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Journal of Neurosciences in Rural Practice

Original Article

Incidence, predictors, and impact of acute post-operative pain after cranial neurosurgery: A prospective cohort study

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ABSTRACT

Objectives: Pain is common after craniotomy. Its incidence and predictors in developing nations are not adequately studied. We aimed to assess the incidence, predictors, and impact of acute post-operative pain after intracranial neurosurgeries.

Materials and Methods: This prospective observational study was conducted in adult patients undergoing intracranial neurosurgeries. After patient consent, ethics committee approval, and study registration, we assessed the incidence of post-operative pain using numerical rating scale (NRS) score. Predictors and impact of pain on patient outcomes were also evaluated.

Results: A total of 497 patients were recruited during 10-month study period. Significant (4–10 NRS score) post-operative pain at any time-point during the first 3 days after intracranial neurosurgery was reported by 65.5% (307/469) of patients. Incidence of significant pain during the 1st post-operative h, on the 1st, 2nd, and 3rd post-operative days was 20% (78/391), 50% (209/418), 38% (152/401), and 24% (86/360), respectively. Higher pre-operative NRS score and pain during the 1st h post-operatively, predicted the occurrence of pain during the first 3 days after surgery, $P = 0.003$ and $P < 0.001$, respectively. Pain was significantly associated with poor sleep quality on the first 2 post-operative nights ($P < 0.001$). Patient satisfaction score was higher in patients with post-operative pain, $P = 0.002$.

Conclusion: Every two in three patients undergoing elective intracranial neurosurgery report significant pain at some point during the first 3 post-operative days. Pre-operative pain and pain during 1st post-operative h predict the occurrence of significant post-operative pain.

Keywords: Acute post-operative pain, Neurosurgery, Incidence, Predictors, Outcomes

INTRODUCTION

Pain is a common consequence after intracranial neurosurgery. Post-operative pain occurs immediately after surgery and usually lasts till 7 days with maximum incidence and intensity during the first 24–48 h.[1,2]

The incidence of acute post-craniotomy pain is between 30% and 90% and depends on several perioperative factors.[3] Pre-operative elements include pre-existing pain, gender, age, anxiety, depression,[4] cultural background, and health-care environment,[5] while intraoperative factors include type of anesthesia,[6] choice of systemic and locoregional analgesia,[4] use of steroids,[7] and duration and location of surgery.[8] Younger age,[9] female gender,[10] infratentorial surgery,[11] and non-frontal surgery[12] are associated with pain after craniotomy. Post-operative pain can result in significant discomfort and distress to patients and lead to poor in-hospital experience, persistent pain, delayed ambulation and hospital discharge, additional costs, and delirium.[13]

Most previous studies on post-craniotomy pain are from the western population. Many factors which influence post-operative pain are different between developed and developing countries. Sociocultural and ethnic differences affect pain perception differently.[14] Analgesia practices in developing countries differ from developed nations with scalp blocks and non-opioid analgesia being more commonly adopted in the intraoperative period. Non-steroidal anti-

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Received: 13 March 2023 **Accepted:** 25 June 2023 **EPub Ahead of Print:** 14 July 2023 **Published:** 10 November 2023 **DOI:** 10.25259/JNRP_141_2023

inflammatory drugs (NSAIDs) and paracetamol (not opioids) are primary analgesics used for post-operative pain treatment in the developing world.[15] These differences might result in different pain incidences, apart from reducing opioid usage.[16] Finally, the burden of pain after intracranial surgery in the Indian subcontinent is not known. This study will fill the current knowledge gap and help in better pain management for our population.

The primary objective of our study was to assess the incidence of acute post-operative pain in adult patients undergoing intracranial neurosurgery. The secondary objectives were to identify potential predictors of pain and assess its impact on in-hospital clinical outcomes.

MATERIALS AND METHODS

This prospective observational study was conducted after obtaining ethics committee approval (NIMHANS/31st IEC (BS and NS DIV.)/2O21 dated 31-August-2021). We registered the study with Clinicaltrials.gov (https://clinicaltrials.gov/ct2/show/NCT05264012) and the Clinical Trial Registry of India (CTRI/2021/09/036525). The current manuscript deals with acute post-craniotomy pain which is part of the project on post-operative pain and neurosurgery.

