Diagnosis and management of pediatric neuropathic pain: Challenges and recent advances

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Abstract

Background: Neuropathic pain in pediatric populations remains underdiagnosed and undertreated due to diagnostic challenges and limited evidence-based interventions. **Objective:** To retrospectively analyze diagnostic approaches, management strategies, and clinical outcomes in pediatric patients with neuropathic pain over a 5-year period. **Methods:** Chart review of 247 pediatric patients (ages 2-18 years) diagnosed with neuropathic pain at tertiary care centers between 2018-2023. This retrospective multicenter study from four tertiary hospitals in the Kingdom of Saudi Arabia (KSA) analyzes diagnostic approaches, management strategies, and clinical outcomes over five years. Data collected included demographics, pain etiology, diagnostic methods, pharmacological and non-pharmacological interventions, and treatment outcomes. **Results:** Cancer-related neuropathy (28.3%) and complex regional pain syndrome (24.7%) were the most common etiologies. Diagnosis relied primarily on clinical assessment (91.5%), with limited use of quantitative sensory testing (12.6%). First-line pharmacotherapy included gabapentin (63.2%) and amitriptyline (41.7%). Multidisciplinary management achieved significant pain reduction (mean NRS decrease 3.8 points, $p<0.001$) compared to pharmacotherapy alone (1.9 points, $p=0.02$). **Conclusion:** Pediatric neuropathic pain management remains challenging with significant variability in diagnostic approaches and treatment protocols. Multidisciplinary care demonstrates superior outcomes.

Keywords: neuropathic pain, pediatric, retrospective study, pain management, diagnosis

1 Introduction

Neuropathic pain, which is a lesion or pathophysiological defect of the somatosensory nervous system, is a unique, compound, and complex pain phenomenon that can have burning, shotting, or electric shock-like symptoms, which are often paradoxical and include allodynia, hyperalgesia. This disorder presents a distinct diagnostic and therapeutic problem in pediatric groups that is not similar to the one in adults [1]. Pain expression, communication barrier, particularly in the younger children, and the similarity with other chronic pain conditions usually complicate the accurate identification and evaluation of the presence of neuropathic pain in children [2]. Although awareness and significant changes in pain management approaches during the last decade contributed to better pain management, it has not yet reached the optimal level, and the subsequent result is considerable patient suffering and functional impairment [3].

Pediatric neuropathic pain clinical landscape is also characterized by severe evidence-based practice gaps [4]. Diagnostic methods are predominantly based on clinical evaluation, and revised objective diagnostic techniques are uncommonly utilized, and treatments guidelines differ significantly among institutions because of a lack of high-quality, pediatric-specific pharmacological research as well as predetermined guidelines [5]. Such variability may result in the delay of diagnosis, the use of in optimal sequence of treatment, and a low clinical outcome. The complete knowledge of the existing real-life experience, the etiological spectrum, delays in diagnosis, patterns of management, and related outcomes are thus important to determine the areas to be improved and standardize the practice [6].

In order to fill these knowledge gaps of critical concern, this retrospective study will investigate the diagnostic patterns, management and clinical outcomes in pediatric patients with neuropathic pain who had been treated in various tertiary care centers during a period of 5 years [7]. This study will examine etiologies prevalent in a large cohort, determine the efficacy of treatments, using both pharmacological and

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non-pharmacological, and determine predictors of treatment success. This is the eventual aim of offering a modern perspective on the issues and facts involved in managing this condition, and thus advising the future nature of clinical practice and research in advancing care to this frail group of patients [8].

2 Methods

2.1 Study Design and Setting

Four tertiary pediatric hospitals took part in this multicenter retrospective chart review, which will be carried out between January 2018 and December 2023. All of the participating institutions received institutional review board approval:

1. King Saud University Medical City – Riyadh
2. King Faisal Specialist Hospital & Research Centre – Riyadh
3. King Abdullah Specialized Children's Hospital – Riyadh
4. University of Hail Medical Center – Hail

2.2 Study Population

2.2.1. Inclusion criteria [9].

1. Age 2-18 years at diagnosis.
2. Recorded diagnosis of neuropathic pain based on International Association to Study Pain (IASP) criteria.
3. Minimum 6-month follow-up.

