INVESTIGATION, THERAPY AND USE OF MOLECULAR BIOMARKER IN CHRONIC KIDNEY DISEASE

Hari Priya Behera ¹*, Swati Mishra ², Sruti Ranjan Mishra ³, Rama Prasad Padhy ⁴, Mahendra Kumar Panigrahi ⁵, Swarna Lichika Satman ⁶, Boi Basanta Kumar Reddy ⁷

 ¹ Assistant Professor, Department of Pharmacology, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
*Corresponding Author Email: haripriyabehera2@gmail.com
² Assistant Professor, Department of Pharmaceutics, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
³ Professor cum Principal, Department of Pharmaceutics, Danteswari College of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁴ Professor cum Vice Principal, Department of Pharmachemistry, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁵ Professor, Department of Pharmacognosy, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁶ Assistant Professor, Department of Pharmacology, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁶ Assistant Professor, Department of Pharmacology, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁷ Professor, Department of Pharmaceutics, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.
⁷ Professor, Department of Pharmaceutics, Danteswari college of Pharmacy, Borpadar, Raipur Road, Jagdalpur, Chhattisgarh, India.

DOI: 10.5281/zenodo.8374747

Abstract

In this article we will discuss anatomy and physiology of kidney in the body. We will define causes, symptoms, stage, complications of chronic kidney disease and use of new technologies of biomarker. When the kidneys are not working properly creatinine levels increased in body, which cause the symptoms of renal failure. Hypertension, tiredness, headache, swelling face and ankles are the symptoms of kidney disease. The Biomarkers use is important for the chronic kidney disease. It is used to confirm the presence of disease. The molecular biomarker in GFR Test is the most important role in chronic renal disease. This study came across the biomarkers of identification of CKD. Disease-specific markers may supplement more general biomarkers. Biomarkers can range from simple physiologic measurements of pulse and blood pressure. Blood samples are test by the help of GFR Test. The GFR is estimated using serum creatinine, a readily available and inexpensive marker. However, serum creatinine varies with age, sex, muscle mass, dietary habits, and medications. Similarly, urine albumin reflects glomerular injury, glomerular permeability, or tubular injury, inflammation, fibrosis, and glomerular hyper filtration .Finally these biomarkers have confirmed the capability to identify early damage, localize injury. Whether the newly identified or kidney biomarkers of underlying pathophysiological processes are purely associations are need to be determine. An approach to biomarker advance that incorporate mutual with regulatory science involving discipline that is required to make sure that balanced, proof based biomarker development keeps speed with technical and medical need.

Keyword: Chronic Kidney Disease, Biomarker, Glomerular Filtration Rate Test, New Technologies Of Biomarker.

INTRODUCTION

The kidneys are vital organs in the body. These are bean formed organs that placed below the rib cage. The proper kidney is normally barely decrease than the left kidney tomake area for the liver(1,2,3). The main role of kidneys is preserving homeostasis(4, 5). Your kidneys remove wastes and extra fluid from your body. The kidney removes wastes, extra fluids and acid from the body (6, 7). This may result in ankle edema, nausea, weakness, restless sleep, and shortness of breath. Without therapy, the damage

may worsen and the kidneys may eventually quit functioning. That is serious and terrible. (8, 9).

The kidney disease mainly 2 types

Acute kidney disease (AKD)

Chronic kidney disease (CKD) (10).

Acute kidney disease

It also called acute renal injury. It is a short-term disease, because sudden decreases the kidney function. The acute kidney disease is of 3 types

Pre-renal:- Decreased blood flows to the kidneys

Inter-renal:- Due to damage the kidney.

Post-renal:- Due to obstruction of urine flows from the kidneys (11, 12).

Chronic kidney disease

It is a long standing disease. It is also called as kidney failure and impaired kidney function. Diabetes, hypertension and heart disease are the cause of kidney failure (13, 14).

BIOMARKER

Biomarker is a technique of diagnosis. For therapeutic intervention biomarker is a character to evaluate as an indicator for pathogenic process and normal biological process (15, 16).

It is characterized by measured and evaluated indication of variety process in these diseases.

Types of Biomarkers

Biomarker is of four types.

Molecular biomarker

Histologic biomarker

Radiographic biomarker

Physiologic biomarker (17).