Consecutive, eligible, and consenting adult patients (≥18 years) undergoing elective intracranial neurosurgeries were recruited. Children, emergency, spine, or surgery under local anesthesia, and patients who cannot/may not respond to our study questions were excluded from the study.

Data regarding age, gender, body mass index, religion, socioeconomic and educational status, domicile, comorbidities, alcohol consumption, pre-operative pain, pre-operative anxiety and depression assessed with hospital anxiety and depression scale, perception about surgery on five-point score, perioperative steroid use, American Society of Anesthesiologists (ASA) grade, surgical site, scalp block, intraoperative opioid dose, use of intraoperative nitrous-oxide or dexmedetomidine, other analgesics (paracetamol, NSAIDs, tramadol), minimum alveolar concentration of volatile anesthetic, durations of surgery and anesthesia were collected from patient's interview, anesthesia information management system and digital patient records.

The primary outcome was the incidence and severity of acute post-operative pain as assessed by numerical rating scale (NRS) score. Pain scores were captured immediately before surgery, in post-anesthesia care unit (PACU) at 15, 30, and 60 min after surgery and for initial 3 days (average and maximum pain during 24-h period). Details regarding post-operative analgesics were obtained. For the purpose of this study, we categorized NRS score 0–3 as no/mild (insignificant) pain and NRS score 4–10 as moderate-to-severe (significant) pain. The impact of significant pain on in-hospital clinical outcomes were evaluated. Following outcome measures were assessed: Duration of post-operative hospital stay, quality of sleep on the first 2 post-operative nights on 1–10 scale (10 being extremely good sleep), patient satisfaction on 1–10 scale (10 being highly satisfied), and day of ambulation after surgery.

With the average incidence of post-craniotomy pain reported as 60% in the literature,[3] and considering possible 5% margin of error, sample size of 368 was considered necessary to achieve 95% confidence level.[17] We expected maximum dropout of 15% for our primary outcome from non-extubation or abnormal consciousness after surgery impending pain assessment. Hence, we adjusted our sample size to 433 patients using formula n*1/(1–0.15).

Data collected was stored in a Microsoft Excel worksheet and analyses were performed using the Statistical Package for the Social Sciences v.28 statistical package. We evaluated the normality of data with Shapiro–Wilk test. Results are expressed as mean ± standard deviation, median and interquartile range or number and percentage (%). Differences between the two groups (significant vs. insignificant pain) were tested using *t*-test or Mann–Whitney test for continuous data and ordinal variables and Chi-square test for categorical variables. Logistic regression was performed to identify predictors of significant pain. $P < 0.05$ was considered as statistically significant.

RESULTS

A total of 497 patients participated in this study from September 2021 to June 2022. Data regarding primary pain outcome were available for 469 patients. No pain scores were available for 25 patients due to the inability to assess pain at any time-point (non-extubation, abnormal consciousness) during the first 3 post-operative days and surgery was abandoned in three patients [Figure 1].

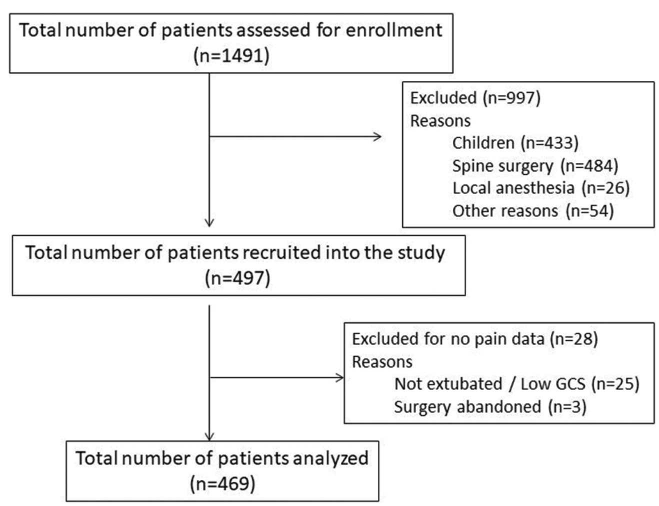

Figure 1: Diagram demonstrating flow of patients in our study.

