Clinical Characteristics, Pain, and Quality of Life Experiences of Trigeminal Neuralgia in a Multi-Ethnic Asian Cohort

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Aims: To describe the clinical characteristics of trigeminal neuralgia (TN) in a multi-ethnic Malaysian population and to relate them to standardized measures of pain severity, anxiety, depression, and quality of life (QoL). **Methods:** Patients fulfilling the International Headache Society (IHS) criteria for TN were prospectively interviewed for their demographic and clinical data. Pain intensity was rated with a visual analog scale (VAS), anxiety and depression were determined by the Hospital Anxiety and Depression Scale (HADS), and QoL was assessed by the Short-Form 36 (SF-36) questionnaire. Chi-square, Mann-Whitney *U*, and Spearman correlation tests were used to test for differences considering a significance level of $P < .05$. **Results**: Of the 75 included patients, 52 (69.3%) were women with a mean ± standard deviation (SD) onset age of 52.0 ± 12.7 years, and 57.3% were Chinese, 24.0% Malay, and 18.7% Indian. Pain was more common on the right side (69.3%) and in the maxillary and mandibular divisions. VAS scores for pain at its worst were higher in anxious/borderline anxious patients compared to non-anxious patients (89.5 ± 15.9 vs 80.9 ± 17.2, respectively; $P < .05$), and VAS scores for pain at its least were higher in depressed/borderline depressed subjects compared to non-depressed subjects (38.4 ± 25.8 vs 23.0 ± 19.2, respectively; $P < .05$). Chinese patients had lower VAS scores for pain at its least compared to Indian patients (19.7 ± 16.1 vs 39.9 ± 24.7; $P < .01$). TN patients scored lower in all eight domains of the SF-36 compared to the general population. Indian patients had lower scores in role limitations due to physical health (8.9 ± 23.2 vs 49.4 ± 43.8; $P < .01$) and social function (56.3 ± 13.6 vs 76.5 ± 23.6; $P < .01$) than Chinese patients, and Malay patients had lower mental health scores compared to Chinese patients (59.1 ± 19.5 vs 73.0 ± 21.0; $P < .01$). **Conclusion:** Clinical characteristics of TN patients were similar to those of other populations. There were differences in pain ratings and QoL between TN patients of different ethnicities, as well as between those with anxiety and depression. *J Oral Facial Pain Headache 2017;31:e15–e20. doi: 10.11607/ofph.1793*

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Trigeminal neuralgia (TN) is characterized by severe pain in the distribution of one or more divisions of the trigeminal nerve.[1] Evidence suggests that TN may be related to compression of the trigeminal nerve root entry zone close to the brainstem, most likely by a tortuous vessel, which leads to demyelination and resulting ectopic excitation and ephaptic transmission of nerve impulses of the demyelinated axons.[2]

TN is an uncommon disease, with a reported annual incidence of 4 to 5 per 100,000, and is higher in women than in men.[3,4] It typically affects the older age groups, with a peak in the 50- to 80-year age group. Its clinical characteristics are well described: it more commonly involves the right side of the face and is in the distributions of the mandibular and/or the maxillary branch of the trigeminal nerve.[1,3,5–7] The pain is typically described as electric shock–like, sharp, stabbing, or lancinating, and attacks can be spontaneous or triggered by mild sensory stimulation of specific areas within the distribution of the affected trigeminal nerve (trigger zones), such as the alveolar mucosa, alae nasi, nasolabial fold, cheek, and lips. Typical triggering stimuli include light touch, face washing, teeth brushing,

talking, eating, and a blowing wind. Management approaches for TN include pain control with medications such as carbamazepine, oxcarbazepine, baclofen, and lamotrigine, or with surgical therapy, which includes microvascular decompression or destructive procedures of the nerve.[8]

