ORIGINAL ARTICLE

J Mycol Infect 2022; 27(4): 63-74
pISSN:1226-4709, eISSN:2465-8278
https://dx.doi.org/10.17966/JMI.2022.27.4.63

JMI

Clinical Features and Risk Factors for Complications of Facial Herpes Zoster in Inpatients

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Background: Few studies have been reported on facial herpes zoster and the risk factors for its complications.

Objective: This study aimed to investigate the clinical features and risk factors with facial herpes zoster.

Methods: We examined the medical records of 676 patients with facial herpes zoster during a 10-year-period from 2011 to 2020. We assessed the proportion of ocular complications, Ramsay-Hunt syndrome, and postherpetic neuralgia in patients with facial herpes zoster according to several clinical factors including age, sex, dermatomes, underlying disease, and time to initiate antiviral treatment.

Results: The incidence of ocular complications was significantly higher in males (Odds ratia [OR], 2.59; 95% CI, 1.26~5.32), and with involvement of ophthalmic branches of the trigeminal nerve (V1: OR, 14.28; 95% CI, 3.62~56.29; V1 inclusion: OR, 20.68; 95% CI, 7.99~53.55), underlying diseases (OR, 1.70; 95% CI, 1.08~2.68) and positive Hutchinson's sign (OR, 3.59; 95% CI, 1.72~7.49). Ramsay-Hunt syndrome was significantly correlated with involvement of VII dermatome (OR, 24.68; 95% CI, 2.97~204.75), and showed considerable significant with otalgia (OR, 3.31; 95% CI 0.98~11.22). Postherpetic neuralgia was significantly higher in those over 60 years of age (OR, 2.03; 95% CI, 1.48~2.78), ocular complications (OR, 2.28; 95% CI, 1.57~3.30), and ear involvement (OR 1.94; 95% CI 1.17~3.20).

Conclusion: These results demonstrated that facial herpes zoster was associated with ocular complications, Ramsay-Hunt syndrome, and postherpetic neuralgia. The incidence of these complications was related to risk factors such as sex, age, dermatome, underlying disease, Hutchinson's sign and otalgia. To decrease the risk of complications associated with facial herpes zoster, patients should receive appropriate antiviral therapy and interdepartmental consultations immediately.

Key Words: Facial herpes zoster, Ocular complication, Postherpetic neuralgia, Ramsay-Hunt syndrome

INTRODUCTION

Herpes zoster is caused by the reactivation of varicella-zoster virus (VZV), which belongs to the human herpesvirus family and remains latent in the sensory nerve ganglia after an earlier attack of varicella. Herpes zoster is an acute inflammatory

Received: August 18, 2022 Revised: September 12, 2022 Accepted: November 8, 2022
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disease common in elderly patients or patients with compromised cellular immunity, and it is characterized by radiating pain along a unilateral sensory dermatome with clustered vesicular rashes[1-3]. Patients with herpes zoster forms a major fraction of patients in dermatology department, since this condition can cause various complications, such as ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia during or after treatment, and also indicate prodromal symptoms of malignant tumors and immunodeficiency[4].

In general, facial herpes zoster occurs when the virus is transported through the cranial nerves. Especially, herpes zoster ophthalmicus occurs when the ophthalmic branch of the trigeminal nerve is involved, leading to ocular complications or permanent blindness[5]. Furthermore, Ramsay Hunt syndrome, also called herpes zoster oticus, occurs when the facial nerve (CN VII) and the vestibulocochlear nerve (CN VIII) are involved, manifested by various symptoms, including facial palsy, otalgia, hearing loss, tinnitus, vertigo, hoarseness, and dysphagia[2,6-8]. Postherpetic neuralgia is generally defined as continuous pain lasting for longer than one month after the development of a skin rash[1,9-11] and occurs more frequently in patients aged 60 years or older, and in cases with severe pain or rash at the acute phase and herpes zoster ophthalmicus[1-3,12]. Since facial herpes zoster may leave neurological sequelae, rapid diagnosis and prompt initiation of treatment are most important[13].

To date, several clinical studies have been reported regarding herpes zoster ophthalmicus[14], Ramsay Hunt syndrome[15], and postherpetic neuralgia[16-18] in the Korean literature for dermatology; however, only two clinical studies have recently been published on facial herpes zoster by Suh et al.[19] and Jeong et al.[20].

