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Assessment of Glomerular Filtration Rate in Diabetic and Hypertensive Patient using Scintigraphy

تقويم معدل الترشيح الكبيبي لدي مرضي السكري وارتفاع ضغط الدم باستخدام النظائر المشعة

A thesis Submitted for Partial Fulfillment of M.Sc. degree in Nuclear Medicine

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الآية

قال تعالي :

﴿وَعَلَّمَكَ مَا لَمْ تَكُنْ تَعْلَمُ ۚ وَكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيمًا﴾

صدق الله العظيم

سوره النساء الآية : 113

DEDDICATION

This thesis is dedicated to my father, who taught me that the best kind of knowledge to have is that which is learned for its own sake. It is also dedicated to my mother, who taught me that even the largest task can be accomplished if it is done one step at a time. I am also very grateful to my brother and my sister .

Acknowledgement

There are a number of people without whom this thesis might not have been written, and to whom I am greatly indebted

I wish to express my special thanks to **Dr. MOHAMMED ELFADEL MOHAMMED** *for his kind assistance, patient helpful, useful advices and continuous encourage, as well as to my closest friends who gave me the best of the knowledge they possess Also I would like to thank all teachers and all my colleagues .*

Abstract

This study was aimed to calculate the GFR in patient whom had diabetic mellitus and hypertensive disease to show how it effecting the GFR. Analytical study designed and conducted in the nuclear medicine department at fedil hospital, in the period from September to December (2016). The data were collected from 35 patients with renal problem where 15 were diagnosis as normal GFR patient, 10 of them were diagnosis as diabetic patient, and 10 were diagnosis as hypertensive patient. Tc^{99m}-DTPA was administrating to the patient intravenously and Gamma camera (SPECT MULTICAM 2000") was used to detect the count and hence GFR were calculated. The result showed that the uptake phase co-offecient for hypertensive was decrease by 6.17cont /second while uptake phase co-offecient for diabetic was decrease by 3.743 cont /second, that meaning the effect of hypertensive is more than that of diabetic. In conclusions we found there is significant difference in absorption co-offecient phase between normal and abnormal (hypertensive and diabetic) one which equal 0.007and 0.013at probability p=0.05 in hypertensive and diabetic with normal respectively done by t-test. On the other hand the secretion phase inconclusive difference these due to the hypertension and diabetic have no direct effect on secretion phase, it function of renal tubule not direct effect thought the blood vessels.

المستخلص

تهدف هذه الدراسة إلي تقويم معدل الترشيح الكبيبي لدي مرضي الضغط والسكري باستخدام النظائر المشعة . وهي تعتبر دراسة تحليلة صممت وأجريت في قسم الطب النووي بمستشفي فضيل في الفترة مابين شهر سبتمبر إلي ديسمبر من عام 2016 وقد تم جمع البيانات من 35 مريضا ممن يعانون من قصور في وظائف الكلي, 15 منهم كان معدل الترشيح الكبيبي في مستوي الطبيعي, و10 مصابون بالضغط , و10 آخرون لديهم داء السكري . تم حقن المرضي بالمادة الصيدلانية المشعة بجرعة مقدارها 5 ملي كوري وبالاستخدام القاما كامير قمنا بحساب معدل الترشيح الكبيبي .وقد أظهرت النتائج ان معدل الامتصاص في مرضي الضغط يتناقص بمقدار 6.17في الثانية بينما ينتاقص في مرضي السكري بمعدل 3.743 في الثانية وهذا يعني ان تاثير الضغط علي معدل الترشيح الكبيبي اعلي من تأثير السكري . وباستخدام الدالة الإحصائية وبقيمة احتمالية تساوي 0.05 وجدنا إن هنالك تأثير في معدل الامتصاص بين كل من المرضي الذين كان لديهم معدل ترشيح كبيبي طبيعي وأولئك الذين يعانون من مرض الضغط والسكري حيث تساوي 0.007 عند المصابين بالضغط و 0.013 للمصابين بالسكري . وفي الجانب الاخر لم يكن هنالك تاثير مباشر علي معدل الافراز اذ انها تعتبر وظيفة مسؤلة منها الانيبيات الكلوية وليست الأوعية الدموية حيث اتضح ان كل من مرض الضغط والسكري تأثر بصورة مباشرة علي الأوعية الدموية .

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List of abbreviation

NM	Nuclear Medicine
UTI	Urinary Tract Infection
GFR	Glomerular Filtration Rate
Tc-99M	Technetium-99m
MDP	Methylene-Diphosphonate
2D	Two-Dimensional Images
PET	Positron Emission Tomography
SPECT	Single Photon Emission Tomography
ADH	Secrete Ant Diuretic Hormone
PCT	Proximal Convoluted Tubule
DCT	Distal Convoluted Tubule
CCr or CrCl	Creatinine clearance rate
BUN	Blood Urea Nitrogen
ACE	Angiotensin-Converting Enzyme
TC DTPA, Acetate	Technetium Diethylene Triaminepenta
Bq	Becquerel
Ci	Curi

Chapter one

Introduction

Chapter One

Introduction

1.1 Background:

Despite recent technical advances in computed tomography, Magnetic resonance, and ultrasound imaging, nuclear medicine (NM) has maintained its crucial role in the functional assessment of the urinary tract, particularly the kidneys. Indeed, nuclear medicine techniques maintain “gold standard” status in the diagnosis of upper urinary tract obstruction and pyelonephriticscarring secondary to urinary tract infection (UTI). Importantly, all NM renal imaging techniques also provide an estimate of relative Renal function. Absolute renal function (e.g.glomerular filtration rate (GFR) in ml/min) canalso be measured by blood sample-based radionuclide methods that are superior in accuracy to routinely used indicators of renal function (e.g. serum creatinine). Finally, renographictechniques also play important roles inthe diagnosis of renovascular hypertension, renal transplant complications, and some lower urinary tract disorders such as vesico-uretericreflux.The main imaging techniques in the investigation of the urinary tract are renography, which has numerous variants, and static DMSAimaging. The techniques and indications for these tests will be considered, along with their strengths and weaknesses.

1.2 Nuclear Medicine:

Is a medical specialty involving the application of radioactive substances in the diagnosis and treatment of disease .

In nuclear medicine procedures, radionuclides are combined with other elements to form chemical compounds, or else combined with existing pharmaceutical compounds, to form radiopharmaceuticals these radiopharmaceuticals, once administered to the patient, can localize to specific organs or cellular receptors. This property of radiopharmaceuticals allows nuclear medicine the ability to image the extent of a disease process in the body, based on the cellular function and physiology rather than relying on physical changes in the tissue anatomy.

In some diseases, nuclear medicine studies can identify medical problems at an earlier stage than other diagnostic tests. Nuclear medicine, in a sense, is "radiology done inside out", or "endo-radiology", because it records radiation emitting from within the body rather than radiation that is generated by external sources like x rays.

Treatment of diseased tissue, based on metabolism or uptake or binding of a particular ligand, may also be accomplished, similar to other areas of pharmacology. However, the treatment effects of radiopharmaceuticals rely on the tissue-destructive power of short-range ionizing radiation.

In the future, nuclear medicine may provide added impetus to the field known as molecular medicine as understanding of biological processes in the cells of living organisms expands; specific probes can be developed to allow visualization, characterization, and quantification of biologic processes at the cellular and subcellular levels. Nuclear medicine is a possible specialty for adapting to the new discipline of molecular medicine because of its emphasis on function and its utilization of imaging agents that are specific for a particular disease process.

A typical nuclear medicine study involves administration of a radionuclide into the body by intravenous injection in liquid or aggregate form, ingestion while combined with food, inhalation as a gas or aerosol, or rarely, injection of a radionuclide that has undergone micro-encapsulation.

Some studies require the labeling of a patient's own blood cells with a radionuclide (leukocyte scintigraphy and red blood cell scintigraphy). Most diagnostic radionuclides emit gamma rays, while the cell-damaging properties of beta particles are used in therapeutic applications. Refined radionuclide’s for use in nuclear medicine are derived from fission or fusion processes in nuclear reactors, which produce radionuclide’s with longer half-lives, or cyclotrons, which produce radionuclide’s with shorter half-lives, or take advantage of natural decay processes in dedicated generators, i.e. molybdenum/technetium or strontium/rubidium.

1.3 Nuclear medicine imaging:-

Diagnostic tests in nuclear medicine exploit the way that the body handles substances differently when there is disease or pathology present.

The radionuclide introduced into the body is often chemically bound to a complex that acts characteristically within the body; this is commonly known as a tracer .

In the presence of disease, a tracer will often be distributed around the body and/or processed differently. For example, the ligand methylene-diphosphonate (MDP) can be preferentially taken up by bone. By chemically attaching technetium-99mto MDP, radioactivity can be transported and attached to bone via the hydroxyapatite for imaging.

Any increased physiological function, such as due to a fracture in the bone, will usually mean increased concentration of the tracer. This often results in the appearance of a "hot spot", which is a focal increase in radio accumulation or a general increase in radio accumulation throughout the physiological system. Some disease processes result in the exclusion of a tracer, resulting in the appearance of a "cold spot". Many tracer complexes have been developed to image or treat many different organs, glands, and physiological processes.

In nuclear medicine imaging, radiopharmaceuticals are taken internally, for example, intravenously or orally. Then, external detectors (gamma cameras) capture and form images from the radiation emitted by the radiopharmaceuticals. This process is unlike a diagnostic X-ray, where external radiation is passed through the body to form an image.

There are several techniques of diagnostic nuclear medicine:-

2D: *Scintigraphy* ("scint") is the use of internal radionuclides to create two-dimensional images
For example:-

Nuclear medicine myocardial perfusions scan with thallium-201 for the rest images andTc-Sestamibi for the stress images. The nuclear medicine myocardial perfusion scan plays a pivotal role in the noninvasive evaluation of coronary artery disease. The study not only identifies patients with coronary artery disease; it also provides overall prognostic information or overall risk of adverse cardiac events for the patient.

A nuclear medicine whole body bone scan. The nuclear medicine whole body bone scan is generally used in evaluations of various bone-related pathology, such as for

bone pain, stress fracture, nonmalignant bone lesions, bone infections, or the spread of cancer to the bone

3D: SPECT is a 3D tomography technique that uses gamma camera data from many projections and can be reconstructed in different planes. Positron emission tomography (PET) uses coincidence detection to image functional processes

For example:-

A nuclear medicine SPECT liver scan with technetium-99m labeled antilogous red blood cells

Whole body positron emission tomography with F18DG

1.4 Problem of the Study:

Hypertensive and diabetic diseases affected the function of several organs of the body one of these organs the renal system. In renal system mainly the Glomerular filtration rate (GFR) is one of functions that might be affected by both diseases; where the function might be slightly differ than the normal relative to the severity of the disease. Therefore assessment of GFR in diabetic and hypertensive patient will reveals and quantifies the effect in renal function versus the normal one and hence management can be done.

1.5 Objectives of the study:

The general objective of this study was to assess of GFR in diabetic and hypertensive patient using DTPA scintigraphy

1.5.1 Specific objectives:

- To find the counts and time of uptake and secretion of the Right and Left kidney
- To find the association of GFR with diabetic and hypertension duration
- To find the effect of patient age, weight, height in GFR (renal scintigraphy).
- To find the significance difference between normal and abnormal (diabetic and hypertension) GFR.

