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EFFECT OF LOW CLEARANCE, DIALYSIS AND DRUGS AFTER TRANSPLANTATION ON TESTOSTERONE, CALCIUM, PHOSPHOROUS, ALBUMIN AND ALKALINE PHOSPHATASE LEVELS IN SUDANESE MALE

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ABSTRACT
As many as 50 to 70% of CKD men have been reported to be hypogonadal on the basis of low concentrations of total and free testosterone. Beside disturbance of minerals and Albumin and Alkaline phosohatase in renal diseases which known as "kidney bone disease", Renal osteodystrophy has been classically described to be the result by the damaged kidney. The present study aimed to evolution the effect of low clearance, dialysis and drugs after transplantation on testosterone, calcium, phosphorous, albumin and alkaline phosphatase levels in Sudanese male. 250 individuals male were included divided as follow 50 had low clearance, 50 in dialysis stage,50 functional renal transplant treated with Tacrolimus (prograf), 50 functional renal transplant treated with cyclosporine and 50 individuals apparently healthy as control group (mean age 45±15 years in all groups). Our finding showed significant decrease testosterone and calcium levels in all cases groups than in control group. The phosphorus levels showed significant decrease in transplant groups and significant increase in low clearance and dialysis groups compared with control, while Albumin levels were significant low in all cases groups except in low clearance group. Also we found negative correlation of testosterone with age and negative correlation of albumin with duration of renal impairment. In conclusion that all groups of renal diseases have low or low-normal levels of testosterone with hypocalcaemia while phosphorus level was increased in low clearance, dialysis and decreased after functional renal transplantation which indicate for sexual dysfunction and bone disease is more suggested in renal diseases patients.

KEYWORDS: low clearance, Dialysis, Testosterone, Drug after Transplantation, Sudanese Male.

INTRODUCTION
Male patients with impaired renal function are at risk of impaired reproductive function.[1] Deteriorating quality of life in some patients with uraemia is also thought to contribute to sexual dysfunction.[2,3] As many as 50 to 70% of CKD stage-5 men have been reported to be hypogonadal on the basis of low concentrations of total and free testosterone[4,5] Alterations on sex steroid production and metabolism (leading to primary hypogonadism and disturbances of the hypothalamic-pituitary axis) are already seen when moderate reductions in the GFR arise[5,6] And disturbance of minerals in renal diseases is hallmarks, also known as "kidney bone disease".[7] Renal osteodystrophy has been classically described to be the result by the damaged kidney due to low activated vitamin D3, calcitriol, hypocalcaemia. High levels of fibroblast growth factor 23 seem now to be the most important cause of decreased calcitriol levels in CKD patients.[8] Both high and low bone turnover diseases are currently observed equally in CKD patients treated by dialysis and all types of renal osteodystrophy are associated with an increased risk of skeletal fractures, reduced quality of life and poor clinical outcomes.[8,9]

Testosterone is steroid hormone and plays an important role in the development of the male reproductive system. In adult males it promotes secondary sexual characteristic including increased muscle growth and body hair.[10] Testosterone is made primarily by the testicles in males. Small amounts are also made by the adrenal glands and the ovaries in females.[11] Levels of testosterone are typically more than five times higher in adult males than females.[12]

Calcium is the most abundant electrolyte in the body. 99% of calcium is stored in the teeth and bones where it helps to make and keep them strong. Moreover, calcium is also critical for muscle contraction, nerve signaling, blood clotting and maintaining normal heart function.[13]

Phosphorus is major of the body's phosphate is found in the bones and teeth where it promotes their formation. It also plays an important role in the body's utilization of carbohydrates and fats. Phosphate is also critical to the synthesis of proteins that promote the growth, maintenance and repair of cells and tissue.[13]

Albumin is the main protein of human blood plasma. It binds water, cations (such as Ca2+, Na+ and K+), fatty acids, hormones, bilirubin, thyroxine (T4) and pharmaceuticals (including barbiturates): its main function is to regulate the colloidal osmotic pressure of blood. Alpha-fetoprotein (alpha-fetoglobulin) is a fetal plasma protein that binds various cations, fatty acids and bilirubin. Vitamin D-binding protein binds to vitamin D and its metabolites, as well as to fatty acids.[14]

