Post-Kidney Transplant Proteinuria in Tripoli Central Hospital

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Abstract

Proteinuria is defined as urinary protein excretion exceeding 150 mg/day. The onset of proteinuria exceeding the normal level is a bad prognostic factor and a negative indicator of kidney function, either in native kidneys or in kidney transplanted patients.

The aim of this study is not only to determine the proportion of protein in the urine of patients with kidney transplantation but also to

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review the different methodologies available for assessing proteinuria and albuminuria. The method by which this is done should be tempered by practical considerations such as ease of use, patient acceptability, efficiency and cost.

*In this research work has been extensive study on the assessment of proteinuria in the population of renal transplant using a sample of **127** (recipient patients). Were Samples collected for this work in random urine samples were tested with Dipstick, and then they were classified according to sensitivity to dipstick. (As Positive or negative the sensitivity of protein).*

The results of the study showed that the prevalence of post-kidney transplant proteinuria is high in our patients, where it found that about 60 recipient patients (47.2%) were positive for proteinuria, which necessitates further evaluation and (67) recipient patients (58.8 %) were negative for proteinuria who do not need any further investigation. Using chi-square, a significant relationship between diabetes mellitus and proteinuria was found, with a correlation of (R = -0.483) P-value (0.000).

***Keywords**: proteinuria, albuminuria, transplant, kidney function.*

الخلاصة

يعرف البروتين (الزلال) في البول على أنه فقد أكثر من 150 مليجرام من الزلال يومياً.

إن ظهور الزلال في البول متجاوزاً المستوى الطبيعي يعتبر عامل إنذاري سيئ ومؤشر سلبي لوظيفة الكلى، سواء في الكلى السليمة أو في مرضى زارع الكلى.

أن الهدف من هذه الدراسة ليس فقط معرفة نسبة الزلال في البول لمرضى زارعي الكلى وإنما أيضا مراجعة الطرق المختلفة لتقييم تواجد نسبة الزلال في البول وهذه الطرق التي يمكن استعمالها يجب موازنتها باعتبارات عملية مثل سهولة الاستعمال وتقبل المريض لها وكفاءتها وتكاليفها.

هذا العمل البحثي عبارة عن دراسة مكثفة حول تقييم وجود الزلال في البول لمرضى زراعة الكلى باستخدام عينة من 127 (مريضًا). تم جمع العينات لهذا العمل في عينات بول عشوائية واختبرت هذه العينات بواسطة شرائط التحاليل (Dipstick) ثم تم تصنيفها طبقا لحساسية هذا الاختبار (إيجابية وسلبية لحساسية البروتين).

استنتجنا من دراستنا هذه بأن وجود الزلال في البول ما بعد زراعة الكلى كانت عالية عند هؤلاء المرضى حيث وجدنا أن 60 مريض وبنسبة 47.2% مصابون بهذا المرض ويحتاجوا إلى مزيد من التقييم. و 67 مريض وبنسبة 8. 58% كانت نتائجهم خالية من هذا المرض ولا يحتاجوا إلى مزيد من الفحوصات. لاحظنا في دراستنا هذه وجود علاقة ذات أهمية بين المتغيرين المرض السكرى الزلال في البول وكان معامل الارتباط يساوى (0.483-) وهذا يثبت وجود علاقة طردية بين المتغيرين وكانت قيمة P- value تساوى (0.000).

Introduction

The kidneys represent the primary organs of Homeostasis in the regulation of both volume and composition of body fluids and the excretion of metabolic waste products in urine (1). Continual function of the kidney is essential to good health playing active roles in urine formation. Under normal physiological state urine is expected to be protein free (2). The production of protein free urine is exclusively carried out by the kidney nephrons. Nephrons are structured to perform an important role of filtration and Reabsorption. Therefore, defective or diseased kidney is associated with defective reabsorption mechanisms and an indication of injured nephrons (3).

Renal transplantation is an established method of renal replacement therapy in patients with end-stage renal failure (4). Despite the improvement achieved in the overall patient and graft survival rates following renal transplantation, some medical problems related to the

grafts such as proteinuria are encountered (5). The appearance of proteins in urine (proteinuria) is a bad prognostic factor and a negative indicator of kidney function, either in native kidneys or in kidney transplanted patients and if not detected and treated early it may lead to loss of the transplanted kidney. The assessment of proteinuria is clinically and diagnostically an important index in renal function generally and particularly that of nephrons (6).

Persistent proteinuria is usually defined as protein excretion of 0.5 to 1.0 g/24 hours for at least three to six months (7). Persistent proteinuria can be the first sign of kidney disease. Persistent proteinuria commonly results from disorders associated with increased glomerular permeability such as nephritic syndrome, glomerulonephritis (e.g., post-infectious, membranous, membrane proliferative, lupus, IgA) and genetic defects (Alport syndrome, mesangial sclerosis). Glomerular proteinuria is an early sign of kidney disease and may also play a role in the progression of glomerular damage (8, 9).

