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The Role of Physical and Rehabilitation Medicine in Preventing Musculoskeletal Complications in Pediatric Hemophilia

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ABSTRAK

Latar Belakang: Hemofilia pada anak merupakan kelainan perdarahan herediter yang menimbulkan komplikasi muskuloskeletal progresif akibat hemartrosis berulang sehingga berisiko menyebabkan disabilitas jangka panjang dan penurunan kualitas hidup. **Tujuan:** Menelaah peran rehabilitasi medik dalam pencegahan komplikasi muskuloskeletal pada hemofilia pediatrik. **Metode:** Penelitian ini merupakan *narrative literature review* dengan penelusuran artikel melalui PubMed, Scopus, dan Google Scholar menggunakan kata kunci terkait hemofilia pediatrik, komplikasi muskuloskeletal, hemartrosis, artropati hemofilik, dan rehabilitasi dan manajemen preventif. Literatur yang diseleksi meliputi penelitian asli, pedoman klinis, dan tinjauan sistematis yang relevan pada populasi anak dan remaja. Analisis dilakukan secara deskriptif-sintesis untuk mengintegrasikan hasil terkait komplikasi muskuloskeletal dan strategi rehabilitasi preventif berbasis fase. **Hasil:** Komplikasi meliputi hemartrosis, sinovitis hemofilik kronik, artropati hemofilik, deformitas sendi, dan hematoma otot yang berdampak pada penurunan kekuatan otot, keterbatasan lingkup gerak sendi, nyeri kronis, pembatasan aktivitas, dan penurunan kualitas hidup. Rehabilitasi preventif yang terintegrasi dengan terapi profilaksis faktor koagulasi, termasuk asesmen fungsional (HJHS dan FISH), protokol RICE fase akut, hidroterapi, latihan penguatan isometrik, latihan lingkup gerak sendi, edukasi proteksi sendi, dan penggunaan ortosis dan alat bantu mobilisasi. **Kesimpulan:** Rehabilitasi medik merupakan pilar profilaksis non-farmakologis yang esensial dalam pencegahan komplikasi muskuloskeletal hemofilia anak.

ABSTRACT

Background: *Pediatric hemophilia is a hereditary bleeding disorder that leads to progressive musculoskeletal complications due to recurrent hemarthrosis, thereby increasing the risk of long-term disability and reduced quality of life.* ***Objective:*** *To examine the role of medical rehabilitation in preventing musculoskeletal complications in pediatric hemophilia.* ***Methods:*** *This study was conducted as a narrative literature review by searching articles through PubMed, Scopus, and Google Scholar using keywords related to pediatric hemophilia, musculoskeletal complications, hemarthrosis, hemophilic arthropathy, and preventive*

rehabilitation and management. The selected literature included original research articles, clinical guidelines, and systematic reviews relevant to children and adolescent populations. A descriptive-synthesis approach was used to integrate findings related to musculoskeletal complications and phase-based preventive rehabilitation strategies. ***Results:*** *Complications include hemarthrosis, chronic hemophilic synovitis, hemophilic arthropathy, joint deformities, and muscle hematomas, which contribute to decreased muscle strength, limited joint range of motion, chronic pain, activity restriction, and reduced quality of life. Preventive rehabilitation integrated with coagulation factor prophylaxis includes functional assessment (HJHS and FISH), the acute-phase RICE protocol, hydrotherapy, isometric strengthening exercises, range of motion exercises, joint protection education, and the use of orthoses and mobility aids.* ***Conclusion:*** *Medical rehabilitation represents an essential non-pharmacological prophylactic pillar in preventing musculoskeletal complications in pediatric hemophilia.*

INTRODUCTION

Pediatric hemophilia remains a significant clinical challenge due to its lifelong bleeding tendency and high risk of progressive musculoskeletal damage. Although characterized by deficiencies of coagulation factor VIII (hemophilia A) or factor IX (hemophilia B) and inherited in an X-linked recessive pattern predominantly affecting boys, the primary clinical burden extends beyond bleeding episodes toward cumulative joint and muscle deterioration. According to the World Health Organization (WHO), inherited bleeding disorders remain a significant global health concern due to their lifelong morbidity and resource-intensive management, particularly in low and middle-income countries. The musculoskeletal system, particularly joints and periarticular muscles, represents the most vulnerable target of recurrent hemorrhage.From early childhood, repeated hemarthrosis during critical phases of growth disrupts normal joint development, alters biomechanics, and progressively compromises motor function. Rather than being isolated acute events, recurrent bleeding episodes initiate a chronic inflammatory cascade that contributes to synovial hypertrophy, cartilage degeneration, and long-term functional limitation. Consequently, children with hemophilia face restrictions in physical activity, participation in play, and school engagement, which collectively diminish long-term quality of life (Marchesini *et al*., 2021; Samman *et al*., 2020).