Alkaline phosphatase is a hydrolase enzyme responsible for removing phosphate groups from many types of molecules, including nucleotides, proteins and alkaloids. The process of removing the phosphate group is called dephosphorylation. As the name suggests, alkaline phosphatases are most effective in an alkaline environment, it present in all tissues throughout the entire body, but is particularly concentrated in the liver, bile duct, kidney, bone, intestinal mucosa and placenta. In the serum, two types of alkaline phosphatase isozymes predominate: skeletal and liver.[15,16]

MATERIALS AND METHODS

Materials

Study design: This is a descriptive analytical case control study.

Study area: The study was conducted in Association Specialize hospital which located in Khartoum state.

Study population

This study included 250 individuals male divided as follow 50 had low clearance, 50 in dialysis stage, 50 functional renal transplant treated with Tacrolimus (prograf), 50 functional renal transplant treated with cyclosporine and 50 individuals apparently healthy as control group (mean age 45±15 years in all groups).

Inclusion Criteria

Patients with renal disease with low clearance or in dialysis or functional renal transplant were included.

Exclusion criteria

Patients without renal disease or prostate or bone disease or any diseases effect parameter of study were excluded.

Samples

About 5ml of venous blood were collected from each patient. The samples collected under aseptic conditions and placed in sterile plane containers and after clotting centrifuged for 3 minutes at 3000 RPM to obtain serum, then kept at _20c till the time of analysis.

Ethical consideration

Patients who voluntarily accepted to participate in the study were informed and included. The study was approved by the Research Committee of Medical Laboratory Science Faculty Sudan University for science & technology.

Statistical analysis

Data analyzed by statistical package for the social science (SPSS) software program version 16. T, test was conducted to show differences between cases and control while person's correlation was used to find the association between variables of. P.value of ≤ 0.05 was considered significant.

METHODOLOGY

Estimation of Calcium, Phosphorus, Albumin and Alkaline phosphatase were done by cobas c311 machine and its reagents, while Testosterone was done by TOSOH machine.

Principle of Testosterone by TOSOH method

This is an ELISA for the quantitative analysis of Testosterone levels in biological fluid. This test kit operates on the basis of competition between the hormone conjugate and the Testosterone in the sample for a limited number of binding sites on the antibody coated plate.

Principle of calcium method

Test principle Method according to Schwarzenbach with o-cresolphthalein complexone. 3 Calcium ions react with o-cresolphthalein complexone (o-CPC) under alkaline conditions to form a violet colored complex. The addition of 8-hydroxyquinoline prevents interference by magnesium and iron.

$$Ca2+ + \text{o-CP} \xrightarrow{\text{Alkaline pH}} \text{calcium-o-CPC complex}$$

The color intensity of the complex formed is directly proportional to the calcium concentration and is measured photometrically. Reagents - **working solutions** R1 CAPS (3-[cyclohexylamino]-1-propanesulfonic acid): 525 mmol/L; NaOH: 400 mmol/L, pH 11.3; nonreactive surfactant R2 o-cresolphthalein complexone: 0.5 mmol/L; 8-hydroxyquinoline: 30 mmol/L; pH 1.3; stabilizer.

Principle of phosphorus method

Molybdate UV. Inorganic phosphate forms an ammonium phosphomolybdate complex having the formula $(NH4)3[PO4(MoO3)12]$ with ammonium molybdate in the presence of sulfuric acid.

Phosphate +ammonium molybdate ⟶ H2SO

The concentration of phosphomolybdate formed is directly proportional to the inorganic phosphate concentration and is measured photometrically **working solutions** R1 Sulfuric acid: 0.36 mol/L; detergent R2 Ammonium molybdate: 3.5 mmol/L; sulfuric acid: 0.36 mol/L; sodium chloride: 150 mmol/L.

