Pathophysiology of Lipid Metabolism in Chronic Renal failure patients

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ABSTRACT

Back ground: Assessing the main pathophysiological changes in individuals with chronic renal failure—which is characterized by either a persistent, substantial drop in glomerular filtration rate or a prolonged, irreversible loss of kidney tissue—is the aim of the study. It is also distinguished by a variety of clinical signs and indications as well as a broad spectrum of metabolic abnormalities.

Material and methods: From July 2019 to July 2021, a cross-sectional study was conducted in Kirkuk City, Iraq, where 100 patients with stage 3-5 chronic renal illness were admitted to private clinics, Azadi Teaching Hospital, and Al-Jamhorri General Hospital over a two-year period. There were forty-six women and fifty-four men. There was a comparable control group selected for comparison. Peripheral venous blood was drawn in five milliliters per usual procedure. A test tube was filled with 2.0 ml of blood, dried EDTA for a complete blood count, and a Hematology Cell Counter (SysmexKX21) for a hematological study.

Results: The hematological parameters and individuals with chronic renal failure were significantly correlated. At a p-value of 0.000, the study's results showed that the VLDL and triglyceride levels were highly statistically significant between the control and study groups, and that 44% of the male patients were between the ages of 40 and 59 and 60 and 79, respectively.

Keywords: Pathophysiology, renal failure, lipid, hematological parameters

Introduction:

It is estimated that up to 50% of the population suffers from chronic kidney disease (CKD), which affects the elderly, individuals with communicable diseases (CDs) such as HIV/AIDS, and those with non-communicable diseases (NCDs) including hypertension and type 2 diabetes mellitus (T2D). [1,2] This condition is associated with numerous metabolic abnormalities [4], a significant and prolonged decline in glomerular filtration rate [3], as well as various clinical signs and symptoms, such as altered sexual function, neurological disorders, skin disorders, osteodystrophy, and digestive problems, as well as hematologic abnormalities and cardiovascular issues [5, 6, 7], are all characteristics of chronic renal failure. The most frequent cause of anemia is hematological, especially when it impacts indices of red blood cells (RBCs). Anemia, the most prevalent, severe, and long-lasting of the several

hematological illnesses, has been found to be more prevalent in Black Africans. [8].

Although anemia can occur at any stage of the disease, it worsens as it progresses and is present in nearly all patients with end-stage kidney disease (CKD stage 5). [9]. Anemia in CKD is primarily caused by the kidneys' inability to produce adequate endogenous erythropoietin, in addition to the decline in GFR. [11, 10]

A patient's quality of life is negatively impacted by untreated anemia in chronic kidney disease (CKD), which also raises their risk of cardiovascular and all-cause death and increases morbidity [9]. Because untreated anemia causes tissue hypoxia and changes renal hemodynamics, it may hasten the deterioration of renal function [12,13].

All existing guidelines have included patients with chronic kidney disease (CKD) among those at high or very high risk, based on GFR values. This is because multiple studies have demonstrated that cardiovascular (CV) mortality increases as GFR decreases [14,15].
Even though the kidney doesn't directly regulate lipoprotein metabolism, end-stage renal disease (ESRD) is frequently associated with high rates of cardiovascular morbidity and death. Rapid atherosclerotic lesions and the progression of renal illness are both significantly impacted by this metabolic shift, which is typified by both quantitative and qualitative changes in lipoproteins [16,17].

This metabolic shift, which is marked by alterations in lipoproteins both quantitatively and qualitatively, has a significant effect on the rapid development of atherosclerotic lesions and most likely the course of renal disease. Hypertriglyceridemia is frequently caused by elevated triglyceride-rich lipoproteins (TRL), which include VLDL, chylomicrons, and their remnants, in people with chronic kidney disease (CKD) [18,19] [20–22]. TRL is broken down less peripherally and produced more hepatically, which results in hypertriglyceridemia [23–25].

