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CLINICAL RESEARCH

Pain assessment and management in the Moroccan haemophilia population: a prospective descriptive study

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A study in Casablanca is the first to look at the prevalence of pain among people with haemophilia in Morocco

Introduction: For people with haemophilia (PwH) who live in developing countries, haemophilia continues to be a condition with serious medical and social consequences. In Morocco, the efforts of patient associations and medical teams have led to the creation of a national programme for haemophilia care since the end of 2012, and the country is no longer solely reliant on World Federation of Hemophilia (WFH) donations for access to factor products. There is growing recognition of the impact of the pain experienced by PwH. To continue to improve treatment for PwH in Morocco, it is important to ensure that they are also able to manage haemophilia-related pain. **Aims:** This study aims to describe the prevalence, characteristics, and effects of pain experienced by PwH in Morocco for the first time, in order to increase understanding, and to support consideration of interventions and improvements in care. **Methods:** We conducted a prospective, descriptive survey of the experience of pain in PwH attending the Department of Clinical Hematology and Pediatric Oncology in Casablanca, using the

Multidimensional Hemophilia Pain Questionnaire (MHQP) approved by the WFH. All PwH with mild, moderate or severe haemophilia and over 18 years of age who presented to the department during the study period were included; consent was obtained. The data collection period lasted 6 months from October 2020 to April 2021. **Results:** 60 PwH completed the questionnaire (51 haemophilia A, 9 haemophilia B; 38 severe, 22 moderate). All respondents had experienced pain, 90% during the previous year and 75% during the last 3 months. 60% reported the occurrence of pain more than once a week. 65% reported that the right knee was the most painful site in the past year, followed by the right ankle (58%). The right knee was also the site of pain with the most negative impact in the past year. 58% responded that the evening was the time of most intense pain. The therapeutic strategies used against pain were pharmacological and non-pharmacological. 60% of respondents reported using analgesics and 50% reported using coagulation factor substitution for pain relief. Regarding non-pharmacological strategies, rest was reported by 40%, elevation of the painful site/change of position by 20%, and ice by 10%. The majority reported being satisfied or very satisfied with the current treatment of their pain by health professionals. **Conclusion:** This study shows that pain is still very present in PwH treated at our haemophilia centre, with a significant impact on different areas of life. There is a need for action to standardise treatment approaches and develop protocols for pain management in PwH.

Keywords: *Haemophilia, Pain management, Health-related quality of life*

Haemophilia is a congenital bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII) in haemophilia A or factor IX (FIX) in haemophilia B. The deficiency is the result of mutations in the respective clotting factor genes. People with haemophilia (PwH) often begin to feel pain at a young age. They may have acute pain secondary to bleeding episodes and/or persistent (chronic) pain due to years of haemarthrosis, often experiencing both, making their pain presentation unusual [1,2]. Life expectancy has increased dramatically in recent decades with the availability of more effective treatments and the use of factor replacement prophylaxis. This increase in life expectancy has been accompanied by multiple age-related comorbidities, including persistent pain [3]. There is growing recognition of the impact of the pain experienced by PwH [4] and a need to better consider pain management as part of haemophilia care [5,6]

For the 80% of PwH who live in developing countries, haemophilia continues to be a condition with serious medical and social consequences. Treatment with anti-haemophilic factor concentrates is often unavailable due to high cost and the absence of social coverage for most patients. This is the case in Morocco, where the number of PwH is estimated to be around 3,700, in the current absence of a national registry [7]. The Association Marocaine des Hémophiles reported 1,229 PwH in the most recently published World Federation of Hemophilia (WFH) Annual Global Survey [8]. PwH in Morocco receive treatment and care through two reference centres, in Rabat and Casablanca, and through regional treatment centres in other cities. The efforts of patient associations and medical teams have led to the creation of a national programme for haemophilia care since the end of 2012. Previously reliant solely on WFH donations for access to factor products, the Moroccan Ministry of Health now purchases factor for use in haemophilia treatment centres, although this continues to be supplemented by WFH aid. Treatment remains mostly limited to episodic on-demand therapy; 20% of haemophilia patients are treated with low-dose prophylaxis, at a dose of 50 IU/kg twice weekly for the majority of patients [9]. All PwH need to attend hospital to receive their treatment. To continue to improve treatment for PwH in Morocco, it is important to ensure that they are also able to manage haemophilia-related pain.

