Taylor & Francis
Taylor & Francis Group

International Journal of Audiology

ISSN: 1499-2027 (Print) 1708-8186 (Online) Journal homepage: http://www.tandfonline.com/loi/iija20

Sudden sensorineural hearing loss: is there a relationship between routine haematological parameters and audiogram shapes?

Pietro Salvago, Serena Rizzo, Antonino Bianco & Francesco Martines

To cite this article: Pietro Salvago, Serena Rizzo, Antonino Bianco & Francesco Martines (2016): Sudden sensorineural hearing loss: is there a relationship between routine haematological parameters and audiogram shapes?, International Journal of Audiology, DOI: 10.1080/14992027.2016.1236418

To link to this article: http://dx.doi.org/10.1080/14992027.2016.1236418

Published online: 07 Oct 2016.

Submit your article to this journal

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at
http://www.tandfonline.com/action/journalInformation?journalCode=iija20

Download by: [Universita di Palermo] **Date:** 07 October 2016, At: 06:12

Taylor & Francis
Taylor & Francis Group

International Journal of Audiology 2016; Early Online: 1–6

International Journal of Audiology

Original Article

Sudden sensorineural hearing loss: is there a relationship between routine haematological parameters and audiogram shapes?

Pietro Salvago[1], Serena Rizzo[1], Antonino Bianco[2], and Francesco Martines[1]

[1]BioNeC Department, Università degli Studi di Palermo, ENT Section, Via del Vespro, Palermo, Italy and [2]Sport and Exercise Sciences Research Unit, Università degli Studi di Palermo, Via Giovanni Pascoli, 6, Palermo, Italy

Abstract

Objective: To investigate the relationship between haematological routine parameters and audiogram shapes in patients affected by sudden sensorineural hearing loss (SSNHL). *Design*: A retrospective study. All patients were divided into four groups according to the audiometric curve and mean values of haematological parameters (haemoglobin, white blood cell, neutrophils and lymphocytes relative count, platelet count, haematocrit, prothrombin time, activated partial thromboplastin time, fibrinogen and neutrophil-to-lymphocite ratio) of each group were statistically compared. The prognostic role of blood profile and coagulation test was also examined. *Study sample*: A cohort of 183 SSNHL patients without comorbidities. *Results*: With a 48.78% of complete hearing recovery, individuals affected by upsloping hearing loss presented a better prognosis instead of flat (18.36%), downsloping (19.23%) and anacusis (2.45%) groups ($p = 0.0001$). The multivariate analysis of complete blood count values revealed lower mean percentage of lymphocytes ($p = 0.041$) and higher platelet levels ($p = 0.015$) in case of downsloping hearing loss; with the exception of fibrinogen ($p = 0.041$), none of the main haematological parameters studied resulted associated with poorer prognosis. ***Conclusions***: Our work suggested a lack of association between haematological parameters and a defined audiometric picture in SSNHL patients; furthermore, only fibrinogen seems to influence the prognosis of this disease.

Keywords: Sudden sensorineural hearing loss, audiogram shape, haematological parameters

Introduction

With an expected incidence of 5–30/100,000 cases per year (Schreiber et al, 2010), sudden sensorineural hearing loss (SSNHL) represents a challenging otological emergency whose pathophysiology, prognosis and treatment remain not completely understood. The most common diagnostic criteria are a sensorineural hearing loss of at least 30 dB over three consecutive frequencies occurring within a 72-h period (Stachler et al, 2012). SSNHL is generally unilateral, isolated and with variable clinical features in terms of hearing loss degree, accompanying symptoms and post-treatment outcomes. It was estimated that approximately half of SSNHL patients has a complete and spontaneous hearing recovery (Wilson et al, 1980; Filipo et al, 2013) even if a short course of corticosteroids is generally prescribed (Kuhn et al, 2011).

It is possible to recognise a specific aetiology only in about 10% of cases (Nosrati-Zarenoe et al, 2007; Chau et al, 2010); however, to explain the inner ear damage, several pathogenetic mechanisms were proposed such as vascular, viral, autoimmune, traumatic and metabolic. Impaired cochlear perfusion remains the most supported hypothesis due to the characteristics of inner ear circulation, constituted by a terminal capillary bed without collateral blood supply; vasospasm, thrombosis or vascular haemorrhage may be responsible of a reduced cochlear blood flow with consequent hypoxia, decrease of metabolic activity and damage of cochlear hair cells (Mosnier et al, 2010; Martines et al, 2011). Additionally, rheological and thrombophilic factors like high plasma viscosity, elevated fibrinogen levels, inherited prothrombotic conditions (e.g. hyperhomocysteinemia, Factor V Leiden mutation) and reduced erythrocyte filterability may increase the risk of SSNHL onset (Suckfull et al, 2002; Fusconi et al, 2012; Lovato et al, 2014).

