

**Prevalence of Musculoskeletal Pain in
Haemodialysis Patients & Its Relation
with Serum Biochemical Markers,
Psychological Status & Work Abilities**

Thesis

*Submitted for partial fulfillment of master degree in
Internal Medicine*

By

Marwa Maher Zenhom

M.B.B.Ch.

Supervised by

Prof. Dr. Magdy Mohammed El-Sharkawy

*Professor of Internal Medicine and Nephrology
Faculty of Medicine, Ain Shams University*

Dr. Cherry Reda Kamel

*Lecturer of Internal Medicine and Nephrology
Faculty of Medicine, Ain Shams University*

**Faculty of Medicine
Ain Shams University**

2014

Contents

Subjects	Page
• List of abbreviations	I
• List of Tables	IV
• List of figures	VI
• Introduction	1
• Aim of the work.....	2
• Review of literature	
- Chapter (1): Musculoskeletal pain.....	3
- Chapter (2): Musculoskeletal pain in haemodialysis patients.....	38
• Patients and Methods.....	112
• Results.....	117
• Discussion.....	132
• Summary	141
• Conclusion.....	144
• Recommendations.....	145
• References.....	146
• Arabic summary	

List of Abbreviations

ABD	: Adynamic bone disease
ACPA	: Anti-citrullinated protein antibodies
ACR/EULAR	: American college of rheumatology/ european league against rheumatism
BMD	: Bone mineral density test
BMI	: Body mass index
BP	: Blood pressure
Ca	: Calcium
Ca MB	: Ca mass balance
Ca x P	: Calcium phosphorus product
CaR	: Calcium-sensing receptor
CCP	: Cyclic citrullinated peptide
CKD	: Chronic kidney disease
CKD-MBD	: Chronic kidney disease mineral bone disease
CRF	: Chronic renal failure
CRP	: C-reactive protein
DCOR	: The three-year dialysis clinical outcomes revisited
DEXA	: Dual-energy x-ray absorptiometry
DMARDs	: Disease-modifying anti rheumatic drugs

DOPPS	: Dialysis outcomes and practice patterns study
ECT	: Electroconvulsive therapy
ESP	: Erythropoiesis stimulating therapy
ESR	: Erythrocyte sedimentation rate
ESRD	: End stage renal disease
ESRF	: End stage renal failure
FDA	: Food & drug administration
FGF-23	: Fibroblast growth factor
GFR	: Glomerular filtration rate
GI	: Gastro intestinal
HB	: Hemoglobin
HD	: Hemodialysis
HDF	: Hemodiafiltration
IL	: Interlukin
iPTh	: Intact parathormone
kDa	: Kilo dalton
KDOQI	: Kidney foundation kidney disease outcomes quality initiative
LDH	: Long haemodialysis
LDL	: Low density lipo protein
LVH	: Left ventricular hypertrophy
MAOI	: Monoamine oxidase inhibitors

MTX	: Methotrexate
NDHD	: Nocturnal daily haemodialysis
NKF	: National kidney foundation
NSAIDs	: Non steroidal anti-inflammatory drugs
P04	: Phosphorus
PRCA	: Pure red cell aplasia
QoL	: Quality of life
RA	: Rheumatoid arthritis
RF	: Rheumatoid factor
rHu-Epo	: Recombinant human erythropoietin
SC	: Subcutaneous
SDHD	: Short daily haemodialysis
SHD	: Standard haemodialysis
SHPT	: Secondary hyperparathyroidism
SSRI	: Selective serotonin reuptake inhibitors
TIBC	: Total iron binding capacity
TNF	: Tumor necrosis factor
TSAT	: Transferrin saturation
VDRA s	: Various vitamin d receptor activators