Proteinuria is associated with an increased death risk in patients with diabetes mellitus or hypertension and even in the general population. Many studies are indicated the dysfunction of the renal allograft and immunosuppressive therapy are usually added to the common risk factors such as virus infection, rejection, diabetes mellitus or drugs, hypertension, and other forms of kidney diseases (10, 11). Proteinuria is also associated with cardiovascular disease. Damaged blood vessels may lead to heart failure or stroke as well as kidney failure (12).

Proteinuria is often measured using a dipstick assay. In this assay, a reagent reacts with albumin producing a color change. Of note, the dipstick test for proteinuria suffers from both false positive errors. False negative tests are often seen in dilute urine (specific gravity <1.005), and

when a protein other than albumin is present in the urine. False positives can be seen in a concentrated urine, a basic urine (pH >8), and a urine contaminated by gross Hematuria or by antiseptic agents (chlorhexidine or benzalkonium chloride) (13).

Methods

All samples were tested with Dipstick. And then they were classified according sensitivity to dipstick. (As Positive or negative the sensitivity of protein). The first groups with a positive dipstick test for protein, these Samples were tested for protein/creatinine ratio (p/c ratio) by machines spectrophotometer type Screen plus. While, the second groups with Negative dipstick test for protein, these samples were tested for Microalbuminuria (MAU) by machines Nycocard.

Dipstick Testing

The dipstick method for detection of proteinuria relies on color change of the indicator dye reaction primarily dependent on the amount of albumin in the urine. A testing dipstick is usually made of paper or cardboard and is impregnated with reagents that indicate some feature of the liquid by changing color. A semi-quantitative test such as a dipstick urine protein is used to screen the generally population for the presence of protein in the random urine sample as part of a routine urinalysis (14)**.** The squares on the dipstick represent the following components in the urine Figure (**1**)**:**

Figure (1) Urine screening tape, protein in urine (albumin) [15]

Proteinuria was measured using a dipstick assay. Reagent reacts with albumin producing a color modify. The dipstick is scale: negative, trace (10-20 mg/dL), 1+ (30 mg/dL), 2+ (100mg/dL), 3+ (300 mg/dL), 4+ (1000-2000 mg/dL). Of note, the dipstick test for proteinuria suffers from both false positive errors. False negative tests are often seen in dilute urine (specific gravity <1.005), and when a protein other than albumin is present in the urine. False positives can be seen in a concentrated urine, a basic urine (pH >8), and a urine contaminated by gross Hematuria or by antiseptic agents (chlorhexidine or benzalkonium chloride).

Spectrophotometer

The urine samples which were positive by the dipstick will be further subjected to measurement of Urinary albumin/ urinary creatinine ratio by Spectrophotometer method. The spectrophotometer is an instrument which measures the amount of light of a specified Wavelength which passes through a medium. According to Beer's law, the amount of light Absorbed by a medium is proportional to the concentration of the absorbing material.

The Clinical Chemistry photometer Screen Plus is an instrument that can be easily placed in any type of clinical laboratory. It affects readings of end point, kinetic, fixed time and differential reaction, in absorbance and concentration, storage of 199 methods with possibility of programming each method with type of reaction, wavelength, working temperature, reading unit, normal values, incubation time and reading intervals (16).

Nycocard

The samples which were negative by dipsticks will be considered for more sensitive urine testing by Measuring the Microalbuminuria

directly Nyco card machine. The Reader pen contains three pairs of Light Emitting Diodes (LED, s) red green and blue. Reflected light from the test sample is measured, relative to a white sample, by a light sensitive Photodiode circuit.

Nycocard was introduced to the market in the early 1990's starting with the non-instrumental Nycocard CRP card-test, followed shortly thereafter by the Nycocard D-Dimer. HbA1c and U-Albumin concluded the range of planned Nycocard tests for the Point of Care market. During these years the Nycocard Reader was also introduced, satisfying requirements for the automatic reading of Nycocard tests (17, 18)

Specimens

Samples random urine to reveal the main causes of post-transplant proteinuria. Informed consent and ethical approval references for all samples were obtained through National kidney transplantation Tripoli Central Hospital (NKTTC, 127/KT). This study was similar with various previous studies include 127 recipient patients from period August 2018 and October 2021.

Sample preparation of dipstick technique

The procedure must be followed exactly to achieve reliable results, Dip the strip into the urine up to the test area for no more than two second. Draw the edge of the strip along the brim of the vessel to remove excess urine; at this time, didn’t make the test areas touched to the brim of the vessel. After the proper time compared the test results carefully with the color chart on the vial label under good light. While comparing, keep the strip horizontally to prevent possible mixing of chemicals when excessive urine is present.