White blood cell (WBC) count represents another peripheral blood index frequently elevated in SSNHL patients (Mattox & Simmons, 1977). The study of WBC subtypes and particularly of

Correspondence: Pietro Salvago, Università degli Studi di Palermo, BioNeC Department, ENT Section, Via del Vespro, Palermo, 90100 Italy. Tel: 0039-091.6251473. E-mail: pietrosalvago@libero.it

(Received 8 May 2016; accepted 9 September 2016)

ISSN 1499-2027 print/ISSN 1708-8186 online © 2016 British Society of Audiology, International Society of Audiology, and Nordic Audiological Society
DOI: 10.1080/14992027.2016.1236418

Abbreviations

SSNHL	sudden sensorineural hearing loss
PTA	pure tone average
Hb	haemoglobin
WBC	white blood cell
N%	neutrophils relative count
L%	lymphocytes relative count
PC	platelet count
Ht	haematocrit
PT	prothrombin time
aPTT	activated partial thromboplastin time
NLR	neutrophil-to-lymphocite ratio
MPV	mean platelet volume
PDW	platelet distribution width

Neutrophil-to-lymphocite ratio (NLR) may be a useful tool to determine inflammation and predict prognosis in subjects with SSNHL (Ulu et al, 2013).

Even if numerous studies previously evaluated the role of haematological parameters as risk and prognostic factors for SSNHL, few of them focused on their possible influence on the audiometric profile. For example, Kanzaki et al (2014) in a retrospective multicentre trial involving 203 SSNHL patients evidenced a negative correlation in hearing recovery rate between high-pitch sloping hearing loss and fibrinogen levels ($p = 0.04$) and between anacusis and WBC ($p = 0.03$). Sagit et al (2013) and Mirvakili et al (2016) instead found no association between hearing loss severity and mean platelet volume (MPV) and platelet count (PC), respectively ($p > 0.05$).

It is clear that studying the aforementioned blood parameters values and the associated pattern of hearing damage may contribute to a better understanding of the underlying cause of SSNHL development. Thus, main purpose of the present study was to investigate the relationship between haematological routine parameters and audiogram shapes in patients affected by SSNHL; the prognostic role of blood profile and coagulation test was also examined.

Materials and methods

Participants and inclusion criteria

A retrospective study was conducted at the Audiology Section of the University of Palermo collecting medical and audiological records from 270 patients diagnosed with SSNHL who were admitted to our tertiary referral centre between January 2001 and December 2014.

A careful analysis of data concerning anamnesis, microotoscopy and audiometric tests was performed to exclude otological diseases as history of middle and inner ear disease with a defined aetiology such as trauma, infection, perilymphatic fistula, magnetic resonance imaging (MRI)-documented retrocochlear disease (e.g. schwannoma), exposure to ototoxic drugs, barotrauma, middle or inner ear malformation, definite Meniere's disease. Additionally, the following comorbidities were used as exclusion criteria: diabetes mellitus, coronary artery disease, congestive heart failure, renal and/or hepatic dysfunction, arterial or venous thrombotic disease, haematological disease, endocrine disorder and autoimmune disease.

Subjects with SSNHL in the better or in the only hearing ear were included when in the presence of a previous audiometry test. A total of 183 patients who met the inclusion criteria were enrolled in the study. Ethical Committee approved our study and a written informed consent was obtained from all participants before the treatment.

Haematological parameters

Haemoglobin (Hb), WBC with the relative count of neutrophils (N%) and lymphocytes (L%), PC, haematocrit (Ht), fibrinogen, prothrombin time (PT), activated partial thromboplastin time (aPTT) in blood samples were measured before the treatment. NLR was calculated as a ratio between the absolute neutrophil and lymphocyte counts (Ulu et al, 2014). Initially, patients with abnormal finding in glucose levels, creatinine, total cholesterol and triglycerides were excluded. Venous blood samples were collected into tubes containing ethylenediaminetetraacetic acid at 8 a.m. following an overnight fast.