Molecular biomarker:

It can be calculated biological samples.

E.g. Serum, plasma, cerebrospinal fluid (CSF) etc (18).

Histologic biomarker:

In this process measurement of grading, staging and history of disease (18).

E.g. Cancer disease, Diabetes

Radiographic biomarker:

It is obtained from image related test.

E.g. CT, MRI, Ultrasound, X-ray, ECG etc. (18).

Physiologic biomarker:

In this process that measurement a particular body process.

E.g. Blood pressure (18).

PATHOPHYSIOLOGY

The both kidneys are two bean formed organs. Those are the part of urinary system. Every day the kidneys filter 189 liters of fluid. The kidney balance the body's fluids, electrolytes and pH balance of the blood. It makes glucose and protein. The kidney produce hormones i.e. calcitriol and erythropoietin. Calcitriol produced by vitamin D, that helps absorb calcium and the erythropoietin helps make red blood cells (RBCs) in body.

Formation of Urine: Urine is formed in 3 main steps.

Glomerular filtration, reabsorption and secretion.

Glomerular filtration: Every kidney consists of thousands and thousands of tiny systems called as nephron. Every nephron has a glomerulus. The glomerulus is a cup like structure called glomerulus capsule. The glomerulus capsule has glomerulus capillaries. The blood passes through the glomerulus capillaries to the kidney. The glomerular filtration begins in the process of urine formation.

Reabsorption: The glomerulus removes waste materials and water from the bloodstream. The filtrate contains waste, but the body prefers other substances.

Secretion: At that same time glomerular reabsorption and as well as glomerular secretion is done in kidney (19, 20).

Causes of Kidney Damage

Chronic kidney disease: Diabetes and hypertension causes of CKD.

Kidney cancer: Genetic disorder, smoking is the cause of kidney cancer.

Kidney stone: Drinking too little water is the cause of kidney stone.

Symptoms of Renal Disease

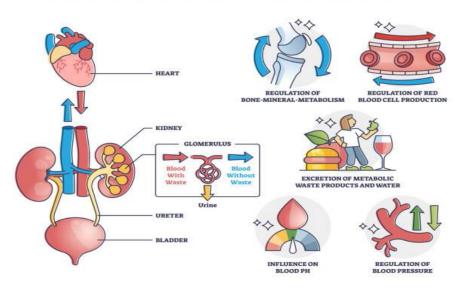
Muscle cramps, swelling ankles, feet, face, dark urine or blood in urine, dry skin, loss of appetite, sleeping problem.

Common Test of Kidney Disease

Advanced Imaging: CT scan, MRI, Ultrasound can show abnormalities of kidney.

Blood Tests: For detection of kidney damage we can prefer blood test.

Uretroscopy: It is also known as endoscope. It is a procedure that uses anuretroscope to look inside the ureters and kidney (21).



FUNCTIONS OF A KIDNEY

Figure 1: (22, 23)

GLOMERULAR FILTRATION RATE (GFR) TEST

Blood will be tested. The GFR test estimates the amount of blood that goes through the filter each minute and also analyzes the levels of creatinine. The waste product creatinine is produced by the body during routine bodily processes. As a result, the most common method for estimating GFR is the estimated GFR test, or eGFR. We shall employ a technique known as a GFR calculator in this procedure. A mathematical formula that estimates the rate of filtration is a GFR calculator.

The results of a blood test to assess levels of a waste product called creatinine that is filtered by the kidneys

Age Weight height Gender Race

An easy test with potentially highly accurate results is the eGFR.

What happens during a GFR test?

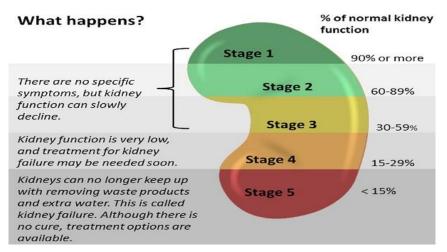


Figure 2: (22,23)

In the normal range GFR of 90 or higher. GFR of 60-89 may have early stage kidney disease. GFR below 15 may have kidney failure (24).

NEW TECHNOLOGY OF BIOMARKER

The biomarkers are used in different types of disease. E.g.: Cancer, Kidney disease, cardiovascular disease, Diabetes, Alzheimer's disease etc.

