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Original Article

Endemic fluorosis and its impact on cases of cervico-dorsal ossification of the posterior longitudinal ligament: An overview

Soumya Ranjan Rana[1], Jwalit Kamlesh Mistry[1], Vikas Janu[1], Pavan Gabra[1], Raghavendra Kumar Sharma[1], Jaskaran Singh Gosal[1], Deepak Kumar Jha[1], Pragyna Paramita Das[2]

[1]Department of Neurosurgery, All India Institute of Medical Sciences, Jodhpur, Rajasthan, [2]Department of Community Medicine, Srirama Chandra Bhanja Medical College, Cuttack, Odisha, India.

ABSTRACT

Objectives: This study has been centered in the state of Rajasthan, to consolidate the significance of high fluoride consumption and endemicity in causing ossification of the posterior longitudinal ligament (OPLL) and tries to identify fluorosis as a predictor of operative as well as post-operative outcome.

Materials and Methods: A single-center retrospective cohort study. Case records of clinico-radiologically diagnosed patients of OPLL were retrospectively evaluated who were managed during a three-year duration (2019–2022). Patients were grouped into Group A: Endemic zone; ground water consumption, Group B: Endemic zone; purified water consumption and Group C: Patients from non-endemic region. Nurick grade and modified Japanese Orthopedic Association (mJOA) scores were used for clinical evaluation. Demographic, clinical, radiological, management, and urinary fluoride were evaluated preoperatively, at discharge, and after three months.

Results: Of the total operated 28 patients, 23 belonged to the fluorosis endemic zone whereas 5 were from a non-endemic zone. Group A showed deterioration in Nurick as well as mJOA scores $P < 0.05$ in the follow-up period. Group C patients showed the best improvement postoperatively followed by Group B. Fluorosis had an impact as an independent variable for clinical outcome, but it was not found to be clinically significant.

Conclusion: Early outcomes of OPLL with fluorosis appear to have a higher risk of deterioration after surgery in comparison to those who are from non-endemic zones or have no fluorosis.

Keywords: Cervical spine, Cervico-dorsal spine, Early post-operative outcome, Fluorosis, Ossified posterior longitudinal ligament

INTRODUCTION

Endemic fluorosis, a condition resulting from prolonged exposure to high levels of fluoride in water of daily consumption, has garnered significant attention due to its adverse effects on skeletal health.[1-3] For a very long time, it has been an issue that keeps getting worse throughout Asia and India. When fluoride levels in the body exceed 3–5 ppm,[1] it can cause a number of harmful effects, including dental fluorosis and diffuse ossification of long bones, ligaments, tendons, and intervertebral disc spaces.[2] One particular area of concern is its potential link to the ossification of the posterior longitudinal ligament (OPLL) in the spine. OPLL is a pathological process characterized by abnormal bone formation within the spinal ligaments, leading to spinal canal stenosis and neurological deficits. After Tsukimoto's meticulous autopsy description in 1960, OPLL, initially reported by Key in 1938, was finally acknowledged.[3] Understanding the intricate relationship between endemic fluorosis and OPLL is crucial for elucidating the mechanisms behind spinal pathologies and devising effective preventive measures and treatments. With excessive fluoride levels in all 33 of its districts' groundwater supplies, Rajasthan is the most severely afflicted state in India. According to studies, the groundwater in 22 out of 30 districts in Rajasthan has fluoride levels >10 ppm. Districts of Bhilwara, Nagaur, Churu, Jaipur, Udaipur, and Sri Ganganagar have been categorized as areas afflicted with alarmingly high levels >20.0 ppm groundwater fluoride levels.[4] Consumption of water with fluoride content >3.0–5.0 ppm is considered hazardous. Previously available literature has emphasized the correlation between high urinary fluoride levels and the

*Corresponding author: Soumya Ranjan Rana, Department of Neurosurgery, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India. sunny.soms@gmail.com

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incidence of OPLL.[1,5] The present study corroborates the same along with finding the implication of fluorosis and endemicity on post-operative outcomes of such patients.

This study has been centered in the state of Rajasthan (western part of India), to assess the significance of high fluoride consumption and endemicity in causing OPLL and its effects on post-operative outcome.

