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Prevalence of common causes of neuropathic pain in Korea: population-based observational study

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Abstract

Objective: To investigate the prevalence of complex regional pain syndrome (CRPS), post-herpetic neuralgia (PHN), trigeminal neuralgia (TN), and diabetic neuropathy (DN), common causes of neuropathic pain encountered in pain clinics.

Methods: We investigated the period prevalence rate of CRPS, PHN, TN, and DN using data from a Korean national electronic database from 2009 to 2013.

Results: The prevalence of CRPS decreased slightly throughout the study period, while the prevalence of PHN increased from 2009 to 2013. The prevalence of TN was reduced over the same period. The prevalence of DN increased from 2009 to 2012 but decreased in 2013. All four neuropathic diseases were more prevalent in individuals aged over 70 years. The prevalence of CRPS, PHN, and TN were more common in women than in men, but DN showed no gender difference.

Conclusion: While the prevalence of CRPS and TN has decreased in Korea, that of PHN and DN has increased. With the exception of DN, the neuropathic diseases were more prevalent in women. Further studies are necessary to investigate the risk factors and socioeconomic burden for each disease, and national efforts are essential to limit the development of these preventable neuropathic diseases.

Keywords

Prevalence, complex regional pain syndrome, post-herpetic neuralgia, trigeminal neuralgia, diabetic neuropathy, neuropathic pain

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Introduction

Neuropathic pain typically persists for several years or even decades, does not respond to conventional analgesic treatment such as non-steroidal anti-inflammatory drugs and opioids, and debilitates the quality of life of the patient.[1] It is important to evaluate the epidemiology of neuropathic pain in the general population to determine its socio-economic burden.[2]

Several studies have examined the prevalence of neuropathic pain. Bouhassira et al.[3] reported that the prevalence of chronic pain with neuropathic characteristics was 6.9% in the general population in France according to a postal survey. In Brazil, the prevalence of chronic pain with neuropathic characteristics was reported to be 10% in the municipality of São Luís.[4] According to Gajria et al.,[5] the prevalence of diagnosis associated with chronic neuropathic pain was 13 per 1000 in one region of London, United Kingdom. To date, however, little has been reported on the prevalence of chronic neuropathic pain attributable to a specific condition such as complex regional pain syndrome (CRPS), post-herpetic neuralgia (PHN), trigeminal neuralgia (TN), or diabetic neuropathy (DN). Although its mechanism has not been clearly described, several studies have defined CRPS as a neuropathic pain state.[6,7] We therefore investigated the prevalence of CRPS as part of neuropathic pain.

Hecke et al.[8] reported the prevalence of PHN (3.9–42.0/100,000 person years [PY]), TN (12.6–28.9/100,000 PY), and painful diabetic neuropathy (15.3–72.3/100,000PY). Sandroni et al.[9] reported that the incidence and prevalence rate of CRPS type 1 in 1990 in Olmsted County were 5.46/100,000 and 20.57/100,000, respectively, and that the female-to-male ratio was 4:1. McDonald et al.[10] reported that the lifetime prevalence of PHN and TN was 0.7/1000 in the London area. Savettieri et al.[11] reported that the prevalence of DN with somatic symptoms was 3 per 1000 people in two Sicilian municipalities according to a door-to-door survey. Mueller et al.[12] reported that the lifetime prevalence of TN was estimated to be 0.3%.

These previous studies were limited to specific regions within a country during a defined study period. Given the regional variability in age and sex ratio within a country, nationwide data are essential to evaluate the effects of a disease on society. Koopman et al.[13] reported an incidence rate of TN (12.6/100,000 PY) in The Netherlands in 2009, while Hall et al.[14] reported an incidence rate of PHN (3.4/1,000 PY) in the UK general population. These studies were not population-based, however, but were instead based on primary care records, and clear diagnostic criteria may not have been used. Other studies by Mueller et al.[12] and Schwaiger et al.[15] used clear diagnostic criteria and face-to-face interviews to collect data.