Herein, we present a retrospective study on clinical presentations and risk factors for ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia comprising 676 patients hospitalized for facial herpes zoster in the department of dermatology at the Dongguk University Gyeongju Hospital during a 10-year period.

MATERIALS AND METHODS

1. Subjects

We conducted this study at the Dongguk University Gyeongju Hospital from Jan 2011 to Dec 2020. This study included patients who were hospitalized for facial herpes zoster at our department of dermatology. We excluded cases with insufficient medical records, unclear diagnosis, hospitalization for postherpetic neuralgia, and loss of follow up. All patients' electronic medical records were reviewed retrospectively. This study was approved by the Institutional Review Board of our hospital (approval No.: 110757-202103-HR-02-02).

2. Clinical characteristics

Medical records of 676 patients, who had been diagnosed with facial herpes zoster and hospitalized, were retrospectively investigated with respect to sex, age, underlying diseases, dermatome distribution, ocular complications, Ramsay Hunt syndrome, postherpetic neuralgia, initiation time of antiviral administration, and length of hospitalization.

3. Clinical classification and definition

Dermatome distribution was grouped according to the ophthalmic (V1), maxillary (V2), and mandibular (V3) branches of the trigeminal nerve, the external auditory canal and ear (VII), and the second (C2) and third (C3) cervical spinal nerves. For ocular complication analysis, dermatome involvement was classified into V1 only, V1 inclusion (V1+V2, V1+V2+V3), and V1 exclusion (V2, V2+V3). For Ramsay Hunt syndrome analysis and postherpetic neuralgia analyses, dermatome involvement was classified into V3 inclusion (V3, V2+V3, V1+V2+V3), VII, and cervical spinal nerve (C2, C3, C2+C3), and into V1, V2, V3, combination of trigeminal nerve branches (V1+V2, V2+V3, V1+V2+V3), VII, and cervical spinal nerve (C2, C3, C2+C3), respectively. Ocular complications were investigated in patients whose ocular involvement was confirmed by the department of ophthalmology at the time of hospitalization, and the degree of ocular involvement was assessed every three days during hospitalization. In particular, we considered that involvement of the dermatome corresponding to the nasociliary branch innervating the tip or side of the nose was accompanied with Hutchinson's sign. Patients were diagnosed with Ramsay Hunt syndrome at the department of otorhinolaryngology based on vesicular rashes in the auricle and external auditory canal, otalgia, or facial nerve palsy. Finally, postherpetic neuralgia was defined when pain persisted a month after the onset of herpes zoster. Time was calculated from the initiation date of systemic antiviral administration after the onset of skin lesions.

4. Statistical analysis

Data were entered into Excel and then transferred to SPSS Version 24.0 (SPSS Inc., Chicago, USA) for analysis.

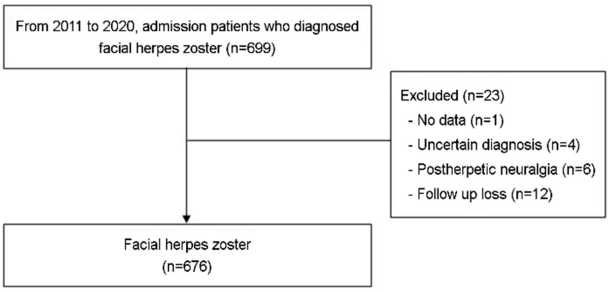

Fig. 1. Flow chart of subject selection

Multivariable logistic regression was employed to assess the association between independent and outcome variables. We used regression diagnostic procedures to check evidence of multi collinearity or overly influential outliers in the models. All variables determined to be important ($p < 0.15$) were incorporated into the multivariable logistic regression analysis by stepwise methods.