1.6Significant of the study:

GFR describes the flow rate of filtered fluid through the kidneys. The importance of this study is to know the effect of some diseases (obstructive disease and nonfunctioning disease) to the GFR, and to know the effect of abnormal percent to the kidney function.

1.7 Overview of the study:

This study consisted of five chapters, with chapter one is an introduction,while chapter two includes a comprehensive literature review and background, and chapter three describe the material and method. Chapter four includes result presentation; finally chapter five will include the discussion and conclusion.

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Chapter two

Background and literature review

Chapter Two

Background and literature review

2.1 Background

2.1.1 Anatomy

The bean-shaped kidneys lie in a retroperitoneal position in the superior lumbar region. Extending approximately from T12 to L3, The right kidney is crowded by the liver and lies slightly lower than the left. An adult's kidney has a mass of about 150 g (5 ounces) and its average dimensions are 12 cm long, 6 cm wide, and 3 cm thick. Each kidney comprises an outer cortex and an inner medulla.The lateral surface is convex. The medial surface is concave and has a vertical cleft called the renal hilum that leads into an internal space within the kidney called the renal sinus. The ureter, renal blood vessels, lymphatic, and nerves all join each kidney at the hilum and occupy the sinus. The kidney is supplied with oxygenated blood via the renal artery and drained of deoxygenated blood by the renal vein. In addition, urine produced by the kidney as part of its excretory function, drains out via narrow "tubules" and the ureter, in turn connected to the bladder.Atop each kidney is an adrenal (or suprarenal) gland, an endocrine gland that is functionally unrelated to the kidney.

2.1.2 Physiology:

The kidney participates in whole-body homeostasis, regulating acid-base balance, electrolyte concentrations, extracellular fluid volume, and blood pressure. The kidney accomplishes these homeostatic functions both independently and in concert with other organs, particularly those of the endocrine system. Various endocrine hormones coordinate these endocrine functions; these include renin, angiotensin II, aldosterone, antidiuretic hormone, and atrial natriuretic peptide, among others.

Reabsorption of vital nutrients :

Glucose at normal plasma levels is completely reabsorbed in the proximal tubule. The mechanism for this is the Na+/glucose transporter. A plasma level of 350 mg/dL will fully saturate the transporters and glucose will be lost in the urine. A plasma glucose level of approximately 160 is sufficient to allow glucosuria, which is an important clinical clue to diabetes mellitus.Amino acids are reabsorbed by sodium dependent transporters in the proximal tubule.

LocationofRe-absorption	Reabsorbed nutrient	Notes
Early proximal tubule	Glucose (100%), amino acids (100%), bicarbonate (90%), Na^+ (65%), Cl^-, phosphate and H_2O (65%)	- PTH will inhibit phosphate excretion. - AT II stimulates Na^+ , H_2O and HCO_3^-reabsorption.
Thin descending loop of Henle	H_2O	-Reabsorbs via medullary hyper tonicity and makes urine hypertonic.
Thick ascending loop of Henle	Na^+ (10–20%), K^+ , Cl^- ; indirectly induces para cellular reabsorption of Mg^{2+}, Ca^{2+}	-This region is impermeable to H_2O and the urine becomes less concentrated as it ascends.
Early distal convoluted tubule	Na^+, Cl^-	-PTH causes Ca^{2+} reabsorption.
Collecting tubules	Na^+(3–5%), H_2O	-Na^+ is reabsorbed in exchange for K^+,, and H^+, which is regulated by aldosterone. -ADH acts on the V2 receptor and inserts aquaporins on the luminal side

Acid-base homeostasis :

Two organ systems, the kidneys and lungs, maintain acid-base homeostasis, which is the maintenance of pH around a relatively stable value. The lungs contribute to acid-base homeostasis by regulating carbon dioxide (CO_2 concentration. The kidneys have two very important roles in maintaining the acid-base balance: to reabsorb and regenerate bicarbonate from urine, and to excrete hydrogen ions and fixed acids (anions of acids) into urine.

Excretion of wastes:

The kidneys excrete a variety of waste products produced by metabolism into the urine. These include the nitrogenous wastes urea, from protein catabolism, and uric acid, from nucleic acid metabolism. The ability of mammals and some birds to concentrate wastes into a volume of urine much smaller than the volume of blood from which the wastes were extracted is dependent on an elaborate countercurrent multiplication mechanism. This requires several independent nephron characteristics to operate: a tight hairpin configuration of the tubules, water and ion permeability in the descending limb of the loop, water impermeability in the ascending loop, and active ion transport out of most of the ascending limb. In addition, passive countercurrent exchange by the vessels carrying the blood supply to the nephron is essential for enabling this function.

Osmolality regulation:

Any significant rise in plasma osmolality is detected by the hypothalamus, which communicates directly with the posterior pituitary gland. An increase in osmolality causes the gland to secrete antidiuretic hormone (ADH), resulting in water reabsorption by the kidney and an increase in urine concentration. The two factors work together to return the plasma osmolality to its normal levels.

ADH binds to principal cells in the collecting duct that translocate aquaporins to the membrane, allowing water to leave the normally impermeable membrane and be reabsorbed into the body by the vasa recta, thus increasing the plasma volume of the body.

There are two systems that create a hyperosmotic medulla and thus increase the body plasma volume: Urea recycling and the 'single effect.'

Urea is usually excreted as a waste product from the kidneys. However, when plasma blood volume is low and ADH is released the aquaporins that are opened are also permeable to urea. This allows urea to leave the collecting duct into the medulla creating a hyperosmotic solution that 'attracts' water. Urea can then re-enter the nephron and be excreted or recycled again depending on whether ADH is still present or not.

The 'Single effect' describes the fact that the ascending thick limb of the loop of Henle is not permeable to water but is permeable to NaCl. This allows for a countercurrent exchange system whereby the medulla becomes increasingly concentrated, but at the same time setting up an osmotic gradient for water to follow should the aquaporins of the collecting duct be opened by ADH.

Blood pressure regulation:

Although the kidney cannot directly sense blood, long-term regulation of blood pressure predominantly depends upon the kidney. This primarily occurs through maintenance of the extracellular fluid compartment, the size of which depends on the plasma sodium concentration. Renin is the first in a series of important chemical messengers that make up the renin-angiotensin system. Changes in renin ultimately alter the output of this system, principally the hormones angiotensin II and aldosterone. Each hormone acts via multiple mechanisms, but both increase the kidney's absorption of sodium chloride, thereby expanding the extracellular fluid compartment and raising blood pressure. When renin levels are elevated, the concentrations of angiotensin II and aldosterone increase, leading to increased sodium chloride reabsorption, expansion of the extracellular fluid compartment, and an increase in blood pressure. Conversely, when renin levels are low, angiotensin II and aldosterone levels decrease, contracting the extracellular fluid compartment, and decreasing blood pressure.

Hormone secretion:

The kidneys secrete a variety of hormones, including erythropoietin, and the enzyme renin. Erythropoietin is released in response to hypoxia (low levels of oxygen at tissue level) in the renal circulation. It stimulates erythropoiesis (production of red blood cells) in the bone marrow. Calcitriol, the activated form of vitamin D, promotes intestinal absorption of calcium and the renal reabsorption of phosphate. Part of the renin–angiotensin–aldosterone system, renin is an enzyme involved in the regulation of aldosterone levels.

2.1.3 Nephron

The kidney consists of over a million individual filtering units called nephrons. Each **nephron** consists of a filtering body therenal corpuscle, and a urine-collecting and concentrating tube the renal tubule.

Renal Capsule*:*

The renal capsule is the part of the kidney nephron in which blood plasma is filtered.

The term "capsule" means "tiny" or "small" body. The renal capsule of each kidney nephron has two parts - they are the Glomerulus which is a network of small blood vessels called capillaries, and the Bowman's Capsule (also known as the Glomerular Capsule), which is the double-walled epithelial cup within which the glomerulus is contained.

Within the glomerulus are glomerular capillaries that are located between the afferent arteriole bringing blood into the glomerulus and the efferent arteriole draining blood away from the glomerulus. The (outgoing) efferent arteriole has a smaller diameter than the (incoming) afferent arteriole. This difference in arteriole diameters helps to raise the blood pressure in the glomerulus.

The area between the double-walls of the Bowman's Capsule is called the capsular space. The cells that form the outer edges of the glomerulus form close attachments to the cells of the inner surface of the Bowman's Capsule. This combination of cells adhered to each other forms a filtration membrane that enables

water and solutes (substances that are dissolved in the water/blood) to pass through the first wall of the Bowman's Capsule into the capsular space. This filtration process is helped by the raised blood pressure in the glomerulus - due to the difference in diameter of the afferent and efferent arterioles.

Renal Tubule:

The renal tubule is the part of the kidney nephron into which the glomerular filtrate passes after it has reached the Bowman's capsule. The first part of the renal tubule is called the **proximal convoluted tubule (PCT)**,The water and solutes that have passed through the proximal convoluted tubule (PCT) enter the Loop of Henle, which consists of two portions - first the

descending limb of Henle, then the ascending limb of Henle. In order to pass through the Loop of Henle, the water (and substances dissolved in it) pass from the renal cortex into the renal medulla, then back to the renal cortex.

When this fluid returns to the renal cortex (via the ascending limb of Henle) it passes into the **distal convoluted tubule (DCT) ,**The distal convoluted tubules of many individual kidney nephrons converge onto a single collecting duct.

The fluid that has passed through the distal convoluted tubules is drained into the collecting duct (far left-hand-side of the diagram above). Many collecting ducts join together to form several hundred papillary ducts. There are typically about 30 papillary ducts per renal papilla (the renal papillae being the tips of the renal pyramids - which point towards the Centre of the kidney). At each renal papilla the contents of the papillary ducts drain into the minor calces - the channels through which the fluid passes, via the major calyx, into the Centre of the kidney - called the renal pelvis.

The operation of the human nephron consists of three processes:

Glomerular filtration
Tubular reabsorption
Tubular secretion

These three processes, which determine the quantity and quality of the urine.

Glomerular filtration:

The first step in the production of urine is called glomerular filtration. Filtration (the foreign of fluids and dissolved substances through a membrane by pressure) occurs in Bowman's capsule when blood enters the glomerular, the blood pressure forces water and dissolved components through the endothelial pores of the capillaries, basement membrane and through the filtration slits of the adjoining visceral wall of the glomerular (Bowman's capsule). The resulting fluid is called the filtrate. In healthy person, the filtrates consist of all the blood accepts for the formed elements and most proteins, which are too large to pass through the endothelial – capsular barrier.

Tubular reabsorption:

In healthy kidneys, nearly all of the desirable organic substances (proteins, amino acids, glucose) are reabsorbed by the cells that line the renal tube. These substances then move into the peritubular capillaries that surround the tubule. Most of the water and many ions are reabsorbed as well, but the amounts are regulated so that blood volume, pressure, and ion concentration are maintained within required levels for homeostasis.

Reabsorbed substances move from the lumen of the renal tubule to the lumen of a peritubular capillary. Movement of substances out of the tubule, then, must occur through the cells, either by active transport (requiring ATP) or by passive transport processes.

