# Role of Musculoskeletal Ultrasound in Detection of Hemophilic Arthropathy

A Thesis

Submitted for Partial Fulfillment of Master Degree in Radiology

By

**Salma Ehab Mohamed Elbastawisy**
M.B.B.Ch,

Under Supervision of

**Prof. Dr. Hossam Moussa Sakr**
Professor of Radiology
Faculty of Medicine, Ain Shams University

**Dr. Nermeen Nasry Keriakos**
Lecturer of Radiology
Faculty of Medicine, Ain Shams University

**Faculty of Medicine**
**Ain Shams University**
**2019**


بسم الله الرحمن الرحيم
قالوا
سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم الحكيم
صدق الله العظيم
سورة البقرة الآية: ٣٢

# Acknowledgments

*First and foremost, I feel always indebted to* **Allah**, *the* ***Most Beneficent*** *and* ***Merciful*** *who gave me the strength to accomplish this work.*

*My deepest gratitude to my supervisor,* **Prof. Dr. Hossam Moussa Sakr,** *Professor of Radiology, Faculty of Medicine, Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision.*

*I would like to express my great and deep appreciation and thanks to* **Dr. Nermeen Nasry Keriakos,** *Lecturer of Radiology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, and her patience in reviewing and correcting this work.*

*Special thanks to my* **Parents,** *my* **Husband** *and all my* **Family** *members for their continuous encouragement, enduring me and standing by me.*

✍ **Salma Ehab Mohamed Elbastawisy**

# List of Contents

*Subject* *Page No.*

**List of Abbreviations** ..... **i**

**List of Tables** ..... **iii**

**List of Figures** ..... **v**

**List of Cases** ..... **ix**

**Introduction** ..... **1**

**Aim of the Work** ..... **6**

**Review of Literature**

Anatomy of the Knee, Elbow & Ankle Joints ..... 7

Technique and Radiological Anatomy ..... 25

Pathology of Hemophilia ..... 57

**Patients and Methods** ..... **84**

**Results** ..... **88**

**Illustrative Cases** ..... **100**

**Discussion** ..... **114**

**Summary** ..... **132**

**References** ..... **136**

**Arabic Summary** ..... **—**

# List of Abbreviations

| Abbr. | | Full-term |
|---|---|---|
| **ACL** | : | Anterior Cruciate Ligament |
| **AMCL** | : | Anterior bundle of the Medial Collateral Ligament |
| **BMD** | : | Bone Mineral Density |
| **CET** | : | Common Extensor Tendon |
| **CFCs** | : | Clotting Factors Concentrates |
| **CFT** | : | Common Flexor Tendon |
| **Cm2** | : | Square centimeters |
| **H2O2** | : | Hydrogen Peroxide |
| **HA** | : | Hemophilic Arthropathy |
| **HEAD-US** | : | Hemophilia Early Arthropathy Detection with Ultrasound |
| **HJHS 2.1** | : | Hemophilia Joint Health Score 2.1 |
| **IL** | : | Interleukin |
| **ITB** | : | Iliotibial Band |
| **JADE** | : | Joint Activity and Damage Exam |
| **LCL** | : | Lateral Collateral Ligament |
| **LS** | : | Longitudinal Section |
| **LUCL** | : | Lateral Ulnar Collateral Ligament |
| **MCL** | : | Medial Collateral Ligament |
| **Mm** | : | Millimeters |
| **MMP** | : | Matrix Metalloproteinases |
| **MRI** | : | Magnetic Resonance Imaging |
| **MSK US** | : | Musculoskeletal Ultrasound |
| **NO** | : | Nitric Oxide |
| **OA** | : | Osteoarthritis |
| **OPG** | : | Osteoprotegin |
| **PCL** | : | Posterior Cruciate Ligament |
| **PD** | : | Power Doppler |
| **POC** | : | Point-Of-Care |
| **PRLI** | : | Posterolateral rotatory Instability |
| **PwH** | : | Patients with Hemophilia |

| | | |
|---|---|---|
| **RA** | : | Rheumtoid Arthritis |
| **RANK-L** | : | RANK Ligand |
| **RCL** | : | Radial Collateral Ligament |
| **SD** | : | Standard deviation |
| **SPSS** | : | Statistical package for social science |
| **TNF** | : | Tumor Necrosis Factor |
| **TS** | : | Transverse Section |
| **US** | : | Ultrasound |
| **USG** | : | Ultrasonography |
| **VEGF** | : | Vascular-Derived Endothelial Growth Factor |
| **VEGFR** | : | Vascular-Derived Endothelial Growth Factor Receptor |
| **vWD** | : | Von Willebrand disease |
| **vWF** | : | Von Willebrand factor |
| **WFH** | : | World Federation of Hemophilia |