MATERIALS AND METHODS

The retrospective cohort study was conducted at a tertiary care public healthcare institute in the western part of India over a period of three years, between 2019 and 2022. It included diagnosed cases of cervical or cervico-dorsal OPLL. Patients were identified based on the demography and accordingly classified. Diagnoses were made as per their presentations as myelopathy, myeloradiculopathy or radiculopathy, and radiological evaluation.

All these patients underwent either anterior or posterior decompression, in the form of anterior cervical discectomy with or without corpectomy with fusion or laminectomy respectively. Decision of operative intervention was taken on the basis of, age, pre-operative kyphosis, K-line measurement, and levels of pathological segment involved.

All patients who were operated on for OPLL-related compressive myelopathy were included in the study while excluding all the cases deemed unfit for any surgical procedure. Patients were categorized into three groups, (A) Those from fluoride-endemic areas having natural sources of water consumption, (B) Those from fluoride-endemic areas having non-natural sources of water consumption (purified), and (C) Those from non-endemic regions. All patients were examined for urinary fluoride. They were evaluated as per the Nurick grading scale and Modified Japanese Orthopedics Association (mJOA) score at the time of admission and on discharge. They were re-evaluated clinico-radiologically after discharge at three months and two years irrespective of the treatment they received. The analysis of postoperative radiology, Nurick grading, and mJOA was then made with the pre-operative data.

Inclusion criteria

- Patients having non-traumatic etiology.
- Patients operated with anterior and posterior decompression.
- Patients having magnetic resonance imaging/computed tomography (CT) findings suggestive of OPLL.
- All patients with urinary fluoride s/o fluorosis status.

Exclusion criteria

- Traumatic spinal cord injury
- Patients with medical comorbidities who are unfit for surgery.

Radiological criteria

Pre-operative X-ray, CT, and magnetic resonance tomography were used as tools to confirm the diagnosis of OPLL. OPLL was categorized into continuous, segmental, mixed, and focused types based on the Japanese Ministry of Public Health and Welfare's recommended classification scheme.[6] Further classification into lordotic and kyphotic spine was done based on Cobb's angle (Angle >10° -Lordotic; Angle <5°-Kyphotic).[7]

Urinary fluoride (diagnosis of fluorosis)

All patients had undergone 24 h urinary fluoride level measurement, irrespective of the category they belong to. It was done based on the ion-selective method. Orion 4-star Plus pH/ISE benchtop meter equipment was used and any value >1.6 mg/L was taken as diagnostic of fluorosis.[8]

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences version 21. Continuous and categorical data were presented as mean ± standard deviation, frequencies, and percentages, respectively. Chi-square and Wilcoxon sign-rank tests were used for statistical analysis to evaluate the association between variables. The difference in difference regression analysis was carried out to find the effect of fluorosis on pre- and post-operative NURICK grade and mJOA score of OPLL patients. $P < 0.05$ was considered significant.

RESULTS

A total of 30 patients were included in our study, of which 2 patients were lost to follow-up on account of death due to natural causes. The demographic representation of the included patients is shown in Table 1. As per the categorization previously mentioned, group A had 17 patients, 6 were from group B, and 5 patients were in group C. Of all the patients, 18 had fluorosis based on the 24 h urinary fluoride estimation. Among the total number of patients with fluorosis, 15 were from group A and the rest from group B. The various sources of water consumption have been depicted in Table 1, showing the most widely used source to be tube wells, followed by canal water. Other sources of water included government supply water (not purified), purified water, rainwater harvesting, and wells (excavation or structure created for accessing groundwater).

As per the distribution of types of OPLL, 16 i.e. 57.1 % patients had continuous type OPLL of which 11 (68.8%) were from group A, 4 (25%) from group B, and 1 (6.2%) patient from group C. 6 patients had segmental OPLL and rest had mixed OPLL. This suggests that the majority of patients with fluorosis and continuous type of OPLL were from group A, although the statistical significance of the same could not be established.

The study population had the majority of patients, i.e., 85.7% with cervical level involvement followed by cervicodorsal and dorsal level, respectively, as shown in Table 2. 13 patients i.e. 76.5% of group A had cervical involvement.

Table 1: Demographic profile of the study population.

