

Original Article



Clinical insights and treatment challenges in trigeminal neuralgia from a retrospective cohort study

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Abstract

Background: Trigeminal neuralgia (TN) is a severely incapacitating condition marked by recurrent, intense facial pain. This disorder significantly diminishes patients' quality of life and is frequently misdiagnosed, owing to symptomatic similarities with other facial pain conditions. The present study aims to meticulously examine the demographic profiles, prevalence of concurrent systemic illnesses, specific pain characteristics, and therapeutic responses among TN patients, enhancing diagnostic precision and optimizing treatment strategies.

Methods: A retrospective study was conducted at the Chronic Orofacial Pain Clinic, Oral Diagnostic Department, Kerman, Iran. This study analyzed data collected from TN patients who were diagnosed between 2016 and 2022, adhering to the International Headache Society criteria. Patient demographics, systemic health conditions, pain characteristics, and treatment outcomes were thoroughly assessed. Statistical analysis was performed using SPSS 26, with Chi-square tests employed to determine statistical significance.

Results: This study involved a cohort of 81 patients, predominantly female (69.1%), with a mean age of 52 years (age range: 25 to 81 years). Systemic conditions were observed in 66.70% of patients ($P=0.003$), with hypertension being the most prevalent (22.20%, $P<0.001$). The maxillary branch (V2) was identified as the most frequently affected anatomical site (43.20%, $P<0.001$). The pain experienced by participants was overwhelmingly unilateral (97.50%, $P<0.001$). Patients characterized the pain using several descriptors, most commonly as electric shock-like (56.80%), piercing/stabbing (54.30%), and radiating (51.90%). Significant triggers for this pain encompassed touching the affected site (59.2%, $P=0.098$) and speaking (35.8%, $P=0.011$). Significant sleep disturbances were observed within the patient cohort. Specifically, 22.2% of patients reported difficulty initiating sleep ($P<0.001$), and 29.6% experienced problems with sleep maintenance ($P=0.004$). Regarding treatment outcomes for TN, 26.90% of patients achieved full recovery ($P<0.001$), while 55.70% demonstrated relative recovery.

Conclusion: The current research underscores the intricate symptoms and profound influence of TN on patients' daily lives, highlighting the critical need for specialized treatment approaches. The enhancement of diagnostic criteria and the development of personalized management plans are crucial for improving treatment efficacy and patients' overall quality of life. Additionally, further research is warranted to investigate a potential correlation between TN and myalgia, which could lead to novel therapeutic strategies.

Keywords: Trigeminal neuralgia, Facial pain, Pain management, Cranial nerve diseases

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Introduction

Trigeminal neuralgia (TN) is an uncommon disorder characterized by brief, intense paroxysms of pain, typically lasting from less than a second to two minutes. The reported prevalence of TN varies across populations, though the mean annual incidence is estimated to be 1.5–2 cases per 100,000 individuals.^{1–4} TN is linked to debilitating pain that profoundly impacts all facets of a patient's life and is often diagnosed with a delay of several months.^{5–7}

A definitive diagnosis of TN typically takes several months following symptom onset, despite the presence of characteristic clinical indicators. This delay is primarily attributable to challenges in diagnosis based on existing criteria. In clinical practice, TN pain is frequently misdiagnosed, as its presentation can be confounded with symptoms characteristic of other facial pain disorders, including migraine, sinusitis, and dental pain. This diagnostic ambiguity often results in patients undergoing



superfluous and ineffectual therapeutic interventions. It has been observed that in some cases, inappropriate dental interventions, including root canal therapy, restorations, and tooth extractions, fail to alleviate pain and may even intensify existing symptoms. Consequently, precise symptom identification and an accurate diagnosis of this condition within pain clinics are crucial for enhancing the quality of life for affected patients.⁸⁻¹²

Given the rarity and unclear origins of this condition, it would be beneficial to conduct thorough evaluations and an epidemiological study of affected individuals. Such research could significantly enhance our understanding of this disorder, leading to improved diagnosis and more effective treatment strategies. Prior descriptive and retrospective studies have investigated the neurological and psychological alterations in TN patients across various communities. These studies have yielded diverse statistical outcomes owing to differences in the studied populations. The current study aimed to assess the demographic features of TN patients and their treatment outcomes by analyzing existing patient medical records from the Chronic Orofacial Pain Clinic at the Oral Diagnostic Department, Kerman, Iran. This study also assessed co-occurring conditions like depression and anxiety, as well as sleep quality, in these patients. The findings of this research have implications for diagnosis, treatment planning, and clinical evaluation of individuals with TN.