The foundation for optimal pain management and treatment is a complete and thorough assessment of the pain. Additionally, and particularly given the increased emphasis on patient-centred care, it is essential to consider the patients' viewpoints to determine the best treatment options [10]. This study aims to describe the prevalence, characteristics, and effects of pain experienced by PwH in Morocco for the first time, in order to increase understanding, to support consideration of interventions, and to highlight potentially important or problematic areas that might be improved in the Moroccan setting.

METHODS

We conducted a prospective, descriptive survey of the experience of pain in PwH attending the Department of Clinical Hematology and Pediatric Oncology in Casablanca using the Multidimensional Hemophilia Pain Questionnaire (MHPQ) approved by the WFH [11].

The MHPQ was developed within a biopsychosocial framework and following IMMPACT (Initiative on Methods, Measurement and Pain Assessment in Clinical Trials) recommendations for pain measures [12]. It consists of four initial items that accurately distinguish between acute and chronic pain, then nine dimensions focused on an in-depth evaluation of the characteristics of pain. Each dimension is examined independently, and the MHPQ does not generate a global pain score. The MHPQ is not currently available in Arabic and an Arabic translation was produced by a certified translator to enable its completion by our patients.

The questionnaire was given to PwH by a haematologist either during their visits to the haematology department or by sending the form by mail. All PwH with mild, moderate and severe haemophilia over the age of 18 years who presented to the haematology department during the study period, either for consultation or to receive treatment, including in the event of bleeding, were eligible for inclusion. Consent was obtained. The data collection period lasted 6 months from October 2020 to April 2021. Approval for the study was given by the Ethical Committee of the Faculty of Medicine at the Hassan II University of Casablanca.

RESULTS

Seventy PwH returned the survey. Ten were excluded due to missing data on pain measures, leaving 60 participants in the final sample from a total of 200 PwH registered at our haemophilia centre. Fifty-one had haemophilia A and 9 had haemophilia B; 32 had severe haemophilia and 22 had moderate haemophilia. Demographic data are provided in Table 1.

All participants had suffered pain, including 90% (54/60) in the previous year and 75% (45/60) in the last 3 months. Sixty percent (36/60) reported the occurrence of pain more than once in a week; 48% (29/60) said that the last manifestation of pain was a week ago. Nineteen percent (11/60) reported that pain was present every week with some days without pain.

Almost half of respondents reported that the right knee was the most painful site in the past year, followed by the left knee in one third of respondents (Figure 1). In the past year, the site of pain with the most negative impact in their life was the right knee in 46% (27/60), followed by the left knee (36%; 21/60), right ankle (26%; 16/60), and left ankle (17%; 10/60). The most common pain factors were bleeding (54%; 32/60) followed by physical exertion (38%; 22/60).

Figure 1. Distribution of most painful joints reported by study participants (N=60)