Heart Disease

Radiographic biomarker is mainly used in the treatment of cardiovascular or heart disease.

Electrocardiogram (EGC) – A device that studies heart rhythm using electrical markers.

Echocardiogram – Non-invasive method based on ultrasound of the chest area.

Stress test – Increase the heart rate with exercise or medication to monitor the heart's response.

Cardiac Computer Tomography (CT) scans – Collection of images around the heart to provide a complete view of the heart.

Cardiac Magnetic Resonance Imaging (MRI) – It is Similar to a CT scan an image of the heart is taken for evaluation (25).

Cancer Disease

Molecular biomarker is mainly used in the treatment of cancer disease.

If you have a tumor, they will most likely use the samples taken during a biopsy of the tumor or during surgery.

A blood or bone marrow sample test leukemia.

For some cancers, other body fluids such as urine might be tested (26).

Diabetes Disease

Molecular biomarker is used in the treatment of diabetes. It is test in blood samples (27).

Alzheimer's Disease

Radiographic and molecular biomarker is used in the Alzheimer's disease.

In this disease, treatment is done through the computed tomography (CT), MRI (28).

It is test in blood or Cerebrospinal fluid (CSF) (29).

Other technology used for biomarker includes in-vitro analyses of metabolite quantification, expression of protein and DNA/RNA (30).

Two Dimensional Gel Electrophoresis is the primary approach for proteomics paintings. It separates the combination samples using 2 one-of-a-kind parts. Proteins are separated by way of the pl fee in 1st size and the relative molecular weight in 2nd dimension (31).

In a laboratory test, an enzyme immunoassay (ELISA) is commonly used. Antibody test in the blood (32, 33).

ELISA is applied in many diagnostic tests.

Detects and Calculates the Presence of Antibodies in the Blood

Auto-antibodies (anti-dsDNA, anti-dsg1, ANA, etc.)

Antibodies against infectious disease (antibacterial, antiviral, antifungal)

Hepatitis A, B, C, HIV, etc.

Detection and Estimation of Tumor Marker Values

Prostate-specific antigen (PSA)

Carcinoembryonic Antigen (CEA)

Detection and Estimation of Hormone Levels

Luteinizing hormone

Follicular stimulating hormone

Prolactin

Testosterone

Recognize Drug Addiction

Amphetamine

Methamphetamine

3, 4-methylenedioxymethamphetamine

Cocaine

Benzoylecgonine (34).

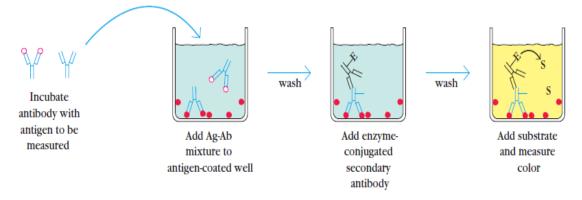


Figure 3: (35)

ELISA technique is based on observance of mass sensing BioCD array suffers from its result variation with change in alkali, buffer and pH (36). Mass biosensors measure protein amount by means of directly converting the protein mass into bodily signal that are extra impartial of the nearby micro-surroundings (37).

Generally serum sample is viscous and terbids in nature for electrochemical immunity assay. Tedious process is also known as purification of serum sample and it also block

the protein detection (38). It is a quantitative method for measurement of antigen or antibody based on the change in electrochemical signal before and after immunoreactions(39).

The plasmonic nano structures the detection of biomarker protein on the surface can used Enhanced Raman Spect (SERS) which is a technique of ultrasensitive vibrational spectroscopy (40).

The fluroscence detection has been most widely used and biomarker proteins are used comparatively easy labeling of biomolecules with fluroscent tag in biological application (40, 41, 42).

BIOMARKERS USED SPECIAL FOR KIDNEY DISEASE

Biological markers (biomarkers), which pick out normal or pathogenic procedures, or responses to remedy, are a treasured for figuring out a affected person's situation. Biomarkers used to diagnose and degree a pathological situation or make a diagnosis about the improvement of sickness. Diabetes can also be detect by this test. There is a rareness of sensitive and specific biomarkers for the early calculation of CKD progression.