Demographic feature	Value
Age	
Average	54±9.43
Sex, %	
Male	85.7
Female	14.3
Education, (%)	
Primary	13 (46.4)
Graduate	2 (7.1)
None	13 (46.4)
Residence, (%)	
Rural	20 (71.4)
Urban	8 (28.6)
Source of water, %	
Canal	21.40
Supply	14.3
Tube-well	**46.40**
Rain-water	7.10
Purified	3.60
Well	7.10

Bold Value: Tube-well as a source of water comprised of highest percentage of consumption.

Irrespective of inclusion of fluorosis and solely analyzing on the basis of endemicity of patients demographically, we found that the improvement in Nurick and m JOA score postoperatively was least amongst group A and most in group C, which was statistically significant ($P < 0.05$) using Wilcoxon sign-ranked test [Table 2].

Analyzing the postoperative outcome of patients on the basis of improvement or deterioration in Nurick grade, we found that 11 patients (39.3%) showed improvement whereas 4 patients (11.3%) showed deterioration. All the deteriorated patients belonged to group A which was statistically significant.

On difference in difference (DID) analysis, fluorosis had an effect on both Nurick and m JOA score with time, although this was not found to be statistically significant, in view of a smaller number of the study population.

Radiologically, in our study, all the patients with continuous OPLL had a mottled appearance with a high density of bone in pre-operative CT scans, which is again indirect evidence of fluorosis. Of the 28 patients – 1 had pre-operative kyphotic deformity with the segmental type of OPLL, i.e., 3.57%. 25 patients had a loss of lordotic curvature (89.2%). There was no such case that had increased kyphosis in post-operative imaging. Two patients with continuous OPLL showed an increase in canal narrowing in post-operative imaging, done after a two-year follow-up. Both these patients were from Group A having high 24 h urinary fluoride levels. Clinically also, both these patients showed deterioration in Nurick as well as mJOA score. Corresponding images of the

Table 2: Duration of symptoms, radiological OPLL distribution, and change in clinical status after surgery.

	Group A (*n*=17)	Group B (*n*=6)	Group C (*n*=5)	*P*-value
Duration of symptoms				
Mean	30.53	8.50	19.00	0.148
SD	28.04	8.59	11.04	
Distribution of OPLL as per the respective vertebral level				**Total**
Involved spinal level distribution, (%)				
Cervical	13 (54.2)	6 (25.0)	5 (20.8)	24 (100)
CD	3 (100)	0	0	3 (100)
Dorsal	1 (100)	0	0	1 (100)
Total	17 (60.7)	6 (21.4)	5 (17.9)	28 (100)
Change in clinical status after surgery				
Pre-op mJOA median (IQR)	12 (6)	7.5 (4)	10 (7)	
Post-op mJOA median (IQR)	16 (4)	14 (5)	15 (7)	
P-value	0.001	0.42	0.78	
Pre-op Nurick median (IQR)	4 (2)	2.5 (3)	2 (4)	
Post-op Nurick median (IQR)	2 (2.5)	1 (1.3)	0 (2)	
P-value	<0.05	0.066	<0.05	

SD: Standard deviation, OPLL: Ossified posterior longitudinal ligament, CD: Cervico-dorsal, Pre-op: Pre-operative, Post-op: Post-operative, mJOA: Modified Japanese Orthopedic Association Score, IQR: Inter-quartile range pre-operative and post-operative periods have been shown in Figures 1-4.

Complications we faced were dural tear and intraoperative cerebrospinal fluid (CSF) leak in 3 patients, 2 patients having continuous OPLL, and 1 having focal OPLL, all these patients were from group A and had high 24 h fluoride level (>1.6 mg/L). However, this was not found to be statistically significant.