Methods

This single-center, retrospective study utilized data from the Orofacial Pain Clinic at the Oral Diagnostic Department of Kerman Dental School, Kerman, Iran. The study population comprised all patients diagnosed with TN between 2016 and 2022. The study protocol received approval from the Ethics Committee of Kerman University of Medical Sciences (ethical code: IR.KMU.REC.1403.112).

The clinical diagnosis of TN was established according to the criteria set forth by the International Headache Society (IHAS)²:

1. Pain attacks that last from under a second to two minutes, affecting one or more branches of the fifth cranial nerve, and include items 2 and 3 on this list.
2. Pain that exhibits at least one of the following traits:
 - a) Intense, sharp, superficial, or stabbing
 - b) Triggered by specific points or stimulating factors.
3. Pain episodes that follow a consistent pattern in the same individual.
4. No neurological deficits are evident in the patient.
5. The pain cannot be linked to any other medical condition.

In the analyzed patient medical records, TN pain characteristics, the presence of diffuse body pain, and levels of anxiety and depression were assessed using the

Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI).¹³ Furthermore, each patient's apnea status was evaluated using the Epworth Sleepiness Scale (ESS).

Data were gathered using a checklist. Demographic characteristics of the patients, specifically age, gender, and occupation, were recorded. Data from patient medical records was coded and assessed anonymously to ensure confidentiality. Patients with incomplete data in their medical records were excluded from the study.

All patients enrolled in this study were contacted by phone to assess their treatment outcome.

Statistical analyses were conducted using SPSS software, version 26 (Cary, NC, USA). The Chi-square test was employed to compare the prevalence of various characteristics and the severity of pain across different patient cohorts.

Results

This descriptive-analytic retrospective study examined 81 TN patients, with a mean age (standard deviation [SD]) of 52 (4.3) years (range: 25-81 years). The patients were predominantly female (69.1%), while males constituted 30.9%. Education levels varied: 46.1% completed high school, 35.9% were illiterate, 9% had an elementary school education, and 9% possessed higher education.

Among TN patients, a substantial majority (66.70%) presented with co-occurring systemic conditions. This proportion was significantly higher than that observed in patients without these conditions (33.30%, $P=0.003$). Hypertension emerged as the most frequently identified systemic comorbidity (22.20%, $P<0.001$), followed by digestive disorders (17.30%) and diabetes (10.00%). Analysis of affected nerve branches revealed that the maxillary branch (V2) was most frequently involved (43.20%, $P<0.001$). As all patients included in the study were contacted for follow-up to evaluate their treatment outcomes, with an average follow-up period of 3 years and 7 months, it was found that 26.9% achieved full recovery from trigeminal neuralgia (TN) ($P<0.001$), while 55.7% experienced partial improvement, reflecting both the chronic nature of TN and the relative efficacy of current treatments (Table 1).

In a study examining pain characteristics in 81 TN patients, a statistically significant proportion reported unilateral pain (97.50%, $P<0.001$). This pain was more frequently observed on the right side (52.60%, $P=0.466$). Furthermore, the most prevalent pain descriptors included electric shock-like (56.80%, $P=0.221$), piercing/stabbing (54.30%, $P=0.439$), and radiating (51.90%, $P=0.732$) sensations. A substantial majority of patients also reported experiencing severe pain (64.00%, $P<0.001$). Beyond the most prevalent pain characteristics, the present study also revealed a statistically significant presence of less frequent pain descriptors, including burning (27.20%,

Table 1. Prevalence of systemic conditions and recovery outcomes in patients with trigeminal neuralgia: A detailed analysis of affected nerve branches