Principle of Albumin method

Colorimetric assay at a pH value of 4.1, albumin displays a sufficiently cationic character to be able to bind with bromcresol green (BCG), an anionic dye, to form a blue-green complex.

Albumin + BCG ⟶ pH 4.1 albumin-BCG complex

The color intensity of the blue-green color is directly proportional to the albumin concentration in the sample and is measured photometrically. Reagents - working solutions R1 Citrate buffer: 95 mmol/L, pH 4.1; preservative R2 Citrate buffer: 95 mmol/L, pH 4.1; bromcresol green: 0.66 mmol/L.

Principle of Alkaline phosphatase method

Colorimetric assay in accordance with a standardized method. In the presence of magnesium and zinc ions, p-nitrophenyl phosphate is cleaved by phosphatases into phosphate and p-nitrophenol.

p-nitrophenyl phosphate + H2O ⟶ ALP phosphate + p-nitrophenol

Working solutions R1 2-amino-2-methyl-1-propanol: 1.724 mol/L, pH 10.44 (30°C); magnesium acetate: 3.83 mmol/L; zinc sulfate: 0.766 mmol/L; N-(2-hydroxyethyl)-ethylenediamine triacetic acid: 3.83 mmol/L R2 p-nitrophenyl phosphate: 132.8 mmol/L, pH 8.44 (30 °C); preservatives.

RESULTS ammonium phosphomolybdate

The statistical analysis was done by SPSS (t, test and person's correlation) showed result as follow:

Testosterone level in all groups: Showed a Significant decrease of testosterone level in all cases group when compared the means with control group (Table 1).

Calcium level in all groups: Showed a Significant decrease of calcium level in all cases group when compared the means with control group (Table 2).

Phosphorus level in kidney all groups: Showed a Significant decrease of Phosphorus level in all transplant groups (cyclosporine and prograf) when compared the means with control group while showed a significant increase in low clearance and dialysis groups (Table 3).

Albumin level in all groups: Showed a Significant decrease of albumin level in all cases group except low clearance group when compared the means with control group. Low clearance group showed no significant result (Table 4).

Alkaline phosphatase activity in all groups: Showed a no Significant of alkaline phosphatase activity in all cases group when compared the means with control group (Table 5).

Correlation (person's): showed a significant negative correlation between serum testosterone and age in all case groups while there was no correlation between testosterone levels and duration in any of groups (Figures 1, 2, 3 and 4).

Correlation (person's): showed a significant negative correlation between serum albumin and duration in low clearance group and kidney transplant (porgraf) group while there was no correlation between albumin levels and duration or age in any of groups (Figures 5,6).

Table 1: Means & P.valus of testosterone levels in cases and control groups.

Testosterone test groups	Means±SD(ng/dl)	P.value
Group of Transplant treated with prograf Control	530 ± 241 662 ± 47.7	0.000
Group of Transplant treated with cyclosporine Control	507 ± 236 662 ± 47.7	0.000
Group of low clearance renal disease Control	535 ± 100 662 ± 47.7	0.000
Group of renal disease in dialysis Control	492 ± 242 662 ± 47.7	0.000

Significant difference consider as P.value ≤ 0.05.

Table 2: Means & P.valus of calcium levels in cases and control groups.

Calcium test groups	Means±SD(mg/dl)	P.value
Group of Transplant treated with prograf Control	8.5±0.37 8.85±0.46	0.000
Group of Transplant treated with cyclosporine Control	8.5±0.64 8.85±0.46	0.01
Group of low clearance renal disease Control	8.4±0.52	0.000

	8.85±0.46	
Group of renal disease in dialysis Control	7.6±2.0 8.85±0.46	0.000

Significant difference consider as P.value ≤ 0.05.

Table 3: Means & P.valus of phosphrous levels in cases and control groups.

Phosphorus test group	Means±SD(mg/dl)	P.value
Group of Transplant treated with prograf Control	3.0±0.64 3.98± 0.44	0.000
Group of Transplant treated with cyclosporine Control	3.0±0.71 3.98± 0.44	0.000
Group of low clearance renal disease Control	4.5±0.71 3.98± 0.44	0.000
Group of renal disease in dialysis Control	4.5±1.8 3.98± 0.44	0.05

Significant difference consider as P.value ≤ 0.05.