DISCUSSION

The incidence of OPLL in the Asiatic population has been reported to be between 2% and 3% in many previous studies.[7,9-11] It has been postulated that the incidence may be higher in fluorotic patients, but no study has defined a clear association between OPLL and fluorosis other than that of Reddy *et al.* in 2018, showing that out of the 30 patients with OPLL, 18 patients had fluorosis.[5] Previously, Reddy had published that OPLL is very commonly observed (37 of 80 people) in endemic areas.[1] In this study, the mean age was 54 which was similar to previously published studies suggesting an association of age with incidences of OPLL. With higher age people have more duration of exposure to fluoride-rich water intake, thereby increasing their chances of suffering from OPLL too. Jolly *et al.*,[12] reported that the advanced stage of fluoride intoxication usually resulted from continuous exposure of an individual to 20–80 mg fluoride ion daily over a period of 10–20 years, and such a heavy exposure is associated with at least 10 ppm levels in the water supply. Similar were the findings of Tsuyama, Kim *et al.*, (in the Korean population), and Wu *et al.*[11-14] (in the Taiwanese population). This also underlines the presence of fluorosis and OPLL in the group B population All 3 patients had ages more than 50 years. Belonging to endemic areas, although these patients had purified water as a source of consumption at the time of presentation, they had a history of depending on natural water sources for daily usage including drinking for more than 30 years. Only one of these 3 patients followed a similar course of post-operative outcome as the group A patients with fluorosis.

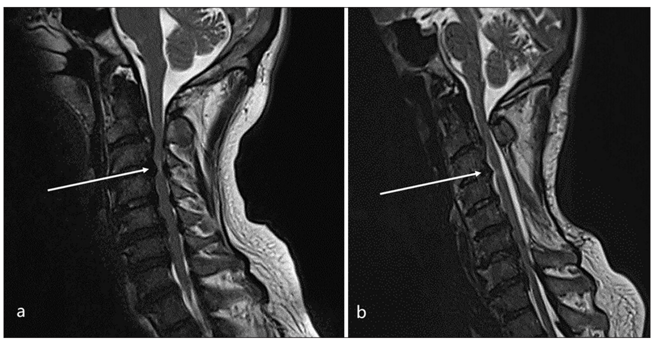

Figure 1: (a) Pre-operative T2W magnetic resonance imaging sagittal view of a Group A patient showing multiple levels of canal stenosis with continuous ossification of the posterior longitudinal ligament (OPLL). White arrow shows the level of maximum cervical canal stenosis and cord signal changes. (b) Post-operative T2W magnetic resonance imaging sagittal view of a Group A patient showing adequate canal decompression at the level of maximum stenosis (white arrow); there remains persistent canal narrowing at adjacent levels.

The majority of the patients (85.7 %) were male, which is similar to other studies, showing a higher incidence of OPLL among males. One patient had pre-operative kyphosis having segmental OPLL, while none of our patients showed a post-operative increase in kyphosis. The major source of fluoride-rich water intake in India is groundwater sources like deep bore wells and wells.[1,15] Similarly, in our study, tube-well constituted 46.40% of all the sources of water consumption followed by canal water. The endemicity and risk factors were then evaluated based on 24 h urine fluoride and radiology, which showed most of our patients with fluorosis had origin from fluoride endemic zones with a history of groundwater intake rich in fluoride. This correlation could not be statistically demonstrated in view of a smaller number of the study population in each demographic group.

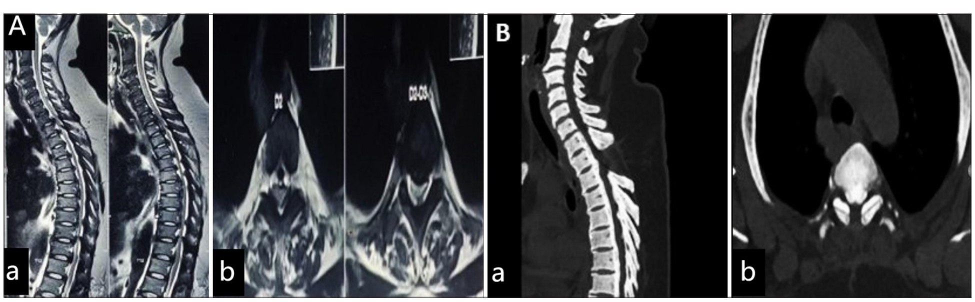

Figure 2: (A) Pre-operative T2W magnetic resonance imaging (a) sagittal and (b) axial view in a Group A patient showing a level of maximum canal stenosis at D2-3 level. (B) Post-operative non-contrast computed tomography spine (a) sagittal and (b) axial view in a Group A patient showing residual canal narrowing because of persistent ossification of the posterior longitudinal ligament and facetal hypertrophy.