Dyslipidemia, a disorder commonly associated with chronic kidney disease (CKD), is characterized by low HDL cholesterol levels and elevated triglycerides. While increased triglycerides and cholesterol are linked to proteinuria, LDL cholesterol (and thus total cholesterol) levels are often not affected. This is due to delayed breakdown of triglyceride-rich lipoproteins without changes in their production rate, leading to downregulation of LDL receptors and lipoprotein lipase, as well as increased triglyceride levels (9).

CKD is also associated with decreased hepatic expression of apolipoprotein A-I (apo A-I) and an increased ratio of apo B to apo A-I (10). Elevated activity of cholesteryl ester transfer protein (CETP) and decreased activity of lecithin-cholesterol acyltransferase (LCAT) contribute to reduced HDL cholesterol levels. Additionally, CKD is linked to lowered HDL cholesterol and diminished anti-inflammatory and antioxidant functions [26, 27]. As CKD progresses, dyslipidemia tends to worsen. Data from the National Health and Nutrition Examination Survey (NHANES) between 2001 and 2010 showed that the use of lipid-lowering medications increased from 18.1% in stage 1 CKD to 44.7% in stage 4 CKD, while the prevalence of dyslipidemia rose from 45.5% in stage 1 to 67.8% in stage 4 CKD [28].
However, only 15% of the 317 peritoneal dialysis patients and 20% of the over 1000 hemodialysis patients in the study had "normal" lipid levels (defined as triglycerides < 150, HDL > 40, and LDL<130 mg/dl).
82% of people with stage 5 CKD had dyslipidemia, according to a larger study that evaluated the issue in over 21,000 incident dialysis patients. The study suggested a threshold of non-HDL cholesterol > 100 mg/dl (2.6 mmol/L) to identify dyslipidemia in these patients [29]. The study aims to assess the main pathophysiological changes in individuals with chronic renal failure.

Material and Methods: -

The study was cross-sectional and involved 100 patients with chronic renal disease in stages three to five.
How much time was spent studying?
The study was conducted over the course of the last two years, from the beginning of July 2019 to the end of July 2021, in the labs of the Kirkuk General Hospital, the Azadi Teaching Hospital, and private clinics in order to find biochemical and hematological indicators. Each and every

patient who reports having chronic renal failure is given serious medical review. after laboratory testing, for precise analysis. The sampling methodology and sample collection procedure: One hundred patients with chronic renal failure were asked to provide a 5 ml peripheral venous blood sample, following standard procedure. The following characteristics were assessed using the Hematology Cell Counter (SysmexKX21): platelets, hemoglobin, packed cell volume, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, white blood cells, red blood cells, lymphocytes, and granulocytes. A full blood count was performed using two milliliters of blood in a test tube with dried EDTA. A test tube was filled with three milliliters of blood serum for lipid profile and chemical analysis. For further analysis, a certified laboratory technician in a hospital collects samples and analyzes them for triglycerides, cholesterol, HLD, LDL, and VLDL [26].

Data analysis:

The statistical analysis of the gathered data was done using SPSS v.21. If the P-value for the chi-square test was less than 0.05, the relationship between the variables was deemed significant. The frequency level was quantified through the use of numbers and percentages. Concerns were raised about the project's ethical status because Kirkuk Medical College and Kirkuk Health Directory approved it before it started.

The inclusion criteria were met by all patients admitted to the nephrology unit of the aforementioned institutions during the study period; however, pregnant and lactating women, as well as any chronic cases with a history of diabetes mellitus, hypertension, or other conditions, were excluded.

Results:

Table 1 displays the four age groups that were formed from the 100 patients with chronic renal failure who were admitted to Azadi Teaching Hospital. Forty-six women and fifty-four men were present. Table 1 shows a comparison of 44.4% of male patients and 47.8% of female patients in the 60–79 and 40–59 age groups (p-values of 0.177 and 0.811, respectively), As in table 1:

Tabel (1) distribution of study sample according to age and gender

Age group	Total patients 100				Total		P. value
	Male patients		Female patients				
	No.	%	No.	%	No.	%	
20-39	0	0.0%	4	8.7%	4	4%	0.133
40-59	24	44.4%	12	26.0%	36	36%	0.177
60-79	24	44.4%	22	47.8%	46	46%	0.811
80-99	6	11.2%	8	17.4%	14	14%	0.559
Total	54	100%	46	100%	100	100%	