Beyond hematologic manifestations such as spontaneous bleeding, hemophilia can also lead to complications affecting multiple organ systems, including the musculoskeletal, gastrointestinal, and nervous systems. Among these, musculoskeletal complications represent the most common and functionally significant clinical manifestations in pediatric patients. Recurrent hemarthrosis, particularly in the ankles, knees, and elbows, may progress to chronic synovitis and eventually to hemophilic arthropathy. This pathological process is progressive in nature and, if not optimally managed, can result in limited joint range of motion, structural deformities, chronic pain, and even permanent disability. In addition to hemarthrosis, intramuscular bleeding contributes to muscle weakness, contractures, and altered biomechanics. Collectively, these complications significantly interfere with daily activities, including play, physical exercise, and school participation (E. C. Rodriguez-Merchan, 2012).

Advances in treatment, particularly through the administration of prophylactic coagulation factor replacement therapy, have substantially improved life expectancy among children with hemophilia. The World Federation of Hemophilia (WFH)

guidelines emphasize that modern hemophilia care should not only focus on bleed control but also on long-term functional preservation and participation outcomes. As survival rates increase, the focus of management has shifted from merely preventing mortality due to acute bleeding to preventing long-term complications and optimizing functional outcomes. The long-term goals now include preserving independence, enhancing quality of life, and promoting active social participation. Physical and Rehabilitation Medicine plays a role as an integral component of comprehensive hemophilia care. Rehabilitation interventions are directed at minimizing the functional consequences of recurrent bleeding episodes. These include reducing pain, improving muscle strength, enhancing joint range of motion, preventing joint deformities secondary to repeated hemarthrosis, and promoting safe physical activity through individualized exercise programs (Wagner *et al*., 2019).

Early and continuous rehabilitation interventions have the potential to significantly reduce the risk of hemophilic arthropathy and long-term disability. Timely implementation of targeted therapeutic exercises, muscle strengthening programs, and joint protection strategies may interrupt the cycle of bleeding and inflammation within the joint. Evidence suggests that appropriate rehabilitation can decrease the frequency and severity of hemarthrosis episodes. Furthermore, structured rehabilitation programs may reduce the progression of musculoskeletal deformities associated with recurrent bleeding. Preventive rehabilitation strategies are particularly important during childhood, when growth and musculoskeletal development are ongoing (Wagner *et al*., 2019). However, existing discussions in the literature remain predominantly descriptive, focusing either on hematologic management or on rehabilitation as a secondary, restorative intervention after joint damage has occurred.

A critical research gap persists in the absence of a clearly articulated prevention-oriented conceptual framework that integrates coagulation prophylaxis, musculoskeletal surveillance, functional assessment, and stage-specific rehabilitation strategies into a unified model of care. In many clinical settings, rehabilitation is still introduced reactively, after joint damage or functional limitations have already developed, rather than proactively as a preventive strategy. Existing literature has largely focused on hematologic control and pharmacologic prophylaxis, while the preventive potential of early and structured rehabilitation interventions has received comparatively less systematic attention. Furthermore, there is limited consensus regarding standardized rehabilitation protocols tailored specifically to different stages of musculoskeletal involvement in children with hemophilia. Variability in assessment tools, exercise prescriptions, and monitoring strategies also reflects a lack of unified, evidence-based guidance.

Conceptually, this review proposes a prevention-oriented framework in which recurrent hemarthrosis represents the initiating event, chronic synovial inflammation and arthropathy constitute the progressive pathological continuum, and structured rehabilitation functions as an interventional modifier capable of disrupting this cycle. Within this framework, prophylactic factor replacement addresses the hematologic trigger, while rehabilitation strategies target biomechanical stress, muscle imbalance, joint instability, and functional decline.

This literature review addresses these gaps by specifically concerning on the preventive role of Physical and Rehabilitation Medicine in pediatric hemophilia, rather than solely its restorative function after complications occur. The novelty of this review lies in its emphasis on early, structured, and stage-specific rehabilitation strategies integrated with coagulation factor prophylaxis to interrupt the cycle of

bleeding, inflammation, and joint degeneration. Unlike previous discussions that primarily describe rehabilitation as supportive therapy, this review conceptualizes rehabilitation as a core preventive pillar within multidisciplinary management. It synthesizes current evidence to clarify how individualized exercise programs, functional monitoring, and musculoskeletal surveillance can be systematically aligned with hematologic treatment plans. By framing rehabilitation within a prevention-oriented and evidence-based model, this review seeks to contribute a more cohesive understanding of its role in reducing hemophilic arthropathy and long-term disability.

METHOD

This study was conducted as a narrative literature review aimed at synthesizing current evidence regarding musculoskeletal complications in pediatric hemophilia and the preventive role of Physical and Rehabilitation Medicine. As a narrative review, this study does not perform a systematic selection of studies or meta-analysis; therefore, a full PRISMA flow diagram is not applicable (Gualtierotti *et al*., 2021). Narrative reviews inherently carry a risk of selection bias, and this study does not formally grade the level of evidence for each included reference. A comprehensive search of electronic databases, including PubMed, Scopus, and Google Scholar, was performed to identify relevant articles published in English. Keywords used in the search strategy included “pediatric hemophilia,” “musculoskeletal complications,” “hemarthrosis,” “hemophilic arthropathy,” “physical therapy,” “rehabilitation,” and “preventive management.” Original research articles, clinical guidelines, systematic reviews, and relevant consensus statements focusing on children and adolescents with hemophilia were included. The selected literature was screened and analyzed to ensure relevance to the objectives of this review (Chigbu *et al*., 2023).

