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Biochemistry Section

Laboratory Profiles of Patients on Hemodialysis - A Retrospective One Year Study in a Rural Tertiary Care Hospital

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ABSTRACT

Introduction: The global prevalence of chronic kidney disease (CKD) is estimated to be 8-16%. Studies have shown that the increased mortality in patients with CKD is due to anemia that leads to cardiovascular disease (CVD), also known as "Cardio renal anemia syndrome". The present study was undertaken to look into the laboratory profiles of end stage renal disease (ESRD) patients.

Aim: To study the laboratory profiles of End stage renal disease (ESRD) patients coming for hemodialysis.

Materials and Methods: The study was a retrospective, cross-sectional study done by collecting data from the medical case records of all patients during a period of one year from January 1st 2014 to December 31st 2014. Records of a total of 140 patients who underwent hemodialysis during this period were taken. The laboratory profiles that was recorded included haemoglobin, serum sodium, potassium, chloride, fasting glucose, calcium and phosphorus.

Results: The mean age of the subjects was 53.5±14.5 yrs. All the patients had moderate anaemia. There was a significant difference in the mean systolic and diastolic blood pressure, serum creatinine and serum urea values between males and females. The mean serum calcium levels were low.

Conclusion: The present study is the first such study in this rural area and shows evidence of a relatively young population with ESRD having moderate anaemia and hypertension. There is evidence of hypocalcaemia and serum phosphorus is on the higher end of the normal range. These findings are usually associated with a higher risk of mortality. With the explosion of diabetes and hypertension in India, chronic kidney disease should be diagnosed and managed as early as possible if not prevented.

Keywords: Anaemia, Chronic kidney disease, End stage renal disease, Hemodialysis

INTRODUCTION

Chronic kidney disease (CKD) is defined as either a reduced Glomerular filtration rate (GFR) of <60 ml/mt/1.73 m^2 or albumin excretion or both over a period of three months. This is a major public health problem throughout the world [1]. The prevalence of CKD in the world according to a study by Jha et al., is around 8-16% [2]. In India the SEEK (screening and early evaluation of kidney disease) study has reported the age-adjusted incidence rate of ESRD (end stage renal disease) to be 229 per million population and it was found that >1,00,000 new patients enter renal replacement programs annually [3]. About 63,538 patients had enrolled in the Indian CKD registry. This registry is a voluntary reporting body of the patients suffering from CKD. Data indicate that out of the subjects enrolled 70% are males and a majority of them have stage 4 and 5 CKD and 20% of them are on renal replacement therapy [4]. A review by Thomas et al., has shown that the increased mortality in patients with CKD is due to anaemia that leads to cardiovascular disease (CVD), also known as "Cardio renal anaemia syndrome"[5]. The other cardiovascular risk factors associated with CKD are increased serum phosphorus level, abnormal calcium-phosphate ion product, parathormone levels and dyslipidemia [5]. Microalbuminuria is another cardiovascular risk factor in diabetic and hypertensive CKD [6]. The present study was undertaken to look into the laboratory profiles of ESRD patients over a period of one year. It was a retrospective study and the population studied was the patients coming for hemodialysis at a tertiary care hospital located in a rural area. The economically backward patients coming for dialysis are funded by a government scheme.

AIM

To study the laboratory profiles of all End stage renal disease (ESRD) patients coming for hemodialysis over a period of one year.

MATERIALS AND METHODS

The study was a retrospective cross-sectional study done at Dr. PSIMS and RF a tertiary care teaching hospital in Chinnaavutapalli, in Krishna district - rural Andhra Pradesh. Data was collected from the medical case records over a period of one year from January 1st 2014 to December 31st 2014. Records of patients who underwent hemodialysis during this period were taken. The inclusion criterion was all subjects on hemodialysis and in stage 5 CKD. Those case records which did not have the relevant data or incomplete data were excluded. Paediatric and pregnant subjects were excluded. The patients included were in stage V CKD as assessed by clinicians based on eGFR (estimated Glomerular Filtration Rate) determined by Cockcroft-Gault equation and on maintenance hemodialysis (MHD). An eGFR value of <15 ml/mt/1.73m^2 is considered stage V CKD [1]. A total of 140 patients met the inclusion criteria. The study was started after obtaining ethical committee clearance from the institute. The laboratory profiles included haemoglobin, serum sodium, potassium, chloride, fasting glucose, calcium and phosphorus. The blood pressure recorded in the case sheet and the clinical diagnosis was noted. The laboratory profiles recorded was after the last dialysis session, irrespective of the number of sessions the patients underwent. The treatment history, diet, drug history, duration and lifestyle factors were not taken into consideration.