Although numerous aspects of TN have been described in the literature—including its epidemiology, clinicopathologic features, and management—few studies have assessed the pain experiences of TN patients. Ethnic differences in pain perception are well recognized, and a recent study using quantitative sensory testing reported differences in somatosensory profiles of various pain modalities between Chinese and Danish patients.[9] In a previous study of patients from Malaysia and Singapore, TN was reported to be more common in Chinese than in Malay patients, but the study did not evaluate differences in their pain perceptions.[6] The recognized impact of neuropathic pain on psychological health and quality of life (QoL) suggests that patients with TN may have a significant disease burden related to the condition. However, no study has evaluated this impact in a multi-ethnic population. This lack of information suggests a need to better understand the characteristics of TN patients and the related disease burden. The aims of this study were to describe the clinical characteristics of TN in a multi-ethnic Malaysian population and to relate them to standardized measures of pain severity, anxiety, depression, and QoL.

Materials and Methods

This was a prospective cross-sectional study in 77 consecutive patients seen at the Neurology Clinic, University of Malaya Medical Centre (UMMC), Kuala Lumpur, between July 2011 and February 2012. The study was approved by the UMMC Medical Ethics Committee (MEC No: 866.5), and all patients gave written informed consent for participation. Patients who fulfilled the International Headache Society (IHS) diagnostic criteria for TN[1] were included in the study.

Patients were interviewed by using a standard questionnaire in English, which is widely spoken and understood in Malaysia. Information obtained were sociodemographic and clinical data, including pain characteristics (ie, site and nerve division involved, nature of the pain, trigger zones, and triggering stimuli). Pain intensity was assessed on a 100-mm visual analog scale (VAS), on which 0 represented no pain at all and 100 represented worst ever pain.[10] Patients were asked to assess pain intensity at its worst, at its least, and on average over the past 4 weeks. Brain magnetic resonance imaging (MRI) findings were recorded when available. The Hospital Anxiety and Depression Scale (HADS) was used to evaluate psychological health. The HADS is a self-administered questionnaire consisting of 7 items related to anxiety and 7 related to depression. Each item is scored, and a total score is calculated for each variable: A score of 0 to 7 is considered no anxiety/depression, 8 to 10 is considered borderline, and 11 to 21 is considered to indicate anxiety/depression.[11] QoL was measured with the health survey Short-Form 36 (SF-36).[12] The SF-36 consists of 36 items measuring 8 domains: physical functioning (PF), role limitations due to physical health (role-physical function [RP]), bodily pain (BP), general health perceptions (GH), vitality (energy and fatigue [VT]), social functioning (SF), role limitations due to emotional health (role-emotional function [RE]), and general mental health (MH). The scores range from 0 (worst QoL) to 100 (best QoL). Results were compared with previously published age-matched normative general Malaysian population data.[13] These eight domains can be recorded into two summary scores: a Physical Component Summary (PCS) score and a Mental Component Summary (MCS) score. The summary scores are standardized to have a population mean of 50 (standard deviation [SD] ± 10.0), thus making it possible to meaningfully compare scores across domains and summary scores.[14] Scores above and below 50 are regarded as above and below the average, respectively.[15]

Descriptive statistics were used to present patient characteristics in frequencies for all categorical variables and to calculate mean and SD for continuous variables. Comparison of categorical data was performed by using chi-square test, and quantitative data were tested for normality by using the Kolmogorov-Smirnov test to select the appropriate test of significance. Also, three pair-wise comparisons with Bonferroni correction were used to determine the differences in VAS score and SF-36 data between the ethnic groups. The level of significance was set at $P < .05$. For correlation analysis between pain severity and QoL, the Spearman correlation test was used. All analyses were performed by using the Statistical Package for Social Science (SPSS) software version 19.0 for Windows.