# List of Tables


| Table No. | Title | Page No. |
|---|---|---|
| **Table (1):** | Main anatomic structures depicted by US and their related sonographic pattern | 38 |
| **Table (2):** | Number and percentage distribution of patients of hemophilic arthropathy according to their baseline characteristics | 89 |
| **Table (3):** | Number and percentage distribution of patients of hemophilic arthropathy according to their clinical presentation | 91 |
| **Table (4):** | Number and percentage distribution of patients of hemophilic arthropathy according to their joints affected | 92 |
| **Table (5):** | Number and percentage distribution of patients of hemophilic arthropathy according to their ultrasonography finding | 93 |
| **Table (6):** | Relationship between the joints affected and their ultrasonography findings | 95 |
| **Table (7):** | Relationship between the joints affected and their US findings | 96 |
| **Table (8):** | Relationship between different US parameters in all the joints involved in the disease and age-groups of the patients examined. | 96 |
| **Table (9):** | Relationship between all examined joints (normal and abnormal joints) and their US parameters/findings | 98 |

**Table (10):** Relationship between patients with normal and abnormal US findings according to their all joints.....99

**Table (11):** HEAD-US score (Hemophilia Early Arthropathy Detection with Ultrasound).....118

**Table (12):** The items included in a number of MSK-US scanning protocols and scoring systems used in the assessment of HA.....124

# List of Figures


| Figure No. | Title | Page No. |
|---|---|---|
| **Figure (1):** | Left knee joint from behind, showing interior ligaments | 9 |
| **Figure (2):** | Head of right Tibia seen from above | 10 |
| **Figure (3):** | Osseous anatomy of the elbow. | 13 |
| **Figure (4):** | Medial and lateral ligamentous stabilizers of the elbow. | 15 |
| **Figure (5):** | Elbow anatomy. | 16 |
| **Figure (6):** | Important bony landmarks and muscle origin and insertion points of the muscles and bones around the ankle | 18 |
| **Figure (7):** | The muscles, tendons, and retinaculae around the ankle joint | 21 |
| **Figure (8):** | The ankle joint ligaments | 22 |
| **Figure (9):** | Patient Position for ultrasound examination (Knee anterior approach) | 27 |
| **Figure (10):** | Quadriceps tendon | 28 |
| **Figure (11):** | Anterior suprapatellar longitudinal approach showing longitudinal view of the quadriceps tendon and the suprapatellar bursa | 29 |
| **Figure (12):** | Articular cartilage of the trochlea | 30 |
| **Figure (13):** | Patellar tendon (Longitudinal view) | 31 |
| **Figure (14):** | Anterior infrapatellar longitudinal approach showing patella, tibia, patellar tendon from the inferior pole of the patella to the tibial tuberosity | 31 |
| **Figure (15):** | Medial collateral ligament. | 32 |

**Figure (16):** Medial meniscus..... 33
**Figure (17):** Pes anserinus complex insertion..... 33
**Figure (18):** The lateral collateral ligament. ..... 34
**Figure (19):** Posterolateral corner of the knee joint..... 35
**Figure (20):** The iliotibial band..... 36
**Figure (21):** Semimembranosus-gastrocnemius bursa..... 36
**Figure (22):** The popliteal vessels in LS. ..... 37
**Figure (23):** Anterior elbow joint anatomy ..... 40
**Figure (24):** Anterior approach for distal biceps tendon evaluation..... 41
**Figure (25):** Distal brachialis muscle evaluation. ..... 42
**Figure (26):** Normal structures of the medial elbow joint ..... 43
**Figure (27):** Ultrasound technique of examination of the medial structures of the elbow..... 44
**Figure (28):** Normal common flexor tendon and ulnar collaterla ligament. ..... 45
**Figure (29):** Common flexor tendon and medial collateral ligament ..... 46
**Figure (30):** Normal common extensor tendon ..... 48
**Figure (31):** Normal distal triceps tendon..... 49
**Figure (32):** The cubital fossa and ulnar nerve ..... 50
**Figure (33):** Anterior ankle position of US examination ..... 51
**Figure (34):** Normal anterior ankle showing the distal tibia, the talus, and the anterior tibiotalar joint..... 52
**Figure (35):** Long-axis view of the normal tibialis anterior tendon..... 52
**Figure (36):** Medial ankle – "Frog-leg" position for assessment of medial ankle ..... 53

**Figure (37):** Short-axis oblique view showing the medial compartment tendons of ankle ..... 54

**Figure (38):** Lateral ankle – Medial tilt of the leg for assessment of lateral ankle ..... 54

**Figure (39):** Short-axis view of peroneus longus and peroneus brevis tendons ..... 55

**Figure (40):** Posterior ankle –the Achilles tendon views..... 56

**Figure (41):** The vicious cycle of hemophilic arthropathy..... 61

**Figure (42):** Schematic representation of a healthy joint and hemophilic arthropathy ..... 61

**Figure (43):** Schematic representation of the mechanisms of blood-induced joint damage in hemophilia. ..... 65

**Figure (44):** Axial ultrasound images used to assess cartilage thickness of the distal femur. ..... 86

**Figure (45):** Pie chart showing percentage distribution of patients of hemophilic arthropathy according to their age.... 90