RESULTS

1. Demographic characteristics of facial herpes zoster

Among the 699 patients who had been clinically diagnosed as herpes zoster in the facial area and then hospitalized in the Department of Dermatology in Dongguk University Gyeongju Hospital during a 10 year period between Jan 2011 and Dec 2020, 23 patients were excluded as follows: one patient with insufficient hospitalization record; four patients with unclear diagnosis; six patients who were hospitalized due to postherpetic neuralgia; and 12 patients lost at follow up (Fig. 1). As shown in Table 1, among the 676 facial herpes zoster patients, 295 were males (43.6%) and 381 were females (56.4%), demonstrating a slight female predominance (M:F = 1:1.3). Three hundred and forty patients (50.3%) were aged <60 years, while 336 (49.7%) were aged ≥60 years, with a mean age of 56.9 ± 18.3 years. Underlying diseases were confirmed in 279 patients (41.3%) as follows: 207 (30.6%) with hypertension, 82 (12.1%) with diabetes, 55 (8.1%) with both hypertension and diabetes, 28 (4.1%) with dyslipidemia, and 14 (2.1%) with malignant tumor. Regarding dermatome distribution, V1 only was most common in 324 (47.9%) patients, whereas V2, V3, V1+V2, V2+V3, V1+V2+V3, VII, C2, C3, and C2+C3 were involved in 69 (10.2%), 39 (5.8%), 14 (2.1%), 13 (1.9%), 3 (0.4%), 52

Table 1. Demographic characteristics of the facial herpes zoster patients (n=676)

	N	%
Sex		
Females	381	56.4
Males	295	43.6
Age		
<60	340	50.3
≥60	336	49.7
Age (mean ± SD)	56.9 ± 18.3	
Underlying disease		
HTN	207	30.6
DM	82	12.1
DM+HTN	55	8.1
Dermatome		
V1	324	47.9
V2	69	10.2
V3	39	5.8
V1+V2	14	2.1
V2+V3	13	1.9
V1+V2+V3	3	0.4
VII	52	7.7
C2	20	3.0
C3	104	15.4
C2+C3	38	5.6
Side		
Right	315	46.6
Left	361	53.4
Ocular complications	184	27.2
Ramsay-Hunt syndrome	27	4.0
Postherpetic neuralgia	378	55.9
Time of antiviral initiation		
≤4 days	322	47.6
> 4 days	354	52.4
Length of hospitalization		
≤7 days	371	54.9
> 7 days	305	45.1

HTN: hypertension, DM: diabetes mellitus, V1: ophthalmic branch of trigeminal nerve, V2: maxillary branch of trigeminal nerve, V3: mandibular branch of trigeminal nerve, VII: facial nerve (cranial nerve 7), C2: 2nd cervical spinal nerve, C3: 3rd cervical spinal nerve

Table 2. Demographic and clinical characteristics of ocular complications (n=423)

	Total patients (n=423)		*p*-value
	Ocular complications (+) (n=184)	Ocular complications (-) (n=239)	
Sex			<0.001***
Female (n=228)	82	146	
Male (n=195)	102	93	
Age			0.397
<60 (n=226)	94	132	
≥60 (n=197)	90	107	
Dermatome			<0.001***
V1 (n=324)	172	152	
V1+V2, V1+V2+V3 (n=17)	7	10	
V2, V2+V3 (n=82)	5	77	
Underlying disease			0.024*
Positive (n=145)	74	71	
HTN (n=133)	68	65	0.032*
DM (n=52)	27	25	0.191
HTN+DM (n=40)	21	19	0.228
Negative (n=278)	110	168	
Hutchinson's sign			<0.001***
Positive (n=52)	34	18	
Negative (n=371)	150	221	
Time of antiviral initiation			0.199
≤4 days (n=192)	77	115	
>4 days (n=231)	107	124	

*p<0.05, ***p<0.001

(7.7%), 20 (3.0%), 104 (15.4%), and 38 (5.6%), respectively. Dermatomes were distributed unilaterally in all 676 patients, 315 (46.6%) on the right side and 361 (53.4%) on the left side. The cases of ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia were 184 (27.2%), 27 (4.0%), and 378 (55.9%), respectively. The time of antiviral therapy initiation was ≤4 days in 322 (47.6%) patients and >4 days in 354 (52.4%). Finally, the length of hospitalization was <7 days in 371 patients (54.9%) and ≥7 days in 305 (45.1%) (Table 1).

2. Ocular complications

Ocular complications were identified in 184 (43.5%) patients of the 423 with V1 or V2 involvement: 172 (53.0%) for V1 (324); 4 (5.8%) for V2 (69); 6 (42.3%) for V1+V2 (14); 1 (7.7%) for V2+V3 (13); and 1 (33.3%) for V1+V2+V3 (3) as summarized in Table 2. The ocular complications in 184 cases comprised 90 (48.9%) patients with conjunctivitis, 63 (34.2%) with keratitis, 17 (9.2%) with uveitis, 6 (3.3%) with glaucoma, 6 (3.3%) with scleritis, and 2 (1.1%) with external ophthalmoplegia.

