



Review

Chronic Pediatric Pain in Low and Middle Income Countries

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Abstract: Chronic pain is a serious health concern and potentially debilitating condition, leading to anxiety, depression, reduced productivity and functionality, and poor quality of life. This condition can be even more detrimental and incapacitating in the pediatric patient population. In low and middle income countries (LMICs), pain services are inadequate or unavailable, leaving most of the world's pediatric population with chronic pain untreated. Many of these children in LMICs are suffering without treatment, and often die in pain. Awareness and advocacy for this population must be prioritized. We reviewed the available literature on the chronic pediatric pain burden in LMICs, barriers to treatments, and current efforts to treat these patients.

Keywords: chronic pediatric pain 1; low income country 2; middle income country 3; low and middle income country 4; pediatric palliative care 5.

1. Introduction

Chronic pain is a serious health concern and potentially debilitating condition, leading to anxiety, depression, reduced productivity and functionality, and poor quality of life. This condition can be even more detrimental and incapacitating in the pediatric patient population. In high income countries [HICs], pediatric chronic pain is treated by specialists in pain clinics or by other physicians whose training has included management of pain, such as anesthesiologists and oncologists. Available services range from a variety of medications, to invasive procedures, to alternative medicine such as acupuncture. Children with terminal conditions often receive palliative treatment for the underlying condition in the form of surgery or medical treatment. In low and middle income countries [LMICs], many of these services are inadequate or unavailable, leaving most of the world's pediatric population with chronic pain untreated [1]. Many of these children in LMICs are suffering without treatment, and often die in pain. Awareness and advocacy for this population must be prioritized.

2. Review

- Low and middle income countries [LMICs]

LMICs are ranked by the World Bank using the Human Development Index [HDI], which averages achievements in three dimensions of human development: a long and healthy life, knowledge, and standard of living. In 2016, low income countries had an average annual gross national income [GNI] of \$2649 and middle income countries of \$6281. By comparison, high income countries' GNI was \$13844 and very high \$39605 [2]. Disparities between HICs and LMICs are not purely economical, but there are large inequalities with treatment of disease, including chronic pain.

- Chronic pain

Pain is described by the International Association for the Study of Pain [IASP] as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage [3].” Acute pain immediately follows an insult or injury. Chronic pain is a separate entity that affects an individual's well-being, is continuous, and recurs beyond the expected normal time of healing or lasts longer than 3 to 6 months. Pain is further divided into nociceptive pain, pain perceived through specific pain receptors on the surface of somatic tissues or viscera, or neuropathic pain, which is caused by damage to nerves. Pediatric neuropathic pain has been rarely studied [4].

Children cannot always communicate effectively, but “the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment [5].” The overall experience of pain is not only caused by noxious stimuli, but by cognitive, affective, and behavioral responses. These are affected by social and cultural context which we are just beginning to understand [4]. In addition to the physical and emotional distress children may experience while in pain, parental distress over pain management is significant and appropriate pain management leads to increased parental satisfaction [6].

Physical symptoms, psychological distress, and social consequences can severely decrease the quality of life of chronic pain patients. Pain can cause diminished mobility, loss of strength, decreased immune system function, inability to eat, concentrate, sleep, or interact with others [7]. Pain experienced very early in life may have effects on nociceptive perception for the rest of the patient's lifespan [8]. Children with chronic pain see effects on daily life, including school attendance, family interactions, and social relationships. A Pakistani study found children with dental pain had difficulty sleeping and playing [9]. Chronic pain sufferers are four times more likely to have anxiety or depression, and there is a high association with abuse and post-traumatic stress disorder [10]. Disability related to pain can have devastating economic consequences on families and countries that cannot afford to have members unable to work due to pain.

- Pain treatment is a human right

Pain treatment is considered an obligation under the right to health as a basic human right, as stated by the IASP and World Health Organization in 2004 [7]. In 2005, the Montreal Statement of Human Right to Essential Medicines stated all have a right to the WHO essential medicines, which includes opioids [11]. The IASP Global Day Against Pain in Children was held in 2005 and focused on pediatric pain. The United Nations Convention of Rights of the Child noted children are a particularly vulnerable part of the population and are therefore entitled to special consideration. In the Declaration of Montreal in 2010, the IASP declared that all people have a right for acknowledgement of their pain and to pain management without discrimination by trained professionals. Failure of government and institutions to provide systems for pain management and failure of health care providers to treat pain within their legal scope of practice was declared to be unethical and a breach of a patient's human rights [12]. Pain is increasingly accepted as requiring treatment, and under-treatment of pain is recognized as causing short- and long-term negative consequences [13]. Current failure of most governments to appropriately treat pediatric pain is not only a failure to meet an agreed-upon human right, but failure to address this vulnerable population.