List of Tables

Table No	Title	Page No
1	Estimated burden of common musculoskeletal conditions.	13
2	Vitamin D Nomenclature.	69
3	Causes of adynamic renal osteodystrophy.	75
4	Comparison of anemia of chronic disease and iron deficiency anemia.	90
5	Descriptive data of 100 hemodialysis patients including Age sex cause of ESRD,duration of dialysis, other comorbid conditions and grade of pain and disability.	117
6	Descriptive Statistics: The age, duration of dialysis,serum markers & blood pressure.	119
7	Inspection abnormalities in the study patients.	120
8	Palpation abnormalities in the study patients.	121
9	Limitation of movement (active & passive) in the study patients.	122
10	Motor examination in the study patients.	123
11	Sensory examination of the study patients.	123
12	Correlation between age, duration of dialysis, serum biochemical markers& blood pressure to with limitation of movement in the study population.	124

Table No	Title	Page No
13	Correlation between age, duration of dialysis, serum biochemical markers& blood pressure to with affection of motor examination in the study population.	125
14	Comparison between level of serum biochemical markers with the different grades of pain and disability.	126
15	Comparison between the positive findings of motor and sensory system examination with the grades of pain and disability.	127

List of Figures

Figure No	Title	Page No
1	Types of musculoskeletal pain.	12
2	Joint impact of osteoarthritis and rheumatoid arthritis.	19
3	Mineral metabolism and bone disease in CKD.	42
4	Mechanisms by which Phosphorus induces PTH secretion.	45
5	The homeostasis of calcium and phosphorus.	47
6	A comparison of serum phosphate relative reduction kinetics during three sequential dialysis prescriptions in six patients.	67
7	Approach to Management of bone metabolism and disease in patients on dialysis.	71
8	When a patient develops CKD, anemia may develop as a result of the presence of any one or the combination of multiple factors.	78
9	Role of hepcidin as a central regulator of systemic iron homeostasis.	81
10	Effect of inflammatory cytokine and hepcidin in iron transport from the reticuloendothelial system to bone marrow.	83
11	Type of anemia in relation with the ferritin level.	89
12	Assesing iron status.	93

Figure No	Title	Page No
13	With the incorporation of 2 additional carbohydrate chains, the half life of darbepoetin alfa is 3 times longer than the rHuEPO. Reprinted with permission from Nature Biotechnology.	96
14	Ling's group examined the effect of extending the darbepoetin alfa dosing to once a month in patients with CKD stages 3 or 4 who were not on dialysis.	97
15	Depression and its effect on medical outcomes.	102
16	Comparison of muscle wasting among patients with different grades of pain and disability.	128
17	Correlation between deformity with different grades of pain & disability.	129
18	The correlation between crepitations of knee & other joints with different grades of pain and disability.	129
19	Correlation between decrease of muscle power with different grades of pain & disability.	130
20	Correlation between limitation of movement with grades of pain and disability.	130
21	Coorelation between glove & stoke hypothesia with different grades of pain & disability.	131
22	Causes of ESKD across the world.	134

Introduction

Musculoskeletal pain is pain that affects the muscles, ligaments and tendons, along with the bones, it can be acute or chronic. Musculoskeletal pain can be localized in one area, or widespread (*Lorenzo and Canalis, 2008*).

The causes of musculoskeletal pain are variable. Muscle tissue can be damaged with the wear and tear of daily activities. It is due to either traumatic causes as trauma to an area e.g jerking movements, auto accidents, fractures, sprains, dislocations, postural strain, repetitive movements, overuse and prolonged immobilization.

Inflammatory causes as: myositis, fibromyalgia, polymyalgia rheumatica, rheumatoid arthritis, psoriatic arthritis and Reiter"s disease.

Neoplastic causes include: primary malignancy of bone (multiple myeloma, osteosarcoma, Ewing sarcoma) or metastatic malignancy of bone, other conditions include, Disruption of blood supply as in sickle cell anemiaosteoporosis Infection, leukemia and bone infection (osteomyelitis) (*Coleman and Holen, 2008*).

Aim of Work

The aim of this study is to detect the prevalence of musculoskeletal pain among haemodialysis patients & to find out its correlation with serum biochemical markers, the psychological status and work abilities.