The statistical analysis of risk factors revealed that ocular

Table 3. Multivariable analysis of factors associated ocular complication (n=423)

	Ocular complications		*p*-value
	OR	95% CI	
Sex			
Male	2.59	1.26~5.32	0.009*
Female (Reference)	1		
Dermatome			
V1	14.28	3.62~56.29	<0.001*
V1+V2, V1+V2+V3	20.68	7.99~53.55	<0.001*
V2, V2+V3 (Reference)	1		
Underlying disease			
Positive	1.70	1.08~2.68	0.023*
Negative (Reference)	1		
Hutchinson's sign			
Positive	3.59	1.72~7.49	0.001*
Negative (Reference)	1		

*p<0.05

complications occurred more frequently in males (102/195: 52.3%) than females (82/228: 36.0%) ($p < 0.001$), and in patients aged ≥60 (90/197; 45.7%) than <60 (94/226: 41.6%). Regarding dermatome distribution, ocular complications occurred most frequently in V1 only (172/324: 53.1%), followed by V1 inclusion (V1+V2, V1+V2+V3) (7/17: 41.2%) and V1 exclusion (V2, V2+V3) (5/82: 6.1%), indicating a statistically significant difference ($p < 0.001$). For underlying diseases, ocular complications occurred in 51.0% (74/145) of cases: 51.1% (68/133) with hypertension, 51.9% (27/52) with diabetes, and 52.5% (21/40) with both hypertension and diabetes, showing a significantly higher frequency in patients with underlying diseases ($p = 0.024$). Although hypertension was associated with a higher risk of developing ocular complications ($p = 0.032$), Bonferroni correction showed that this association was not statistically significant. Ocular complications occurred in 65.4% (34/52) of cases with Hutchinson's sign and 40.4% (59/179) of cases without Hutchinson's sign, revealing a significantly higher frequency in cases with Hutchinson's sign ($p < 0.001$). Finally, ocular complications occurred in 40.1% (77/192) of patients with ≤4 days of antiviral initiation, and 46.3% (107/231) of cases with >4 days, suggesting no significant difference (Table 2).

In multivariable logistic regression analysis, ocular complications increased significantly with male sex (odds ratio [OR], 2.25; 95% CI, 1.45~3.47), V1 only, and V1 inclusion dermatome (*vs.* V1 exclusion; V1 only: OR, 14.28; 95% CI, 3.62~56.29; V1 inclusion: OR, 20.68; 95% CI, 7.99~53.55), underlying disease (OR, 1.70; 95% CI, 1.08~2.68) and Hutchinson's sign (OR, 3.59; 95% CI, 1.72~7.49) (Table 3).

3. Ramsay Hunt Syndrome

After omitting three cases with V3 exclusion (V1, V2, or V1+V2), 269 patients with herpes zoster, whose dermatome involvement included V3 (V3, V2+V3, V1+V2+V3), VII, or cervical spinal nerves (C2, C3, C2+C3), were highly associated with auricular and periauricular involvement. As described in Table 4, Ramsay Hunt syndrome occurred in 24 (8.9%): 23 (95.8%) with VII and one (4.2%) with V3. Clinical symptoms included ear skin lesions in all 24 patients (100%), skin lesions with otalgia in 19 patients (79.2%), facial nerve involvement only without skin lesions in 19 patients (79.2%), vestibulocochlear nerve involvement only in three patients (12.5%), and concurrent facial and vestibulocochlear nerve involvement in two patients (8.3%).

The statistical analysis of risk factors revealed that the Ramsay Hunt syndrome occurred more frequently in males (13/108; 12.0%) than females (11/161; 6.8%), and in patients aged <60 (15/123; 12.2%) than those ≥60 (9/146; 6.2%), although no statistical significance could be reached. Dermatome involvement of VII, V3, and spinal nerves was 44.2% (23/52), 1.8% (1/55) and 0%, respectively, indicating the frequent occurrence of the Ramsay Hunt syndrome with VII ($p = 0.006$). The Ramsay Hunt syndrome occurred in 6.3% (6/96) of cases with underlying diseases: 4.9% (4/81) of patients with hypertension, 9.4% (3/32) of patients with diabetes, and 5.9% (1/17) of patients with hypertension and diabetes. Furthermore, this condition occurred more frequently in patients with otalgia than in patients without otalgia (39.6% (19/48) *vs.* 2.3% (5/221)), respectively, and in patients with than without ear involvement (30.4% (24/77) *vs.* 0%), indicating a statistically significant difference ($p < 0.001$). The Ramsay Hunt syndrome occurred in 9.7% (13/134) of cases with prompt administration of antiviral agents (≤4 days) and 8.1% (11/135) of cases with delayed administration (>4 days), showing no significant difference (Table 4).

