Statistical Assessment of Electrophysiological Pattern among Sudanese Patients in the Period from 2009 to 2014

A Thesis Submitted in Partial Fulfillment Required for
M.Sc in Human Physiology

By: Mohamed Nazar Mohamed Abdalla
Supervisor: Associate Prof. Mohammed Salah Eldin Al Magzoub

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DEDICATION

I dedicate my dissertation work to my family and many friends. A special feeling of gratitude to my loving parents Dr. Nazar and Dr. Amani. And also my brothers Mujahid, Amin and Ali.
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I wish to thank my supervisor prof. Mohamed Salah Al Majzoup who was more than generous with his expertise, his countless hours of reflecting, reading, encouraging, and most of all patience throughout the entire process.

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## Preface

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Abstract

Neurologic disorders are not uncommon in Sudan. The current work is a retrospective observational analytic study aimed to determine the pattern of neurologic disorders in Khartoum.

It was carried out in Elmagzoub Neuroscience clinic faculty of medicine, national ribat university from January 2009 to December 2014. Neurophysiological data (Nerve Conduction Study, Electromyelogram and Evoked Potential tests Results) were collected, processed and analyzed using SPSS 20 (statistical package for social sciences).

The study targeted 3178 patients. The majority of them (70.4%) presented in the age group between 25 years to 64 years old. The mean age at presentation was (38.74 ± 5.65) years with equal male to female ratio. Mononeuropathy was the most common condition (35.30%) with carpal tunnel syndrome comprising nearly half of them. This followed by polyneuropathies (19.06%), Myopathies (9.59%), rededucopathies and plexopathies (6.92%), disorders diagnosed by evoked potentials (3.99%), myasthenia gravis (2.07%), and Motor neuron disease (1.32%) while a minority of patients suffer from other neurological disorders representing (0.25%) . On the other hand 21.46% of patients showed no significant findings.

The current study gives a clue about the neurological deficits as studied electrophysiologicaly. Sudan like many developing countries lacks necessary equipment and trained staff in this field which is essential for the diagnosis of many neurological conditions. Furthermore the service is only available in Khartoum, which is very unsatisfactory for physicians and also patients. Hence the health authorities should pay more weight to solve this problem by establishing a training program for neuroscientist in all states.
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**Abbreviations**

NCS: Nerve conduction study.

EMG: Electromyography.

CTS: Carpal tunnel syndrome.

BP: Brachial plexus.

GBS: Guillain-Barre syndrome.

MG: Myasthenia gravis.

DM: Dermatomyositis.

PM: Polymyositis.

DMD: Duchenne muscular dystrophy
CHAPTER I

INTRODUCTION
1.1 Anatomy of innervation of upper and lower limbs

1.1.1. Innervation of Upper limb:
The motor and sensory supply of the upper limb is provided by the brachial plexus which is formed by the ventral rami of spinal nerves C5-T1. In the posterior triangle of the neck these rami form three trunks from which fibers enter the axilla region to innervate the muscles of the anterior and posterior compartments of the limb. In the axilla cords are formed to split into branches including the five terminal branches listed below. The muscles of the upper limb are innervated segmentally proximal to distal so that the proximal muscles are innervated by higher segments (C5—C6) and the distal muscles are innervated by, lower segments (C8—T1).

Motor innervations of upper limb by the five terminal nerves of the brachial plexus:

• The musculocutaneous nerve innervates all the muscles of the anterior compartment of the arm.
• The median nerve innervates all the muscles of the anterior compartment of the forearm except flexor carpi ulnaris and the ulnar part of the flexor digitorum profundus. It also innervates the three thenar muscles and the first and second lumbricals.
• The ulnar nerve innervates the muscles of the forearm and hand not innervated by the median nerve.
• The axillary nerve innervates the deltoid and teres minor.
• The radial nerve innervates the posterior muscles of the arm and forearm\(^{(1)}\)

The dorsal scapular nerve innervates rhomboid major and minor.

• The long thoracic nerve innervates serratus anterior.
• The suprascapular nerve innervates supraspinatus and infraspinatus
• The lateral pectoral nerve innervates pectoralis major
• The medial pectoral nerve innervates pectoralis major and minor
• The upper subscapular nerve innervates subscapularis
• The thoracodorsal nerve innervates latissimus dorsi
• The lower subscapular nerve innervates subscapularis and teres major
• The medial antebrachial cutaneous nerve innervates the skin of medial arm
• The lateral antebrachial cutaneous nerve innervates the skin of medial forearm

1.1.1. Innervations of the Lower limb:
The sensory and motor innervation to the lower limb is supplied by the lumbosacral plexus, which is formed by the ventral rami of the lumbar and sacral spinal nerves with additional contributions from the subcostal nerve (T12) and coccygeal nerve (C0). Based on distribution and topography, the lumbosacral plexus is subdivided into the lumbar plexus (T12-L4) and the Sacral plexus (L5-S4); the latter is often further subdivided into the sciatic and pudendal plexuses.

The lumbar plexus is formed lateral to the intervertebral foramina by the ventral rami of the first four lumbar spinal nerves (L1-L4), which all pass through psoas major. The larger branches of the plexus exit the muscle to pass sharply downward to reach the abdominal wall and the thigh (under the inguinal ligament); with the exception of the obturator nerve which pass through the lesser pelvis to reach the medial part of the thigh through the obturator foramen. The nerves of the lumbar plexus pass in front of the hip joint and mainly support the anterior part of the thigh.

The iliohypogastric (T12-L1) and ilioinguinal nerves (L1) emerge from the psoas major near the muscle’s origin, from where they run laterally downward to pass anteriorly above the iliac crest between the transversus abdominis and abdominal internal oblique, and then run above the inguinal ligament. Both nerves give off muscular branches to both these muscles. Iliohypogastric supplies sensory branches to the skin of the lateral hip region, and its terminal branch finally pierces the aponeurosis of the abdominal external oblique above the inguinal ring to supply sensory branches to the skin there. Ilioinguinalis exits through the inguinal ring and supplies sensory branches to the skin above the pubic symphysis and the lateral portion of the scrotum. The genitofemoral nerve (L1, L2) leaves psoas major below the two former nerves, immediately divides into two branches that descends along the muscle’s anterior side. The sensory femoral branch supplies the skin below the inguinal ligament, while the mixed genital branch supplies the skin and muscles around the sex organ. The lateral femoral cutaneous nerve (L2, L3) leaves psoas major laterally below the previous nerve, runs obliquely and laterally downward above the
iliacus, exits the pelvic area near the iliac spine, and supplies the skin of the anterior thigh.

The obturator nerve (L2-L4) passes medially behind psoas major to exit the pelvis through the obturator canal, after which it gives off branches to obturator externus and divides into two branches passing behind and in front of adductor brevis to supply motor innervation to all the other adductor muscles. The anterior branch also supplies sensory nerves to the skin on a small area on the distal medial aspect of the thigh. The femoral nerve (L2-L4) is the largest and longest of the nerves of the lumbar plexus. It supplies motor innervation to iliopsoas, pectineus, sartorius, and quadriceps; and sensory branches to the anterior thigh, medial lower leg, and posterior foot.

The nerves of the sacral plexus pass behind the hip joint to innervate the posterior part of the thigh, most of the lower leg, and the foot. The superior (L4-S 1) and inferior gluteal nerves (L5-S2) innervate the gluteus muscles and the tensor fasciae latae. The posterior femoral cutaneous nerve (S1-S3) contributes sensory branches to the skin on the posterior thigh. The sciatic nerve (L4-S3), the largest and longest nerve in the human body, leaves the pelvis through the greater sciatic foramen. In the posterior thigh it first gives off branches to the short head of the biceps femoris and then divides into the tibial (L4-S3) and common fibular nerves (L4-S2). The fibular nerve continues down on the medial side of biceps femoris, winds around the fibular neck and enters the front of the lower leg. There it divides into a deep and a superficial terminal branch. The superficial branch supplies the peroneus muscles and the deep branch enters the extensor compartment; both branches reaches into the dorsal foot. In the thigh, the tibial nerve gives off branches to semitendinosus, semimembranosus, adductor magnus, and the long head of the biceps femoris. The nerve then runs straight down the back of the leg, through the popliteal fossa to supply the ankle flexors on the back of the lower leg and then continues down to supply all the muscles in the sole of the foot. The pudendal (S2-S4) and coccygeal nerves (S5-Co2) supply the muscles of the pelvic floor and the surrounding skin. The lumbosacral trunk is a communicating branch passing between the sacral and lumbar plexuses containing ventral fibers from L4. The coccygeal nerve, the
last spinal nerve, emerges from the sacral hiatus, unites with the ventral rami of the two last sacral nerves, and forms the coccygeal plexus. (2)

1.2. Physiology of nerve and muscle:
The basic unit of living tissue is the cell. Cells are specialized in their anatomy and physiology to perform different tasks. All cells exhibit a voltage difference across the cell membrane. Nerve cells and muscle cells are excitable. Their cell membrane can produce electrochemical impulses and conduct them along the membrane. In muscle cells, this electric phenomenon is also associated with the contraction of the cell. In other cells, such as gland cells and ciliated cells, it is believed that the membrane voltage is important to the execution of cell function.

The origin of the membrane voltage is the same in nerve cells as in muscle cells. In both cell types, the membrane generates an impulse as a consequence of excitation. This impulse propagates in both cell types in the same manner. The following is a short introduction to the anatomy and physiology of nerve cells.