Once outside of the tubule and in the interstitial fluids, substances move into the peritubular capillaries or vasa recta by passive processes.

The reabsorption of most substances from the tubule to the interstitial fluids requires a membrane-bound transport protein that carries these substances across the tubule cell membrane by active transport. When all of the available transport proteins are being used, the rate of reabsorption reaches a transport maximum (Tm), and substances that cannot be transported are lost in the urine.

The following mechanisms direct tubular reabsorption in the indicated regions:

- Active transport of Na^+ (in the PCT, DCT, and collecting duct). Because Na^+ concentration is low inside tubular cells, Na^+ enters the tubular cells (across the luminal membrane) by passive diffusion. At the other side of the tubule cells, the basolateral membrane bears proteins that function as sodium-potassium (Na^+-k^+) pumps. These pumps use ATP to simultaneously export Na^+ while importing k^+. Thus, Na^+ in the tubule cells is transported out of the cells and into the interstitial fluid by active transport. The Na^+ in the interstitial fluid then enters the capillaries by passive diffusion. (The k^+ that is transported into the cell leaks back passively into the interstitial fluid.)
- Symporter transport (secondary active transport) of nutrients and ions (in the PCT and nephron loop). Various nutrients, such as glucose and amino acids, and certain ions (k^+ and Cl^-) in the thick ascending limb of the nephron loop are transported into the tubule cells by the action of Na^+ symporters. A Na^+ symporter is a transport protein that carries both Na^+ and another molecule, such as glucose, across a membrane in the same direction. Movement of glucose and other nutrients from the tubular lumen into the tubule cells occurs in this fashion. The process requires a low concentration of Na^+ inside the cells, a condition maintained by the Na^+-k^+ pump operating on the basolateral membranes of the tubule cells. The movement of nutrients into cells by this mechanism is referred to as secondary active transport, because the ATP-requiring mechanism is the Na^+-k^+ pump and not the symporter itself. Once inside the tubular cells, nutrients move into the interstitial fluid and into the capillaries by passive processes.
- Passive transport of H_2O by osmosis (in the PCT and DCT). The buildup of Na^+ in the peritubular capillaries creates a concentration gradient across which water passively moves, from tubule to capillaries, by osmosis. Thus, the reabsorption of Na^+ by active transport generates the subsequent reabsorption of H_2O by passive transport, a process called obligatory H_2O reabsorption.
- Passive transport of various solutes by diffusion (in the PCT and DCT, and collecting duct). As H_2O moves from the tubule to the capillaries, various solutes such as k^+, Cl^-, HCO_3^-, and urea become more concentrated in the tubule. As a result, these solutes follow the water, moving by diffusion out of the tubule and into capillaries where their concentrations are lower, a process called solvent drag. Also,

the accumulation of the positively charged Na^+ in the capillaries creates an electrical gradient that attracts (by diffusion) negatively charged ions (Cl^-, HCO_3^-).

- H_2O and solute transport regulated by hormones (in the DCT and collecting duct). The permeability of the DCT and collecting duct and the resultant reabsorption of H_2O and Na^+ are controlled by two hormones
- Aldosterone increases the reabsorption of Na^+ and H_2O by stimulating an increase in the number of Na^+-k^+ pump proteins in the principal cells that line the DCT and collecting duct.
- Antidiuretic hormone (ADH) increases H_2O reabsorption by stimulating an increase in the number of H_2O-channel proteins in the principal cells of the collecting duct.

Tubular Secretion:

- In contrast to tubular reabsorption, which returns substances to the blood, tubular secretion removes substances from the blood and secretes them into the filtrate. Secreted substances include H^+, k^+, NH_4^+ (ammonium ion), creatinine (a waste product of muscle contraction), and various other substances (including penicillin and other drugs). Secretion occurs in portions of the PCT, DCT, and collecting duct.
- Secretion of H^+. Because a decrease in H^+ causes a rise in pH (a decrease in acidity), H^+ secretion into the renal tubule is a mechanism for raising blood pH. Various acids produced by cellular metabolism accumulate in the blood and require that their presence be neutralized by removing H^+.

In addition, CO_2, also a metabolic byproduct, combines with water (catalyzed by the enzyme carbonic anhydrase) to produce carbonic acid (H_2CO_3), which dissociates to produce H^+, as follows:

$$CO_2 + H_2O \longleftrightarrow H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

- This chemical reaction occurs in either direction (it is reversible) depending on the concentration of the various reactants. As a result, if HCO_3^- increases in the blood, it acts as a buffer of H^+, combining with it (and effectively removing it) to produce CO_2 and H_2O. CO_2 in tubular cells of the collecting duct combines with H_2O to

form H^+ and HCO_3^- The CO_2 may originate in the tubular cells or it may enter these cells by diffusion from the renal tubule, interstitial fluids, or peritubular capillaries. In the tubule cell, Na^+/H^+ antiporters, enzymes that move transported substances in opposite directions, transport H^+ across the luminal membrane into the tubule while importing Na^+. Inside the tubule, H + may combine with any of several buffers that entered the tubule as filtrate (HCO_3^-, NH_3, or HPO_4^{2-}). If HCO_3^- is the buffer, then H_2CO_3 is formed, producing H_2O and CO_2. The CO_2 then enters the tubular cell, where it can combine with H_2O again. If H^+ combines with another buffer, it is excreted in the urine. Regardless of the fate of the H^+ in the tubule, the HCO_3^- produced in the first step is transported across the basolateral membrane by an HCO_3^-/Cl^- antiporter. The HCO_3^- enters the peritubular capillaries, where it combines with the H^+ in the blood and increases the blood pH. Note that the blood pH is increased by adding HCO_3^- to the blood, not by removing H^+.

- Secretion of NH_3. When amino acids are broken down, they produce toxic NH_3. The liver converts most NH_3 to urea, a less toxic substance. Both enter the filtrate during glomerular filtration and are excreted in the urine. However, when the blood is very acidic, the tubule cells break down the amino acid glutamate, producing NH_3. and HCO_3^-. The NH_3. combines with H^+, forming NH_4^+, which is transported across the luminal membrane by a Na + antiporter and excreted in the urine. The HCO_3^- moves to the blood (as discussed earlier for H^+ secretion) and increases blood pH.
- Secretion of k^+ Nearly all of the k^+ in filtrate is reabsorbed during tubular reabsorption. When reabsorbed quantities exceed body requirements, excess k^+ is secreted back into the filtrate in the collecting duct and final regions of the DCT. Because aldosterone stimulates an increase in Na^+/k^+ pumps, k^+ secretion (as well as Na^+ reabsorption) increases with aldosterone.

2.1.4 Mechanism of urine concentration:

The excretion of concentration urine begins with high concentration of solutes in the interstitial fluid in the medulla of the kidney the high medulary concentration is ma is maintained by two principal factors include: Solutes reabsorption from various

parts of the renal tubules , Countercurrent mechanism which based on the anatomical arrangement of the juxtamedullary nephrons and vasarecta.

Urine is expelled from the urinary bladder by an act called micturition, commonly known as urination or voiding. This response is brought about by a combination of involuntary and voluntary nerve impulses. The average capacity of the urinary bladder exceed 200 to 400ml, stretch receptors in the urinary bladder wall transmit impulses to the lower portion of the spinal cord. These impulses, by way of sensory tracts to the cortex, initiate a conscious desire to expel urine and, by way of a center in the sacral cord, a subconscious reflex referred to as the micturition reflex. Parasympathetic impulses transmitted from the micturition reflex center of the sacral area of the spinal cord reach the urinary bladder wall and internal urethral sphincter, bringing about contraction of the detrusor muscle of the urinary bladder and relaxation of the internal sphincter. Then the conscious portion of the brain sends impulses to the external sphincter, the sphincter relaxes, and urination takes place. Although emptying the urinary bladder is controlled by reflex, it may be initiated voluntarily and stopped at will because of cerebral control of external sphincter and certain muscles of the urogenital (Pelvic) diaphragm.

Renal function, in nephrology, is an indication of the state of the kidney and its role in renal physiology. Glomerular filtration rate (GFR) describes the flow rate of filtered fluid through the kidney. Creatinine clearance rate (CCr or CrCl) is the volume of blood plasma that is cleared of creatinine per unit time and is a useful measure for approximating the GFR. Creatinine clearance exceeds GFR due to creatinine secretion, which can be blocked by cimetidine. In alternative fashion, overestimation by older serum creatinine methods resulted in an underestimation of creatinine clearance, which provided a less biased estimate of GFR. Both GFR and CCr may be accurately calculated by comparative measurements of substances in the blood and urine, or estimated by formulas using just a blood test result (eGFR and eCCr).

Most doctors use the plasma concentrations of the waste substances of creatinine and urea (U), as well as electrolytes (E), to determine renal function. These measures are adequate to determine whether a patient is suffering from kidney disease.

However, blood urea nitrogen (BUN) and creatinine will not be raised above the normal range until 60% of total kidney function is lost. Hence, the more accurate Glomerular filtration rate or its approximation of the creatinine clearance is measured whenever renal disease is suspected or careful dosing of nephrotoxic drugs is required.Elevated protein levels in urine mark some kidney disease. The most sensitive marker of proteinuria is elevated urine albumin. Persistent presence of more than 30 mg albumin per gram creatinine in the urine is diagnostic of chronic kidney disease .

2.1.5 GFR(Glomerular Filtration Rate) :

Glomerular filtration rate (GFR) is the volume of fluid filtered from the renal (kidney) glomerular capillaries into the Bowman's capsule per unit time.The GFR, about 125 mL/min (180 liters/day), is regulated by the following:

- Renal auto regulation is the ability of the kidney to maintain a constant GFR even when the body's blood pressure fluctuates. Auto regulation is accomplished by cells in the juxtaglomerular apparatus that decrease or increase secretion of a vasoconstrictor substance that dilates or constricts, respectively, the afferent arteriole.

Neural regulation of GFR occurs when vasoconstrictor fibers of the sympathetic nervous system constrict afferent arterioles. Such stimulation may occur during exercise, stress, or other fight-or-flight conditions and results in a decrease in urine production.

Hormonal control of GFR is accomplished by the renin/angiotensinogen mechanism. When cells of the juxtaglomerular apparatus detect a decrease in blood pressure in the afferent arteriole or a decrease in solute (Na + and Cl –) concentrations in the distal tubule, they secrete the enzyme renin.

Renin converts angiotensinogen (a plasma protein produced by the liver) to angiotensin I. Angiotensin I in turn is converted to angiotensin II by the angiotensin-converting enzyme (ACE), an enzyme produced principally by capillary endothelium in the lungs. Angiotensin II circulates in the blood and increases GFR by doing the following:

-Constricting blood vessels throughout the body, causing the blood pressure to rise

-Stimulating the adrenal cortex to secrete aldosterone, a hormone that increases blood pressure by decreasing water output by the kidneys.