All of the hematological indicators between males and females are statistically significantly correlated (p value 0.00) in Table 2, with the exception of MCH, which does not exhibit any significant link (p value 0.0423). Boys' and girls' triglyceride levels are statistically significantly correlated (p. value = 0.000), as Table 3 demonstrates. Additionally, a statistically significant correlation (p. value = 0.00) exists between VLDL and gender. For both men and women, however, there is a weak statistical correlation between HDL and LDL (p. values 0.011 and 0.006, respectively), as its clarified in table 2:

Table (2) Hematological parameters between male and female patients

Hematological parameters	Male patients		Female patients		p- value
WBC	Normal	48	Normal	47	0.00
	Abnormal	2	Abnormal	3	0.00
Lymphocyte %	Normal	50	Normal	48	0.00
	Abnormal	0	Abnormal	2	0.00

Granulocyte %	**Normal**	**45**	**Normal**	**49**	**0.00**
	Abnormal	**5**	**Abnormal**	**1**	**0.00**
RBC	**Normal**	**46**	**Normal**	**48**	**0.00**
	Abnormal	**4**	**Abnormal**	**2**	**0.00**
Hb	**Normal**	**50**	**Normal**	**35**	**0.00**
	Abnormal	**0**	**Abnormal**	**15**	**0.00**
PCV	**Normal**	**50**	**Normal**	**47**	**0.00**
	Abnormal	**0**	**Abnormal**	**3**	**0.00**
MCV	**Normal**	**44**	**Normal**	**42**	**0.00**
	Abnormal	**6**	**Abnormal**	**8**	**0.00**
MCH	**Normal**	**37**	**Normal**	**27**	**0.423**
	Abnormal	**13**	**Abnormal**	**23**	**0.00**
MCHC	**Normal**	**39**	**Normal**	**38**	**0.00**
	Abnormal	**11**	**Abnormal**	**12**	**0.00**
Platelate	**Normal**	**46**	**Normal**	**49**	**0.00**
	Abnormal	**4**	**Abnormal**	**1**	**0.00**

Male and female VLDL levels had a larger statistically significant link (p. value = 0.00) than female triglyceride levels (p. value = 0.000), as seen in Table 3. But there is a statistically significant difference between the LDL and HDL levels in males and females (p. value 0.011, 0.006), as its shown in table 3:

Table (3) Biochemical test between patients and controls

Biochemical parameters	Patients		Control		P. Value
Cholesterol Mg/dl	**40**	**Normal**	**43**	**Normal**	**0.424**
	10	**Abnormal**	**7**	**Abnormal**	
Triglyceride	**40**	**Normal**	**37**	**Normal**	**0.000**
	10	**Abnormal**	**13**	**Abnormal**	
HDL	**45**	**Normal**	**34**	**Normal**	**0.006**
	5	**Abnormal**	**16**	**Abnormal**	
LDL	**50**	**Normal**	**44**	**Normal**	**0.011**
	0	**Abnormal**	**6**	**Abnormal**	
VLDL	**7**	**Normal**	**35**	**Normal**	**0.000**
	43	**Abnormal**	**15**	**Abnormal**	

Discussion:

The ages of the males and girls differed statistically significantly, as seen in Table 1. 100 consecutive pre-dialysis CKD patients who were followed up with for two years, a total of 100 age- and sex-matched control volunteers, along with patients, were included in a case-control study conducted by Oluseyi et al. [27]. The study revealed that the male-to-female ratio was 1.7:1, and the mean ages of the CKD patients and control individuals were 46.98 ± 16.81 years and 47.57 ± 15.97 years, respectively. Renal

mass declines by about 10% every ten years between the ages of 30 and 80, which explains this. Moreover, renal cortical thickness declines by 10% for each decade of age, indicating a decline in the number of functioning nephrons.

Healthy aging, however, does not significantly alter single-nephron GFR or glomerular volume [28]. In a different study, Xu Lengnan et al. looked at how aging affected the renal function of a healthy Beijing community [29]. According to their evaluation of several glomerular filtration rate estimation equations, people's renal function remained largely constant as they aged, despite the fact that different eGFR models yielded data that differed among various subject populations. After age 40, GFR decreases in a similar manner, and renal blood flow decreases by 10% every ten years.