1.2.1 Nerve Cell:
1.2.1.1 The Main Parts of the Nerve Cell:
The nerve cell may be divided on the basis of its structure and function into three main parts: The cell body, also called the soma; numerous short processes of the soma, called the dendrites; and the single long nerve fiber called the axon. The body of a nerve cell is similar to that of all other cells. The cell body generally includes the nucleus, mitochondria, endoplasmic reticulum, ribosomes, and other organelles. Nerve cells are about 70 - 80% water; the dry material is about 80% proteins and 20% lipid. The cell volume varies between 600 and 70,000 µm$^3$ (3). The short processes of the cell body, the dendrites, receive impulses from other cells and transfer them to the cell body (afferent signals). The effect of these impulses may be excitatory or inhibitory. A cortical neuron may receive impulses from tens or even hundreds of thousands of neurons (4).

The long nerve fiber, the axon, transfers the signal from the cell body to another nerve or to a muscle cell. Mammalian axons are usually about 1 - 20 µm in diameter. Some axons in larger animals may be several meters in length. The axon may be covered with an
insulating layer called the myelin sheath, which is formed by Schwann cells (named for the German physiologist Theodor Schwann, 1810-1882, who first observed the myelin sheath in 1838). The myelin sheath is not continuous but divided into sections, separated at regular intervals by the nodes of Ranvier (named for the French anatomist Louis Antoine Ranvier, 1834-1922, who observed them in 1878).

1.2.1.2 The Cell Membrane:
The cell is enclosed by a cell membrane whose thickness is about 7.5 - 10.0 nm. Its structure and composition resemble a soap-bubble film since one of its major constituents, fatty acids, has that appearance \(^{(5)}\). The fatty acids that constitute most of the cell membrane are called phosphoglycerides. A phosphoglyceride consists of phosphoric acid and fatty acids called glycerides. The head of this molecule, the phosphoglyceride, is hydrophilic. The fatty acids have tails consisting of hydrocarbon chains which are hydrophobic (repelled by water). If fatty acid molecules are placed in water, they form little clumps with the acid heads that are attracted to water on the outside and the hydrocarbon tails that are repelled by water on the inside. If these molecules are placed very carefully on a water surface they orient themselves so that all acid heads are in the water and all hydrocarbon tails protrude from them. If another layer of molecules were added and more water put on top, the hydrocarbon tails would line up with those from the first layer to form a double (two molecules thick) layer. The acid heads would protrude into the water on each side and the hydrocarbons would fill the space between. This bilayer is the basic structure of the cell membrane.

From the bioelectric viewpoint the ionic channels constitute an important part of the cell membrane. These are macromolecular pores through which sodium, potassium, and chloride ions flow through the membrane. The flow of these ions forms the basis of bioelectric phenomena.

1.2.1.3 The Synapse:
The junction between an axon and the next cell with which it communicates is called the synapse. Information proceeds from the cell body unidirectional over the synapse, first along the axon and then across the synapse to the next nerve or muscle cell. The part of
the synapse that is on the side of the axon is called the presynaptic terminal; that part on
the side of the adjacent cell is called the postsynaptic terminal. Between these terminals
there exists a gap, the synaptic cleft, with a thickness of 10 - 50 nm. The fact that the
impulse transfers across the synapse only in one direction, from the presynaptic terminal
to the postsynaptic terminal, is due to the release of a chemical transmitter by the
presynaptic cell. This transmitter, when released, activates the postsynaptic terminal. The
synapse between a motor nerve and the muscle it innervates is called the neuromuscular
junction.

1.2.2 MUSCLE CELL:

There are three types of muscles in the body:

- Smooth muscle.
- Striated muscle (skeletal muscle).
- Cardiac muscle.

**Smooth muscles** are involuntary (i.e., they cannot be controlled voluntarily). Their cells
have a variable length but are in the order of 0.1 mm. Smooth muscles exist for example
in the digestive tract, in the wall of the trachea, uterus, and bladder. The contraction of
smooth muscle is controlled from the brain through the autonomic nervous system.

**Striated muscles** are also called skeletal muscles because of their anatomical location,
are formed from a large number of muscle fibers that range in length from 1 to 40 mm and
in diameter from 0.01 to 0.1 mm. Each fiber forms a (muscle) cell and is distinguished by
the presence of alternating dark and light bands. This is the origin of the description
"striated," as an alternate terminology of skeletal muscle. The striated muscle fiber
corresponds to an (unmyelinated) nerve fiber but is distinguished electrophysiologically
from nerve by the presence of a periodic transverse tubular system (TTS), a complex
structure that, in effect continues the surface membrane into the interior of the muscle.
Propagation of the impulse over the surface membrane continues radially into the fiber via
the TTS, and forms the trigger of myofibrillar contraction. The presence of the TTS affects
conduction of the muscle fiber so that it differs (although only slightly) from propagation
on an (unmyelinated) nerve fiber. Striated muscles are connected to the bones via
tendons. Such muscles are voluntary and form an essential part of the organ of support and motion.

**Cardiac muscle** is also striated, but differs in other ways from skeletal muscle: not only is it involuntary, but also when excited it generates a much longer electric impulse than does skeletal muscle, lasting about 300 m.sec. Correspondingly, the mechanical contraction also lasts longer. Furthermore cardiac muscle has a special property: The electric activity of one muscle cell spreads to all other surrounding muscle cells, owing to an elaborate system of intercellular junctions.

1.2.3 BIOELECTRIC FUNCTION OF THE NERVE CELL:
The membrane voltage (transmembrane voltage) \( V_m \) of an excitable cell is defined as the potential at the inner surface \( \phi_i \) relative to that at the outer \( \phi_o \) surface of the membrane, i.e. \( V_m = (\phi_i) - (\phi_o) \). This definition is independent of the cause of the potential, and whether the membrane voltage is constant, periodic, or nonperiodic in behavior. Fluctuations in the membrane potential may be classified according to their character in many different ways. According to Bullock, these transmembrane potentials may be resolved into a resting potential and potential changes due to activity. The latter may be classified into three different types:

1. Pacemaker potentials: the intrinsic activity of the cell which occurs without external excitation.

2. Transducer potentials across the membrane, due to external events. These include generator potentials caused by receptors or synaptic potential changes arising at synapses. Both subtypes can be inhibitory or excitatory.

3. As a consequence of transducer potentials, further response will arise. If the magnitude does not exceed the threshold, the response will be nonpropagating (electrotonic). If the response is great enough, a nerve impulse (action potential impulse) will be produced which obeys the all-or-none law and proceeds unattenuated along the axon or fiber.
1.2.4 EXCITABILITY OF NERVE CELL:
If a nerve cell is stimulated the transmembrane voltage necessarily changes. The stimulation may be excitatory (i.e., depolarizing; characterized by a change of the potential inside the cell relative to the outside in the positive direction, and hence by a decrease in the normally negative resting voltage) or inhibitory (i.e., hyperpolarizing, characterized by a change in the potential inside the cell relative to the outside in the negative direction, and hence by an increase in the magnitude of the membrane voltage). After stimulation the membrane voltage returns to its original resting value. If the membrane stimulus is insufficient to cause the transmembrane potential to reach the threshold, then the membrane will not activate. The response of the membrane to this kind of stimulus is essentially passive. Notable research on membrane behavior under subthreshold conditions has been performed by Lorente and Davis (6) (7). If the excitatory stimulus is strong enough, the transmembrane potential reaches the threshold and the membrane produces a characteristic electric impulse, the nerve impulse. This potential response follows a characteristic form regardless of the strength of the trans-threshold stimulus. It is said that the action impulse of an activated membrane follows an all-or-none law. An inhibitory stimulus increases the amount of concurrent excitatory stimulus necessary for achieving the threshold. The electric recording of the nerve impulse is called the action potential. If the nerve impulse is recorded magnetically, it may be called an action current.

1.2.5 THE GENERATION OF THE ACTIVATION:
The generation of the activation is discussed only in general terms. The concentration of sodium ions (Na\(^+\)) is about 10 times higher outside the membrane than inside, whereas the concentration of the potassium (K\(^+\)) ions is about 30 times higher inside as compared to outside. When the membrane is stimulated so that the transmembrane potential rises about 20 mV and reaches the threshold - that is, when the membrane voltage changes from -70 mV to about -50 mV (these are illustrative and common numerical values) - the sodium and potassium ionic permeability of the membrane will change. The sodium ion permeability increases very rapidly at first, allowing sodium ions to flow from outside to inside, making the inside more positive. The inside reaches a potential of about +20 mV. After that, the more slowly increasing potassium ion permeability allows potassium ions to
flow from inside to outside, thus returning the intracellular potential to its resting value. The maximum excursion of the membrane voltage during activation is about 100 mV; the duration of the nerve impulse is around 1 ms, while at rest, following activation, the Na-K pump restores the ion concentrations inside and outside the membrane to their original values.

1.2.6 CONCEPTS ASSOCIATED WITH THE ACTIVATION PROCESS:
Whether an excitatory cell is activated depends largely on the strength and duration of the stimulus. The membrane potential may reach the threshold by a short, strong stimulus or a longer, weaker stimulus. The smallest current adequate to initiate activation is called the rheobasic current or rheobase. Theoretically the rheobasic current needs an infinite duration to trigger activation. The time needed to excite the cell with twice rheobase current is called chronaxy. Accommodation and habituation denote the adaptation of the cell to a continuing or repetitive stimulus. This is characterized by a rise in the excitation threshold. Facilitation denotes an increase in the excitability of the cell; correspondingly, there is a decrease in the threshold. Latency denotes the delay between two events. In the present context it refers to the time between application of a stimulus pulse and the beginning of the activation. Once activation has been initiated, the membrane is insensitive to new stimuli, no matter how large the magnitude. This phase is called the absolute refractory period. Near the end of the activation impulse, the cell may be activated, but only with a stimulus stronger than normal. This phase is called the relative refractory period.