Glomerular filtration rate (GFR) can be calculated by measuring any chemical that has a steady level in the blood, and is freely filtered but neither reabsorbed nor secreted by the kidneys. The rate therefore measured is the quantity of the substance in the urine that originated from a calculable volume of blood. The GFR is typically recorded in units of volume per time, e.g., milliliters per minute ml/min.

$$\text{GFR} = \frac{\text{urine concentration} \times \text{urine flow}}{\text{plasma concentration}}$$

There are several different techniques used to calculate or estimate the glomerular filtration rate (GFR or eGFR) :

Measurement using inulin:

The GFR can be determined by injecting inulin into the plasma. Since inulin is neither reabsorbed nor secreted by the kidney after glomerular filtration, its rate of excretion is directly proportional to the rate of filtration of water and solutes across the glomerular filter. Compared to the MDRD formula, the inulin clearance slightly overestimates the glomerular function. In early stage renal disease, the inulin clearance may remain normal due to hyperfiltration in the remaining nephrons. Incomplete urine collection is an important source of error in inulin clearance measurement

Creatinine-based approximations of GFR:

In clinical practice, however, creatinine clearance or estimates of creatinine clearance based on the serum creatinine level are used to measure GFR. Creatinine is produced naturally by the body (creatinine is a break-down product of creatinine phosphate, which is found in muscle). It is freely filtered by the glomerular, but also actively secreted by the peritubular capillaries in very small amounts such that creatinine clearance overestimates actual GFR by 10-20%. This margin of error is acceptable, considering the ease with which creatinine clearance is measured. Unlike precise GFR measurements involving constant infusions of inulin, creatinine is already at a steady-state concentration in the blood, and so measuring creatinine clearance is much less cumbersome. However, creatinine estimates of GFR have their

limitations. All of the estimating equations depend on a prediction of the 24-hour creatinine excretion rate, which is a function of muscle mass. One of the equations, the Cockcroft and Gault equation (see below) does not correct for race, and it is known that African Americans, for example, both men and women, have a higher amount of muscle mass than Caucasians; hence, African Americans will have a higher serum creatinine level at any level of creatinine clearance.

A common mistake made when just looking at serum creatinine is the failure to account for muscle mass. Hence, an older woman with a serum creatinine of 1.4 may actually have a moderately severe degree of renal insufficiency, whereas a young muscular male, in particular if African American, can have a normal level of renal function at this serum creatinine level. Creatinine-based equations should be used with caution in cachectic patients and patients with cirrhosis. They often have very low muscle mass and a much lower creatinine excretion rate than predicted by the equations below, such that a cirrhotic patient with a serum creatinine of 0.9 may have a moderately severe degree of renal insufficiency.

Creatinine Clearance CCr:

One method of determining GFR from creatinine is to collect urine (usually for 24-hours) to determine the amount of creatinine that was removed from the blood over a given time interval. If one removes, say, 1440 mg in 24 hours, this is equivalent to removing 1 mg/min. If the blood concentration is 0.01 mg/mL (1 mg/dL), then one can say that 100 mL/min of blood is being "cleared" of creatinine, since, to get 1 mg of creatinine, 100 mL of blood containing 0.01 mg/mL would need to have been cleared.

Creatinine clearance (CCr) is calculated from the creatinine concentration in the collected urine sample (UCr), urine flow rate (V), and the plasma concentration (PCr). Since the product of urine concentration and urine flow rate yields creatinine excretion rate, which is the rate of removal from the blood, creatinine clearance is calculated as removal rate per min (UCr×V) divided by the plasma creatinine concentration. This is commonly represented mathematically as

$$Ccr = \frac{Ucr \times V}{Pcr}$$

The common procedure involves undertaking a 24-hour urine collection, from empty-bladder one morning to the contents of the bladder the following morning, with a comparative blood test then taken. The urinary flow rate is still calculated per minute, hence:

$$Ccr = \frac{\text{Urine creatinine} \times \text{urine volume in 24 hours}}{\text{Plasma creatinine} \times 24 \times 60\text{mins}}$$

To allow comparison of results between people of different sizes, the CCr is often corrected for the body surface area (BSA) and expressed compared to the average sized man as mL/min/1.73 m2. While most adults have a BSA that approaches 1.7 (1.6-1.9), extremely obese or slim patients should have their CCr corrected for their actual BSA.

$$Ccr - corrected = \frac{Ccr \times 1.73}{BSA}$$

BSA can be calculated on the basis of weight and height.

The creatinine clearance is not widely done any more, due to the difficulty in assuring a complete urine collection. When doing such a determination, to assess the adequacy of a complete collection, one always calculates the amount of creatinine excreted over a 24-hour period. This amount varies with muscle mass, and is higher in young people vs. old, in blacks vs. whites, and in men vs. women. An unexpectedly low or high 24-hour creatinine excretion rate voids the test. Nevertheless, in cases where estimates of creatinine clearance from serum creatinine are unreliable, creatinine clearance remains a useful test. These cases include "estimation of GFR in individuals with variation in dietary intake (vegetarian diet, creatinine supplements) or muscle mass (amputation, malnutrition, muscle wasting), since these factors are not specifically taken into account in prediction equations.

2.1.6 Pathology:

Pyelonephritis (infection of kidney pelvis):

Bacteria may infect the kidney, usually causing back pain and fever. A spread of bacteria from an untreated bladder infection is the most common cause of pyelonephritis.

Glomerulonephritis:

An overactive immune system may attack the kidney, causing inflammation and some damage. Blood and protein in the urine are common problems that occur with glomerulonephritis. It can also result in kidney failure.

Kidney stones (nephrolithiasis):

`Minerals in urine form crystals (stones), which may grow large enough to block urine flow. It's considered one of the most painful conditions. Most kidney stones pass on their own but some are too large and need to be treated.

Nephrotic syndrome:

Damage to the kidneys causes them to spill large amounts of protein into the urine. Leg swelling (edema) may be a symptom..

Diabetic nephropathy:

High blood sugar from diabetes progressively damages the kidneys, eventually causing chronic kidney disease. Protein in the urine (nephrotic syndrome) may also result.

Hypertensive nephropathy:

Kidney damage caused by high blood pressure. Chronic renal failure may eventually result.

Kidney cancer:

Renal cell carcinoma is the most common cancer affecting the kidney. Smoking is the most common cause of kidney cancer.

Nephrogenic diabetes insipidus:

The kidneys lose the ability to concentrate the urine, usually due to a drug reaction. Although it's rarely dangerous, diabetes insipidus causes constant thirst and frequent urination.

2.2Previous study

Jagdish et al. (1987) described evaluation of renal function in diabetics employing two different methods, the objectives of their study was to evaluate renal function by endogenous creatinine clearance and compare this with GFR, employing gamma camera using technetium diethylenetriaminepenta acetate (TC DTPA), to correlate type of diabetes, duration, glycemic control, blood pressure and large vessel disease, serum creatinine and lipids with severity of renal decomposition and to conduct follow up studies on renal function to assess the rate of progression of diabetic renal disease. The data was collected using 27 cases of diabetes mellitus were selected, going by the criteria of 24 hour urinary albumin excretion >250 mg/24 hours from the Endocrinology wards and out-patient of Endocrinology Unit at All India Institute of Medical Sciences, New Delhi. There were 18 males and 9 females. 13 patients were IDDM type while 14 were NIDDM type. Mean ages in IDDM - 27.1 years and NIDDM 58.5 yrs. while mean duration of DM was IDDM-7.1 yrs and NIDDM-11.1 yrs. Endogenous creatinine clearance measured by accurately timed collection of 24 hour urine, twice and mean of two values taken. Glycosylated hemoglobin estimation was done by colorimetric method. GFR Tc DTPA using gamma camera and radioisotope method was based on plasma clearance of injected TC 99m DTPA, determined by serial collection of blood samples. The result showed that Routine investigation in two groups, IDDM and NIDDM revealed mean values of Hb A1C of 12.23% and 11.66% (Table I) respectively, reflecting poor control at the time of inclusion in the study. Lipid profile also revealed raised values in both the groups (Table I). Glomerular filtration rate in the groups was studied and classified into 3 groups as : Group I with GFR > 100 ml/mt, Group II with GFR 50-100 ml/mt, Group III with GFR <50 ml/mt. Total number of cases studied in these groups was 8, l0 and 9 respectively (Table II). A direct correlation between 24 hour urinary albumin, serum creatinine and glomerular filtration was observed (Table III). In the conclusion the present study it was observed that endogenous creatinine clearance if done meticulously gives a fairly accurate measure of GFR. Gamma camera method though more accurate and sensitive is slightly more expensive. In follow up studies up to 1½ years in 5 cases with advanced renal involvement there was rapid decline in GFR (30 ml/year) which is probably 2-3 times as compared to earlier data from West. It was further observed that IDDM group was free of large vessel disease in this sample

group of 27 cases. Incidence of small vessel disease is independent of LVD and this may be dependent on racial factors. It is concluded that in assessment of diabetic renal disease advancement, critical criteria for defining advanced renal involvement be S. creatinine>2.5 ml/dl and GFR <50 ml/mt beyond which a nephrologists should intervene and offer a life plan to a diabetic.

Hiromichi et al. (1998) described decrease in glomerular filtration rate in Japanese patients with type 2 diabetes is linked to atherosclerosis, the objective of their study was to assessed the effects of atherosclerosis on the glomerular filtration rate (GFR) in patients with type 2 diabetes and who had micro- or normoalbuminuria. The data was collected using total of 61 Japanese patients with type 2 diabetes were recruited from inpatients of Osaka City University Hospital. They ranged in age from 40 to 69 years (28 men and 33 women). Each subject collected a 24-h urine sample for quantitative analysis of albumin. Absence of albuminuria was defined as a urinary albumin excretion level of 30 mg/24 h (n = 36) and microalbuminuria as a level of 30–300 mg/24 h. The GFRwas estimated using 99mTc diethylenetriaminepentaaceticrenogram method. As indexes of atherosclerosis, we measured the intimal-medial thickness (IMT) and distensibility of the carotid artery using high-resolution B-mode ultrasonagraphy and an echo-tracking system. We measured the resistance index (RI) of the renal interlobar arteries by pulsed Doppler sonography. The result showed the clinical characteristics of type 2 diabetic patients with and without microalbuminuria did not differ except for duration of diabetes, which was longer in the patients with microalbuminuria. GFR also did not differ between the patients with and without microalbuminuria. GFR was significantly correlated with the patient's age (r = 0.256, P 0.05), carotidIMT (r = 0.326, P 0.05), carotid stiffness (r = 0.449, P 0.001), and renal arterial RI (r = 0.365, P 0.05). In multiple re g ression analysis, independent factors associated with GFR were carotid IMT ($R2$ = 0.108, P = 0.0102), carotid stiffness ($R2$ = 0.208, P = 0.0003), an n d renal artery RI ($R2$ = 0.130, P = 0.0043). In the conclusion the decline in GFR in type 2 diabetic patients in the early stages of nephropathy may be due in part to atherosclerosis

Nik et al. (2010) described sensitivity of serum creatinine in assessing renal function in type 2 diabetes mellitus with normal urinary protein excretion. The aim of their study was to determine the sensitivity of serum creatinine in assessing renal

function in type 2 diabetes mellitus patients who have no proteinuria on routine urine dipstick testing. The data was collected using Type 2 DM patients with normoalbuminuria confirmed on urine ACR were selected from endocrine clinic. All patients had their renal profile taken and subsequently the GFR measurements were performed using 99mTc-DTPA renal dynamic imaging. The result showed that a total of 93 subjects had their GFR measured by both the DTPA and MDRD methods. The mean GFR by DTPA method was 79.96 ± 29.53 mls/min/1.73m2 and the median by the MDRD methods was 82.00 (35.00) mls/min/1.73m2. Thirty two (34%) of the subjects were in Stage 1, 37 (39%) were in CKD Stage 2, 22 (23%) were in stage 3 and 2 subjects (0.02%) were in CKD stage 4. Among them 37 (39%) subjects had a normal creatinine level despite the renal impairment (false negative results). The use of serum creatinine to estimate renal function in a patient with GFR. In the conclusion he sensitivity of serum creatinine as an index of renal function dropped to 60% when the GFR dropped to below 60 mls/min/1.73m2. It is wise not to rely on serum creatinine when CKD is suspected in DM patients.