- Lost Disability-Adjusted Life Years [DALYs]

DALYs [Disability-Adjusted Life Years] include years of life lost from premature death and years lived with disability [YLD] and is the most widely used measure of the global burden of disease. Chronic diseases caused 54% of DALYs and 78.6% of non-communicable diseases [NCDs] in 2010 [14]. Musculoskeletal disorders accounted for 21.3% of YLDs and 22.7% of mental disorders. Eight out of twelve top disabling NCDs were related to chronic pain: low back pain, neck pain, migraines, arthritis, other musculoskeletal disorder, depression, anxiety, and drug use disorder [14]. Low back pain was the leading cause of YLDs [15]. Chronic pain syndrome includes multiple somatic complaints with psychological components, such as somatoform disorder or fibromyalgia, and has a prevalence of one to four percent of the global population [16]. Patients with chronic pain have increased disability and decreased ability to participate in economic productivity, which can have a large and often devastating impact on families and communities in LMICs. Pediatric pain patients have high levels of pain-associated disability [8] [17]. Low back, neck pain, and migraines are leading causes of YLD in older children and adolescents [18]. Despite high disability attributed to migraines, headaches, and musculoskeletal disorder, they have been a low health care priority [18].

- Chronic pain burden in LMICs

The World Health Organization estimates that 5.5 billion people [83% of the world's population] have no or inadequate treatment for moderate to severe pain, including no access to controlled medicines [12]. Millions of cancer and HIV patients suffer from moderate to severe pain with no treatment, including 1 million end stage AIDS patients every year, 5.5 million terminally ill cancer patients, and 0.8 million trauma victims [19]. Prevalence of chronic pain varies with gender, age, occupational stress, socioeconomic status, population density, and education [16].

A meta-analysis of the prevalence of chronic pain without clear etiology in LMICs using 68 reports found the prevalence of unspecified chronic pain to be 34% amongst the general population and 62% in the elderly. Low back pain prevalence was as high as 52%, headaches 51%, and musculoskeletal pain 79% amongst workers. In the elderly population, 19% of the population had widespread pain. This study, however, found significant heterogeneity in the assessment of pain and therefore standardization of chronic pain definitions and measurements is warranted for future measurements and research for accurate prevalence assessments [20]. A survey of 17 countries found a chronic pain prevalence of 37.3% in developed countries and 41.1% in developing countries with higher prevalence in females and the elderly. Within the developing countries, there was wide variability from 28.4% prevalence in Lebanon to 58.2% in Ukraine, potentially showing cultural differences that warrant further studies [21].

In addition to the high prevalence of pain of 34% in LMICs, 1 in 10 people develop chronic pain every year worldwide [16]. In addition to inequalities between HICs and LMICs, even within LMICs there is inequality, with the poorest countries carrying the highest burden of chronic pain and decreased availability of treatment [22]. A survey of emergency rooms in central Africa found inadequate pain treatment [23].

- Chronic pediatric pain burden in LMICs

Chronic pain in children may be caused by chronic diseases [inflammatory bowel disease, sickle cell, rheumatologic disorders], trauma, life threatening diseases [cancer, HIV], or may be idiopathic such as headaches [4]. Pediatric chronic pain is complex, with nociceptive, affective, sociocultural, behavioral, and cognitive components, and therefore requires multimodal management [24]. A systematic review on the epidemiology of chronic pain in children and adolescents found the prevalence rates of pain to be 8-83% for headaches, 4-53% for abdominal pain, 14-24% for back pain, 4-40% for musculoskeletal pain, 4-49% for multiple pains, and 5-88% for other pains. Although the review included mostly high and very high income countries, it found that lower socioeconomic

status was associated with higher pain prevalence [25]. Similarly, a Brazilian study found higher dental pain in children with lower socioeconomic status and lower parental educational levels [26].

Children in LMICs with chronic pain are particularly vulnerable to pain and suffering due to inadequate availability of pain treatment, low personnel capacity with few pain specialists, poor training, cultural differences including language barriers that make it difficult to assess pain, and limited resources [27]. In Malawi, during a 15 month observation period, assessment and management of pediatric pain was not performed [28] and in another review, pain management was not available for pediatric palliative care patients [29]. Nurses in Morocco felt "powerless" because they could not alleviate the suffering of children in pain. Physicians and nurses in Morocco did not feel they had the resources or training to assess and treat pain [30].