Sample preparation of protein

1ml of working reagent were added into three Cuvette- Blank, Standard, and Sample. 20 µl demineralised water was added into Cuvette Blank, 20 µl standards was also added into Cuvette standard. Finally, add 20 µl specimens (urine) into Cuvette sample. Mix well. Let stand at least for 10 minutes at room temperature. Read absorbance at 600 nm (578-612) against reagent blank.

Sample preparation of creatinine

1ml working reagent (Mix proportionally 1:1 the reagent R1 and R2) was added into three Cuvette- Blank, Standard, and Sample. 100 µl standards was added into Cuvette standard, Then 100 µl of specimen (urine diluted 1/10) was added into Cuvette Sample. Mix well. Let stand at least for 30 sec. Read absorbance at 492 nm (490-510) against reagent blank.

Sample preparation of Microalbuminuria

50µl of urine sample or C/Control to test tube was added with R1 (Dilution liquid), Mixed well, and then 50 µl diluted urine was added to a TD (Test Device). Allowed the diluted sample to soak completely into the membrane (approximately 50 sec). Additionally, 50µl of R2/Conjugated to test device, allowed the conjugate to soak completely into the membrane (approximately 50 sec). Immediately 50µl of R3/ washing solution was added to test device. Allowed the washing solution to soak completely into the membrane (approximately 50 sec).The result within 5 minutes using the Nycocard system.

Statistical Analysis

The laboratory results were confronted with the results of the proteinuria by using correlation coefficient (chi-square correlation). SPSS statistical software was used to calculate chi-square correlation, P value considered statistically significant if < 0.05 level.

Results

Gender distribution

The records included in the study **127** patient's renal transplants were performed between August 2018 and October 2021. There were 82 patient's male (64.6 %), and 45 patients female (35.4%). See Figure (2).

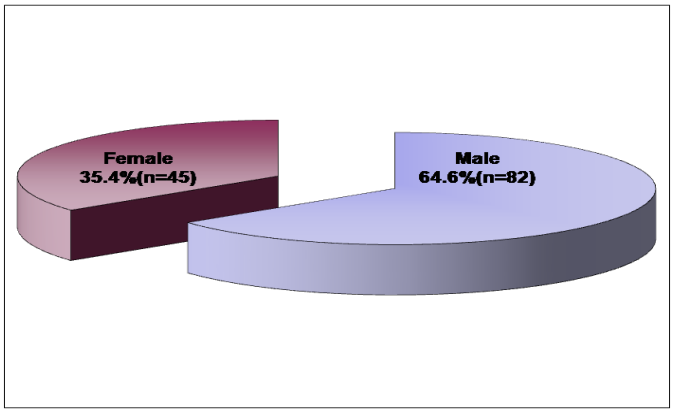


Figure (2) : Gender distribution

Patients age groups

The studied sample was divided to eight groups according to age of patients. See Figure (3) which is: Group one (7-14 years) contains 2.4% of the total sample. Group two (15-22 years) contains 8.7% of the total sample. Group three (23-30 years) contains 19.7% of the total sample. Group four (31-38 years) contains 23.6% of the total sample. Group five (39-46 years) contains 17.3% of the total sample. Group six (47-54 years)

contains 13.4% of the total sample. Group seven (55-62 years) contains 12.6% of the total sample. Group eight (63-70 years) contains 2.4% of the total sample. It was found that 23.6% of patients with proteinuria are aged between 31 years to 38 years.

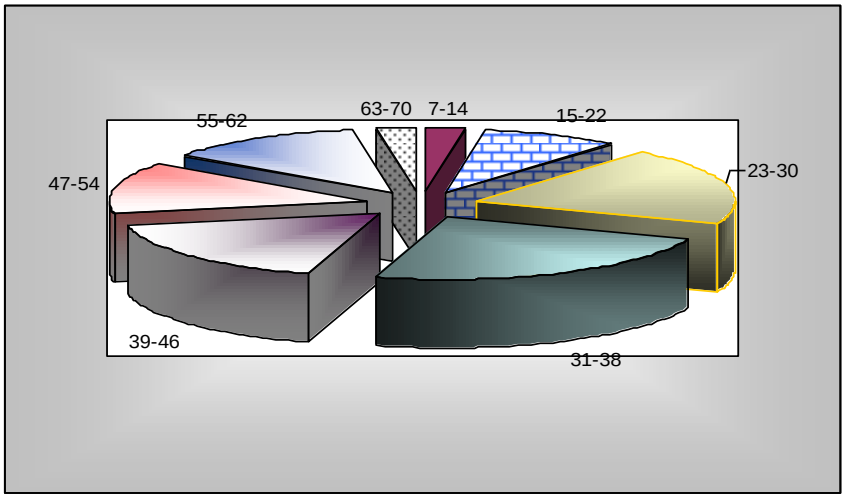
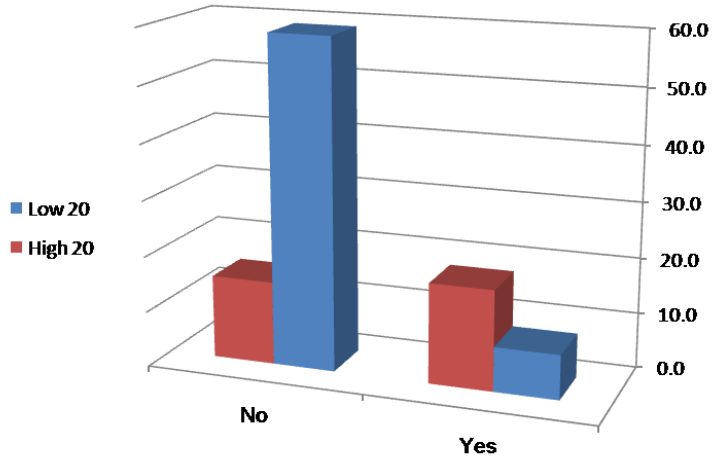