LIU et al. (2009) described The Applicability of Modified Assessment Equation for Glomerular Filtration Rate in Diabetic Nephropathy. The aim of their study was to evaluate the applicability of modified formulas based on plasma creatinine levels in Chinese patients with diabetic nephropathy. The data was collected using a total of 67 patients with diabetic nephropathy were investigated. Glomerular filtration rate (GFR) was estimated with Chinese equations, Ruijin equation, and MDRD1 equation and abbreviated MDRD equation. The accuracy of estimated GFRs was compared with sGFR by 99mTc-DTPA-GFR in these patients. The result showed that the Bland-Altman analysis demonstrated that Ruijin equation was more consistent with sGFR than the other equations. But the consistency limits of GFRs estimated by all the equations and sGFR were beyond the professional threshold value well defined in advance. Linear regressions showed that the slope of Ruijin equation was closer to the identical line. 30% and 50% accuracy of Ruijin equation were higher than the other equations. But 30% accuracy of Ruijin equation was still less than 70%. When compared the accuracy of estimated GFRs with sGFR in different stages of CKD, GFR estimated by Ruijin equation showed good results. In the conclusion when plasma creatinine was checked with enzymatic method, modified GFR estimation equations may show evident bias in Chinese patients with diabetic

nephropathy. More clinical trials must be done to test the application of modified GFR estimation equations in Chinese patients with diabetic nephropathy.

Gang et al. (2005) described GFR determined in conjunction with 99m Tc-DTPA; the aim of their study was to assess the GFR requires numerous blood samples obtained over period of several hours to determine plasma concentration of injected radiopharmaceutical. The data was collected using less than 40 min of imaging time and single blood sampling. The 99m-Tc-DTPA clearances was measered with Jackonmothed during the rotune 99m-Tc-DTPA in 63 patient, in the 23 cases among 63 creatinine clearances was accounted simultaneously. The result showed that the range of clearances DTPA from 19.9 ml\min to 170ml\min and the correlation of clearances DTPA and creatinine clearances was described by Y 16.2570+0.7852X(X=Cl DTPA,Y=Clceratinine) and the correlation coefficient r was 0.88. In the conclusion 99m-Tc-DTPA renal clearances measurment with Jackonmothedclinicalyusefull to account GFR that can be done with 99m-Tc-DTPA renal scintigraphy simultaneously.

Delpassand et al, (2000) describedDetermination of Glomerular Filtration Rate Using a Dual-Detector Gamma Camera and the Geometric Mean of Renal Activity. The purpose of their study was to use of a dual-detector gamma camera to measure the glomerular filtration rate (GFR).The data was collected using Thirty-three patients with a wide range of renal function participated in this study. The GFR was measured using a dual-detector gamma camera by calculating the geometric mean of activity from each kidney and using an outline background. These results were compared with the GFR estimates obtained from Tc-99m DTPA plasma clearance using a multiple blood sample method. The result showed that Correlation was excellent between GFR estimated using the dual-detector gamma camera and GFR measured using the plasma clearance of Tc-99m DTPA with multiple blood samples ($r = 0.89$). The correlation was especially strong in children younger than 13 years ($r = 0.94$).In the conclusion, measuring the GFR using a dual-detector gamma camera and calculating the geometric mean of renal activity yields relatively accurate results.

LI et al. (2010) described Diagnostic accuracy of various glomerular filtration ratesestimating equations in patients with chronic kidney disease and diabetes, the aim of their study was to compare the performance of the modification of diet in renal disease (MDRD) equation based on creatinine with the five cystatin C-based formulae for estimation of GFR in patients with CKD and diabetes.The data collected using 166 patients with CKD and 91 patients with type 2 diabetes were enrolled in this study. Cystatin C was measured by using the particle-enhanced immunonephelometric method and estimated formulae proposed by five different investigator teams (Stevens, Ma, Rule, Macisaac and Perkins). The plasma clearance of 99mTc-DTPA was determined as measured GFR (mGFR).The result showed that the CKD patients, the bias and accuracy for the Ma and Macisaac equations were superior compared with the MDRD, and the mean results for the Ma formula were closer to mGFR than the other equations in CKD stages 2–5. The differences between Macisaac and mGFR in CKD stages 2–4 were significantly less than those in CKD stage 1 or 5. Stevens and Rule's formulae revealed a similar bias and accuracy compared with the MDRD equation. The MDRD formula had a higher accuracy in CKD stages 3–5 as compared with the results in other stages. For diabetic patients, the mean results between Macisaac and mGFR were closer than those of other equations in mGFR ≥90 ml·min-1·1.73 m-2 stage. In GFR 60–89 ml·min-1·1.73 m-2 stage, the MDRD formula showed the smallest difference compared with other equations. All equations overestimated GFR in the cases with GFR <60 ml·min-1·1.73 m-2 stages. The MDRD formula hada greater accuracy within 50% of mGFR than the equations based on cystatin C in diabetic patients. Perkins formula showed a large positive bias and low accuracy, therefore it may not be suitable for assessing GFR in patients with CKD and diabetes.In the conclusion the formulae for estimating GFR based on cystatin C or creatinine have different trends and accuracies in patients with CKD and diabetes, especially in patients with various GFR levels. The equations based on cystatin C provide less accurate results than MDRD formulae, at least in the diabetic patients. Therefore, whether the formulae based on cystatin C are superior to MDRD formula requires further investigation in large diverse populations.

Chapter three

Materials and Method

Chapter Three

Material and Method

In this chapter describe the material used to collect the data and method of the study which include study area, study variable, study design, study sampling, method of data collection and method of data analysis.

3.1 Materials:

In this study adose calibrator was used to measure the activity of radiopharmaceutical before administration to the patient, as well the data acquired form the region of interest using SPECT gamma camera in the renal scintigraphy**.**

3.1.1 Dose calibrator (ISOMED 1010):

PC-based dose calibrator ISOMED 1010

was used the dose calibrator model ISOMED 1010 and ISOMED 2000 manufactured by MED Nuklear- Medizintechnnikcompany, with specification of :

Activity range: 40kBq – 300GBq.

Resolution: 0.001 MBq

Energy range:25Kev – 3Mev.

Shielding: 4mmPb basic shielding.

Detector: pressurized fill with argon.

Response time: max 3 seconds.

Principle of operation:The typical radioisotope calibrator contains an ionization chamber, a high voltage power supply, an electronic amplifier, and a display unit on which one can select the radioisotope to be calibrated. The ionization chamber is cylindrical in shape and is used to measure the total amount of ionization produced by the sample to be calibrated. The ionization chamber contains Argon gas under high pressure, and the hermetically sealed chamber contains two electrodes

having an electric potential between them. When the vial or syringe containing the radionuclide is placed into the chamber, the Argon gas is ionized, the ion pairs migrate toward the anode and cathode and an electrical current flows between them. This current is proportional to the activity of the measured radioisotope. The magnitude of this current is usually very small (on the microampere level), even if large amounts of activity are present. A device called an electrometer, designed for quantifying very small electric currents, is used and its output is displayed in either mCi or MBq. Dose calibrator function is based on a number of parameters.

3.1.2 Gamma camera (SPECT/MULTICAM 2000") :

Was used **SPECTMULTICAM 1000/MULTICAM 2000**medical imaging systems model MED Nuclear- Medizintechnnik company with dual head and camera large field of view and collimator low energy general purpose .

3.2Methods:

3.2.1 Study design:

This is analytical cross-sectional study where the samples were selected conveniently.

3.2.2 Population of the study

This experimentalstudy, where the patients were selected randomly conducted whom they suffered from kidney disease when they referred to nuclear medicine department in fedail hospital for renal function evaluation, from September to December in 2016.

Exclusion criteria:

All patients with obstructive uropathy and renal failure were excluded from this study.

3.2.3 Sample size

The sample size of this study consist of35patients from both gender whom ages range being from 20 to 80 years, where 15 were diagnosis as normal GFR patient,10 of them were diagnosis as diabetic patient, and 10 were diagnosis as hypertensive patient.

3.2.3 Method of data collection:

Renal scintigraphy withGFR:

- Radiopharmaceutical: 99mTc-DTPA (diethylenetriaminepentaacetic acid).

- Dose: 5 mci .
- Method of Administration: intravenously in one bolus, use butterflyfor adiuretic (furosemide 20 mg).
- Patient Preparation: Instruct patient to hydrate well (water; up to 10 mL/kg) and void just before test, the hydration should continue between studies.

Procedure:

- Before start the scan should be measure the count of syringe before and after injection to calculate the GFR.
- Place the patient in supine position and the camera posterior to the patient, in the pelvic kidney we use two detectors one anterior and one posterior to the patient.
- Position camera by point source over xiphoid, umbilicus, pubic symphysis, and sides in field of view.
- Inject 5mCi 99mTc-DTPA intravenously in one bolus and start the study.

3.2 4Study variable:

Study variable is the data of patient; the variable was collected from GFR, patient ID, disease background, kidney size, patient age, patient weight and height (BMI), count for each frame and patient gender.

3.2.5 Method of Data analysis:

The result of this study analyzed using Exile and SPSS (statistical package for social studies), The result will be shown in a form of correlation between renal scintigraphy with GFR and creatinine clearance result and obtain the linear association between the GFR and patient (age, weight , height) .

