








Clinical Characteristics and Treatment Outcomes in Patients with Trigeminal Neuralgia: An Analysis of Cases from a Tertiary Care Center

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ABSTRACT

Objective: To determine the clinical characteristics and treatment outcomes in patients with trigeminal neuralgia in a tertiary care setting. **Material and Methods:** The data of patients diagnosed with trigeminal neuralgia over a nine-year period in this tertiary care center from the archives of the Medical Records Department were included. Two observers documented the clinical data and treatment outcomes in a specially designed proforma. A p-value of <0.05 was considered statistically significant. A comparison of categorical variables was done using the Chi-square/Fisher exact test. A comparison of continuous variables was done using the Mann-Whitney U test. **Results:** There were 34 males and 24 females with a mean age of onset of neuralgia at 52.02 years. The estimated prevalence of trigeminal neuralgia from this tertiary care center in Karnataka, India, is 0.007%. There was a female dominance regarding the reported symptoms that triggered pain (p=0.031), with talking and chewing being the most common triggers. Primary and classical variants were the most common types. Medical management was the sole treatment of choice for nine participants; surgery was performed for 49 and 14 participants underwent a combination therapy. **Conclusion:** No single best treatment option has been established for this disorder. Further clinical trials with promising pain management regimens need to be conducted to strengthen the existing evidence for improving the quality of life of these individuals.

Keywords: Facial Nerve Diseases; Facial Neuralgia; Trigeminal Nerve Diseases.

■ Introduction

Trigeminal neuralgia is a chronic orofacial pain condition that causes paroxysmal, electric shock-like pain in the orofacial region innervated by the trigeminal nerve. It is characterized by stereotypic lancinating pain on the face that is usually precipitated by innocuous stimuli (allodynia) and is mostly unilateral in nature [1]. The bilateral nature of presentation poses a diagnostic challenge as it can mimic other neurological disorders causing pain [2]. The epidemiology and prevalence of trigeminal neuralgia across the global ranges from 0.03 to 0.3% [3,4]. Pain in trigeminal neuralgia typically lasts for seconds to less than a few minutes and commonly involves the maxillary and mandibular divisions [3,5,6]. Atypical clinical presentations coupled with diagnostic delays often lead to a negative impact on patients' quality of life, which adds to the challenges of management strategies [7].

The protocol for the management of primary trigeminal neuralgia usually starts with pharmacological therapy combined with a close follow-up visit. Imaging protocols are employed to rule out central abnormalities as a source of pain. The surgical mode of management offers promising outcomes but is least preferred by the patients. Most often, combined medical and surgical approaches are also employed [4].

The severity and the nature of pain experienced by individuals with this neuralgic condition warrant the need to adopt an interdisciplinary team approach. This comprehensive team usually comprises pain and palliative care specialists, neurologists, neurosurgeons, and an oral physician who intricately designs a custom-made regimen for pain management. The nature of the presentation of pain in these patients often mimics dental or orofacial foci, owing to which these individuals seek dental consultations. Timely recognition of allodynia and identification of clinical trigger zones in affected patients is crucial for prompt referral and initiation of therapeutic interventions [8].

Trigeminal neuralgia lacks a universally accepted optimal treatment strategy, complicating comparisons among various therapeutic approaches. Moreover, variations in management regimens between clinical and tertiary care settings further contribute to this complexity. The guidelines for diagnosis and management have been established through a consensus panel including all stakeholders [9-11]. Various studies have evaluated the clinical and treatment outcomes in patients with trigeminal neuralgia in clinical settings [5,6,12-16]. However, most of the literature lacks documentation of the type of trigeminal neuralgia and pain characteristics as per the International Classification of Headache Disorders-3 (ICHD-3) and the International Headache Society [3,17]. Additionally, the lack of standardized referral protocols and variability in management strategies exacerbate these gaps in the literature.

Therefore, there is a need for research that conducts comprehensive analyses of the clinical features and treatment outcomes among trigeminal neuralgia patients in hospital-based setup. Hence, this study was performed to determine the clinical characteristics and treatment outcomes in patients with trigeminal neuralgia in a tertiary care setting.