Hearing evaluation and treatment

Air conduction pure-tone average thresholds at frequencies 0.25–0.5-1-2-4 kHz ($PTA_{0.25\text{-}4\,kHz}$) were calculated for each ear (Suzuki et al, 2015) and were used to classify hearing loss degree as follows: mild, 21 dB or greater but less than 41 dB; moderate, 41 dB or greater but less than 71 dB; severe, 71 dB or greater but less than 91 dB; and profound, greater than 91 dB hearing loss. Hearing assessment was performed during the initial visit and one-month post-treatment. Pre-treatment and post-treatment audiograms were examined and hearing thresholds at 250, 500, 1000, 2000 and 4000 Hz were recorded. Audiogram patterns were categorised as ''upsloping'' (hearing loss affecting 250, 500 Hz more), ''flat'' (less than 20 dB difference between the highest and the lowest threshold), ''downsloping'' (hearing loss affecting 4000, 8000 Hz more) and ''anacusis'' (thresholds of 90 dB or more in each test frequency) (Alimoglu et al, 2011). Patients were divided into four groups according to audiogram shape.

Criteria adopted to categorise audiological improvement were based on those used by Furuhashi et al (2002): (1) complete recovery: a post-treatment $PTA_{0.25\text{–}4\ kHz} \leq 25$ dB H; 2) marked improvement: a $PTA_{0.25\text{–}4\ kHz}$ improvement >30 dB HL; (3) slight improvement: a $PTA_{0.25\text{–}4\ kHz}$ improvement >10 dB HL but <30 dB HL; (4) nonrecovery: a $PTA_{0.25\text{–}4\ kHz}$ improvement <10 dB HL.

All subjects were treated with oral prednisone 1 mg/kg/day (maximum daily dose =60 mg) for at least 12 days; the dose was tapered every 4 days. No patients underwent hyperbaric oxygen therapy (HBO). Salvage intratympanic steroid injection (ITSI) was performed after failure (slight improvement or no recovery) in initial systemic steroid treatment since 2009. ITSI was performed introducing a solution of 4 mg/ml dexamethasone to fill completely the middle ear through a puncture of the posteroinferior portion of the tympanic membrane with a 25-gauge spinal needle. During the procedure, the patient was in the supine position with the head tilted 45° to the unaffected side; after the injection, patients were instructed to maintain this position for 30 min avoiding swallowing, speaking and movements of the head. ITSI was repeated once a week for a maximum of five consecutive weeks.

Table 1. Demographic and clinical characteristics of the total cohort.

	Audiogram				
Cohort	Upsloping	Flat	Downsloping	Anacusis	p *value*
No. of patients	41 (22.4)	49 (26.77)	52 (28.42)	41 (22.41)	
Gender					
Male	24 (58.53)	19 (38.78)	38 (73.07)	20 (49.79)	0.005
Female	17 (41.47)	30 (61.22)	14 (26.93)	21 (51.21)	
Mean age	38.35 ± 10.83	45.79 ± 15.17	42.71 ± 12.85	44.54 ± 14.92	ns
Side					
Left	24 (58.53)	26 (53.06)	29 (55.76)	27 (65.85)	ns
Right	17 (41.47)	23 (46.94)	23 (44.24)	14 (34.15)	
Smoking					
Yes	16 (39.03)	14 (28.58)	23 (44.24)	13 (31.71)	ns
No	25 (60.97)	35 (71.42)	29 (55.76)	28 (68.29)	
Tinnitus					
Yes	28 (68.29)	39 (79.59)	37 (71.15)	33 (80.48)	ns
No	13 (31.71)	10 (20.41)	15 (28.85)	8 (19.52)	
Vertigo					
Yes	9 (21.96)	15 (30.62)	14 (26.93)	20 (48.79)	0.048
No	32 (78.04)	34 (69.38)	38 (73.07)	21 (51.21)	
Treatment delay	4.45 ± 2.17	5.17 ± 2.21	4.76 ± 2.74	5.93 ± 5.56	ns
Mean $PTA_{0.25–4\ kHz}$					
Pre-treatment	50.9 ± 18.65	63.25 ± 16.81	54.3 ± 18.37	105.7 ± 11.7	<0.0001
Post-treatment	29.19 ± 16.28	45.83 ± 22.54	40.16 ± 22.6	84.41 ± 30.91	<0.0001
ITS					
Yes	8 (19.52)	14 (28.58)	21 (40.39)	13 (31.71)	ns
No	33 (80.48)	35 (71.42)	31 (59.61)	28 (68.29)	

Statistical analysis

Group data were expressed as percentages and quantitative variables as mean ± standard deviations. Statistical comparisons between two or more groups were made using χ^2 test and/or Fisher's exact test, Student's paired *t*-test and analysis of variance (ANOVA) test when appropriate. A multivariate analysis of significance with Bonferroni's *post hoc* test was performed to study the relationship between haematological parameters and audiogram shapes (Wilks' effect). Significance was set at $p < 0.05$. The STATISTICA Software, Palermo, Italy (Vers. 8.0 for Windows) was adopted.