Why we choose biomarkers in CKD?

It can be measure easily, exactly & reproducibly.

It can with sensitivity signify the kidney response to treatment.

It can identify specific types of kidney disease (43, 44, 45, 46).

CONCLUSION

Biomarker studies has expanded vastly in the formerly ten times with aiming of allowing nephrologists to identify order detriment ahead. Valuable interventions are the reason to identify order conditions. In discovery lores, medical product development, and healthcare biomarkers are critical to the fabric for the individual and population. Lots of promising biomarkers of order health that are introduced in the pathophysiology- sense medium of renal damage have established the eventuality to progress clinical treatment of order conditions. For opinion of AKI and CKD biomarkers may revise. Whether the lately linked or order biomarkers of bolstering pathophysiological processes are purely associations are need to be determine. An approach to bio- marker strengthen that consists of collaborative with nonsupervisory wisdom concerning multiple disciplines is demanded to make sure that rational, proof-predicated fully biomarker development keeps pace with scientific and medical want.

References

- 1) National Institutes of Health. National Institute of Diabetes and Digestive and Kidney Diseases. Kidney disease statistics for the United States.
- Baranski A. Basic Anatomy of the Kidney, Ureters and the Urinary Bladder, and Their Functions. InKidney Transplantation: Step-by-Step Surgical Techniques 2023 Apr 27 (pp. 1-32). Cham: Springer International Publishing.
- 3) Taco E, Noguera E. RENAL ANATOMY. Advanced Anesthesia Review. 2023 Mar 17:405.
- 4) Finco DR. Kidney function. InClinical biochemistry of domestic animals 1997 Jan 1 (pp. 441-484). Academic Press.

- 5) Macías Ruiz MD, Cuenca Bermejo L, Veronese N, Fernández Villalba E, González Cuello AM, Kublickiene K, Raparelli V, Norris CM, Kautzky-Willer A, Pilote L, Barbagallo M. Magnesium in Kidney Function and Disease—Implications for Aging and Sex—A Narrative Review. Nutrients. 2023 Mar 31;15(7):1710.
- 6) Kidney E. NIDDK.(2022)
- 7) 7.Steinbrenner I, Sekula P, Kotsis F, von Cube M, Cheng Y, Nadal J, Schmid M, Schneider MP, Krane V, Nauck M, Eckardt KU. Association of osteopontin with kidney function and kidney failure in chronic kidney disease patients: the GCKD study. Nephrology Dialysis Transplantation. 2023 Jun;38(6):1430-8.
- 8) Nwankwo CU, OBASI SC, Obasi SC. Renal failure: implication for health education. International Journal of Research. 2015 May;9(1):1-0.
- 9) Veltkamp DM, Wang Y, Meuleman Y, Dekker FW, Michels WM, van der Boog PJ, de Vries AP. Age and gender differences in symptom experience and health-related quality of life in kidney transplant recipients: a cross-sectional study. Nephrology Dialysis Transplantation. 2023 Jan 27:gfad023.
- 10) Jackson T. Companion and Non-Companion Animals' Impact on People Living with Kidney Disease: A Qualitative Content Analysis (Doctoral dissertation).
- 11) Rahman M, Shad F, Smith MC. Acute kidney injury: a guide to diagnosis and management. American family physician. 2012 Oct 1;86(7):631-9.
- 12) Turgut F, Awad AS, Abdel-Rahman EM. Acute kidney injury: Medical causes and pathogenesis. Journal of Clinical Medicine. 2023 Jan 3;12(1):375.
- 13) Pruthy S. Chronic kidney disease-Symptoms and causes [WWW Document]. Mayo Clinic. URL https://www. mayoclinic. org/diseases-conditions/chronic-kidney-disease/symptomscauses/syc-20354521 (accessed 7.20. 22). 2022.
- 14) Jeong J, Sprick JD, DaCosta DR, Mammino K, Nocera JR, Park J. Exercise modulates sympathetic and vascular function in chronic kidney disease. JCI insight. 2023 Feb 2;8(4).
- 15) Bienaimé F, Muorah M, Metzger M, Broeuilh M, Houiller P, Flamant M, Haymann JP, Vonderscher J, Mizrahi J, Friedlander G, Stengel B. Combining robust urine biomarkers to assess chronic kidney disease progression. Ebiomedicine. 2023 Jul 1;93.
- 16) Arriaga-Canon C, Contreras-Espinosa L, Aguilar-Villanueva S, Bargalló-Rocha E, García-Gordillo JA, Cabrera-Galeana P, Castro-Hernández C, Jiménez-Trejo F, Herrera LA. The clinical utility of IncRNAs and their application as molecular biomarkers in breast cancer. International Journal of Molecular Sciences. 2023 Apr 18;24(8):7426.
- 17) Faiman B, Kurtin SE, Persinger R. Biomarker Pursuit: Keeping Current With Novel Biomarkers in Hematology/Oncology. Journal of the Advanced Practitioner in Oncology. 2023 Apr;14(3):223.
- 18) Ilori TO. and Boston Medical Center, Boston, MA 02118, USA 7. Department of Biostatistics, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, 21205, USA 8. Cancer Innovation Laboratory, Center for Cancer Research, National Cancer Institute and Basic Research program, Frederick National Laboratory, Frederick, MD 21702, USA.
- Price T, Palokas M, Patel N. Nursing assessments of women with hypertensive disorders during labor in an academic medical center in Mississippi: a best practice implementation project. JBI Evidence Implementation.2023 Apr 7:10-97.
- 20) Bhargava R, Li H, Tsokos GC. Pathogenesis of lupus nephritis: the contribution of immune and kidney resident cells. Current Opinion in Rheumatology. 2023 Mar 1;35(2):107-16.
- 21) de Paula BL, Pinheiro BV, Segura-Ortí E, Barros FS, Veras PM, Ávila KS, Lucinda LM, Garcia MA, Reboredo MM. Association Between Protocols of the Sit-to-Stand Test and Lower Limb Muscle Force Output in Patients on Hemodialysis and Subjects Without Chronic Kidney Disease. Journal of Renal Nutrition.2023 Feb 13.
- 22) 17,600+ Kidney Function Stock Photos, Pictures & Royalty-Free Images iStock | Kidney function test (istockphoto.com)