■ Material and Methods

Study Design and Ethical Clearance

This was a cross-sectional study that was performed on patients diagnosed with trigeminal neuralgia (ICD code: 50.0) in our tertiary care center from the archives of the Medical Records Department. The study protocol was approved by the Institutional Ethics Committee (IEC 201/2021).

Participants

A total of 12,41,541 outpatients visited this tertiary care hospital from January 2012 to January 2021. Of these, 94 participants were diagnosed with trigeminal neuralgia. Thirty-six patient records were excluded since there was incomplete data and lost to follow-up. Patients who were diagnosed with trigeminal neuralgia with concomitant neuromuscular diseases were also excluded.

Data Collection

Two observers independently systematically screened and analyzed patient records. In case of doubt, consensus was reached on consultation with a third expert. A specially designed proforma was drafted for documenting the clinical data (demographics, clinical symptoms according to ICHD-3 criteria - International Classification of Headache Disorders, past drug history, current drug therapy with titration, dose and duration, surgical management, referral protocols employed and the diagnosis of the type of neuralgia: primary/secondary/ classical variants.) from the patient records.

Statistical Analysis

The data of the study participants included was entered into a Microsoft Excel spreadsheet (Microsoft Corp., Redmond, WA, USA). All the analysis was performed using Statistics for Windows, version 26 (IBM Corp., Armonk, NY, USA). A p-value of <0.05 was considered statistically significant. Comparison of categorical variables was done using the Chi-square and Fisher exact tests. A comparison of continuous variables was done using the Mann-Whitney U test.

■ Results

A total of 58 patient records with trigeminal neuralgia (34 males and 24 females) were included for final analysis, with ages ranging between 27 and 86 years (mean 52.02 years). Twenty-four (41.3%) participants were diagnosed with left-side neuralgia, 33 (56.8%) with the right side, and one participant (1.7%) was diagnosed with bilateral involvement. The most affected division was the mandibular nerve (31%) (Table 1).

Table 1. Distribution of participants according to the division of involvement of trigeminal neuralgia.

Division of Involvement	Male N (%)	Female N (%)	Total N (%)
Ophthalmic division (V1)	3 (8.8)	3 (12.5)	6 (10.3)
Maxillary division (V2)	3 (8.8)	3 (12.5)	6 (10.3)
Mandibular division (V3)	12 (35.2)	6 (25)	18 (31.0)
V1 + V2 involvement	9 (26.5)	2 (8.3)	11 (18.9)
V1 + V3 involvement	1 (2.9)	0 (0.0)	1 (1.7)
V2 + V3 involvement	4 (11.7)	6 (25)	10 (17.2)
V1 + V2 + V3 involvement	2 (5.8)	4 (16.6)	6 (10.3)
Total	34 (58.6)	24 (41.4)	58 (100.0)

Primary trigeminal neuralgia was diagnosed in 28 participants (48.3%). There was no association between trigeminal neuralgia variants and gender (Table 2).

Table 2. Association of the variants of trigeminal neuralgia with gender.

Variants	Male N (%)	Female N (%)	Total N (%)	p-value
Primary Trigeminal Neuralgia	13 (38.2)	15 (62.5)	28 (48.3)	0.069
Classical Trigeminal Neuralgia	20 (58.8)	8 (33.3)	28 (48.3)	0.056
Secondary Trigeminal Neuralgia	1 (2.9)	1 (4.2)	2 (3.4)	>0.99

The majority of the participants reported specific precipitating factors that initiated the episode of pain by innocuous stimuli. There was female dominance regarding the reported symptoms that triggered pain ($p=0.031$), with talking and chewing being the most common triggers ($p<0.05$) (Table 3). The characteristics of pain and its association with gender are depicted in Table 4.

Table 3. Association of the ICHD-3 Criteria with gender.