Variable	Category	Subcategory	N	%	P value
Systemic conditions	No systemic conditions		27	33.30%	0.003
	With systemic conditions		54	66.70%	
	Most prevalent systemic conditions	Hypertension	18	22.20%	<0.001
		Digestive disorders	14	17.30%	
		Diabetes	8	10.00%	
		Hyper/hypothyroidism	7	8.60%	
		Cardiac diseases	6	7.70%	
		Others	28	34.20%	
Nerve branches affected	V2 (maxillary)		35	43.20%	<0.001
	V3 (mandibular)		15	18.50%	
	V1 (ophthalmic)		14	17.10%	
	V2 & V3 combined		8	9.90%	
Recovery	Complete recovery		22	26.90%	<0.001
	Relative recovery		45	55.70%	
	No recovery		6	7.40%	
	Loss to follow-up		8	9.90%	

$P < 0.001$), throbbing (16.00%, $P < 0.001$), and compressive sensations (12.30%, $P < 0.001$). These findings highlight the multifaceted and severe impact of this condition on those afflicted (Table 2).

Among all TN patients, extraoral triggers were the most common precipitating factor for pain (50.8%, $P = 0.001$), followed by intraoral stimuli (32.3%, $P = 0.001$), and then combined stimuli (16.9%). Activities significantly associated with pain onset included touching the affected site (59.2%, $P = 0.098$) and speaking (35.8%, $P = 0.011$). Interestingly, chewing (50.6%, $P = 0.914$) did not show any statistically significant differences in triggering pain compared to not chewing. Several other factors were identified as highly significant triggers, such as taking food into the mouth (26.0%, $p < 0.001$), toothbrushing (13.6%, $P < 0.001$), exposure to cold air (14.8%, $P < 0.001$), consuming warm or cold foods (11.1%, $P < 0.001$), yawning (6.1%, $P < 0.001$), and resting the head on a pillow (5.9%, $P < 0.001$). These findings emphasize the intricate nature of pain management in TN, thereby underscoring the imperative for individualized therapeutic approaches that target specific pain triggers (Table 3).

A total of 39.7% of patients reported nocturnal awakenings attributable to pain, though this finding was not statistically significant ($P = 0.064$). Concomitant symptoms were frequently observed, with numbness (17.3%), tingling (14.8%), and prickling (11.1%) being the most frequent. Less prevalent, though still present, symptoms included dizziness and vertigo (both 7.4%). A notable finding was that 33.3% of patients did not report frequent symptoms like tearing and eye redness, even though these were observed in 12.3% and 11.1% of patients, respectively ($P < 0.001$). This diverse symptomatic presentation underscores the intricate and individualized

nature of TN, emphasizing the necessity of personalized diagnostic and management strategies (Table 4).

Significant sleep disturbances were frequently observed in TN patients, underscoring the extensive influence of this condition on their overall well-being. A considerable proportion of these patients reported difficulty initiating sleep (22.2%, $P < 0.001$) and maintaining sleep (29.6%, $P = 0.004$). Snoring was also reported by 25.9% of patients ($P = 0.001$). In addition, irregular sleep patterns and the use of sleeping pills represented less frequent but still notable concerns, affecting 6.2% ($P < 0.001$) and 8.6% ($P < 0.001$) of the population, respectively. Furthermore, 24.7% of patients experienced post-awakening fatigue ($P < 0.001$), indicating a substantial impairment in sleep quality among a considerable number of individuals afflicted with this condition. These results underscore the imperative for comprehensive management approaches that simultaneously address both pain and sleep disturbances in TN individuals (Table 5).

Discussion

This study analyzed the clinical characteristics of TN patients who presented to the Orofacial Clinic in the Oral Diagnostic Department of Kerman Dental School, Kerman, Iran, between 2016 and 2022. The mean age of these patients was 52 years (age range: 25 to 81 years). This finding aligns with previous research indicating that TN typically affects individuals aged 50 to 70 years.¹⁴ Furthermore, hypertension was identified as the most prevalent systemic comorbidity among these patients, affecting 22.2%. This finding aligns with Katusic et al's research that posited a potential link between hypertension and an elevated risk of TN.¹⁵ Consequently, effective blood pressure management combined with

Table 2. Detailed analysis of pain characteristics and severity among patients with trigeminal neuralgia