Results

A total of 77 patients were recruited into the study. Two were excluded, as they had painful trigeminal neuropathy attributed to space-occupying lesions. Therefore, 75 patients fulfilled the IHS criteria of classical TN, with 12 (16.0%) having the typical purely paroxysmal pain and 63 (84.0%) having concomitant persistent facial pain (Table 1). Of the 75 TN patients, 69.3% were female and 30.7% were

male, representing a ratio of 2.26:1 (Table 1). Their ages ranged from 20 to 84 years, with a mean age of 60.2 ± 12.0 years. The age of onset of the first episode of TN ranged from 18 to 81 years (mean 52.0 ± 12.7 years). The majority had onset of symptoms in the fourth and fifth decades of life. Of the 75 patients, 57.3% were Chinese, 24.0% were Malay, and 18.7% were Indian. There were no differences in the distribution of the two subtypes of classic TN among the different ethnic groups.

Pain was unilateral in 98.7% of the patients and was more common on the right side in 69.3%. Bilateral involvement was noted in one patient, but did not occur at the same time on both sides (Table 2): The patient developed right TN after the left TN had resolved. The most frequently affected divisions of the trigeminal nerve were the maxillary [V2] (29.3% of patients) and mandibular [V3] (28.0%) alone, and the isolated ophthalmic branch [V1] was the least frequently affected (8.0%). Women had more V2 involvement, either isolated or in combination with other divisions, compared to men (39 [75.0%] vs 9 [39.1%]; odds ratio [OR] 4.67; 95% confidence interval [CI] 1.64 to 13.33). There was no statistically significant association between the side of the face affected and the division of the trigeminal nerve that was likely to be involved. There were no significant differences in distribution of pain among the different ethnic groups (Table 3).

More than one type of pain characteristic was described in 48 (64.0%) of the patients. Sharp, stabbing pain was the most common pain described, followed by an electrical shock–like sensation (Table 4). Trigger zones were observed in 97.3% of the patients, and these varied widely in location, with the most common being the alveolar mucosa followed by the nasolabial fold (Table 4). There were also many types of triggering stimuli, and the majority of patients reacted to more than one type (Table 4). There were no differences in the character of the pain, trigger zones, or triggering factors among the different ethnic groups (data not shown). Of the 77 patients, MRI was performed in 51 (66.2%). MRI showed trigeminal nerve compression by an aberrant vascular loop in 33.3% of these patients and a tumor in 3.9% (schwannoma and meningioma).

VAS scores for pain at its worst, least, and average over the last 4 weeks were compared according to gender, ethnicity, and presence of anxiety or depression. VAS was not assessed in one patient, as the patient was blind. Mean VAS of pain at its worst and at its least were 84.5 ± 17.1 and 26.8 ± 21.8, respectively. There were no significant differences in worst and least VAS between men and women. Comparison of the different ethnic groups revealed that ethnic Chinese patients had significantly lower VAS scores for pain at its least compared to Indian patients (19.7 ± 16.1 vs 39.9 ± 24.7; $P < .01$) (Fig 1). There were no significant differences in VAS scores between Chinese and Malay patients or between

Table 1 Demographic Data of Malaysian Trigeminal Neuralgia Patients (N = 75)

Patient characteristics	n (%)
Subtype of classical TN	
Purely paroxysmal	12 (16.0)
Concomitant persistent facial pain	63 (84.0)
Age, y (mean ± SD)	60.2 ± 12.0
Gender	
Male	23 (30.7)
Female	52 (69.3)
Ethnicity	
Malay	18 (24.0)
Chinese	43 (57.3)
Indian	14 (18.7)
Age at Onset (y)	
< 20	1 (1.3)
20–29	4 (5.3)
30–39	4 (5.3)
40–49	21 (28.0)
50–59	28 (37.3)
60–69	9 (12.0)
70–79	7 (9.3)
≥ 80	1 (1.3)

Table 2 Distribution of Side of Face and Division of Nerve Involved in Malaysian Trigeminal Neuralgia Patients

Division	Bilateral	Right	Left	Total, n (%)
V1	0	5	1	6 (8.0)
V2	1	15	6	22 (29.3)
V3	0	12	9	21 (28.0)
V1 + V2	0	9	1	10 (13.3)
V2 + V3	0	5	3	8 (10.7)
V1 + V2 + V3	0	6	2	8 (10.7)
Total, n (%)	1 (1.3)	52 (69.3)	22 (29.3)	75 (100)

