Title –

**Introduction**

Trigeminal neuralgia is a type of facial pain characterized by brief intermittent episodes of lancinating shock like sensation confined to distribution of one or more branches of trigeminal nerve with no neurological deficit; severely disabling the daily life activities and quality of life. The estimated in incidence is 0.1 to 0.3 % in general population. Classical trigeminal neuralgia is attributed to the compression of the trigeminal nerve at root entry zone by superior cerebellar artery. Other rare causes of neurovascular conflict include Anterior inferior cerebellar artery, superior petrosal vein, transverse pontine vein, dolichoectatic vertebral artery, persistent primitive trigeminal artery or combination of artery and vein. The chronic vascular conflict causes abutment, displacement, distortion, or atrophy of the nerve causing facial pain explained by ‘IGNITION HYPOTHESIS’.

Neurovascular conflict is thought to be important etiological factor for the development of trigeminal neuralgia due to the evidence of relief of symptoms with microvascular decompression. But it has been observed that not all patients with neurovascular conflict develop trigeminal neuralgia and the pathological alterations can be observed in patients with no neurovascular conflict suggesting other mechanisms like ischemia, inflammation, multiple sclerosis, hyperexcitability of nerve linked to mutation in calcium channel TRPM7 attributing to development of syndrome. Arachnoiditis is a common observation noted during microvascular decompression with negative prognostic ability. CSF biomarkers of the neuronal inflammation and cell death like Clec11a, LGMN, MFG-E8, ANGPTL-4 along with substance P, VIP are noted to be elevated in patients with trigeminal neuralgia coupled with decrease in beta-endorphins, serotonin, and dopamine. Although the biomarkers are noted to be elevated in the CSF globally, there is selective inflammation of trigeminal nerve with no evidence of coexisting pathology in adjacent cranial nerves. Hence this study aims to evaluate the inflammatory microenvironment of CP angle cistern selectively, in comparison to the cisternal CSF with other pathologies.

**Key words** – CSF biomarkers; Cistern; Trigeminal Neuralgia; Neuroinflammation; Neurovascular conflict.

**Abbreviations**: CSF – Cerebrospinal fluid; TRPM7 – Transient Receptor Potential cation channel subfamily M member 7; Clec11a – C type lectin domain containing 11A; LGMN – Legumain; MFGE8 – Milk Fat globule -EGF factor 8 protein; ANGPTL-4 Angiopoietin like 4; VIP- Vasoactive intestinal polypeptide

**Objectives**

Primary

To explore cisternal inflammatory microenvironment in TN in relation to a control group

Secondary

To establish basis of pathophysiology of trigeminal neuralgia.

**Materials and Methods**

**Study design**

In this prospective observation study, patient referred to Sree Chitra Tirunal institute for medical sciences and technology, who fulfilled the criteria for classical trigeminal neuralgia and are candidates for surgical treatment with microvascular decompression between 2023 to 2025 are eligible to study. The cisternal CSF of TN patients are analyzed in relation to age matched control group of patients undergoing surgery for cp angle lesions.

**CSF collection**

**Proximity extension analysis**

**Statistical analysis**

The categorical and ordinal variables are expressed as numbers (proportions) and medians (interquartile range) respectively. The demographic data between the two groups are compared with chi-square and or Mann – Whitney U test depending on the distribution of the data. Principal component analysis (PCA) is performed to investigate if there are global differences between trigeminal neuralgia and controls.

Differences in CSF biomarker between trigeminal neuralgia and controls are to be assessed by linear regression analysis for each biomarker, adjusted to age and sex. P Value <0.05 is considered statistically significant.

**Expected outcomes**

Identification of CSF biomarkers in cisternal space specific to trigeminal neuralgia; to better understand the pathophysiology.

To predict the outcome in negative explorations of microvascular decompressions for Trigeminal Neuralgia.