These days, nephrology clinics frequently see senior citizens. There are three factors that make this epidemiological finding significant. Firstly, a nephrologist is the main care physician for a patient who has a clear chronic renal disease but does not require dialysis. These days, nephrology clinics frequently see senior citizens. There are three factors that make this epidemiological finding significant. Firstly, a nephrologist is the main care physician for a patient who has a clear chronic renal disease but does not require dialysis. In the past decade, the number of elderly individuals sent to nephrologists has significantly increased. Third, patients who were referred to a nephrology global follow-up had more advanced renal illness and higher burdens of CVD comorbidities [30].

In a similar study, Liying et al. examined the connection between blood lipid levels and lipid ratios and Chronic Kidney Disease (CKD) in a Chinese population. in China through the use of a cross-sectional survey to collect data. Using multivariable logistic regressions and multivariate regression models, the results demonstrated that the lipid profile was statistically substantially linked to chronic kidney disease (CKD) in males but not to any of the serum lipids or lipid ratios in women. The only accurate measure of CKD in men, they found, is serum TG. However, women's chronic kidney disease cannot be predicted by lipid ratios or serum lipid levels alone. 33.

The impact of hemodialysis on the lipid profiles of patients with chronic renal failure was examined in a different study by Lokesh et al. Thirty CRF patients who had never had hemodialysis were in Group I, thirty healthy controls were in Group II, and thirty CRF patients were in Group III. They found that, in comparison to controls, group II and group III had considerably lower HDL values, significantly higher blood triglyceride and VLDL levels, and no significant change in LDL and total cholesterol levels. They hypothesized that this dyslipidemia pattern was present in both CRF patients with and without hemodialysis [32].

In their investigation of biochemical changes in patients with chronic kidney failure, focusing on complete blood count and anemia, Muhammad Naeem et al. found that while the mean corpuscular hemoglobin (MCH) was within the reference range (27–33 pg), the mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) values were below their respective reference ranges (80–90 fl and 33.3–35.5 g/dl) [31]. Patients with severe chronic renal disease often experience an inflammatory state characterized by increased cytokine production, oxidative stress, vitamin D deficiency, malnutrition, and heightened susceptibility to infections.

Inflammation exacerbates arterial calcification, atherosclerosis, sarcopenia, anemia, and the progression of chronic kidney disease. Instead of just one of these adverse situations, it seems that several of them affect hematological markers like RDW and MPV. Red blood cell (RBC) and hemoglobin (Hb) levels dropped, per a study by Md. Ashrafur et al. Similar findings were seen in our investigation, which revealed substantial differences in all hematological parameters except MCH [35]. Routine hematological markers have been connected in recent studies to poor clinical outcomes in patients with chronic renal illness. Regardless of whether these interactions are generally linked to residual renal function, chronic inflammation, or renal anemia, a recent study

attempts to uncover and ascertain the cause of these interactions.

A recent study of patients with advanced chronic kidney disease (CKD) discovered that a high RDW was linked to several clinical features, including anemia, elevated CRP levels, diabetes mellitus, cardiovascular disease, comorbidity score, decreased renal function, advanced age, and male gender. After correcting for a number of covariates, the regression model indicated that higher RDW levels would more accurately reflect the inflammatory condition, anemia, and comorbidity burden of CKD patients. Conversely, patients with low MPV and CKD had lower renal function and higher platelet counts. Low MPV and low eGFR were still associated even after a number of variables were taken into account. Chronic kidney disease (CKD) patients with advanced stages may be one reason of this. Moreover, there were associations between MPV and CRP and albumin levels [37]. Individuals with chronic inflammation, high comorbidity burden, and end-stage renal disease (ESRD) may have low MPV readings rather than normal or high ones. Abdullah et al. conducted a second study in Kirkuk City to investigate the relationship between serum magnesium and Helicobacter pylori-specific IgG antibodies and serum lipid profiles [38].