Table 3 Comparisons of Pain Distribution of Trigeminal Neuralgia Patients Among the Ethnic Groups

	Malay, n (%)	Chinese, n (%)	Indian, n (%)	*P* value
Side				
Right	15 (83.0)	30 (69.8)	7 (50.0)	NS
Left	3 (16.7)	12 (27.9)	7 (50.0)	
Bilateral	0 (0)	1 (2.3)	0 (0)	
Division				
V1	1 (5.6)	4 (9.3)	1 (7.1)	NS
V2	6 (33.3)	10 (23.3)	6 (42.9)	
V3	2 (11.1)	16 (37.2)	3 (21.4)	
V1 + V2	4 (22.2)	4 (9.3)	2 (14.3)	
V2 + V3	2 (11.1)	5 (11.6)	1 (7.1)	
V1 + V2 + V3	3 (16.7)	4 (9.3)	1 (7.1)	

NS = nonsignificant.

Table 4 Pain Characteristics of Malaysian Trigeminal Neuralgia Patients

Character of pain	n (%)	Trigger zone	n (%)	Triggering stimuli	n (%)
Sharp, stabbing	46 (61.3)	Alveolar mucosa	27 (36.0)	Eating	64 (85.3)
Electrical shock–like	42 (56.0)	Nasolabial fold	14 (18.7)	Face washing	57 (76.0)
Pulling	17 (22.7)	Cheek	7 (9.3)	Tooth brushing	55 (73.3)
Throbbing	12 (16.0)	Lips	6 (8.0)	Touching	54 (72.0)
Burning	12 (16.0)	Jaw	6 (8.0)	Talking	54 (72.0)
Pricking	12 (16.0)	Eyebrow	3 (4.0)	Wind blowing	33 (44.0)
Dull aching	8 (10.7)	Forehead	3 (4.0)	Swallowing	13 (17.3)
Numbness	5 (6.7)	Chin	2 (2.7)		
		Tongue	2 (2.7)		
		None	2 (2.7)		

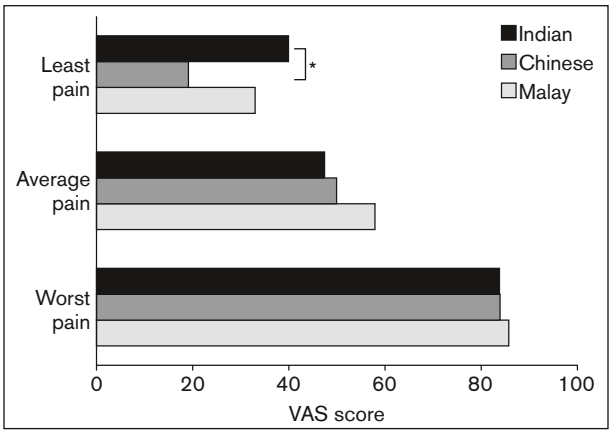

Fig 1 Comparisons of visual analog scale (VAS) scores of pain at its worst, least, and on average among the three ethnic groups. *P < .01.

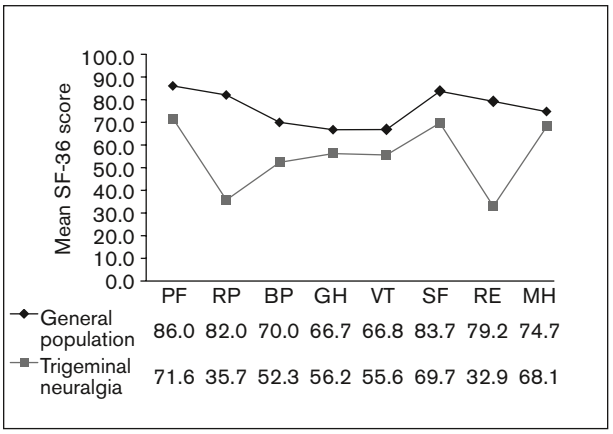

Fig 2 Comparison of SF-36 domain mean scores between TN patients and the general Malaysian population.[13] Scores for all eight domains were lower than the general population. PF = physical function; RP = role-physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role-emotional; MH = mental health.

