بسم الله الرحمن الرحيم

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College of Graduate Studies

Measurement of Normal Median Nerve Area at the Level of the Wrist Joint in Adult Using Diagnostic Ultrasonography

قياس المساحة الطبيعية للعصب الاوسط علي مستوي الرسغ للبالغين باستخدام الموجات فوق الصوتية التشخيصية

A thesis Submitted for Partial Requirements of M.Sc. Degree in Medical Diagnostic Ultrasound

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الايـة

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قال تعالي:

(سَنُرِيهِمْ آيَاتِنَا فِي الآفَاقِ وَفِي
أَنْفُسِهِمْ حَتَّى يَتَبَيَّنَ لَهُمْ أَنَّهُ الْحَقُّ أَوَلَمْ
يَكْفِ بِرَبِّكَ أَنَّهُ عَلَى كُلِّ شَيْءٍ شَهِيدٌ)

سورة فصلت

الايه 53

Dedication

To my beloved mother

To my great father

To my brothers and sister

To all knowledge seekers

Acknowledgment

I humbly thank Allah Almighty," the Merciful and the Beneficent, who gave me health, thoughts and co-operative people to ".enable me achieve this goal

Special vote of thanks to my :supervisor

***Dr. /* Babiker Abd Elwahab .Awad Alla**

My thanks to everyone who helps me in way or another to make this work appear to light, especial thanks to Ribat University Hospital *staff and my college, also thanks to Dr.* ***Raga Ahmmed Aburaida***

Abstract

This a cross sectional descriptive study carried out in order to know the normal area measurements of median nerve at the wrist joint for adult. The study was done in College of Medical Radiological Sciences and .Ribat University Hospital, Khartoum, Sudan from April to august 2016

There were 100 subjects, of age above 17 years, selected randomly all subjects had not any symptoms related to median nerve pathology. Musculoskeletal ultrasound scanning using 7-10 MHz transducers were performed for the wrist joints and the median nerve area of both hands .were obtained

The results of this thesis states that the mean of right and left median nerve area (MNA), were (7.32±2.51) mm2, and (6.43±2.14) mm2 respectively, with no significant difference between males and females. The study found out that, there is linear increase in the median nerve area in relation to increase in the patient's age and weight, by 0.163±0.024 and 0.17±0.03 mm^2/year for right and left median nerve area respectively, and by (0.04±0.02) and (031±0.01) $mm^{2/}$/kg for the right and left median nerve area respectively. Moreover the normal median nerve has a hypo .(echogenicity (hypoechoic

The study conclude that the median nerve area measurement is important to detect any abnormal increment in MNA and ultrasound is a best modality to scanning the median nerve in means of availability, cost and ease of use, so it’s recommended to use ultrasound confidently as a .diagnostic modality to detect any median nerve injury

ملخص البحث

اجريت هذة الدراسة من اجل معرفة المساحة الطبيعية للعصب الاوسط عند منطقة مفصل الرسغ للبالغين. اقيمت هذة الدراسة بكلية علوم الاشعة الطبية التابعهة لجامعة السودان للعلوم والتكنلوجيا ومستشفي الرباط الجامعي , بولاية الخرطوم عاصمة جمهورية السودان في الفترة من ابريل الي اغسطس 2016م.

حيث أُخذ عدد 100 شخص عشوائيا , من عمر 18 سنة فما فوق , بعد التاكد من عدم معاناتهم من اي اعراض متعلقة بامراض للعصب الاوسط. وتم فحصهم بالموجات فوق الصوتية عند مفصل الرسغ, واثناء الفحص تم قياس مساحة المقطع العرضي للعصب الاوسط لكلتا اليدين.

وجدت الدراسة ان متوسط مساحة المقطع العرضي للعصب الاوسط لليد اليمني واليسري هو (7.32±2.51) مم^2 و(6.43±2.14) مم^2 علي الترتيب. مع عدم وجود تغيير ملحوظ في مساحة مقطع العصب الاوسط بين الزكور والاناث.

واثبتت الدراسة ان مساحة المقطع العرضي للعصب الاوسط تزيد بزيادة بعض العوامل المتعلقه بالشخص كالعمر والوزن بنسب متفاوتة (0.163±0.024) و (0.17±0.03) ملم مربع/السنة لليدين اليمني واليسري علي الترتيب, وبذيادة (0.04±0.02) و (0.03± 0.01) ملم ^{2}/كجم لليدين اليمني واليسري علي الترتيب.

واثبتت الدراسة ايضا ان العصب الاوسط يظهر بمستوي صدي منخفض مقارنة بما حوله.

خلصت الدراسة الي ان قياس مساحة المقطع العرضي للعصب الاوسط مهم جدا في تشخيص اي ذيادة غير طبيعية في مساحة العصب وأن سهولة الكشف بالموجات واتاحيتها وقلة تكاليفها جعلنها افضل وسيلة لتصوير العصب الاوسط, لذلك اوصت الدراسة باستخدام التصوير بالموجات فوق الصوتية بثقة عالية في الكشف عن امراض العصب الاوسط.

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List of abbreviations

MN	Median nerve
CSA	cross-sectional area
CTS	carpal tunnel syndrome
ADC	apparent diffusion coefficient
FA	fractional anisotropy
DML	distal motor latency
SNAPs	sensory nerve action potentials
TCL	transverse carpal ligament
SMA	spinal muscular atrophy
ALS	Amyotrophic lateral sclerosis
EMG	Electromyographic
CMT	Charcot-Marie-Tooth
PNS	peripheral nervous system
CNS	central nervous system
SPSS	Statistical Package for Social Sciences
US	Ultrasound
MHz	Megahertz

Chapter one

:Introduction .1.1

Musculoskeletal ultrasonography is non-invasive diagnostic exam which provide immediate information in the structure and the characteristics of the median nerve. The Median Nerve extends along the middle of the arm and forearm to the hand. It arises by two roots, one from the lateral and one from the medial cord of the brachial plexus; these embrace the lower part of the axillary artery, uniting either in front of or lateral to that vessel. Its fibers are derived from the sixth, seventh, and eighth cervical and first thoracic nerves. As it descends through the arm, it lies at first lateral to the brachial artery; about the level of the insertion of the Coracobrachialis it crosses the artery, usually in front of, but occasionally behind it, and lies on its medial side at the bend of the elbow, where it is situated behind the lacertus fibrosus (bicipital fascia), and is separated from the elbow-.(joint by the Brachialis (Peter L, W, 1995

In the forearm it passes between the two heads of the Pronator teres and crosses the ulnar artery, but is separated from this vessel by the deep head of the Pronator teres. It descends beneath the Flexor digitorum sublimis, lying on the Flexor digitorum profundus, to within 5 cm. of the transverse carpal ligament; here it becomes more superficial, and is situated between the tendons of the Flexor digitorum sublimis and Flexor carpi radialis. In this situation it lies behind, and rather to the radial side of, the tendon of the Palmaris longus, and is covered by the skin and fascia. It then passes behind the transverse carpal ligament into the palm of the hand. In its course through the forearm it is accompanied by the median artery, a .(branch of the volar interosseous artery (Peter L, W, 1995

Ultrasonically, in the transverse plane, the median nerve appears hypoechoic with a hyperechoic border, containing multiple bright reflectors. The median nerve is also rounded or oval in the proximal wrist, becoming progressively flatter as it passes through the carpal tunnel. Within the carpal tunnel, the median nerve is intimately related to the flexor retinaculum. In the longitudinal plane, the median nerve is seen anterior to the flexor digitorum tendons, coursing in a parallel plane. The nerve is easily differentiated from the tendons lying posteriorly, as the nerve lacks the tendons' characteristic fibrillar pattern (Devin Dean, .(2007

Carpal tunnel syndrome is a median nerve entrapment syndrome that has become the second most common reason for employee loss of work, following low back pain and ahead of shoulder pain. Patients who present with CTS typically complain of chronic tingling in their fingers, often .(worse at night, in the distribution of the median nerve (Lee D et al. 1999 Studies have shown that if the cross-sectional area of the median nerve as measured during ultrasound imaging exceeds 15 mm2, there is good correlation with abnormal EMG's and carpal tunnel disease can be .(confirmed. (Lee D et al. 1999

The advantage of the using ultrasound imaging it is mobility and low cost as well as ability to measure the dimension of the nerve, check for the presence of masses or cyst and evaluate the structure and echogenicity of .(the nerve (Paul and Scott, 2008

:Problem of the study .1.2

There is no local stander of normal medial nerve area measurement in adult Sudanese, also median nerve area might follow body characteristic .such as age, gender, weight, and height as well as subject occupation

:Objectives .1.3

The general objective of this study is to measure normal median nerve area at the level of the wrist joint in adult using diagnostic .ultrasonography

:Specific objective

To determine the normal median nerve area at the level of the wrist - .joint

.To evaluate the echogenicity of normal median nerve -

To correlate between normal measurements of median nerve area in - .both hand

To correlate between normal measurement of median nerve area and - .gender, age, weight, height and occupation

:Over view of the study .1.4

This study is concerned with normal median nerve measurement in -:Sudanese people, its falls into five chapters

Chapter one: is an introduction, which include introductory notes on median nerve anatomy, physiology, pathology, as well as statement of the problem and study objectives.

Chapter two: include a comprehensive scholarly literature reviews concerning the previous studies.

Chapter three: deals with the methodology, where it provides an outline of material and methods used to acquire the data in this study as well as the method of analysis approach.

Chapter four: presenting the results.

Chapter five: include discussion of results, conclusion and recommendation followed by references and appendices.

Chapter two
Theoretical background

2.1. Anatomy of the median nerve:

2.1.1. Anatomical course of the median nerve:

The Median Nerve extends along the middle of the arm and forearm to the hand. It arises by two roots, one from the lateral and the other from the medial cord of the brachial plexus; these embrace the lower part of the axillary artery, uniting either in front of or lateral to that vessel. Its fibers are derived from the sixth, seventh, and eighth cervical and first thoracic nerves. As it descends through the arm, it lies at first lateral to the brachial artery; about the level of the insertion of the Coracobrachialis it crosses the artery, usually in front of, but occasionally behind it, and lies on its medial side at the bend of the elbow, where it is situated behind the lacertus fibrosus (bicipital fascia), and is separated from the elbow-joint by the Brachialis (Peter L, W, 1995).

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the Palmaris longus, and is covered by the skin and fascia. It then passes behind the transverse carpal ligament into the palm of the hand. In its course through the forearm it is accompanied by the median artery, a branch of the volar interosseous artery (Peter L, W, 1995).

In the arm the line of the median nerve is practically the same as that for the brachial artery; at the bend of the elbow the nerve is medial to the artery. The course of the nerve in the forearm is marked by a line starting from a point just medial to the center of one joining the epicondyles, and extending to the lateral margin of the tendon of Palmaris longus at the wrist. (Peter L, W, 1995).

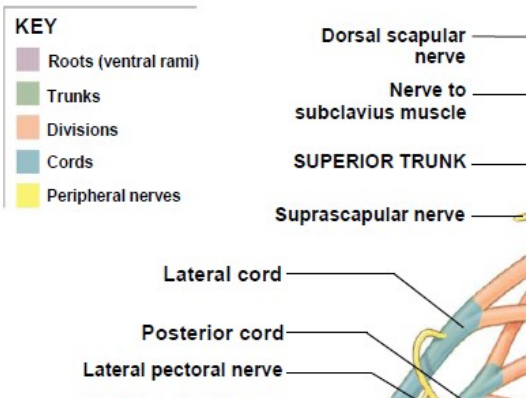

Figure 2.1 shows the Brachial plexus and median nerve origin (*Steven Bassett, 2012*).

2.1.2. Branches of the median nerve:

With the exception of the nerve to the Pronator teres, which sometimes arises above the elbow-joint, the median nerve gives off no branches in the arm. As it passes in front of the elbow, it supplies one or two twigs to the joint. In the forearm its branches are: muscular, volar interosseous, and palmar. The muscular branches (rami musculares) are derived from the nerve near the elbow and supply all the superficial muscles on the front of the forearm, except the Flexor carpi ulnaris. The volar interosseous nerve (n. interosseous [antibrachii] volaris; anterior interosseous nerve) supplies the deep muscles on

the front of the forearm, except the ulnar half of the Flexor digitorum profundus. It accompanies the volar interosseous artery along the front of the interosseous membrane, in the interval between the Flexor pollicis longus and Flexor digitorum profundus, supplying the whole of the former and the radial half of the latter, and ending below in the Pronator quadratus and wrist-joint

.((Peter L, W, 1995

The palmar branch (ramus cutaneous palmaris n. mediani) of the median nerve arises at the lower part of the forearm. It pierces the volar carpal ligament, and divides into a lateral and medial branch; the lateral branch supplies the skin over the ball of the thumb, and communicates with the volar branch of the lateral antibrachial cutaneous nerve; the medial branch supplies the skin of the palm and communicates with the palmar cutaneous branch of the ulnar. The median nerve enters the forearm between the two heads of the muscle, and is separated from the ulnar artery by the ulnar head. (Peter

.(L, W, 1995

In the palm of the hand the median nerve is covered by the skin and the palmar aponeurosis, and rests on the tendons of the Flexor muscles. Immediately after emerging from under the transverse carpal ligament the nerve becomes enlarged and flattened and splits into a smaller, lateral, and a larger, medial portion. The lateral portion supplies a short, stout branch to certain of the

muscles of the ball of the thumb, viz. The Abductor brevis, the Opponens, and the superficial head of the Flexor brevis, and then divides into three proper volar digital nerves; two of these supply the sides of the thumb, while the third gives a twig to the first Lumbricalis and is distributed to the radial side of the index finger (Peter L,

.(W, 1995

The medial portion of the nerve divides into two common volar digital nerves. The first of these gives a twig to the second Lumbricalis and runs toward the cleft between the index and middle fingers, where it divides into two proper digital nerves for the adjoining sides of these digits; the second runs toward the cleft between the middle and ring fingers, and splits into two proper digital nerves for the adjoining sides of these digits; it communicates with a branch from the ulnar nerve and sometimes sends a twig to the third Lumbricalis. Each proper digital nerve, opposite the base of the first phalanx, gives off a dorsal branch which joins the dorsal digital nerve from the superficial branch of the radial nerve, and supplies the integument on the dorsal aspect of the last phalanx. At the end of the digit, the proper digital nerve divides into two branches, one of which supplies the pulp of the finger, the other ramifies around and beneath the nail. The proper digital nerves, as they run along the fingers, are placed superficial to the corresponding arteries (Peter L,

.(W, 1995

All the muscles of the superficial layer are supplied by the median nerve, excepting the Flexor carpi ulnaris, which is supplied by the ulnar (Peter L, W, 1995).