Results

Table 1 depicts the main demographic and clinical characteristics of the whole sample studied. One hundred eighty-three SSNHL patients, 101 males (55.19%) and 82 females (54.81%) were enrolled, with a Sex ratio of 1.23 and an average age at the SSNHL onset of 43 ± 13.73 years. Subjects were classified in four groups according to audiogram shape: the first, composed by 41 patients (22.4%) who suffered from an upsloping hearing loss; the second, which included 49 individuals (26.77%) affected by a flat hearing loss; the third and the fourth, respectively, constituted by 52 subjects (28.43%) with a downsloping hearing loss and 41 patients (22.4%) suffering from anacusis. Groups were similar in terms of age ($p = 0.063$) and smoking ($p = 0.363$), but different with respect to sex ($p = 0.005$).

The evaluation of accompanying symptoms revealed a higher percentage of vertigo (48.79%) in patients with anacusis with respect to the others groups ($p = 0.048$). The mean duration from the SSNHL onset to therapy was studied, resulting in 4.45 ± 2.17, 5.17 ± 2.21, 4.76 ± 2.74 and 5.93 ± 5.56 days of treatment delay, respectively, in subjects with an upsloping hearing loss, flat hearing loss, downsloping hearing loss and anacusis ($p = 0.21$); particularly, the 93.44% of the total sample received a treatment within 7 days.

As shown in Figure 1, the study of mean pre-treatment $PTA_{0.25–4\ kHz}$ evidenced a mean hearing threshold of 50.9 ± 18.65 dB HL and 54.3 ± 18.37 dB HL in the upsloping and downsloping groups, instead of patients with flat hearing loss (63.25 ± 16.81 dB HL) and anacusis (105.7 ± 11.7 dB HL) who were characterised by lower threshold values ($p < 0.0001$). Specifically, from the comparison of the distribution of hearing loss degree, it resulted a higher percentage (82.94%) of mild and moderate hearing impairment in the first group with respect to flat (51.03%) and downsloping groups (69.23%) ($p = 0.001$).

A mean hearing improvement of about 20 dB HL after therapy was observed independently of the audiogram curves, even if patients affected by an upsloping hearing loss presented better post-treatment mean $PTA_{0.25–4\ kHz}$ values (29.19 ± 16.28 dB HL) ($p < 0.0001$). A complete PTA improvement occurred in 40 patients (21.86%), a marked in 25 (13.66%), a slight in 41 (22.4%) whereas no recovery was observed in 77 SSHL cases (42.08%).

Audiological evaluation of patients revealed a heterogeneous hearing recovery with respect to the audiogram shape (Figure 2): in fact, with a 48.78% of complete hearing recovery, individuals suffering of upsloping hearing loss presented a better prognosis instead of flat (18.36%), downsloping (19.23%) and anacusis (2.45%) groups who were characterised by poorer post-treatment outcomes ($p = 0.0001$).

Table 2 represents the main haematological parameters examined. The multivariate analysis of complete blood count values revealed lower mean percentage of lymphocytes (21.19 ± 7.84%) in case of downsloping hearing loss ($p = 0.041$); a statistical