Malay and Indian patients. Based on the HADS, 21 patients (28.0%) were found to have anxiety and 8 (10.7%) to have depression. Another 10 patients (13.3%) had both borderline anxiety and depression. Combined anxiety and borderline anxiety patients had significantly higher VAS scores for pain at its worst compared to those who were not anxious (89.5 ± 15.9 vs 80.9 ± 17.2; P < .05), while combined depression and borderline depression patients had significantly higher VAS scores for pain at its least compared to patients who were not depressed (38.4 ± 25.8 vs 23.0 ± 19.2; P < .05). No significant ethnic differences were found between TN patients with combined anxiety and borderline anxiety or between combined depression and borderline depression.

Results from the SF-36 showed that TN patients had a significantly impaired QoL: The scores of all eight domains of the SF-36 were significantly reduced compared with the Malaysian general population[13] (Fig 2). RP and RE domains were the most affected. Mean summary scores for physical health (PCS) and mental health (MCS) components were 41.4 ± 8.5 and 43.6 ± 11.9, respectively, and both were below that of the normal population.[13] Pain severity at its least correlated negatively with all eight domains of the SF-36, as well as with the two summary scores. The correlation was significant for the GH domain (r = –.306, P < .01). There were no significant differences in any of the eight domains between genders. Among the different ethnic groups, only Indian patients had significantly lower RP and SF mean scores compared to ethnic Chinese patients, and Malay patients had significantly lower MH scores compared to ethnic Chinese patients (Table 5).

Discussion

This study described the clinical findings of 75 patients with TN from a university hospital in Malaysia. Clinical characteristics of Malaysian TN patients were similar to those previously reported in the literature, including the distinctive features of an older age of onset and a higher prevalence in women, on

Table 5 Pairwise Comparison of the Short-Form 36 Domains Between Ethnic Groups

		Mean SF-36							
		Physical health scores (mean ± SD)				Mental health scores (mean ± SD)			
Ethnicity	n	PF	RP	BP	GH	VT	SF	RE	MH
Malay	18	70.0 ± 24.5	23.6 ± 37.8	51.4 ± 31.5	57.3 ± 22.8	55.3 ± 19.9	63.9 ± 25.3	20.4 ± 38.1	59.1 ± 19.5
Chinese	43	75.5 ± 21.9	49.4 ± 43.8	54.4 ± 24.7	57.6 ± 21.4	57.8 ± 20.4	76.4 ± 23.6	44.9 ± 48.7	73.0 ± 21.0
P value		NS	NS	NS	NS	NS	NS	NS	< .01
Malay	18	70.0 ± 24.5	23.6 ± 37.8	51.4 ± 31.5	57.3 ± 22.8	55.3 ± 19.9	63.9 ± 25.2	20.4 ± 38.1	59.1 ± 19.5
Indian	14	61.8 ± 21.5	8.9 ± 23.2	47.3 ± 18.0	50.4 ± 16.8	49.3 ± 18.4	56.2 ± 13.6	11.9 ± 30.9	64.3 ± 16.5
P value		NS	NS	NS	NS	NS	NS	NS	NS
Chinese	43	75.5 ± 21.9	49.4 ± 43.8	54.4 ± 24.7	57.6 ± 21.4	57.8 ± 20.4	76.5 ± 23.6	44.9 ± 48.7	73.0 ± 21.0
Indian	14	61.8 ± 21.5	8.9 ± 23.2	47. 3± 18.0	50.4 ± 16.8	49.3 ± 18.4	56.3 ± 13.6	11.9 ± 30.9	64.3 ± 16.5
P value		NS	< .01	NS	NS	NS	< .01	NS	NS

PF = physical function; RP = role-physical; BP = bodily pain; GH = general health; VT = vitality; SF = social function; RE = role-emotional; MH = mental health; NS = nonsignificant; SD = standard deviation. Mann-Whitney *U* test.

the right side, and in the maxillary and/or mandibular divisions.[3,5,7,16] There were no significant differences between ethnic groups in terms of clinical characteristics.