Musculoskeletal pain

General organization of musculoskeletal system:

The musculoskeletal framework of the body is composed of at least 213 bones and the associated tendons, ligaments, muscle and cartilages. The skeletal system has variety of important functions, including the support of soft tissues, blood cell production, mineral and lipid storage, and through its relationships with the muscular system, the support and movement of the body as a whole. Skeletal system disorders can thus affect many other systems, skeletal system is in turn influenced by the activities of other systems. For example, weakness or paralysis of skeletal muscles will lead to a weakening of the associated bones.

The four general categories of bones are long bones, short bones, flat bones, and irregular bones (*Authors of Gray's Anatomy, 2004*).

The periosteum is a fibrous connective tissue sheath that surrounds the outer cortical surface of bone, except at joints where bone is lined by articular cartilage, which contains blood vessels, nerve fibers, and osteoblasts and osteoclasts. The periosteum is tightly attached to the outer cortical surface of bone by thick collagenous fibers, called Sharpey's fibers, which extend into underlying bone tissue. The endosteum is a

membranous structure covering the inner surface of cortical bone, trabecular bone, and the blood vessel canals (Volkman's canals) present in bone. The endosteum is in contact with the bone marrow space, trabecular bone, and blood vessel canals and contains blood vessels, osteoblasts, and osteoclast (*Eriksen et al., 2008*).

The adult human skeleton is composed of 80% cortical bone and 20% trabecular bone overall, Cortical bone and trabecular bone are normally formed in a lamellar pattern, in which collagen fibrils are laid down in alternating orientations . Lamellar bone is best seen during microscopic examination with polarized light, during which the lamellar pattern is evident as a result of birefringence. The mechanism by which osteoblasts lay down collagen fibrils in a lamellar pattern is not known, but lamellar bone has significant strength as a result of the alternating orientations of collagen fibrils, similar to plywood. The normal lamellar pattern is absent in woven bone, in which the collagen fibrils are laid down in a disorganized manner. Woven bone is weaker than lamellar bone. Woven bone is normally produced during formation of primary bone and may also be seen in high bone turnover state (*Kobayashi et al., 2007*).

The living skeleton is dynamic and undergoing continuous remodeling. The remodeling process involves bone deposition

by osteoblasts and bone resorption by osteoclasts, the net result of the remodeling varies depending on:

1. *The age of the individual:* During development, bone deposition occurs faster than bone resorption, and the skeleton grows larger. At maturity, bone deposition and resorption are in balance; as the aging process continues, the rate of bone deposition declines and the bones become less dense. This gradual weakening, called *osteopenia*, begins at age 30–40 and may ultimately progress to *osteoporosis*.

2. *The applied physical stresses:* Heavily stressed bones become thicker and stronger, and lightly stressed bones become thinner and weaker.

Skeletal weakness can therefore result from muscular disorders, such as *myasthenia gravis* or the *muscular dystrophies*, and conditions that affect CNS motor neurons, such as spinal cord injuries, demyelination disorders, or multiple sclerosis (*IBlair & Athanasou, 2006*).

3. *Circulating hormone levels:* Changing levels of growth hormone, androgens and estrogens, thyroid hormones, parathyroid hormone, and calcitonin increase or decrease the rate of mineral deposition in bone. As a result, many

disorders of the endocrine system will have an impact on the skeletal system. For example:

- Conditions affecting the skin, liver, or kidneys can interfere with calcitriol production.
- Thyroid or parathyroid disorders can alter thyroid hormone, parathyroid hormone, or calcitonin levels.
- Pituitary gland disorders or liver disorders can affect GH or somatomedin production.
- Reproductive system disorders can alter circulating levels of androgens or estrogens

4. *Rates of calcium and phosphate absorption and excretion:*

For bone mass to remain constant, the rate of calcium and phosphate excretion, primarily at the kidneys, must be balanced by the rate of calcium and phosphate absorption at the digestive tract. Problems that affect the calcium and phosphate absorption will have a direct effect on the skeletal system.

5. *Genetic and environmental factors:* Genetic or environmental factors may affect the structure of bone or the remodeling process (*Amling et al., 2007*).