The activation process encompasses certain specifics such as currents, potentials, conductivities, concentrations, ion flows, and so on. The term action impulse describes the whole process. When activation occurs in a nerve cell, it is called a nerve impulse; correspondingly, in a muscle cell, it is called a muscle impulse. The bioelectric measurements focus on the electric potential difference across the membrane; thus the electric measurement of the action impulse is called the action potential that describes the behavior of the membrane potential during the activation. Consequently we speak for instance of excitatory postsynaptic potentials (EPSP) and inhibitory postsynaptic potentials (IPSP). In bio-magnetic measurements it is the electric current that is the
source of the magnetic field. Therefore it is logical to use the term action current to refer to the source of the bio-magnetic signal during the action impulse.

1.2.7. CONDUCTION OF THE NERVE IMPULSE IN AN AXON:
The activation propagates in an axon as an unattenuated nerve impulse was proposed by Ludving Hermann (1872,1905). He suggested that the potential difference between excited and unexcited regions of an axon would cause small currents, now called local circuit currents to flow between them in such a direction that they stimulate the unexcited region\(^8\).

Although excitatory inputs may be seen in the dendrites and/or soma, activation originates normally only in the soma. Activation in the form of the nerve impulse (action potential) is first seen in the root of the axon - the initial segment of the axon, often called the axon hillock. From there it propagates along the axon. If excitation is initiated artificially somewhere along the axon, propagation then takes place in both directions from the stimulus site. The conduction velocity depends on the electric properties and the geometry of the axon.

An important physical property of the membrane is the change in sodium conductance due to activation. The higher the maximum value achieved by the sodium conductance, the higher the maximum value of the sodium ion current and the higher the rate of change in the membrane voltage. The result is a higher gradient of voltage, increased local currents, faster excitation, and increased conduction velocity. The decrease in the threshold potential facilitates the triggering of the activation process.

The capacitance of the membrane per unit length determines the amount of charge required to achieve a certain potential and therefore affects the time needed to reach the threshold. Large capacitance values with other parameters remaining the same which mean a slower conduction velocity. The velocity also depends on the resistivity of the medium inside and outside the membrane since these also affect the depolarization time constant. The smaller the resistance, the smaller the time constant and the faster the conduction velocity. The temperature greatly affects the time constant of the sodium conductance; a decrease in temperature decreases the conduction velocity.
The above effects are reflected in an expression derived by Muler and Markin using an idealized nonlinear ionic current function. For the velocity of the propagating nerve impulse in unmyelinated axon \(^{(9)}\).

1.3. Pathology of Peripheral nerve, neuromuscular junction and muscles:

There are variable pathological processes affecting normal nerves, these include:

1.3.1.1. Inflammation:

Neuritis is a general term for inflammation of a nerve or the general inflammation of the peripheral nervous system. Symptoms depend on the nerves involved, but may include pain, paresthesia (pins-and-needles), paresis (weakness), hypoesthesia (numbness), anesthetia, paralysis, wasting, and disappearance of the reflexes.

Causes of neuritis include:

Physical injury, Cancer, Celiac disease, Diabetes, hypothyroidism, porphyria, Vitamin B12 deficiency, infection: like diphtheria, herpes zoster, leprosy, Lyme disease. Chemical injury such as chemotherapy, radiation therapy. Underlying conditions including: alcoholism, autoimmune disease, Guillain-Barre syndrome, Beriberi (vitamin B1 deficiency). \(^{(10)}\)

Types of neuritis include:

- Brachial neuritis
- Cranial neuritis such as Bell's palsy
- Optic neuritis
- Vestibular neuritis
- Wartenberg's migratory sensory neuropathy
- Vitamin B6 deficiency and toxicity

1.3.1.2. Degeneration:

Axonal injuries initially lead to acute axonal degeneration, which is rapid separation of the proximal and distal ends within 30 minutes of injury. Degeneration follows with swelling of the axolemma. There are two types:
**Anterograde** degeneration (Wallerian Degeneration) Affecting the:

- Injured neuron
- Neurons functionally connected to the injured neuron

**Retrograde** Degeneration extends up to the first node of Ranvier proximal to the injury site as follow:

- Swelling of the cell
- Displacement of the nucleus to periphery
- Fragmentation and reduction of Golgi apparatus
- Disappearance of neurofibrils

**Wallerian degeneration:**
Process that results when a nerve fiber is cut or crushed in which the part of the axon separated from the neuron's cell body. Pre-degeneration reactions:

- Decentralization of the nucleus
- Increased ribosomes surrounding the nucleus
- Immune response:

Macrophages start attacking the Schwann cells of the distal segment

- Nervous system reaction:

All adjacent neurons start extending sprouts of their axons. The axon of the distal segment is broken down by enzymes. (11) Pathophysiology:

- Axonal degeneration: Axis cylinder (axolemma) swells and breaks up into small pieces. The axon of the distal segment is broken down by enzymes. The products of this action is carried by retrograde transport to the soma then debris appear in the space occupied by axis cylinder and the myelin sheath disintegrate into fat droplets.

- Myelin clearance: Immune response, macrophages start attacking the Schwann cells of the distal segment. Macrophages invade and remove the debris of axis cylinder. (12)
1.3.1.3. Metabolic Neuropathy:

Background
The term metabolic neuropathy includes a wide spectrum of peripheral nerve disorders associated with systemic diseases of metabolic origin. These diseases include diabetes mellitus, hypoglycemia, uremia, hypothyroidism, hepatic failure, polycythemia, amyloidosis, acromegaly, and porphyria, disorders of lipid/glycolipid metabolism, nutritional/vitamin deficiencies, and mitochondrial disorders, among others. The common hallmark of these diseases is involvement of peripheral nerves by alteration of the structure or function of myelin and axons due to metabolic pathway dysregulation.

Diabetic mellitus is the most common cause of metabolic neuropathy, followed by uremia.

Pathophysiology:
Little is known about the mechanisms underlying metabolic peripheral neuropathy. Metabolic impairment causes demyelination or axonal degeneration.

Diabetic polyneuropathy; although controversial, most studies suggest that diabetic polyneuropathy has a multifactorial etiology. Results from the diabetes control and Complications Trial (DCCT) demonstrated that hyperglycemia and insulin deficiency contribute to the development of diabetic neuropathy and that glycaemia reduction lowers the risk of developing diabetic neuropathy by 60% over 5 years\(^{13}\)\(^{14}\). Decreased bioavailability of systemic insulin in diabetes may contribute to more severe axonal atrophy or loss. Different levels of involvement of peripheral nerve are found in type 1 and type 2 diabetes, with milder compromise in type 2\(^{15}\)\(^{16}\). Studies in rats have demonstrated involvement of the polyol pathway. Myoinositol and taurine depletion have been associated with reduced \(\text{Na}^+/\text{K}^+\)-ATPase activity and decreased nerve conduction velocities (NCVs), all of which are corrected by aldose reductase inhibitors in rat studies. Recent studies have suggested that aldose reductase inhibitors may also improve NCVs and protect small sensory fibers from degeneration. Unfortunately, treatment with these agents so far has failed to show any significant benefits in humans.

Sural nerve biopsies from patients with diabetes have demonstrated changes suggestive of microvascular insufficiency, including membrane basement thickening, endothelial cell
proliferation, and vessel occlusions (17). Rats with diabetes have been shown to have reduced blood flow to the nerves. Ischemia from vascular disease induces oxidative stress and injury to nerves via an increase in the production of reactive oxygen species. Some studies have suggested that antioxidant therapy may improve NCVs in diabetic neuropathy. These findings suggest that the metabolic and vascular hypotheses may be linked mechanistically.

Another mechanism in diabetic neuropathy is impaired neurotrophic support. Nerve growth factor (NGF) and other grow factors, such as NT3, IGF-I, and IGF-II, may be decreased in tissues affected by diabetic neuropathy. Other factors such as abnormalities in vasoactive substances and nonenzymatic glycation have demonstrated possible involvement in diabetic neuropathy development.

A glycoprotein called laminin promotes neurite extension in cultured neurons. Lack of expression of the laminin beta2 gene may contribute to the pathogenesis of diabetic neuropathy.

Recent studies suggest that microvasculitis and ischemia may play significant roles in development of diabetic lumbosacral radiculoplexoneuropathy. (18)

A role for hypoglycemia has also been demonstrated; peripheral nerve damage has been demonstrated in insulinoma and in animal models of insulin-induced hypoglycemia.

**Uremic polyneuropathy:**

In uremic polyneuropathy, conduction velocity slowing is believed to result from inhibition of axolemma-bound Na+/K+ -ATPase by uremic toxins leading to intracellular sodium accumulation and altered resting membrane potentials. Eventually this results in axonal degeneration with secondary segmental demyelination.

**Thyroid neuropathy:**

Little is known about thyroid neuropathy but studies have shown microvascular and endoneurial ischemic involvement like that in diabetes. In rats with hypothyroidism no significant changes of NCVs occurred 5 months after onset but alterations in latencies in
brainstem evoked potentials have been demonstrated. The earliest observation was the deposit of mucopolysaccharide-protein complexes within the endoneurium and perineurium, but these studies await confirmation. Reductions in myelinated fibers, mostly of large diameter, and Renaut bodies have been noted. Other studies have shown axonal degeneration. Rarely hyperthyroidism may be associated with polyneuropathy. (19)

1.3.2. Neuromuscular junction pathology:
The neuromuscular junction is a specialized synapse between a neuron and the muscle it innervates. It allows efferent signals from the nervous system to contact muscle fibers causing them to contract. In vertebrates, the neuromuscular junction is always excitatory, therefore to stop contraction of the muscle. Inhibition must occur at the level of the efferent motor neuron. In other words the inhibition must occur at the level of the spinal cord.