In multivariable logistic regression analysis, the Ramsay

Table 4. Demographic and clinical characteristics of Ramsay-Hunt syndrome (n=269)

	Total patients (n=269)		*p*-value
	Ramsay-Hunt syndrome (+) (n=24)	Ramsay-Hunt syndrome (-) (n=245)	
Sex			0.142
Female (n=161)	11	150	
Male (n=108)	13	95	
Age			0.084
<60 (n=123)	15	108	
≥60 (n=146)	9	137	
Dermatome			0.006†
V3, V2+V3, V1+V2+V3 (n=55)	1	54	
VII (n=52)	23	29	
C2, C3, C2+C3 (n=162)	0	162	
Underlying disease			0.252
Positive (n=96)	6	90	
HTN (n=81)	4	77	0.132†
DM (n=32)	3	29	1.000†
HTN+DM (n=17)	1	16	1.000†
Negative (n=173)	18	155	
Otalgia			<0.001***
Positive (n=48)	19	29	
Negative (n=221)	5	216	
Ear involvement			<0.001***
Positive (n=77)	24	53	
Negative (n=192)	0	192	
Periauricular involvement			0.313†
Positive (n=10)	0	10	
Negative (n=259)	24	235	
Time of antiviral initiation			0.655
≤4 days (n=134)	13	121	
>4 days (n=135)	11	124	

***p<0.001, †by Fisher's exact test

Hunt syndrome increased significantly with VII dermatome involvement (OR, 24.68; 95% CI, 2.97~204.75) and showed a considerable significance with otalgia (OR, 3.31; 95% CI, 0.98~11.22) (Table 5).

4. Postherpetic neuralgia

Of the 676 patients with facial herpes zoster, postherpetic neuralgia occurred in 378 patients (55.9%) as shown in Table

Table 5. Multivariable analysis of factors associated Ramsay-Hunt syndrome (n=269)

	Ramsay-Hunt syndrome		*p*-value
	OR	95% CI	
Dermatome			
VII	24.68	2.97~204.75	0.003*
C2, C3, C2+C3	-	-	0.996
V3, V2+V3, V1+V2+V3 (Reference)	1		
Otalgia			
Positive	3.31	0.98~11.22	0.054
Negative (Reference)	1		

*$p<0.05$

Table 6. Demographic and clinical characteristics of postherpetic neuralgia (n=676)

	Total patients (n=676)		*p*-value
	Postherpetic neuralgia (+) (n=378)	Postherpetic neuralgia (-) (n=298)	
Sex			0.881
Female (n=381)	214	167	
Male (n=295)	164	131	
Age			<0.001***
<60 (n=340)	163	177	
≥60 (n=336)	215	121	
Dermatome			0.057
V1 (n=324)	192	132	
V2 (n=69)	35	34	
V3 (n=39)	17	22	
V1+V2, V2+V3, V1+V2+V3 (n=30)	17	13	
VII (n=52)	36	16	
C2, C3, C2+C3 (n=162)	81	81	
Underlying disease			0.032*
Positive (n=234)	144	90	
HTN (n=207)	128	79	0.039
DM (n=82)	51	31	0.222
HTN+DM (n=55)	35	20	0.229
Negative (n=442)	234	208	
Ocular complications			<0.001***
Positive (n=184)	125	59	

Table 6. Demographic and clinical characteristics of postherpetic neuralgia (n=676) (Continued)