Table 4: Means & P.valus of albumin levels in cases and control groups.

Albumin test groups	Means±SD(g/dl)	P.value
Group of Transplant treated with prograf Control	4.1±0.65 4.3±0.53	0.018
Group of Transplant treated with cyclosporine Control	3.9±0.44 4.3±0.53	0.000
Group of low clearance renal disease Control	4.2±0.81 4.3±0.53	0.30
Group of renal disease in dialysis Control	3.2±1.0 4.3±0.53	0.000

Significant difference consider as P.value ≤ 0.05.

Table 5: Means & P.valus of alkaline phosphatase activity in cases and control groups.

Alkaline phosphataes test groups	Means±SD(IU/l)	P.value
Group of Transplant treated with prograf Control	89.1 ±43.1 100.4 ±4.6	0.73
Group of Tra nsplant treated with cyclosporine Control	95.2 ±32.3 100.4 ±4.6	0.26
Group of low clearance renal disease Control	99.6 ±54.3 100.4 ±4.6	0.91
Group of renal disease in dialysis Control	88.5 ±51.0 100.4 ±4.6	0.10

Significant difference consider as P.value ≤ 0.05.

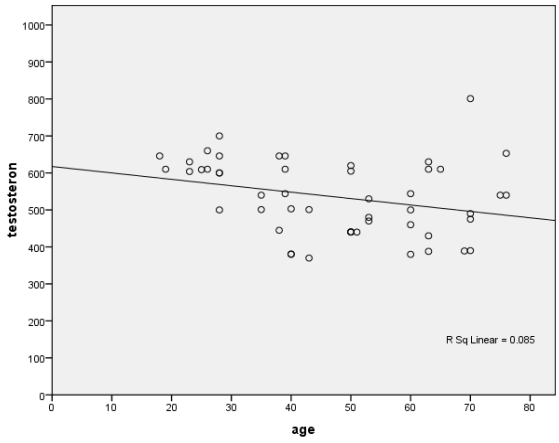

Figure 1: Correlation of testosterone level and age in low clearance group(r= -0.291 P.value 0.040) Correlation is significant at the 0.05 level

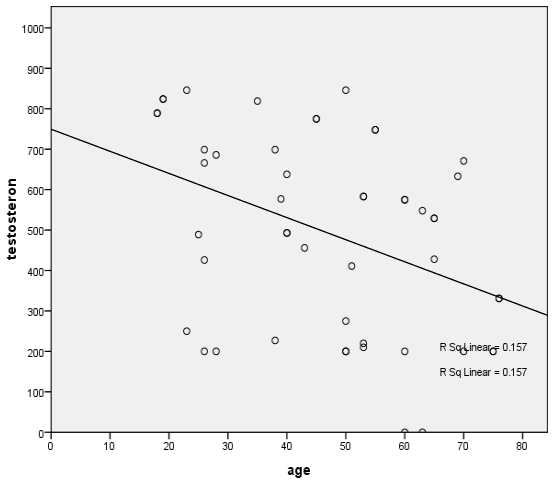

Figure 2: Correlation of testosterone level and age in Dialysis group(r= -0.397 P.value 0.004)

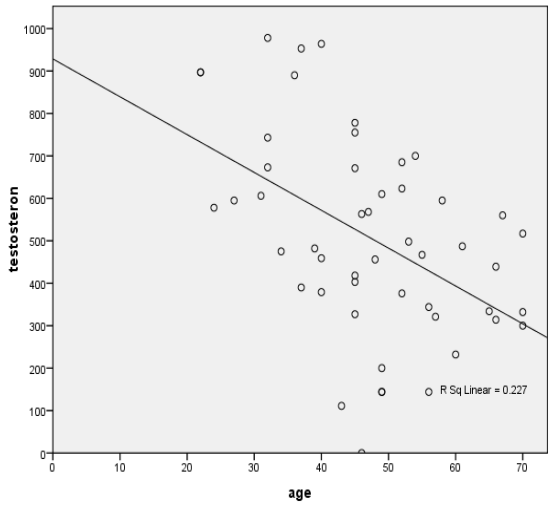

Figure 3: Correlation of testosterone level and age in kidney transplant (cyclosporine group)(r= -0.477 P.value 0.000)