Significant post-operative pain at any assessment time-point during first 72-h period after cranial neurosurgery was reported by 65.5% (307/469) patients. Incidence of significant pain during the first 1 h after surgery, on the 1st, 2nd, and 3rd post-operative days was 20% (78/391), 50% (209/418), 38% (152/401), and 24% (86/360), respectively. Patients available for pain assessment varied across 3 days due to poor neurological status, non-extubation, or early hospital discharge.

The median NRS scores were 0 (0–3) versus 5 (4.75–6) between insignificant and significant pain groups in the first 1 h. The median NRS scores were 1 (1–2) versus 3 (2–5) and 0 (0–3) versus 5 (5–7) for average and maximum NRS scores, respectively, on the 1st post-operative day between the two groups. The average and maximum median NRS scores were 0 (0–3) versus 4 (3–5) and 0 (0–3) versus 5 (5–6) for day 2, and 0 (0–3) versus 4 (3–5) and 3 (0–3) versus 5 (5–5) for day 3 after surgery, respectively. Most patients received fixed-dose regimen of diclofenac (n = 357), followed by paracetamol (n = 63), and both diclofenac and paracetamol (n = 9) in post-operative period. Figure 2 demonstrates median NRS scores across various time-points in patients with and without significant pain after brain surgery.

The risk factors with potential for association with acute significant post-operative pain after intracranial surgery on univariate analysis are shown in [Table 1]. No difference was noted between the groups for site and approach of surgery (frontal and parietal vs. temporal and occipital craniotomy vs. trans-nasal trans-sphenoidal surgery) or type of post-operative non-opioid analgesics (diclofenac, paracetamol or both). No patient received opioids during the first 3 post-operative days. On univariate analysis; pre-operative pain, anxiety, depression, non-usage of steroids, and pain during the first 1-h after surgery were associated with the occurrence of significant pain in initial 3 post-operative days ($P < 0.1$). These factors were analyzed using multivariate regression to identify predictors of acute significant pain. Only pre-operative pain and pain during initial 1 h after surgery remained predictors of significant post-operative pain [Table 2]. Pre-operative pain (headache) was reported by 19% of patients in the insignificant pain group and 34.4% of patients in the significant pain group. The effect of significant pain on clinical outcomes is informed in [Table 3]. There was no difference in the duration of hospital stay or day to ambulation, but patients with significant pain had lower scores for post-operative sleep. Satisfaction was, however, better in patients with significant pain.

DISCUSSION

Despite pain being a common problem after craniotomy, only few studies evaluated post-operative pain in detail. Most previous studies had small sample size, were retrospective in nature, published decades ago, were from developed world, and evaluated few risk factors. One study involving 37 patients