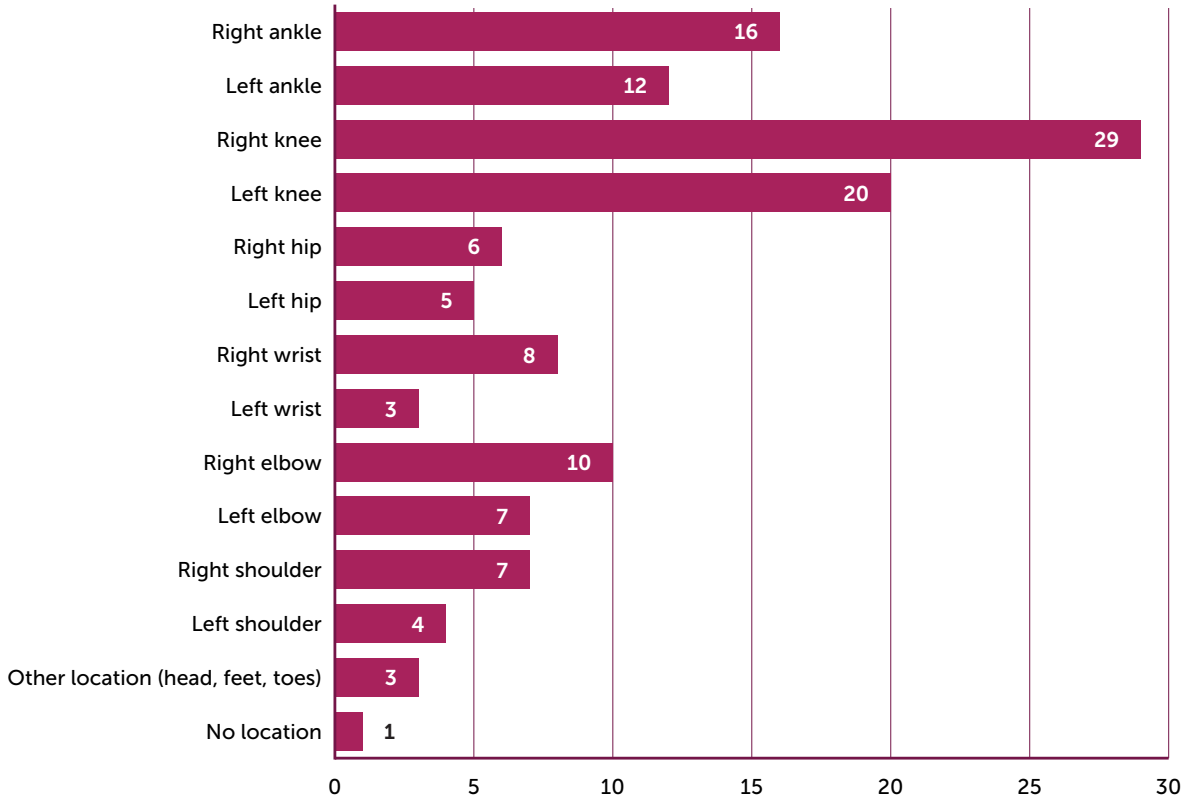

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Table 1. Participant demographics (N=60)

	NUMBER (N)
Gender	
Male	60 (100%)
Female	0
Age range	
18-30	42 (70%)
31-45	15 (25%)
45-59	2 (3.3%)
>60	1 (1.6%)
Haemophilia type	
Haemophilia A	51 (85%)
Haemophilia B	9 (15%)
Haemophilia severity*	
Severe	38 (63%)
Moderate	22 (37%)
Mild	0
Inhibitor status	
Inhibitors	6 (10%)
No inhibitors	54 (90%)
Treatment regimen	
Low dose prophylaxis	8 (13%)
On-demand treatment	52 (87%)

The majority of respondents reported moderate pain (27%; 16/60) or severe pain (36%) during bleeding episodes, with one quarter saying they experienced the worst possible pain. Physical efforts caused severe pain for 46% (28/60) of respondents, with 19% (11/60) experiencing the worst possible pain. Walking up and down stairs resulted in moderate or severe pain for 60% of respondents. Resting or staying still provided relief for 29% (17/60) of respondents, but one quarter reported experiencing severe pain during rest. False movements led to severe pain or the worst possible pain for over half of respondents. Detailed results can be found in Table 2.

Over half of respondents (58%; 35/60) said that evening was the time when their pain was most intense. The impact of pain on quality of life was evaluated using a scale from 0 to 10. Over half (54%; 32/60) had a significant or total impact of pain with a score >7 on general activity, 46% on mood, 50% (30/60) on walking ability, 42% (25/60) on daily activity, 31% (18/60) on social life, 29% (17/60) on sleep, 42% (25/60) on enjoyment of life.

Therapeutic strategies used against pain were pharmacological and non-pharmacological. Sixty percent of respondents (36/60) reported using analgesics and 50% (30/60) reported using coagulation factor substitution for pain relief. For non-pharmacological strategies, rest was reported by 40%, (24/60), elevation of the painful site/change of position by 20% (12/60) and ice by 10% (6/60). No respondents reported using compression (see Table 3).

The majority of respondents reported being satisfied (63%; 39/60) or very satisfied (19%; 11/60) with the current treatment of their pain by health professionals (Figure 2).

DISCUSSION

The results of this study offer, for the first time, insights into pain among PwH in Morocco. Despite the majority of respondents reporting that they were satisfied with how their pain was being managed, all respondents still experience pain, many of them on a frequent or persistent basis, with 90% having experienced pain relating to their haemophilia during the previous year. These findings are consistent with the results reported in a studies of pain among PwH in Portugal, where the incidence was 77% [13], and Germany, where 86% of PwH surveyed reported regularly experiencing haemophilia-related pain [14].