While there is paucity of pediatric chronic pain prevalence studies in LMICs available, the Global Burden of Disease 2013 Study found that within the largest 50 countries, there was a 2% prevalence of pediatric low back and neck pain and 5.5 % migraines for the developing group [18]. At a cancer hospital in Jordan, 48% of pediatric patients had pain, 11% had "a lot" of pain, with only 22% receiving analgesics. Only one child was ordered continuous opioids, all other medications were ordered as needed, showcasing cultural differences from HICs [31]. In Malawi, 27% of children referred for palliative care complained of pain [32]. In Indian children, chronic daily headache has a prevalence of 6.3% [33] and 10% of school-aged children have chronic abdominal pain [34]. An Indian paper described a chronic pain incidence of 23% in children who presented with a history of abdominal pain [35]. Pelvic pain was present in 37% of adolescent girls in Indian schools and colleges [36]. In a survey of two schools in Sri Lanka, 35.2% of children reported abdominal pain [37]. Colombian children experienced recurrent abdominal pain in 10-15% of school-aged children and up to 75% of teenagers, with 21% with enough pain to affect daily living. Most cases [85-90%] had no structural basis for the pain and were deemed functional [38]. Five percent of patients in a Colombian study were found to have temporomandibular joint pain [39]. Amongst Nigerian teenagers, low back pain was present in 51.8% in their lifetime, 38.4% in the last 12 months, and 22.3% in the last month. About 41% reported recurrence of the pain and 13.1% had been absent from school due to the pain [40]. In a cohort of Congolese children, the reported prevalence of orofacial pain was 19-21% and nasal pain was 18-20% [41]. In Vietnam, 47.1% of children in kindergarten and preschool had mouth pain, likely secondary to untreated caries [42].

Infectious diseases are common in LMICs and can cause chronic pain. In Haiti, 37% pediatric patients with Tungiasis wounds reported pain. Chronic ear pain was prevalent in 44% of patients with HIV infection in Angola [43]. Twenty percent of pediatric patients with cerebral malaria in Mali reported headaches [44]. Also in Mali, a study looking for schistosomiasis prevalence also found 27.2% of participants had abdominal pain and 23.2% headaches [45]. A large study in Kenya described a 51.1% prevalence of abdominal pain in children with cryptosporidiosis [46]. Children with HIV/AIDS in Colombia had 19% prevalence of abdominal pain [47].

The adult literature shows wide heterogeneity with respect to pain assessment scales. Because children cannot all readily communicate, assessment many times must be done through observation of behavior and will vary with age, cognitive development, and sociocultural context [4]. Pain assessment scales are in regular use in HICs, but there are few studies addressing use of pain scales in LMICs. Chronic dental pain prevalence was reported as 25-27% in Nigeria. In this study, the Visual Analog Scale and the Full Cup Test were of similar sensitivity for pain assessments [48]. Indian children in East Delhi assessed their post dental extraction pain as 0.73-4.38/10 using both a visual analog scale and faces pain scale, with decreasing pain with older age. In that setting, the Wong-Baker faces pain rating scale was found to be the more sensitive pain assessment tool [49]. The six-grades faces pain scale was validated in South Africa for postoperative pain in children [50].

- Current efforts in LMICs

Specialist care is rare in LMICs and task shifting is common [51]. When available, specialized care tends to be clustered around cities and therefore is unavailable to rural communities [29]. Most pain is treated by general practitioners, and there are few pain specialists. In Mozambique, an African country with a population of over 25 million people, there are just 2 physicians and 2 nurses specifically trained in pain management. There are 4 pain clinics with 9 anesthesiologists, 1 pediatrician, and 5 rotating resident staff; 3 of these are outside of the capital. The clinic will see pediatric patients, but few children are brought for help, almost all oncology patients. One pain physician saw only 5 pediatric patients in a one year period. Similarly, in Kenya, anesthesiologists will provide pain care, with few pain specialists in the country. Zimbabwe has only one adult chronic pain specialist and one palliative care specialist, both in the capital city. In Uganda in 2000, new laws allowed specially trained nurses and clinical officers to prescribe morphine to ensure further availability of the drug to those who need it [52].

A systematic review of the availability of pediatric palliative care in LMICs found that 12 out of 19 countries had access to specialized training [29]. When present, ratios of palliative care service to population are significantly lower in LMICs than HICS. In Kenya, ratios are 1:4.28 million and Pakistan 1:158 million. By comparison, the ratio of services in the United Kingdom is 1:43,000 [53]. Despite most children requiring palliative care services spending a significant amount of time in the hospital, inpatient palliative care is growing at a slow pace. Developed programs are available in Malawi and South Africa. Furthermore, pediatric palliative care training opportunities are few. A multi-disciplinary certificate course for pediatric palliative care has scaled-up training in Tanzania, Uganda and South Africa. This has been in an effort to establish Beacon centers for palliative care for children. Courses have been conducted in Kenya, Zambia, Malawi, and Uganda [54]. In Zimbabwe, the government has formulated the National Strategy for Palliative Care 2020 to address policy, education, and medicine availability for palliative care [55].