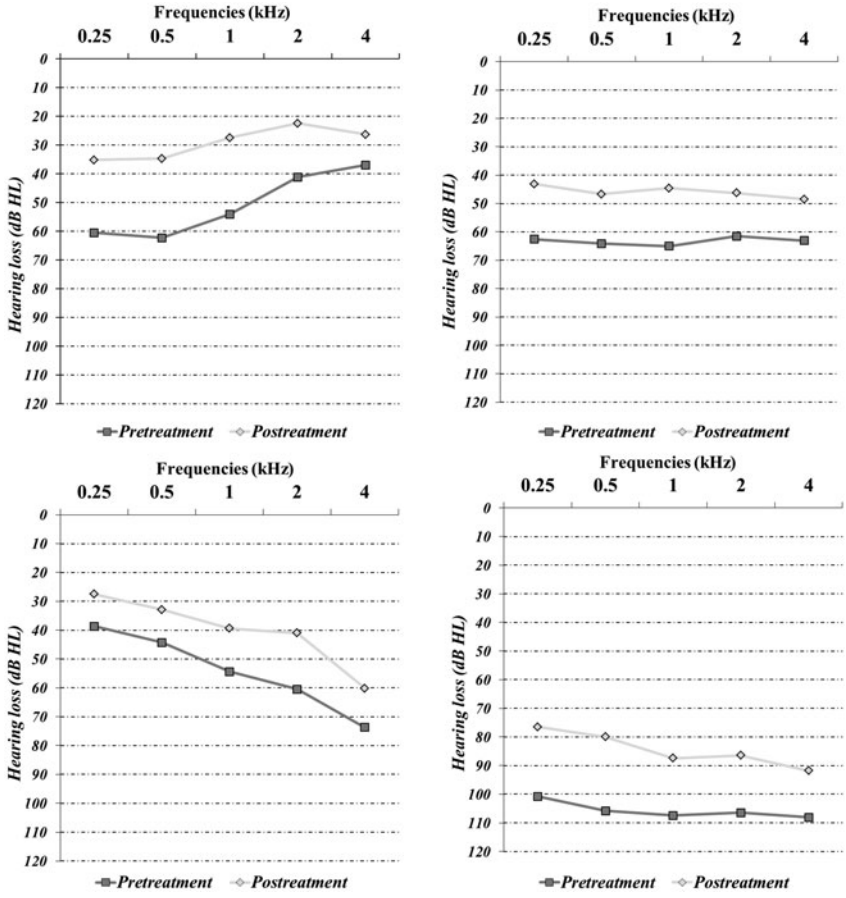

Figure 1. Pre-treatment and post-treatment $PTA_{(0.25–4\ kHz)}$ in case of upsloping hearing loss (1), flat hearing loss (2) downsloping hearing loss (3) and anacusis (4).

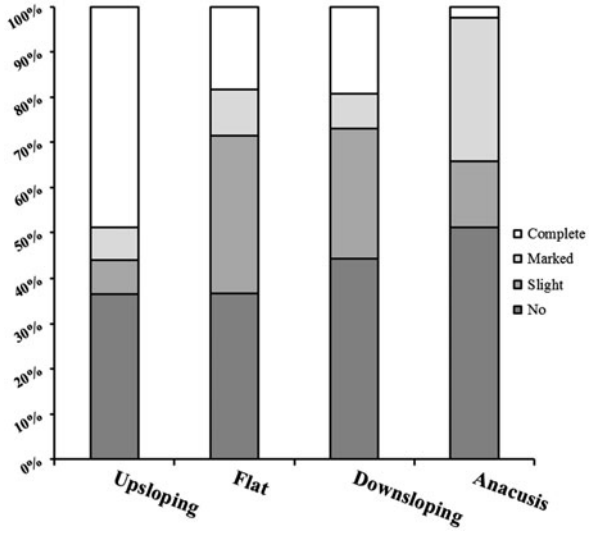

Figure 2. Relative frequencies of hearing recovery for each audiogram shape group.

significant difference ($p = 0.015$) was also evidenced in case of PC, with patients affected by downsloping hearing impairment having a slight increase (~20,000–30,000/μl) in mean PC with respect to other groups. Concerning fibrinogen, aPTT, PT, Hb, WBC, Ht and NLR, no significant variations between patients with different audiogram shapes were identified ($p > 0.05$).

Finally, with the exception of fibrinogen, none of the main haematological parameters studied resulted correlated with prognosis; in fact, fibrinogen levels showed a significant positive trend with prognosis ($p = 0.041$), with higher mean values found in patients characterised by slight (329.48 ± 98.61 mg/dl) or no (320.8 ± 78.61 mg/dl) improvement.

Discussion

Even if cochlear microcirculatory disturbances, viral, immunologic and inflammatory reasons have been suggested as possible causes of SSNHL, the exact etiopathogenesis of this otological emergency remains still unclear.

In the last years, many authors studying the role of blood and coagulation parameters as risk factors and potential prognostic biomarkers for SSNHL, tried to understand the main pathogenetic mechanism of hearing loss onset, often with contradictory conclusions.

Platelet parameters (PC, MPV, PDW) are indexes of haemostasis and its dysfunction and have been investigated as potential risk factors for SSNHL due to its similar clinical manifestation to that of vascular disorders. In particular, MPV is a well-studied indicator of platelet activation: in fact, platelets of larger volume are characterised by more granules, larger adhesion receptors and a

Table 2. Multivariate analysis on the association between mean haematological parameters values and audiogram shapes ($p = 0.013$).