The discussion is organized into three main sections. The first section outlines the fundamental aspects of pediatric hemophilia, including definitions, epidemiology, etiology, genetic inheritance patterns, and clinical bleeding manifestations. The second section examines musculoskeletal complications, including hemarthrosis, chronic hemophilic synovitis, hemophilic arthropathy, articular deformities, and muscle hematomas, as well as their long-term functional consequences such as reduced muscle strength, decreased joint range of motion, and chronic pain. The third section focuses on the preventive role of rehabilitation medicine, covering principles of preventive rehabilitation, functional assessment strategies, pain and joint health evaluation, the Functional Independence Score in Haemophilia (FISH), and stage-specific interventions during acute and maintenance phases. Preventive rehabilitation strategies discussed include hydrotherapy, muscle strengthening exercises, range of motion training, joint protection education, and the use of assistive devices and orthoses. Through this structured approach, the review aims to provide a comprehensive and prevention-oriented synthesis of current evidence.

RESULTS AND DISCUSSION

Pediatric Hemophilia and Its Musculoskeletal Complications

Hemophilia is one of the most frequently reported congenital hematologic disorders after thalassemia and represents a significant health burden in the pediatric population. Genotypically, hemophilia is classified into three main types: hemophilia A, B, and C. Hemophilia A results from a deficiency or dysfunction of coagulation factor VIII, whereas hemophilia B and C are caused by abnormalities in factors IX

and XI, respectively. Clinically, these disorders are characterized by prolonged and excessive bleeding following minor trauma or, in severe cases, spontaneous bleeding episodes. Although hemophilia is primarily a hereditary condition, acquired forms associated with autoantibodies targeting clotting factors have also been described (Mannucci, 2020). The chronic and recurrent nature of bleeding in affected children underlies the progressive musculoskeletal morbidity observed over time.

According to the World Federation of Hemophilia (WFH) Global Report 2024, the estimated prevalence of hemophilia is approximately 1 in 10,000 live births, with around 489,000 individuals worldwide living with the condition (Federation & Report, 2024).Hemophilia A accounts for approximately 80-85% of all cases and is significantly more common than hemophilia B. The prevalence of hemophilia A is estimated at 17.1 per 100,000 males, whereas hemophilia B affects approximately 3.8 per 100,000 males. Due to its X-linked recessive inheritance pattern, males are predominantly affected, while females are typically carriers. In regions with a high rate of consanguineous marriages, such as Egypt, the prevalence is reported to be higher. Hemophilia C is rarer, occurring in approximately 1 in 100,000 children, and factor XI deficiency is notably more prevalent among individuals of Ashkenazi Jewish descent in the Middle East, with a reported prevalence of approximately 8% (Federation & Report, 2024; Matuk-Villazon *et al*., 2021).

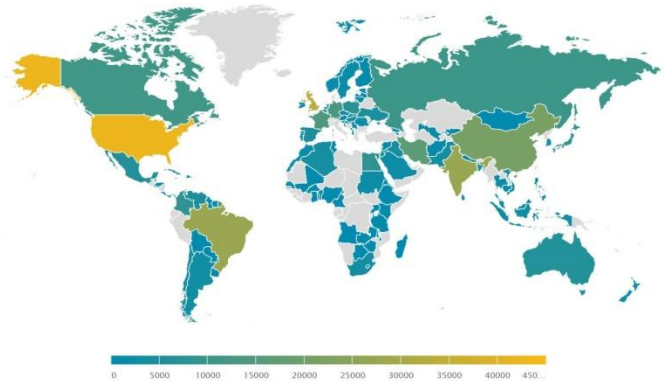

Figure 1. Global distribution of hemophilia cases (WFH 2024) (Federation & Report, 2024)

Hemophilia is primarily caused by mutations in genes encoding specific coagulation factors and is almost always inherited. More than 1,000 distinct mutations have been identified in the genes encoding factors VIII and IX, with approximately 30% arising from spontaneous mutations (López-Arroyo *et al*., 2021). These genes are located on the long arm of the X chromosome, explaining the X-linked recessive inheritance pattern observed in hemophilia A and B. All daughters born to fathers with hemophilia will be obligate carriers, while carrier mothers have a 50% probability of having affected sons and a 50% probability of having carrier daughters. This inheritance pattern has significant implications for genetic counseling and early diagnosis. Early identification of affected children is essential to initiate timely prophylactic therapy and preventive strategies to minimize long-term complications.