ICHD-3 Criteria	Male N (%)	Female N (%)	p-value
Precipitated by innocuous stimuli (Allodynia)	23 (67.6)	22 (91.7)	0.031*
Brushing	10 (29.4)	8 (33.3)	0.751
Precipitated by innocuous stimuli (Allodynia)	23 (67.6)	22 (91.7)	0.031*
Talking	6 (17.6)	13 (54.2)	0.004*
Chewing	18 (52.9)	19 (79.2)	0.041*
Washing face	3 (8.8)	7 (12.5)	0.684
Shaving	13 (38.2)	0 (0.0)	0.076
Touching face	4 (11.8)	0 (0.0)	0.134
Eating warm and cold food	12 (35.3)	8 (33.3)	0.877
Exposure to cold air	6 (17.6)	4 (16.7)	>0.99
After head bath	7 (20.6)	7 (29.2)	0.452
Pain at rest	2 (5.9)	1 (4.2)	>0.99
Others (Jaw movements/touching the gums of teeth)	17 (50.0)	20 (83.3)	0.009*

*Statistically significant: Chi-square or Fisher exact test.

Table 4. Characteristics of pain and its association with gender.

Variables	Male N (%)	Female N (%)	p-value
Nature of Pain			
Electric shock like	13 (38.2)	12 (50.0)	0.373
Shooting, stabbing or sharp pain	11 (32.4)	10 (41.7)	0.467
Dull continuous pain	9 (26.5)	2 (8.3)	0.102
Severe intensity	18 (52.9)	15 (62.5)	0.469
Duration of Pain			
Pain lasting from a fraction of second to two minutes	5 (14.7)	4 (16.7)	>0.99
Pain lasting for more than two minutes	15 (44.1)	10 (41.7)	0.853

The correlation between the variants of trigeminal neuralgia and various referral protocols adopted for the study population is depicted in Table 5.

The imaging technique employed for the visualization of the nerve anatomy was magnetic resonance imaging (MRI). T1 weighted MRI was performed for 40 participants (68.9%), and 35 (60%) underwent FIESTA (Fast imaging employing steady-state acquisition) sequence. A percentage of 56.9% (21 males and 12 females) of the participants had a visible neurovascular conflict, which led to neuralgic pain. On the other hand, about 36.2% ($n=21$) of the participants underwent medical management, while 84.5% ($n=49$) of them underwent surgical interventions for the control of pain. The age of onset of the neuralgic pain had no association with the choice of therapy (medical/surgical) initiated.

Seventeen participants had a history of a polydrug regimen, and 14 individuals were under a single-drug regimen at the time of presentation to our tertiary care center. Pregabalin, carbamazepine, oxcarbazepine, and gabapentin were drugs that the participants had taken in the past. Carbamazepine was the most prescribed medication with a dose range of 200 to 700mg per day for a duration ranging from 7 days to 72 months. Medical management was the sole treatment of choice for 9 of the 58 participants. Surgical management was performed

for 49 participants and 14 underwent a combination of medical and surgical management for trigeminal neuralgia. Eighteen individuals underwent radiofrequency ablation, seven presented microvascular decompression and one of them underwent balloon compression.

A total of 42.9% of the participants with primary trigeminal neuralgia underwent medical management (single/polytherapy), whereas 46.9% of them underwent surgical management. 52.4% (n=11) of the participants with classical trigeminal neuralgia underwent medical management and 49% (n=24) underwent surgical management. Of the two individuals with secondary trigeminal neuralgia, one of them underwent surgical management alone and the other underwent both medical and surgical management. None of the study participants underwent sole surgical treatment modality. The association of the variants of trigeminal neuralgia with medical and surgical treatment modalities is depicted in Tables 6 and 7. Association of characteristics of pain with the surgical treatment modalities is depicted in Table 8.

Table 5. Correlation between the variants of trigeminal neuralgia and various referral protocols adopted for the study population.

Trigeminal Neuralgia	Dental			Pain Clinic			ENT			Neurology			Neurosurgery		
	Present N (%)	Absent N (%)	p-value	Present N (%)	Absent N (%)	p-value	Present N (%)	Absent N (%)	p-value	Present N (%)	Absent N (%)	p-value	Present N (%)	Absent N (%)	p-value
Primary	13 (52.0)	15 (45.5)	0.621	21 (58.3)	7 (31.8)	0.05	5 (62.5)	23 (46.0)	0.464	10 (41.7)	18 (52.9)	0.397	10 (40.0)	18 (54.5)	0.272
Classical	11 (44.0)	17 (51.5)	0.571	14 (38.9)	14 (63.6)	0.067	3 (37.5)	25 (50.0)	0.707	13 (54.2)	15 (44.1)	0.451	13 (52.0)	15 (45.5)	0.821
Secondary	1 (4.0)	1 (3)	>0.99	1 (2.8)	1 (4.5)	>0.99	0 (0.0)	2 (4.0)	>0.99	1 (4.2)	1 (2.9)	>0.99	2 (8.0)	0 (0.0)	0.181

Table 6. Association of the variants of trigeminal neuralgia with the medical management.