2.2.2. Exclusion criteria [10].

1. Incomplete medical records.
2. Mixed pains without apparent neuropathic element.
3. Patients receiving palliative care having less than 3 months of survival.

2.3 Data Collection

2.3.1. EMRs were audited regarding.

1. Demographics (age, sex, comorbidities).
2. Pain etiology and duration.
3. Methods of diagnosis used.
4. Pain assessment tools used.
5. Pharmacological (drug, dose, duration) interventions.
6. Non-pharmacological interventions.
7. Outcomes of treatment at 3 months, 6 months and 12 months.
8. Adverse events.

2.4 Outcome measures

1. **Primary:** The change in the degree of pain (NRS 0-10 or age-specific scales).
2. **Secondary:** Medication adherence, adverse events, secondary functionality, healthcare use.

2.4.1. Statistical analysis. Descriptive statistics, t tests of changes in pain scores paired, chi square test of changes in categorical variables, and automatic regression of outcomes by multivariate. Significance set at $p<0.05$. Statistical analysis done in SPSS version 28.0 [11].

3 Results

3.1 Patient demographics

1. Total patients analyzed: 247.
2. Mean age: 12.4 years (SD 4.2).
3. Sex distribution: 58.3% female, 41.7% male.
4. Median follow-up: 18 months (range 6-60 months).

3.2 Pain etiology

Etiology	n (%)
Cancer-related (chemotherapy-induced, tumor compression)	70 (28.3%)
Complex regional pain syndrome (CRPS)	61 (24.7%)
Post-surgical neuropathy	38 (15.4%)
Peripheral nerve injury	32 (13.0%)
Metabolic/genetic disorders	21 (8.5%)
Spinal cord injury	15 (6.1%)
Other/idiopathic	10 (4.0%)

3.3 Diagnostic approaches

3.3.1. Methods of clinical assessment.

1. Comprehensive history and physical exam: 226 patients (91.5).
2. Pediatric pain scales: 183 patients (74.1%).
3. Pain drawings: 156 patients (63.2%).

3.3.2. Objective diagnostic tools.

1. Quantitative sensory testing (QST): 31 patients (12.6%).
2. Nerve conduction studies: 67 patients (27.1%).
3. Skin biopsy of small fiber neuropathy: 8 (3.2) patients.
4. Structural etiology/MRI/imaging: 124 patients (50.2%).

3.3.3. The pain evaluation mechanisms used.

1. Numeric Rating Scale (NRS, ages 8 +): 178 patients (72.1%).
2. Faces Pain Scale-Revised (ages 4-12): 94 (38.1) patients.
3. FLACC scale (2-7 years old or non-verbal): 23 patients (9.3%).
4. Neuropathic Pain Scale-Child (NPS-C): 42 patients (17.0%).

3.4 Time to diagnosis

3.4.1. All medians. 8.3 months (0.5-72 months) time between the onset and diagnosis of the symptoms.

3.4.2. Issues related to delayed diagnosis.

1. Age <8 years (OR 2.8, 95% CI 1.6-4.9).
2. Non-cancer etiology (OR 2.1, 95% CI 1.3-3.4).
3. First presentation to non-specialist (OR 3.4, 95% CI 2.0-5.8).

3.5 Pharmacological management

3.5.1. First-line agents.

Medication	n (%)	Mean dose (mg/kg/day)	Response rate
Gabapentin	156 (63.2%)	15-35	58.3%
Amitriptyline	103 (41.7%)	0.2-1.0	51.5%
Pregabalin	47 (19.0%)	3-8	61.7%
Duloxetine	28 (11.3%)	0.5-1.5	53.6%

Response defined as ≥30% pain reduction at 8 weeks.