In order to determine whether hemodialysis had any effect on the lipid profiles of CRF patients getting dialysis vs those not, a similar study was conducted in Kirkuk City. comprise 30 patients with chronic renal failure and 15 individuals who appear to be in good condition. Triglycerides, HDL-C, LDL-C, VLDL-C, and blood total cholesterol were all measured enzymatically.

Although most of the data fell within the normal ranges, there was a significant difference in all values between hemodialysis and non-dialysis patients, except for LDL, which was over the range. Individuals with chronic kidney disease (CKD), particularly those who continue hemodialysis, will benefit from these improved outcomes. [39].

Conclusions:

The triglyceride and VLDL levels of men and women are statistically significantly correlated. Males and females have a weak statistical correlation between HDL and LDL.

3. All hematological indicators display a substantial statistical association between males and females, with the exception of MCH. Male participants in the study were mostly between the ages of 40 and 59 and 60 and 79.

Recommendation:

Further research might be conducted on a bigger population to ascertain the relationship between the hameatological markers and the incidence of renal failure. Advanced diagnostic methods can be used to determine chronic renal failure. In a randomized controlled trial, increasing the sample size can improve outcomes and reduce biases. In order to determine the types and causes of anemia in CKD, further hematological abnormalities associated with the severity of CKD might be examined. Other indicators, such as vitamin B12 and iron, may be investigated to ascertain their correlation with the incidence of chronic failure.

References:

1. Lozano R, Naghavi M, Foreman K, *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010.*Lancet* 2012;380:2095–128. **doi: 10.1016/S0140-6736(12)61728-0.**

2. Eckardt KU, Coresh J, Devuyst O, *et al*. Evolving importance of kidney disease: from subspecialty to global health burden. *Lancet* 2013;382:158–69. **doi.org/10.1016/S0140-6736(13)60439-0**

3-Dewardener, H.E. An outline of normal and abnormal function. In: The kidney 4th edition Churchill Livingstone New York.1986; 181-235. DOI: https://doi.org/10.18203/2320-6012.ijrms20162251

4- Mathenge R.N, Mcligego, S.O., Mutua, A.K. and Otieno, L.S The spectrum of echocardiographic finding in chronic renal failure. E. A. M. J.2003;70(3): 97-103.

5-Moronkola O.A, Ojediran M.M,and Amosu A. Menstrual disorder in chronic renal failure patients attending renal clinics in Ibadan, Nigeria. AH Sci. 2006; 6 (3): 155-160. DOI: 10.33545/gynae.2020.v4.i2f.549

6. Webster AC, Nagler EV, Morton RL, Masson P: Chronic kidney disease . Lancet. 2016, 389:1238-52.10.1016/S0140-6736(16)32064-5.

7-Wickramasinghe MP, Perera DM, Kahandawaarachchi KA: Dietary prediction for patients with chronic kidney disease (CKD) by considering blood potassium level using machine learning algorithms. ILSC. 2018, 300-3. **DOI: 10.1109/LSC.2017.8268202**

8. Astor BC, Muntner P, Levin A, et al. Association of kidney function with anemia: the third national health and nutrition examination survey (1988-1994). A I M. 2002;162:1401–8. DOI: 10.1001/archinte.162.12.1401

9. Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc. N. 2012;23:1631–4. **DOI: 10.1681/ASN.2011111078**

10. Kazmi WH, Kausz AT, Khan S, et al. Anemia: an early complication of chronic renal insufficiency. Am J K D. 2001;38:803–12. DOI: 10.1053/ajkd.2001.27699

11. Kutuby F, Wang S, Desai C, et al. Anemia of chronic kidney disease. Dis Mon 2015;61:421–4. https://doi.org/10.3389/fmed.2021.642296

12. Webster AC, Nagler EV, Morton RL, et al. Chronic kidney disease. Lancet 2017;389:1238–52. https://doi.org/10.1016/S0140-6736(16)32064-5

13. Go, A.S.; Chertow, G.M.; Fan, D.; McCulloch, C.E.; Hsu, C.Y. Chronic kidney disease and the risks of death, cardiovas-cular events, and hospitalization. New Engl. J. Med. **2004**, 351, 1296–1305. DOI: 10.1056/NEJMoa041031