In recent years, many countries have implemented the use of electronic medical records systems, thus enabling nationwide epidemiologic research.[16,17] In Korea, all citizens have been covered by the National Health Insurance Service (NHIS) since 1989, and the Health Insurance Review and Assessment Service (HIRA) under NHIS has computerized all medical records since 2005. It is therefore possible to investigate the incidence or prevalence of specific diseases and their yearly change in Korea.

Because few studies to date have reported the nation-wide annual prevalence of rare neuropathic diseases, we sought to investigate the prevalence of CRPS, PHN, TN, and DN using HIRA data and to determine whether the prevalence of these rare neuropathic diseases changed from 2009 to 2013 in Korea.

Materials and methods

Ethical statement and informed consent

This study was approved by the institutional review board (IRB) of Bucheon

St. Mary's Hospital of the Catholic University of Korea (no. HIRB00E92001). The need for informed consent was waived by the IRB because this study used existing data that were in the public domain.

Data source

Demographic data including age and sex are collected by the NHIS according to an individual's Korean identification (ID) number. All medical procedures including diagnosis, physical and laboratory examination, treatment, prescription, nursing procedures, and hospitalization are also reported in the HIRA computerized database by Korean ID number.

Population data from 2009 to 2013 were used in this study and were obtained from the National Statistical Office of South Korea (http: //kosis.kr).

Case definition

Patients with CRPS, PHN, TN, and DN were identified by searching the data using the International Classification of Disease 9th revision code (ICD-9) and the relevant domestic HIRA codes for CRPS (M890 for CPRS type 1, G564 for CRPS type 2), PHN (G530), TN (G500), and DN (G590 for diabetic mononeuropathy, G632 for diabetic poly-neuropathy). For CRPS, cases of CRPS type 1 and CRPS type 2 were taken together, while cases of diabetic mononeuropathy and diabetic poly-neuropathy were taken together for DN.

The prevalence rate was calculated by dividing the number of cases of CRPS, PHN, TN, and DN by the population for a given year and multiplying by 100,000. In the present study, prevalence rate is expressed as cases per 100,000 persons.

Given that variability in population factors such as gender proportion and age throughout the study period may have affected the number of cases identified, we standardized the prevalence rate to the population in 2009 to determine whether there were changes over time in the prevalence of neuropathic disease.

Statistical analysis

All variables were described by number or percentage. Standardization was performed for comparison by year, gender, and age using a direct method. The standardized rate was calculated using the population of 2009 as a standard population. Statistical analyses were performed using SAS 9.4 (SAS Institute, Inc, Cary, NC).

Statistical analysis in our study was supported by consultation with the Medical Statistical Office of the Catholic Research Coordinating Center (https://cmccrcc.cmcnu.or.kr/).

Results

The prevalence of CRPS showed a trend towards a gradual reduction over time, from 32.8 per 100,000 in 2009 to 26.3 per 100,000 in 2013. Prevalence was highest for the age group 70 to 79 years from 2009 to 2012 in both males and females, but was highest in the age group $\geq$80 years in 2013 among males. CRPS was more prevalent in women than in men (ratio 1:1.2, Table 1).

The prevalence of PHN increased from 161.5 per 100,000 in 2009 to 224.6 per 100,000 in 2013. Prevalence was highest for the age group 70 to 79 years in men and $\geq$80 years in women, and was more prevalent overall in women (ratio 1:1.7, Table 2).

The prevalence of TN decreased slightly from 81.8 per 100,000 in 2009 to 76.8 per 100,000 in 2013. Prevalence was highest for the age group 70 to 79 years in both men and women, and was more prevalent in women (ratio 1:2.2, Table 3).

The prevalence of DN increased from 80.7 per 100,000 in 2009 to 124.7 per

Table 1. Standardized prevalence of CRPS in Korea 2009–2013.

