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Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio as Novel Markers for Diagnosis of Sudden Sensorineural Hearing Loss: A Systematic Review and Meta-analysis

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Background: Sudden sensorineural hearing loss (SSNHL) is a common otologic disease characterized by a loss of hearing greater than 30 dB in three consecutive frequencies which occurs in less than 72 hours. **Objective:** To investigate the role of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) on sudden sensorineural hearing loss (SSNHL). **Search strategy:** A PubMed, Science Direct, Scopus, OVID, EMBASE and Google Scholar search (date last searched April 2016) without any time, language and location restriction was done. **Inclusion criteria:** All case-control studies, which have been investigated the relationship of NLR and PLR with the occurrence of SSNHL were included in our meta-analysis. **Results:** A total of 5 case-control studies were included in the study. All 5 studies have been reported NLR of patients and control groups (611 patients and 804 controls). Our analysis showed that the mean NLR of patients is 1.12 (0.82-1.43) unit higher than that of controls with 95% CI which is statistically significant. Also, 3 studies have been reported PLR of patients and control groups (512 patients and 705 controls). Our analysis showed that the mean PLR of patients is 0.57 (0.08-1.05) unit higher than that of controls with 95% CI which is statistically significant too. **Conclusions:** This meta-analysis confirmed the relationship of NLR and PLR with SSNHL. Therefore, these parameters can be considered as new markers in diagnosis of SSNHL.

Keywords: Sudden sensorineural hearing loss, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio

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INTRODUCTION

Sudden sensorineural hearing loss (SSNHL), which has been identified by Dekleyn in 1944, is a subset of sudden hearing loss that has the sensory-neural origin.[1] SSNHL is a common otologic emergency which is defined as more than 30 dB hearing loss in at least three consecutive frequencies in a standard pure tone audiogram (PTA). Sudden sensorineural hearing loss usually reaches its maximum pick quickly.

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In the occurrence of this disorder, patients often experience a sudden hearing loss which then progresses quickly and other sudden hearing losses occur.[2-8]

Current literature shows that only 10-15% of SSNHL cases have established causes and more than 85% of the cases occur without any established causes which is called idiopathic sudden sensorineural hearing loss.[6,9] The severity of hearing loss in this condition varies in a range from a slight hearing impairment to complete deafness. In clinical references the severity of hearing loss is categorized into 3 categories named low, medium and high hearing loss. Also, the type of hearing loss in this condition is varied and can include the low

frequencies, high frequencies or both.[6] Various aspects and causes of SSNHL is unknown and the etiology, risk factors, prognostic features and treatment protocols of the condition still remains controversial.[3,10] Studies show that the prevalence of SSNHL is varied among 5 to 30 cases per 100000 populations[3,6,7,11-13] with an increasing trend in recent epidemiological studies.[14] Platelets are the smallest blood cells. They play an important role in the formation of vascular thrombosis, coagulation processes, inflammation and atherosclerosis. Platelets are heterogeneous in terms of their volume and density.[15]

Although the primary role of platelets is keeping the hemostasis and thrombosis at the site of damage and bleeding, but it is known that it has a dominant role in inflammatory processes and immune response.[15] Various studies have shown that platelet parameters have relationship with some clinical events such as ischemic events, heart attack, infarction, vascular thrombosis, acute or chronic syndromes, autoimmune diseases and inflammatory conditions.[3,16]

Given that, according to previous studies, cardiac ischemic events associated with mean platelet volume (a platelet parameter)[16] as well as the clinical manifestation of sudden sensorineural hearing loss which similar to vascular diseases with the sudden appearance of one-sided signs[17] and also because some researchers believe that the sudden sensorineural hearing loss could be related to a kind of disruption in the blood supply to the inner ear due to its sudden occurrence[18] therefore the hypothesis of the existing a relationship between platelet parameters and occurrence and severity of SSNHL is under consideration. The aim of this meta-analysis was to analyze the results of previous studies which have been done in order to investigate the relationship of neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) with the occurrence of SSNHL.

MATERIALS AND METHODS

Search strategies:

This meta-analysis was performed according to a recommended protocol for systematic reviews. We searched PubMed, MEDLINE, Science Direct, OVID, Scopus, EMBASE and Google Scholar (date last searched April 2016) with using keywords and text words haring loss, sudden hearing loss, sudden sensorineural hearing loss, platelet, platelet parameters, lymphocyte, neutrophil, blood cells, neutrophil to lymphocyte ratio and platelet to lymphocyte ratio with "Or" and "And" operations in the title and abstract of articles. Also, the lists of retrieved studies' references were searched manually. No restrictions for language, time or geographical location were placed. Search was done by 2 researchers independently and the third researcher checked the agreement of retrieved studies with those 2 researchers.