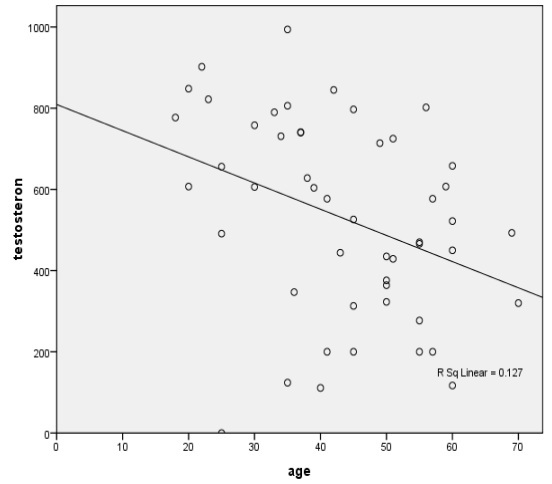

Figure 4: Correlation of testosterone level and age in kidney transplant (prograf) group (r= -0.356 P.value 0.011)

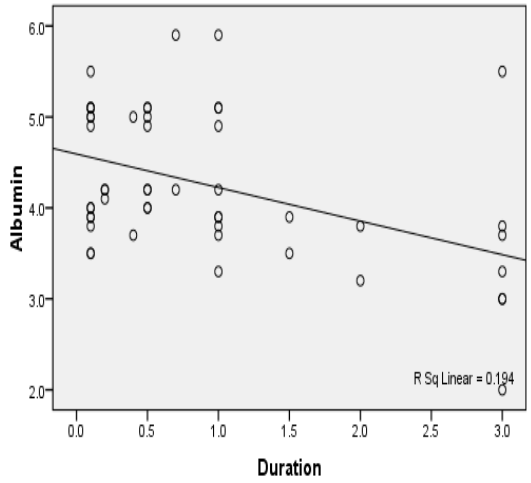

Figure 5: Correlation of albumin level and duration in low clearance group (r= -0.441 P.value 0.001)

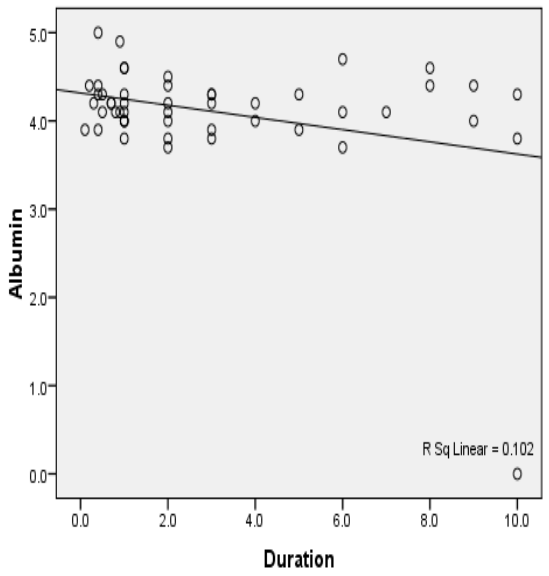

Figure 6: Correlation of albumin level and duration in kidney transplant (prograf) (r= -0.319 P.value 0.02)

DISCUSSION

Our study Showed a Significant decrease of testosterone level in all cases group when compared the means with control group (Table 1). Sex hormone disturbance is common finding in chronic renal failure and uremic men[17] previous studies report that stimulation of testosterone secretion with administration of human chorionic gonadotropin (HCG), a compound with luteinizing hormone-like actions, produces only a blunted response in uremic men[18] and low testosterone levels and impaired Leydig cell sensitivity to HCG are first detectable with only moderate reductions in the GFR.[19] Also our finding showed decrease of testosterone level in patients receiving dialysis which agreed with[4,20-22] and increase of testosterone level from dialysis to transplant indicate for functional transplant[23] and we found level of testosterone in cyclosporine lower than in tacrolimus (prograf) in groups of functional transplantation which agreed with.[24]

