. [16]	37	22 (59)	0	NA
All patients*	537	325 (61)	63	18 (29)

NA: not applicable.
*Not including those papers that did not report differences in recovery rates between unilateral and bilateral cases

mumps, syphilis, hepatitis B and C, and Lyme serology or titers can be useful diagnostic tools. Dedhia et al. [21] suggested testing for mutations in the gap junction beta-2 (*GJB2*) and *GJB6* genes, which code for connexin 26 and 30, respectively; however, this tends to cause a congenital hearing loss, rather than an SSNHL [31].

One study reports a singular use of a streptococcal throat swab [20]. Beta-hemolytic streptococcal infections can cause sensorineural hearing loss, which can respond to steroid therapy [32].

Computed tomography (CT) scanning can be used to find structural anomalies such as an enlarged vestibular aqueduct, absent/hypoplastic cochlear nerve, syndrome of common cavity, or Mondini dysplasia, which can be associated with the development of hearing loss in childhood [13,21,33]. Enlarged vestibular aqueduct is usually associated with an enlarged endolymphatic sac, seen on magnetic resonance imaging (MRI) [34]; however, Dedhia et al. [21] reported a discrepancy between MRI and CT; hence, both modalities can be considered. MRI can also show features of congenital cytomegalovirus infection [35]; however, this tends to cause a more progressive hearing loss [36].

In reality, one cannot expect to do all these investigations for each child presenting with SSNHL, and as such, investigations should be tailored to each child depending on the history and systemic examination. Indeed, where reported, despite these tests, 67% of patients with SSNHL in the papers analyzed remained idiopathic (Table 2).

Treatment

The mainstay of treatment of SSNHL in children is steroids. The specific steroids used and their route of administration, however, differed slightly in the papers studied, and many did not give specific details of treatments used, but where possible, this is detailed later and summarized in Table 2.

Tarshish et al. [20] gave most patients systemic steroids, the specifics of which were not recorded. Others also received antivirals or antibiotics, depending on the clinical need.

Pitaro et al. [13] used at least 7 days of oral prednisolone (1 mg/kg/day) or intravenous hydrocortisone (1 mg/kg/day) divided over 3 doses. If no improvement was seen with systemic steroids, patients were given 1 mg of dexamethasone intratympanically, twice a day for 7 days as salvage therapy. Dedhia et al. [21] also described initial use of systemic oral steroid, followed by salvage intratympanic steroid, although only for those patients whose hearing worsened after systemic steroid treatment. Specific regimens were not recorded. Chen et al. [9] used 7 days of methylprednisolone at 1 mg/kg/day that was then tapered, along with mecobalamine (a vitamin B12 derivative).

Ha et al. [8] used 1.5 mg/kg/day prednisolone, which was tapered, but the course length was not described. They also used intratympanic steroid in some patients; however, the selection criteria for these patients was not discussed. Kim et al. [14] used 4 days of prednisolone at 1 mg/kg/day before tapering over 10 days. They also used intratympanic steroid injection for salvage treatment if no improvement in hearing was seen after administration of the systemic steroid.

Inci et al. [17] used 1 mg/kg/day of methylprednisolone, tapering gradually, and hyperbaric oxygen for all patients. Kizilay et al. [18] used 1

mg/kg prednisolone, reducing the dose by 10 mg every second day from a minimum of 5 to 11 days total treatment. Na et al. [15] used a similar regimen, but did not describe it in such detail. Wu et al. [10] gave all their patients prednisolone at 1 mg/kg/day for 7 to 14 days before tapering and adenosine triphosphate (ATP) and mecobalamine for a month.

Övet et al. [19] offered intratympanic and systemic steroids to all their patients. Those who consented had 0.3–0.5 mL of 4 mg/mL intratympanic dexamethasone and 14 days of oral methylprednisolone, initially at 1 mg/kg/day, tapering 10 mg every 3 days. Those who did not consent to intratympanic steroid had oral methylprednisolone alone.

Li et al. [11] used a plethora of treatments. Along with the more widely used steroids, they mentioned low-salt diet, vasodilators, fibrinolytics, plasma volume expansion, antivirals, anti-inflammatories, diuretics, and hyperbaric oxygen.