	2013		2012		2011		2010		2009		
Age group (y)	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Population	Prevalence
Men											
Total	6,533	23.4	6,471	24.0	6,345	24.2	6,601	25.9	7,429	24,929,939	29.8
<10	9	0.4	9	0.4	8	0.3	16	0.6	47	2,553,592	1.8
10–19	83	2.5	73	2.2	74	2.1	126	3.5	187	3,599,148	5.2
20–29	480	13.9	467	13.5	516	14.7	496	13.9	507	3,636,509	13.9
30–39	510	12.5	528	12.7	528	12.5	619	14.5	607	4,269,498	14.2
40–49	831	18.3	917	20.3	891	19.7	930	20.6	1,045	4,439,164	23.5
50–59	1,406	34.8	1,417	36.2	1,295	34.3	1,340	37.8	1,517	3,261,648	46.5
60–69	1,543	71.4	1,618	77.7	1,626	80.5	1,712	85.6	2,065	1,920,187	107.5
70–79	1,423	109.5	1,287	103.3	1,239	108.0	1,191	111.2	1,294	997,027	129.8
≥80	406	114.5	322	98.9	317	105.9	309	109.4	296	253,166	116.9
Women											
Total	8,103	29.2	7,736	28.6	7,641	29.1	8,187	32.2	8,879	24,843,206	35.7
<10	3	0.1	3	0.1	7	0.3	16	0.7	39	2,369,377	1.6
10–19	69	2.3	58	1.9	62	2.0	83	2.6	141	3,212,502	4.4
20–29	204	6.5	213	6.7	221	6.8	298	9.0	342	3,391,753	10.1
30–39	482	12.3	455	11.4	485	12.0	575	14.0	644	4,102,035	15.7
40–49	861	19.7	906	20.9	983	22.7	1,202	27.8	1,393	4,290,331	32.5
50–59	1,897	47.6	1,912	49.3	1,801	48.0	1,924	54.6	2,134	3,246,429	65.7
60–69	1,854	80.2	1,819	81.0	1,846	84.0	1,870	85.3	1,993	2,127,305	93.7
70–79	2,171	122.4	1,899	110.1	1,736	106.9	1,762	113.8	1,769	1,480,410	119.5
≥80	744	88.8	615	78.4	619	84.5	601	87.1	548	623,064	88.0
Total	14,636	26.3	14,207	26.3	13,986	26.6	14,788	29.0	16,308	49,773,145	32.8

Note: Standard population was that in 2009. Prevalence is cases per 100,000.

Table 2. Standardized prevalence of PHN in Korea 2009–2013.

	2013		2012		2011		2010		2009		
Age group (y)	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Population	Prevalence
Men											
Total	48,519	168.2	44,712	160.4	39,116	145.7	34,383	132.3	30,688	24,929,939	123.1
<10	45	1.9	30	1.2	42	1.7	35	1.4	43	2,553,592	1.7
10–19	475	14.5	508	15.0	442	12.6	407	11.3	405	3,599,148	11.3
20–29	1,254	36.3	1,366	39.5	1,164	33.3	1,102	30.9	1,022	3,636,509	28.1
30–39	3,069	75.0	2,834	68.1	2,518	59.8	2,345	54.9	2,142	4,269,498	50.2
40–49	5,274	116.1	5,001	110.9	4,445	98.4	4,113	91.1	3,682	4,439,164	82.9
50–59	10,327	255.5	9,360	239.0	8,153	216.0	6,783	191.4	5,934	3,261,648	181.9
60–69	12,515	579.4	11,767	564.7	10,585	524.0	9,381	469.2	8,518	1,920,187	443.6
70–79	12,651	973.6	11,384	913.4	9,696	845.3	8,304	775.6	7,340	997,027	736.2
≥80	3,524	994.1	3,079	946.0	2,543	849.4	2,267	802.8	1,973	253,166	779.3
Women											
Total	79,138	281.2	74,678	272.9	64,461	242.9	56,323	219.2	49,701	24,843,206	200.1
<10	39	1.7	43	1.9	41	1.8	52	2.3	41	2,369,377	1.7
10–19	475	16.0	486	15.9	480	15.2	400	12.4	342	3,212,502	10.6
20–29	1,723	54.9	1,821	57.5	1,631	50.5	1,451	44.0	1,345	3,391,753	39.7
30–39	3,829	97.6	3,660	91.4	3,058	75.6	2,856	69.7	2,490	4,102,035	60.7
40–49	7,742	176.8	7,650	176.8	6,679	154.3	6,221	143.6	5,691	4,290,331	132.6
50–59	19,690	494.2	18,643	481.0	15,972	425.5	13,246	375.9	11,245	3,246,429	346.4
60–69	19,404	839.1	18,402	819.7	16,298	741.8	14,515	662.2	13,110	2,127,305	616.3
70–79	19,671	1109.3	18,085	1049.0	15,209	936.4	13,216	853.9	11,759	1,480,410	794.3
≥80	7,429	886.7	6,775	863.8	5,788	789.8	5,039	729.9	4,182	623,064	671.2
Total	127,657	224.6	119,390	216.5	103,577	194.2	90,706	175.6	80,389	49,773,145	161.5