Parameter	*Upsloping*	*Flat*	*Downsloping*	*Anacusis*	*p value*
Fibrinogen (mg/dl)	303.22 ± 61.53	332.48 ± 84.86	296.4 ± 59.05	324.58 ± 91.27	ns
aPTT	26.96 ± 12.8	27.33 ± 4.6	28 ± 4.53	26.5 ± 3.59	ns
PT	99.41 ± 12.8	99.35 ± 12.87	97.65 ± 15.52	107.41 ± 20.46	ns
Haemoglobin (g/dl)	14.24 ± 1.31	13.51 ± 1.66	13.9 ± 1.32	13.96 ± 1.38	ns
WBC (10^3/μl)	9.16 ± 2.83	9.14 ± 3.33	9.22 ± 2.91	9.2 ± 4.08	ns
Neutrophils (%)	64.86 ± 11.25	67.06 ± 10.11	71.35 ± 10.61	67.9 ± 13.13	ns
Lymphocytes (%)	27.63 ± 10.33	25.98 ± 8.5	21.19 ± 7.84	25.56 ± 12.91	0.041
NLR	2.93 ± 1.83	3.19 ± 2.68	3.61 ± 3.02	3.78 ± 3.58	ns
PC (10^3/μl)	243.22 ± 33.76	256.41 ± 55.17	264.69 ± 57.24	227.58 ± 65.16	0.015
Haematocrit (%)	42.83 ± 2.79	40.62 ± 5.08	41.62 ± 3.37	41.71 ± 3.54	ns

higher enzymatic and metabolic activity (Park et al, 2001; Kamath et al, 2002); so the presence of an elevated MPV may indicate dysfunction of haemostasis and could support the hypothesis of vascular impairment in the pathogenesis of SSNHL. Mirvakili et al (2016) in a prospective case–control study showed no association between PC, MPV and PDW and occurrence of SSNHL; only PDW resulted correlated with the severity of hearing loss ($p = 0.043$). On the contrary, Sagit et al (2013) and Seo et al (2014) analysing, respectively, haematological data of 31 and 348 SSNHL patients evidenced a significant difference in PC values between subjects with and without SSNHL. Furthermore, Yasan et al (2013), Wittig et al (2014), Quaranta et al (2015), Kum et al (2015) did not recognise PC as prognostic factor for hearing recovery ($p > 0.05$).

WBC and its subtypes are well-known inflammatory markers in cardiovascular diseases (Madjid et al, 2004), but, in patients affected by SSNHL, a high WBC count may reflect immune-mediated cochlear ischemic changes that can lead to extensive inner ear tissue damage (Kanzaki et al, 2014). In particular, Seo et al (2014) and Kum et al (2015) showed lower values of lymphocyte count in patients with less than 15 dB HL of hearing gain with respect to the initial hearing loss. Masuda et al (2012), İkincioğulları et al (2014) and Quaranta et al (2015) instead did not observe any correlation between lymphocyte count and recovery rate.

Other works instead, on the basis of fibrinogen rheological properties, highlighted the association between high fibrinogen levels and reduced blood flow in the inner ear with major risk of SSNHL onset (Suckfull et al, 2002; Canis et al, 2012; Bao et al 2015). Quaranta et al (2015) did not find any significant difference in terms of fibrinogen level between patients with and without hearing improvement ($p = 0.22$). In contrast, Wittig et al (2014), in a retrospective review including 173 SSNHL patients, recognised hyperfibrinogenaemia as independent prognostic factors for better hearing recovery ($p = 0.032$). Finally, Kanzaki et al (2014) analysing the correlation between various potential blood factors and hearing recovery rate demonstrated a negative correlation for fibrinogen ($p = 0.04$) in case of high-pitch sloping hearing loss and for WBC count ($p = 0.03$) in patients suffering from total deafness.

The analysis of our results may be summarised as follows: first, in line with other studies (Zadeh et al, 2003; Cvorović et al, 2008; Kuhn et al, 2011), our data confirmed the association between audiometric pattern and hearing recovery, with patients affected by severe or profound hearing loss having poor prognosis ($p = 0.0001$). Second, multivariate analysis failed to recognise a clear distinction between different audiometric curves in terms of haematological profile. In fact, of the 10 blood parameters examined, only higher PC ($p = 0.015$) and lower L% ($p = 0.041$) values were found to be statistically different in patients suffering from downsloping hearing loss. Third, the study of fibrinogen levels evidenced different mean values in patients suffering from upsloping hearing loss (303.22 ± 61.53 mg/dl), flat hearing loss (332.48 ± 84.86 mg/dl), downsloping hearing loss (296.4 ± 59.05 mg/dl) and anacusis (324.58 ± 91.27 mg/dl), but without any significant difference. However, in line with Kanzaki et al (2014), fibrinogen level seems to influence the prognosis ($p = 0.041$); in fact, lower mean values (<300 mg/dl) were found in patients characterised by marked and complete recovery with respect to subjects who presented a slight (329.48 ± 98.61 mg/dl) or no hearing improvement (320.8 ± 78.61 mg/dl).