- 23) Glomerular Filtration Rate (GFR) Test: MedlinePlus Medical Test
- 24) Holt A, Rahm J, Hopper HA, Hunt DL. Acute Kidney Injury: Iterative Development of an Audit Tool for Trauma Patients. Journal of Trauma Nursing. 2023 Mar 1;30(2):108-14.
- 25) Gupta UC, Gupta SC, Gupta SS. An Evidence-Based Review of Diabetes Care: History, Types, Relationship to Cancer and Heart Disease, Co-Morbid Factors, and Preventive Measures. Current Nutrition & Food Science. 2023 May 1;19(4):399-408.
- 26) Hathaway CA. The Association of Kidney Function Biomarkers with Ovarian Cancer Risk and the Mediating Effects of Inflammation (Doctoral dissertation, Nova Southeastern University).
- 27) Pilvenyte G, Ratautaite V, Boguzaite R, Ramanavicius A, Viter R, Ramanavicius S. Molecularly imprinted polymers for the determination of cancer biomarkers. International Journal of Molecular Sciences. 2023 Feb 18;24(4):4105.
- 28) Yilmaz E, Ismaila N, Bauman JE, Dabney R, Gan G, Jordan R, Kaufman M, Kirtane K, McBride SM, Old MO, Rooper L. Immunotherapy and biomarker testing in recurrent and metastatic head and neck cancers: ASCO Guideline. Journal of Clinical Oncology. 2023 Feb 10;41(5):1132-46.
- 29) Menegaut L, Laubriet A, Crespy V, Leleu D, Pilot T, Van-Dongen K, Pais de Barros JP, Gautier T, Petit JM, Thomas C, Nguyen M. Inflammation and Oxidative Stress Markers in Type 2 Diabetes Patients with Advanced Carotid Atherosclerosis. medRxiv. 2023:2023-07.
- 30) Gustavsson A, Norton N, Fast T, Frölich L, Georges J, Holzapfel D, Kirabali T, Krolak-Salmon P, Rossini PM, Ferretti MT, Lanman L. Global estimates on the number of persons across the Alzheimer's disease continuum. Alzheimer's & Dementia. 2023 Feb;19(2):658-70.
- 31) Padala SP, Newhouse PA. Blood-based biomarkers in Alzheimer's disease: a mini-review. Metabolic Brain Disease. 2023 Jan;38(1):185-93.
- 32) He H, Wu C, Saqib M, Hao R. Single-molecule fluorescence methods for protein biomarker analysis. Analytical and Bioanalytical Chemistry. 2023 Jan 7:1-5.
- 33) Nakagawa M, Tomioka Y, Sakuma C, Kurosawa Y, Shibata T, Arakawa T, Akuta T. Development of a novel two-dimensional gel electrophoresis protocol with agarose native gel electrophoresis. Electrophoresis. 2023.
- 34) Yu Q, Trinh HD, Lee Y, Kang T, Chen L, Yoon S, Choo J. SERS-ELISA using silica-encapsulated Au core-satellite nanotags for sensitive detection of SARS-CoV-2. Sensors and Actuators B: Chemical. 2023 May 1;382:133521.
- 35) elisa diagram Bing images
- 36) Shinde A, Illath K, Kasiviswanathan U, Nagabooshanam S, Gupta P, Dey K, Chakrabarty P, Nagai M, Rao S, Kar S, Santra TS. Recent Advances of Biosensor-Integrated Organ-on-a-Chip Technologies for Diagnostics and Therapeutics. Analytical Chemistry. 2023 Jan 30;95(6):3121-46.
- 37) Ma C, Zhang Z, Tan T, Zhu JJ. Recent Progress in Plasmonic based Electrochemiluminescence Biosensors: A Review. Biosensors. 2023 Jan 29;13(2):200.
- Karim MR, Comet L, Beyan O, Cochez M, Rebholz-Schuhmann D, Decker S. A Biomedical Knowledge Graph for Biomarker Discovery in Cancer. arXiv preprint arXiv:2302.04737. 2023 Feb 9.
- Nguyen CM, Sallam M, Islam MS, Clack K, Soda N, Nguyen NT, Shiddiky MJ. Placental Exosomes as Biomarkers for Maternal Diseases: Current Advances in Isolation, Characterization, and Detection. ACS sensors. 2023 Jul 14.
- 40) Kukkar D, Chhillar M, Kim KH. Application of SERS-based nanobiosensors to metabolite biomarkers of CKD. Biosensors and Bioelectronics. 2023 Apr 17:115311.
- 41) Meeseepong M, Ghosh G, Shrivastava S, Lee NE. Fluorescence-Enhanced Microfluidic Biosensor Platform Based on Magnetic Beads with Highly Stable ZnO Nanorods for Biomarker Detection. ACS Applied Materials & Interfaces. 2023 Apr 27;15(18):21754-65.