14. Gansevoort, R.T.; Correa-Rotter, R.; Hemmelgarn, B.R.; Jafar, T.H.; Heerspink, H.J.L.; Mann, J.F.; Matsushita, K.;Wen, C.P. Chronic kidney disease and cardiovascular risk: Epidemiology, mechanisms, and prevention. Lancet 2013, 382, 339–352. https://doi.org/10.1161/CIRCULATIONAHA.120.050686

15. Verdoia M,Barbieri L,Schaffer A,Bellomo G,Marino P,De Luca G; Novara Atherosclerosis Study (NAS) group. Impact of renal function on mean platelet volume and its relationship with coronary artery disease: A single-centre cohort study. *Thromb Res*. 2016;141:139-44. DOI: 10.1016/j.thromres.2016.03.018

16- Abraham G, Moorthy AV, Aggarwal V: Chronic kidney disease: a silent epidemic in Indian subcontinent-strategies for management. J Indian Med Assoc. 2006, 104:689-91. PMID: 17474287

17. Speer, T.; Zewinger, S.; Fliser, D. Uraemic dyslipidaemia revisited: Role of high-density lipoprotein. N. Dial. T. 2013, 28, 2456–2463. DOI: 10.1093/ndt/gft080

18. Vaziri, N.D. Dyslipidemia of chronic renal failure: The nature, mechanisms, and potential consequences. Am. J. P. P. 2006, 290, F262–F272. DOI: 10.1152/ajprenal.00099.2005

19.Quaschning,T.;Krane,V.;Metzger,T.;Wanner, C.Abnormalities in uremicl ipoprotein metabolism and its impact on cardiovascular disease. Am. J. K. D. 2001, 38, S14–S19. DOI: 10.1053/ajkd.2001.27384

20. Wanner, C.; Quaschning, T. Dyslipidemia and renal disease: Pathogenesis and clinical consequences. C.O.N.H. 2001, 10, 195–201. DOI: 10.1097/00041552-200103000-00007

21. Mesquita, J.; Varela, A.; Medina, J.L. Dyslipidemia in renal disease: Causes, consequences and treatment. E.N.J. 2010, 57, 440–448. DOI: 10.1097/00041552-200103000-00007

22. Barbagallo, C.M.; Averna, M.R.; Sparacino, V.; Galione, A.; Caputo, F.; Scafidi, V.; Amato, S.; Mancino, C.; Cefalù, A.B.; Notarbartolo, A. Lipoprotein (a) levels in end-stage renal failure and renal transplantation. Nephron 1993, 64, 560–564. DOI: 10.1159/000187400

23. Vaziri, N.D.; Moradi, H. Mechanisms of dyslipidemia of chronic renal failure. Hemodial. Int. 2006, 10, 1–7. DOI: 10.1111/j.1542-4758.2006.01168.x

24. Lacquaniti, A.; Bolignano, D.; Donato, V.; Bono, C.; Fazio, M.R.; Buemi, M. Alterations of Lipid Metabolism in Chronic Nephropathies: Mechanisms, Diagnosis and Treatment. Kidney Blood Press. Res. 2010, 33, 100–110. DOI: 10.1159/000302712

25. Chan,M.K.; Persaud,J.; Varghese,Z.; Moorhead,J.F. Pathogenicrolesofpost-heparin lipases in lipid abnormalities in hemo dialysis patients. Kidney Int. 1984, 25, 812–818. DOI: 10.1038/ki.1984.94

26. Muhammad Naeem, Arsalan Ashraf, Hafiz Muhammad Zeshan Safdar, Mahnoor Qayyum

Khan, Shuja Ur Rehman, Rimsha Iqba, Mohsin Raza, Jabir Ali, Ghafoor Ahmad. Biochemical Changes in Patients with Chronic kidney Failure In Relation to Complete Blood Count and Anemia. 2020.IJB,Vol. 16, No. 1, p. 267-271 DOI: 10.12692/ijb/16.1.267-271

27. Oluseyi A. Adejumo, Enajite I. Okaka2 and Louis I. Ojogwu. Lipid profile in pre-dialysis chronic kidney disease patients in southern Nigeria. GMJ. 2016. DOI.104314/gmj.v.50i1.