3.5.2. Second-line/adjuvant therapies.

1. Topical lidocaine: 89 patients (36.0%).
2. Topical capsaicin: 23 patients (9.3%).
3. Tramadol: 34 patients (13.8%).
4. Low dosage ketamine infusions: 19 (7.7%) patients.
5. Cannabinoids: 7 patients (2.8%).

3.5.3. Polypharmacy.

1. Single agent: 102 patients (41.3%).
2. Two agents: 98 patients (39.7%).
3. Three or more: 47 (19%) patients.

3.6 Non-pharmacological interventions

Intervention	n (%)	Integrated with pharmacotherapy
Physical therapy	187 (75.7%)	180 (96.3%)
Cognitive-behavioral therapy	142 (57.5%)	138 (97.2%)
Occupational therapy	98 (39.7%)	95 (96.9%)
Transcutaneous electrical nerve stimulation (TENS)	67 (27.1%)	67 (100%)
Acupuncture	31 (12.6%)	29 (93.5%)
Mirror therapy (primarily CRPS)	28 (11.3%)	28 (100%)
Spinal cord stimulation	4 (1.6%)	4 (100%)

3.7 Treatment outcomes

3.7.1. Change in the intensity of pain at 6 months. The multidisciplinary approach (pharmacotherapy and at least 2 non-pharmacological interventions, n=164) was used.

1. Baseline mean NRS: 7.6 (SD 1.4).
2. 6-month mean NRS: 3.8 (SD 1.9).
3. Mean reduction: 3.8 points (95% CI 3.4-4.2, p<0.001).

3.7.2. Pharmacotherapy alone (n=83).

1. Baseline mean NRS: 7.4 (SD 1.5).
2. 6-month mean NRS: 5.5 (SD 2.1).
3. Mean reduction: 1.9 points (95% CI 1.4-2.4, p=0.02).

3.7.3. Improvement in functioning 6 months.

1. Multidisciplinary: 68.4% vs 43.4% pharmacotherapy alone, p<0.001.
2. Sporting/recreation: 54.3% vs 28.9%, p=0.001.
3. Improvement in sleep quality (2 points on PSQI): 71.3% vs 38.6%, p<0.001.

3.7.4. Response stratification.

1. Excellent response (reduction in the level of pain by more than 50%): 38.1%.
2. Moderate response (30-49% reduction): 31.2%.
3. Minimal response (<30% reduction): 30.7%.

3.8 Adverse events

3.8.1. Medication-related adverse events.

1. Sedation/drowsiness: 34.8%.
2. Weight gain: 17.8%.
3. Dizziness: 22.7%.
4. Gastrointestinal symptoms: 19.4%.
5. Mood changes: 8.9%.
6. Discontinuation due to adverse events: 21.5%.

3.8.2. Serious adverse events. None reported.

3.9 Predictors of treatment success

Multivariate logistic regression analysis identified independent predictors of good response (≥30% pain reduction):

Factor	Odds Ratio	95% CI	p-value
Multidisciplinary care	4.2	2.3-7.6	<0.001
Early diagnosis (<6 months from onset)	2.8	1.6-4.9	<0.001
Age ≥10 years	1.9	1.1-3.2	0.018
CRPS etiology	2.3	1.3-4.1	0.004
Psychological intervention	2.6	1.5-4.5	0.001
Medication adherence >80%	3.1	1.8-5.3	<0.001

3.10 Healthcare utilization

3.10.1. Pre-diagnosis (12 months prior).

1. Mean emergency department visits: 4.2 (SD 3.1).
2. Mean specialist consultations: 5.7 (SD 3.8).
3. Mean hospital admissions: 1.3 (SD 1.6).

3.10.2. Post-diagnosis (12 months after).

1. Mean emergency department visits: 1.4 (SD 1.8), $p<0.001$.
2. Mean specialist consultations: 3.1 (SD 2.4), $p<0.001$.
3. Mean hospital admissions: 0.4 (SD 0.8), $p<0.001$.