One hypothesis to explain the increasing incidence of TN with age is that elongation of aging arteries and "sagging" of the brain cause pulsatile compression and hyperactive dysfunction of the trigeminal nerve.[17] The increased preponderance in women might be explained by a longer lifespan in women, as well as postmenopausal osteoporosis resulting in progressive basilar impression and trigeminal nerve compression.[3,5] Reasons for the predilection to the right side and maxillary and mandibular divisions are unknown, but anatomical observations have shown that the foramen ovale and rotundum are asymmetrical, with the right side being narrower.[18,19] It was hypothesized that in cases of TN caused by vascular compression, the narrower foramina led to a secondary entrapment of the maxillary and mandibular trigeminal nerve branches.[20]

The prevalence of anxiety in TN patients was higher compared to the general population of Malaysia.[21] Conversely, the prevalence of depression in TN patients was about the same as the general population.[22] However, whether the anxiety and depression preceded or was caused by TN could not be determined, as they were assessed with the HADS and scored only at the time of the study interview. Pain intensity scores were not significantly different between genders, but were correlated with anxiety and depression. Interestingly, pain at its worst was felt to be more severe in anxious subjects, but there was less tolerance for pain at its least in depressed subjects. This finding may be a reflection of differences between these two psychological disorders. In addition, VAS scores for pain at its least were lower among ethnic Chinese compared to Indian patients (suggesting Chinese patients have a greater tolerance for baseline pain compared to Indian patients), but all ethnic groups experienced pain to a similar degree when it reached its maximum intensity. A lower perception of pain intensity between Chinese and other ethnic groups has been reported in neighboring Singapore (which has a similar multiethnic population) for other chronic pain conditions, namely osteoarthritis and headache.[23,24] These differences between ethnicities may be explained by differences in sociocultural background, psychological sensitivities (eg, expectations, pain beliefs), and biologic responses to pain.[25]

TN patients have more problems with work and other daily activities due to physical health and emotional problems compromising their QoL.[26,27] In the present study, TN patients scored lower on all eight SF-36 domains compared with the general Malaysian population. RP and RE domains were the most affected, reflecting the common perception among TN patients that their illness is severe and disabling, which limits their ability to carry out their activities. The lower PCS and MCS scores indicate that both physical and mental well-being were impaired in the TN patient population. Lower QoL scores were inversely correlated with VAS scores of pain at its least. This suggests that baseline pain severity was more important than maximum pain intensity, which may be brief and episodic, and that the former should be a better marker for response to therapy. In addition, there were ethnic differences in QoL scores, with Indian patients scoring lower on RP and SF domains compared to ethnic Chinese patients, and with Malay patients scoring lower on the MH domain compared to Chinese patients. Again, these differences could be explained by differences in socioeconomic status and cultural factors, including the way symptoms are perceived, mental and bodily distress and needs are expressed, and attitudes toward those seeking professional health care.[28,29]

The study limitations included a relatively small sample size from a hospital-based study, which may have led to an over-representation of patients with more severe and disabling disease. The cross-sectional design also did not allow the evaluation of the temporal course of TN. In addition, other less readily measurable factors that may contribute to ethnic differences in pain perception, including socioeconomic status, cultural factors, and spiritual perceptions of illness, were not assessed.

Conclusions

The clinical characteristics of TN in the Malaysian population were similar to other populations, and TN patients also experienced a poorer QoL compared to the general population. Interestingly, there were differences in the perception of pain intensity and QoL between ethnic groups, as well as between those with anxiety and depression. Recognizing these unique characteristics could help to successfully manage this group of patients.

Acknowledgments

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