The Abductor brevis, Opponens, and lateral head of the Flexor pollicis brevis are supplied by the sixth and seventh cervical nerves through the median nerve; the medial head of the Flexor brevis, and the Adductor, by the eighth cervical through the ulnar nerve. The two lateral Lumbricales are supplied by the sixth and seventh cervical nerves, through the third and fourth digital branches of the median nerve; the two medial Lumbricales and all the Interossei are supplied by the eighth cervical nerve, through the deep palmar branch of the ulnar nerve. The third Lumbricalis frequently receives a twig from the median. (Peter L, W, 1995).

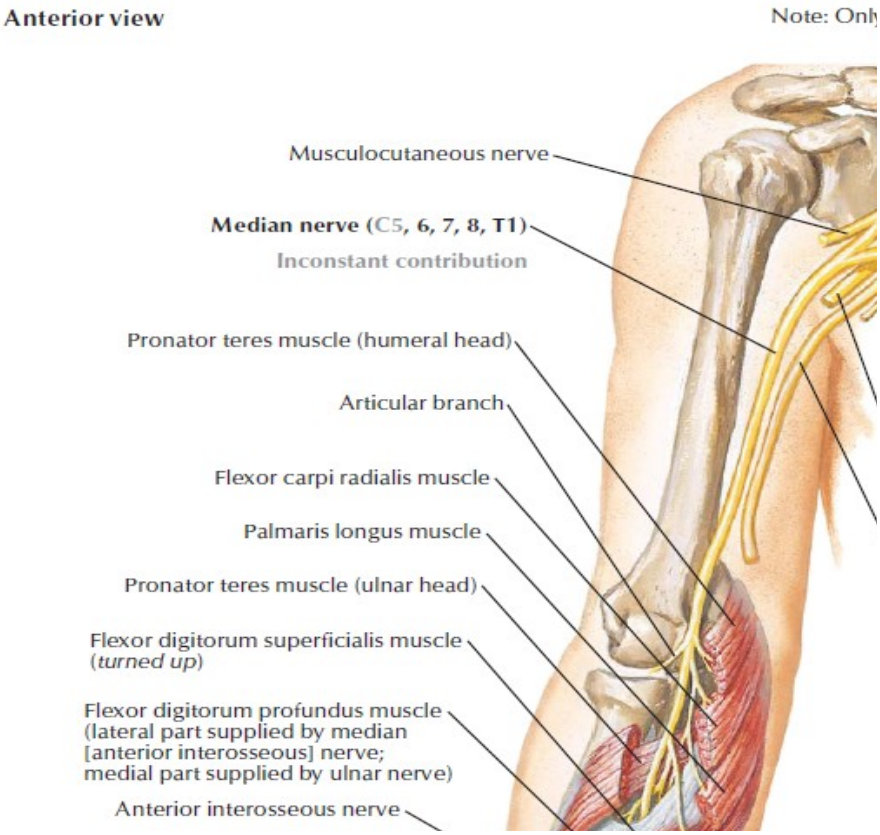

Figure 2.2 shows course of the median nerve through the arm, forearm, hand and its branches (Frank .(H et al, 2004

Median nerve .2.2 :physiology

The median nerve belongs to the peripheral nervous system which refers to parts of the nervous system outside the brain and spinal cord. In the peripheral nervous system, bundles of nerve fibers or axons conduct .information to and from the central nervous system

Neuronal function is complex and involves numerous processes in nerve transmission. Generation of a nerve impulse (action potential) of a sensory neuron occurs as a result of a stimulus such as light, a particular chemical, or stretching of a cell membrane by sound. Conduction of an impulse along a neuron occurs from the dendrites to the cell body to the axon. Transmission of a signal to another neuron across a synapse occurs via chemical transmitter. This substance causes the next neuron to be electrically

stimulated and keeps the signal going along a nerve .((Chawla, 2016

The sensory (afferent) division carries sensory signals by way of afferent nerve fibers from receptors in the central nervous system (CNS). It can be further subdivided into somatic and visceral divisions. The somatic sensory division carries signals from receptors in the skin, muscles, bones and joints. The motor (efferent) division carries motor signals by way of efferent nerve fibers from the CNS to effectors (mainly glands and muscles). It can be further subdivided into somatic and visceral divisions. The somatic motor division carries signals to the skeletal .(muscles (Chawla, 2016

The reflex arc control many autonomic and somatic functions, and consists of Receptors, afferent, center, efferent and effectors. The receptor Found at the .(peripheral ends of afferent neurons (Hakim, 2013

Reflexes are classified according to the site of the receptors to superficial reflexes (receptors in the skin), deep reflexes (receptors within the muscles), and visceral reflexes (receptors in viscera). The afferent enters the spinal cord through the dorsal root, the efferent leaves the spinal cord through the ventral root to supply the effectors, the effectors may be a muscle or a gland that do the effect, The center or synapse is the site of integration

of the reflex (the synapse between afferent and efferent neurons) (Hakim, 2013).

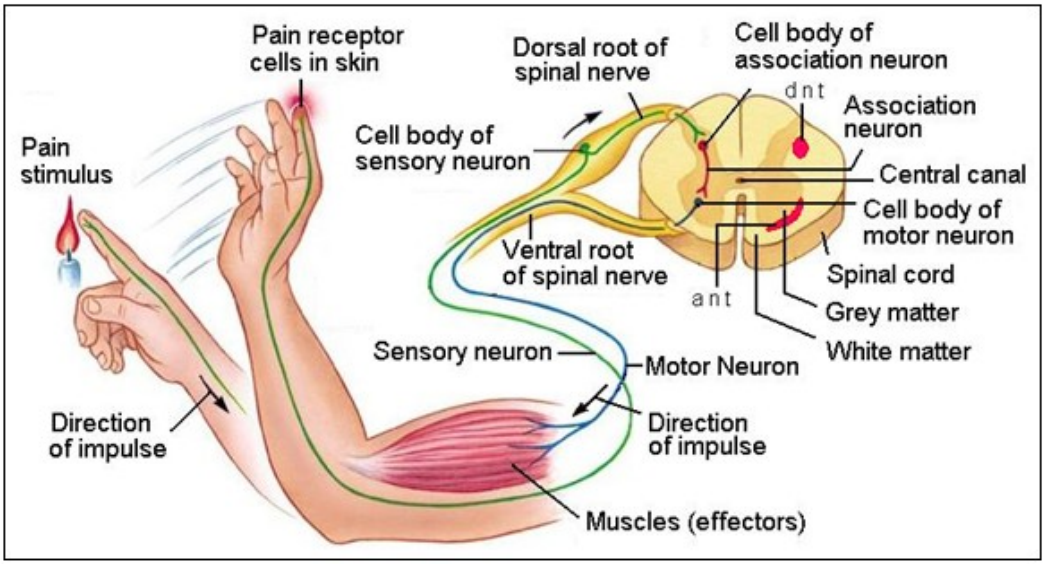

Figure 2.3 a diagram of a reflex arc (Tognolini, 2016).

2.3. Diseases of the Peripheral Nerves and Motor Neurons:

The peripheral nervous system (PNS) includes all structures related to the Schwann cells from the pia-arachnoid membrane to the nerve endings. The first (olfactory) and second (optic) cranial nerves are not considered peripheral nerves. These nerves are extensions of the central nervous system (CNS) and contain oligodendroglia instead of Schwann cells. The other cranial nerves, spinal motor and sensory nerves, and peripheral components of autonomic nervous system are included in PNS. Disorders that affect peripheral nerves can affect one or more components of the nerve fiber. Disorders

predominantly affecting myelin are demyelinating neuropathies. When disease process affects distal portion of axons with preservation of parent cell bodies in dying-back manner, this is axonopathy or axonal neuropathy. Disorders affecting cell bodies in dorsal root ganglia and their axons are neuronopathies. Neuropathies may be generalized and symmetrical (polyneuropathy) or focal and affect one (unifocal or mononeuropathy) or multiple (mononeuropathy multiplex) nerves (Weisberg, 1996).

:Symptoms and signs can be motor, sensory, or autonomic

Motor Findings: Weakness or paralysis in neuropathies is usually hypotonic in type and is associated with muscle

.(wasting (atrophy) (Weisberg, 1996

Weakness can develop acutely in external compression of a superficial nerve ("Saturday night" or "crossed leg" paralysis), when penetrating trauma injures a nerve, or when vascular occlusion causes infarction of nerves as in diabetic femoral neuropathy or ophthalmoplegia (third cranial nerve) or in vasculitis such as in polyarteritis nodosa. Subacute onset of weakness takes less than 4 weeks as is usually seen in para-infectious polyneuropathies. Weakness in chronic neuropathies progresses slowly over several months to years. Patients show distal wasting of muscles. Chronic neuropathies are usually due to hereditary or toxic-metabolic causes. Pescavus, hammer toes, kyphoscoliosis and other orthopedic deformities are associated with chronic

hereditary neuropathies due to muscle imbalance ((Weisberg, 1996).

Weakness in mononeuropathies is localized to muscles innervated by affected nerve. Weakness in polyneuropathies usually begins distally in feet and hands and progresses in ascending symmetrical fashion to involve legs and arms and sometimes facial, bulbar, and respiratory muscles. Initial proximal weakness in neuropathies suggests a radicular (nerve roots) involvement or more likely primary muscle involvement (myopathy). Fasciculations are a rare occurrence in neuropathies and, when present, suggest distal motor axonal involvement or more likely anterior horn cell disease (Weisberg, 1996).

Myokymia or undulating worm-like rhythmic movements of muscle is rarely seen in neuropathies. Sensory disturbances appear in two different ways. Positive sensory symptoms occur when aberrant sensation occurs in the absence of normal stimulation. Negative symptoms occur when adequate stimuli fail to produce a sensory response. Positive sensory symptoms: A sensation of tingling (paresthesia) in the hands or feet over the distribution of one or more nerves is a frequent complaint in sensory neuropathies and can be the first sign of nerve involvement. Some patients experience a peculiar unpleasant sensation of tingling in the feet that occurs

mainly during the night and that can be temporarily relieved by movement of the affected limb, the neuropathic pain restless legs syndrome. Ischemic pain of peripheral vascular disease, which has to be differentiated from this, occurs during activity rather than at rest and improves with rest. Paresthesias are characteristic of acquired neuropathies, whereas numbness is seen in congenital neuropathies. Dysesthesia, or unpleasant feeling triggered by any ordinary stimuli, is usually evident after partial nerve injury or during recovery from some neuropathies

.((Weisberg, 1996

A burning sensation, hyperesthesia, or exaggerated normal feeling, hyperpathia, is felt when stimulus is moving rather than when stationary pressure is applied. Dysesthesias, hyperesthesias, and hyperpathias can occur in diabetic and alcoholic neuropathies and in some neuropathies associated with malignancies (multiple myeloma). Terms frequently used in reference to abnormal sensation in some peripheral neuropathies are neuralgia, which implies stabbing or throbbing pain in distribution of a nerve as is found in tic douloureux, herpetic neuritis, and causalgia, which implies burning, persistent pain that radiates distally along an injured nerve trunk. When causalgic pain is associated with autonomic dysfunction, such as abnormal sweating, trophic skin and nail changes,

or edema, it is known as reflex sympathetic dystrophy or complex regional pain syndrome (Weisberg, 1996).

Negative sensory symptoms, Sensory loss can be an early sign and occasionally the only sign of peripheral neuropathy; however, it frequently is associated with motor disturbances. Sensory loss can be limited to one nerve trunk as in herpetic neuritis or, more frequently, can be bilateral, symmetrical, and distal in stocking or glove distribution as seen in polyneuropathies (Weisberg, 1996).

Sensory findings: Loss of all modalities of sensation in distal distribution with gradual return of sensation is usually produced by conduction blocks caused by demyelination, Loss of touch-pressure, vibratory, and position sense with preservation of pain and temperature, so-called sensory ataxia, is seen in tabes dorsalis, but also is seen in some diabetic neuropathies and Friedreich'sataxia. This type of sensory deficit is due to large fiber loss**,** Selective loss of pain and temperature with preservation of touch-pressure is seen in leprosy and some hereditary sensory neuropathies. This type of sensory deficit is due to loss of small myelinated sensory fibers, pure sensory syndrome with positive (dysesthesia) and negative (hypesthesia) phenomena and associated with sensory ataxia is seen in neuronopathies and is due to damage to nerve cell bodies in dorsal root ganglia (Weisberg, 1996).

Autonomic Findings: Orthostatic hypotension without change in the pulse rate is probably the most important and earliest abnormality in some autonomic neuropathies. Painless nocturnal diarrhea, heat intolerance, and localized excessive sweating in unaffected areas with anhidrosis in affected areas may be the complaint of some patients. Other symptoms of autonomic dysfunction include bladder (atonic) dysfunction manifested by difficulty voiding, sexual impotence, retrograde ejaculation, decreased tearing, and pupillary abnormalities. Autonomic involvement is seen predominantly in diabetic and amyloid neuropathies, but maybe seen in neuropathies of other etiologies (Weisberg, 1996).

Laboratory Tests: The diagnosis of peripheral neuropathy can be confirmed by electrophysiologic studies. Nerve conduction studies define distribution and extent of neuropathy and differentiate between axonal and demyelinating process. Based upon nerve condition velocities, it is possible to suggest the etiology of the neuropathy in some cases. The presence of multifocal conduction blocks indicates acquired demyelinating neuropathy, whereas hereditary neuropathies show uniform slowing of conduction velocities. Nerve conduction studies can localize level of lesion in compressive (entrapment) neuropathies (Weisberg, 1996).

Laboratory investigation should include a complete blood cell count, erythrocyte sedimentation rate, fasting blood

glucose, serum protein and plasma immunoelectrophoresis, liver function tests, chest roentgenograms, thyroid function tests, and serum vitamin B12and folate levels. Cryoglobulins, urinary porphyrins, and heavy metals should be ordered in selected cases. Ganglioside-monosialic (GMI) acid antibodies are detected in some patients with multifocal neuropathies and lower motor neuron disease. Myelin-associated glycoprotein (MAG) and sulfate-3-glucuronyl paragloboside are detected in some patients with inflammatory neuropathies. Commercially available motor and sensory neuropathy diagnostic panels are already available. Deoxyribonucleic acid analyses for the CMT1Aduplication and for peripheral neuropathy with liability to pressure palsies are also commercially available. Cerebrospinal fluid (CSF) protein is elevated in some neuropathies, most frequently in Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy. Finally nerve biopsy can be helpful in diagnosis of neuropathies caused by vasculitis (polyarteritis nodosa), autoimmunity, infections, and amyloid (Weisberg, 1996).