Study selection:

All of the case control studies which have been done to study the relationship of NLR and PLR with the occurrence of SSNHL were included in the meta-analysis. For this purpose, full texts of all articles were retrieved through an extended search. The repeated or unrelated studies were removed and the investigation of the results of the reminding studies was done to prevent bias caused by reprint (publication bias of transverse and longitudinal). The inclusion criteria of remaining studies were investigated and those that have the inclusion criteria selected to meta-analysis.

Inclusion criteria:

All case-control studies which have been done on age and sex-matched patients and controls were included in the study.

Data Extraction:

The required data from selected studies including the title of article, first author, publication year and location of study, sample size of patients and control group, number of withdrawals and the mean and standard deviation of NLR and PLR of patients and control subjects were extracted and entered to EXCELL software.

Data analysis:

Data analysis was done using STATA ver.11 software. The index of heterogeneity between studies was determined using Cochran (Q) and I-squared tests. Given that the existing heterogeneity between studies random effect model was used to estimate the standardized difference of NLR and PLR of patients and controls. Inverse variance method and Cohen statistics were used for estimation. The point estimations of standardized difference of NLR and PLR were calculated using forest plot and 95% confidence interval. In this plot, the size of square represents the weight of each study and its booth sides' lines represent 95% confidence interval. P value < 0.01 was considered statistically significant.

RESULT

A total number of 17900 studies were retrieved from our search from which 16970 ones were removed by limiting the search. From reminding 926 studies, 672 studies were removed because of overlapping of searched databases. The reviewing of titles and abstracts of 254 studies indicated that 193 studies are unrelated. The remaining 61 studies were selected to investigating the full text after that 56 studies were removed from study due to their inappropriateness. The remaining 5 studies were entered to be assessed based on the

inclusion criteria from them 5 studies were found to be appropriate for our study (Fig.1). All of these 5 studies have reported NLR of patients and controls (611 patients and 804 controls) and 3 studies have reported PLR of patients and controls (512 patients and 705 controls). The characteristics of primary studies which have reported NLR and PLR of patients and controls are presented in Table.1 and Table.2. In all of 5 studies which have reported NLR, the NLR of patients were statistically higher than controls. Analyzing the results of these studies showed that the mean NLR of patients is 1.12 (0.82-1.43) unit higher than that of controls with 95% CI which is statistically significant. The heterogeneity between these studies was relatively high (I-squared=79.5%, Q=19.5, P=0.001). These results are presented in Fig.2.

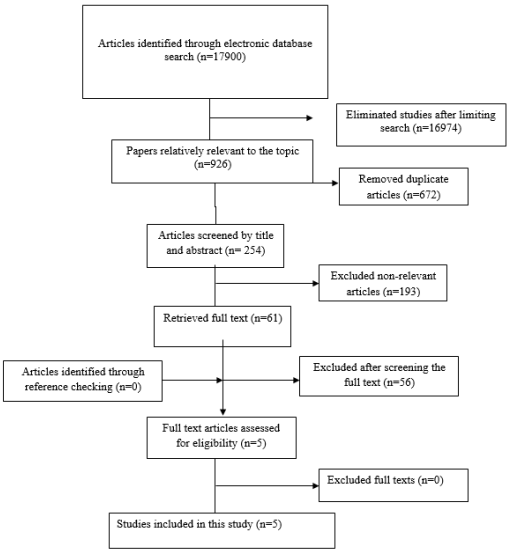

Figure 1
Literature search and review flowchart for selection of primary studies.

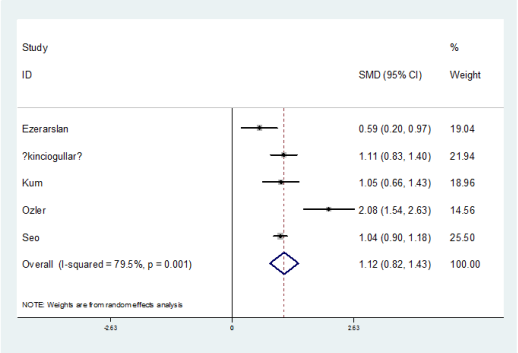

Figure 2
The difference of NLR of patients and control groups (CI=95%)

Also, in all of 3 studies which have reported PLR, the PLR of patients were statistically higher than controls. Analyzing the results of these studies showed that the mean PLR of patients is 0.57 (0.08-1.05) unit higher than that of controls with 95% CI which is statistically significant. The heterogeneity between these studies was relatively high (I-squared=90.9%, Q=21.95, P<0.001). These results are presented in Fig.3.