	Total patients (n=676)		*p*-value
	Postherpetic neuralgia (+) (n=378)	Postherpetic neuralgia (-) (n=298)	
Conjunctivitis (n=90)	54	36	<0.001†***
Keratitis (n=63)	47	16	
Scleritis (n=6)	5	1	
Uveitis (n=17)	12	5	
Glaucoma (n=6)	6	0	
Oculomotor nerve palsy (n=2)	1	1	
Negative (n=492)	253	239	
Hutchinson's sign			0.788
Positive (n=52)	30	22	
Negative (n=624)	348	276	
Ramsay-Hunt syndrome			0.251
Positive (n=27)	18	9	
Negative (n=649)	360	289	
Otalgia			0.271
Positive (n=59)	33	27	
Negative (n=617)	345	271	
Ear involvement			0.133
Positive (n=80)	51	29	
Negative (n=596)	327	269	
Periauricular involvement			0.316
Positive (n=12)	5	7	
Negative (n=664)	373	291	
Time of antiviral initiation			<0.001***
≤4 days (n=322)	151	171	
＞4 days (n=354)	227	127	

*p<0.05, ***p<0.001, †by Fisher's exact test

6. The analysis of risk factors revealed that this condition was more prevalent among males (164/295; 56.2%) than females (167/214; 55.6%) and in patients aged ≥60 years (215/336; 64.0%) than those aged <60 years (163/340; 47.9%), showing a significant difference ($p < 0.001$). Regarding dermatome distribution, postherpetic neuralgia occurred in 59.3% (192/342) of V1, 50.7% (35/69) of V2, 43.6% (17/39) of V3, 56.7% (17/3) of two or more dermatomes (V1+V2, V2+V3, V1+V2+V3), 69.2% (36/52) of VII, 50.0% (81/162) of cervical spinal nerves (C2, C3, C2+C3), resulting in a descending order of occurrence, although not reaching statistical significance, as follows: VII>V1>two or more dermatomes>V2>cervical spinal nerves>V3. Postherpetic neuralgia occurred in 61.5% (144/234) of cases with underlying diseases: 61.8% (128/207) with hypertension, 62.2% (51/82) with diabetes, and 63.6% (35/55) with hypertension and

Table 7. Multivariable analysis of factors associated postherpetic neuralgia (n=676)

	Postherpetic neuralgia		*p*-value
	OR	95% CI	
Age			
≥60	2.03	1.48~2.78	<0.001*
<60 (Reference)	1		
Ocular complication			
Positive	2.28	1.57~3.30	<0.001*
Negative (Reference)	1		
Ear involvement			
Positive	1.94	1.17~3.20	0.01*
Negative (Reference)	1		

*p<0.05

diabetes, suggesting a significantly higher incidence of this condition with underlying diseases (p = 0.024). Although postherpetic neuralgia was found in a greater number of patients with hypertension (p = 0.039), no statistical significance was identified after Bonferroni correction. Among 184 patients with ocular complications, 125 (67.9%) were involved with postherpetic neuralgia, showing a statistical significant trend (p < 0.001): 100.0% (6/6) of cases with glaucoma, 83.3% (5/6) of cases with scleritis, 74.6% (47/63) of cases with keratitis, 70.6% (12/17) of cases with uveitis, 60.0% (54/90) of cases with conjunctivitis, and 50.0% (1/2) of external ophthalmoplegia, indicating higher incidence of postherpetic neuralgia in patients with conjunctivitis, keratitis, scleritis, uveitis, and glaucoma except external ophthalmoplegia. Patients with Ramsay Hunt syndrome (18/27; 66.7%) were more frequently involved with postherpetic neuralgia compared to those without the syndrome (360/649; 55.5%), although not reaching statistical significance. Cases with delayed initiation of antiviral administration at >4 days were more frequently involved with postherpetic neuralgia than cases with ≤4 days, indicating a statistically significant difference (p < 0.001) (Table 6).

In multivariable logistic regression analysis, postherpetic neuralgia increased significantly with patients aged >60 years old (OR, 2.03; 95% CI, 1.448~2.78), ocular complication (OR, 2.28; 95% CI, 1.57~3.30), and ear involvement (OR, 1.94; 95% CI, 1.17~3.20) (Table 7).

DISCUSSION

Herpes zoster is an infectious dermatologic disease caused by VZV that is characterized by the manifestation of vesicular skin rashes. Although most cases are healed without specific sequelae, in some patients this disease is accompanied by neurological complications of which postherpetic neuralgia is the most common. However, in cases where the facial area is also involved, this disease may induce systemic complications such as ocular complications or Ramsay Hunt syndrome[21]. However, to the best of our knowledge, there have only been a few studies in the Korean literature for dermatology, such as Suh et al.[19] and Jeong et al.[20], investigating the effect of this disease when the entire facial area is involved. Therefore, the present study investigated the clinical presentations and risk factors for ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia in 676 patients with facial herpes zoster.