The clinical manifestations of hemophilia in neonates and young children, particularly those with severe disease, commonly include soft tissue and intramuscular bleeding, bleeding related to medical procedures such as venipuncture, central line insertion, circumcision, and heel pricks, as well as mucocutaneous bleeding such as epistaxis and gingival bleeding (Nogami & Shima,

2017; “WFH Guidelines for the Management of Hemophilia,” 2020). Extracranial bleeding may also occur. Serious but not immediately life-threatening bleeding episodes most frequently involve joints (hemarthrosis), accounting for approximately 70-85% of cases, followed by deep muscle bleeding (10-20%) and mucosal bleeding (5-12%). Life-threatening bleeding, occurring in approximately 5-10% of cases, includes intracranial hemorrhage (<5%), upper airway bleeding, and gastrointestinal bleeding. Among these manifestations, recurrent joint bleeding plays a central role in the development of chronic musculoskeletal complications.

Musculoskeletal involvement is reported in more than 75% of individuals with hemophilia and represents the most common long-term complication (Berntorp *et al*., 2021; E. Rodriguez-Merchan *et al*., 2011; “WFH Guidelines for the Management of Hemophilia,” 2020). The spectrum of musculoskeletal complications includes hemarthrosis, chronic hemophilic synovitis, hemophilic arthropathy, articular deformities, and muscle hematomas. Hemarthrosis is typically preceded by a tingling or aura-like sensation before intra-articular bleeding becomes clinically evident. Once blood accumulates within the synovial cavity, the joint becomes warm, swollen, extremely painful, and is often maintained in a flexed position to alleviate discomfort. Recurrent hemarthrosis initiates a vicious cycle of inflammation, synovial hypertrophy, and cartilage destruction, ultimately leading to progressive joint degeneration.

Diagnosis of hemarthrosis can be established using magnetic resonance imaging (MRI) and/or ultrasonography. Current recommendations suggest intravenous administration of coagulation factor concentrates at doses of 20-30 U/kg body weight, combined with short-term rest, immobilization in an antalgic position using bandages or splints, and appropriate analgesia (Berntorp *et al*., 2021; Kovač *et al*., 2025). Intra-articular blood aspiration remains controversial; according to recent WFH recommendations, it is considered potentially hazardous due to the risk of recurrent bleeding and septic arthritis (Kovač *et al*., 2025). Moreover, aspiration does not address the underlying coagulation factor deficiency and may require repeated procedures, thereby increasing the cumulative risk of complications.

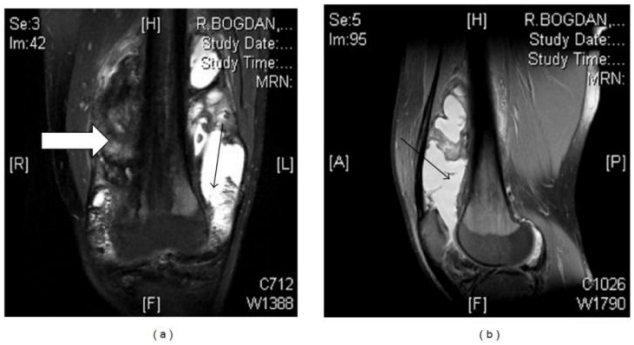

Figure 2. MRI findings of hemarthrosis in a 27-year-old patient with hemophilia Anteroposterior view (a) shows intra-articular blood on the lateral side (black arrow) and severe synovitis medially (white arrow). Lateral view (b) demonstrates the same hemarthrosis (black arrow). (E. C. Rodriguez-Merchan, 2012)

Chronic hemophilic synovitis (CHS) represents a semi-irreversible stage of joint involvement that develops particularly in the setting of recurrent hemarthrosis. Once synovitis is established, as confirmed by ultrasonography, computed tomography (CT), and/or magnetic resonance imaging (MRI), early rehabilitation and modification

of physical activity are essential to prevent progression to chronic synovial disease (Gualtierotti *et al*., 2021). The pathophysiological process begins with the deposition of iron and hemosiderin derived from intra-articular bleeding. Iron oxidation generates reactive oxygen species (ROS), which irritate synoviocytes and chondrocytes lining the articular cartilage. Simultaneously, necrosis and oxidative stress trigger synovial inflammation, resulting in the production of pro-inflammatory cytokines such as tumor necrosis factor alpha (TNFα), interferon gamma (IFNγ), prostaglandins, and interleukin-6 (IL-6). Clinically, CHS is characterized by classical signs of inflammation, including joint redness (rubor), pain (dolor), and warmth (calor), yet without established structural deformity, which distinguishes it from advanced hemophilic arthropathy (Gualtierotti *et al*., 2021).

Hemophilic arthropathy is a long-term complication resulting from recurrent hemarthrosis and represents the progressive structural endpoint of chronic synovial inflammation. Persistent alterations in synovial cell metabolism and structure lead to progressive joint destruction and long-term functional disability if not adequately managed (Gualtierotti *et al*., 2021; Kovač *et al*., 2025; Wyseure *et al*., 2016). Repeated bleeding episodes overwhelm the synovium's capacity to clear iron, leading to hemosiderin accumulation within the synovial membrane. Free iron catalyzes the conversion of hydrogen peroxide (H_2O_2) into reactive oxygen species, which further amplify synovial activation and chondrocyte apoptosis. Chronic synovial inflammation lasting more than six weeks promotes synovial membrane remodeling, excessive proliferation of the basement membrane, and thickening of the synovial lining with villous projections extending into the joint cavity. This process reduces synovial fluid volume and lubrication capacity, thereby accelerating cartilage damage. The inflammatory cascade is mediated by IL-1β, IL-6, TNFα, and IFNγ, while hypoxic intra-articular conditions upregulate hypoxia-inducible factors (HIF-1α and HIF-2α) and vascular endothelial growth factor-A (VEGF-A), stimulating neoangiogenesis that paradoxically increases the risk of future bleeding episodes (Gualtierotti *et al*., 2021; Kovač *et al*., 2025; Wyseure *et al*., 2016).