Variable	Category	Subcategory	N	%	P-value
Pain characteristics	Pain laterality	Unilateral	79	97.50%	<0.001
		Bilateral	2	2.50%	
	Side involvement	Right	43	52.60%	0.466
		Left	36	44.90%	
	Electric shock-like	Yes	46	56.80%	0.221
		No	35	43.20%	
	Piercing/stabbing	Yes	44	54.30%	0.439
		No	37	45.70%	
	Radiating	Yes	42	51.90%	0.732
		No	39	48.10%	
	Burning	Yes	22	27.20%	<0.001
		No	59	72.80%	
	Throbbing	Yes	13	16.00%	<0.001
		No	68	84.00%	
	Compressive	Yes	10	12.30%	<0.001
		No	71	87.70%	
	Heavy	Yes	7	8.60%	<0.001
		No	74	91.40%	
	Tender	Yes	5	6.20%	<0.001
		No	76	93.80%	
	Sharp	Yes	5	6.20%	<0.001
		No	76	93.80%	
	Gripping	Yes	5	6.20%	<0.001
		No	76	93.80%	
	Dull	Yes	4	4.90%	<0.001
		No	77	95.10%	
	Concussion	Yes	4	4.90%	<0.001
		No	77	95.10%	
	Appalling/frightening	Yes	4	4.90%	<0.001
		No	77	95.10%	
	Frustrating	Yes	1	1.20%	<0.001
		No	80	98.80%	
	Tearing	Yes	1	1.20%	<0.001
		No	80	98.80%	
	Pain severity	Severe	52	64.00%	<0.001
		Moderate	22	26.70%	
		Mild	8	9.30%	
	Pain between attacks	Yes	29	35.90%	0.011
		No	52	64.10%	

surgical decompression procedures could culminate in a reduction in pain for these individuals, given that surgical decompression has been shown to lower blood pressure.¹⁶

In alignment with the characteristics of this disorder and findings from previous research,^{10, 14, 17-20} a significant majority of patients (64%) reported experiencing severe pain. Of these, 52.6% indicated pain on the right side. This

Table 3. Pain triggers in trigeminal neuralgia: An analysis of stimulants and activities affecting patients

Variable	Category	Subcategory	N	%	P-value
Triggering factors	Stimulants	Intraoral	26	32.30%	0.001
		Extraoral	41	50.80%	
		Both	14	16.90%	
	Touching area	Yes	48	59.20%	0.098
		No	33	40.80%	
	Chewing	Yes	41	50.60%	0.914
		No	40	49.40%	
	Speaking	Yes	29	35.80%	0.011
		No	52	64.20%	
	Taking food into mouth	Yes	21	26.00%	<0.001
		No	60	74.00%	
	Toothbrushing	Yes	11	13.60%	<0.001
		No	70	86.40%	
	Cold air	Yes	12	14.80%	<0.001
		No	69	85.20%	
	Warm/cold foods	Yes	9	11.10%	<0.001
		No	72	88.90%	
	Yawning	Yes	5	6.10%	<0.001
		No	76	93.90%	
	Placing head on pillow	Yes	5	5.90%	<0.001
		No	76	94.10%	
	Trigger points in masticatory muscles	Yes	26	31.90%	0.001
		No	55	68.10%	

lateralization of pain could potentially be explained by the hypothesis that the foramen ovale and foramen rotundum are smaller on the right side.²¹

The mean duration of the condition before patient referral was 3.5 years, characterized by a mean of 12 daily attacks. This observation aligns with findings reported by Bohlouli et al.¹⁷. These painful episodes significantly impair patients' quality of life.²⁰ The most commonly identified triggers, both intraoral and extraoral, were touching the affected site (59.2%) and chewing (50.6%). In a study conducted by Maarbjerg et al the most frequently identified triggers were speaking, chewing, and touching.²⁰ This observation may be attributed to the engagement of orofacial and cervical muscles during these activities, which is associated with subtle movements within the cervical-cranial junction.²²

In this study, masticatory muscles were identified as the trigger point in 31.9% of patients, a finding that aligns with prior retrospective research. These consistent results suggest that jaw movements initiate TN in over half of all cases. Furthermore, a study by Katusic et al reported that 78% of TN instances were linked to pain following stimulation of trigger zones.¹⁵ In a four-year study, researchers observed that approximately 80% of TN cases exhibited pain initiation upon tactile stimulation of either

Table 4. Impacts and accompanying symptoms of pain in patients with trigeminal neuralgia