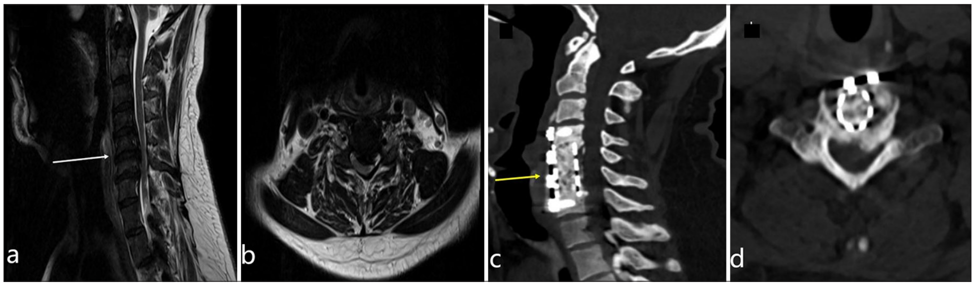

Figure 3: Pre-operative T2W magnetic resonance imaging cervical spine (a) sagittal and (b) axial view in a Group B patient with segmental ossification of the posterior longitudinal ligament (OPLL), maximum compression at C5-6 level (white arrow). Post-cervical corpectomy and cage fixation: Non-contrast computed tomography cervical spine (c) sagittal showing fusion in the region of cage placement (yellow arrow) and (d) axial view, in the same Group B patient with segmental OPLL.

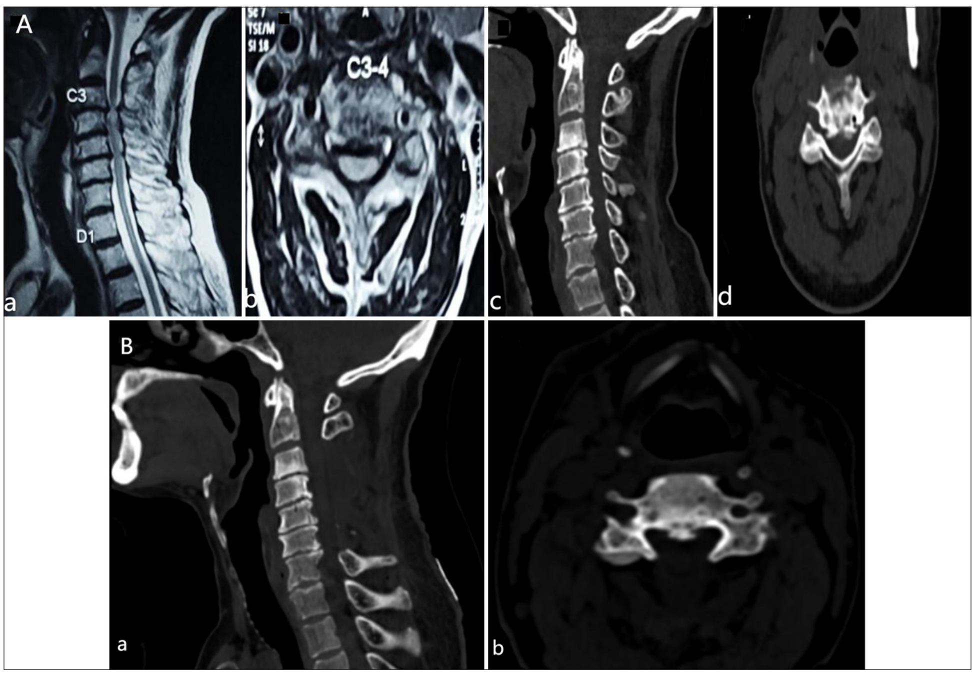

Figure 4: (A) Pre-operative T2W magnetic resonance imaging cervical spine (a) sagittal and (b) axial view in a Group C patient with segmental ossification of the posterior longitudinal ligament (OPLL), maximum compression at C3-4 level with (c and d) corresponding non-contrast computed tomography (NCCT) sagittal and axial view. (B) Post-cervical laminectomy and decompression: NCCT cervical spine (a) sagittal and (b) axial view, in the same Group C patient with segmental OPLL.