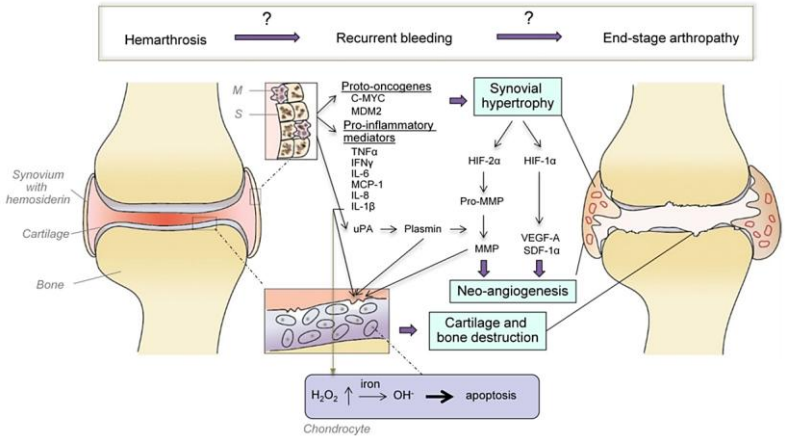

Figure 3. Pathogenesis of hemophilic arthropathy (Kovač *et al*., 2025).

The final stage of hemophilic arthropathy involves progressive cartilage degradation and osteophyte formation. Articular cartilage is composed of chondrocytes embedded in a matrix rich in type II collagen and proteoglycans, particularly aggrecan, which confer tensile strength and elasticity necessary for load-bearing activities such as walking and standing. Chondrocyte survival depends on

oxygen diffusion from synovial fluid and intact proteoglycan-glycosaminoglycan (GAG) metabolism. Pro-inflammatory cytokines released by macrophages and synoviocytes disrupt GAG metabolism and activate apoptotic pathways in chondrocytes, leading to progressive cartilage thinning and joint surface irregularity (Gualtierotti *et al*., 2021; Kovač *et al*., 2025; Wyseure *et al*., 2016).Clinically, the joints most frequently affected include the elbows, knees, and ankles, which are particularly vulnerable due to repetitive mechanical stress and frequent bleeding episodes.

Articular deformities arise as a consequence of chronic synovial remodeling, fibrosis, and structural musculoskeletal adaptation, particularly in weight-bearing joints such as the knees, hips, and ankles, as well as in the elbows and fingers. Synovial epithelial hyperactivation driven by pro-inflammatory cytokines including IL-1, IL-6, and TNFα promotes fibroblast recruitment and excessive extracellular matrix deposition. Fibroblasts secrete collagen types I, III, and IX, laminin, and elastin, contributing to synovial thickening and fibrosis (Ray *et al*., 2022). Concurrently, hemosiderin deposition and oxidative stress induce collagen fiber polarization and increased tissue stiffness. Over time, these processes alter joint biomechanics and lead to characteristic postural and gait abnormalities. Patients commonly develop flexion deformities of the elbows, knees, and hips, lumbar hyperlordosis, ankle plantarflexion, pelvic asymmetry due to leg length discrepancy, and disproportional body alignment secondary to muscle atrophy and fibrosis (Kathy Mulder, 2016).

Muscle hematoma is another significant musculoskeletal manifestation in hemophilia and is frequently associated with physical trauma such as falls or minor injuries. Clinically, it presents with swelling, pain, warmth, and overlying ecchymosis. Although most intramuscular bleeds resolve spontaneously without long-term motor impairment, fewer than 5% of severe cases may progress to compartment syndrome. In instances where blood resorption is incomplete, interstitial clots may organize into a mass known as a pseudotumor, which can impair muscle contraction and functional activity. Hemophilic pseudotumors, although rare (approximately 2-5%), represent a serious complication due to iron-mediated oxidative damage leading to periosteal destruction, rhabdomyolysis, bone cyst formation, and nerve irritation (Gualtierotti *et al*., 2021; Kovač *et al*., 2025; Wyseure *et al*., 2016). Collectively, these musculoskeletal complications underscore the progressive and multifactorial nature of joint and muscle damage in pediatric hemophilia, reinforcing the importance of early preventive strategies.