Chapter four

Results

Chapter Four

Results

Table 4-1 the mean ± standard deviation of body characteristics and renal function in normal patient

Variable	Mean ± SD		
	Normal	Hypertensive	Diabetic
Age	22±17.5	38±14.1	48±10.5
BMI	14.7±5.9	18.7±3.9	44±15.6
Total GFR	78±14.7	26±24.45	17.6±6.2

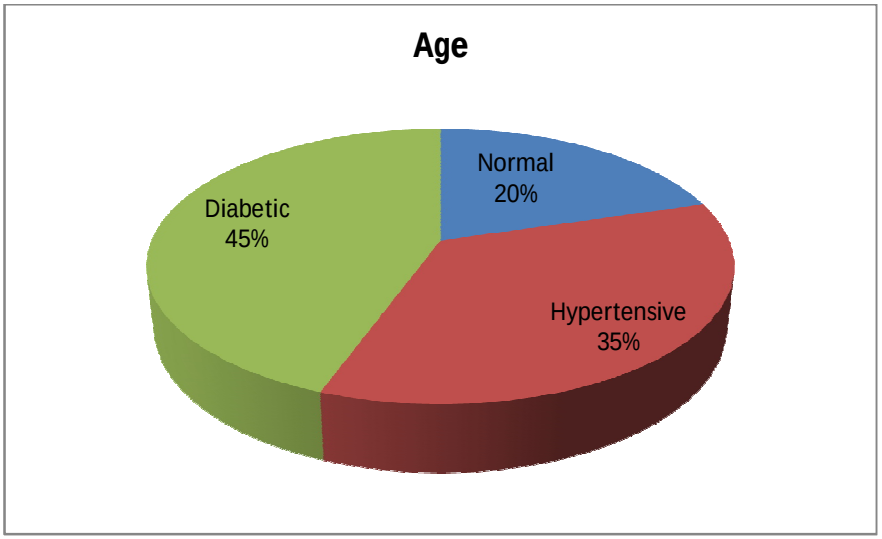

Figure 4:1 a pie graph shows age percentage distribution

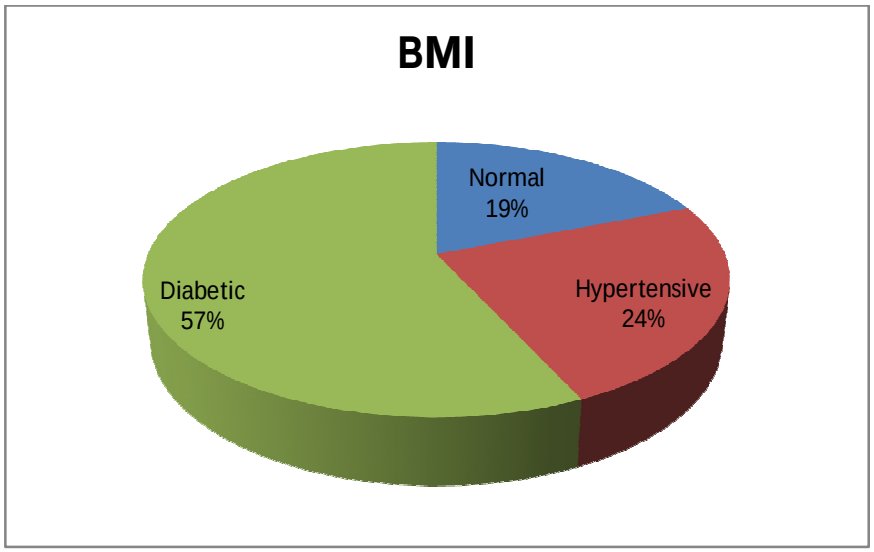

Figure 4:2 a pie graph shows BMI percentage distribution

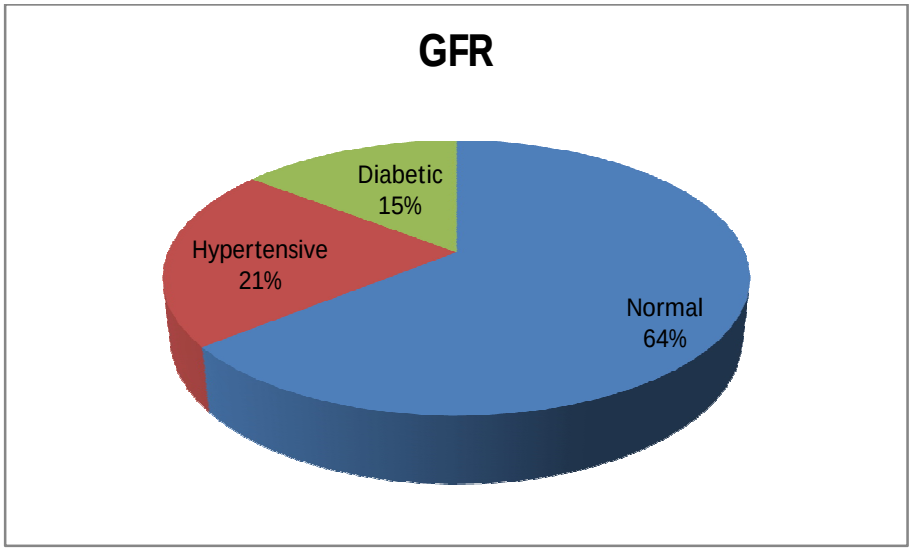

Figure 4:3a pie graph shows GFR percentage distribution

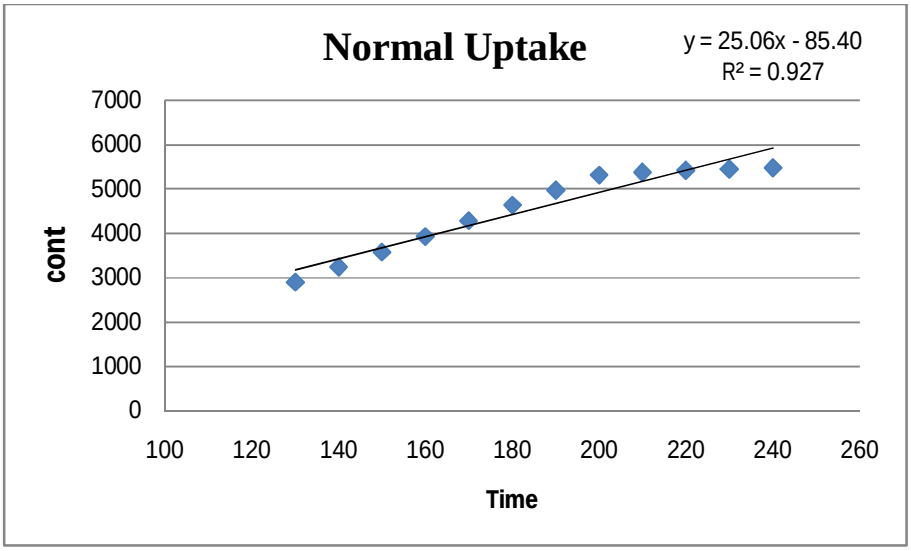

Figure 4:4a scatter plot show the uptake phase versus time in normal patient.

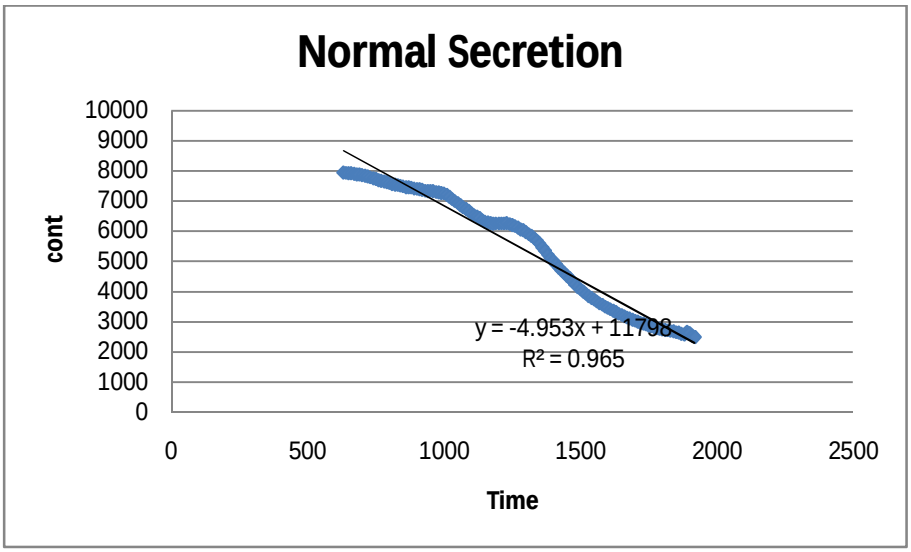

Figure 4:5a scatter plot show the secretion phase versus time in normal patient.

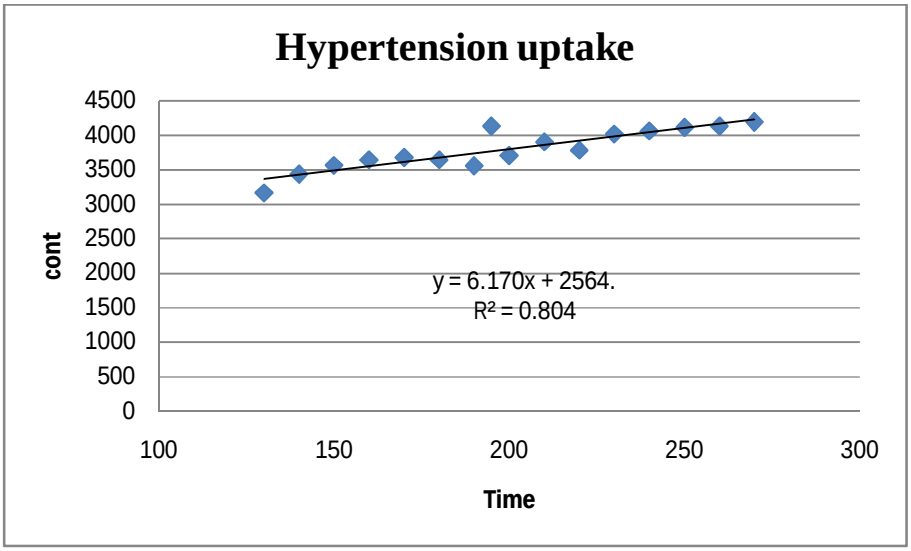

Figure 4:6 a scatter plot show the uptake phase versus time in hypertension patient.

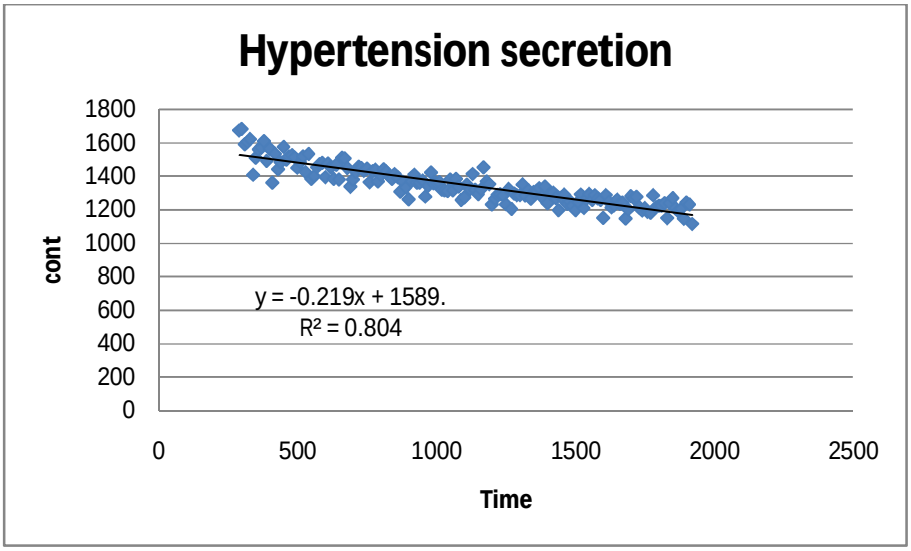

Figure 4:7a scatter plot show the secretion phase versus time in hypertension patient.