Note: Standard population was that in 2009. Prevalence is cases per 100,000.

Table 3. Standardized prevalence of TN in Korea 2009–2013.

	2013		2012		2011		2010		2009		
Age group (y)	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Population	Prevalence
Men											
Total	13,239	47.8	13,472	50.0	13,458	51.2	13,412	52.2	12,895	24,929,939	51.7
<10	18	0.8	17	0.7	20	0.8	18	0.7	25	2,553,592	1.0
10–19	290	8.9	301	8.9	334	9.5	353	9.8	356	3,599,148	9.9
20–29	779	22.6	790	22.8	885	25.3	922	25.9	840	3,636,509	23.1
30–39	1,642	40.1	1,732	41.6	1,777	42.2	1,677	39.2	1,744	4,269,498	40.8
40–49	2,191	48.3	2,360	52.3	2,413	53.4	2,464	54.6	2,378	4,439,164	53.6
50–59	2,837	70.2	2,813	71.8	2,735	72.5	2,691	75.9	2,583	3,261,648	79.2
60–69	2,579	119.4	2,718	130.4	2,612	129.3	2,720	136.0	2,660	1,920,187	138.5
70–79	2,465	189.7	2,386	191.4	2,304	200.9	2,169	202.6	1,953	997,027	195.9
≥80	609	171.8	554	170.2	540	180.4	548	194.1	510	253,166	201.4
Women											
Total	28,857	105.9	30,086	113.3	29,757	114.2	28,635	112.4	27,801	24,843,206	111.9
<10	23	1.0	29	1.3	23	1.0	19	0.8	31	2,369,377	1.3
10–19	462	15.6	576	18.8	612	19.3	540	16.7	587	3,212,502	18.3
20–29	1,388	44.2	1,551	49.0	1,636	50.7	1,630	49.4	1,714	3,391,753	50.5
30–39	2,850	72.6	3,212	80.2	3,285	81.2	3,132	76.4	3,271	4,102,035	79.7
40–49	4,718	107.7	5,050	116.7	5,315	122.8	5,155	119.0	5,037	4,290,331	117.4
50–59	7,083	177.8	7,139	184.2	6,871	183.0	6,412	182.0	5,983	3,246,429	184.3
60–69	5,630	243.5	5,941	264.6	5,739	261.2	5,788	264.1	5,542	2,127,305	260.5
70–79	5,230	294.9	5,213	302.4	4,889	301.0	4,765	307.9	4,495	1,480,410	303.6
≥80	1,830	218.4	1,842	234.9	1,715	234.0	1,525	220.9	1,466	623,064	235.3
Total	42,096	76.8	43,558	81.6	43,215	82.7	42,047	82.3	40,696	49,773,145	81.8

Note: Standard population was that in 2009. Prevalence is cases per 100,000.