Figure (3): Patients age groups

According to risk factors of the study is divided to several factors:

Diabetes Mellitus (DM)

Diabetes mellitus disease is considered as an important cause of renal failure was diagnosed in 27 patients. All are negative with dipstick (i.e. no Macroalbuminuria) .Positive Microalbuminuria (High) proteinuria were diagnosed in 19 patients (14.9%) while low proteinuria was diagnosed in 8 patients (6.2%) in our center. See Figure (4) . In our study, we found a significant correlation between heavy proteinuria and prevalence of diabetes mellitus (P-value= 0.000), which means the first hypothesis is true.



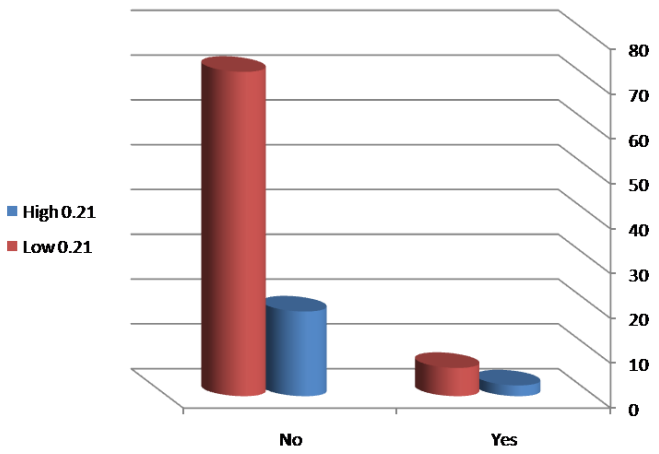
High 20:+ve for Microalbuminuria >20mg/l

Low 20:-ve for Microalbuminuria <20mg/l

Figure (4) show correlation between diabetes and Microalbuminuria

Hypertension (Macroalbuminuria)

Hypertension is a major cause of renal failure was diagnosed in 35 patients. Positive Macroalbuminuria (High) proteinuria was diagnosed in 8 patients (6.2%). while low Macroalbuminuria was diagnosed in 27 patients (21.2%) in our center See Figure (5) . which means the result was not the same with the second hypothesis.



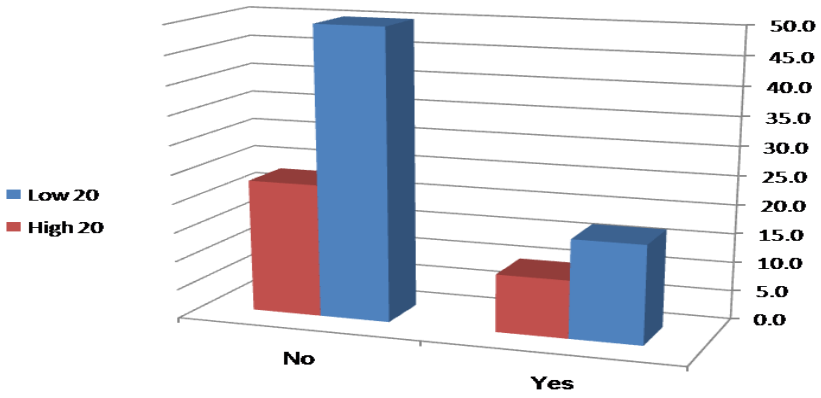
High 0.21:+ve for Macroalbuminuria > 0.21mg/dl