**Figure (46):** Diagram showing synovial thickening, synovial hyperemia, joint effusion, hemoarthrosis and osteochondral changes relationship with age. ..... 98

**Figure (47):** Bar chart showing relationship between the joints with normal and abnormal US findings in all the examined group ..... 99

**Figure (48):** Illustrative Case (1) ..... 101

**Figure (49):** Illustrative Case (1) ..... 102

**Figure (50):** Illustrative Case (1) ..... 102

**Figure (51):** Illustrative Case (2) ..... 103

**Figure (52):** Illustrative Case (2) ..... 103

**Figure (53):** Illustrative Case (3) ..... 105

**Figure (54):** Illustrative Case (3) ..... 106

**Figure (55):** Illustrative Case (3) ..... 106
**Figure (56):** Illustrative Case (3) ..... 107
**Figure (57):** Illustrative Case (4) ..... 108
**Figure (58):** Illustrative Case (4) ..... 109
**Figure (59):** Illustrative Case (4) ..... 109
**Figure (60):** Illustrative Case (5) ..... 110
**Figure (61):** Illustrative Case (5) ..... 111
**Figure (62):** Illustrative Case (5) ..... 111
**Figure (63):** Illustrative Case (5) ..... 111
**Figure (64):** Illustrative Case (6) ..... 112
**Figure (65):** Illustrative Case (7) ..... 113
**Figure (66):** Illustrative Case (7) ..... 114
**Figure (67):** Illustrative Case (7) ..... 114

# List of Cases


| Case No. | Page No. |
|---|---|
| **Case (1)** | 100 |
| **Case (2)** | 102 |
| **Case (3)** | 103 |
| **Case (4)** | 107 |
| **Case (5)** | 109 |
| **Case (6)** | 111 |
| **Case (7)** | 112 |

# Introduction

Hemophilia is an X-linked heritable coagulopathy which occurs in approximately 1 in 10,000 individuals. Hemophilia A (factor VIII deficiency) comprises about 80% of cases while hemophilia B (factor IX deficiency), comprises about 20% of cases. The prevalence of hemophilia A in males is 1 in 5000-10,000, while hemophilia B is estimated at 1 in 25,000-30,000 males. ***(Pulles et al., 2016)*** Von Willebrand disease (vWD) is a bleeding disorder of variable severity, caused by deficiency of von Willebrand factor (VWF), which is a multimeric plasma protein and an extracellular adapter molecule, linking platelets to the extracellular matrix and mediates their adhesion at the sites of endothelial injury ***(Sadler, 2003).***

The severity of the hemophilia is classified as mild, moderate or severe, depending on the degree of factor activity. Patients with factor levels between 5 and 40% are classified as mild, those with activity between 1 and 5 % are moderate and those with less than 1% factor level in blood are considered to have severe hemophilia ***(Constantine et al., 2009).*** Generally, the severity of bleeding has an inverse correlation with the clotting factor level. Patients with severe hemophilia (factor level <1 %) suffer spontaneous bleedings, whereas in the mild form of the disease (factor level >5%) bleeding only occurs after major trauma or after surgery. Spontaneous bleeding occurs mainly in the large synovial joints ***(Pulles et al., 2016).***

In patients affected with severe hemophilia (i.e., plasma factor VIII or IX < 1 U/dL), joint bleeding (haemarthrosis) is the most frequent manifestation in both children and adults ***(Melchiorre et al., 2017).*** Intra-articular bleeding triggers joint changes such as: synovitis and cartilaginous damage, which may even start after exposure to the first bleeding episode through activation of inflammatory mediators i.e. cytokines, eventually leading to progressive and permanent bone and joint damage ***(Izquierdo, 2017; Melchiorre et al., 2011; Seuser et al., 2018)***.

Factors contributing to hemophilic joint damage include recurrent hemoarthrosis, synovial inflammation and soft tissue hypertrophy ***(von Drygalski et al., 2018*)** and the most commonly affected joints are the knees, ankles and elbows (***Di Minno et al., 2017; Izquierdo, 2017).***

Target joints are defined as the joints that sustain several consecutive bleeding episodes (> 3 bleeds) within a short period of time (< 6 months). These target joints are the most prone to develop the hemophilic bony and soft tissue changes ***(Izquierdo, 2017).*** Although the use of prophylaxis against joint bleeding is increasing worldwide, a high percentage of patients still develop degenerative changes in their joints despite using this regimen ***(Di Minno et al., 2017).***