28- Yu-Hsiang Chou, Yung-Ming Chen, aging and Renal Disease: Old Questions for New Challenges, aging Dis. 2021 Apr; 12(2): 515–528. doi: 10.14336/AD.2020.0703

29- Xu -Lengnan, Chen Aiqun, Sun Ying, Li Chuanbao, and Mao Yonghui, The effects of aging on the renal function of a healthy population in Beijing and an evaluation of a range of estimation equations for glomerular filtration rate, aging (Albany NY). 2021 Mar 15; 13(5): 6904–6917. doi: 10.18632/aging.202548

30- Kazuyoshi Okada; Mitsuru Yanai; Susumu Takahashi, Aging and Chronic Kidney Disease , *Kidney Blood Press Res* (2014) 38 (1): 109–120. DOI: 10.1159/000355760

31. Liying Zhang, Zhiyong Yuan, Wu Chen, Shanying Chen, Xinyu Liu, Yan Liang, Xiaofei Shao and Hequn Zou. Serum Lipid Profiles, Lipid Ratios and Chronic Kidney Disease in a Chinese Population. Int. J. E. R. P. H. 2014,11,7622-7635. DOI: 10.3390/ijerph110807622

32. Dr. Lokesh Rao Magar.S1 , Dr.Anwar Miya Mohammad 2 , Dr. Sandhya Anil.S 3. A Study of Lipid Profile in Chronic Renal Failure Patients Undergoing Hemodialysis. IOSR .Volume 15, June. 2016), PP 01-03 DOI: 10.5958/2395-1184.2015.00025.X

33. Muhammad Naeem, Arsalan Ashraf, Hafiz Muhammad Zeshan Safdar, Mahnoor Qayyum Khan, Shuja Ur Rehman, Rimsha Iqba, Mohsin Raza, Jabir Ali, Ghafoor Ahmad. Biochemical Changes in Patients with Chronic kidney Failure In Relation to Complete Blood Count and Anemia. 2020.IJB,Vol. 16, No. 1, p. 267-271 DOI: 10.12692/ijb/16.1.267-271

34-. Lu YA,Fan PC,Lee CC,Wu VCC,Tian YC,Yang CW,et al.. Red cell distribution width associated with adverse cardiovascular outcomes in patients with chronic kidney disease. *BMC Nephrol*. 2017;18:361. DOI: 10.1186/s12882-017-0766-4

35-.Md. Ashrafur Rahman 1, Yeasna Shanjana 2, Md.Shakil Ahmed3. Hematological Abnormalities and comorbidities are Association with the severity of kidney Disease: A hospital- based Cross- sectional study in Bangaladesh. Pathol. 2022. DOI: 10.1177/2632010X221114807

36. Chu SG,Becker RC,Berger PB,Bhatt DL,Eikelboom JW,Konkle B,et al.. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost*. 2010;8:148-56. DOI: 10.1111/j.1538-7836.2009.03584.x

37- Mach, F.; Baigent, C.; Catapano, A.L.; Koskinas, K.C.; Casula, M.; Badimon, L.; Chapman, M.J.; De Backer, G.G.; Delgado, V.; Ference, B.A. Guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). Eur. Heart J. **2020**, 41, 111–188. DOI: 10.1093/eurheartj/ehz455

38 - Raoof A Abdullah , Nooruldeen MY, Shamoon MS, Relationship of Helicobacter Pylori Specific IgG Antibodies with Serum Magenisum and Serum Lipid Profile in Patients on Maintenance Hemodialysis, Kirkuk journal of medical sciences, 2015; 3(1): 48-55. DOI :10.32894/kjms.2021.169517

39- Jasim AY, AZEEZ FS, Qaism RY, Saad AM, Lipid profil in non dialysis and haemodiaylsis chronic renal failure patients in kirkuk city , Biochemical and Cellular Archives , 2019 : 19(1):1653-1656 DOI: 10.35124/bca.2019.19.1.1653