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Introduction

- Trigeminal neuralgia (TN) is an infrequent neurologic disorder that causes severe pain in the facial region
- The incidence rate is approximately four per 100,000 per population, affecting mostly females and those above 40 years of age
- TN can involve one or more divisions of the fifth cranial nerve (CN V), with the maxillary and mandibular branches being more commonly affected than the ophthalmic branch
- The pain is usually unilateral and has a slight right sided predominance .The pain is often described as lancinating, sharp, shooting or “electric shocklike
- Common triggering factors include talking, chewing, tooth brushing, touching, or even a cool breeze
- The etiopathogenesis of TN is not entirely clear, and many cases have no apparent cause. However, it is widely accepted that in many cases, TN is related to neurovascular compression at or near the dorsal root entry zone of the nerve
- Only less than 10% of TN is believed to be caused by traumatic compression of CN V either by tumors, cysts, arteriovenous malformations, or demyelinating conditions, such as multiple sclerosis
- Although diagnosis is usually made on the basis of clinical signs or symptoms, magnetic resonance imaging may be necessary to exclude specific pathology in the posterior cranial fossa
- Patients with TN respond well to medication, and pharmacotherapy is considered the first line of management.Only refractory TN cases are considered for surgical treatment
- The most effective drugs for treating TN are anticonvulsants :carbamazepine(90%), baclofen, gabapentin, phenytoin sodium, oxcarbazepine, sodium valproate, and lamotrigine
- Although many aspects of TN have been addressed in the literature, most of the-studies have been based on Caucasian/Western populations. With regard to Malaysian patients, only two articles focusing on the demographic and clinical features of patients with TN seen at oral-maxillofacial medicine clinics have been published, both with relatively small populations of patients

METHODS AND MATERIALS

- This was a retrospective multicenter research study, involving data on patients with TN from **eight hospital based oral-maxillofacial medicine clinics located in major cities within Malaysia** **Study design**
- Records of consecutive patients diagnosed as having TN from **January 1, 2001, to December 31, 2012**, were retrieved and assessed for suitability to be included into the study.
- Only patients diagnosed as having TN by **oral-maxillofacial medicine specialists** following the diagnostic criteria published in the first and second editions of the **International Classification of Headache Disorders (ICHD)**
- **Followed-up** for a minimum period of **6 months** with complete patient records were included in the study. Cases with incomplete records (missing data points) were excluded from the study.
- Records of 354 patients were retrieved; of these, 34 were excluded as they were incomplete records (missing data), and thus a **final number of 320 cases** were included.

RESULTS

- Demographic characteristics

Clinical features ^{†‡}	Gender ^{†‡}		Total (n, [%]) ^{†‡}	P-value [§]
	Male (n) [†]	Female (n) [‡]		
Age [‡]	^{†‡}	^{†‡}	^{†‡}	^{†‡}
Median age ^{†‡} [interquartile range] ^{†‡}	60.2 [11.98] (123) ^{†‡}	57.8 [9.92] (197) ^{†‡}	58.2 [13.00] (320) ^{†‡}	.073 [§]
Side [‡]				
Right [‡]	54 ^{†‡}	126 ^{†‡}	180 (56.3) ^{†‡}	.001 [§]
Left [‡]	67 ^{†‡}	69 ^{†‡}	136 (42.5) ^{†‡}	^{†‡}
Bilateral [‡]	2 ^{†‡}	2 ^{†‡}	4 (1.3) ^{†‡}	^{†‡}
Total, n, (%) ^{†‡}	123 (38.4) ^{†‡}	197 (61.6) ^{†‡}	320 (100) ^{†‡}	^{†‡}
Branch of fifth cranial nerve [‡]				
Maxillary only ^{†‡}	51 ^{†‡}	72 ^{†‡}	123 (38.4) ^{†‡}	.265 [§]
Mandibular only ^{†‡}	57 ^{†‡}	92 ^{†‡}	149 (46.6) ^{†‡}	^{†‡}
Ophthalmic and maxillary ^{†‡}	6 ^{†‡}	4 ^{†‡}	10 (3.1) ^{†‡}	^{†‡}
Maxillary and mandibular ^{†‡}	5 ^{†‡}	21 ^{†‡}	26 (8.1) ^{†‡}	^{†‡}
Ophthalmic, maxillary, and mandibular ^{†‡}	4 ^{†‡}	8 ^{†‡}	12 (3.8) ^{†‡}	^{†‡}
Total, n, (%) ^{†‡}	123 (38.4) ^{†‡}	197 (61.6) ^{†‡}	320 (100) ^{†‡}	^{†‡}

1. TN occurred most frequently in the later decades of life, predominantly the **sixth decade**. The patients' age ranged **between 26 and 91 years**. TN was diagnosed at a **mean age 58.7**.
2. TN presented predominantly in **females (61.6%)**.
3. The majority of patients were from the ethnic Malay group (56.3%), followed by Chinese (24.7%) and Indian (8.8%). ("Others") was made up of other Malaysian indigenous ethnic groups. **There were no statistically significant differences in age between the different ethnic groups**