- 42) Cao Y, Wang Z, Fu B, Li H, Zhang X, Guo DY, Li L, Pan Q. Bifunctional ratiometric fluorescent probe for sensing anthrax spore biomarker and tetracycline at different excitation channels. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2023 Jan 15;285:121915.
- 43) Sezer B, Kodaman Dokumacıgil N, Kaya R, Güven S, Türkkan ÖN, Çiçek N, Alpay H, Kargül B. Association between serum biomarkers and oral health status in children with chronic kidney disease: A cross-sectional study. Clinical oral investigations. 2023 Apr 4:1-0.
- 44) Kubota M, Zhang BS, Li SY, Yoshida Y, Wang H, Adachi A, Matsutani T, Mine S, Machida T, Kamitsukasa I, Wada T. Serum anti-TSTD2 antibody as a biomarker for atherosclerosis-induced ischemic stroke and chronic kidney disease. Medicine International. 2023 Jan 1;3(1):1-0.
- 45) Luo M, Zhang Z, Lu Y, Feng W, Wu H, Fan L, Guan B, Dai Y, Tang D, Dong X, Yun C. Urine metabolomics reveals biomarkers and the underlying pathogenesis of diabetic kidney disease. International Urology and Nephrology. 2023 Apr;55(4):1001-13.
- 46) Fassett RG, Venuthurupalli SK, Gobe GC, Coombes JS, Cooper MA, Hoy WE. Biomarkers in chronic kidney disease: a review. Kidney international. 2011 Oct 2;80(8):806-21.