4 Discussion

This retrospective study of 247 children with neuropathic pain supports the diagnosis and management difficulties of the condition and defines the usefulness of the multidisciplinary approach.

4.1 Diagnostic challenges

The median difference to diagnosis of 8.3 months highlights consistent recognition challenges among pediatric neuropathic pain. Delayed diagnosis was especially late in younger children (<8 years), probably due to the weakness associated with verbal communication and the use of behavioral pain measurement. Low use of objective diagnostic methods (QST 12.6% and skin biopsy 3.2%), points to perceiving impediments such as no pediatric normative data, equipment, and issues with patient cooperation [12].

The overwhelming use of clinical assessment (91.5) is consistent with the realities of the present-day pain management in children but questions the accuracy and consistency of the diagnosis. Age-specific neuropathic potential pain screening tools are also still in need of development and validation.

4.2 Management patterns

Gabapentin was the most commonly prescribed agent as the first choice (63.2%), regardless of the absence of maximum high-quality evidence specific to children, as it had an acceptable safety profile and had clinical experience in children. The overall response rates (51.5-61.7) of all first-line agents were only modest, which underscores the refractory phenomenon of pediatric neuropathic pain and the necessity of using multimodal modalities [13].

The fact that multidisciplinary care reduces pain by a statistically significant margin (3.8 vs 1.9 with pharmacotherapy alone, $p<0.001$) is a significant discovery. Combined strategies on physical, psychological and functional domains led to clinically significant outcomes on several outcome measures. These results are compatible with international guideline requirements on full-scale pain management packages.

4.3 Special etiologic considerations

The biggest subgroup (28.3%) was cancer-related neuropathic pain which is a symptom of the chemotherapy neurotoxicity and the tumor effects. The patients with CRPS (24.7%) showed a comparatively better prognosis, especially when there was early progressive multidisciplinary care involving physical therapy and the psychological assistance. Neuropathy post-surgery (15.4) was often not identified, with the median delay of 11.2 months of diagnosis implying that this disease should be more closely monitored after surgery [6].

4.4 Effect of early intervention

A diagnosis within 6 months of the onset of the symptoms was connected in a positive manner with improved treatment outcomes (OR 2.8, $p<0.001$). The presented finding highlights the significance of neuropathic pain education among primary caregivers and the presence of systematic screening protocols amongst high-risk populations (oncology, post-surgical, metabolic disorders).

4.5 Psychological components

Combination of cognitive-behavioral therapy was related to better results (OR 2.6, $p=0.001$) and biopsychosocial character of pediatric chronic pain. It seems essential to address the issues of anxiety, depression, catastrophizing, and fear of pain to manage them in a comprehensive manner.

4.6 Medication adherence and adverse events

A medication adherence over 80% was a strong predictor of treatment success (OR 3.1, $p<0.001$), whereas the adverse events resulted in discontinuation of 21.5% of patients. Most problematic (34.8% and 17.8% respectively) were sedation and weight gain, especially with gabapentinoids and tricyclic antidepressants.

Close dose titration, education of patients/their families, and anticipatory adverse event control are crucial [8].

4.7 Healthcare resource impact

Drastic changes in emergency department visits (4.2 to 1.4, $p<0.001$) and hospitalizations (1.3 to 0.4, $p<0.001$) post-diagnosis and treatment initiation indicate important changes in the healthcare system other than patient symptom improvement. Early detection and proper treatment seem to be cost efficient even though multidisciplinary practices are resource based [13].

4.8 Study limitations

This retrospective study possesses some limitations such as the possible selection bias (tertiary care centers), missing documentation, absence of control groups and non-standard treatment regimes. Direct comparison is inhibited by the variability in pain assessment tools in relation to age groups and institutions. Only a subset of patients had long-term outcomes after 12 months. The future of such controlled trials is to provide evidence-based protocols of managing pediatric neuropathic pain.