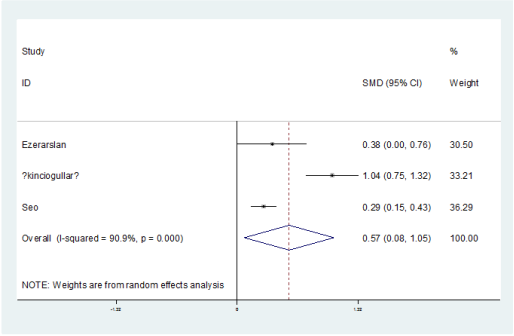

Figure 3
The difference of PLR of patients and control groups (CI=95%)

Table 1. Characteristics of primary studies which have reported NLR of patients and controls

No.	First author	Publication year	Country	Sample size		NLR, patients		NLR, controls		P value
				Case	Control	Mean	SD	Mean	SD	
1	Ezerarslan (19)	2016	Turkey	62	49	3.10	2.40	2.00	0.80	0.002
2	İkincioğulları (20)	2014	Turkey	102	119	4.02	3.57	1.32	0.22	0.001
3	Kum (21)	2015	Turkey	59	59	3.24	2.26	1.53	0.47	0.001
4	Ozler (22)	2014	Turkey	40	40	5.53	1.72	2.73	0.81	0.0001
5	Seo (23)	2014	Korea	348	537	4.48	3.92	1.83	0.87	0.001

Table 2. Characteristics of primary studies which have reported PLR of patients and controls

No.	First author	Publication year	Country	Sample size		PLR, patients		PLR, controls		P value
				Case	Control	Mean	SD	Mean	SD	
1	Ezerarslan (19)	2016	Turkey	62	49	143	83	118	31.2	0.032
2	İkincioğulları (20)	2014	Turkey	102	119	148.595	70.553	95.298	25.509	0.001
5	Seo (23)	2014	Korea	348	537	169.25	102.88	146.75	55.14	0.001

DISCUSSIONS

Sudden sensorineural hearing loss is a common otologic disorder which reports show that its prevalence is increasing worldwide. This disorder, often needs urgent attention and can be considered as an emergency due to its unknown etiology and prognostic features.[2,24] Although in many cases, the severity of SSNHL is mild but in some cases it can be leaded to long-term or permanent hearing loss or even deafness or disturbing condition for patients such as tinnitus.[25,26] Also, because the disease occurs suddenly, often it has negative psychological effects on patients which in turn reduce their quality of life.[27] So far, the treatment of this disease has not been satisfactory due to its diverse etiologies.[28] In addition, the number of controlled studies on various aspects of the disease is low due to a very heterogeneous pathology, the high rate of spontaneous recovery of patients as well as the delayed care seeking or referring of patients to various clinical specialties.[6,21] On the other hand, given that according to previous studies, cardiac ischemic events are associated with some platelet parameters such as mean platelet volume.[16] as well as the similarity of clinical manifestation of sudden sensorineural hearing loss to vascular disease with sudden occurrence and unilateral signs.[17] Some writers believes that the main cause of SSNHL could be a corruption of blood supply to the inner ear[18], in recent years some researchers have attempted to examine the relationship between different platelet parameters and the occurrence and severity of SSNHL in their studies. Some of these studies are the studies of Seo et al. (2014)[23], Blaha et al. (2014)[29], Ulu et al. (2013)[3], Karli et al. (2013)[16] and Sagit et al. (2013).[30] Our objective in this meta-analysis was to analyze the results of the studies which have been done on the relationship of NLR and PLR with the occurrence of sudden sensorineural hearing loss. For this purpose, an extensive search was done; many studies were retrieved and the relevant ones were entered into the meta-analysis. In summary, our meta-analysis booth of these parameters has statistical relationship with the occurrence of SSNHL. Therefore, they can be considered as novel markers for the diagnosis of SSNHL. However, given that the number of studies on this subject is few, it seems that making a definitive conclusion about the relationship of these parameters and the occurrence of SSNHL needs more studies.

CONCLUSIONS

Our meta-analyzed showed that the NLR and PLR have statistical relationship with the occurrence of sudden sensorineural hearing loss. Therefore, they can be considered as novel markers for the diagnosis of SSNHL.

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