100,000 in 2012, and subsequently decreased slightly to 115.3 per 100,000 in 2013. Prevalence was highest for the age group 70 to 79, and no gender difference was observed (ratio 1:1.0, Table 4).

Discussion

In the present study, we report the standardized prevalence rates of CRPS, PHN, TN, and DN over a 5-year period in Korea. Our study is the first to report the prevalence of four rare neuropathic diseases and their change by year in a single-ethnic Asian country with a population over 50 million.

CRPS usually occurs from trauma, is extremely painful, and is associated with a particularly poor quality of life as well as extensive health-care and societal costs.[18] Few studies to date have reported the prevalence of CRPS, however. Because CRPS type 1 and CRPS type 2 were considered together in our study, direct comparison with other studies may be difficult, although the prevalence of CRPS type 1 in our raw data was 17.8/100,000 in 2013, which was comparable to that reported by Sandroni et al.[9] (20.57/100,000).

The prevalence of CRPS in Korea decreased slightly throughout the study period. Given that few studies to date have examined the change in prevalence or incidence of CRPS over time, the cause of this reduction is difficult to identify. As trauma is the main cause of CRPS, a reduced occurrence of trauma might be one reason for this reduction, although we were unable to obtain national statistics on trauma to verify this.

PHN is the most common complication of herpes zoster (HZ). Although several studies have examined the incidence of herpes zoster and PHN, few have reported on the prevalence of PHN. McDonald et al.[10] reported that the lifetime prevalence of PHN was 0.7/1000. Direct comparison with our data was not possible, however, because they investigated lifetime prevalence while we examined prevalence within a specified period of time.

Our findings show that the prevalence of PHN has increased persistently from 2009 to 2013. We consider the increasing age of the population in Korea to be the main reason for this observation. PHN can be prevented by vaccination to reduce the incidence of HZ[11] and better management of acute HZ,[19] meaning that primary physicians and health policy makers should strongly recommend HZ vaccination to older individuals and provide active treatment for acute HZ.

TN is a unilateral painful disorder characterized by brief electric shock-like pain with abrupt onset and termination in the distribution area of the trigeminal nerve.[20] McDonald et al.[10] reported that the lifetime prevalence of TN was 0.7/1000 in the London area using data from a General Practice Linkage Scheme with the National Hospital for Neurology and Neurosurgery. Sjaastad and Bakketeig[21] reported two cases of TN among 1838 parishioners in the age group 18 to 64 years using a face-to-face questionnaire. Using a self-assessment questionnaire and face-to-face interviews with clear diagnostic criteria, Mueller et al.[12] reported that the estimated lifetime prevalence of TN in Essen city, Germany was 0.3%. Tallawy et al.[22] reported that the prevalence of TN was 28/100,000 in people aged >37 years in Al Quseir City, Red Sea Governorate, Egypt using a door-to-door survey. In our study, the prevalence of TN was 51/100,000, Although we examined the prevalence for a defined period of time while McDonald et al.[10] and Mueller et al.[12] investigated lifetime prevalence. While Tallawy et al. and Sjaastad and Bakketeig implemented an age limit in their study population, we included patients of all ages. In the study of Mueller et al., [12] 7 of 10 patients with TN were women, resulting in an estimated male-to-female ratio of 1:2.3, which

Table 4. Standardized prevalence of DN in Korea 2009–2013.