Low 0.21:-ve for Macroalbuminuria < 0.21mg/dl

Figure (5) show correlation between blood pressure and Macroalbuminuria

Microalbuminuria

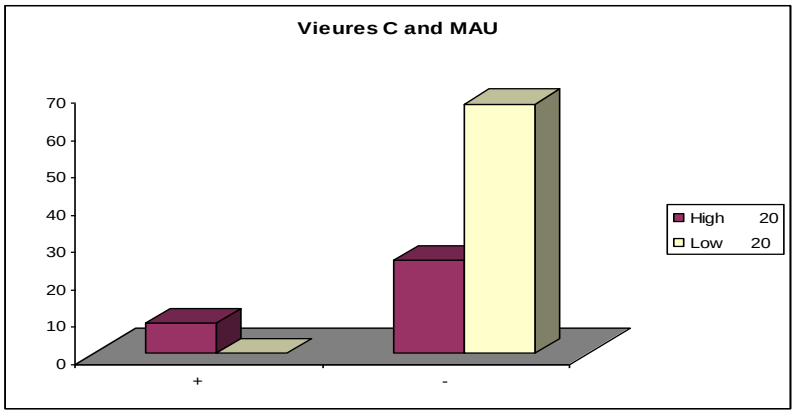
Hypertension is a major cause of renal failure was diagnosed in 35 patients. Positive Microalbuminuria (High) proteinuria were diagnosed in 10 patients (7.8%), while low proteinuria was diagnosed in 17 patients (13.3%) in our center. See Figure (6). Which means the result was not the same with the second hypothesis.



High 20:+ve for Microalbuminuria >20mg/l
Low 20:-ve for Microalbuminuria <20mg/l
Figure (6) show correlation between blood pressure and Microalbuminuria

Viral hepatitis C (Microalbuminuria)

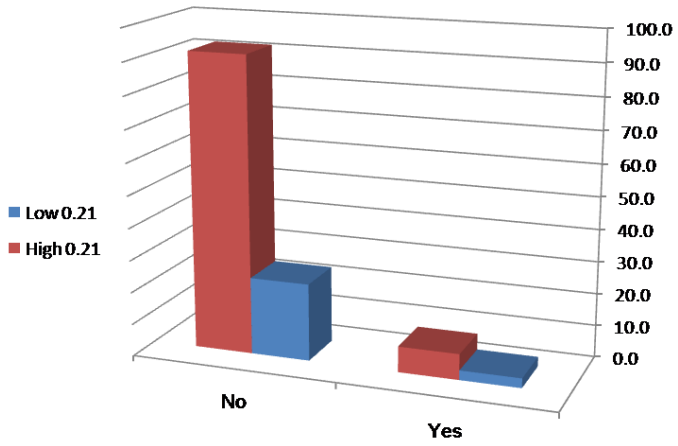
Viral hepatitis C is another cause of renal failure was diagnosed in 11 patients. Positive Microalbuminuria (High) proteinuria was diagnosed in 8 patients (6.2%) in our center See Figure (7). which means the result was not the same with the third hypothesis.



High 20:+ve for Microalbuminuria >20mg/l
Low 20:-ve for Microalbuminuria <20mg/l
Figure (7): show correlation between Virus C and Microalbuminuria

Macroalbuminuria

Viral hepatitis C is another cause of renal failure was diagnosed in 11 patients. Positive Macroalbuminuria (High) was diagnosed in 3 patients 2.3% In our center. See Figure (8). Which means the result was not the same with the third hypothesis.



High 0.21:+ve for Macroalbuminuria > 0.21mg/dl

Low 0.21:-ve for Macroalbuminuria < 0.21mg/dl

Figure (8) show correlation between Virus C and Macroalbuminuria

Hyperlipidemia

Hyperlipidemia was found in 19 patients which is 14.9% of patient's abnormal lipid profile and 96 patients 75.6% had normal after kidney transplantation the patient See Figure (9). Which means the result was not the same with the second hypothesis.

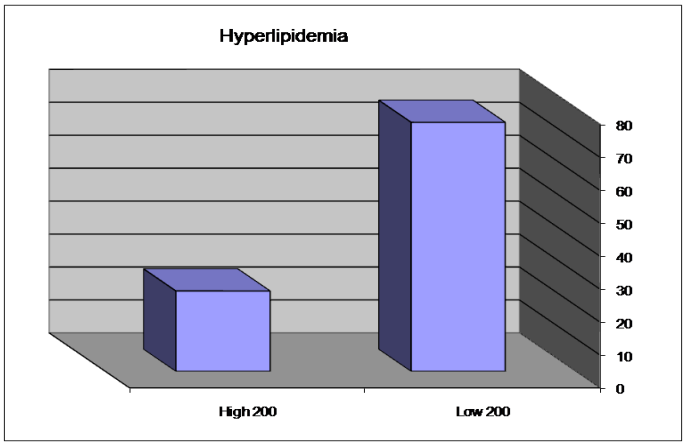


Figure (9) Hyperlipidemia

Anemia

Anemia was found in 68 patients which is 53% of patients presented with anemic, 55 patients 43.3% had normal and 4 patients 3.1% had high normal. Of our study generally is a complication of kidney disease and not a cause of proteinuria but anemia is highly associated with kidney transplantation See Figure (10).