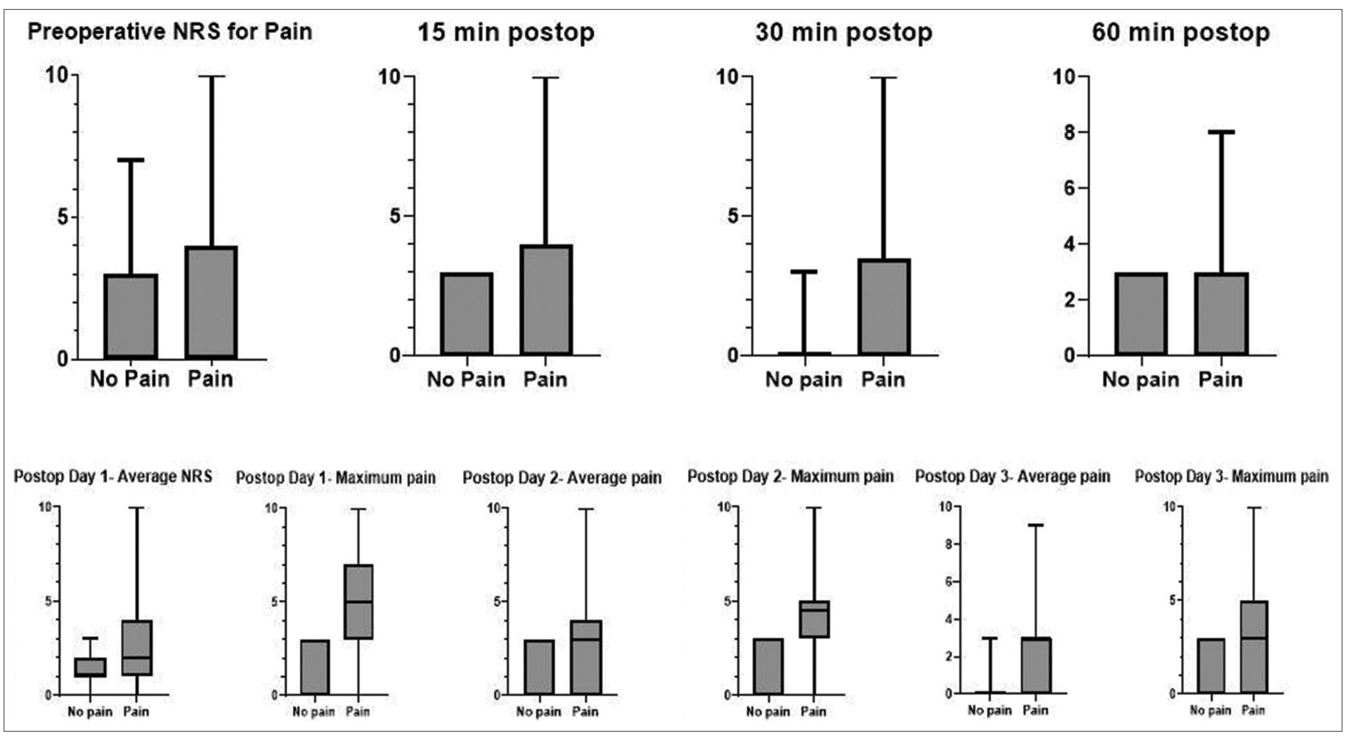

Figure 2: Box plot showing comparison of numerical rating scale scores (median and interquartile range) for pain at different assessment time-points.

Table 1: Comparison of predictors for significant acute post-operative pain after intracranial neurosurgery on univariate analysis.

Variables	Insignificant pain	Significant pain	*P*-value
Age (years)	42 (31–54)	42 (32–50)	0.770
Female gender	76 (47%)	151 (49%)	0.698
BMI (kg/m^2)	24.28 (22.04–26.47)	24.14 (22.04–26.53)	0.606
Hindu religion	148 (91%)	267 (87%)	0.148
Rural domicile	138 (85%)	264 (89%)	0.245
Illiterate status	32 (20%)	77 (25%)	0.250
Unemployed status	101 (63%)	188 (61%)	0.765
Below poverty line status	92 (57%)	196 (64%)	0.301
Chronic alcoholism history	8 (5%)	21 (7%)	0.546
ASA grade	2 (2–2)	2 (2–2)	0.160
Pre-operative NRS pain score	0 (0–3)	0 (0–4)	<0.001
Pre-operative anxiety score	0 (0–7)	3 (0–9)	<0.001
Pre-operative depression score	0 (0–6)	0 (0–7)	0.066
Positive perception score about surgery	5 (5–5)	5 (4–5)	0.278
Infratentorial craniotomy	32 (20%)	67 (22%)	0.636
Pre-operative scalp block	93 (58%)	194 (63%)	0.272
Intraoperative morphine dose (mg/kg/h)	0.05 (0.03–0.10)	0.06 (0.03–0.10)	0.318
Intraoperative nitrous-oxide use	24 (15%)	37 (12%)	0.391
Intraoperative dexmedetomidine use	33 (21%)	58 (19%)	0.712
Perioperative steroid use	51 (32%)	134 (44%)	0.013
Surgery duration (h)	3.45 (2.4–5)	3.48 (2.5–4.4)	0.614
Intraoperative MAC of anesthetic	0.9 (0.8–1.0)	0.9 (0.8–1.0)	0.290
Maximum NRS score during 1st h after surgery	0 (0–3)	0 (0–4)	<0.001

BMI: Body Mass Index, ASA: American Society of Anesthesiologists, NRS: Numerical rating scale, MAC: Minimum alveolar concentration. Values expressed as mean±standard deviation, median and interquartile range or number (percentage)

Table 2: Predictors of significant acute post-operative pain after brain surgery on multivariate analysis.