- Drug shortages

The WHO Pain Relief Ladder recommendations for mild to severe pain include different levels of opioids, as well as adjunct pain medications that work in other pain receptor systems. The WHO calls strong opioids such as morphine “absolutely necessary,” and it is recommended as the drug of choice for moderate to severe pain in pediatric patients [4, 56]. The weak opioid codeine, morphine, and fentanyl patches are part of the WHO’s List of Essential Medicines [57]. The UN Economic and Social Council has called for adequate opioid availability for medical use and the International Narcotics Control Board is charged with ensuring availability as well as that drugs are not diverted to illicit markets [58]. Although the Single Convention on Narcotics Drugs declared narcotics essential in the treatment of pain four decades ago, most of the world population still does not have access to these medications [59]. There are huge inequalities with access to opioid analgesics, with six developed countries accounting for 79% and developing countries accounting for 6% of the global consumption of morphine [60].

LMICs suffer from drug supply chain problems, with rural hospitals often having minimal, inadequate, or no medications available. Further, there are many restrictions on opioids and essential medicines, making shortage of opioids even worse than other medications [12]. Due to restrictive regulations, healthcare workers are afraid of legal sanctions for legitimate narcotic use for patients. In some countries, overly restrictive regulations for licit drugs deprive the majority of the population access to opioids when needed for medical reasons [61]. Jordan has restrictive laws for ordering and dispensing opioids, leading to inadequate public access [31]. Where governments have accepted and enacted pain regulation, there is often failure to act on policies. Even when available, pain medication is expensive, with morphine costing over a month’s wage in some LMICs and

therefore not accessible to the destitute [7, 30, 31]. Use of alternative medicines and local healers is common in many LMICs. Complementary medicines were specifically used for pain in Nigeria [62].

A systematic review in LMICs found that only 7 out of 21 countries reported full access to essential analgesic drugs [29]. Two thirds of the world had little to no access to opioids for pain relief and only 7.5% of the population had adequate access in 2010 [63]. In Africa, 39% of palliative care providers did not have access to opioids [27]. In Malawi, a main hospital only had aspirin readily available for pain treatment, which should not be used in children [27].

The WHO recommends countries prioritize appropriate pain management through comprehensive policies and regulation addressing educational, supply, and cultural barriers. Multidisciplinary teams with both pharmacological and non-pharmacological approaches are recommended to ameliorate chronic pain. Needs assessments with current burden of pain as well as cost estimates must be done. Pain management ought to be undertaken on every level of the system, from community workers to tertiary care centers. Given that chronic pain has major economic impacts due to patients often being unable to work, countries will save resources by treating pain [4].

- Why insufficient efforts

There are many reasons for the inaccessibility of adequate pain treatment, the paucity of global pain data, and the why pain has not been a priority. Attitudes towards pain will depend on culture, religion, and political environment, and this will change how pain is perceived and accepted [7, 64]. For example, many providers still believe that opioids will cause harm to patients and society due to dependence, which is an unfounded belief for legitimate medical use [7], [27]. Nurses in central Africa believed opioids caused addiction, taking pain medicine was a sign of weakness, and that pain relief could interfere with healing [23]. Some cultures believe showing pain to be weakness, and children in pain may have been taught not to express their concerns [30]. In Malawi, children with significant acute pain such as open fractures were silent and Kenyan nurses valued stoicism [28]. Parents of pediatric chronic cancer pain patients in Jordan believed that pain was from God and therefore must not be treated. They also believed that children should be responsible for complaining of pain, not asked [31]. These beliefs and attitudes ultimately lead to under treatment of pediatric pain.

Global pain is a new field with limited literature and little research. Pain is subjective and currently there are no easy ways to measure physiologic changes due to pain. Even with the pain assessment methods and scales that exist, there is such high heterogeneity that it is difficult to compare them. The reason for this is both lack of standardization and necessity, as pain rating scales need to be adapted to local environments. There are large gaps in pediatric research available, where studies have focused on acute pain in children. The WHO has called on the scientific community to research pediatric chronic pain and treatments. In addition to medication research, they call for the development and validation of measurement tools for persistent pain [4]. Standardization of measurement tools and prevalence studies will allow measurements of the current problem of pediatric pain and guide future efforts to alleviate suffering in children.