Similar to the results reported by Suh et al.[19] and Jeong et al.[20], the frequency of herpes zoster with respect to dermatome distribution was the highest in V1 (47.9%), followed by C3 (15.4%), V2 (10.2%), VII (7.7%), V3 (5.8%), C2+C3 (5.6%), C2 (3.0%), V1+V2 (2.1%), V2+V3 (1.9%), and V1+V2+V3 (0.4%). However, the frequency of this disease in patients with V1 innervated by the ophthalmic branch was 47.9%, which was lower than the 59.2% reported in Suh et al.[19]. Furthermore, this frequency in patients with VII accompanied by ear involvement and Ramsay Hunt syndrome was 7.7%, which was slightly higher than the 6.3% reported by Suh et al.[19].

Ocular complications of herpes zoster include conjunctivitis, keratitis, uveitis, scleritis, glaucoma, oculomotor palsy, ptosis, retinal necrosis, and optic neuritis[3,12,22-27]. Male patients were found to be more susceptible to ocular complications (52.3%) than females (36.0%). Kim and Suh[14], Ando and Kohmoto[12] have reported that it occurred more frequently in patients over 80 years of age. Similarly, occurrence in the present study was the highest in patients over 80 years of age at 70.6%. However, there was a slight difference as shown in Jeong et al., in which the highest frequency was 83.8% for patients in their 60's. The incidence in patients aged over 60 years was 45.7% contrary to 41.6% in patients aged less than 60 years, with no statistically significant difference. In this study, V1 or V2 were involved in 43.5%, which was higher than the 22.8% reported in Suh et al.[19]. The ophthalmology literature accepts that that the larger the area of the three trigeminal nerve branches, the higher the likelihood of occurrence of ocular complications[28]. In this study, the odds ratio was higher in V1 inclusion (multi lesion) than V1 only. According to Jeong et al.[20], the occurrence of ocular complications was higher in patients with underlying diseases, such as hypertension and diabetes, but there was no statistically significant difference. In contrast, the present study confirmed that this higher incidence was statistically significant. The positive rate of Hutchinson's sign in which skin lesions occur either at the tip or side of the nose corresponding to the nasopharyngeal branch accounts for 20~70% in patients with herpes zoster ophthalmicus[1]. In this study, the positive rate of Hutchinson's sign was 18.5%, which was similar with the 17% reported in Ando and Kohmoto[12]. The incidence of ocular complications was 65.4% in patients with Hutchinson's sign, which was higher and statistically significant compared to the incidence of 40.4% without Hutchinson's sign, a finding consistent with previous studies[12,22,24]. Differences pertaining to the time of antiviral initiation (≤4 days and ≥4 days) were not significant. It is thought that the patients with severe ocular symptoms were hospitalized earlier. The incidence of ocular complications was higher in the patient group with hospitalization of ≥7 days than the group with ≤7 days; however, this finding may be a result of the prolonged treatment period due to the accompanying ocular complications.

Ramsay Hunt syndrome occurs when VZV invades the geniculate ganglion present in the facial and auditory nerves. This condition can cause facial palsy, tinnitus, and nystagmus accompanied by severe ear pain. Rarely, it can also cause dizziness and sensorineural hearing loss by invading the vestibular organ[2]. In this study, the incidence of Ramsay Hunt syndrome was 8.9%, which was slightly higher than 4.7% and 5.6% in patients with facial palsy reported in Min et al.[15] and Suh et al.[19], respectively. However, an accurate comparison could not be made due to the different patient groups. Dermatome distribution revealed that the VII nerve group was most commonly invaded at 85.2%, an incidence that was statistical significant and similar to the 78.2% rate shown in Suh et al.[19]. Regarding the clinical symptoms in patients with Ramsay Hunt syndrome, ear skin lesion was the most common symptom shown in 100% of cases, while skin lesion accompanied by otalgia was found in 79.2% of cases. The likelihood of occurrence of Ramsay Hunt syndrome was high and statistical significant in cases with a skin lesion in the ear or otalgia. Consequently, Ramsay Hunt syndrome must be suspected in such cases, and a consultation with an ENT specialist is necessary. In contrast, there was no statistically significant difference for the occurrence of Ramsay Hunt syndrome based on the time of administration of the antiviral drug on the fourth day. This was initially thought to be due to the relatively small number of patients with Ramsay Hunt syndrome. The duration of hospitalization was significantly higher ($p < 0.001$) in the group with ≥7 days than in the group with ≤7 days (17.3% *vs.* 1.4%), but it is thought to be a result of the prolonged treatment period due to the accompanying Ramsay Hunt syndrome.