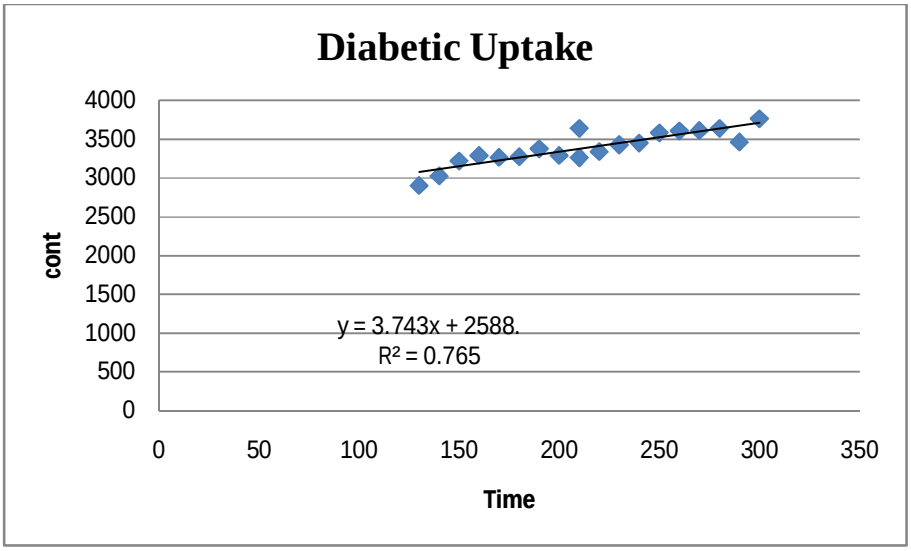

Figure 4:8 a scatter plot show the uptake phase versus time in diabetic patient.

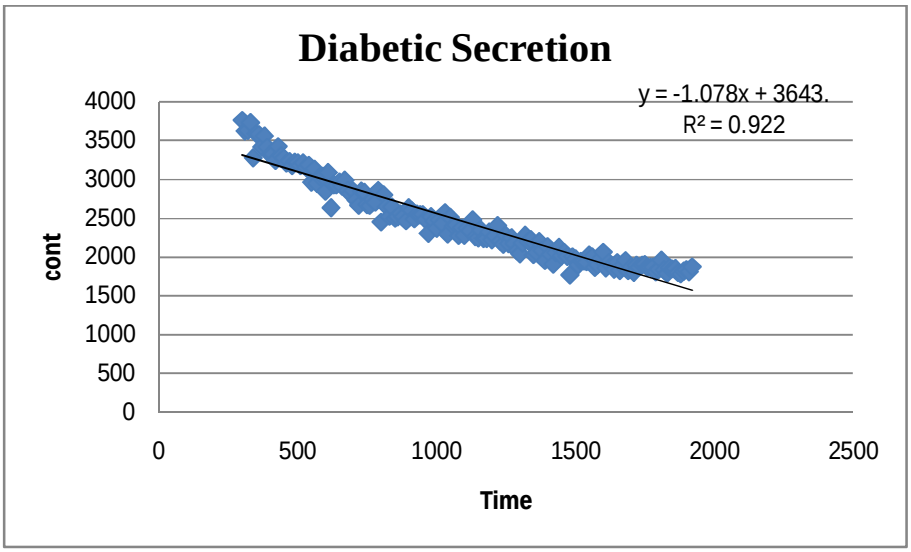

Figure 4:9a scatter plot show the secretion phase versus time in diabetic patient.

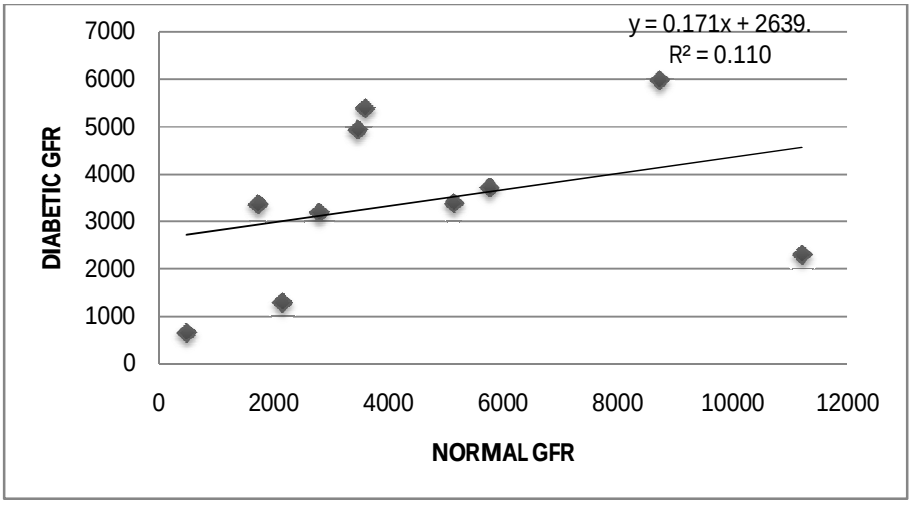

Figure 4:10a scatter plot show direct linear relationship between GFR in normal patient and diabetic using renal scintigraphy.

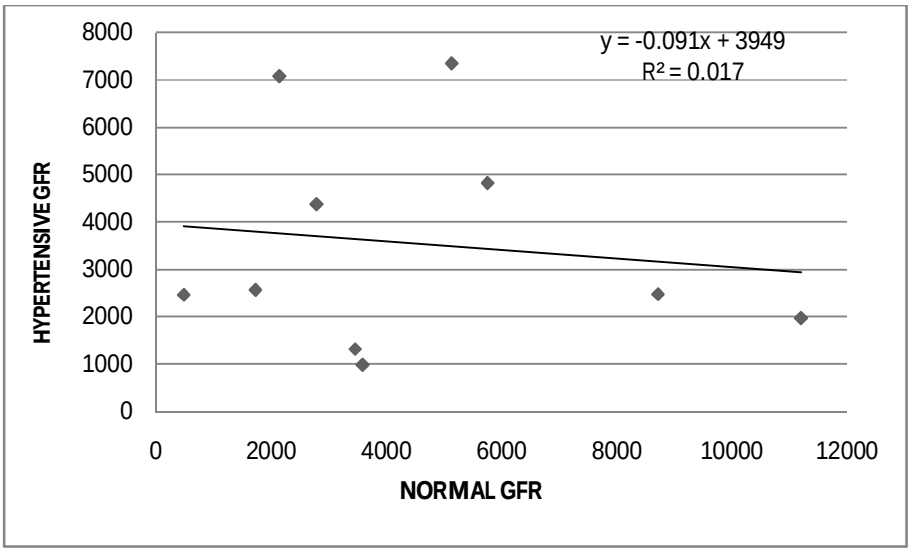

Figure 4:11a scatter plot show inverse linear relationship between of GFR in normal patient and hypertension using renal scintigraphy.

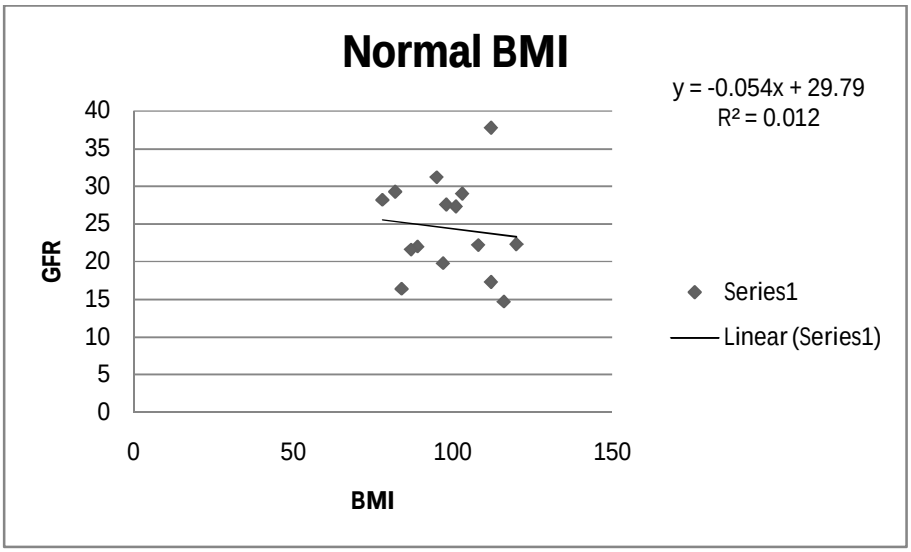

Figure 4:12a scatter plot show an inverse linear relationship between GFR and BMI in normal patient

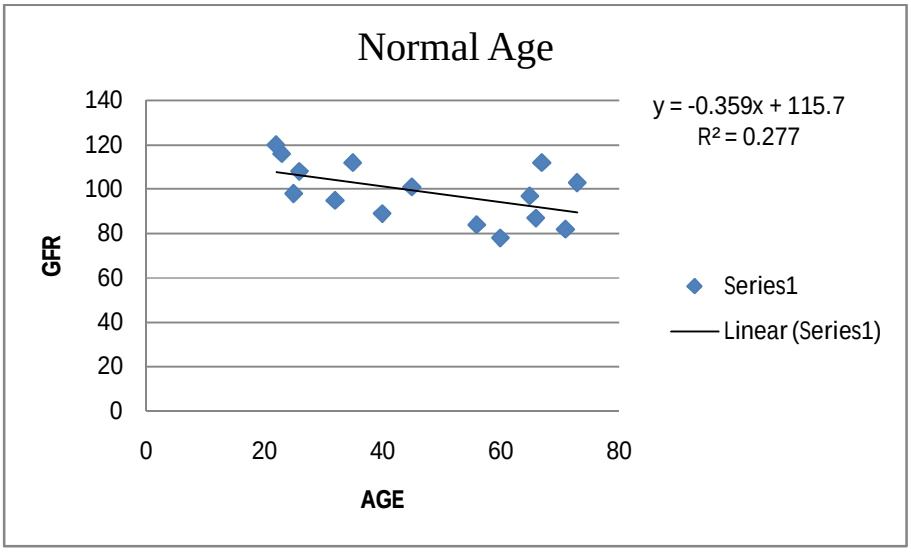

Figure 4:13a scatter plot show an inverse linear relationship between GFR and age in normal patient

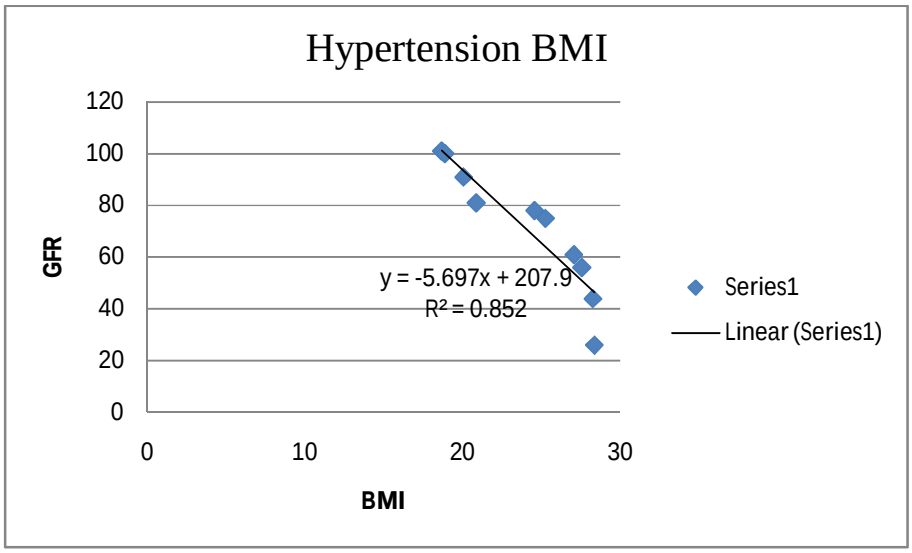

Figure 4:14a scatter plot show an inverse linear relationship between GFR and BMI in hypertensive patient