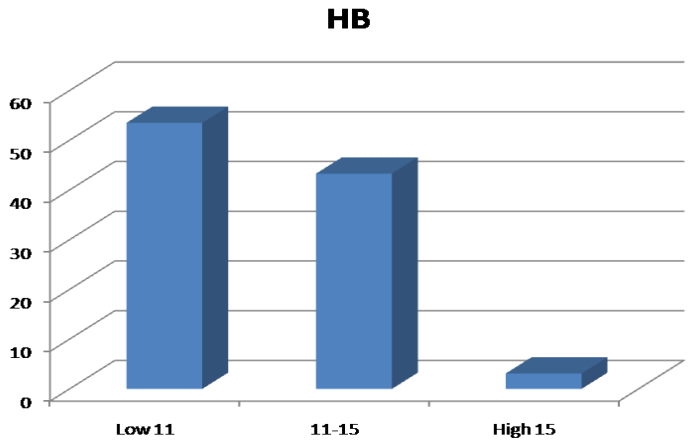


Figure (10) Anemia

Discussion

The study of the prevalence and risk factors of proteinuria in the renal transplant population in Libyan is a very important step in the follow up of this type of patients in order to keep a stable kidney function. And to evaluate the magnitude of the degree of proteinuria and guide the anticipation of these risk factors to prevent or at least to reduce the consequences of its complication on the transplanted graft or even the patient life as a whole (19).

This study is similar to many other previous studies; it was done on one hundred and twenty-seven patients (82 males, 45 females) from the period August 2018 to October 2021. it has been discovered that 60 patients (47.2%) were positive for proteinuria who necessitate further evaluation, and 67 patients (52.7%) were negative for proteinuria who do not need any further investigation.

From the 47.2% patients who are positive for proteinuria, 33 patients (25.9%) were positive for Microalbuminuria (Microalbuminuria is defined as a range from 30-300 mg/day). And 27 patients (21.2%) were positive for Macroalbuminuria. (Macroalbuminuria is defined as above 300 mg/day). Diabetes mellitus was found in 27 patients (21.2%) from these patient 18 patients (14.2%) was positive for Microalbuminuria.

The development of post-transplant diabetes mellitus has an adverse effect upon patient survival and correlates with increased cardiovascular mortality, which is the most prevalent cause of poor long-term survival with PTDM. Medications like prednisone and cyclosporine are known causes of PTD Recurrence of diabetic nephropathy (glomerular pathology) may contribute to presence of proteinuria (20).

Hypertension was found in 35 patients (27.5%) out of these 127 patients of these 10 patients (7.8 %) were positive for Microalbuminuria and 8 patients (6.2%) were positive for Macroalbuminuria**.**

In situations where the blood pressure is chronically elevated, the delicate filtering structures of the kidneys are exposed to abnormally high pressures, which they are not designed to handle. One result of this increased pressure is a gradual deterioration of the vessel structures that form the actual filter. This deterioration is much like making the holes larger. As the size of the holes increases, progressively larger substances are able to pass through this initial barrier into the kidney, where they eventually become part of the urine (21).

Hepatitis C virus was found in 11 recipient patients (8.6%) from these 8 recipient patients (6.2%) were positive for Microalbuminuria and 3 patients were Positive for Macroalbuminuria (2.3%). and Hepatitis B virus was found in 3 recipient patients out of 127 recipient patients (2.3%).

Hepatitis C infection has been linked to distinct histological patterns of immune complex glomerulonephritis. The association with mesangial proliferative glomerulonephritis, de novo or recurrent (with or without cryoglobulinemia), has now been extensively documented in recipients of kidney transplants and well-known cause of proteinuria. These results are similar with many other previous studies (22).

The present study has not included the effect of the immunosuppressive drugs such as cyclosporine or prednisolone or MMF as they applied to all patients thus it has not constituted a variable. Rejection also might be a cause of proteinuria in some patients but we excluded patients with abnormal renal profile (high serum urea or high serum creatinine) that might be contributed to acute or chronic rejection.

Hyperlipidemia was found in 19 patients (14.9%), After kidney transplantation the patient lifestyle starts to change as might become less motivated for exercise prefer low profile activity and might be more liberal in food as may eat more freely fat-containing food. furthermore, certain drugs being taken post-transplantation including Prednisone may increase the cholesterol level by stimulating hepatic production of lipoproteins. Several studies have shown a positive correlation between serum cholesterol level and daily prednisone dose steroid with draw alphas been associated with 17% reduction into total cholesterol level (23).