4.9 Clinical implications

The major clinical practice implications are as follows:

1. Increasing the suspiciousness towards neuropathic pain among high-risk children.
2. Early specialist referral in case of the suspicion of neuropathic pain.
3. Multidisciplinary team intervention since diagnosis.
4. Personal treatment programs based on pharmacological and non-pharmacological interventions.
5. Frequent observation of adverse events and drug regulation.
6. Psychological assistance as standard element of care.

5 Conclusion

The retrospective study of 247 pediatric patients supports the idea that the diagnosis and management of neuropathic pain are still challenging, with there still being a lot of delays to the diagnosis and inconsistent methods of treatment. Multidisciplinary care is shown to have an obvious advantage over pharmacotaherapy alone, which produces clinically significant pain relief and functional improvement. The earliest diagnosis, interdisciplinary holistic intervention, and the fusion of psychological support become the key success factors.

There are still serious gaps in objective diagnostic studies, age-specific assessment tests, and evidence of pharmacological intervention specific to children. The current research priorities involve validation of diagnostic criteria, prospective trial studies of treatment regimens, optimal timing and sequence of intervention and longitudinal outcome studies.

Healthcare systems are advised to focus on creating easy access pediatric pain services that are able to operate multidisciplinary, improve training of primary care providers and create systematic screening procedures among the high-risk groups. It is only under such holistic strategies that results to children with neuropathic pain will have any significance.

References

[1] Anghelescu, Doralina L., and Jessica Michala Tesney. "Neuropathic pain in pediatric oncology: a clinical decision algorithm." Pediatric Drugs 21.2 (2019): 59-70.

[2] Jensen, Troels S., et al. "Painful and non-painful diabetic neuropathy, diagnostic challenges and implications for future management." Brain 144.6 (2021): 1632-1645.

[3] Andrejic, Nikola, et al. "Neuropathic pain management: A focused review of current treatments and novel data from main ongoing clinical trials." Expert Opinion on Investigational Drugs 34.4 (2025): 287-299.

[4] Hess, Courtney W., et al. "Application of PainDETECT in pediatric chronic pain: how well does it identify neuropathic pain and its characteristics?." Pain Reports 8.6 (2023): e1109.

[5] Einhorn, Lisa M., Jonathan Hudon, and Pablo Ingelmo. "The pharmacological treatment of neuropathic pain in children." Current Neuropharmacology 22.1 (2024): 38-52.

[6] Coluzzi, Flaminia, et al. "The Challenge of Managing Neuropathic Pain in Children and Adolescents with Cancer." Cancers 17.3 (2025): 460.

[7] Schindler, Emmanuelle AD, and Mark J. Burish. "Recent advances in the diagnosis and management of cluster headache." Bmj 376 (2022): e059577.

[8] Bielewicz, Joanna, et al. "Diagnosis and management of neuropathic pain in spine diseases." Journal of Clinical Medicine 12.4 (2023): 1380.

[9] de Leeuw, Thomas G., et al. "Diagnosis and treatment of chronic neuropathic and mixed pain in children and adolescents: results of a survey study amongst practitioners." Children 7.11 (2020): 208.

[10] Kumar, Chandan, et al. "Pediatric neuropathic pain: challenges and treatment modalities." Biochemical & Cellular Archives 24.2 (2024): 2029.

[11] Hange, Namrata, et al. "Managing chronic neuropathic pain: recent advances and new challenges." Neurology Research International 2022.1 (2022): 8336561.

[12] Rugnath, Renira, et al. "A literature review: the mechanisms and treatment of neuropathic pain—a brief discussion." Biomedicines 12.1 (2024): 204.

[13] van Velzen, Monique, Albert Dahan, and Marieke Niesters. "Neuropathic pain: challenges and opportunities." Frontiers in Pain Research 1 (2020): 1.