2.3.1. Neuropathies associated with systemic diseases:

2.3.1.1. Diabetic neuropathy:

Clinical signs and symptoms of neuropathy are seen in approximately 20% of diabetic patients, but electrophysiologic studies done in asymptomatic diabetics demonstrate higher percentage of subclinical involvement. Rarely, the neuropathy can be initial sign of diabetes. The longer duration and more poorly controlled the diabetic, the increased risk of neuropathy. Rarely neuropathy symptoms are initial presenting sign of diabetes and with treatment, symptoms recede. In addition, distal painful extremity paresthesias may occur 4weeks after initiation of insulin therapy and achievement of normoglycemic state axonal nerve injury occurs as glucose is not available for nerve metabolism; however, with normalization of blood glucose with insulin, symptoms resolve. Diabetes is major risk factor for all entrapment neuropathies. There are different patterns of diabetic neuropathy; symmetric polyneuropathies, focal and multifocal neuropathies. Symmetric polyneuropathies: Distal, symmetrical, sensory polyneuropathy of insidious onset is most common form. Symptoms usually start with paresthesias of feet and legs

.(in typical length related pattern (Weisberg, 1996

The hands are rarely affected and if affected, first consider alternate diagnosis e.g. cervical radiculopathy, carpal tunnel syndrome syrinx. The anterior midline of the abdomen (truncal neuropathy) may be affected. Burning paresthesias of feet that are worse during night can be seen. Leg weakness is rare. Are flexia of Achilles tendon is constant feature. There is loss of pain and touch in

stocking-glove distribution. Acute painful neuropathy can occur and is preceded by rapid and profound weight loss. It is most frequently seen in males and can be associated with impotence (Weisberg, 1996).

Symptoms subside with adequate control of diabetes and weight gain. In some patients there is predominant loss of vibratory, position, and deep pain sensation with neuropathic arthropathy and nonreactive pupils resembling tabes dorsalis (diabetic pseudotabes). Transient painful paresthesias can be described by some diabetic patients following treatment with insulin (treatment induced neuropathy). The symptoms improve with tight glycemic control. Proximal symmetric lower limb motor neuropathy, also known as diabetic amyotrophy, can occur. It is insidious in onset and is associated with poorly defined pain and prominent weakness and wasting in proximal distribution. Autonomic neuropathy, Autonomic involvement increases risk of death in diabetic patients. Due to loss of sensation in diabetic patients, pain less myocardial ischemia may occur. Autonomic dysfunction includes pupillary abnormalities that are frequent and consist of miosis, diminished light reflex, and absence of pupillary dilation in dark as result of sympathetic denervation. Tachycardia and postural hypotension can also occur. Painless nocturnal diarrhea or diarrhea after meals is most frequent gastrointestinal

autonomic dysfunction. Impotence correlates with presence of neuropathy (Weisberg, 1996).

Bladder a tony with overflow incontinence and large residual of volume after micturition indicate parasympathetic denervation. Focal and multifocal neuropathies: Acute, painful mononeuropathies caused by nerve ischemia occur in diabetes and include mainly femoral mononeuropathy and diabetic ophthalmoplegia. In femoral mononeuropathy, patient develops severe pain in distribution of femoral nerve (thigh) accompanied by weakness and atrophy of quadriceps muscle with patellar areflexia. In diabetic ophthalmoplegia, third nerve is most commonly affected but with no pupillary involvement. Pupillary sparing seen in diabetic third nerve involvement differentiates it from compression of the third nerve by intracranial carotid artery aneurysms or neoplasms. Sixth cranial nerve is less frequently affected by ischemic diabetic cranial neuropathy (Weisberg, 1996).

Other presentations of diabetic nerve disease include multiple, painful, asymmetric, usually motor neuropathy (multiple mononeuropathy). Treatment of diabetic neuropathies consists of strict control of diabetes and maintenance of ideal body weight. Vitamin supplementation and aldolase reductase inhibitors have produced no improvement of sensory symptoms. Tricyclic antidepressants e.g., Amitriptyline (Elavil) or nortriptyline (Pamelor), 75 to 100mgat bedtime, frequently relieves

pain in patients with sensory neuropathies, but anti-epileptic drugs (which block sodium channels) either individually or in combination, can also be used for neuropathic pain (Weisberg, 1996).

2.3.1.2. Uremic Polyneuropathy:

Uremic polyneuropathy occurs more frequently in males and has insidious onset, usually correlating with renal failure. Clinical manifestations are those of dysesthesias, cramps, and restless legs syndrome. The neuropathy is distal symmetric mixed sensory motor neuropathy that predominantly affects legs. Some improvement of neuropathy can occur after dialysis, but only renal transplantation results in sustained improvement (Weisberg, 1996).

2.3.1.3. Alcoholic Neuropathy:

Alcoholic neuropathy is most likely result of dietary deficiency rather than direct neurotoxic effect of alcohol. Alcoholic neuropathy is slowly progressive and manifests predominantly with distal sensory dysesthesias of feet. Patients describe pain as burning or stabbing. Hands involvement is late and less severe. Variable weakness and muscle atrophy also occur. Loss of stretch reflexes and autonomic skin changes are frequent. Autonomic involvement with hypothermia and postural hypotension is also frequent. Treatment consists of dietary improvement,

abstinence from alcohol, and vitamin supplements (especially thiamine and other B vitamins) (Weisberg, 1996).

2.3.1.4. Amyloid Neuropathy:

Peripheral nerves can be involved in primary systemic amyloidosis and rarely in secondary (chronic infection) amyloidosis. The most frequent form of amyloid neuropathy occurs in familial form known as foot disease or Andrade's disease. It usually starts in young adulthood and progresses slowly for 10 to15 years. Neuropathy is usually sensory. Autonomic involvement is very frequent with predominant gastrointestinal problems (diarrhea). Cardiac arrhythmias, vitreous opacity, and renal involvement along with positive family history are characteristic of this disorder. Amyloid deposits can be demonstrated in nerve or rectal biopsies (Weisberg, 1996).

2.3.1.5. Monoclonal Gammopathies:

A gammopathy is disorder in which there is abnormal proliferation of lymphoid cells producing immunoglobulins. In monoclonal gammopathies, single clone of plasma cells in bone marrow produces immunoglobulin consisting of two heavy polypeptide chains of the same class and subclass and two light polypeptide chains of same type. The monoclonal proteins are classified according to their type of heavy chain. IgG, IgA, and IgM monoclonal

gammopathies are sometimes associated with neuropathies. Neuropathies in monoclonal gammopathies are most likely associated with sclerotic myeloma, multiple myeloma, amyloidosis, macroglobulinemia, or lymphoma. Neuropathies associated with monoclonal gammopathy are rare and, when present, are more frequent in males older than 50. They are usually mixed sensory-motor and are seen predominantly in distal legs. They respond to treatment of the underlying process. If these diseases have been excluded, patient is classified as having a monoclonal gammopathy of undetermined significance (MGUS) with associated neuropathy. Antibodies that are active in MGUS associated with peripheral neuropathy are usually of IgM class. These antibodies are frequently directed against myelin associated glycoprotein (MAG), and neuropathy is frequently demyelinating and predominantly sensory (Weisberg, 1996).

2.3.2. Infectious and post infectious neuropathies:

2.3.2.1. Herpes Zoster (Shingles):

Herpes zoster the most frequent infectious neuritis in adults and is due to reactivation of varicella-zoster virus in ganglia and associated sensory axons. It is associated with dermal pain, frequently in thoracic area, with or without vesicular rash along course of affected nerve (Weisberg, 1996).

Human Immunodeficiency Virus Infection .2.3.2.2 :((Acquired Immune Deficiency Syndrome

Peripheral neuropathy is most frequent neurologic disorder in infection with human immunodeficiency virus (HIV). Type of neuropathy correlates with stage of infection. In early asymptomatic stages, inflammatory demyelinating neuropathy and Guillain-Barré-like syndrome can occur; however, this may begin with bilateral facial weakness and weakness may descend rather than ascend as is characteristic of Guillain-Barré neuropathy (Weisberg, 1996).(

CSF pleocytosis and laboratory evidence of HIV infection differentiate these neuropathies from idiopathic ones. In early symptomatic phase of infection; vasculitic syndrome that is probably due to immune complex deposits in blood vessel can produce some mononeuropathies or multiple mononeuropathy. During late immunocompromised stage, most frequent form is distal symmetric polyneuropathy. This is typically painful sensory polyneuropathy involving feet and distal leg. At this stage, cytomegalovirus infection (CMV) is frequently found and produces radiculo polyneuropathy or myelopathy. Drugs used for treatment of HIV disease are common causes of neuropathy ((Weisberg, 1996).

Leprous Neuropathy .2.3.2.3:

Leprous neuropathy is disease endemic in tropical areas and is due to direct invasion of nerve by Mycobacterium leprae. Neuropathy is frequently associated with skin lesions and is mixed sensorimotor neuropathy with features of multiple mononeuropathy predominantly affecting cool areas of skin. Painless injury as result of sensory loss is main manifestation. Nerve enlargement is prominent finding. The organisms can be demonstrated in skin or nerve biopsies. Antibiotic treatment (dapsone, clofaximine, and rifampin) arrests progression and disease

.(may reverse neuropathy (Weisberg, 1996

Acute Inflammatory Demyelinating .2.3.2.4

:(Polyneuropathy (Guillain-Barré Syndrome

Acute idiopathic polyneuritis is immunologically mediated demyelinating polyneuropathy that affects all ages and both sexes equally. The disease is usually preceded by acute infectious illness, including Campylobacter jejuni, viral or Mycoplasma infection, surgery, or immunization (rabies, swine influenza) or can occur in patients with malignant disease (lymphomas) or lupus erythematous. The disease is characterized by rapidly progressive motor weakness, frequently symmetrical, with or without mild ataxia at onset and frequently of ascending nature beginning distally in the legs, progressing to upper extremities, and ending with severe respiratory paralysis. There can be involvement of cranial nerves causing facial

paralysis, and external ophthalmoplegia with sixth nerve palsy, which is most frequent extraocular finding. Progression of weakness varies from3 days to 4 weeks. Areflexia is usually generalized and occurs early; this is constant feature. Although paresthesias are frequently early complaint, sensory signs are mild. Autonomic dysfunction can cause cardiac arrhythmias and postural hypotension, but bladder or bowel dysfunction at onset or persisting during disease is rare. Functional recovery usually begins 2 to 4weeks after stabilization of symptoms and is complete in most patients. Areflexia can be permanent residual finding (Weisberg, 1996).

A variant of the disease includes acute onset of ophthalmoplegia, ataxia, and Areflexia with or without weakness of the extremities (Fisher syndrome). Rapid onset of symmetrical cranial nerve dysfunction (polyneuritis cranialis) can also be a variant. Pure pandysautonomia of rapid onset with full recovery is considered another variant, and in some cases predominant autonomic symptoms can precede typical course of Guillain-Barré syndrome. Autonomic symptoms can cause sudden death. The increase in CSF protein with less than10 cells/ml (albuminocytologic dissociation) strongly supports the diagnosis when found after first week of symptoms or when progressive rise of protein content is demonstrated from serial lumbar punctures ((Weisberg, 1996).

Nerve conduction studies confirm demyelinating process by showing reduction in conduction velocity, conduction block or abnormal temporal dispersion in motor nerves, prolonged distal latencies. Treatment consists of maintaining adequate respiratory function and instituting respiratory assistance when vital capacity falls below 12 to 15 ml/kg or when there is decreased blood oxygen saturation. Cardiovascular status should be monitored to control autonomic dysfunction. Passive bedside physiotherapy should be started immediately and followed throughout recovery. There is convincing evidence that plasmapheresis early in disease course reduces duration of acute hospital care, shortens duration of ventilator dependency, and hastens motor recovery. One session every other day with exchange of 40 to 50 ml/kg should be done to achieve cumulative exchange of 200 to 250 ml/kg. Intravenous immune globulin in dosage 0.4 gm per kilogram per day for 5 days is as effective as or superior to plasma exchange. Treatment with high-dose immuneglobulin as described, combined with 0.5gm of methylprednisolone/day, is more effective than treatment

.(with immune globulin alone (Weisberg, 1996

Chronic Inflammatory Demyelinating .2.3.2.5

:Polyneuropathy

Chronic recurrent inflammatory demyelinating polyneuropathy is rare form of both motor and sensory

polyneuropathy or polyradiculoneuropathy that affects distal and proximal limbs. Onset of symptoms is usually insidious, and course is slowly progressive, either stepwise or relapsing. Motor weakness predominates, but sensory loss is found in most patients. Muscle atrophy is of lesser degree than would be expected from amount of weakness. CSF protein is elevated without increased cell count. Respiratory involvement is less frequent than in Guillain-Barré syndrome, and there is greater fluctuation of functional impairment. Treatment includes intermittent intravenous immune globulin treatment with or without methylprednisolone, intermittent plasmapheresis, chronic steroid therapy, or immunosuppression with cyclophosphamide (Cytoxan) or azathioprine (Imuran) ((Weisberg, 1996).

.2.3.3 Neuropathies Associated with Connective Tissue Disorders:

Neuropathies associated with connective tissue disorders are usually of ischemic vascular origin caused by arteritis. Clinical evidence of neuropathy in rheumatoid arthritis, other than carpal tunnel syndrome, is not frequent but when present is due to arteritis and occurs in patients with longstanding disease, destructive joint disease, rheumatoid nodules, and high titers of rheumatoid factor. The disease can appear as progressive, distal (legs first), sensorimotor polyneuropathy or can have features of

multiple mononeuropathy. Neuropathy in polyarteritis nodosa occurs in 50% of patients with this disease and can be initial manifestation. The neuropathy appears as multiple mononeuropathy with involvement of two or more nerves in an acute fashion, with pain and paresthesias in distribution of affected nerve, followed by weakness. The distribution can also be that of diffuse, distal, and symmetrical sensorimotor polyneuropathy. Treatment consists of corticosteroids and immunosuppression. Neuropathy in systemic lupus erythematosus occurs infrequently; it can be initial symptom of disease and indicates diffuse vasculitis and poor prognosis. The disease appears as progressive symmetrical, distal, sensorimotor neuropathy with elevated CSF protein

.((Weisberg, 1996

More rarely the disease can appear as multiple mononeuropathy. Cranial Neuropathies Cranial nerves can be affected by several disease processes without involvement of spinal nerves. They can be individually affected or else several nerves can be involved. When cranial mononeuropathies or polyneuropathies are associated with impaired function in corticospinal, spinothalamic, or cerebellar tracts, lesion is within brain stem. Pure mononeuropathies or polyneuropathies localize lesion outside brain stem. The most common cranial neuropathy is discussed below. Bell's Palsy (Idiopathic Facial Paralysis) Bell's palsy is an acute disease of facial (seventh cranial) nerve of unknown causes that produces

edema and compressive ischemia of nerve within its bony canal within temporal bone (Weisberg, 1996).