More than 80% of all bleeding in haemophilia involves joints, with the knee, ankle, elbow, and wrist the most often affected [14]. Consequently, the most prevalent sites of both acute and chronic pain are

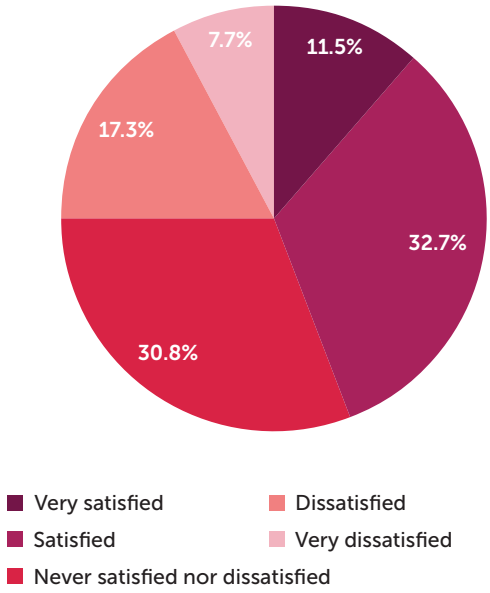
Table 2. Reported pain intensity in different situations (N=60)

	NO PAIN	MILD PAIN	MODERATE PAIN	SEVERE PAIN	WORST PAIN POSSIBLE
During bleeding episodes	4%	7%	27%	37%	25%
During physical efforts	6%	14%	15%	46%	19%
While walking up and down stairs	17%	15%	29%	31%	8%
After resting or staying still	29%	19%	21%	25%	6%
During rest	35%	26%	17%	15%	7%
After false movements	6%	21%	17%	31%	25%

Table 3. Therapeutic strategies used, with reported response rate (N=60)

TREATMENT STRATEGY	% OF RESPONDENTS (N)
Pain medication (analgesics, creams)	60% (36)
Rest	40% (24)
Elevation/change of position	20% (12)
Ice	10% (6)
Coagulation factor replacement	50% (30)
Prayer	6 (10%)

Figure 2. Participant satisfaction with management of their pain by healthcare professionals (%)



these joints, as a result of haemarthrosis and resulting haemarthropathy. Studies in the UK and Germany report the most common joint affected in adult PwH as being the ankle [15,16]. In our study, the knee was reported as the most painful joint. Studies in other countries where access to haemophilia treatment, and particularly prophylaxis, is limited also show the knee joint as being most affected by haemarthrosis [17,18]. It has been suggested that prophylaxis not only helps to reduce joint bleeds but, in doing so, helps PwH to engage in more physical activity [15]. In turn, this can result in more impact and strain on the ankle and make bleeding into this joint more likely [15].

Our study indicates that pain is not currently well treated Moroccan haemophilia population, suggesting that it is under-recognised and undervalued. Undervaluing haemophilia-related pain can result in inadequate use of available pain management techniques [19]. Uncertainty around therapeutic options due to coagulation issues may also result in ineffective or inappropriate pain management. Half of the participants in our study reported that their pain was treated effectively with factor replacement therapy. This was one of the most widely used 'pain management' techniques and also the technique that reportedly brought the most relief. In the case of haemarthrosis, use of factor replacement is key to stop the bleeding episode that is causing pain. However, it can be difficult for PwH to make a distinction between acute pain caused by a bleed and persistent pain caused by arthropathy [20]. Pain must be constant and/or intermittent, lasting more than three months, and happening more than once a week in order to be classified as chronic [21]. Where home treatment is available, many PwH treat pain with factor automatically as they have always been told that pain can mean a bleed and if they are in doubt they should treat it as such [22]. All PwH in Morocco can receive on-demand factor replacement treatment following haemarthrosis to stop bleeding, but this can only be accessed via a hospital treatment centre. When PwH come to the hospital for factor treatment to manage a bleeding episode, bleeds are typically confirmed by a combination of clinical evaluation, medical history assessment, and joint imaging (X-rays, ultrasounds), so this should not be an issue among our patients.