Qian et al. [12] gave all their patients 3 days of oral prednisolone at 1 mg/kg/day and 7 to 14 days of dipyridamole and alprostadil. Those with profound hearing loss (>80 dB loss) or flat audiograms were also given batroxobin (a fibrinolytic). Some children were also given intratympanic methylprednisolone and/or postauricular betamethasone. The selection criteria for this were not described.

Finally, Chung et al. [16] used 1 mg/kg/day of oral prednisolone for 7 days before tapering over 7 days and a 5-day continuous infusion of 5 mL/kg/day of dextran, a low molecular-weight plasma volume expander.

The most widely used treatment for SSNHL in children within the analyzed papers was systemic steroid. Intratympanic steroid was used in addition to or as a salvage, but never on its own.

Recovery

A range of improvement parameters were utilized and characterized as "recovery" within the current literature (Table 1). Siegel's criteria was most commonly used, being a measure in 6 studies [37], although this audiological criteria was modified by an additional 2 authorship groups; and 2 groups used a self-defined scale of complete, partial, and no recovery, whereas mean pure tone audiogram was also used by 2 papers.

For this analysis, "improvement" was classed as any improvement in hearing after the initial episode of SSNHL as defined by the included papers. Table 2 shows the treatment given to patients in each of the papers analyzed (where possible) and shows the proportion of patients showing improvement.

Table 3 shows the proportion of patients showing any improvement from each treatment, pooled across the papers. The paper by Li et al. [11] was excluded from this data because the proportion of each treatment used for their patients are not described. A total of 594 patients were included for this post-treatment analysis of which 521 were unilateral and 73 were bilateral.

There was an overall hearing improvement rate of 56 % in the studies analyzed with systemic steroids, which was the most commonly used treatment. Most papers do not state whether oral or intravenous therapy was used, although in a small number of patients where this was recorded, intravenous therapy appeared to be slightly superior. However, intravenous therapy requires lengthy admission to hospital and increases the treatment burden (cannulation, and so on) for young people.

Intratympanic steroid appears to be effective, both when used as a first-line treatment, increasing the recovery rate from 60% with steroids alone to 83%, and as a salvage treatment. In this case, the use of intratympanic steroid when systemic steroid failed led to an improvement in hearing in 55% of the patients. Hyperbaric oxygen, used by 1 paper with 43 children, did not appear to increase recovery rate when added to standard systemic steroid therapy. Of the 14 children not treated for their SSNHL, only 1 showed signs of improvement.

One paper [10] reported a 100% recovery rate with systemic steroids, adenosine triphosphate (ATP), and mecobalamine, although this data is difficult to extrapolate beyond this isolated study. Another study [9] just using steroid and mecobalamine showed a recovery rate of 31%.

When bilateral SSNHL was identified (73 individuals), improvement occurred in 29% (21 patients) demonstrating a much poorer prognosis than when SSNHL is identified unilaterally (Table 4).

CLINICAL AND RESEARCH CONSEQUENCES

Methodologically, this paper is limited by the degree of heterogeneity within the current pediatric literature that restricts the possible analysis along with the comparatively poor evidence base surrounding treatment options for pediatric patients with SSNHL. Standardization of "improvement parameters" would allow comparison of treatment regimens. In particular, the opportunity to evaluate the prognosis of bilateral SSNHL as distinct from unilateral SSNHL is of interest given its profound impact on the affected child and family.

Given the comparative rarity of the pathology, multi-center research collaboration is likely to form the best approach for understanding the condition in the future. Inner ear therapeutics undertaken within the adult field offer future opportunities that may translate to the pediatric population. Patient and parental interpretation of the risks of these therapies need to be assessed with reference to current understanding of audiological outcome and potential resolution with standard therapies.

Discussion with the patient and their parents regarding the potential prognosis of this condition has previously been difficult. This paper allows clinicians to explain that from the published literature, the chances of improvement stand at 56%. This is a worse prognosis than adult data in which an estimated spontaneous improvement of 65%-66% of cases is noted [38,39].

CONCLUSION

A pooled analysis of pediatric SSNHL demonstrates significant heterogeneity in the assessment and treatment of these patients along with outcomes of improvement. To create an evidence-based guideline for the management of these rare patients, consensus agreement on audiological standards for improvement and subsequent monitoring would be beneficial.

The role of steroid in primary treatment is indicated, but the potential impact and timing of intratympanic steroid treatment as an analogous primary treatment or salvage therapy remains unclear. Future focus in these areas is particularly pertinent given the worse overall prognosis of the condition within the pediatric population.

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