Also showed a significant negative correlation between serum testosterone and age in all case groups while there was no correlation between testosterone levels and duration in any of groups this finding agreed with.[25,26] While Serum Calcium Showed a Significant decrease of calcium level in all cases group when compared the means with control group and increase of means in groups of functional transplantation more than before (Table 2). There are many factors that may lead to elevation of calcium after successful kidney transplantation: (A) correction of hyperphosphatemia, (B) improved 1, 25(OH) 2 vitamin D production from the allograft and (C) elevated serum PTH our finding agreed with.[8, 27-30] Result of Serum Phosphorus Showed a Significant decrease of Phosphorus level in all transplant groups (cyclosporine and prograf) when compared the means with control group while showed a

significant increase in low clearance and dialysis groups (Table 3). Hyperphosphatemia is more prevalent in pre-transplant patients, while hypophosphatemia is observed much more frequently after renal transplantation especially in the first few weeks postoperatively.[31-34] Decreased phosphorus reabsorption in the proximal tubule, potentially related to persistently elevated PTH or FGF-23 levels and a quasi "hungry bone syndrome" seem to be mechanisms responsible for post-transplantation hypophosphatemia. Hypophosphatemia has been associated with severe alterations in bone turnover that include a decrease in osteoblast activity that leads to rickets and osteomalacia[31,35] Several recent studies indicate that posttransplantation hypophosphatemia frequently is independent of PTH[36] suggesting that FGF-23(37-39) or perhaps additional humoral factors (other phosphatonins) contribute to phosphaturia in the early post-transplant period[33,34] Both pre-transplant[40] and posttransplant[41] serum phosphorous derangements appear to be associated with anemia and mortality risk in kidney transplant recipients.[42]

Other finding the Albumin level in kidney diseases: Showed a Significant decreased in all cases group except low clearance group when compared the means with control group. Low clearance group showed no significant result (Table 4). and showed a significant negative correlation between serum albumin and duration in low clearance group and transplant (porgraf) group while there was no correlation between albumin levels and duration or age in any of groups we think that due to dialysis, external losses and inflammation which reported.[43-45] In conclusion that all groups of renal diseases have low or low-normal levels of testosterone with hypocalcaemia while phosphorus level was increased in low clearance, dialysis and decreased after functional renal transplantation which indicate for sexual dysfunction and bone disease is more suggested in renal diseases patients.