Onset is sudden or can develop in few hours or days. It occurs in either gender and at any age. Many of patients are diabetic. Facial palsy can develop in patients with basilar meningitis (sarcoid, neoplastic, including leukemia). The most significant finding is infranuclear (peripheral) facial palsy, which can be partial or complete and can be associated with or preceded by retroauricular (mastoid) pain and decreased taste. Some patients can have hyperacusis (uncomfortable sensation in the ear in response to loud noise) and excessive or decreased lacrimation. Recovery tends to be rapid (weeks) and complete in 80% of patients. Prognostic indicators for delayed or partial recovery include age over forty, complete paralysis with decreased tearing, decreased taste, retroauricular pain, and electromyographic evidence of denervation 10 days after onset of symptoms. Treatment consists of protecting the cornea with eye patch during sleep or when going out doors Corticosteroids can have beneficial effect when used within 72 hours of onset (60 mg/day for 4 days, then taper to 5 mg/day in 10 days.) and there is evidence that Acyclovir, used for herpes infection, is effective. No evidence exists that surgical decompression improves outcome (Weisberg, 1996).

2.3.4. Toxic neuropathies:

A great variety of toxic agents produce damage to peripheral nerves usually to distal portion of axon. Only a few that have unique features are discussed (Weisberg, 1996).

2.3.4.1. Heavy Metals:

Lead produces pure motor neuropathy of radial nerve (wrist drop), which can be unilateral or bilateral. Arsenic poisoning is characterized by mixed polyneuropathy with predominant sensory symptoms usually affecting the lower extremities. Thallium produces mixed polyneuropathy with marked synesthesia and is associated with severe hair loss (Weisberg, 1996).

2.3.4.2. Drugs:

Streptomycin affects cochlear part of eighth nerve. Isoniazid produces polyneuropathy by creating pyridoxine deficiency. Ethambutol and amphotericin can also produce polyneuropathy. With longstanding use, anticonvulsants e.g. phenytoin, frequently produce subclinical symptoms. Antineoplastic agents including vincristine and nitrogen mustard can produce neuropathies. Cisplatin commonly causes sensory neuronopathy. Industrial agents, mainly solvents including n-hexane and related compounds,

acrylamide, or organophosphates can produce an axonal neuropathy (Weisberg, 1996).

2.3.5. Inherited primary peripheral neuropathies:

Hereditary Motor and Sensory Neuropathies or the Charcot-Marie-Tooth Polyneuropathy Syndrome These are genetically and clinically heterogeneous group of disorders of peripheral nerves characterized by insidious onset and slowly progressive weakness of distal muscles and mild sensory impairment. Symptoms appear in first decade or early in second decade. Children with disease often walk on their toes, and adults complain of abnormalities of gait, foot deformities, or loss of balance (Weisberg, 1996).

Pescavus develops as disease progresses. Atrophy of distal legs can be prominent feature ("stork leg" or inverted champagne bottle appearance). Tripping over objects on floor and ankle sprains are frequent as result of weakness of dorsiflexion of foot produced by weakness of peroneal and anterior tibialis muscles. Weakness of the intrinsic hand muscles usually occurs late. The most frequent complaints concerning hand involvement are difficulty using zippers, difficulty buttoning and unbuttoning, and difficulty manipulating small objects when using fine finger movements. In severe cases, wasting of hand muscles gives appearance of claw hands. Muscle stretch reflexes

disappear early at ankle and later on at patella. Plantar reflex is flexor or absent (Weisberg, 1996).

Sensory involvement to any significant degree is rare, but decreased pain to pinprick in stocking distribution is seen in some patients. Electrophysiological studies distinguish two major forms of Charcot-Marie-Tooth (CMT) that have same clinical phenotype and some variable clinical features. CMT type 1 (CMT1) is a demyelinating neuropathy with moderate to severely decreased motor NCV, absent reflexes, and, in some slender patients, enlarged (hypertrophic), visible, or palpable nerves. Patients with CMT type 2 (CMT2), neuronal axonal form, have normal NCVs, normal muscle stretch reflexes, and normal size nerves. Genetics of CMT CMT1 can be inherited as autosomal-dominant (AD), autosomal-recessive (AR), or X-linked disorder. AD CMT1 is most frequently observed pattern, whereas AR CMT1 is rare. In 70% of AD CMT1 patients, disease locus shows DNA duplication in a segment of chromosome17 (17p11.2p12) that encodes membrane-associated myelin protein with apparent molecular weight of 22 kd (PMP22). CMT 1 B is linked to markers on chromosome 1 (1q21.2q23) that encode for protein zero (Po) myelin. The dominant X-linked form, CMTX (sq1213), has missense mutation in segment of X chromosome that encodes conexin-32 protein. All these proteins are found in peripheral nerve myelin and to

play a role in keeping compaction of myelin layers ((Weisberg, 1996).

2.3.6. Hereditary Neuropathy with Liability to Pressure Palsies (HNPP):

This disorder, which is also called familial recurrent polyneuropathy or tomaculous neuropathy, was originally described in a family in which three generations had recurrent peroneal neuropathy after digging potatoes in a kneeling position. Hereditary neuropathy with liability to pressure palsies (HNPP) can cause periodic episodes of numbness, muscular weakness, atrophy, and in some cases palsies that follow relatively minor compression or trauma of peripheral nerves. Carpal tunnel syndrome and other entrapment neuropathies are frequent manifestations of HNPP. Electrophysiologic studies sometimes show mildly slow nerve conduction velocity in clinically affected individuals as well as in asymptomatic carriers. Conduction blocks can also be seen. Peripheral nerves show segmental demyelination and remyelination with tomaculous or sausage-like focal thickening of myelin sheath. Refsum's Disease (Heredopathia Atactica Polyneuritiformis) Refsum's disease is hereditary metabolic disorder transmitted as autosomal recessive trait as result of deficiency of phytanic acid α-hydroxylase and accumulation of phytanic acid in tissues and blood. The disease starts in childhood and is manifested by chronic

polyneuropathy associated with cerebellar ataxia, retinitis pigmentosa, deafness, and pupillary abnormalities. The disease responds to diet low in phytanic acid. Hereditary Sensory Neuropathies Hereditary sensory neuropathies are rare hereditary disorders characterized by sensory loss of dissociated type resembling syringomyelia. These neuropathies can appear early or late in life and are frequently associated with painless traumatic deformities, ulcers of the extremities, and autonomic dysfunction

.((Weisberg, 1996

:Diseases of motor nerves .2.3.7

Amyotrophic Lateral Sclerosis (Motor Neuron Disease, Lou Gehrig's Disease) Amyotrophic lateral sclerosis (ALS), also known as motor neuron disease and often referred to as Lou Gehrig's disease, is a devastating paralytic and fatal disorder of adult patients caused by degeneration of large motor neurons of brain and their corticospinal tract, motor neurons of brain stem, and anterior horn cells of spinal cord. As contrasted with peripheral neuropathy, in ALS there is involvement of both lower and upper motor neuron system. There is no sensory disturbances as disorder is entirely motor. Symptoms usually begin insidiously and there is frequently 12 to 24 month delay in diagnosis and hopefully with enhanced awareness of this disorder, the delay in diagnosis will decrease. The disease usually affects middle-aged patients (males more than females possibly related to involvement of androgen

receptor) and risk factors may include exercise, smoking, Gulf War experience, genetics (role of superoxide dismutase), and glutamate excitoxicity. The dis-ease is characterized by progressive weakness and early wasting (amyotrophy) of muscles with fasciculations and presence of upper motor neuron signs. There is striking sparing of bladder and bowel control, sparing of sensation, and preservation of sexual function, intellect, and eye movements (Weisberg, 1996).

Clinical presentation varies according to group of neurons or tracts affected. It usually consists of progressive, usually symmetrical, distal weakness of legs or hands. Leg muscle cramps are frequent early complaint. Weight loss and progressive wasting of muscles associated with fasciculations in upper and lower limbs, hypotonia, diminished reflexes indicate anterior horn cell involvement. Spasticity of legs with hyperreflexia and bilateral Babinski signs indicate corticospinal tract involvement. Weakness progresses proximally and affects neck muscles and bulbar musculature to cause difficulty swallowing and speech impairment. Respiratory muscle paralysis is the terminal effect. Emotional liability with uncontrollable bouts of laughing or crying, dysarthria, difficulty swallowing, spastic tongue without fasciculations, and hyperactive jaw jerk can occur (pseudobulbar palsy). Course is relent-less, progressing to death within 3 to 7 years or more. Diagnosis is established by EMG-NCV which shows normal nerve condition

velocities and electromyographic evidence of widespread denervation with re innervation. Muscle biopsy shows severe denervation (fascicular) atrophy (Weisberg, 1996).

The differential diagnosis includes cervical spondylitic myelopathy and other cervical cord lesions including tumors, disk herniations, syringomyelia, or foramen magnum lesions that can be diagnosed by myelography or CT/MRI scanning. Lead and mercury intoxications, thyroid and parathyroid disease, and familial or tropical spastic paraparesis should be excluded. There is a reluctance to make diagnosis of ALS due to poor prognosis and diagnostic certainty needs to be high before this diagnosis is explained to the patient. There are multiple variants of ALS dependent upon whether the upper or lower motor neuron is predominantly involved and whether the disease begins in the extremities or bulbar region. Progressive bulbar palsy can be the first manifestation of motor neuron disease. Speech impairment and difficulty swallowing are early signs associated with tongue atrophy and fasciculations. Symptoms progress to respiratory impairment or aspiration pneumonia. Clinical course usually lasts less than 3 years. Progressive bulbar palsy is final stage of most patients with amyotrophic lateral sclerosis. In progressive spinal muscular atrophy (PSMA), predominant findings are progressive muscle atrophy and fasciculations with lack of corticospinal tract involvement. This can be confused with unusual muscle disease

inclusion body myositis, which begins with distal muscle weakness. The progression of this type of motor neuron disease is slower. However, most patients eventually develop upper motor neuron signs and follow regular course of amyotrophic lateral sclerosis. Some patients with primary lateral sclerosis (PLS) have progressive spastic paraparesis (PLS) that later affects upper limbs and that eventually shows signs of lower motor neuron involvement. Rarely, clinical presentation remains as pure

.(upper motor neurons signs (Weisberg, 1996

Care of patients with amyotrophic lateral sclerosis requires multidisciplinary approach. Physical therapy to increase usefulness of preserved muscles is important. Feeding gastrostomy improves general nutrition of patients with dysphagia and prevents aspiration pneumonia. Ventilatory assistance when necessary should be discussed with patient and family early in disease course. There is no effective therapeutic agent but Riluzole which is glutamate antagonist may slow disease progression especially if utilized early. There is some suggestive evidence that anti-oxidants and creatine may be effective therapeutic strategies. Five to 10% of cases are familial, transmitted in autosomal dominant pattern. There is evidence that genetic defect in some families is linked to chromosome21 (D21S58) segment that encodes for Superoxide Dismutase 1, an important neuronal antioxidant. A clinically heterogeneous group of hereditary lower motor neuron diseases that predominantly affect

infants and young patients is known as progressive spinal muscular atrophy (SMA). Regardless of age of onset, they are linked to chromosome5. The disease is inherited through autosomal recessive gene. This heterogeneous disease has several clinical presentations with different ages of onset. When present at birth (Werdnig-Hoffman), it is manifested by floppiness, abdominal breathing, fasciculations of tongue, and evidence of denervation on electromyography and muscle biopsy. And form of spinal muscular atrophy appears in infancy. Patients with this form have a longer survival span. Another intermediate type of spinal muscular atrophy with the same type of inheritance but with onset in adolescence is characterized by predominantly proximal muscle involvement and normal life span (Kugelberg-Welander type). In this form of SMA, weakness and atrophy are frequently proximal and simulate myopathy; however, in contrast with a myopathy muscle stretch reflexes are usually absent in Kugelberg-Welander syndrome. Electrophysiologic studies and muscle biopsy are necessary for diagnosis. Bracing and physical and occupational therapy to stretch or prevent contractures and to prevent scoliosis improves quality of patient's life (Weisberg, 1996).

2.3.8. Carpal tunnel syndrome:

The carpal tunnel is open-ended proximally and distally, but behaves like a closed compartment physiologically and maintains its own distinct tissue fluid pressure levels.

It is a fibro-osseous canal that is bounded by the concave arch of the carpal bones dorsally and the flexor retinaculum palmarly. The hook of the hamate, triquetrum, and pisiform form the ulnar border; the radial border consists of the scaphoid, trapezium, and the fascial septum overlying the FCR. The flexor retinaculum consist of three zones: a proximal zone that is continuous with the deep forearm fascia, a central zone that is composed of the transverse carpal ligament (TCL), and a third zone that consists of the aponeurosis between the thenar and hypothenar muscles. The median nerve at the wrist has approximately 30 fascicles. The motor recurrent branch often consists of two fascicles that are situated in a volar position, with the various sensory groups in the radial, ulnar and dorsal positions of the main trunk. The motor branch can be separated from the main trunk without harm for up to 100 mm proximal to the thenar muscles. The sensory fibers travel within the common digital nerves to the thumb, index and middle, as well as the communicating branch to the third web space (David J.

.(2006

:Pathophysiology .2.3.8.1

There are two potential sites of compression anatomically. The first is at the proximal edge of the TCL where compression may be produce by acute wrist flexion. This account for the positive Phalen’s test (wrist flexion test) in CTS. The second is adjacent to the hook of the hamate,

where an hourglass deformity of the median nerve may be seen. Patients with compression in this area will have a positive median nerve compression (Durkan’s) test but a negative Phalen’s test. Compression within the carpal tunnel may also result from any lesion that takes up space within the canal, such as flexor tenosynovitis, hematoma, palmar carpal dislocation, distal radius fractures, tumors and ganglia. Although many cases have been attributed to a non-specific synovitis, synovial biopsies typically fail to show evidence of inflammation. They do reveal edema and vascular sclerosis, which may be secondary to compression rather than the primary event (David J. 2006).