Variables	B	S.E.	Wald	df	Sig.	Exp (B)	95%CI	
							Lower	Upper
Maximum NRS pain score in 1st post-operative hour	0.223	0.052	18.28	1	<0.001	1.250	1.129	1.385
Pre-operative NRS pain score	0.153	0.051	9.05	1	0.003	1.165	1.055	1.287
Pre-operative anxiety score	0.027	0.026	1.11	1	0.292	1.028	0.977	1.081
Pre-operative depression score	−0.025	0.034	0.56	1	0.455	0.975	0.913	1.042
Perioperative steroid use	0.293	0.233	1.58	1	0.209	1.340	0.849	2.117

NRS: Numerical rating scale, S.E.: Standard error, df: Degrees of freedom, Sig.: Significant, CI: Confidence interval

Table 3: Comparison of clinically important outcomes between significant and insignificant pain groups after intracranial neurosurgery.

Variables	Overall insignificant pain	Overall significant pain	*P*-value
Duration of post-operative hospital stay (days)	6 (3.5–10)	5 (3–8)	0.193
Sleep quality on night-1 after surgery	6 (4–7)	5 (3–7)	<0.001
Sleep quality on night-2 after surgery	7 (5–8)	6 (5–7)	<0.001
Patient satisfaction score	5.5 (5–6)	6 (5–8)	0.002
	Day-wise no significant pain (%)	**Day-wise significant pain (%)**	***P*-value**
Day-1 ambulation	112 (54)	105 (51)	0.492
Day-2 ambulation	166 (67)	112 (74)	0.180
Day-3 ambulation	215 (81)	67 (78)	0.643

Values expressed as median and interquartile range or number (percentage)

noted 60% incidence of post-operative pain with two-thirds reporting it as moderate-to-severe and maximum pain during the first 48 h after brain surgery.[9] A 64% incidence of pain was observed among 58 patients[18] and 192 patients,[19] with both studies involving acoustic neuroma surgery. Another study in 256 patients noted 55% incidence of moderate-to-severe pain during the first 24 h after craniotomy.[6] Similarly, 69% and 48% incidences of significant pain (NRS ≥4) on the 1st and 2nd day, respectively, were observed after intracranial surgery in 187 patients.[2] Our incidence of 65% in larger sample is similar to that reported in earlier studies suggesting that despite recent advances, post-craniotomy pain remains a challenge in perioperative patient care. Previous studies reported the use of post-operative opioids for analgesia along with non-opioid drugs.[6,7,20] Pain incidence in our study was not different despite non-usage of post-operative opioids. This suggests that non-opioid analgesia fare similarly in providing pain relief in the presence of locoregional analgesia.

Pre-operative pain predisposes to post-craniotomy pain.[8,19] This finding was noted in our study too. Hence, it is important to assess and manage pre-operative pain effectively to reduce the development of post-operative pain.

Females[9] and younger patients[6,8,9] had higher incidence of pain after intracranial surgery. The median age of our study population was 42 years, and age did not predict post-operative pain. An earlier study too did not observe age contributing to post-operative pain.[21] We did not observe association between gender and pain which is similar to earlier studies.[6,8] One study noted ASA Grade III patients reporting more pain than ASA Grade I.[8] This was not seen in our study.

Pain is a personal experience; pain behavior and response are influenced by previous experiences, beliefs, expectations, sociocultural and psychological factors, and caregiver attitude.[5,14,22,23] Anxiety and depression can affect post-operative pain.[3,24] However, previous reports are conflicting in craniotomy patients.[9,25] We observed that pre-operative anxiety but not depression was associated with post-operative pain on univariate analysis. Unemployment and less education were associated with post-operative pain in orthopedic patients.[26] We did not observe association of religion, socioeconomic status, education, and domicile with post-operative pain.

Infratentorial[2,21] and non-frontal surgeries[12] are associated with post-operative pain. However, we did not observe effect of surgical site (supratentorial vs. infratentorial, and between supratentorial sites - frontal and parietal [less muscle retraction] vs. temporal and occipital [more muscle retraction] vs. trans-nasal trans-sphenoidal [minimally invasive]) on post-operative pain. This finding matches with an earlier study.[6]

Scalp block or incision site infiltration reduces analgesic requirement and post-operative pain.[11] Scalp block reduces the nociceptive response to skull pin insertion better than pin-site infiltration.[27] Another study demonstrated decreased intraoperative opioid consumption but similar post-operative pain with scalp block when compared to local infiltration.[28] We did not see the difference in post-operative pain between patients receiving and not receiving scalp block. This could be due to all patients receiving incision site local anesthetic infiltration in our study.