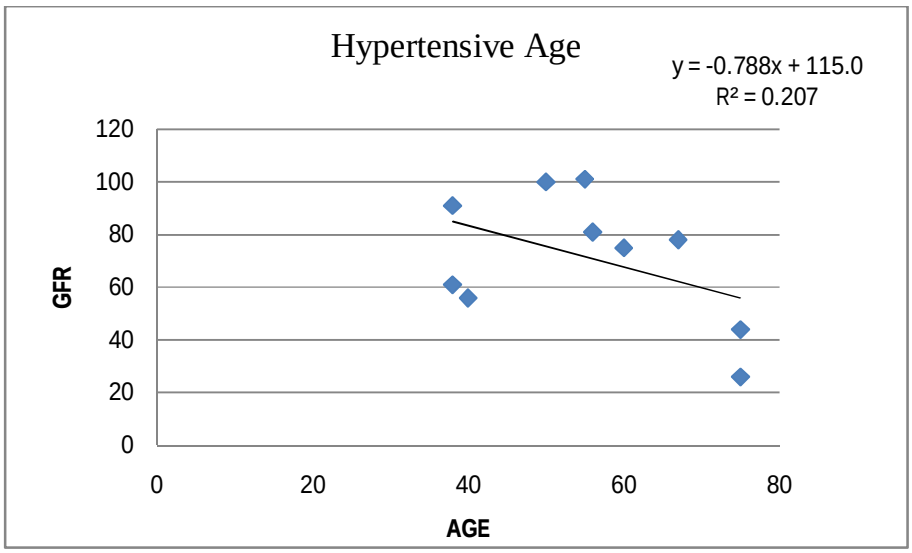

Figure 4:15 a scatter plot show an inverse linear relationship between GFR and age in hypertensive patient

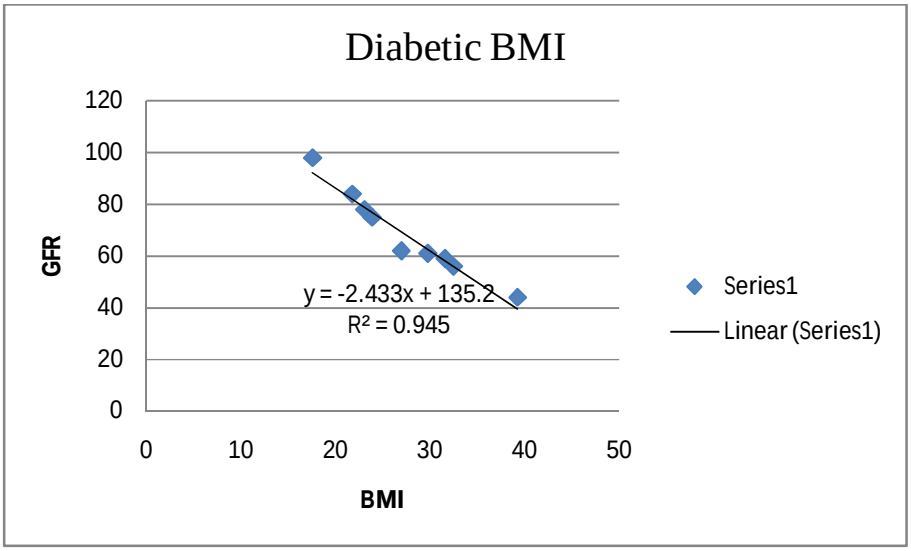

Figure 4:16a scatter plot show an inverse linear relationship between GFR and BMI in Diabetic patient

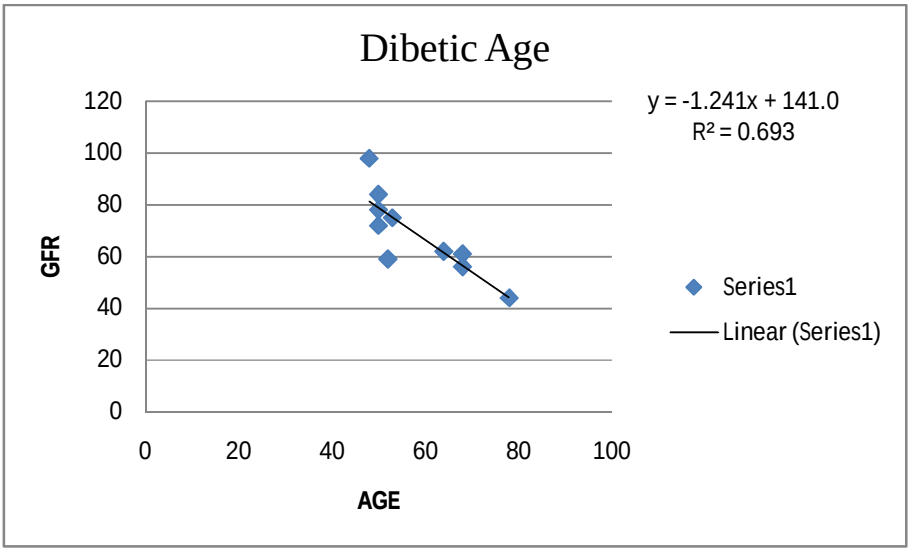

Figure 4:17a scatter plot show an inverse linear relationship between GFR and age in Diabetic patient

Table 4- 2 T-test for Equality of Means in absorption phase

	t	Sig. (2-tailed)
For hypertensive	3.215	.007
For diabetic	2.873	.013

Table 4- 3 ANOVA test for secretion phase

Average	Sum of Squares	Mean Square	F	Sig.
Between Groups	3.996	1.998	.786	.466
Within Groups	68.625	2.542		
Total	72.621			

Chapter five

Discussion, Conclusion and Recommendations

Chapter Five

Discussion, Conclusion and Recommendation

5.1 Discussion

The sample of this study included 35 patients with normal abnormal result of GFR using renal scintigraphy, where the main objective was to assessment of Glomerular filtration rate (GFR) in diabetic and hypertensive patient using DTPA scintigraphy.

The mean age and BMI of the normal patients participated in this study was 22±17.5 years and 14.7±5.9 kg/m^2 respectively, which reflect middle age and underweight body mass index.

The mean age and BMI of the diabetic patients participated in this study was 48±10.15 years and 44±15.6 kg/m^2 respectively, which reflect old age and obesity body mass index.

The mean age and BMI of the hypertensive patients participated in this study was 38±14.1 years and 18.7±3.9 kg/m^2 respectively, which reflect middle age and normal body mass index. While their mean GFR using renal scintigraphy method was 78±14.7 ml /min, 17.6±6.6ml/min and 26±24.4 ml/min in normal , diabetic and hypertensive patient respectively (Table 4-1) .

The presented result as shown in Figure (4-4) shows that the normal patient uptake co-offecient is 25.06count/second whileFigure (4-5) shows that the normal patient secretion co-offecient is -4.953count /second.

The following four figures two of them explain the uptake phase versus time and the other two shows secretion phase versus time, all hypertensive and diabetic one respectively.

The uptake phase co-offecient for hypertensive (Figure 4-6) wasdecrease by6.17cont /second While Figure (4-8) shows uptake phase co-offecient for diabetic wasdecrease by 3.743 cont /second, that meaning the effect of hypertensive is more than that of diabetic .

As shows in the table (4-2) which use the t-test there is significant difference in absorption co-offecient phase between normal and abnormal (hypertensive and diabetic) one which equal 0.007and 0.013at probability p=0.05 in hypertensiveand diabetic with normal respectively. On the other hand the secretion phase inconclusive difference show in table(4-3) these due to the hypertension and diabetic have no direct effect on secretion phase ,it function of renal tubule not direct effect thought the blood vessels .

Age and body mass index (BMI) also influenced the result of GFR. In case of age, GFR decreased linearly when age increases by 0.359cont /second ,0.788cont/second and1.241count/second in case of normal and hypertensive and diabetic respectively .Concerning BMI also it has an inverse linear relationship with the value of GFR using renal scintigraphy.

5-2 Conclusion

This study was carried out in order to assessment of Glomerular filtration rate (GFR) in diabetic and hypertensive patients using DTPA scintigraphy

The data of this study collected from 35 patients their renal function was assessed using renal Scintigraphy this study conducted in Fedail Hospital (FH), Khartoum state / Sudanwhere the data were collected prospectively.

The results of this study showed that there is a direct effect in GFR in diabetic and hypertensive.

5.3 Recommendation

- Another study can be done for abnormal patients i.e. those with renal function disorder including the duration of diseases
- Similar study can done to investigate the effect of stone and obstruction in kidney function
- Large sample can be incorporated in similar study to highlight the effect of age, BMI and gender.
- The researcher also recommending to develop nuclear medicine center and increase its number in Khartoum and rest of Sudan states to be able to cover the high people residency and provide good medical services to the patient

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Appendix

6.1 Appendix:

Master data sheet

number	Age	Gender	Height	Weight	BMI	Total GFR ml/min	Disease
1	50	1	182	87	26.3	62	3
2	68	1	156	53	21.8	75	3
3	50	1	173	69	23.1	44	3
4	52	1	165	65	23.9	61	3
5	64	2	171	87	29.8	56	3
6	68	1	153	92	39.3	78	3
7	78	2	170	51	17.6	84	3
8	48	2	152	75	32.5	98	3
9	50	1	167	88	31.6	59	3
10	53	1	154	64	27	72	3
11	67	2	167	77	27.6	78	2*
12	38	2	163	72	27.1	91	2*
13	56	1	177	77	24.6	81	2*
14	75	2	157	46	18.7	26	2*
15	60	1	165	77	28.3	75	2*
16	55	2	154	60	25.3	101	2*
17	50	2	176	88	28.4	100	2*
18	75	1	161	52	20.1	44	2*
19	38	2	172	56	18.9	61	2*
20	40	2	153	49	20.9	56	2*
21	35	1	154	41	17.3	84	1*
22	56	2	178	52	16.4	98	1*
23	25	1	168	78	27.6	101	1*

24	45	1	167	76	27.3	95	1*
25	32	1	157	87	31.2	82	1*
26	71	2	149	65	29.3	116	1*
27	23	2	181	48	14.7	78	1*
28	60	1	163	75	28.2	120	1*
29	22	1	154	53	22.3	108	1*
30	26	2	159	56	22.2	78	1*
31	40	1	177	69	14.7	89	1*
32	66	2	168	61	22	87	1*
33	65	1	171	58	21.6	97	1*
34	73	2	167	81	19.8	103	1*
35	67	2	156	92	29	112	1*

1= male 2= female

1* = Normal 2* = Diabetic 3=Hypertension