:History .2.3.8.2

The patient typically complains of numbness and paresthesia in the median nerve distribution. Initially the symptoms occur at night, owing to a combination of wrist flexion during sleep and fluid shifts that occur within the horizontal position, which increases the carpal canal pressure. In this early stage of nerve compression the symptoms are of a vascular nature, which culminate in endoneurial edema. With early compression the symptoms are intermittent and the edema is reversible. As the symptoms progress, they become more frequent during the day and are precipitated by gripping and pinching activities as well as those tasks requiring repetitive wrist flexion. When there are constant symptoms, there is

usually myelin damage and/or chronic endoneurial edema

.((David J. 2006

:Physical examination .2.3.8.3

CTS represents a constellation of signs and symptoms in which no one test absolutely confirms its diagnosis. A positive Tinel's sign may be present over the median nerve at the wrist, and produces paresthesia in the thumb and radial $2^{1/2}$ digits. Phalen's test consist of passive wrist flexion for 1minute, which when positive produces subjective paresthesia in a median nerve pattern. This is best performed with the elbow extended because simultaneous wrist and elbow flexion may reproduce ulnar nerve symptoms as well. Direct compression of the nerve or the Durkan's test is thought to be more sensitive. Szabo et al. found that if a patient had an abnormal hand diagram, abnormal sensibility by SWT testing, a positive Durkan's test, and night pain, the probability of having CTS was 0.86. If all four of these conditions were normal,

.(the probability of having CTS was 0.0068 (David J. 2006

:Electrodiagnostic studies .2.3.8.4

The nerve conduction study can yield useful information, but the severity of the preoperative condition deficit does not provide significant data for prediction of the final outcome or return to work after carpal tunnel release. There are some caveats for nerve conduction studies in

CTS. First, sensory abnormalities usually occur before motor abnormalities. In other words, the distal sensory latencies are often slow before the distal motor latency. This is not surprising, because 94% of the axons in the median nerve at the wrist level are sensory. The sensory nerve axons are larger than the motor axons and hence more susceptible to compression. If the distal motor latency (DML) is abnormal in the presence of normal sensory nerve action potentials (SNAPs), extra care must be taken to rule out anterior horn cell disease or a C8 radiculopathy, although isolated recurrent motor branch compression has been reported. Second, the nerve conduction studies may not return to normal after decompression owing to retrograde fiber degeneration or incomplete remyelination, even in the presence of a full

.(clinical recovery (David J. 2006

:Sonographic anatomy of the median nerve .2.4

Ultrasonically, in the transverse plane, the median nerve appears hypoechoic with a hyperechoic border, containing multiple bright reflectors. The median nerve is also rounded or oval in the proximal wrist, becoming progressively flatter as it passes through the carpal tunnel. Within the carpal tunnel, the median nerve is intimately related to the flexor retinaculum. In the longitudinal plane, the median nerve is seen anterior to the flexor digitorum tendons, coursing in a parallel plane. The nerve is easily differentiated from the tendons lying posteriorly, as the nerve lacks the tendons' characteristic fibrillar pattern (i.e. its fibrillar

.(pattern is not as pronounced

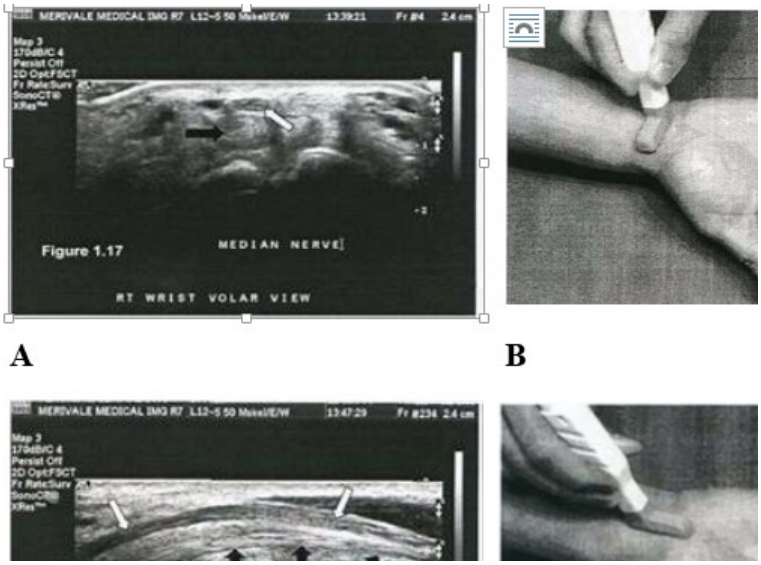

Figure 2.4. **A**: Short axis, the median nerve - flexor pollicis longus (white arrow) the tendon (black arrow). **B&D**: probe position of the in the volar aspect of the wrist **C**: Median Nerve – Long axis, the median nerve flexor (white arrows), pollicis longus tendon (black arrow) (Devin Dean, 2007).

2.5. Previous studies:

Bathala, L, et al, 2014 studied Normal values of median nerve cross-sectional area obtained by ultrasound along its course in the arm with electrophysiological correlations, in 100 Asian subjects. The objective of this study is to obtain normative cross-sectional area (CSA) values for median nerve by ultrasound at predetermined sites and correlate them with electrophysiological variables in healthy Asian subjects. Methods of this study was examination of the median nerve ultrasonographically in 100 healthy volunteers, mean age 39 years (range, 18–75 years). CSA of the median nerve was measured at wrist, mid-forearm, mid-arm, and axilla. All subjects underwent simultaneous standardized nerve conduction studies. Results of this study shows The mean median nerve CSAs ± SD at the distal wrist crease was 7.2 ± 1 mm^2; mid-forearm 4.8 ± 0.9 mm^2; mid-arm 6.1 ± 1 mm^2; axilla 5.9 ± 0.9 mm^2. The CSA at the wrist was the largest compared

with other levels ($P < 0.001$), and it increased with advancing age($P < 0.002$).And concluded as these a normative data show that median nerve CSA is not uniform along its length. There are differences between gender, and values increase with advancing age. ((Bathala, L, et al, 2014).

Burg EW, et al, 2013, studied Difference in normal values of median nerve cross-sectional area between Dutch and Indian subjects. Ultrasound (US) measurement of the median nerve cross-sectional area (CSA) at the wrist is a useful diagnostic test for carpal tunnel syndrome (CTS). We compared median nerve normal values between samples of Indian and Dutch populations. The methods followed in this study were examination of the median nerve by US at the wrist in 100 healthy volunteers in India and 137 volunteers in The Netherlands using the same protocol. The result was the Median nerve CSA at the wrist (7.0 ± 1.1 mm (2)) in the Indian cohort was lower in comparison to the Dutch cohort (8.3 ± 1.9 mm (2); $P < 0.05$). This difference was still present after controlling for age, height, and weight ($P = 0.001$). The study concluded as the CSA normal values for the median nerve were different between the examined population samples even after correcting for age, height, and weight. This enforces the idea that laboratories around the world should obtain their own normative data (Burg EW, et al, 2013).

Yao L, Gai N, 2004 studied Median nerve cross-sectional area and MRI diffusion characteristics: normative values at the carpal tunnel. One of the objectives of this study is to examine normal values for median nerve cross-sectional area (CSA), apparent diffusion coefficient (ADC), and fractional anisotropy (FA).Materials were, Twenty-three wrists in 17 healthy volunteers underwent MRI of the wrist at 3 T. In 13 subjects, DTI was performed at a B value of 600 mm (2)/s. Median nerve CSA, ADC, and FA were analyzed at standardized anatomic levels. The study result were the Mean (SD) median nerve CSA within the proximal carpal tunnel was 10.0 (3.4) mm (2). The mean (SD) FA of the median nerve was 0.71 (0.06) and 0.70 (0.13) proximal to and within the carpal tunnel, respectively. There was a significant difference between nerve CSA and ADC, but not FA, at the distal forearm and proximal carpal tunnel. Nerve CSA, ADC, and FA did not differ between men and women or between dominant and non-dominant wrists. Nerve CSA at the proximal carpal tunnel was positively correlated with subject age and body mass index. The study concluded as the results suggest a 90% upper confidence limit for normal median nerve CSA of 14.4 mm (2) at the proximal carpal tunnel, higher than normal limits reported by many ultrasound studies. We observed a difference between the CSA and ADC, but not the FA, of the median nerve at the distal forearm and proximal carpal tunnel levels (Yao L, Gai N, 2009).

Marciniak et al, 2013 studied High-Resolution Median Nerve Sonographic Measurements. The study was objected to study relationships between median wrist and forearm sonographic measurements and median nerve conduction studies. The methods followed was study population consisted of a prospective convenience sample of healthy adults. Interventions included high-resolution median nerve sonography and median motor and sensory nerve conduction studies. Main outcome measures included median motor nerve compound muscle action potential amplitude, distal latency, and conduction velocity; sensory nerve action potential amplitude and distal latency; and sonographic median nerve cross-sectional area. Median motor nerve and sensory nerve conduction studies of the index finger were performed using standard published techniques. A second examiner blinded to nerve conduction study results used a high frequency linear array transducer to measure the cross-sectional area of the median nerve at the distal volar wrist crease (carpal tunnel inlet) and forearm (4 cm proximally), measured in the transverse plane on static sonograms. The outer margin of the median nerve was traced at the junction of the hypoechoic fascicles and adjacent outer connective tissue layer. The study results as fifty median nerves were evaluated in 25 participants. The compound muscle action potential amplitude with wrist stimulation was positively related to the cross sectional area, with the area increasing by 0.195 mm2 for every millivolt increase

in amplitude in the dominant hand (95% confidence interval, 0.020, 0.370 mm2; P < .05) and 0.247 mm2 in the non-dominant hand (95% confidence interval, 0.035, 0.459 mm2; P <.05). There was no significant linear association between the wrist median cross sectional area and median motor and sensory distal latencies. Conduction velocity through the forearm was not significantly linearly associated with the forearm area or forearm-to-wrist area ratio (tapering ratio). The wrist area was inversely related to the sensory nerve action potential amplitude. The study were concluded as although associations were found between median nerve conduction study amplitudes and sonographic nerve measurements, they were not found for other parameters. Studying these relationships may increase our understanding of when to best use these procedures .((Marciniak et al, 2013

Chapter three

Materials & methods

:Materials .3.1

:Study population .3.1.1

The data of this study were collected of subjects not suffer of any median .nerve disease

:Sampling .3.1.2

The sample of this study in 100 volunteers with different age, gender, .weight, height, and occupations have normal median nerve

:Inclusion criteria .3.1.3

Subjects not suffering from any symptoms related to median nerve injury .with ages above 17 years

:Exclusion criteria .3.1.4

.Patient with history of median nerve disease and children

:Machines .3.1.5

The data was collected using (E-CUBE, medical system) Ultrasound machine made in coria, and (Siemens medical system) ultrasound machine made in Germany, each with linear array 7-10 MHz, using coupling gel, Weight Measuring equipment and Height Measuring Tape were used for measuring body .characteristics

:Methods .3.2

:Study design .3.2.1

This is a retrospective cross sectional study where the volunteers were .selected randomly

:Area of study and duration .3.2.2

It was conducted in ultrasound department of College of Medical Radiological Sciences of Sudan University of Sciences and Technology and Ribat University Hospital, Khartoum state of Sudan republic, during the period from April .to august 2016

:Sonographic Technique .3.2.3

The median nerve was examined with a real time linear transducer having a short focal zone (1 to 4cm), volunteers were examined with their forearm resting comfortably on a flat surface with the elbow in mid flexion and their wrist in supination, Proper time gain compensation and dynamic range were used, Imaging was performed in the transverse plane at the level of the palmar crease, with the ulnar artery being the medial landmark of the carpal tunnel, the width and the anterio-posterior diameter were measured then the median nerve area was calculated for .both hands

:Data collection .3.2.4

The data was collected using the following variables: median nerve areaof both hands, echogenicity (ultrasound findings), Age, gender, .weight, height and occupations

Data analysis .3.2.5

The data was analyzed by using Statistical Packaged for Social Studies .(SPSS) and Excel under windows

Chapter four

Results

Statistical Methods: the use of comparative analytical method using the SPSS statistical program based descriptive statistics and comparative and relationship hypothesis tests (0.05 sig. level), to demonstrate the differences in (both Right and Left MNA) with respect to .(gender, age, height, weight, and occupations

The test was used for (simple linear regression, binary logistic regression, ANOVA, t-tests and correlations) to study the hypothesis which states there were significant .differences in MNA

.Table 4.1. Frequency distribution of person's age

Percent	Frequency	Age group
10.0	10	20>
67.0	67	20-25
8.0	8	26-30
5.0	5	31-35

3.0	3	36-40
2.0	2	41-45
5.0	5	46-50
100.0	100	Total

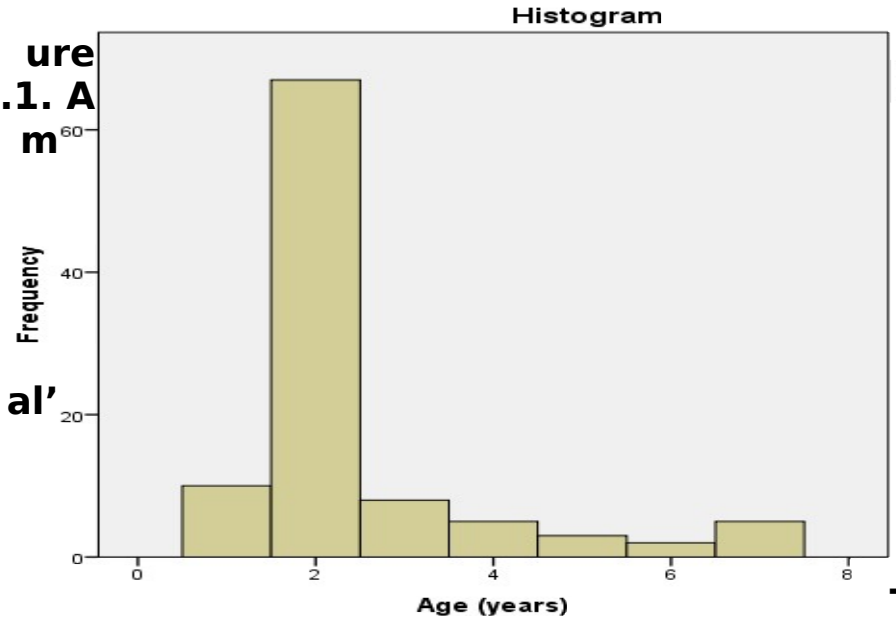

Figure 4.1. A histogram plot shows distribution of the individual's ages

Table 4.2. Frequency distribution of person's weights

Percent	Frequency	(Weight (kg
6.0	6	50>
45.0	45	50-60
26.0	26	61-70
12.0	12	71-80
6.0	6	81-90
2.0	2	91-100