Variable	Category	Subcategory	N	%	P-value
Pain Impacts	Waking from sleep due to pain	Yes	32	39.70%	0.064
		No	49	60.30%	
	Accompanying symptoms	others	17	21.00%	<0.001
		Numbness	14	17.30%	
		Tingling	12	14.80%	
		Prickling	9	11.10%	
		Dizziness	6	7.40%	
		Vertigo	6	7.40%	
		Muscular weakness (myasthenia)	4	4.90%	
		Impaired hearing	3	3.70%	
		Blurred vision	2	2.50%	
		Loss of Equilibrium	2	2.50%	
	Most common symptoms	Difficulty eating food	2	2.50%	<0.001
		Nausea/vomiting	2	2.50%	
		Head heaviness	2	2.50%	
		Not reported symptoms	27	33.30%	
		Tearing	10	12.30%	
		Eye redness	9	11.10%	
		Runny nose	3	3.70%	
		Perspiration	2	2.50%	
		Hypersalivation	2	2.50%	
		Stuffed nose	2	2.50%	
		Others	26	32.10%	

Table 5. Prevalence and sleep disturbances in patients with trigeminal neuralgia

Variable	Category	Subcategory	N	%	P-value
Sleep issues	Difficulty falling asleep	Yes	18	22.20%	<0.001
		No	63	77.80%	
	Sleep maintenance problems	Yes	24	29.60%	0.004
		No	49	60.30%	
	Snoring	Yes	21	25.90%	0.001
		No	49	60.30%	
	Irregular sleep	Yes	5	6.20%	<0.001
		No	76	93.80%	
	Use of sleeping pills	Yes	7	8.60%	<0.001
		No	74	91.40%	
	Tiredness after waking up	Yes	20	24.70%	<0.001
		No	61	75.30%	

intraoral or extraoral regions. The critical question of whether this localized area functions as a trigger point or is a manifestation of central sensitization remains an unresolved logical inquiry. It has been acknowledged by researchers that trigger points are associated with TN. In numerous instances, these trigger points are situated

extra orally, specifically in the perioral region.^{7,21,23} The prevailing hypothesis suggests that these points arise from the convergence of impulses at the level of the second-order neurons (within the trigeminal ganglion) and third-order neurons (thalamus). At these convergence points, a single neuron is responsible for integrating sensory input from multiple distinct anatomical areas. Exposure to multiple high-intensity impulses, characteristic of conditions like TN, leads to the sensitization of second- and third-order neurons. This neuronal sensitization subsequently manifests as allodynia, where normally non-painful stimuli trigger pain attacks.^{8,9,24}

In the current research, 56.2% of patients exhibited oral habits. Given that oral habits are a known cause of masticatory muscle pain and a substantial proportion of TN patients present with these habits, a potential link between TN and myalgia is suggested. Furthermore, Gerwin proposed that in instances where TN co-occurs with orofacial muscle trigger points, TN may stimulate these trigger points, with their subsequent activation acting as a precipitant for neuralgia episodes.²²

In the current study, the V2 nerve branch was implicated most often (43.20%). This finding aligns with prior research, as Siqueira et al identified V2 and V3 as the most commonly affected branches.²⁵ Similarly, Ibrahim et al's study, which is consistent with the present findings, also reported V2 as the most frequently involved branch.¹⁴ The increased involvement of these two specific branches may be attributed to the somatotopic organization of sensory fibers within the trigeminal ganglion. This arrangement leads to a higher incidence of vascular compression affecting the superior-external or inferior regions of the nerve ganglion, relative to the nerve root.¹⁶

A significant discovery in this study concerns the trigger zone for pain. The majority of patients (87.3%) initially reported intraoral pain, which is most frequently localized in the upper left (39.2%) and upper right (35.3%) regions.