Variants of Trigeminal Neuralgia		Medical Management			Single Drug Therapy			Polydrug Therapy		
		Absent N (%)	Present N (%)	p-value	Absent N (%)	Present N (%)	p-value	Absent N (%)	Present N (%)	p-value
Primary	Present	18 (51.4)	9 (42.9)	0.534	21 (50)	7 (43.8)	0.672	13 (48.1)	15 (48.4)	0.986
	Absent	17 (48.6)	12 (57.1)		21 (50)	9 (56.3)		14 (51.9)	16 (51.6)	
Classical	Present	16 (45.7)	11 (52.4)	0.629	20 (47.6)	8 (50.0)	0.871	12 (44.4)	16 (51.6)	0.586
	Absent	19 (54.3)	10 (47.6)		22 (52.4)	8 (50.0)		15 (55.6)	15 (48.4)	
Secondary	Present	1 (2.9)	1 (4.8)	>0.99	1 (2.4)	1 (6.3)	0.479	2 (7.4)	0 (0.0)	0.212
	Absent	34 (97.1)	20 (95.2)		41 (97.6)	15 (93.8)		25 (92.6)	31 (100.0)	

Table 7. Association of the variants of trigeminal neuralgia with the surgical management.

Variants of Trigeminal Neuralgia		Surgical Management			RF Ablation			Microvascular Decompression		
		Absent N (%)	Present N (%)	p-value	Absent N (%)	Present N (%)	p-value	Absent N (%)	Present N (%)	p-value
Primary	Present	4 (57.1)	23 (46.9)	0.7	20 (52.6)	7 (38.9)	0.336	27 (55.1)	0 (0.0)	0.011*
	Absent	3 (42.9)	26 (53.1)		18 (47.4)	11 (61.1)		22 (44.9)	7 (100.0)	

Classical	Present	3 (42.9)	24 (49)	>0.99	16 (42.1)	11 (61.1)	0.184	21 (42.9)	6 (85.7)	0.048*
	Absent	4 (57.1)	25 (51)		22 (57.9)	7 (38.9)		28 (57.1)	1 (14.3)	
Secondary	Present	0 (0.0)	2 (4.1)	>0.99	2 (5.3)	0 (0.0)	>0.99	1 (2.0)	1 (14.3)	0.236
	Absent	7 (100.0)	47 (95.9)		36 (94.7)	18 (100.0)		48 (98)	6 (85.7)	

*Statistically significant: Chi-square or Fisher exact test.

Table 8. Association of characteristics of pain with the surgical treatment modalities.

Characteristics of Pain			Radiofrequency Ablation			Microvascular Decompression		
			Absent N (%)	Present N (%)	p-value	Absent N (%)	Present N (%)	p-value
Nature of Pain	Electric shock like	Present	15 (39.5)	9 (50.0)	0.457	24 (49.0)	0 (0.0)	0.016*
		Absent	23 (60.5)	9 (50.0)		25 (51.0)	7 (100.0)	
	Shooting, stabbing or sharp pain	Present	15 (39.5)	5 (27.8)	0.394	18 (36.7)	2 (28.6)	>0.99
		Absent	23 (60.5)	13 (72.2)		31 (63.3)	5 (71.4)	
	Dull continuous pain	Present	5 (13.2)	6 (33.3)	0.146	11 (22.4)	0 (0.0)	0.324
		Absent	33 (86.8)	12 (66.7)		38 (77.6)	7 (100.0)	
	Severe intensity	Present	21 (55.3)	12 (66.7)	0.418	30 (61.2)	3 (42.9)	0.429
		Absent	17 (44.7)	6 (33.3)		19 (38.8)	4 (57.1)	
Duration of Pain	Pain lasting from a fraction of second to two minutes	Present	5 (13.2)	3 (16.7)	0.703	8 (16.3)	0 (0.0)	0.577
		Absent	33 (86.8)	15 (83.3)		41 (83.7)	7 (100.0)	
	Pain lasting for more than two minutes	Present	16 (42.1)	9 (50.0)	0.579	23 (46.9)	2 (28.6)	0.443
		Absent	22 (57.9)	9 (50.0)		26 (53.1)	5 (71.4)	