3.0	3	111-120
100.0	100	Total

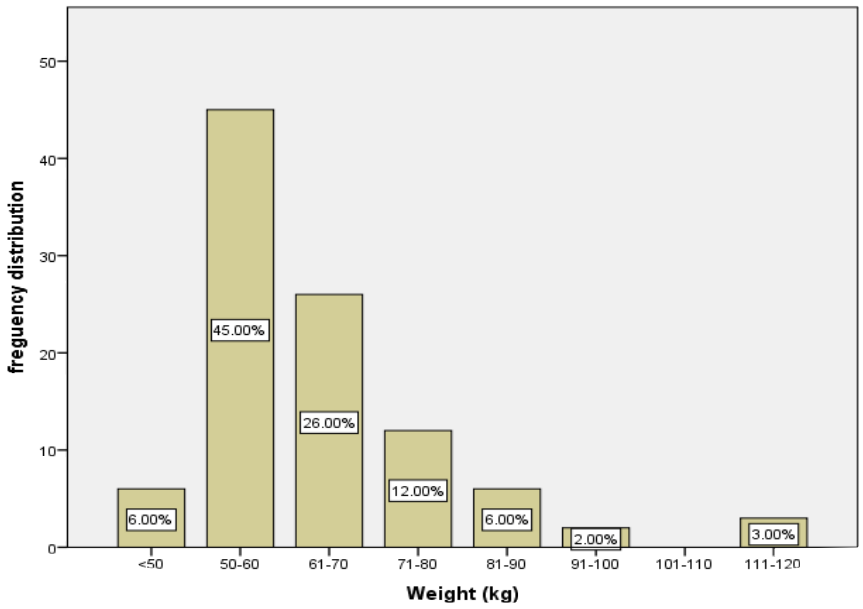

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Figure 4.2. a histogram plot shows distribution of .the individual's weight

.4.3 The linear relationship between age and MNA (Right and Left)

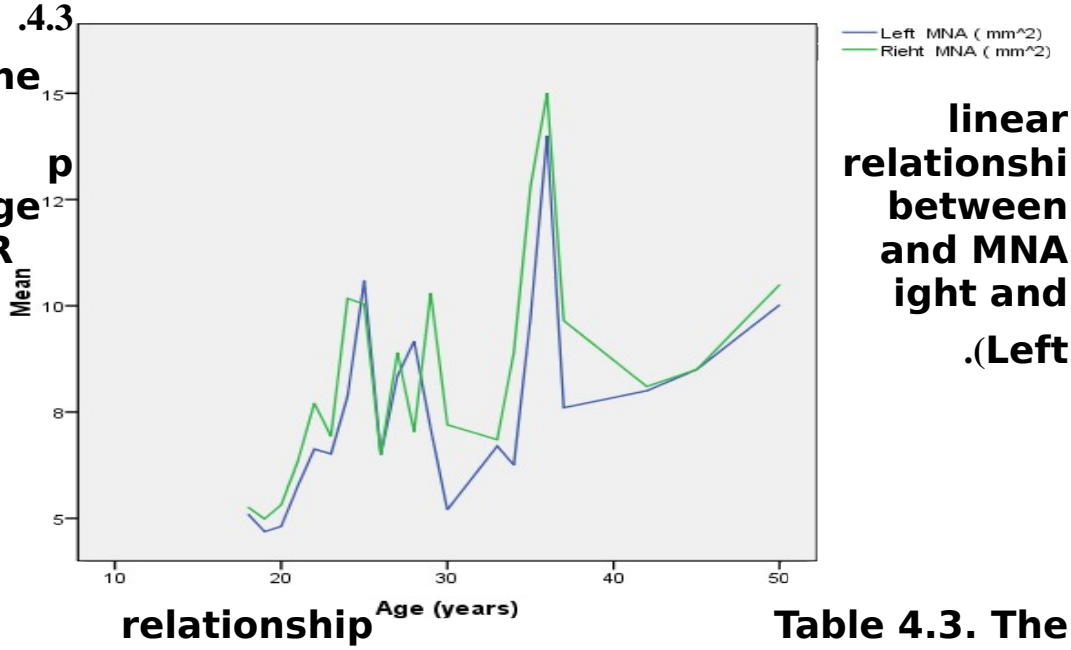

Table 4.3. The relationship between age and MNA (Right and Left).

Model	Unstandardized Coefficients		T	.Sig
	B	Std. Error		
1 (Constant)	2.544	615.	4.134	000.
(Age (years	163.	024.	6.786	000.
2 (Constant)	2.978	678.	4.396	000.
(Age (years	174.	027.	6.554	000.

Table 4.4. Frequency Distributions of gender and .MNA means

Std. Error Mean	Std. Deviation	Mean	N	Gender	
284.	2.108	6.63	55	Female	(Left MNA (mm^2
319.	2.137	6.43	45	Male	
288.	2.137	7.15	55	Female	(Right MNA mm^2
374.	2.510	7.32	45	Male	

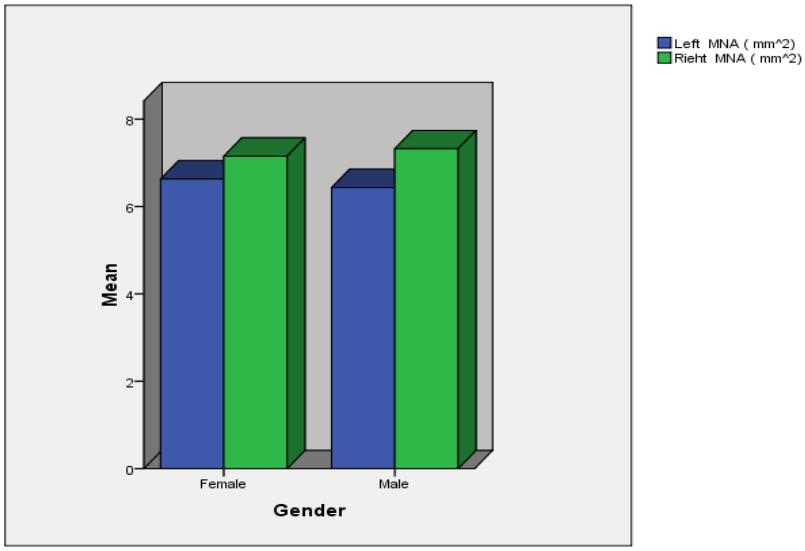

Figure 4.4.The means of (Right and Left) MNAs with .gender

Table 4-5. T-test for Equality of Means of two groups .in both MNAs

		t-test for Equality of Means					
	95% Confidence Interval of the Difference	Std. Error Difference	Mean Difference	Sig. (2-tailed)	Df	T	
	Upper Lower						
Right MNA ((mm²	Equal variances assumed	465.	169.-	716.	98	365.-	753. 1.092-
Left MNA ((mm²	Equal variances assumed	426.	198.	644.	98	463.	1.044 649.-

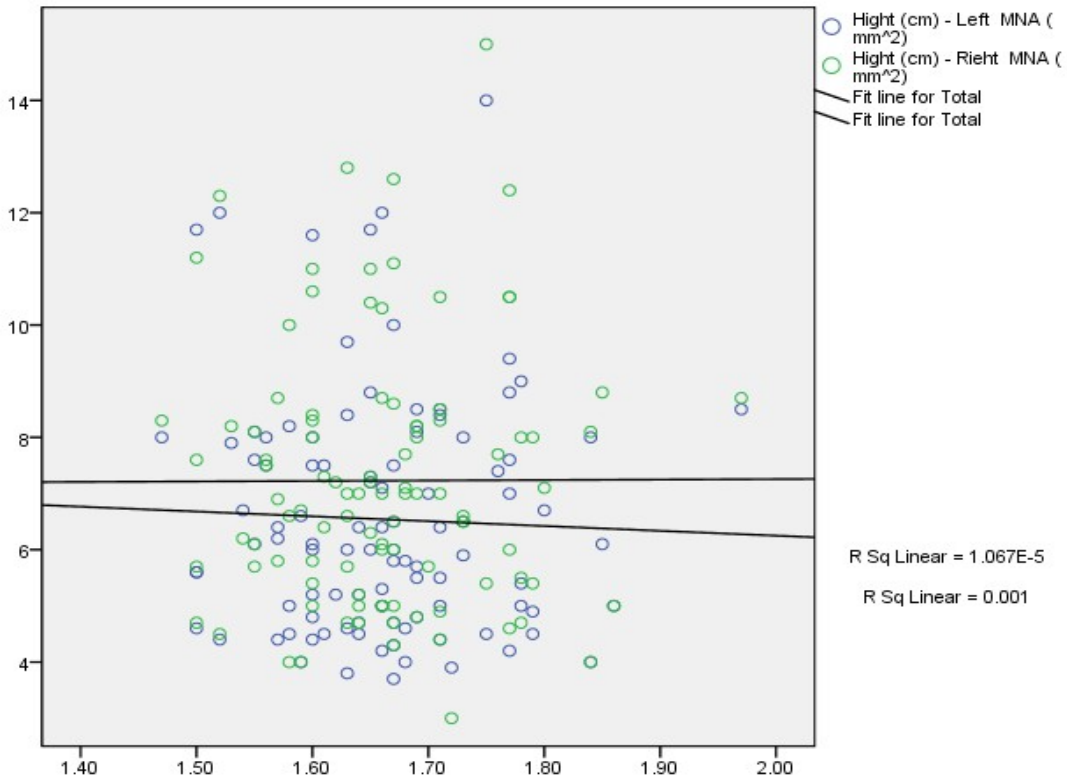

Figure 4.5. The linear relationship between Height and MNA (Right and Left).

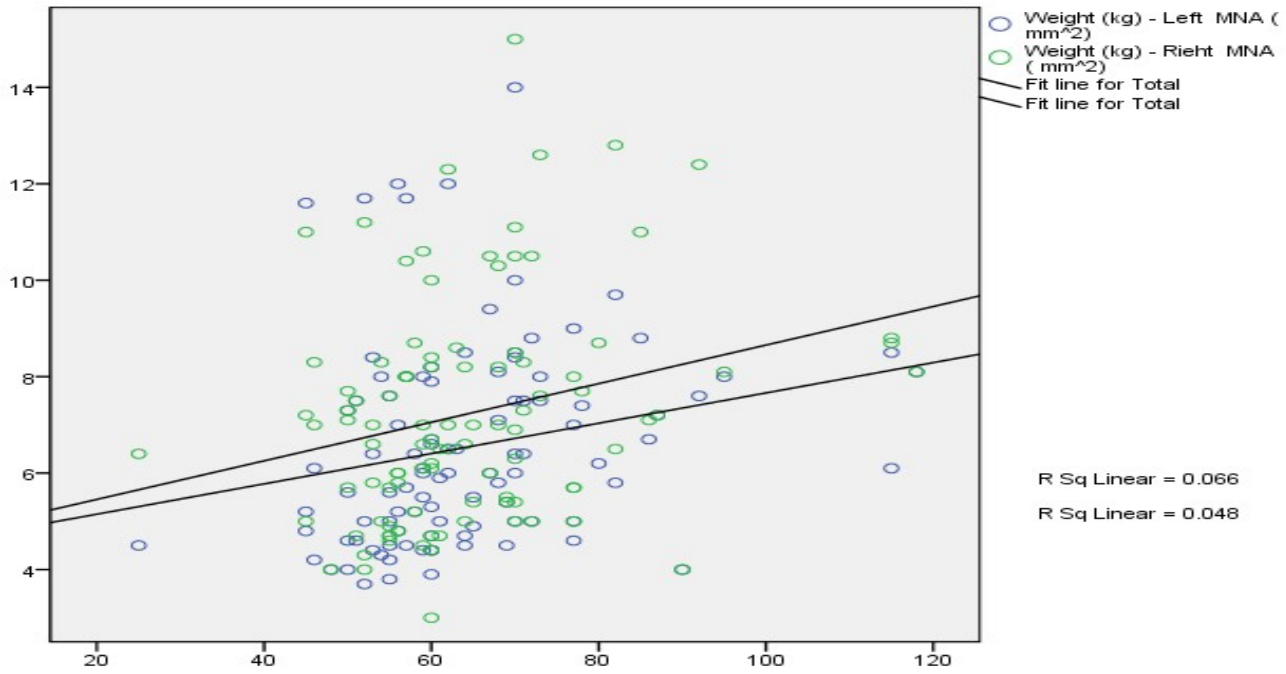

Figure 4.6. The linear relationship between Weight and MNA (Right and Left).

Table 4-6. The relationship between Weight and MNA (Right and Left).

Model		Unstandardized Coefficients		T	.Sig
		B	Std. Error		
1	(Constant)	4.656	1.006	4.627	000.
	(Weight (kg	040.	015.	2.622	010.
2	(Constant)	4.520	932.	4.847	000.
	(Weight (kg	031.	014.	2.224	028.