REFERENCES

1. Handelsman DJ, Liu PY. Androgen therapy in chronic renal failure. Baillieres Clin Endocrinol Metab, 1998; 12: 485–500.
2. Holdsworth SR, de Kretsler DM, Atkins RC. A comparison of hemodialysis and transplantation in reversing the uraemic disturbance of male reproductive function. Clin Nephrol, 1978; 10: 146–50.
3. Salvatierra O, Fortmann JL, Belzer FO. Sexual function of males before and after renal transplantation. Urology, 1975; 5: 64–6.
4. Albaaj F, Sivalingham M, Haynes P, McKinnon G, Foley RN, Waldek S, O'Donoghue DJ, Kalra PA: Prevalence of hypogonadism in male patients with renal failure. Postgrad Med J, 2006; 82: 693–696.
5. Juan Jesús Carrero, Abdul Rashid Qureshi, Low Serum Testosterone Increases Mortality Risk among Male Dialysis Patients.J Am Soc Nephrol. 2009; 20(3): 613–620.
6. Handelsman DJ, Dong Q: Hypothalamo-pituitary gonadal axis in chronic renal failure. Endocrinol Metab Clin North Am, 1993; 22: 145–161.
7. Kalantar-Zadeh K, Shah A, Duong U, Hechter RC, Dukkipati R, Kovesdy CP. Kidney bone disease and mortality in CKD. Kidney Int Suppl. 2010; (117): S10–21.
8. Torres PU, Bover J, Mazzaferro S, de Vernejoul MC, Cohen-Solal M "When, how and why a bone biopsy should be performed in patients with chronic kidney", Seminars in Nephrology. 2014; 34(6): 612–25.
9. Bover J, Ureña P, Brandenburg V, Goldsmith D, Ruiz C, DaSilva I, Bosch RJ "Adynamic bone disease: from bone to vessels in chronic kidney disease". Seminars in Nephrology. 2014; 34(6): 626–40.
10. Heffner LJ, Schust DJ. The Reproductive System at a Glance. John Wiley & Sons. p.2010; 17. ISBN 9781405194525.
11. Puri D. Textbook of Medical Biochemistry (3rd ed.). Elsevier Health Sciences. 2014; 631. ISBN 9788131238059.
12. Jump up^ Burtis CA, Ashwood ER, Bruns DE (2012). Tietz Textbook of Clinical Chemistry and Molecular Diagnostics (5th ed.). Elsevier Health Sciences. p. 1975. ISBN 978-1-4557-5942-2.
13. Tietz Fundamentals of Clinical Chemistry, 6th edition. Carl A. Burtis, Edward R. Ashwood, and David E. Bruns, editors. St Louis, MO: Saunders/Elsevier, 2008; 976. ISBN 978-0-7216-3865-2.
14. Farrugia, Albert. "Albumin Usage in Clinical Medicine: Tradition or Therapeutic?". Transfusion Medicine Reviews. 2010; 24(1): 53–63.
15. Tamás L, Huttová J, Mistrk I, Kogan G. "Effect of Carboxymethyl Chitin-Glucan on the Activity of Some Hydrolytic Enzymes in Maize Plants". Chem. Pap. 2002; 56(5): 326–329.
16. Appendix E: Stem Cell Markers". Stem Cell Information. National Institutes of Health, U.S. Department of Health and Human Services. Retrieved 2013-09-24.
17. Palmer BF. Sexual dysfunction in uraemia. J Am Soc Nephrol, 1999; 10: 1381–8.
18. Stewart-Bentley M, Gans D, Horton R: Regulation of gonadal function in uremia. Metabolism, 1974; 23: 1065-1072.
19. Dunkel L, Raivio T, Laine J, Holmberg C: Circulating luteinizing hormone receptor inhibitor(s) in boys with chronic renal failure. Kidney Int, 1997; 51: 777-84.
20. Handelsman D. Hypothalamic-pituitary gonadal dysfunction in renal failure, dialysis and renal transplantation. Endocr Rev., 1985; 6151–182.182.
21. Singh A, Norris K, Modi N.Pharamacokinetics of a transdermal testosterone system in men with end-stage renal disease receiving maintenance