Because chronic pain is a complex disorder that has physiological, psychological, and cultural components, management is best accomplished with multidisciplinary teams, which are limited in low-resource settings. In LMICs, there is poor training of healthcare workers with respect to pain. Even in situations where a pain specialist is available, support providers such as physical therapists, psychiatrists, psychologists, and social workers may not be available and treatment will be limited and therefore inadequate. Social support, complementary medicine [yoga, acupuncture], and rehabilitation programs may decrease pain and are helpful with or without needed specialists and medications. Pediatric pain and distress may be reduced with anxiety-reducing skills, education,

breathing, muscle relaxation, hypnosis, and imagery [8]. When developing programs to treat chronic pain, efforts to increase this support staff would be a low cost method to decrease the global burden of pain and its related disability.

- Efforts to improve access to chronic pain treatment

Current efforts to improve global capacity to appropriately treat chronic pain include framing pain as a human right, and appealing to ethical practice and good medicine. Regulatory efforts include negligence and criminal law, elder abuse law, and deregulation of practices that limit opioid availability [7, 58]. Guidelines have been created to help countries analyze their own regulatory systems, as well as workshops and seminars [56]. The last decade has seen an increase in scientific literature relating to pain and awareness efforts, starting with the “Global Day Against Pain” in 2004. Guidelines and standards have been created by the IASP, WHO, and other organizations. The WHO recently created guidelines specific to pediatrics, the WHO Guidelines on the pharmacological treatment of persisting pain in children with medical illnesses [4]. These describe classification of pain, medical evaluation, treatment, and legal information and are available in multiple languages. Efforts to improve the availability of pain medications are underway [7].

The IASP has created the Developing Countries Working Group to award grants for educational projects focused on the treatment of pain in LMICs [65]. The World Federation of Societies of Anaesthesiologists has anesthesia-based fellowships in 16 countries spanning 8 specialties. These target young physicians who want to return to their countries and preferably practice in a teaching hospital. Pain fellowships are located in India, Thailand, South Africa, Argentina, and Brazil, with potential to train 10 fellows per year. Fellowships are as short as 2 months and as long as 1 year, consistent with the American 1-year pain fellowship [66]. Other efforts by the WFSA include information and publications about pain management [67].

Given that most pain management in LMICs is administered by non-anesthetists, the Australia and New Zealand College of Anaesthetists has developed a 3-day training course called Essential Pain Management designed to teach local practitioners to recognize, assess, and treat pain using real-life scenarios. Participants are also given teaching skills to run their own workshops [68] [69]. In South Africa, a home-based pediatric palliative care training and support package was developed to equip community workers in rural areas to provide palliative care to very sick children [70]. A Malawi pediatric palliative care team works in both hospital and home settings, and pain control was described as adequate for pediatric oncology patients by authors at the Queen Elizabeth Central Hospital [71]. Other successful pediatric palliative care teams in LMICs have been described, and comprehensive palliative care was achieved in low resource settings, even with no broader systemic support [29, 53].

Other NGOs and organizations have programs where specific LMIC providers are brought to be trained abroad. For example, the head of the pain service of Mozambique was invited for a 2 year PhD in palliative care in Portugal as part of a United Nations Educational Scientific and Cultural Organization [UNESCO] initiative. ChildKind is another program that, although not specific to LMICs, hopes to decrease childhood pain worldwide. The program includes a package sent to interested institutions with guidelines, policies, protocols, audit strategies, and educational modules in order to create a pediatric pain management plan. ChildKind principles, including creating evidence-based written policy, assessing all children for pain, and having treatment plans apply to high and low resource settings and the program offers technical expertise to institutions that may help LMIC initiatives [13].

3. Conclusions

The last decade has seen increased efforts to decrease the suffering of chronic pain patients with increased awareness, advocacy, and creation of guidelines. There is a paucity of data of pain patients in LMICs, and almost no data on pediatric chronic pain. Billions of children are suffering with chronic pain every year, with personal and national economic impacts. Research into chronic pain in pediatric patients is desperately needed, including defining the prevalence of persistent pain, validation of assessment tools that are culturally appropriate and best methods of pain relief in different regions. Healthcare is often limited in LMICs, making the most effective manner to integrate palliative care being through existing services for children. Governments must be encouraged to address drug supply issues and legislation that prevents chronic pain patients from receiving needed medications. Practitioners must be trained in the recognition, assessment, and proper treatment of pain. Education is also warranted in settings where culture prevents proper pain diagnosis and treatment. The work to decrease chronic pediatric pain suffering is only beginning.

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