Cyclosporine was found to cause an increase in serum cholesterol that was independent of its known suppression of glomerular filtration. There are two possible mechanisms that may account for cyclosporine induced hypercholesterolemia. Cyclosporine lipophilic endecapeptide that is transported in the blood in association with lipoproteins may enter cells via the LDL receptor; hypercholesterolemia might occur because of an abnormal interaction between LDL and the LDL receptor secondary to the presence of cyclosporine in the LDL particle. Cyclosporine may also inhibit hepatic 26 hydroxylase, an important enzyme in bile acid synthesis and reduce the excretion of free cholesterol in bile, resulting in systemic hypercholesterolemia (23, 24).

In this study, 68 out of 127 patients (53%) were anemic. Anemia generally is a complication of kidney disease and not a cause of proteinuria, however, anemia is highly associated with kidney transplantation and mainly due to drugs used or associated with recurrence of the primary disease before transplant like glomerulonephritis the cause of lowered hemoglobin in the stable long-term kidney transplant patient may be due to many things (25). Some

causes may be related to the kidney itself or medications given to prevent rejection. Following kidney transplantation, in the vast majority of patients, there is correction of previous anemia from the new kidney making normal amounts of erythropoietin (EPO), and the bone marrow responds appropriately. In certain cases, the transplanted kidney may produce insufficient quantities of EPO for several reasons. First, the kidney could be from an older donor of smaller stature and may not have produced normal amounts of EPO in the donor. Second, there could be kidney tissue damage during the time the kidney was prepared for transplantation and was stored in a cold state (25, 26).

Important in the immunosuppressive treatment plan of all kidney transplant patients is the drug treatment plan designed to prevent rejection. At least two types of drugs can affect the kidney or bone marrow so the patient might become anemic after a long period of normal kidney transplant function. The first class of such drugs is called calcineurin inhibitors (cyclosporine). These drugs, while preventing rejection of the kidney, actually have some degree of toxic effect upon the kidney. Taken over many years, they may alter function of the transplanted kidney and actually contribute to CKD, leading to diminished production of EPO and anemia. Another class of drugs that prevent rejection is the ant metabolite group (MMF: CellCept). These drugs have a well-known effect on the marrow and can cause anemia (27).

We acknowledge that a limitation of this study is the limited number of samples and absence of protocol graft collecting samples for center policy; however, this limitation diminishes its significance when we consider that proteinuria presence and its impact were shown by some authors to improve graft outcome (28).

Another limitation is the lack of qualitative differentiation of urinary protein, considering that glomerular proteinuria could have a different impact on graft outcome, as underlined in previous studies (29).

Conclusion

Persistent of proteinuria was associated with loss of kidney function; the magnitude of persistent proteinuria directly correlates to the rate of loss of kidney function. Proteinuria is strong and independent predictor of increased risk for cardiovascular morbidity and mortality, especially in certain high-risk groups such as diabetics, hypertensive, the elderly, and those post kidney transplantation.

This paper was concluded the prevalence of post transplant proteinuria, high levels in patients at percentage 47.2%. Major factors contribute to proteinuria were hypertension (27.5%) followed by diabetes mellitus (21.2%) either before the kidney transplantation or diabetes mellitus developed after the transplantation followed by Hyperlipidemia (14.9%). liver viral infection (11.2%). Early detection and management of these predisposing factors to proteinuria promptly will improve the graft and patient survival.

Conflict of interest: The authors declare no conflict of interests.

Acknowledgement

The authors express their thanks to the staff at National kidney transplantation Tripoli Central Hospital for their technical assistance.

References

1-Kasiske, BL., Vazquez, M., Harmon, E., 2000. Recommendations for the outpatient surveillance of renal transplant recipients. Nephrology journal, (11)15, pp.69-86.

2- Kris, W., Elgar, M., Johnson, R., ally, J., 2020. Comprehensive clinical nephrology. journal of kidney failure, pp. 11-110.

3- Hoy, E., Douglas, R., Hughson, M., Cass, A., Johnson, K., Bertram, J., 2003. A stereological study of glomerular number and volume, Preliminary findings in a multiracial study of kidneys at autopsy. Kidney international journal, (63)83, pp.31-37.

4- Dan, W., Caroline, J., Fares, D., 2019. Structural determinants of glomerular permeability. Renal physiology journal, (4) 281, pp.579-96.

5- Anderson, S., Tank, J., Brenner, M.,2000. Renal and Systemic Manifestations of Glomerular Disease. The Kidney, Philadelphia, pp.1871-1900.

6- Lund, U., Rippe, A., Venturoli, D., Tenstad, O., Grubb, A., Rippe, B., 2003. Glomerular filtration rate dependence of sieving of albumin and some neutral proteins in rat kidneys. Physiol Renal Physiol, (6)284, pp.1226-34.

7- Ponticelli, C., Grazian, G., 2012. Proteinuria after kidney transplantation. National library of medicine, (9)909, pp.909-917.

8-Dien, D., Messina, M., Debiase, C, 2019. Relationship between early proteinuria and long term outcome of kidney transplanted patients from different decades of donor age. BM Nephrol (20) 12, pp. 420-433.