The main strength of our work is that it demonstrated a lack of association between haematological parameters and a defined audiological SSNHL picture. However, even if we tried to apply strict criteria in the selection of patients to reduce the effect of confounding factors, our results are limited by the retrospective design and the relative small sample size of the study. Further investigations are required to provide a clear evidence of our suggestions.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

Alimoglu, Y., Inci, E., Edizer, D.T., Ozdilek, A. & Aslan, M. 2011. Efficacy comparison of oral steroid, intratympanic steroid, hyperbaric oxygen and oral steroid + hyperbaric oxygen treatments in idiopathic sudden sensorineural hearing loss cases. *Eur Arch Otorhinolaryngol*, 268, 1735–1741.

Bao, F., Zhang, S., Zhang, Y., Zhu, X. & Liu, W. 2015. The correlation analysis of coagulation detection and blood routine parameters of sudden hearing loss. *Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi*, 29, 52–56.

Canis, M., Heigl, F. & Suckfuell, M. 2012. Fibrinogen/LDL apheresis is a promising rescue therapy for sudden sensorineural hearing loss. *Clin Res Cardiol Suppl*, 7, 36–40.

Chau, J.K., Lin, J.R., Atashband, S., Irvine, R.A. & Westerberg, B.D. 2010. Systematic review of the evidence for the etiology of adult sudden sensorineural hearing loss. *Laryngoscope*, 120, 1011–1021.

Cvorović, L., Deric, D., Probst, R. & Hegemann, S. 2008. Prognostic model for predicting hearing recovery in idiopathic sudden sensorineural hearing loss. *Otol Neurotol*, 29, 464–469.

Filipo, R., Attanasio, G., Russo, F.Y., Viccaro, M., Mancini, P., et al. 2013. Intratympanic steroid therapy in moderate sudden hearing loss: a

randomized, triple-blind, placebo-controlled trial. *Laryngoscope*, 123, 774–778.

Furuhashi, A., Matsuda, K., Asahi, K. & Nakashima, T. 2002. Sudden deafness: Long-term follow-up and recurrence. *Clin Otolaryngol Allied Sci*, 27, 458–463.

Fusconi, M., Chistolini, A., de Virgilio, A., Greco, A., Massaro, F., et al. 2012. Sudden sensorineural hearing loss: a vascular cause? Analysis of prothrombotic risk factors in head and neck. *Int J Audiol*, 51, 800–805.

İkincioğulları, A., Köseoğlu, S., Kılıç, M., Atan, D., Özcan, K.M., et al. 2014. New inflammation parameters in sudden sensorineural hearing loss: neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. *Int Adv Otol*, 10, 197–200.

Kamath, S., Blann, A.D. & Lip, G.Y. 2001. Platelet activation: Assessment and quantification. *Eur Heart J*, 22, 1561–1571.

Kanzaki, S., Sakagami, M., Hosoi, H., Murakami, S. & Ogawa, K. 2014. High fibrinogen in peripheral blood correlates with poorer hearing recovery in idiopathic sudden sensorineural hearing loss. *PLoS One*, 9, e104680.

Kuhn, M., Heman-Ackah, S.E., Shaikh, J.A. & Roehm, P.C. 2011. Sudden sensorineural hearing loss: a review of diagnosis, treatment, and prognosis. *Trends Amplif*, 15, 91–105.

Kum, R.O., Ozcan, M., Baklaci, D., Kum, N.Y., Yilmaz, Y.F., et al. 2015. Investigation of neutrophil-to-lymphocyte ratio and mean platelet volume in sudden hearing loss. *Braz J Otorhinolaryngol*, 81, 636–641.

Lovato, A., Tormene, D., Staffieri, C., Breda, S., Staffieri, A., et al. 2014. Sudden hearing loss followed by deep vein thrombosis and pulmonary embolism in a patient with Factor V Leiden mutation. *Int J Audiol*, 53, 625–628.

Madjid, M., Awan, I., Willerson, J.T. & Casscells, S.W. 2004. Leukocyte count and coronary heart disease: implications for risk assessment. *J Am Coll Cardiol*, 44, 1945–1956.

Masuda, M., Kanzaki, S., Minami, S., Kikuchi, J., Kanzaki, J., et al. 2012. Correlations of inflammatory biomarkers with the onset and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol*, 33, 1142–1150.

Martines, F., Dispenza, F., Gagliardo, C., Martines, E. & Bentivegna, D. 2011. Sudden sensorineural hearing loss as prodromal symptom of anterior inferior cerebellar artery infarction. *ORL J Otorhinolaryngol Relat Spec*, 73, 137–140.

Mattox, D.E. & Simmons, F.B. 1977. Natural history of sudden sensorineural hearing loss. *Ann Otol Rhinol Laryngol*, 86, 463–480.