Release of acetylcholine vesicles from the presynaptic terminal occurs only after adequate depolarization of the efferent nerve. Once a motor nerve action potential reaches the presynaptic nerve terminal it causes an increase in intracellular calcium concentration by causing an increase in ion conductance through voltage gated calcium channels. This increase in calcium concentration allows the acetylcholine vesicles to fuse with the plasma membrane at the presynaptic membrane, in a process called exocytosis, thus releasing acetylcholine into the synapse. Once acetylcholine is present in the synapse it is able to bind to nicotinic acetylcholine receptors increasing conductance of certain cations, sodium and potassium in the postsynaptic membrane and producing an excitatory end plate-current. As cations flow into the postsynaptic cell, it causes a depolarization, as the membrane voltage increases above normal resting potential. If the signal is of sufficient magnitude, then an action potential will be generated postsynaptically. The action potential will propagate through the sarcolemma to the interior of the muscle fibers eventually leading to an increase in intracellular calcium levels and subsequently initiating the process of excitation—contraction coupling. Once coupling begins it allows the sarcomeres of the muscles to shorten, thus leading to the contraction of the muscle.
Neuromuscular junction diseases are a result of a malfunction in one or more steps of the above pathway. As a result normal functioning can be completely or partially inhibited with the symptoms largely presenting themselves as problems in mobility and muscle contraction as expected from disorders in motor end plates. Neuromuscular junction diseases can also be referred to as end plate diseases or disorders.

Among neuromuscular diseases some can be autoimmune disease or hereditary disorders. They can affect either presynaptic mechanisms or postsynaptic mechanisms preventing the junction from functioning normally. The most studied diseases affecting the human acetylcholine receptor are myasthenia gravis and some forms of congenital myasthenic syndrome. Other diseases include the Lambert-Eaton syndrome and botulism.

1.3.2.1. Myasthenia gravis:
It is a neuromuscular disease that leads to fluctuating muscle weakness and fatigue. In the most common cases muscle weakness is caused by circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction, inhibiting the excitatory effects of the neurotransmitter acetylcholine on nicotinic receptors at neuromuscular junctions. Alternatively in a much rarer form muscle weakness is caused by a genetic defect in some portion of the neuromuscular junction that is inherited at birth as opposed to developing through passive transmission from the mother's immune system at birth or through autoimmunity later in life. (20)

Myasthenia is treated with medications such as acetylcholinesterase or immunosuppressants and in selected cases thymectomy. The disease is diagnosed in 3 to 30 people per million per year. Diagnosis is becoming more common due to increased awareness. (21)

Myasthenia gravis is believed to be caused by variations in certain genes. The antibody in myasthenia gravis attacks normal human protein, targeting a protein called an acetylcholine receptor or a related protein called a muscle-specific kinase. (22)
Human leukocyte antigens have been associated with MG receptibility. Many of these genes are present among other autoimmune diseases. Relatives of MG patients have a higher percentage of other immune disorders. \(^{(23)}\)

The thymus gland cells form part of the body's immune system. In those with myasthenia gravis the thymus gland is large and abnormal. It sometimes contains clusters of immune cells which indicate lymphoid hyperplasia and it is believed that the thymus gland may give wrong instructions to immune cells. \(^{(24)}\)

**Associated conditions:**
Myasthenia gravis is associated with various autoimmune diseases, including: \(^{(25)}\) \(^{(26)}\) \(^{(27)}\)

- Thymoma
- Thyroid diseases
- Diabetes
- Systemic lupus erythematos
- Preecious anaemia
- Rheumatoid arthritis

**Diagnosis:**

Blood tests:

If the diagnosis is suspected serology can be performed:

- One test is for antibodies against the acetylcholine receptor, \(^{(28)}\) the test has a reasonable sensitivity of 80-96%, but in ocular myasthenia the sensitivity falls to 50%.

- A proportion of the patients without antibodies against the acetylcholine receptor have antibodies against the MuSK protein. \(^{(29)}\)

- For Lambert-Eaton syndrome Ca channel gated antibodies.

**Electro-diagnostics:**
Muscle fibers of patients with MG are easily fatigued and a test called the repetitive nerve stimulation test can be performed. In single-fiber electromyography, which is considered to be the most sensitive (although not the most specific) test for MG. A small diameter needle electrode is inserted into different areas of a particular muscle to record the action potentials from several samplings of different individual muscle fibers. Two muscle fibers belonging to the same motor unit are identified, and the temporal variability in their firing patterns is measured. Frequency and proportion of particular abnormal action potential patterns, called "jitter" and "blocking", are diagnostic. Jitter refers to the abnormal variation in the time interval between action potentials of adjacent muscle fibers in the same motor unit. Blocking refers to the failure of nerve impulses to elicit action potentials in adjacent muscle fibers of the same motor unit.\(^{(30)}\)

**Ice test:**
Applying ice for two to five minutes to the muscles reportedly has a sensitivity and specificity of 76.9% to 98.3%, respectively, for the identification of MG. Acetylcholinesterase is thought to be inhibited at the lower temperature, and this is the basis for this diagnostic test. This generally is performed on the eyelids when a ptosis is present and is deemed positive if there is a >2mm raise in the eyelid after the ice is removed.\(^{(31)}\)

**Edrophonium test:**
This test requires the intravenous administration of edrophonium chloride or neostigmine drugs that block the breakdown of acetylcholine by cholinesterase (acetylcholinesterase inhibitors)\(^{(32)}\). This test is cautiously used usually in the I.C.U as it causes bradycardia which requires attention\(^{(33)}\)(34).

1.3.2. 2. Lambert-Eaton myasthenic syndrome (LEMS):
Lambert-Eaton myasthenic syndrome (LEMS) is similar to myasthenia gravis in that it is an immune-mediated response acting against a specific protein in the neuromuscular junction. The difference is that LEMS is a result of an autoimmune response on the voltage gated calcium channels of the presynaptic membrane. The antibodies attack the voltage gated calcium channels of the P/Q type. Abnormal activity of this ion channel, which usually causes the initiates the process of acetylcholine vesicles from the
presynaptic membrane once the membrane is sufficiently depolarized, causes less acetylcholine to be released into the synapse. LEMS is about 20 times rarer than myasthenia gravis.

LEMS also differs from myasthenia gravis in that it is usually associated with small-cell lung cancer, which is present in 60% percent of patients. It seems that as cancer develops, the body will begin to develop antibodies against the cancer, and in some cases the antibodies can also attack the calcium channels present at the presynaptic membrane. In the cases where no cancer is present in the patient, there is usually an underlying different autoimmune disease which causes the immune system to become hyperactive attacking its own antigens. (35)

1.3.2.3. Neuromyotonia:
Neuromyotonia is classified into three types. The most common form of this disease is acquired neuromyotonia which is the result of an autoimmune attack on rectifier voltage-gated potassium channels. This causes the presynaptic membrane to remain hyperpolarized making it difficult for adequate depolarizations to occur.

1.3.3. Pathology of Muscles disorders:
There are two major common muscle disorders:

1.3.3.1. Polymyositis (PM) ("inflammation of many muscles") is a type of chronic inflammation of the muscles (inflammatory myopathy) related to dermatomyositis and inclusion body myositis.

Signs and Symptoms:
Symptoms include pain with marked weakness and/or loss of muscle mass in the muscles of the head, neck, torso and upper arms and legs. The hip extensors are often severely affected leading to particular difficulty in ascending stairs and rising from a seated position. Dysphagia or other problems with esophageal motility occur in as many as 1/3 of patients. Low grade fever and peripheral adenopathy may be present. Foot drop in one or both feet can be a symptom of advanced polymyositis and inclusion body myositis. Polymyositis is also associated rarely with interstitial lung disease.
Polymyositis may represent a modest increased risk for non-Hodgkin lymphoma and lung and bladder cancers. (36)

Polymyositis tends to become evident in adulthood presenting with bilateral proximal muscle weakness often noted in the upper legs due to early fatigue while walking. Sometimes the weakness presents itself as an inability to rise from a seated position without help or an inability to raise one's arms above one's head. The weakness is generally progressive, accompanied by lymphocytic inflammation (mainly cytotoxic T cells).

Polymyositis like dermatomyositis strikes females with greater frequency than males. The skin involvement of dermatomyositis is absent in polymyositis.

**Causes:**
The cause of polymyositis is unknown and may involve viruses and autoimmune factors. Cancer may trigger polymyositis and dermatomyositis possibly through an immune reaction against cancer that also attacks a component of muscles. (37)

**Diagnosis:**
Diagnosis is depend on, including history and physical examination, elevation of creatine kinase, electromyograph (EMG) alteration, and a positive muscle biopsy.

Sporadic inclusion body myositis (sIBM): IBM is often confused with polymyositis or dermatomyositis that does not respond to treatment. SIBM comes on over months to years while polymyositis comes on over weeks to months. Polymyositis tends to respond well to treatment at least initially but IBM does not.

**Treatment:**
The first line treatment for polymyositis is corticosteroids. Followed with physiotherapy.

**1.3.3.2. Muscle dystrophies: (Muscular dystrophy)**
Muscular dystrophy (MD) is a group of muscle diseases that weaken the musculoskeletal system and hamper locomotion. (38) (39) Muscular dystrophies are characterized by
progressive skeletal muscle weakness, defects in muscle proteins and the death of muscle cells and tissue. (40)

It soon became evident that the disease had more than one form. The other major forms are Becker, limb-girdle, congenital, facioscapulohumeral, myotonic, oculopharyngeal, distal and Emery-Dreifuss muscular dystrophy. (41) Duchenne and Becker muscular dystrophies being caused by a mutation of a gene located on the X chromosome, predominantly affect males, although females can sometimes have severe symptoms as well. Most types of MD are multi-system disorders with manifestations in body systems including the heart, gastrointestinal system, nervous system, endocrine glands, eyes and brain.