	2013		2012		2011		2010		2009		
Age group (y)	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Standardized prevalence	Cases	Population	Prevalence
Males											
Total	33,288	116.6	34,462	124.9	25,908	96.6	21,287	82.7	20,104	24,929,939	80.6
<10	3	0.1	1	0.0	1	0.0	0	0	1	2,553,592	0
10–19	72	2.2	47	1.4	33	0.9	20	0.6	23	3,599,148	0.6
20–29	161	4.7	160	4.6	119	3.4	89	2.5	90	3,636,509	2.5
30–39	975	23.8	981	23.6	702	16.7	588	13.8	558	4,269,498	13.1
40–49	3,673	80.9	4,127	91.5	2,972	65.8	2,516	55.7	2526	4,439,164	56.9
50–59	9,335	231.0	9,950	254.1	6,990	185.2	5,529	156	5181	3,261,648	158.8
60–69	10,650	493.0	11,110	533.2	8,857	438.5	7,584	379.3	7185	1,920,187	374.2
70–79	7,914	609.0	7,725	619.8	5,654	492.9	4,564	426.3	4241	997,027	425.4
≥80	1,581	446.0	1,486	456.5	1,085	362.4	905	320.5	779	253,166	307.7
Females											
Total	31,862	114.0	33,645	124.4	25,473	96.5	21,206	83.5	20,056	24,843,206	80.7
<10	4	0.2	4	0.2	0	0.0	0	0	0	2,369,377	0
10–19	58	2.0	36	1.2	26	0.8	20	0.6	21	3,212,502	0.7
20–29	134	4.3	150	4.7	101	3.1	120	3.6	121	3,391,753	3.6
30–39	533	13.6	578	14.4	451	11.2	401	9.8	425	4,102,035	10.4
40–49	2,068	47.2	2,282	52.8	1,918	44.3	1,814	41.9	1772	4,290,331	41.3
50–59	6,736	169.1	7,461	192.5	5,724	152.5	4,636	131.6	4419	3,246,429	136.1
60–69	9,896	427.9	10,869	484.2	8,214	373.9	6,899	314.8	6728	2,127,305	316.3
70–79	10,539	594.3	10,613	615.6	7,578	466.6	6,263	404.6	5717	1,480,410	386.2
≥80	2,875	343.2	2,761	352.0	1,973	269.2	1,600	231.8	1289	623,064	206.9
Total	65,150	115.3	68,107	124.7	51,381	96.6	42,493	83.1	40160	49,773,145	80.7

Note: Standard population was that in 2009. Prevalence is cases per 100,000.

was similar to that in our study. The differences between our study and those reported previously may be explained by differences in methodology, ethnicity, and proportion of older individuals in the general population.

Several studies have reported on the prevalence of neuropathy in a diabetic population.[23,24] However, there are few reports of the prevalence of DN in the general population. McDonald et al.[10] reported that the lifetime prevalence of diabetic polyneuropathy was 2 per 1000 persons in an unselected urban population. Savettieri et al.[11] reported that the prevalence of diabetic neuropathy with somatic symptoms was 3 per 1000 persons in two Sicilian municipalities according to a door-to-door survey. In our study, the prevalence of DN was 80.7 to 115.3/100,000 lower than that reported in the previous studies. As for TN, these differences can be explained by differences between our study and those reported previously.

The prevalence of DN increased from 2009 to 2012 and was highest in the group aged 70 to 79 years, with no gender difference. An increasing diabetic population in Korea is considered the main reason for this increased prevalence. DN can be prevented by reducing the incidence of diabetes or improving glucose control in patients that have diabetes,[25] indicating that both individual and social efforts are required.

A limitation of our study is its reliance on diagnosis codes in a computerized database instead of on medical records that include symptoms and signs; cases that were misdiagnosed or over-diagnosed could therefore not be eliminated. Moreover, variability caused by changes in diagnostic criteria could not be accounted for. Furthermore, we used period prevalence because HIRA data were collected year by year. Other studies used point prevalence or life-time prevalence, meaning that direct comparison was difficult.

Our findings show that, despite a reduction in the prevalence of CRPS and TN during the study period, the prevalence of PHN and DN was increased. Preventive methods to reduce PHN and DN are therefore warranted in clinical practice.

In conclusion, we reported the period prevalence and change in prevalence for four neuropathic diseases. Further studies are necessary to investigate the risk factors and socioeconomic burden associated with each disease.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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