hemodialysis and healthy hypogonadal men. J Clin Endocrinol Metab, 2001; 862437–2445.2445.
22. Lim V, FangV Gonadal dysfunction in uremic men. A study of the hypothalamo-pituitary-tisticular axis before and after renal transplantation. Am J Med, 1975; 58655–662.662.
23. Lim VS, Fang VS: Restoration of plasma testosterone levels in uremic men with clomiphene citrate. J Clin Endocrinol Metab, 1976; 43: 1370-1377.
24. Bowman AR1, Sass DA, Dissanayake IR, Ma YF, Liang H, Yuan Z, Jee WS, Epstein S. The role of testosterone in cyclosporine-induced osteopenia. J Bone Miner Res. 1997; 12(4): 60715.
25. Feldman HA, Longcope C, Derby CA, et al. Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study. J Clin Endocrinol Metab. 2002; 87: 589–598.
26. Morley JE, Kaiser FE, Perry HM, 3rd, et al. Longitudinal changes in testosterone, luteinizing hormone and follicle-stimulating hormone in healthy older men. Metabolism. 1997; 46: 410–413.
27. Julian B. A., Quarles L. D., Niemann K. M. W. Musculoskeletal complications after renal transplantation: pathogenesis and treatment. American Journal of Kidney Diseases. 1992; 19(2): 99–120.
28. Evenepoel P., Van Den Bergh B., Naesens M., et al. Calcium metabolism in the early posttransplantation period. Clinical Journal of the American Society of Nephrology. 2009; 4(3): 665–672.
29. Messa P., Cafforio C., Alfieri C. Clinical impact of hypercalcemia in kidney transplant. International Journal of Nephrology. 2011; 2011: 9.
30. Felsenfeld AJ, Gutman RA, Drezner M, Llach F. Hypophosphatemia in long-term renal transplant recipients: effects on bone histology and 1,25-dihydroxycholecalciferol. Mineral and electrolyte metabolism. 1986; 12(5-6): 333–341.
31. Moorhead JF, Wills MR, Ahmed KY, Baillod RA, Varghese Z, Tatler GL. Hypophosphataemic osteomalacia after cadaveric renal transplantation. Lancet. 1974; 20; 1(7860): 694–697.
32. Rosenbaum RW, Hruska KA, Korkor A, Anderson C, Slatopolsky E. Decreased phosphate reabsorption after renal transplantation: Evidence for a mechanism independent of calcium and parathyroid hormone. Kidney international. 1981; 19(4): 568–578.
33. Levi M. Post-transplant hypophosphatemia. Kidney international. 2001; 59(6): 2377–2387.
34. Green J, Debby H, Lederer E, Levi M, Zajicek HK, Bick T. Evidence for a PTH-independent humoral mechanism in post-transplant hypophosphatemia and phosphaturia. Kidney international. 2001; 60(3): 1182–1196.
35. Wilkins GE, Granleese S, Hegele RG, Holden J, Anderson DW, Bondy GP. Oncogenic osteomalacia: evidence for a humoral phosphaturic factor. The Journal of clinical endocrinology and metabolism. 1995; 80(5): 1628–1634.
36. Bhan I, Shah A, Holmes J, et al. Post-transplant hypophosphatemia: Tertiary 'Hyper-Phosphatoninism'? Kidney international. 2006; 70(8): 1486–1494.
37. Evenepoel P, Naesens M, Claes K, Kuypers D, Vanrenterghem Y. Tertiary 'hyperphosphatoninism' accentuates hypophosphatemia and suppresses calcitriol levels in renal transplant recipients. American journal of transplantation. 2007; 7(5): 1193–1200.
38. Trombetti A, Richert L, Hadaya K, et al. Early post-transplantation hypophosphatemia is associated with elevated FGF-23 levels. European journal of endocrinology / European Federation of Endocrine Societies. 2011; 164(5): 839–847.
39. Evenepoel P, Meijers BK, de Jonge H, et al. Recovery of hyperphosphatoninism and renal phosphorus wasting one year after successful renal transplantation. Clinical journal of the American Society of Nephrology: CJASN. 2008; 3(6): 1829–1836.
40. Sampaio MS, Molnar MZ, Kovesdy CP, et al. Association of pretransplant serum phosphorus with posttransplant outcomes. Clinical journal of the American Society of Nephrology: CJASN; 2011; 6(11): 2712–2721.
41. Connolly GM, Cunningham R, McNamee PT, Young IS, Maxwell AP. Elevated serum phosphate predicts mortality in renal transplant recipients. Transplantation. 2009; 87(7): 1040–1044.
42. Kovesdy CP, Mucsi I, Czira ME, et al. Association of serum phosphorus level with anemia in kidney transplant recipients. Transplantation. 2011; 91(8): 875–882.
43. Kaplan AA, Halley SE, Lapkin RA, Graeber CW: Dialysate protein losses with bleach processed polysulphone diabyzens. Kidney mt. 1995; 47: 573-578.
44. George A.Kaysen. Biological Basis of Hypoalbuminemia in Esrd J Am Soc Nephrol, 1998; 9: 2368-2376.
45. Yeun JY1, Kaysen GA. Factors influencing serum albumin in dialysis patients. Am J Kidney Dis. 1998; 32(6 Suppl 4): S118-25.