Discussion

Trigeminal neuralgia is a severe, painful, and uncommon clinical entity characterized by brief lancinating pain in the face along the distribution of the trigeminal nerve. This disorder is mostly unilateral, with a predilection for middle-aged females [1]. The prevalence of trigeminal neuralgia estimated from dental care centers in various parts of India has been reported [5,12,14,16]. However, we present data on patients who were diagnosed and managed for trigeminal neuralgia in a tertiary care hospital. The estimated prevalence of trigeminal neuralgia from this tertiary care center in Karnataka, India, is 0.007%.

According to the International Classification of Headache Disorders-3 (ICHD-3) and International Headache Society [3,17-19] the criteria for the diagnosis of trigeminal neuralgia is as follows: "A. Recurrent paroxysms of unilateral facial pain in the distribution(s) of one or more divisions of the trigeminal nerve, with no radiation beyond, and fulfilling criteria B and C; B. Pain has all of the following characteristics: 1. Lasting from a fraction of a second to 2 min. 2. Severe intensity. 3. Electric shock-like shooting, stabbing or sharp in quality; C. Precipitated by innocuous stimuli within the affected trigeminal distribution; and D. Not better accounted for by another ICHD-3 diagnosis."

Although the literature supports a female preponderance from a global perspective [3], the present study showed contrasting results (58.6% males and 41.4% females). Similar observations were reported in an Indian study by Sunitha et al [5]. The mean age of onset of trigeminal neuralgia in our study population was 52.02 years, which is in concordance with other similar studies [16,20,21]. Right-side neuralgia was more commonly reported (56.8%) than the left side. A similar trend was noted in the studies by Debta et al. [12], Sunitha et al. [5] and Katheriya et al. [16]. The most affected division was the mandibular branch (31%). When multiple divisions were involved, a combination of ophthalmic and maxillary (V1 + V2) as well as maxillary and mandibular divisions (V2+V3) were affected. A similar pattern was reported in a systematic review by Toledo et al. [3] and a study on Asian cohorts [22].

International Headache Society has classified facial pain arising due to cranial nerve abnormalities with the exclusive classification of trigeminal neuralgia into three variants, namely the classical, secondary, and idiopathic (primary) forms [18]. In this study, 48.3% were diagnosed with primary and classical variants (each) and only 3.4% had trigeminal neuralgia secondary to facial trauma. Also, there was a statistically significant association between classical trigeminal neuralgia affecting the male gender compared to the other variants ($p=0.056$). However, only a single study from Sweden [23] reported of primary trigeminal neuralgia affecting the female gender. The precise clinical categorization according to the variants is crucial for treatment planning and pain management; however, studies performed on a similar cohort of patients lack these vital data [13,24-26].

Trigger zones are typical areas on the face in trigeminal neuralgia, which, on stimulation, can initiate a pain episode. Analysis of trigger zone sites has been documented in studies by Debta et al. [12] and Ayele et al. [15]. Allodynia, which means a painful response to non-noxious stimuli, is a typical feature of trigeminal neuralgia, and the current study showed females had a statistically higher response to stimuli causing pain than the male gender ($p=0.031$). Other movements that triggered an episode of pain in females were jaw movements and touching the gums of teeth ($p=0.009$). Talking and chewing were the most common triggering activities in the present study, which is in accordance with Jainkittivong et al. [26].

The majority of patients in this study reported severe intensity electric shock-like pain with pain episodes lasting for more than two minutes. Similar observations were made regarding the nature of pain by Debta et al. [12], and Ayele et al. [15]. However, the duration of each episode of pain is not documented in other studies [5,6,14,16].