Table 4.7. Distributions of MNAs with respect to .individual's occupations

		95% Confidence Interval for Mean							
Maximum	Minimum	Upper Bound	Lower Bound	Std. Error	Std. Deviation	Mean	N		
8	4	5.88	5.19	172.	1.336	5.53	60	Student	Left MNA ((mm^2
12	5	8.07	6.71	329.	1.611	7.39	24	Radiographic specialists	
14	6	10.97	7.95	685.	2.374	9.46	12	Police	
12	12	.	.	.	.	11.70	1	Statistician	
9	9	.	.	.	.	8.80	1	Technician	
5	5	.	.	.	.	4.90	1	Security	
6	6	.	.	.	.	6.00	1	Doctor	
14	4	6.96	6.12	211.	2.113	6.54	100	Total	
10	3	6.57	5.78	197.	1.527	6.17	60	Student	Right MNA ((mm^2
13	5	8.83	7.28	376.	1.842	8.05	24	Radiographic specialists	
15	7	12.08	8.98	704.	2.438	10.53	12	Police	
10	10	.	.	.	.	10.40	1	Statistician	
11	11	.	.	.	.	11.00	1	Technician	
5	5	.	.	.	.	5.40	1	Security	
6	6	.	.	.	.	6.00	1	Doctor	
15	3	7.69	6.77	230.	2.301	7.23	100	Total	

Figure 4-7.Means of occupation groups in both MNAs:

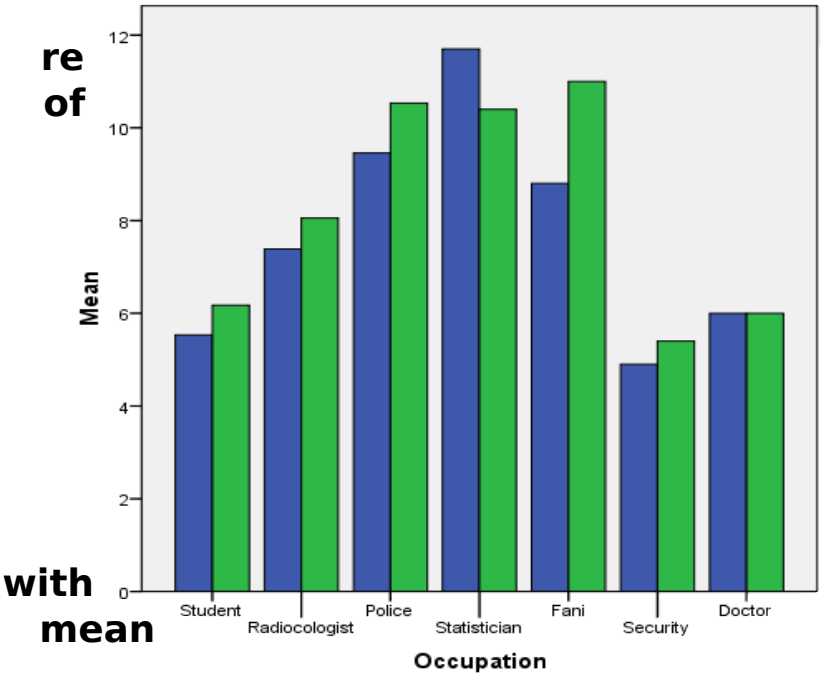

Table 4.8. Occupations with mean difference respect to .of MNAs

Left MNA ((mm²	Between Groups	214.955	6	35.826	14.680	000.
	Within Groups	226.969	93	2.441		
	Total	441.924	99			
Right MNA ((mm²	Between Groups	243.362	6	40.560	13.425	000.
	Within Groups	280.984	93	3.021		
	Total	524.346	99			

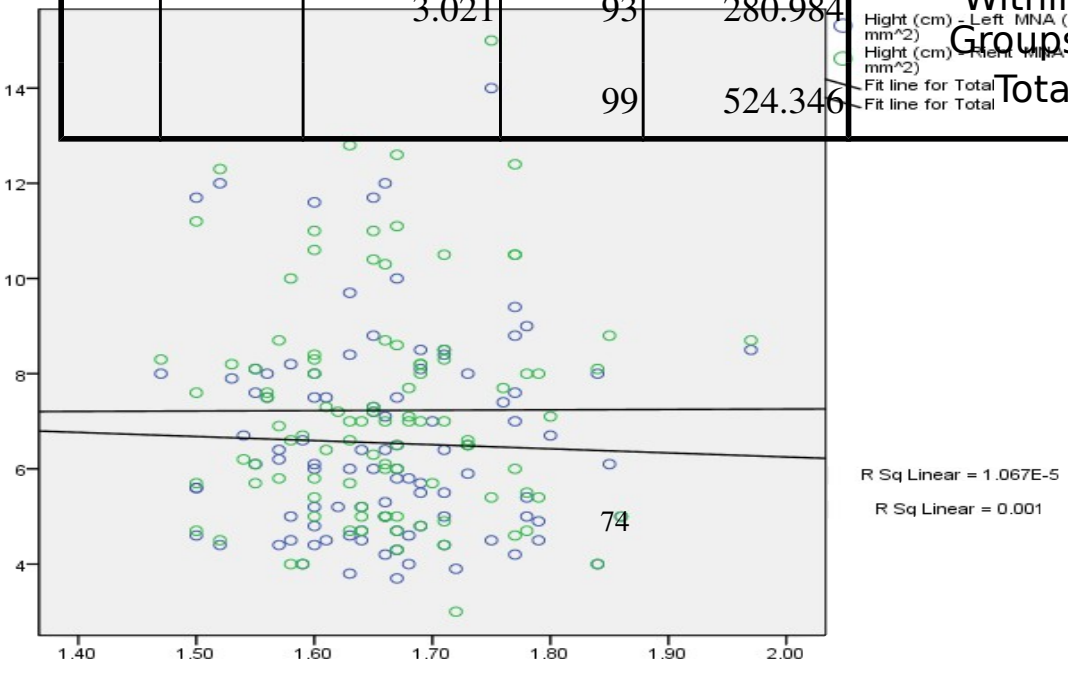

Figure 4-8 the linear relationship between Height .(and MNA (Right and Left

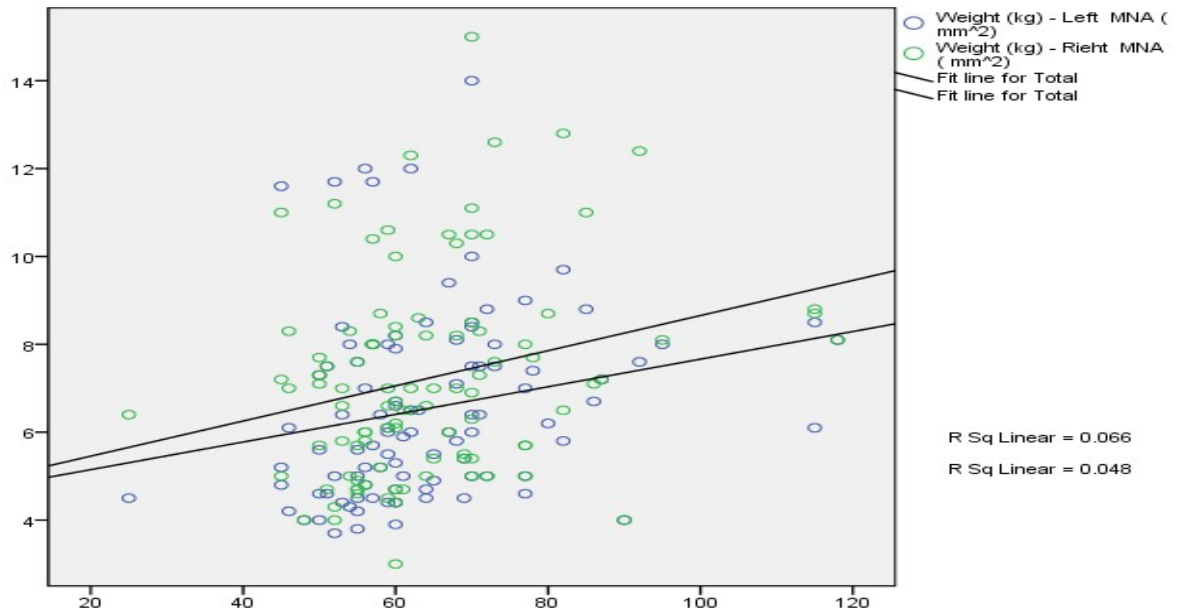

Figure 4.9. The linear relationship between Weight .and MNA (Right and Left

Table 4.9. Relationship between Weight and MNA (Right .(and Left

.Sig	T	Unstandardized Coefficients		Model	
		Std. Error	B		
000.	4.627	1.006	4.656	(Constant)	1
010.	2.622	015.	040.	(Weight (kg	
000.	4.847	932.	4.520	(Constant)	2
028.	2.224	014.	031.	(Weight (kg	

.Table 4.10. A Case Classification

Observed		Predicted		
		Echogenicity		Percentage Correct
		H	G	
Echogenicity	H	94	0	100.0
	G	6	0	0.

The cut value is .500

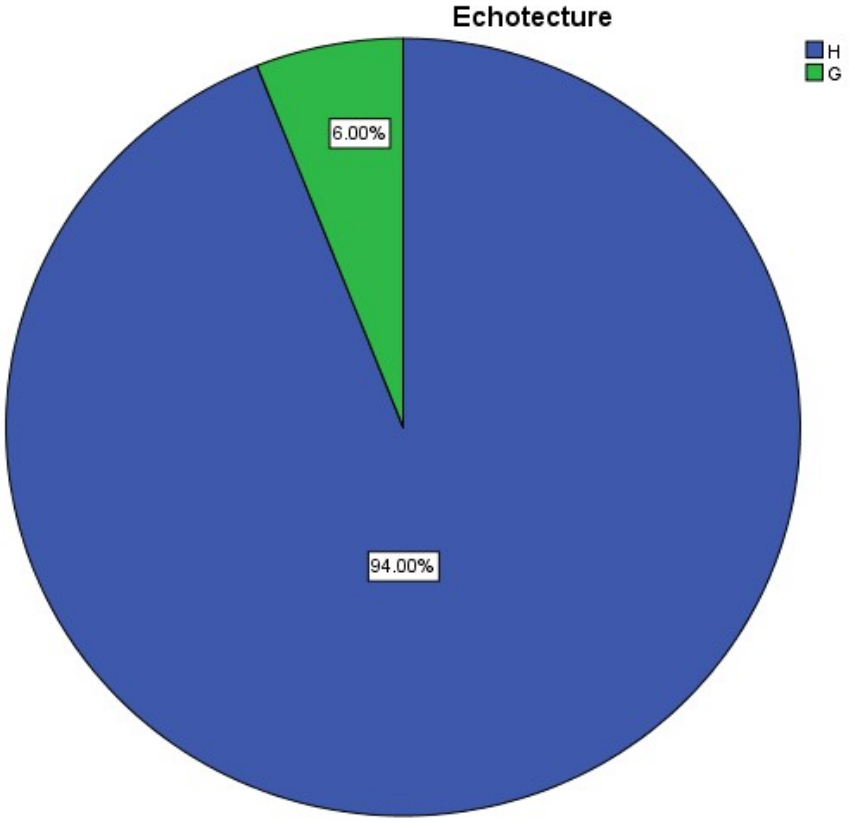

Figure 4.10. A pie chart shows the percentage of .normal median nerve echogenicity

Table 4.11. Contribution of each MNA measurements to Echogenicity.

(Exp(B	.Sig	Df	Wald	.S.E	B	
1.432	030.	1	4.698	166.	359.	LeftMNA
005.	000.	1	14.346	1.423	5.389-	Constant
1.275	130.	1	2.297	160.	243.	RightMNA
010.	001.	1	10.679	1.424	4.655-	Constant

Chapter five

5.1. Discussion:

As mentioned earlier, the general objective of this study was to measure the normal median nerve area at the level of the wrist joint in adult using diagnostic ultrasonography. The data of this study was collected from healthy individual, 100 individual underwent musculoskeletal ultrasound for the median nerve at the wrist joint, and the Median Nerve Area (MNA) of both hand was calculated.

The results of this study reveals that the means of the RT MNA for male and females were 7.32±2.51, and 7.15±2.14 respectively, and the means of the LT MNA for males and females were 6.43±2.14, and 6.63±2.11 respectively, table (4-4) And fig (4-4); same as the result

found in the previous study of (Bathala, L, et al, 2014) and ((Burg EW, et al, 2013).

Also shows that there is no statistically significant difference between the means of MNAs for males and females table (4.6). And this means that the gender do not affect MNA.

Much more the study reveals that there was positive relationship between age and MNA fig. (4-3), that's to say when patient's age increases by 1year the RT & LT MNA increases by 0.163±0.024 and 0.17±0.03 mm^2 respectively table (4-4). Those linear relationships can be stated in the formula: RT MNA=0.16*age + 2.544, LT MNA=0.17*age+2.99, and that what documented by (Yao L, Gai N, 2004, Bathala, L, et al, 2014 and Burg EW, et al, 2013) in a previous studies.

Regarding the relation between person's heights and MNA for both gender the study reveals that there was no variation in the MNA, can be explained by the person Height fig (4.5).

Related to the weight of individuals and MNA the study found that there was positive relationship between weight and MNA fig. (4.6), that's to say when patient's weight increases by 1kg the RT & LT MNA increases by .040±0.02 and .031±0.01 mm^2/kg respectively table (4.8). Those

linear relationships can be stated in the formula: RT MNA = 0.04 * weight + 4.66, LT MNA = 0.03 * weight + 4.52 .respectively

concerning the effect of person's occupations and MNA, table (4.9), the study conclude that the occupation greatly affect the MNA measurement and this was based on table (4.10) take a look at the Sig. values in the last column; The Sig. values are 0.0000 for both right MNA left MNA. So it conclude that there was statistically significant .differences between Occupations in MNA Means

From the results the study found out that patient's age has an effect on the echogenicity of the MN table (4-10), it can say that younger persons have normal echogenicity (hypoechoic), and this is based on the odds of "H"(hypoechoic) was 1.171 times greater for Youngers than Elders, and 96% of median nerve echogenicity was .(hypoechoic fig (4-10

Statistical Methods: the use of comparative analytical method using the SPSS statistical program based descriptive statistics and comparative and relationship hypothesis tests (0.05 sig. level), to demonstrate the differences in (Median Nerve Area) of both hands with respect to (age, gender, height, weight and occupations). The test was used for (simple linear regression, binary logistic regression, t-tests, f-test and correlations) to study

the hypothesis which states there are significant differences in Median Nerve Area.

5.2. Conclusion:

This is a retrospective cross sectional study conducted to know the normal measurements of the Median Nerve Area, and to identify the relationships between these measurements and the individual body characteristics in adult.

The data was collected by doing musculoskeletal ultrasound scanning using 7-10 MHz transducers, 100 subjects with ages above 17 years were selected randomly, from whom have not any symptoms related to median nerve pathology, at period from April- to August, 2016.

The results of this study states that the mean of RT and LT MNA, were (7.32 ± 2.51) mm2, and (6.43 ± 2.14) mm2 respectively, with no significant difference between males and females.

The study conclude that there was linear increasing relationship between the median nerve area and patient's age and weight, by (0.163 ± 0.024) and (0.17 ± 0.03) mm^2/year

for RT and LT MNA respectively, and by (040 ± 0.02) and (0.031 ± .0.01) $mm^{2/}$kg for the RT and LT MNA respectively

of cases shows hypoechoic nerve echogenicity and 96%

found that there were statistically significant differences between Occupations and MNA Means, and the odds of "hypoechoic" is 1.171 .times greater for Youngers than Elders

The study find out that there was no variation in MNA, can be explained .by person Height

5.3. Recommendations:

- High resolution musculoskeletal ultrasound is a respectful modality, and should be used confidently in measurements and evaluation of median nerve .area and pathologies
- In order to improve image quality, patients should be well positioned, and ultrasound machines must be .well adjusted to have better resolution
- Another factors like ethnics...etc.), that might affect the median nerve area were not included here. There

for other studies should be done to cover these factors.