Acute pain management should enable PwH to continue with their daily activities and prevent the onset of chronic pain. Stromer et al. recommend that acute pain management should start when a threshold on the Numeric Rating Scale (NRS) of NRS >3 (at rest) | NPRS >4 (in motion) is reached, and that pharmacological intervention options should adhere to the concept of mechanism-based medication [23]. There are no evidence-based guidelines or protocols that establish a stepped approach to pain management in haemophilia, but early phases of pain management include use of over-the-counter analgesics. The WFH advises against the use of NSAIDs by PwH during bleeding episodes although celecoxib may be used in certain situations and has a lower risk of gastrointestinal complications [24,25]. Some studies have indicated a reluctance among PwH to use analgesics, often despite them being effective, due to side effects or perceived risk of addiction [26,27]. Sixty percent of participants in our study reported using analgesics to treat their pain, which could indicate a reliance on medication over other pain management strategies.

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Our study suggests that the RICE approach (Rest, Ice, Compression, Elevation) is underutilised as a pain control strategy. Only 10% of participants said they used ice; rest and elevation were used individually more frequently. However, no participants used compression and our results suggest little combining of the techniques that make up RICE. Non-pharmacological therapy for pain management in PwH has been the mainstay of conservative treatment [28]. RICE continues to be recommended by the WFH to relieve pain from haemarthrosis, particularly in the absence of access to clotting factor treatment or haemostatic agents [3], and a combined approach using pharmacological and non-pharmacological strategies is recommended as optimal for pain management in PwH [3,29]. Although some participants in our study use non-pharmacological interventions to help manage their pain, there is a need for patient education to support the use of techniques such as RICE.

In terms of other interventions to support better pain management among the PwH treated at our hospital, physical medicine and rehabilitation is a consideration. These play a significant part in multimodal pain management, supplementing treatments for acute pain and preventing and treating chronic haemophilic arthropathy and the pain that results from it. Various physical therapy techniques are used in the treatment of chronic pain, and PwH can benefit from exercise programmes combining proprioception, strength, proprioceptive retraining, flexibility and stretching, balance, and general function [30]. A 3-year observational study of 93 Finnish PwH showed that pain was reduced by 26% with physical therapy and 4.6% with inpatient rehabilitation, compared with a slight deterioration in pain in untreated patients [30]. Using a personalised approach, exercise can be used in pain management by people with severe haemophilia, tailored to the specific goals of individual patients by medical professionals who are familiar with their condition [31]. PwH treated at our centre have access to physiotherapy, and it will be important to involve the physiotherapist in discussions about pain management as we look to improve this aspect of haemophilia care.

A study by Witkop et al. found that PwH who experience both acute and chronic pain are more likely to experience depression and have a lower quality of life [32]. Chronic pain is recognised to be highly correlated with the worst physical and mental health-related quality of life among PwH in terms of both general pain and psychological factors [33]. Conversely, psychological health has been hypothesised to help mitigate the impact of pain on functional restrictions or disability [34]. Psychological treatment is not always necessary for PwH who experience persistent pain, but it is important to be aware of signs that might indicate a need for intervention, including abnormal pain experience and behaviour, poor stress management, interpersonal conflicts and substance addiction [23]. In the case of our institute, integrative therapeutic planning is not available; this type of intervention is typically only achievable in large institutions in Morocco.

Limitations

Our study did not look at the socio-economic aspects of pain among participants, but studies elsewhere have indicated that this has an impact [1,35,36]. Future research should include an overall clinical assessment of PwH who experience pain, with a comparison of socio-economic factors between those who do and do not suffer from pain in our local setting.

CONCLUSION

Pain in haemophilia is both acute and chronic and can be debilitating. PwH often learn to live with their pain but this does not mean they should have to live with it. To improve the quality of care, it is important for every health care professional to better understand this pain. This means it is important to really speak with patients to find out more about their pain, and to find ways to manage that pain better on an individual basis. Pain assessment is an essential component of proper treatment for PwH. However, the most important limitation in the treatment of pain associated with haemophilia is probably the absence of evidence-based treatment guidelines or best practices.

This study shows that pain is very present in PwH treated at our centre in Morocco, with impact on different areas of life. It will enable us to look critically at the need for interventions, and in so doing to improve patient care and haemophilia-related pain management. It should allow us to better direct therapeutic education sessions and to extend their content to non-drug alternative techniques in accordance with patient expectations. There is a need for action to standardise treatment approaches and develop protocols for pain management in PwH.

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Informed consent has been obtained from the participants in the study reported in this paper.

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