Long-Term Impact of Musculoskeletal Complications in Pediatric Hemophilia

One of the most prominent consequences is reduced muscle strength, often described as hemophilia-associated sarcopenia. This reduction in muscle strength is attributed to two principal mechanisms: the direct cytotoxic effects of blood components on muscle tissue and the indirect consequences of pain and fear of bleeding during physical activity (Cruz-Montecinos *et al*., 2020). Intramuscular hematomas occur in approximately 10-20% of patients with hemophilia, and among these individuals, 40-60% demonstrate measurable muscle weakness assessed through hand grip strength, gait speed, or reduced muscle mass determined by bioelectrical impedance analysis (BIA) (Cruz-Montecinos *et al*., 2020). A study involving 41 children with hemophilia reported that hemophilic arthropathy was significantly associated with decreased muscle strength and altered joint biomechanics. In the upper extremities, unilateral elbow arthropathy was linked to weakness of elbow flexors and extensors, potentially compromising joint stability and motor control during functional activities. In the lower extremities, a significant

reduction in plantarflexor muscle strength was observed, which may impair gait efficiency and balance (Cruz-Montecinos *et al*., 2020).

Reduced joint range of motion (ROM) is another major long-term sequela of recurrent bleeding and chronic joint inflammation. Limitation of ROM results from pain, progressive fibrosis and structural joint deformity, as well as psychological fear of excessive movement that might trigger bleeding episodes. Approximately 40-80% of patients with hemophilia experience progressive ROM limitation, particularly those who do not receive adequate prophylactic coagulation therapy or structured physical rehabilitation, leading to recurrent hemarthrosis (Din, 2021). A survey-based study involving 152 patients diagnosed with hemophilia for more than three years reported that 64% of participants experienced movement restriction due to pain, while 45% were unable to freely move their wrists, fingers, and knees because of stiffness (Din, 2021). Persistent ROM limitation alters normal biomechanics, increases joint loading in compensatory patterns, and accelerates degenerative changes. Over time, this mechanical imbalance contributes to worsening arthropathy and functional decline.

Chronic pain represents a central and persistent manifestation of musculoskeletal involvement in hemophilia. Pain may arise from overt bleeding or microbleeding within joints and muscles and can occur either during movement or spontaneously at rest. Pathophysiologically, chronic inflammation triggered by iron deposition and oxidative stress leads to progressive cartilage thinning and exposure of nociceptive nerve endings within the periosteum (Fouda *et al*., 2022). Ferrous iron (Fe^{2+}) exerts apoptotic effects on chondrocytes and synoviocytes, promoting cartilage degradation and joint surface irregularity. As cartilage deteriorates, friction between adjacent bone surfaces increases during movement, resulting in mechanical pain. Pro-inflammatory cytokines such as IL-1, IL-6, and prostaglandins further exert nociceptive effects on periosteal pain receptors, amplifying pain perception (Fouda *et al*., 2022). Chronic pain has been identified as a primary determinant of daily functional limitation and is strongly correlated with poorer general health status and increased depressive symptoms (Buckner *et al*., 2019).

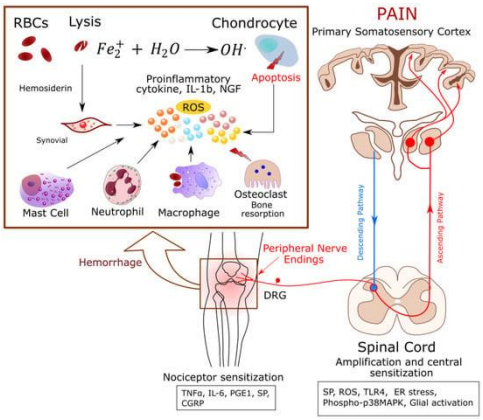

Figure 4. Mechanism of pain in hemophilia (Fouda *et al*., 2022)

Activity limitation and participation restriction constitute broader functional consequences of chronic musculoskeletal damage. In children, activity restriction is often influenced by pain and fear of hemarthrosis, whereas in adults, structural fibrosis and established deformities play a larger role. Historically, between 1970 and 2000, patients with hemophilia were frequently advised to avoid physical activity regardless of intensity or type. However, subsequent recommendations, including those aligned with the World Federation of Hemophilia guidelines, demonstrated that

inappropriate restriction of physical activity is associated with poorer physical and cardiovascular fitness and lower quality of life (Goto *et al*., 2020). Progressive functional limitations restrict children's ability to participate in school, recreational, and social activities. Recurrent bleeding episodes and hospitalizations often result in repeated school absenteeism, which negatively affects academic performance and psychosocial development (Budiarty & Nafianti, 2020). Increased dependence on caregivers or mobility aids such as canes, crutches, or wheelchairs is also significantly correlated with higher pain severity (Buckner *et al*., 2019).

Ultimately, the cumulative burden of chronic pain, joint damage, muscle weakness, and activity restriction leads to a substantial decline in quality of life. Reduced quality of life in children with hemophilia is driven by multiple interconnected factors, including chronic pain, hemophilic arthropathy, physical activity limitations, and frequent hospital visits (Azeredo-da-Silva *et al*., 2023). Children with more severe arthropathy tend to report poorer physical domain scores, while psychosocial impairment is exacerbated by gait abnormalities, multiple joint involvement, and persistent pain (Budiarty & Nafianti, 2020). A study involving 88 patients with hemophilia identified a significant negative correlation between functional disability severity and overall quality of life (Kavia *et al*., 2021).