The use of non-opioid analgesics during surgery results in similar post-operative pain scores as compared to opioids.[29] Dexmedetomidine use reduces opioid requirements during craniotomy.[30] However, intraoperative opioid dose and dexmedetomidine use were similar in our patients with and without significant post-operative pain. Nitrous-oxide use did not influence post-operative pain in our study. We observed lower incidence of post-operative pain on univariate analysis with perioperative steroid use. This is in line with earlier reports[6,7] and reflects the mechanism of prostaglandin synthesis inhibition, anti-inflammatory effect, increased endorphins, and mood alteration contributing to beneficial effects on pain perception. We did not observe relationship between surgery duration and post-operative pain. This finding was similar to previous study.[6] Earlier studies were inconsistent about risk factors for pain after intracranial surgery. One study in 47 patients undergoing brain tumor surgery could not identify any predictors for post-operative pain.[31] Despite larger sample, assessing more factors, and including different intracranial procedures, we found only pre-operative pain and pain during the first post-operative hour as predictors of significant pain.

Post-operative pain results in longer hospital stays and delayed ambulation after hip fracture surgery.[32] However, we did not observe association between post-operative pain, hospital stay, and ambulation. Unlike in patients undergoing hip surgery where operative site pain directly affects ambulation, post-operative pain may not necessarily preclude ambulation after craniotomy. In the absence of delayed ambulation, hospital discharge time was also similar.

There are no previous studies evaluating sleep and pain after intracranial surgeries. Post-operative pain resulted in poor sleep among patients undergoing orthopedic[33] and arthroplasty surgeries.[34] Sleep quality score was significantly lower on the first two post-operative nights in patients with significant pain vis-à-vis insignificant pain in our study. This emphasizes the need for good pain relief irrespective of type of surgery to improve post-operative sleep.

A previous survey of post-operative pain and patient satisfaction across all types of surgeries from India documented high satisfaction rates despite >65% of patients experiencing pain.[35] Similar findings were reported earlier where despite significant pain, patients did not appear dissatisfied.[23] However, one study noted poor patient satisfaction with higher pain.[2] The median satisfaction scores in our study were comparable clinically (6 vs. 5.5) in patients with and without significant pain but were statistically different. Patient satisfaction assessment in this study was not specific to pain but included overall perioperative care. This suggests that satisfaction is more likely aligned with patient expectations and how they are met, than actual pain experienced after surgery.

The strength of this study is its large, prospective observational nature assessing several perioperative factors and evaluation of impact of pain on clinical outcomes. However, this study has certain limitations. Average and maximal pain was assessed for the first 3 post-operative days. More frequent assessments and for longer periods might provide more insight into pattern of pain distribution and experience. Our hospital does not have acute pain services and post-operative opioids are not routinely administered. Despite this, we observed similar incidence of post-operative pain to that reported in previous studies where post-operative opioids were used. Comparison of combined loco-regional and non-opioid analgesia versus opioids for post-operative pain requires further investigation.

CONCLUSION

Two-thirds of patients undergoing elective intracranial neurosurgery report significant pain at some point during the first 3 post-operative days. For effective post-operative pain management, it is important to address pre-operative pain and ensure pain relief continues in PACU. Post-operative pain affects sleep quality but not ambulation or hospital stay after craniotomy. Despite significant pain, patient satisfaction may be higher if expectations are met. Anesthesiologists, neurosurgeons, and nurses involved in perioperative care should be aware of the magnitude of post-operative pain and its influence on post-operative course and put more efforts in addressing modifiable risk factors to reduce acute post-operative pain.

Declaration of patient consent

Institutional Review Board (IRB) permission was obtained for the study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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How to cite this article: Sriganesh K, Kramer BW, Wadhwa A, Akash V, Bharadwaj S, Umamaheswara Rao G, *et al*. Incidence, predictors, and impact of acute post-operative pain after cranial neurosurgery: A prospective cohort study. J Neurosci Rural Pract 2023;14:637-43.