Apart from the nine major types of muscular dystrophy listed above, several MD-like conditions have also been identified. Normal intellectual, muscular, behavioral, bowel and sexual function are noticed in individuals with other forms of MD and MD-like conditions. (42) (43)

MD-affected individuals with susceptible intellectual impairment are diagnosed through molecular characteristics but not through problems associated with disability. (44)

However, a third of patients who are severely affected with DMD may have cognitive impairment, behavioral, vision and speech problems.

**Signs and symptoms:**
- Progressive muscular wasting
- Poor balance
- Drooping eyelids
- Atrophy
- Scoliosis (curvature of the spine and the back)
- Inability to walk
- Frequent falls
- Waddling gait
- Calf deformation
- Limited range of movement
• Respiratory difficulty
• Joint contractures
• Cardiomyopathy
• Arrhythmias
• Muscle spasms
• Gowers' sign

Causes:
These conditions are generally inherited, and the different muscular dystrophies follow various inheritance patterns. However, mutations of the dystrophin gene and nutritional defects (with no genetics history) at the prenatal stage are also possible in about 33% of people affected by DMD. The main cause of the Duchenne and Becker types of muscular dystrophy is the muscle tissue’s cytoskeletal impairment to properly create the functional protein dystrophin and dystrophin-associated protein complex.

Dystrophin protein is found in muscle fiber membrane. Its helical nature allows it to act like a spring or shock absorber. Dystrophin links actin in the cytoskeleton and dystroglycans of the muscle cell plasma membrane known as the sarcolemma (extracellular). In addition to mechanical stabilization dystrophin also regulates calcium levels. Recent studies on the interaction of proteins with missense mutations and its neighbors showed high degree of rigidity associated with central hub proteins involved in protein binding and flexible subnetworks having molecular functions involved with calcium.

Types:

Duchenne muscular dystrophy: (DMD),
Duchenne muscular dystrophy (DMD) is the most common childhood form of muscular dystrophy. It generally affects only boys (with extremely rare exceptions), becoming clinically evident when a child begins walking. By age 10 the child may need braces for walking and by age 12. Most patients are unable to walk. Life span ranges from 15 to 45 with few exceptions. In the early 1990s researchers identified the gene for the protein dystrophin which, when absent, causes DMD. The amount of dystrophin correlates with
the severity of the disease (i.e., the less dystrophin present, the more severe the phenotype). Since the gene is on the X chromosome, this disorder affects primarily males and females who are carriers have milder symptoms. Sporadic mutations in this gene occur frequently accounting for a third of cases. The remaining two-thirds of cases are inherited in a recessive pattern.

Dystrophin is part of a complex structure involving several other protein components. The "dystrophin-glycoprotein complex" helps anchor the structural skeleton (cytoskeleton) within the muscle cells, through the outer membrane (sarcolemma) of each, cell to the tissue framework (extracellular matrix) that surrounds each cell. Due to defects in this assembly, contraction of the muscle leads to disruption of the outer membrane of the muscle cells and eventual weakening and wasting of the muscle.

**Becker muscular dystrophy: (DMD),**
Becker muscular dystrophy (BMD) is a less severe variant of Duchenne muscular dystrophy and is caused by the production of a truncated but partially functional form of dystrophin. Survival is usually into old age. (49) Affects only boys (with extremely rare exceptions).

Congenital muscular dystrophy, Age at onset: birth; symptoms include general muscle weakness and possible joint deformities; disease progresses slowly; shortened life span. (50)

**Congenital muscular dystrophy:**
It includes several disorders with a range of symptoms. Muscle degeneration may be mild or severe. Problems may be restricted to skeletal muscle, or muscle degeneration may be paired with effects on the brain and other organ systems. A number of the forms of the congenital muscular dystrophies are caused by defects in proteins that are thought to have some relationship to the dystrophin-glycoprotein complex and to the connections between muscle cells and their surrounding cellular structure. Some forms of congenital muscular dystrophy show severe brain malformations such as lissencephaly and hydrocephalus.

**Distal muscular dystrophy:**
Distal muscular dystrophies' age at onset: 20 to 60 years; symptoms include weakness and wasting of muscles of the hands, forearms, and lower legs; progress is slow and not life-threatening.

**Miyoshi myopathy:**
One of the distal muscular dystrophies which causes initial weakness in the calf muscles and is caused by defects in the same gene responsible for one form of LGMD (Limb Girdle Muscular Dystrophy).

**Emery-Dreifuss muscular dystrophy: (EMD, LMNA),**
Emery-Dreifuss Muscular Dystrophy patients normally present in childhood and the early teenage years with contractures. Clinical signs include muscle weakness and wasting starting in the distal limb muscles and progressing to involve the limb-girdle muscles. Most patients also suffer from cardiac conduction defects and arrhythmias which increase the risk of stroke and sudden death if not treated.

There are three subtypes of Emery-Dreifuss Muscular Dystrophy, distinguishable by their pattern of inheritance: X-Linked, autosomal dominant and autosomal recessive. The X-linked form is the most common. Each type varies in prevalence and symptoms. The disease is caused by mutations in the LMNA gene, or more commonly, the EMD gene. Both genes encode for protein components of the nuclear envelope. However, how these mutations cause the pathogenesis is not well understood. (51)

**Facioscapulohumeral muscular dystrophy, (DUX4),**
Facioscapulohumeral muscular dystrophy (FSHD) initially affects the muscles of the face, shoulders, and upper arms with progressive weakness. Symptoms usually develop in the teenage years. Some affected individuals become severely disabled. The pattern of inheritance is autosomal dominant, but there are a significant number of spontaneous mutations. Seminal research published in August 2010 documents that two defects are needed for FSHD, which for the first time provides a unifying theory for the underlying genetics of FSHD. The first is the deletion of D4Z4 repeats and the second is a "toxic gain of function" of the DUX4 gene. (52) (53)

**Limb-girdle muscular dystrophy: (LGMD)**
Limb-girdle muscular dystrophy (LGMD). It affects both boys and girls. LGMDs all show a similar distribution of muscle weakness, affecting both upper arms and legs. Many forms of LGMD have been identified showing different patterns of inheritance (autosomal recessive vs. autosomal dominant). In an autosomal recessive pattern of inheritance, an individual receives two copies of the defective gene, one from each parent. The recessive LGMDs are more frequent than the dominant forms and usually have childhood or teenage onset. The dominant LGMDs usually show adult onset. Some of the recessive forms have been associated with defects in proteins that make up the dystrophin-glycoprotein complex. Though a person normally leads a normal life with some assistance, in some extreme cases death from LGMD occurs due to cardiopulmonary complications. (54)

Myotonic muscular dystrophy: (DMPK, ZNF9),
Myotonic muscular dystrophy is an autosomal dominant condition that presents with myotonia (delayed relaxation of muscles) as well as muscle wasting and weakness. Myotonic dystrophy varies in severity and manifestations and affects many body systems in addition to skeletal muscles, including the heart, endocrine organs, eyes, and gastrointestinal tract. Myotonic muscular dystrophy type 1 (DM1), also known as Steinert disease, is the most common adult form of muscular dystrophy. It results from the expansion of a short (CTG) repeat in the DNA sequence of the DMPK (myotonic dystrophy protein kinase) gene. Myotonic muscular dystrophy type 2 (DM2) is much rarer and is a result of the expansion of the CCTG repeat in the ZNF9 (zinc finger protein 9) gene. While the exact mechanisms of action are not known, these molecular changes may interfere with the production of important muscle proteins.

Oculopharyngeal muscular dystrophy: (PABPN1),
Oculopharyngeal MD's age at onset: 40 to 70 years; symptoms affect muscles of eyelids, face, and throat followed by pelvic and shoulder muscle weakness, has been attributed to a short repeat expansion in the genome which regulates the translation of some genes into functional proteins.

Diagnosis:
The diagnosis of muscular dystrophy is based on the results of muscle biopsy, increased creatine phosphokinase (CPK3), electromyography, electrocardiography and DNA analysis.

A physical examination and the patient's medical history will help the doctor determine the type of muscular dystrophy. Specific muscle groups are affected by different types of muscular dystrophy.

Often there is a loss of muscle mass which may be hard to see because some types of muscular dystrophy cause a buildup of fat and connective tissue that makes the muscle appear larger which called-pseudohypertrophy. (55)

**Management:**
There is no known cure for muscular dystrophy, although significant headway is being made with antisense oligonucleotides. (56) Physical therapy, occupational therapy, orthotic intervention (e.g., ankle-foot orthosis), speech therapy and orthopedic instruments (e.g., wheelchairs, standing frames and powered mobile arm supports) may be helpful.
Inactivity (such as bed rest, sitting for long periods) and bodybuilding efforts to increase myofibrillar hypertrophy can worsen the disease.

There is no specific treatment for any of the forms of muscular dystrophy. Physiotherapy, aerobic exercise, prednisone supplements may help to prevent contractures and maintain muscle tone in only D.M.D. Orthoses (orthopedic appliances used for support) and corrective orthopedic surgery may be needed to improve the quality of life in some cases. The cardiac problems that occur with Emery-Dreifuss muscular dystrophy and myotonic muscular dystrophy may require a pacemaker.

The myotonia occurring in myotonic muscular dystrophy may be treated with medications such as quinine, phenytoin, or mexiletine, but no actual long term treatment has been found.

**1.3.4. Optic neuropathy:**
It refers to damage of the optic nerve due to any cause. Damage and death of these nerve cells, or neurons, leads to characteristic features of optic neuropathy. The main symptom is loss of vision with colors appearing subtly washed out in the affected eye.

**Electrophysiological tests:**
Visual evoked potential (VEP) measure the cortical activity in response to flash or pattern stimulus. They are abnormal in the presence of any lesion along the anterior visual pathway. VEPs are used commonly in patients with demyelinating disease to detect occult optic nerve dysfunction and to identify a second site of involvement as part of the neurological assessment. A more recent technology, multifocal VEP, has been shown to be of useful values in detecting optic neuritis patients at high-risk patients to develop clinically definite multiple sclerosis (57).