Preventive Rehabilitation Principles and Functional Assessment

The overarching goals of rehabilitation applicable to both children and adults include improving physical fitness, preventing joint contractures due to recurrent bleeding and chronic synovial inflammation (de Kleijn *et al*., 2022). Functionally, hemophilic arthropathy remains the leading cause of activity limitation, particularly in patients who do not receive adequate prophylactic coagulation therapy. Therefore, structured functional assessment is essential to define rehabilitation targets and guide multidisciplinary management ("WFH Guidelines for the Management of Hemophilia," 2020). Pain assessment constitutes a critical component of evaluation, as 40-80% of children with hemophilia report either acute pain during bleeding episodes or chronic pain secondary to microbleeds and joint contractures. Commonly used tools include the Numerical Rating Scale (NRS), the Wong-Baker FACES Scale for younger children or those with communication difficulties, and the FLACC scale (Face, Legs, Activity, Cry, Consolability) for children under three years old, all of which have demonstrated clinical utility in pediatric settings (Paredes *et al*., 2020). In addition to pain evaluation, joint health assessment using the Hemophilia Joint Health Score (HJHS) provides a structured method to quantify structural damage, functional limitation, pain, and inflammatory signs in major target joints such as knees, ankles, and elbows. The HJHS (score range 0-13 per joint) enables clinicians to monitor disease progression, evaluate therapeutic effectiveness, and adjust treatment strategies accordingly (Ay *et al*., 2024).

Complementing structural joint evaluation, the Functional Independence Score in Haemophilia (FISH) measures patients' ability to perform eight domains of daily living, with a total score ranging from 8 to 32, where higher scores indicate greater independence. FISH has been validated as a reliable tool for monitoring functional capacity, evaluating treatment outcomes, and guiding individualized rehabilitation planning (Tlacuilo-Parra *et al*., 2010). Imaging modalities, particularly musculoskeletal ultrasonography, further enhance early detection and monitoring of hemarthrosis by identifying joint effusion, structural damage, inflammatory changes, and complications such as pseudotumor formation (Gualtierotti *et al*., 2024). In the acute phase of hemarthrosis, preventive rehabilitation emphasizes early intervention using the RICE protocol (Rest, Ice, Compression, Elevation), applied intensively

within the first 0-48 hours, gradually tapered during the subacute phase (48-72 hours), and subsequently transitioned into active rehabilitation during the maintenance phase (>72 hours) (Stromer *et al*., 2021). (Adequate pain control primarily with acetaminophen/paracetamol, followed by selective COX-2 inhibitors or low-dose opioid combinations when necessary supports early mobilization and prevents secondary joint stiffness (Stromer *et al*., 2021).

Maintenance-Phase Preventive Rehabilitation in Pediatric Hemophilia

Maintenance-phase preventive rehabilitation aims to restore muscle performance, preserve joint range of motion (ROM), prevent recurrent bleeding, and reduce long-term musculoskeletal disability. Hydrotherapy represents a cornerstone intervention, particularly through the Halliwick method performed in thermoneutral water (33-34°C), allowing joint movement and muscle activation with reduced axial load due to buoyancy. A 12-week program (two 50-minute sessions per week; total 24 sessions) consisting of warm-up (walking in water), deep-water cycling, respiratory muscle training, and swimming has been shown to significantly improve maximal voluntary isometric contraction (MVIC) and electromyographic (EMG) muscle activity without triggering hemarthrosis, while also enhancing activities of daily living (ADL) performance and improving at least one lower-limb joint score on the Hemophilia Joint Health Score (HJHS) (Feldberg *et al*., 2021).

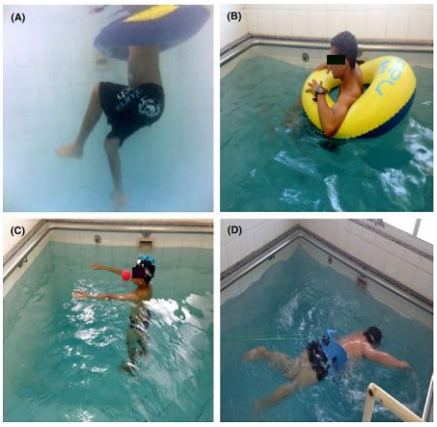

Figure 5. Components of the Halliwick hydrotherapy program in hemophilia

Similarly, a randomized controlled trial demonstrated that a 4-week hydrotherapy program (two sessions per week; 5-minute warm-up, 30-45-minute strengthening and stretching including hamstring stretching, quadriceps strengthening, isometric and isotonic exercises, followed by 5-minute cooldown at 27-35°C) significantly reduced pain (1-10 scale) and improved joint ROM measured using the Norkin and White approach (Mazloum *et al*., 2014). Beyond aquatic therapy, muscle strengthening particularly isometric exercise is strongly recommended by WFH guidelines, as it allows contraction of key muscle groups (quadriceps, hamstrings, gluteal muscles) without excessive joint movement, thereby minimizing mechanical stress and bleeding risk ("WFH Guidelines for the Management of Hemophilia," 2020). Progressive strengthening protocols are structured into levels for major muscle groups frequently affected by bleeding (Kathy Mulder, 2016); (1) hamstrings, progressing from supine isometric contraction to resisted seated extension; (2) iliopsoas rehabilitation following prolonged psoas bleeding, initiated only after complete rest and gradual progression to controlled hip activation to avoid pseudotumor formation; (3) quadriceps strengthening, beginning with supine isometric sets and advancing to wall-supported semi-squats with graded duration and