- Medical history

With regard to medical comorbidities that may contribute to trigeminal neuropathy:

-34 patients: diabetes mellitus

-12 patients: some form of craniofacial trauma before diagnosis

- 5 patients: a history of stroke and
- 3 patients: some form of connective tissue disease, such as systemic lupus erythematosus.
- No patients from this cohort had a history of multiple sclerosis
- Clinical features

Table II. Comparison of clinical features of patients with trigeminal neuralgia with data from other Asian studies^{4,5}

			Total n (%) ^{4,5}		
Clinical features ^{4,5}	Present study ^{4,5}	Loh et al. ^{4,5} (1998) ^{2,4,5}	Ariyawardana et al. ^{4,5} (2003) ^{23,4,5}	Jainkittiwong et al. ^{4,5} (2011) ^{10,4,5}	Yadav et al. ^{4,5} (2015) ^{3,4,5}
Number of patients, n ^{4,5}	320 ^{4,5}	44 ^{4,5}	61 ^{4,5}	188 ^{4,5}	72 ^{4,5}
Gender					
Male ^{4,5}	123 (38.4) ^{4,5}	16 (36.3) ^{4,5}	26 (43.0) ^{4,5}	70 (37.2) ^{4,5}	23 (31.9) ^{4,5}
Female ^{4,5}	197 (61.6) ^{4,5}	28 (63.7) ^{4,5}	35 (57.0) ^{4,5}	118 (62.8) ^{4,5}	49 (68.1) ^{4,5}
Age ^{4,5}	58.2 (13.00) ^{4,5}	54.9 ^{4,5}	Not available ^{4,5}	52.5 ^{4,5}	54.9 ^{4,5}
Median age (interquartile range [IQR])/Mean ^{4,5} (standard deviation ^{4,5} [SD]) ^{4,5}		(SD not available) ^{4,5}		(IQR not available) ^{4,5}	(SD not available) ^{4,5}
Side					
Right ^{4,5}	180 (56.3) ^{4,5}	24 (54.5) ^{4,5}	42 (68.9) ^{4,5}	119 (63.3) ^{4,5}	45 (62.5) ^{4,5}
Left ^{4,5}	136 (42.5) ^{4,5}	17 (38.6) ^{4,5}	19 (31.1) ^{4,5}	67 (35.6) ^{4,5}	27 (37.5) ^{4,5}
Bilateral ^{4,5}	4 (1.3) ^{4,5}	3 (6.8) ^{4,5}	0 (0.0) ^{4,5}	2 (1.1) ^{4,5}	0 (0.0) ^{4,5}
Branch of fifth cranial nerve ^{4,5}					
Maxillary only ^{4,5}	123 (38.4) ^{4,5}	13 (29.5) ^{4,5}	21 (34.0) ^{4,5}	47 (25.0) ^{4,5}	27 (37.5) ^{4,5}
Mandibular only ^{4,5}	149 (46.6) ^{4,5}	22 (50.0) ^{4,5}	40 (66.0) ^{4,5}	57 (30.3) ^{4,5}	41 (56.9) ^{4,5}
Ophthalmic and maxillary ^{4,5}	10 (3.1) ^{4,5}	1 (2.3) ^{4,5}	0 (0.0) ^{4,5}	17 (9.0) ^{4,5}	0 (0.0) ^{4,5}
Maxillary and mandibular ^{4,5}	26 (8.1) ^{4,5}	8 (18.2) ^{4,5}	0 (0.0) ^{4,5}	55 (29.3) ^{4,5}	4 (5.6) ^{4,5}
Ophthalmic, maxillary, and mandibular ^{4,5}	12 (3.8) ^{4,5}	0 ^{4,5}	0 (0.0) ^{4,5}	12 (6.4) ^{4,5}	0 (0.0) ^{4,5}

1. TN was seen to present most **frequently as a unilateral** condition with bilateral involvement in only 1.3% of the cases.
2. **Right-sided** unilateral involvement was seen more commonly (56.3%) than involvement of the left side only
3. The **CN V3 branch** was the most frequently involved branch of the trigeminal nerve in this series of patients with 149 (46.6%) patients having pain solely in the mandibular division. The least frequently involved branch was the ophthalmic division, with only 6.9% of the patients having some involvement of this branch. **No cases of TN solely affecting the ophthalmic division were seen in this cohort of patients**
4. TN was mostly described by these patients as **“sharp or shooting pain” (45%)**, followed by “throbbing pain” (19.1%), “electric shock/current-like pain” (16.6%), and “stabbing pain” (9.1%)
5. The most commonly reported trigger factor in this cohort of patients was **eating or chewing (36.3%)**. Almost a quarter of the patients **(23.4%) reported no triggering factor** or activity. In these patients, the pain was completely **spontaneous**

● Management

1. 39 patients (12.2%) were sent for neuroimaging (8 for computed tomography and 31 for magnetic resonance imaging) as a result of atypical clinical findings. Of these patients, 7 (2.2%) had some form of tumor involving the trigeminal nerve.
2. **Carbamazepine** was the **first-line drug** of choice in most instances (87.5%). Other drugs used included gabapentin, lamotrigine, pregabalin, baclofen, phenytoin, and amitriptyline. In 12.2% of patients, various combinations of

medications were used to achieve adequate pain control as monotherapy was unsuccessful.