**Acute demyelinating optic neuritis:**
Optic neuritis can be the initial manifestation of multiple sclerosis (MS). Optic neuritis is more common in females with a peak age of onset between 30-40 years. Initiating treatment with beta-la interferon should be strongly considered in high-risk patients (patients with a single demyelinating event who had magnetic resonance imaging (MRI) evidence of previous subclinical disease activity (defined as > or = 2 T2-weighted hyperintense lesions, 1 of which was periventricular or ovoid, on unenhanced MRI scans) (58).since this has been found to decrease the risk of conversion to clinically definite multiple sclerosis by 50%.

Optic neuritis improves in 90% of cases over several weeks to near normal visual acuity. The use of intravenous steroids was found to hasten the visual recovery but not the final visual outcome (59). However, the early use of steroids may be warranted to minimize axonal loss of the optic nerve which has been found to occur early in the disease. (60)

**Inflammatory (non-demyelinating) optic neuropathy:**
This category comprises many entities in which the optic nerve is involved by either an ocular or systemic inflammatory process. Optic disc swelling frequently occurs with posterior uveitis and retinitis. Therefore when evaluating optic disk swelling it is useful to look for evidence of anterior or posterior segment inflammation. Optic neuropathy can
also occur in the context orbital inflammatory disease (orbital pseudo tumor). MRI of the orbit will show inflammation of the optic nerve sheath (optic perineuritis) (61).

The optic nerve can be involved in a variety of systemic auto-immune and infectious disorders such as Neuromyelitis optica sarcoidosis, systemic lupus erythematosus, Behcet's disease inflammatory bowel disease, Sjogren's syndrome Wegener's granulomatosis, syphilis, Lyme disease and cat-scratch disease. (62) (63)

Auto-immune optic neuropathy is a recurrent, steroid-responsive optic neuropathy. The anti-nuclear antibody (ANA) and anti-cardiolipin antibody are frequently positive (64) (65). The diagnosis is made by performing a skin biopsy, which often shows evidence of vasculitis when studied with immune-florescence.

**Hereditary optic neuropathy:**
The hereditary optic neuropathies are a broad category including autosomal inherited diseases (dominant, recessive, X-linked) and diseases caused by inheritance of defective mitochondrial genome. Mitochondrial dysfunction may be a final common pathway among these disorders. (66) (67) Hereditary optic neuropathies can be isolated or associated with other neurological signs and symptoms.

Patients with dominant optic neuropathy (Kjers' type) often present in the first decade of life with bilateral symmetric visual loss. Visual acuity can range from 20/20 to 20/400. (68) Visual field testing frequently reveals bilateral central or cecocentral scotomas. In some cases, a central hemianopic bitemporal visual field defect is found, which in the absence of positive family history may erroneously lead to a search for a chiasmal lesion. Patients will have color vision deficit along the tritan (blue-yellow) axis. The optic disc will show temporal pallor and in some cases severe excavation and cupping. There various responsible genetic mutations occur in the OPA 1 gene located on the chromosome 3 q region. (69)

Recessive optic neuropathy is rare and tends to present in the first year of life. It can be associated with diabetes mellitus, diabetes insipidus, and deafness (Wolfram syndrome). (70) An X-linked optic atrophy has also been described and the genetic mutation has been localized to Xp11.4—Xp11.2 (OPA2). (71) Optic neuropathy can also occur in neurological
conditions such as spinocerebellar degeneration, Friedreich's ataxia, and olivo-ponto-cerebellar atrophy.

Leber's hereditary mitochondrial optic neuropathy (LHON) classically presents with acute unilateral, painless, visual loss. However, some cases may stay asymptomatic or have a chronic course. (72) Sequential bilateral involvement may occur weeks or months later. Visual filed defects tend to be central or cecocentral as the papillo-macular bundle is first and most severely affected. (73) LHON has four primary mitochondrial genome mutations; G11778A, G3460A and T14484C and T10663C. The disease affects males more than females with a ratio of 2.5:1 for the G11778A and G3460A mutation and 6:1 ratio for the T14484C mutation. The frequencies of mutation may vary across different countries and newer mutations have been described worldwide (74) "Some patients may demonstrate neurological manifestations such as peripheral neuropathy, ataxia, dystonia and cardiac conduction defects. (75) These patients fall in the spectrum mitochondrial encephalomyelopathies and their clinical manifestations may vary considerably. (76)
CHAPTER II

METHODOLOGY
2.1. Material and Methods:

2.1.1. Study design: This study is a retrospective observational analytic study.

2.1.2. Study area: The study has been conducted in Khartoum state, Sudan.

2.1.3. Population and sampling: Study population was all Sudanese patients suffering from neurological disorders attended Elmagzoub Neuroscience clinic, Faculty of Medicine, the National Ribat University, Khartoum Sudan. The study was conducted in the period from January 2009 to December 2014. The sample size was 3178 subjects. Neurophysiological data (Nerve Conduction Study, Electromyogram and Evoked Potential tests Results) were collected, processed and analyzed using SPSS 20(statistical package for social sciences).

2.2. Neurophysiological tests:

2.2.1. Nerve conduction study:

Equipment and procedure

Data collected using 4 and 8 channels EMG machines (Viaysis select and quest).

Machines settings: Sensitivity—20 μV/division, Low frequency filter— 20 Hz, High frequency filter—2 kHz, Sweep speed—2 msec./division. Data was saved in a standard Microsoft Excel database. Temperature maintained in the range between 20 and 26°C. Body temperature was recorded from the axilla by a digital thermometer.

Data was collected for the following parameters: distal latency measured from the onset of action potential, peak latency, amplitude of sensory nerve action potential (SNAP) and compound muscle action potential (CMAP) conduction velocity.

Electrodes placement technique

The recording electrodes are performed using adhesive conductive pads placed onto the skin overlying the target muscle. The active electrode is placed over the muscle belly and the reference over an electrically inactive site (usually the muscle tendon) distal to the active electrode. A ground electrode is also placed somewhere between the stimulating (active electrodes) and recording electrodes (the cathode) providing a zero voltage reference point.
2.2.2 Electromyography (EMG):
Electromyography is the clinical study of the electrical activity of muscle fibers individually and collectively and it is often done at the same time as NCS test performed. This electrical activity can be recorded via surface or needle electrodes. It is evaluated during needle insertion, during periods of rest (spontaneous activity), and during periods of voluntary muscle contraction.

Needle Electrodes:
Needle electrodes measure the electric potential difference between two sites. They are usually monopolar or concentric. With the monopolar electrode made of stainless steel needle with a very finely sharpened point covered with insulating material over its entire length except for a 0.5mm exposure at the tip. The needle serves as the active recording site, and a surface electrode placed on the skin some distance away serves as the reference electrode.

Concentric Electrode:
Consist of a cannula with an insulated wire down the middle the active electrode is the small tip of the center wire or wires, and the reference electrode is the outside cannula. If there are two central wires (bipolar) the reference and active electrodes are at the tip and the outside cannula act as the ground.

Single Fiber Electrode:
Used for special studies consisting of 0.5-0.6mm stainless steel cannula with 25µm fine platinum wire inside its hollow shaft.

RECORDING:
The best approach to the electromyographic study of each muscle consists of four separate stages. Each stage is evaluated at multiple recording sites by redirecting the needle after skin insertion at two or more places:

1- Insertional activity
   With insertion of the electrode into a muscle it is normal to see brief bursts of electrical activity due to mechanical irritation and depolarization of muscle fibers that minimally exceed the time of the needle movement (~50 ms). Individually,
these bursts can consist of high frequency of varying shapes and sizes or fibrillations, positive sharp waves, or complex repetitive discharges.

2- Spontaneous activity at complete rest
3- Qualitative or quantitative motor unit action potential (MUAP) waveform analysis during minimal voluntary contraction
4- Recruitment of MUAPs during increasing voluntary muscle contraction to maximal levels (the interference pattern).

The picture seen in a myopathic disorders is very different from a neuropathic one:

Myopathic MUAPs reflect the smaller motor units and are characterized by lower amplitude, shorter duration and increase number of phases unlike the neuropathic MUAPs which is characterized by increase in amplitude.

2.2.3. Evoked potential:
Evoked response is an electrical potential recorded from the nervous system of a human or other animal following presentation of a stimulus as distinct from spontaneous potentials as detected by electroencephalography (EEG), electromyography (EMG), or other electrophysiological recording method. Evoked potential amplitudes tend to be low, ranging from less than a microvolt to several microvolts, compared to tens of microvolts for EEG, millivolts for EMG, and often close to a volt for ECG. To resolve these low-amplitude potentials against the background of ongoing EEG, ECG, EMG, and other biological signals and ambient noise, signal averaging is usually required. The signal is time-locked to the stimulus and most of the noise occurs randomly allowing the noise to be averaged out with averaging of repeated responses. Signals can be recorded from cerebral cortex, brain stem, spinal cord and peripheral nerves. Usually the term "evoked potential" is reserved for responses involving either recording from or stimulation of, central nervous system structures. Thus evoked compound motor action potentials (CMAP) or sensory nerve action potentials (SNAP) as used in nerve conduction studies (NCS) are generally not thought of as evoked potentials though they do meet the above definition.
This test has different types:

- Sensory evoked potentials (SEP) are recorded from the central nervous system following stimulation of sense organs.

- Visual evoked potential (VEP) Electrode placement is extremely important to elicit a good VEP response free of artifacts. In a typical (one channel) setup one electrode is placed 2.5 cm above the inion and a reference electrode is placed at Fz. For a more detailed response two additional electrodes can be placed 2.5 cm to the right and left of Oz.