Intraoperatively, patients planned for anterior decompression were either operated with discectomy or corpectomy and fusion, whereas those planned for posterior decompression were operated with laminectomy. It was ensured to keep the laminectomy as extensive as possible to achieve adequate decompression and avoid a redo procedure. The cases who presented with circumferential OPLL were operated with a posterior decompression as mentioned in a study by Modi *et al.*[16] The following steps were given importance during posterior decompression:

1. Using a high-speed drill and bone scalpel – thereby avoiding using Kerrison and Rongeurs, which have been shown to cause added compression at the operative level.
2. Lateral guttering first – Using a high-speed drill, it was practiced as a routine to start with making a lateral gutter in laminae of planned levels. This method was adopted to prevent dural tears while decompressing the bone directly overlying the thecal sac.
3. Start decompression from the less affected side: As per the pre-operative assessment, the decompression was

started from the side of lesser compression, to remove bone from the area of lower risk of dural tear.

4. Any pulling of the segment of bone attached to the dura was avoided – for such areas following the thinning of bone using a drill, egg shelling of that part was done.

The comparative outcomes of these patients based on either endemicity or fluorosis have never been studied in detail. One solitary study published in the Journal of Orthopedics in 2019 by Modi *et al*.[16] has looked for pre-operative and post-operative outcomes in patients with OPLL without a definitive diagnosis of fluorosis. Our study has demonstrated the effect of fluorosis on patient outcomes and its relationship with endemicity. The patients were studied for their post-operative outcome after classifying them separately on the basis of endemicity and presence or absence of fluorosis as per urinary fluoride measurement. We found that fluorosis had a direct impact on the improvement in the patient's neurological status in follow-up examinations. There was also clear improvement in radiological improvement, with incidences of recurrence of canal narrowing in patients with fluorosis (although it was not found to be significant). The intraoperative incidents of CSF leak due to dural tear were also found in 2 patients with fluorosis who belonged to the endemic region, which again could not be corroborated statistically. These patients were managed with sterile re-suturing of the wound site along with administration of oral acetazolamide, although 1 patient required re-exploration and repair of the dural defect. None of these cases had post-operative signs of meningitis. The effect of fluorosis with time on Nurick grade and mJOA score was found to be positive but not statistically significant on DID analysis. As far as post-operative complications are concerned, 2 patients had abdominal distension and constipation operated for dorsal canal stenosis. Both the patients were from group B and had normal urinary fluoride levels. This finding was statistically not significant.

The limited sample size stands as a drawback in consolidating our findings. A prospective randomized controlled study with a larger sample size can prove instrumental in overcoming the limitations of our study. The characteristics (age, sex, number of patients, and surgical techniques) matched comparison, although preferred, it was not possible due to a smaller patient sample size. Including patients from endemic regions of Rajasthan enhances the credibility of our study as far as optimum evaluation of fluorosis and OPLL is concerned.

CONCLUSION

The patients with fluorosis having cervical/cervico-dorsal OPLL in the endemic zone are likely to have poorer outcomes, irrespective of the method of decompression. Being a resident of a fluoride-endemic region is an independent risk factor for poor outcomes irrespective of diagnostic confirmation for fluorosis in these cases. On account of the severity of canal stenosis, patients with fluorosis also stand at a relatively higher risk of intraoperative complications such as dural tears. Above all, Nurick grade and mJOA score proved to be reliable as a modality for uniformly comparing the outcomes in patients with cervical or cervico-dorsal canal stenosis with OPLL.

Authors' contributions: SRR and VJ: Concept. SRR, VJ, RS, JSG, and PD: Design. SRR: The definition of intellectual content. SRR and RS: Literature search. SRR, JM, VJ, PG, RKS, JSG, and DKJ: Clinical studies. SRR, JM, and PG: Experimental studies. SRR, VJ, and PG: Data acquisition. SRR, PG, and PPD: Data analysis. SRR, PG, and PPD: Statistical analysis. SRR, VJ, RKS, JSG, and DKJ: Manuscript preparation. VJ, RKS, JSG, and DKJ: Manuscript editing. VJ, RKS, JSG, and DKJ: Manuscript review.

Ethical approval: Institutional Review Board approval is not required, as this is a retrospective study.

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Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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