repetition; (4) gastrocnemius strengthening, progressing from seated dorsiflexion to wall-supported calf stretch; and (5) forearm flexor training, crucial in preventing compartment-related complications, progressing from simple gripping to weight-bearing extension exercises.

ROM exercises are equally essential to prevent contracture and hemophilic arthropathy. Knee ROM progresses from heel slides in supine to seated flexion-extension and prone knee flexion; elbow ROM advances from gravity-assisted extension to assisted table-supported extension; ankle ROM includes multidirectional active movements ("alphabet drawing"), seated dorsiflexion stretching, and wall-assisted dorsiflexion mobilization (Kathy Mulder, 2016). Joint protection education is critical, given that children with hemophilia have a 5-6 times higher bleeding risk compared to healthy peers, necessitating avoidance of high-contact or high-velocity sports such as football, rugby, boxing, racing, and skiing, while encouraging safer activities like swimming, golf, cycling, table tennis, and walking (Biasoli *et al*., 2022; Wang *et al*., 2016). Protective strategies include external protective gear (knee pads, elbow pads, helmets), orthoses (braces, elastic compressive sleeves), and proper footwear such as insoles to optimize load distribution (Gouw *et al*., 2019; E. Rodriguez-Merchan *et al*., 2011).

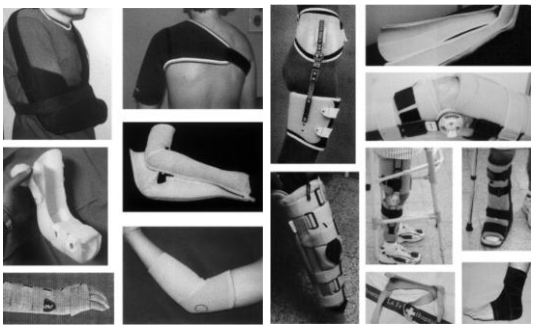

Figure 6. Upper and lower limb orthoses in pediatric hemophilia (Querol *et al*., 2002)

The use of mobility aids and orthoses is phase-dependent. In the acute phase, temporary immobilization with splints is indicated for severe pain, joint instability, and tissue protection (Querol *et al*., 2002; "WFH Guidelines for the Management of Hemophilia," 2020). During the subacute phase, crutches or walkers facilitate gradual weight-bearing in the presence of muscle atrophy or mild contracture while preventing overload of target joints. In the chronic phase of established hemophilic arthropathy, orthoses such as Ankle-Foot Orthosis (AFO), Knee-Ankle-Foot Orthosis (KAFO), and customized insoles are indicated to correct deformity, address chronic instability, and improve biomechanical alignment. Collectively, maintenance-phase rehabilitation integrates hydrotherapy, progressive strengthening, ROM exercises, joint protection education, and appropriate orthotic support to prevent recurrent bleeding, preserve musculoskeletal integrity, and optimize long-term functional independence in pediatric hemophilia.

Despite these recommendations and evidence-based strategies, practical implementation of preventive rehabilitation can be challenging in low-resource settings. Barriers include limited access to hydrotherapy facilities, insufficient numbers of specialized physical and rehabilitation medicine (PRM) practitioners, financial constraints, and lack of locally adapted protocols. Reliance on home-based exercise programs, caregiver training, and tele-rehabilitation may provide feasible

alternatives, though effectiveness may vary compared to structured clinical programs.

CONCLUSION AND RECOMMENDATION

Pediatric hemophilia is a hereditary bleeding disorder with a high risk of long-term musculoskeletal complications, primarily due to recurrent hemarthrosis, muscle bleeding, and progressive hemophilic arthropathy, which collectively contribute to functional limitation, disability, and reduced quality of life extending into adulthood. The management paradigm has shifted from merely controlling acute bleeding episodes toward preventing long-term complications and optimizing functional outcomes through structured physical exercise programs, including progressive muscle strengthening, maintenance of joint range of motion, and careful selection of safe physical activities. Early, continuous, and well-integrated rehabilitation implemented alongside coagulation factor prophylaxis is essential, particularly during the critical growth and developmental phases of childhood, to achieve effective secondary prevention. Therefore, medical rehabilitation should not be viewed solely as a post-complication therapeutic modality but as a fundamental non-pharmacological prophylactic pillar within a comprehensive multidisciplinary approach, and it is strongly recommended that individualized, phase-based rehabilitation programs be routinely incorporated into standard pediatric hemophilia care to prevent long-term disability and maximize functional independence and quality of life.

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