- VEP Waves: The VEP nomenclature is determined by using capital letters stating whether the peak is positive (P) or negative (N) followed by a number which indicates the average peak latency for that particular wave. For example, P100 is a wave with a positive peak at approximately 100 ms following stimulus onset. And it is a usually measured wave. The average amplitude for VEP waves usually falls between 5 and 10 microvolts.

- Auditory evoked potential: Auditory evoked potential can be used to trace the signal generated by a sound through the ascending auditory pathway. The evoked potential is generated in the cochlea, goes through the cochlear nerve through the cochlear nucleus superior olivary complex, lateral lemniscus, to the inferior colliculus in the midbrain, on to the medial geniculate body and finally to the cortex. Auditory evoked potentials (AEPs) are a subclass of event-related potentials (ERP)s. ERPs are brain responses that are time-locked to some "event" such as a sensory stimulus, a mental event (such as recognition of a target stimulus), or the omission of a stimulus. For AEPs, the "event" is a sound. AEPs (and ERPs) are very small electrical voltage potentials originating from the brain recorded from the scalp in response to an auditory stimulus such as different tones, speech sounds.
• Somatosensory evoked potential Somatosensory Evoked Potentials (SSEPs) are used in neuro-monitoring to assess the function of a patient's spinal cord during surgery. They are recorded by stimulating peripheral nerves, most commonly the tibial nerve, median nerve or ulnar nerve, typically with an electrical stimulus. The response is then recorded from the patient's scalp because of the low amplitude of the signal once it reaches the patient's scalp and the relatively high amount of electrical noise caused by background EEG, scalp muscle EMG or electrical devices in the room, the signal must be averaged. The use of averaging improves the signal-to-noise ratio. Typically in the operating room over 100 and up to 1,000 averages must be used to adequately resolve the evoked potential.
CHAPTER III

RESULTS AND DISCUSSION
RESULTS

3.1. Age and gender:
This study targeted 3178 cases. Gender distribution among the study population was nearly equal as shown in table (1). The mean age group is (38.74 ± 5.65) years, while the majority of them fall in the age group between 25 years to 64 years old table (2).

<table>
<thead>
<tr>
<th>Gender distribution</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1591</td>
<td>50%</td>
</tr>
<tr>
<td>Male</td>
<td>1587</td>
<td>50%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3178</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 1: Gender distribution

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5 years old</td>
<td>71</td>
<td>2.2%</td>
</tr>
<tr>
<td>from 5 to 24 years old</td>
<td>378</td>
<td>11.9%</td>
</tr>
<tr>
<td>from 25 to 44 years old</td>
<td>1135</td>
<td>35.71%</td>
</tr>
<tr>
<td>from 45 to 64 years old</td>
<td>1101</td>
<td>34.64%</td>
</tr>
<tr>
<td>more than 64 years old</td>
<td>493</td>
<td>15.6%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3178</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 2: age groups

3.2. The presenting complains:
The main presenting complains were **Sensory** (numbness, pain and paresthesia) and **Motor** (weakness and wasting) this might be localized or generalized in some conditions. And they were of acute onset or chronic as showed in table (3.1) and (3.2)

<table>
<thead>
<tr>
<th>Cause of the clinical presentation</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic</td>
<td>319</td>
<td>10.03%</td>
</tr>
<tr>
<td>Non Traumatic</td>
<td>2859</td>
<td>89.97%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3178</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 3.1: the clinical presentation

3.3. Types of electrophysiological tests:
Different types of neuro-electrophysiological tests were done, where 67.4 % of the subjects performed the nerve conduction study only, On the other hand, 26.1% did
electromyography together with nerve conduction study test. Distribution of the tests shown in table (4)

<table>
<thead>
<tr>
<th>Types of Tests</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCS</td>
<td>2137</td>
<td>67.3%</td>
</tr>
<tr>
<td>NCS and EMG</td>
<td>833</td>
<td>26.2%</td>
</tr>
<tr>
<td>Evoked Potentials</td>
<td>208</td>
<td>6.5%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3178</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

*Table 4: types of tests done to the subjects*

### 3.4. Pattern of the findings

The tests' led to various types of neurological disorders, 21.46% of the cases depicted normal findings. In contrast, patients suffered from mononeuropathies registered the highest percentage at 35.30% as in table (5)

<table>
<thead>
<tr>
<th>Types of disorder</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal results</td>
<td>682</td>
<td>21.46%</td>
</tr>
<tr>
<td>Mononeuropathies</td>
<td>1122</td>
<td>35.30%</td>
</tr>
<tr>
<td>Polyneuropathies</td>
<td>606</td>
<td>19.06%</td>
</tr>
<tr>
<td>Plexopathies and radiculopathies</td>
<td>220</td>
<td>6.92%</td>
</tr>
<tr>
<td>Muscular disorders</td>
<td>305</td>
<td>9.59%</td>
</tr>
<tr>
<td>Disease of the neuromuscular junction</td>
<td>66</td>
<td>2.07%</td>
</tr>
<tr>
<td>Motor Neuron disorders</td>
<td>42</td>
<td>1.32%</td>
</tr>
<tr>
<td>Disorders diagnosed via evoked potentials</td>
<td>127</td>
<td>3.99%</td>
</tr>
<tr>
<td>Other diseases</td>
<td>8</td>
<td>0.25%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>3178</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

*Table 5: distribution of the findings*

#### 3.4.1. Mononeuropathies:

There were 1122 patients suffered from upper and lower limbs mononeuropathies as illustrated in table (6)
The most affected nerve was the median nerve at the wrist level (Carpel Tunnel Syndrome) at 66.25%. Traumatic lesions are considered and most of them referred from the military hospital due to bullet or gun shot. This is shown in table (7)

<table>
<thead>
<tr>
<th>Types of disorder</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Upper limbs</td>
<td>880</td>
<td>78.43%</td>
</tr>
<tr>
<td>The Lower limbs</td>
<td>242</td>
<td>21.56%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1122</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 6: distribution of Mononeuropathies

### 3.4.1.1. Nerves of the upper limbs:

The most affected nerve was the median nerve at the wrist level (Carpel Tunnel Syndrome) at 66.25%. Traumatic lesions are considered and most of them referred from the military hospital due to bullet or gun shot. This is shown in table (7)

<table>
<thead>
<tr>
<th>Types of disorder</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Traumatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTS</td>
<td>583</td>
<td>67.08%</td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>121</td>
<td>13.92%</td>
</tr>
<tr>
<td>Median nerve (at forearm level)</td>
<td>49</td>
<td>5.63%</td>
</tr>
<tr>
<td>Radial Nerve</td>
<td>44</td>
<td>5.06%</td>
</tr>
<tr>
<td>Posterior interosseous Nerve (at forearm level)</td>
<td>18</td>
<td>2.07%</td>
</tr>
<tr>
<td>Axillary Nerve</td>
<td>14</td>
<td>1.61%</td>
</tr>
<tr>
<td>Musculocutaneous Nerve</td>
<td>4</td>
<td>0.46%</td>
</tr>
<tr>
<td>Subscapular nerve</td>
<td>2</td>
<td>0.23%</td>
</tr>
<tr>
<td>Suprascapular nerve</td>
<td>2</td>
<td>0.23%</td>
</tr>
<tr>
<td>Mixed upper limb nerves</td>
<td>32</td>
<td>3.68%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>869</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 7: distribution of upper limbs Mononeuropathies

Moreover, there were 11 patients with non-traumatic facial nerve injury.

### 3.4.1.2. Nerves of the lower limbs:

Meanwhile, the most affected nerve in the lower limbs are the sciatic nerve and peroneal nerve as shown in table (8)
3.4.2 Polyneuropathies:
19.06% of all cases (3178 patients) suffered from different types of polyneuropathies, the majority were counted as having acquired polyneuropathies as in table (9).

<table>
<thead>
<tr>
<th>Types of disorder</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquired Polyneuropathy</td>
<td>556</td>
<td>91.7%</td>
</tr>
<tr>
<td>Hereditary Polyneuropathy</td>
<td>50</td>
<td>8.3%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>606</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 9: distribution of Polyneuropathies

3.4.2.1 Acquired Polyneuropathies:
They are classified into two groups: showed in table (10)

<table>
<thead>
<tr>
<th>Acquired Polyneuropathies</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axonal polyneuropathy</td>
<td>349</td>
<td>62.77%</td>
</tr>
<tr>
<td>Demyelinating Polyneuropathy</td>
<td>207</td>
<td>37.23%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>556</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 10: distribution of Acquired Polyneuropathies

3.4.2.1.1 Axonal polyneuropathy
There were 270 patients have sensorimotor polyneuropathy and the rest shown in table (11.1)
<table>
<thead>
<tr>
<th>Acquired Polyneuropathies</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensorimotor axonal polyneuropathy</td>
<td>270</td>
<td>77.36%</td>
</tr>
<tr>
<td>Motor axonal Polyneuropathy</td>
<td>64</td>
<td>18.33%</td>
</tr>
<tr>
<td>Sensory axonal Polyneuropathy</td>
<td>15</td>
<td>4.29%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>349</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 11.1: distribution of Axonal Polyneuropathies

### 3.4.2.1. Demyelinating polyneuropathy:

The demyelinating polyneuropathies are Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) and Acute Inflammatory Demyelinating Polyneuropathy (AIDP) (Guillain-Barré syndrome). This is showed in table (11.2)

<table>
<thead>
<tr>
<th>Polyneuropathies</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>CIDP</td>
<td>114</td>
<td>55.07%</td>
</tr>
<tr>
<td>AIDP</td>
<td>93</td>
<td>44.934%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>207</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 11.2: distribution of Demyelinating Polyneuropathies

### 3.4.2.2. Hereditary Polyneuropathies:

In contrast, there were 50 patients with hereditary polyneuropathies. 86.84% of them had HMSN and 13.16% suffer from HMN

### 3.4.3. Plexopathies and Radiculopathies:

There were 220 case have plexopathies and radiculopathies. Most of them are traumatic and due to gun shot and these referred from the military hospital as represented in table (12)

<table>
<thead>
<tr>
<th>Plexopathies and Radiculopathies</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial plexopathies</td>
<td>117</td>
<td>53.18%</td>
</tr>
<tr>
<td>Lumbosacral plexopathies</td>
<td>8</td>
<td>3.63%</td>
</tr>
<tr>
<td>Cervical Radiculopathies</td>
<td>56</td>
<td>25.45%</td>
</tr>
<tr>
<td>Lumbosacral Radiculopathies</td>
<td>39</td>
<td>17.27%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>220</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Figure 12: distribution of Plexopathies and Radiculopathies
3.4.4 Muscular disorders:
Acquired myopathies were dominating and constitute two thirds of all cases which was 205 patients represented in:

3.4.4.1. Acquired muscular disorders:
More than 80% of them were diagnosed with polymyositis and the remaining diseases in figure (2).