9- Akbari, A., Hussian, N., Karpinski, J., Knoll, G., 2007. Chronic kidney disease management comparison between renal transplant patients with chronic kidney disease. Nephron, (7)13, pp.100-107.

10- Campistol, G., Garcia, M., Alarcon, A., 2006. Angiotensin II receptors blockage in kidney transplantation, Design and progress of the allograft study. world transplant congress meeting (22)27, pp.510.

11- Rigatto, C., Parfrey, P., Foley, R., Negrijn, C., Tribula, C., Jeffery, J., 2002. Congestive heart failure in renal transplant recipient, Risk factors outcome, and relationship with ischemic heart disease. Soc Nephrol, (13), pp. 1084-90.

12- Opelz, G., Zeier, M., Lau, G., Moerth, C., Dohler, B., 2006. No improvement of patients or graft survival in transplant recipients treated with angiotensin-converting enzymes inhibitors or angiotensin II type 1 receptors blocker, A collaborative transplant study report, Soc Nephrol, (17), pp. 3257-62.

13- Hor, T., Baldwin, D., 2006. Urinary albumin excretion in patients with diabetes after renal transplantation. Transplant Proc, (38), pp. 2879-89.

14- Gorriz, L., Martinez, A., Proteinuria, detection and role in native renal disease progression. Transplant Review (26)1, pp. 3-13.

15- Croker, J., Burnett, D., 1998. The Science of Laboratory Diagnosis. Medical Media Oxford, (4) 1, pp. 391-398.

16- Rendina, A., George, B., 1976. Experimental Methods in Modern Biochemistry W.B. Saunders Company: Philadelphia. 1976. PP.46-55.

17- Knoll, G., Fergusson, D., Chasse, M., Hebert, P., Wells, G., Tibbles, A., 2016. Ramipril versus placebo in kindney transplant patients with

proteinuria, a multicentre, double-blind, randomized controlled trial. Lancet Diabetes Endocrinal (4) 4, pp. 318-26.

18- Amer, H., Lieske, J., Rule, A., Kremers, W., Larson, T., Franco, R., 2013. Urine high and low molecular weight proteins one-year post-kidney transplant, relationship to histology and graft survival. Soc transplant Surg, 13(3), pp. 676-84.

19- Akansha, A., Micheal, G., Ison, A., Lara, D., 2022. Long term infection complication of kidney transplantation. Clinical journal of American Society of Nephrology. 17(2), pp. 286-95.

20- Kaul, D., Vece, G., Blumberg, E., Lahoz, R., Ison, M., Green, M., Pruett, T., Nalesnik, M., Tlusty, S., Wilk, A., Wolf, C., Michaels, M., 2020. Ten years of donor-derived disease, A report of the disease transmission advisory committee. journal of transplant, (5) 11, pp. 1678-89.

21- Jaques, D., Saudan, P., Martinez., 2021. Relationship between renal function and blood pressure recipients, a longitudinal study. BMC nephrol, (3)22, pp. 186-97

22-Dzekova, P., Sikole, A., 2017. Hepatitis C virus infection in kidney transplant patients, current treatment options. Exp Clin transplant, 15 (6), pp. 587-93.

23-Szili, T., Sokooti, S., Oste, M., 2022. Remnant lipoprotein cholesterol is associated with incident new onset diabetes after transplantation (NODAT) in renal transplant recipients, results of transplant Lines and cohort studies. Cardiovasco Diabetrol, 41 (21), pp. 933-42.

24- Arnav, A., Agarwal, A., Ramesh, G., Prasad, V., 2016. Post-transplant dyslipidemia mechanisms, diagnosis and management. world journal of transplantation, 6 (1), pp. 2220-30.

25- Schechter, A., Gafter, G., Shepshelovich, D., 2019. Post renal transplant anemia, severity, causes and their association with graft and patients survival. BMC Nephrol (20), pp.655-61.

26- Hibrand, L., Hoitsma, A., Koene, R., 1992. Post-transplant hemoglobin levels and host kidney status. Transpl Int, 2 (24), pp. 423-29.

27- Daniel, W., Daniel, C., Andrew, M., 2022. Kidney transplantation in adults, anemia and the kidney transplant recipients. Journal of transplant, 3 (13), pp. 223-28.

28- Naesens M, Lerut E, Emonds M-P, Herelixka A, Evenepoel P, Claes K, et al. Proteinuria as a noninvasive marker for renal allograft histology and failure: an observational cohort study. J Am Soc Nephrol JASN. 2016;27(1):281–92.

29- Hosaka B, Park SI, Felipe CR, Garcia RG, Machado PGP, Pereira AB, et al. Predictive value of urinary retinol binding protein for graft dysfunction after kidney transplantation. Transplant Proc. 2003;35(4):1341–3.