3. With regard to side effects of medications,

-**Dizziness(87.3%.)** was the most commonly

-The least frequently adverse effects were altered levels of liver enzymes (2.5%), carbamazepine induced **Stevens Johnson syndrome (SJS) (1.3%)**, and leukopenia (1%).

DISCUSSION

1. As TN is quite uncommon in relatively younger patients (<40 years of age), it is advisable to conduct thorough clinical and radiographic assessments to exclude TN secondary to tumors or demyelinating conditions in young patients or those with atypical clinical findings or pain symptomology
2. Although most of our patients described the pain primarily as **intense, sharp, shooting pain**, some described their pain as “**throbbing pain,**” “**pulling,**” or “**stabbing pain.**”
3. Description of pain is significantly influenced by the culture, language, and prior pain experience of the individual, and it is imperative that the clinician elucidate and record detailed pain symptomology and perform a thorough clinical assessment before arriving at a diagnosis of TN
4. In our study, we discovered that the right side was more commonly affected than the left side, with a ratio of 1.3:1 (excluding bilateral cases). There is a possibility of **anatomic variants** on the right trigeminal nerve. **Neto et al.** showed that in most cases, **the foramen ovale on the right of the human skull is narrower than that on the contralateral side.** Both of these foramina are the passage through which the maxillary and mandibular branches pass. Thus, **Neto et al. hypothesized that the propensity of TN to be present on the right side of face may be caused by entrapment of the second and third divisions of the trigeminal nerves when crossing these foramina.**
5. Patients with TN involving the maxillary division, the ophthalmic division, or both may have been managed by physicians, otorhinolaryngologists, or even ophthalmologists and neurologists
6. TN-like trigeminal neuropathy has also at times been found to precede the features of some connective tissue diseases, such as **Sjogren syndrome, systemic lupus erythematosus, mixed connective tissue disease, and systemic sclerosis.**
7. In this study, all our patients were treated pharmacologically. **Most were treated with carbamazepine**, and they responded favorably. Other drugs, including gabapentin, lamotrigine, pregabalin, baclofen, phenytoin, and amitriptyline, were used for patients who did not respond to carbamazepine
8. Watson stated that about 40% patients treated with carbamazepine experience side effects. The most frequently reported side effects of carbamazepine were **drowsiness, dizziness, and gastrointestinal disturbances.** Other possible side effects are **leukopenia, abnormal liver function, cerebellar dysfunction, aplastic anemia, and hepatitis**
9. The **most serious potential side effects** of carbamazepine are **severe cutaneous adverse reaction, SJS, and toxic epidermal necrolysis.** Only four of our patients treated with carbamazepine developed carbamazepine-induced SJS
10. Chung et al. were the first to describe the relationship between human leucocyte antigen (**HLA**)-**B*1502** and **SJS** induced by **carbamazepine** in the Han-Chinese

11. A study in Malaysia showed that HLA-B*1502 was also present in **75%** of Malay patients with carbamazepine-induced SJS or toxic epidermal necrolysis
12. A major limitation of this study is its retrospective nature. In-depth information on pain symptomology and duration of disease were not uniformly available
13. Neuroimaging is recommended when the clinical findings are more suggestive of TN secondary to tumors or other pathologic processes; however, what is important and most useful is performing a thorough clinical examination, with emphasis on CN examinations and pain symptomology

CONCLUSIONS

- This study has demonstrated that there is very little difference between Caucasian and Malaysian TN patients in terms of their clinical and demographic features
- Prominent involvement of the mandibular branch may be a feature that is unique to Asian patients
- Asian patients with TN are quite likely to present initially at dental clinics for management of their pain because of the frequent involvement of the mandibular division
- As carbamazepine is still the main pharmacologic agent used for the management of TN, HLA-B*1502 testing before initiation of therapy in Malaysian patients is advisable.

題號	題目
1	有關三叉神經痛的敘述，下列何者錯誤？
	(A)好發率：女性 > 男性 (B)單側好發：右側 > 左側 (C)單側好發：左側 > 右側 (D)有觸覺刺激引發區
答案 (C)	出處：Oral and Maxillofacial Pathology, 3E CH 18
題號	題目
2	下列那一種顱顏疼痛，男性比女性較常見？
	(A)三叉神經痛 (trigeminal neuralgia) (B)叢發型頭痛 (cluster headache) (C)緊張型頭痛 (tension headache) (D)偏頭痛 (migraine)
答案 (B)	出處：Oral and Maxillofacial Pathology, 3E CH 18