![Figure 2: distribution of acquired myopathies](image)

3.4.4.2. Hereditary Muscular disorders:
In addition to the acquired myopathies there were also the hereditary myopathies. The commonest disorders were myotonia dystrophica, limb girdle Muscle Dystrophy and duchenne’ Muscular Dystrophy as in table (13).
3.4.5. Degenerative Motor neuron disorders:
There were fifty four patients with degenerative motor neuron disorders forty two of them had motor neuron disorders; the commonest type is the amyotrophic lateral sclerosis. The remaining twelve suffered from Spinal Muscular Atrophy (SMA).

3.4.6. Neuromuscular junction disorders:
There were 66 cases of myasthenia gravis as a neuromuscular junction disorder elicited by repetitive nerve stimulation (RNS).

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myotoniadystrophica</td>
<td>25</td>
<td>25%</td>
</tr>
<tr>
<td>Limb girdle Muscle Dystrophy</td>
<td>20</td>
<td>20%</td>
</tr>
<tr>
<td>Duchenne’ Muscular Dystrophy</td>
<td>21</td>
<td>21%</td>
</tr>
<tr>
<td>Undiagnosed myopathies</td>
<td>14</td>
<td>14%</td>
</tr>
<tr>
<td>Emery-Driefuss muscular dystrophy</td>
<td>5</td>
<td>5%</td>
</tr>
<tr>
<td>Myotonia congenita becker type</td>
<td>4</td>
<td>4%</td>
</tr>
<tr>
<td>Isaacs Syndrome</td>
<td>4</td>
<td>4%</td>
</tr>
<tr>
<td>Facioscapulhumeral muscular dystrophy</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Schwartz Jompel Syndrome</td>
<td>2</td>
<td>2%</td>
</tr>
<tr>
<td>Mitochondrial disorder (Kears-Sayre Syndrome)</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td>MERRF</td>
<td>1</td>
<td>1%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>100</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 13: distribution of hereditary myopathies
3.5. Disorders diagnosed via evoked potentials:
Different types of evoked potential tests were done, there were 122 significant results, visual evoked potential was done for more than 90% of them. 93.44% of these cases had optic neuropathy as illustrated in table (14).

<table>
<thead>
<tr>
<th>Other disorders diagnosed via evoked potentials</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic Neuropathy</td>
<td>114</td>
<td>89.77%</td>
</tr>
<tr>
<td>Migraine</td>
<td>5</td>
<td>3.93%</td>
</tr>
<tr>
<td>blind eye</td>
<td>4</td>
<td>3.14%</td>
</tr>
<tr>
<td>Pontobulbar Palsy with Deafness</td>
<td>2</td>
<td>1.57%</td>
</tr>
<tr>
<td>Leber Hereditary Optic Neuropathy</td>
<td>2</td>
<td>1.57%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>127</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

Table 14: distribution of the significant results obtained from evoked potential tests

* Evoked potential showed lack of potentiation or enhancement in five patients with migraine.

3.4.8. Other diseases:
Finally, there were 8 conditions classified under the other diseases and these diseases represented in table (15)

<table>
<thead>
<tr>
<th>Other diseases</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>spinal cord lesion</td>
<td>3</td>
</tr>
<tr>
<td>congenital hypomyelination</td>
<td>2</td>
</tr>
<tr>
<td>Spino cerebellar ataxia</td>
<td>2</td>
</tr>
<tr>
<td>Bloch Sulzberger Syndrome</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>8</strong></td>
</tr>
</tbody>
</table>

Table 15: distribution of the other diseases
Discussion

Nerve conduction study and Electromyography are of great help in the diagnosis of peripheral nervous system disorders, especially the primary motor and sensory neurons, plexuses, neuromuscular junction and muscles.

These tests also localize the lesion, provide information about the nerve pathophysiology and assess the severity of the disorder. They also give a clue about the etiology for many disorders.

This is a retrospective observational analytic study aimed to determine the pattern of neurologic disorders in 3178 Sudanese patients referred to our Neuroscience clinic. It was found that Nerve disorders were dominating and comprising 54.36% of all the study group. This was followed by muscle disorders 9.59%, plexopathies and radiculopathies 6.92%, Disorders diagnosed by Evoked potentials were 3.99%, Disorders of the Neuro muscular junction 2.07%, Motor neuron disease comprises 1.32% while other neurological deficit showed a percentage of 0.25%.

Mononeuropathies encountered 65% of all nerve disorders (35.3% of the total study population). Nearly half of them was carpal tunnel syndrome. This differ from study performed in the USA in a purpose of getting the prevalence of CTS, our results showed a higher percentage and this could be attributed to the fact that our patients seek medical advice very late in the course of the disease i.e. when there is a severe muscle weakness or wasting of the thenar muscles.

On the other hand, Polyneuropathy was found to be 19.06% of all patients, Sensori-motor axonal neuropathy was the commonest presentation (mounting 48.56% of all the polyneuropathies) followed by Motor and sensory neuropathy. This is in accordance to a study performed in Nigeria which showed a similar percentage of Sensori-motor neuropathy. (78)

Interestingly acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) where found to affect 15.34% of all the polyneuropathies. This is in agreement with a Mexican study conducted for a period of seven years where the main condition handled and reported was acute inflammatory demyelinating polyneuropathy accounted for 19.7%
of all cases \(^{(79)}\). However our study included other variants, namely the axonal type, acute motor axonal neuropathy (AMAN) and the overlapping Bickerstaff’s encephalitis and (GBS). \(^{(80)}\)

Interestingly plexopathies and radiculopathies showed considerable percentage in our study with brachial plexopathies dominating. This is attributed to the fact that most patients are referred from the military hospital with traumatic lesions induced by bullets and gun shots and they comprise about 90% of all plexopathies. This is matching the literature as most plexopathies have underlying traumatic etiology. \(^{(81)}\)

According to muscular disorders, we found that polymyositis is the most frequent acquired myopathy with a percentage of 56.39 of all myopathies. Whereas dermatomyositis showed a percentage of 13.17. This differs from a study performed in Argentina where they found a low percentage of both disorders \(^{(82)}\). This again could be explained by the fact that patients came late in the course of the disease where the findings could obviously be elicited.

In neuromuscular diseases, using repetitive nerve stimulation (RNS) technique, this study showed that myasthenia gravis affected 2.07% of the study population, This percentage is much less than being reported in the literature. \(^{(83)}\)

Regarding Motor neuron disorders (MND), we found that amyotrophic lateral sclerosis (ALS) is the commonest disorder, with a percentage of 77.78% of all the MND. This is less than a study performed in California where ALS represented 87% of all the MND. \(^{(84)}\) This perhaps because the patients seek this particular investigation very late.

Evoked potentials mainly the visual test (VEP) in this study were conducted in patients suspected to have MS. A considerable number of patients conducted the test were found to have optic neuritis which support the diagnosis of central demyelination (neuromyelitis optica, M.S). This is similar to a study performed in Minnesota, USA where they concluded that the incidence of optic neuritis with MS is increasing significantly. \(^{(85)}\)
Sudan like many developing countries lacks necessary equipment and trained staff in this field which is essential for the diagnosis of many neurological conditions. Furthermore the service is only available in Khartoum, which is very unsatisfactory for physicians and also patients. Hence the health authorities should pay more weight to solve this problem by establishing a training program for neuroscientist in all states.

The current results give a clue about the neurological deficits as studied electrophysiologically. Further studies recruiting other electrophysiological center in Khartoum is recommended.
CHAPTER IV

CONCLUSION AND RECOMMENDATION
5.1. Conclusion and Recommendations:

Neurological problems are common. In every 100 patients underwent neuroelectrophysiological tests only 21 of them turned over with no significant results on the other hand, the majority had a nerve disorders while 9 patients had muscular disease and only 2 patients had neuromuscular disease.

Wide ranges of nerve disorders were diagnosed via neuro electrophysiological tests. The commonest deficits among Sudanese patients were Mononeuropathies according to this study followed by Polyneuropathies and then Plexopathies and radiculopathies.

Upper limbs nerves was the commonest nerves affected by mononeuropathies especially carpel tunnel syndrome. The ulnar nerve came second. Regarding the Lower limbs nerves, Sciatic Nerve and the peroneal nerve were the most frequent nerves affected.

Polymyositis was the commonest muscular disease.

Epidemiological studies allow for information to be obtained on specific problems. This will help authorities to aid risk prevention, and provide a road map for prevention and control of these problems. Sudan like many developing countries, trained staff in clinical neurophysiology and necessary equipment are needed to help in the diagnosis of many neurological conditions. The service is available only in Khartoum, which is very unsatisfactory for physicians and also patients.
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