- Also the study recommend to assess the normal median nerve area measurements in other different states in the country. So as to have our own local values, hence we are here in Sudan have different environments and very vary habits.

- It’s notice that some sonologists does not include the median nerve area measurements in case of wrist ultrasound examination, which may missing some pathologies. Therefore it's better to follow standard protocols to improve their techniques.

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:Appendices

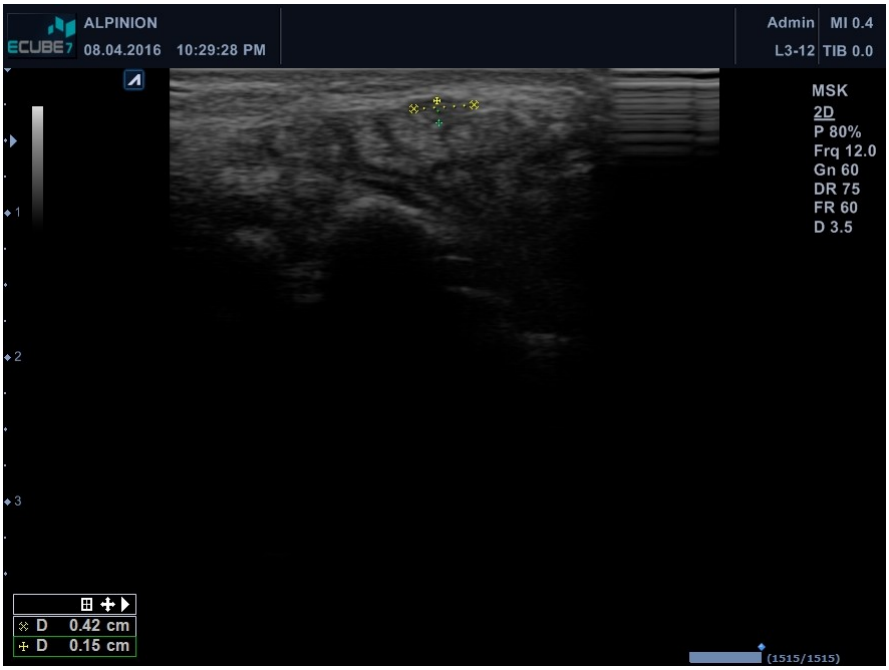

Image 1. US image of 27 yeas male shows normal median nerve cross sectional area.

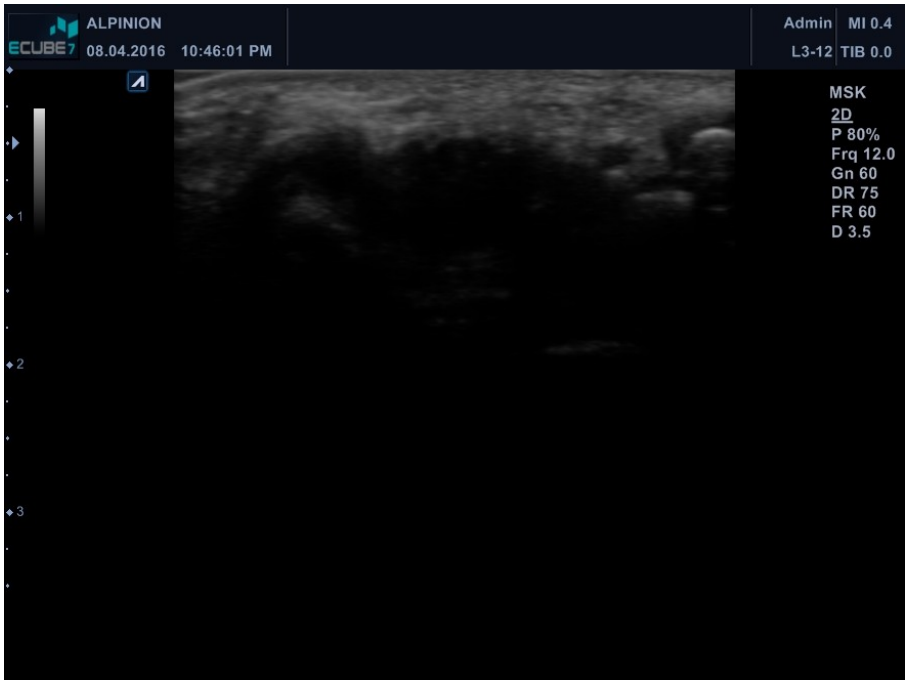

Image 2. US image of 25 yeas male shows normal median nerve cross sectional area.

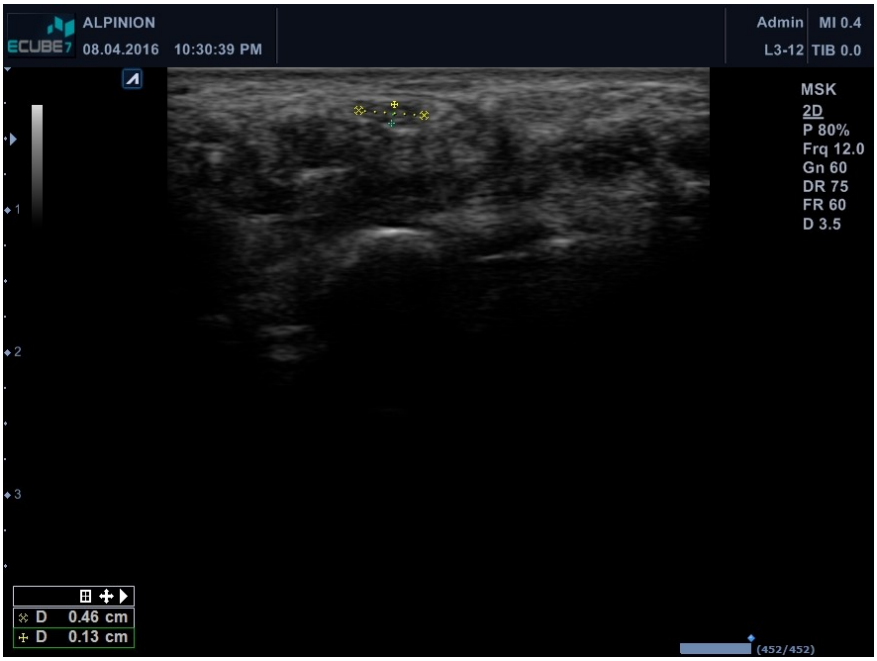

Image 3. US image of 28 yeas female shows normal median nerve cross sectional area.

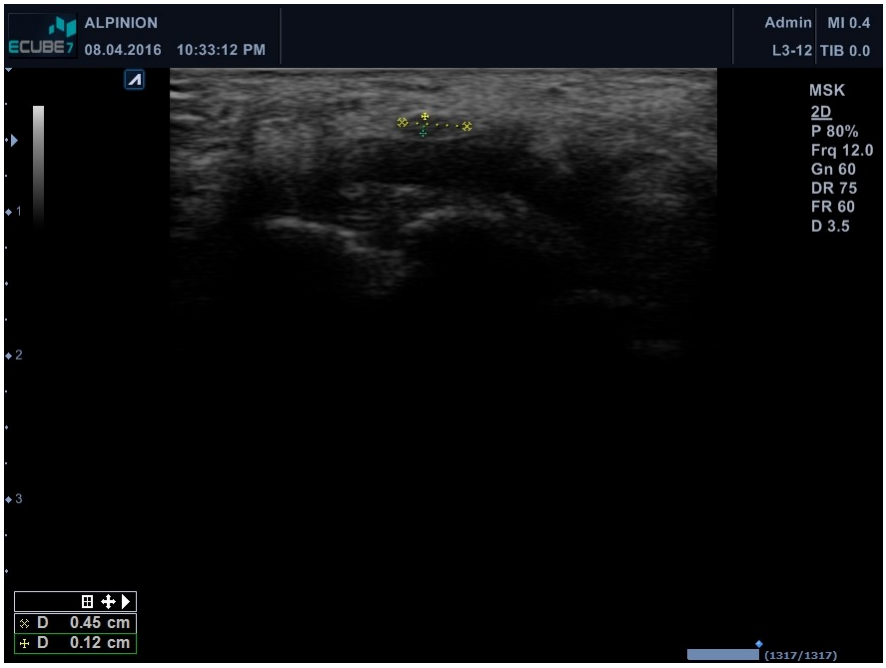

Image 4. US image of 24 yeas male shows normal .median nerve cross sectional area

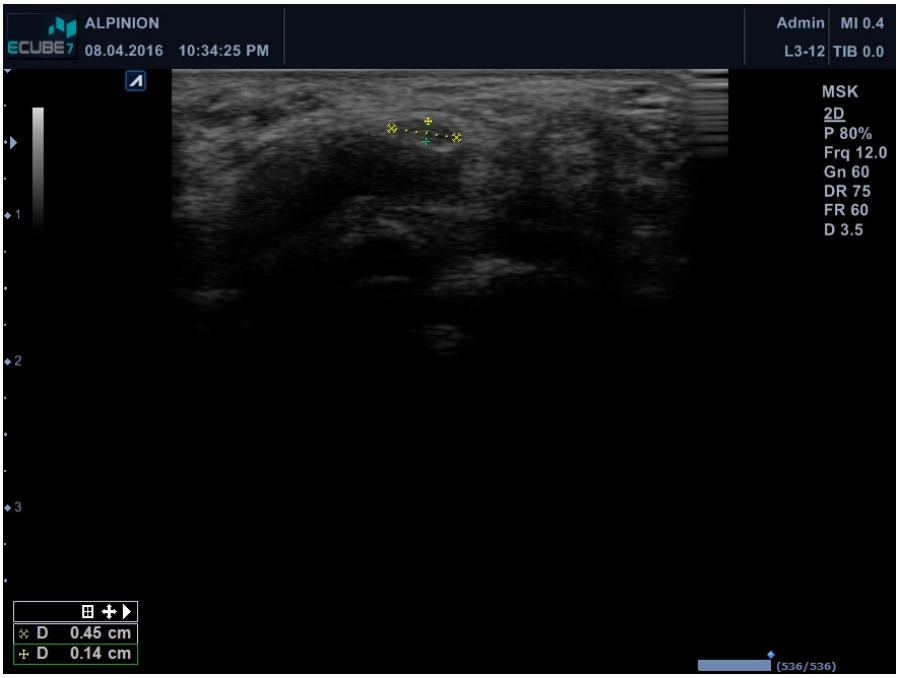

Image 5. US image of 26 yeas male shows normal .median nerve cross sectional area

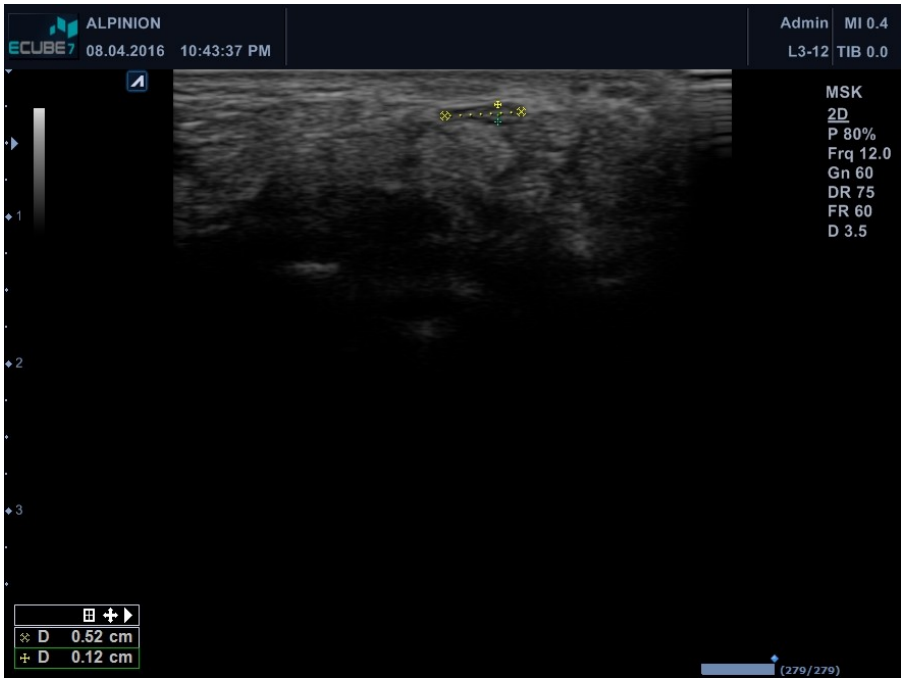

Image 6. US image of 19 years female shows normal median nerve cross sectional area.

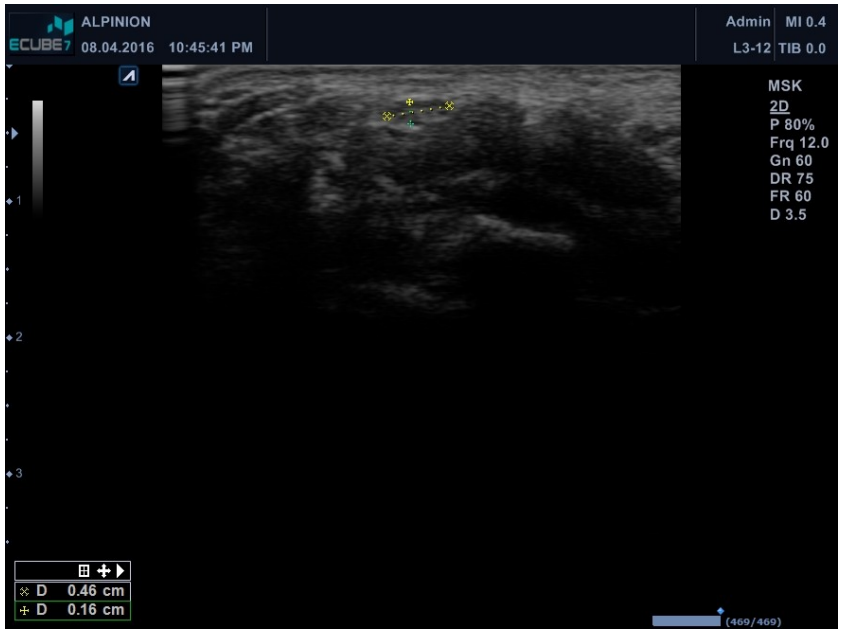

Image 7. US image of 25 yeas male shows normal median nerve cross sectional area.