Mirvakili, A., Dadgarnia, M.H., Baradaranfar, M.H., Atighechi, S., Zand, V., et al. 2016. Role of platelet parameters on sudden sensorineural hearing loss: a case-control study in Iran. *PLoS One*, 11, e0148149.

Mosnier, I., Stepanian, A., Baron, G., Bodenez, C., Robier, A., et al. 2010. Cardiovascular and thromboembolic risk factors in idiopathic sudden sensorineural hearing loss: a case-control study. *Audiol Neurootol*, 16, 55–66.

Nosrati-Zarenoe, R., Arlinger, S. & Hultcrantz, E. 2007. Idiopathic sudden sensorineural hearing loss: results drawn from the Swedish national database. *Acta Otolaryngol*, 127, 1168–1175.

Park, Y., Schoene, N. & Harris, W. 2002. Mean platelet volume as an indicator of platelet activation: methodological issues. *Platelets*, 13, 301–306.

Quaranta, N., Squeo, V., Sangineto, M., Graziano, G. & Sabbà, C. 2015. High total cholesterol in peripheral blood correlates with poorer hearing recovery in idiopathic sudden sensorineural hearing loss. *PLoS One*, 10, e0133300.

Sagit, M., Kavugudurmaz, M., Guler, S. & Somdas, M.A. 2013. Impact of mean platelet volume on the occurrence and severity of sudden sensorineural hearing loss. *J Laryngol Otol*, 127, 972–976.

Schreiber, B.E., Agrup, C., Haskard, D.O. & Luxon, L.M. 2010. Sudden sensorineural hearing loss. *Lancet*, 375, 1203–1211.

Seo, Y.J., Jeong, J.H., Choi, J.Y. & Moon, I.S. 2014. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio: novel markers for diagnosis and prognosis in patients with idiopathic sudden sensorineural hearing loss. *Dis Markers*, 2014, 702807.

Stachler, R.J., Chandrasekhar, S.S., Archer, S.M., Rosenfeld, R.M., Schwartz, S.R., et al. 2012. Clinical practice guideline: sudden hearing loss. *Otolaryngol Head Neck Surg*, 146, S1–S35.

Suckfull, M., Wimmer, C., Reichel, O., Mees, K. & Schorn, K. 2002. Hyperfibrinogenemia as a risk factor for sudden hearing loss. *Otol Neurotol*, 23, 309–311.

Suzuki, H., Koizumi, H., Ohkubo, J., Hohchi, N., Ikezaki, S., et al. 2016. Hearing outcome does not depend on the interval of intratympanic steroid administration in idiopathic sudden sensorineural hearing loss. *Eur Arch Otorhinolaryngol*, 273, 3101–3107.

Ulu, S., Bucak, A., Ulu, M.S., Ahsen, A., Duran, A., et al. 2014. Neutrophil-lymphocyte ratio as a new predictive and prognostic factor at the hearing loss of diabetic patients. *Eur Arch Otorhinolaryngol*, 271, 2681–2686.

Ulu, S., Ulu, M.S., Ahsen, A., Yucedag, F., Aycicek, A., et al. 2013. Increased levels of mean platelet volume: a possible relationship with idiopathic sudden hearing loss. *Eur Arch Otorhinolaryngol*, 270, 2875–2878.

Ulu, S., Ulu, M.S., Bucak, A., Ahsen, A., Yucedag, F., et al. 2013. Neutrophil-to-lymphocyte ratio as a new, quick, and reliable indicator for predicting diagnosis and prognosis of idiopathic sudden sensorineural hearing loss. *Otol Neurotol*, 34, 1400–1404.

Wilson, W.R., Byl, F.M. & Laird, N. 1980. The efficacy of steroids in the treatment of idiopathic sudden hearing loss. A double-blind clinical study. *Arch Otolaryngol*, 106, 772–776.

Wittig, J., Wittekindt, C., Kiehntopf, M. & Guntinas-Lichius, O. 2014. Prognostic impact of standard laboratory values on outcome in patients with sudden sensorineural hearing loss. *BMC Ear Nose Throat Disord*, 14, 6.

Yasan, H., Tüz, M., Yariktaş, M., Aynali, G., Tomruk, O., et al. 2013. The significance of routine laboratory parameters in patients with sudden sensorineural hearing loss. *Indian J Otolaryngol Head Neck Surg*, 65, 553–556.

Zadeh, M.H., Storper, I.S. & Spitzer, J.B. 2003. Diagnosis and treatment of sudden-onset sensorineural hearing loss: a study of 51 patients. *Otolaryngol Head Neck Surg*, 128, 92–98.