The incidence of postherpetic neuralgia is known to be high in the presence of herpes zoster ophthalmicus, severe pain, and rash in the acute phase, and in elderly patients ≥60 years of age[1-3,12]. By age, Jeong et al.[20] reported that postherpetic neuralgia was present in 63.2% of patients aged ≥60 years old, which was similar to the incidence rate found in the present study (64.0%, $p < 0.001$). Furthermore, the incidence of postherpetic neuralgia was higher in patients with underlying diseases (61.5%). Kim and Suh[14] reported that 50% of patients with ocular complications had postherpetic neuralgia, and this was reported to be 48.4% and 42.4% in Suh et al.[19] and Jeong et al.[20], respectively. In the present study, this incidence rate was higher (67.9%), showing a statistically significance difference. This result might be due to the difference in the patient groups; hence, further investigations with a greater number of patients will be necessary to validate these findings. In particular, considering ocular complications, Szeto et al.[29] reported that postherpetic neuralgia was statistically significant only in uveitis (15.2%). However, in this study, postherpetic neuralgia occurred in 100% of cases with glaucoma, 83.3% of cases with scleritis, 74.6% of cases with keratitis, 70.6% of cases with uveitis, 60.0% of cases with conjunctivitis, and 50% of cases with ocular motor palsy. Moreover, the incidence of postherpetic neuralgia was high in all ocular complications except ocular motor palsy. The incidence of postherpetic neuralgia in patients with and

without Ramsay Hunt syndrome was 66.7% and 55.5%, respectively, and the difference was not statistically significant. The average length of time elapsed before patients visited the hospital and started receiving antiviral treatment was 5.1 days, which was slightly different from the 4.2 days reported in previous studies[15,16]. Multivariable analysis showed no significant difference between the groups that started antiviral treatment within and after four days, suggesting that early antiviral treatment initiation did not reduce the incidence of postherpetic neuralgia. The average length of hospital stay was 6.9 days, and the incidence of postherpetic neuralgia was significantly higher among patients whose hospital stay was ≥7 days. Our findings indicate that more severe pain and skin rashes during the acute phase associated with longer hospital stay with increased incidence of postherpetic neuralgia.

This study has some limitations. First, the patient group included only inpatients, thus the number of patients with severe symptoms was relatively high. In the future, studies on more cases, including outpatients, are necessary to supplement the limitations of this study. Second, this study was conducted as a retrospective study with medical record analysis in a single institution. Therefore, the information was limited with reliance on the records. However, this study may be considered to be of great significance in that it was able to investigate the clinical features and risk factors for ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia in a patient group with facial herpes zoster comprising 676 participants.

CONCLUSIONS

This study was conducted retrospectively to investigate the clinical features and risk factors for ocular complications, Ramsay Hunt syndrome, and postherpetic neuralgia in 676 patients with facial herpes zoster who had been hospitalized in our dermatology department from January 2011 to December 2020.

The incidence of ocular complications was found to be higher in males than in females, in cases of dermatome V1 invasion, in the presence of comorbidities, such as hypertension, and in patients with a positive Hutchinson's sign. The incidence of Ramsay Hunt syndrome was higher in patients with otalgia. The incidence of postherpetic neuralgia was higher in the elderly patients (≥60 years of age), with ocular complications, and ear involvement.

In conclusion, it is necessary to analyze the related risk factors in advance to minimize potential complications and provide appropriate treatments at an early stage for patients hospitalized with facial herpes zoster. If other diseases are suspected, the respective departments should be consulted.

CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

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ETHICAL APPROVAL STATEMENT

The study was approved by the Institutional Review Board of (IRB No. 110757-202103-HR-02-02). This study was conducted in accordance with the principles of the Declaration of Helsinki.

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