Dental consultations are often sought to identify and rule out oral foci of pain that may mimic pain in trigeminal neuralgia. 43.1% of the individuals in this study had a dental referral subsequent to the diagnosis of this condition. Though 84.4% of the patients were suspected of having neuralgia-like pain conditions, they were referred to Neurology and Neurosurgery for expert diagnosis and subsequent management. 62% of the patients had a visit to the exclusive Pain clinic in our tertiary care center. This reiterates the importance of oral diagnosticians in the team of orofacial pain diagnosis and management. Studies done in India and elsewhere have not addressed the vital role of referral and a multidisciplinary team approach for the effective management of trigeminal neuralgia [8,23].

The imaging protocol commonly employed for the identification of morphological aberrations leading to trigeminal neuralgia is T1 weighted- magnetic resonance imaging (T1W). This section usually enables clear visualization and subsequent planning. However, in a small subset of patients, the axial sections may not clearly depict the nerve distortions (previous microvascular decompression, atrophy and prominent blood vessels). Fast imaging employing steady-state acquisition (FIESTA) MRI is the preferred modality of choice for imaging such

anomalies [27]. In this study, 68.9% of the participants underwent T1W MR imaging, whereas 60% of them underwent FIESTA sequencing. The significance of FIESTA coupled with MRI has shown promising results in the radiosurgical treatment planning in these patients [27,28]. The findings from this study reinforce the importance of employing the appropriate higher imaging modalities for diagnosis and management of this condition which is feasible in a tertiary care setup. The analysis of this parameter is not performed in other studies [5,12,16,20].

Medical management forms the first line of treatment for trigeminal neuralgia. In this study, pharmacotherapy was the sole treatment modality in 15.5% of the cases. 27.5% of them had a monotherapy regimen, while 53.4% were administered polytherapy. At the same time, findings by Singhota et al. reported the majority of individuals under a monotherapy regimen (60.5%) [8]. Carbamazepine was the most employed drug in both mono and polydrug regimens. The second most administered drug was Pregabalin (50-150 mg) for a maximum duration of seven months for effective pain control. However, other similar studies have shown carbamazepine and oxcarbazepine as the preferred drug of choice [8,14]. Drugs used for refractory cases are Oxcarbazepine, Meganeuron®, Nervigen Plus®, Amitriptyline, Gabaneuron, Gabapentin, Gabantip®, Maxmala®, Prelogic® and Amneurite®. These drugs are well-established in the pharmacological regimen for trigeminal neuralgia [29]. A total of 24.1% (n=14) of the participants were classified as non-responders to medical therapy and, hence, had to undergo surgical intervention.








The majority (84.4%) of the participants underwent surgical management (microvascular decompression, radiofrequency ablation and balloon compression). None of them had adverse outcomes at one-year follow-up visits. Radiofrequency ablation was the most frequently performed surgical technique in our tertiary care center. These findings are in accordance with the study by Singhota et al. [8]. The surgical interventions and outcomes have not been addressed in other studies performed in this cohort in higher dental settings [5,14,16].

The present study addressed the population attending a tertiary care center for trigeminal neuralgia, describing the clinical course, diagnosis, and treatment outcomes of these participants. The data gathered from this study represents a subset of people seeking pain management through a multidisciplinary panel of medical experts. The medical and surgical protocols adopted for these patients with outcomes were documented. The limitations of the study design bring in an inherent interobserver bias and this single-center experience may not be representative of the population under study. Dependence on the archives for data retrieval led to cases with overlapping features and incomplete data regarding the clinical and treatment outcomes owing to which few cases had to be excluded. This paves the way for future multicentric prospective studies on clinical characteristics, diagnosis and treatment outcomes.

■ Conclusion

Trigeminal neuralgia is a debilitating, painful orofacial condition that adds to a significant disease burden to these individuals. Though surgical interventions are definitive, pharmacotherapy forms the main pillar of therapy as most patients are reluctant for surgery. Since there is no single best treatment option that is established for this disorder, further clinical trials with promising pain management regimens need to be established.

■ Authors' Contributions

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■ Financial Support

None.

■ Conflict of Interest

The authors declare no conflicts of interest.

■ Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

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