A significant finding of this study, aligning with prior research, highlights the severe nature of TN pain. Patients most characterized their pain as an electric shock (56.8%), piercing or stabbing (54.3%), and radiating (51.9%). TN pain is considered by some researchers to be the most excruciating pain experienced by humans. Historically, it has been referred to as "tic douloureux" or the "impact of a sword." While the precise cause of this severe, electric shock-like pain remains unclear, many researchers hypothesize that the intense severity and unique quality of TN pain are inherent to its etiology. One critical mechanism contributing to TN is the demyelination of central nervous system (CNS) nerve fibers, leading to ephaptic transmission of impulses. This phenomenon is analogous to an electrical short circuit between two wires, resulting from an abnormal interaction between two neurons. It remains unclear why the pain associated

with TN is often characterized as an electric shock at the sensory level.^{14,18} Additionally, Liao et al observed that trauma leads to demyelination through the activation of Schwann cells.¹⁹

Research investigating symptoms associated with TN is limited. However, a notable epidemiological study conducted in Germany identified tingling as the most frequently reported accompanying symptom.²⁶ This finding is consistent with observations from the current study. Local numbness emerged as another symptom in this study, occurring more frequently than paresthesia, characterized by prickling or tingling sensations. A primary etiological factor for these sensory disturbances is a disorder affecting the myelin sheath of neurons, which, as previously discussed, is also a significant contributor to the etiology of TN.²⁴

A significant majority of patients (67.8%) in this study had a history of receiving treatment. Carbamazepine was the most frequently utilized therapeutic agent (32.1%), recognized as the gold standard for management.²⁷ This finding aligns with other research indicating that carbamazepine is commonly the primary pharmaceutical intervention. The therapeutic mechanism of this drug is primarily attributed to its inhibitory effect on voltage-dependent sodium channels. This action leads to the stabilization of stimulated neuronal membranes, thereby preventing their re-excitation.^{9,10,14,18,20,28} Furthermore, a notable proportion of patients, specifically one-third, presented with active trigger points in their masticatory muscles, necessitating interventions focused on myofascial pain treatment.

In the current study, the majority of patients exhibited mild depressive symptoms, aligning with observations from Tolle et al's study. Conversely, other studies have indicated significantly elevated levels of anxiety and depression, up to three times higher than those found in control subjects. These studies further suggest that such heightened anxiety and depression are contributing factors to chronic pain experienced by these patients.^{10,29,30}

Approximately 22.2% of patients reported experiencing difficulty falling asleep, while 29.6% reported issues with sleep maintenance. These sleep disturbances could potentially be attributed to the irritation of trigger zones caused by contact with pillows or bed sheets. Furthermore, a study conducted by Di Stefano et al. revealed that 38% of their patients awoke from sleep due to pain, and similar findings regarding impaired sleep quality in TN patients were also reported by Baghaei, Lavaee, and Roosta.^{31,32}

In the current study, 48.1% of the participants experienced autonomic symptoms, with eye tearing being the most common. This finding aligns with Simms and Honey, who reported autonomic signs and symptoms in two-thirds of their patients, with eye tearing as the most frequent manifestation.^{32,33}

One additional observation from this study revealed

that 59.3% of patients experienced pain in other bodily regions. The most commonly reported locations were headaches (49.4%) and TMD (14.8%), a finding aligned with previous research.¹⁸

A significant strength of this study was the extended follow-up period, averaging three years and seven months. During this time, a considerable proportion of patients achieved positive outcomes: 26.9% experienced complete recovery, while 53.7% reported relative recovery. Conversely, 19.4% showed no recovery. These findings align with existing literature, suggesting a comparatively favorable treatment success rate when patients are monitored over time. Additionally, complete recovery was documented in more than one-fourth of the patients. These outcomes could serve as a benchmark for assessing treatment efficacy in subsequent follow-up assessments. Nevertheless, approximately one-fifth of patients remain unrecovered, suggesting a potential requirement for alternative therapeutic interventions. Consequently, additional research is warranted to assess the potential complications and benefits associated with patient follow-ups across diverse medical conditions.

Conclusion

Given the potential for sleep disorders and depression to intensify pain, addressing these conditions is recommended to enhance patients' quality of life. Furthermore, the prevalence of oral habits leading to muscular pain among a significant portion of these patients suggests a possible correlation between TN and myalgia. Should future research substantiate this relationship, it could significantly enhance our capacity to provide effective assistance and treatment to these patients, thereby alleviating their discomfort.

Authors' Contribution

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Competing Interests

No conflict of interest.

Data Availability Statement

All data related to the study are available within the text.

Ethical Approval

Ethical approval was obtained from Kerman University of Medical Sciences (ethical code: IR.KMU.REC.1403.112).

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