STARISTICAL ANALYSIS

The results were recorded on Microsoft excel sheet and tabulated. Data are reported as mean and standard deviation. Students t-test was used to establish the differences between means of continuous variables and the results were considered significant when p <0.05.

RESULTS

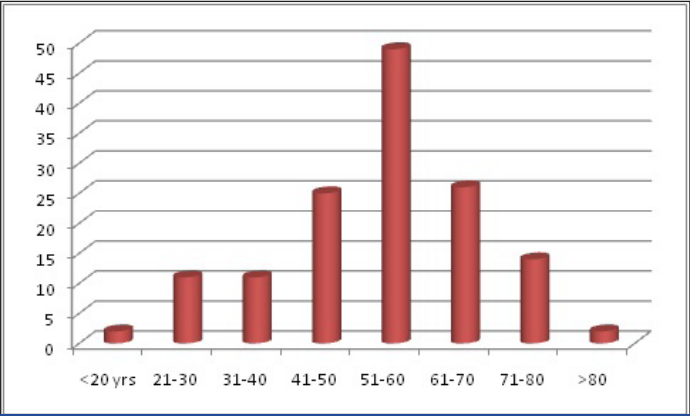
A total of 140 patients were included in the study. The demographic and laboratory profiles are given in [Table/Fig-1]. There was no significant age difference between the sexes. Out of 140 patients 20 were diabetics, 43 were hypertensive, 31 had a diagnosis of both diabetes and hypertension and 46 were neither diabetic nor hypertensive, but had other causes of CKD like analgesic nephropathy (10), infective cause of nephropathy (22) and for some the cause was not known (8). All the patients had moderate anaemia. There was a significant difference in the mean systolic and diastolic blood pressure between males and females, [Table/Fig-1]. There was a significant difference in serum creatinine and serum urea values between males and females (p<0.0001). There was no significant difference between the sexes in the other parameters. There were no significant differences in these parameters in those below 60 yrs of age and those above 60 years [Table/Fig-2]. The p-value was > 0.05. In all the patients mean serum calcium levels were low. The mean values of serum sodium were slightly lower in females when compared to males; [Table/Fig-1], though not statistically significant p value >0.05.

Parameters	Males (76) Mean ± SD	Females (64) Mean ± SD
Age (in yrs)	55.2±14.8	52.6±14.2
Hemoglobin (in g%)	9.07±2.4	8.9±1.9
Systolic blood pressure in (mmHg)	162.5±13.7	179.6±30.4 (p=≤0.0001)
Diastolic blood pressure (in mmHg)	89.8±17.0	84.2±12.4 (p=≤0.01)
Serum glucose (in mg/dl) (fasting)	125.3±63.2	135.2±64.2
Serum urea (in mg/dl)	104.7±49.5	84.7±44.3 (p=≤0.0001)
Serum creatinine (in mg/dl)	5.9±2.9	4.4±2.5 (p=≤0.0001)
Serum sodium (in meq/l)	136.5±6.8	134.7±7.9
Serum potassium (in meq/l)	4.5±1.0	4.4±0.9
Serum calcium (in mg/dl)	8.2±0.8	8.2±0.6
Serum phosphate (in mg/dl)	3.9±0.5	4.1±0.3

[Table/Fig-1]: Gender differences in the clinico-demographic and laboratory parameters

Parameters	age≥60 yrs	age≤ 60yrs
Number	54	86
Hemoglobin (in g%)	9.0±2.5	8.9±1.9
Systolic blood pressure (in mmHg)	145.3±25.4	149.6±29.4
Diastolic blood pressure (in mmHg)	86.5±16.1	87.8±14.8
Serum phosphorus (in mg/dl)	3.9±0.4	4.0±0.4
Serum calcium (in mg/dl)	8.1±0.7	8.2±0.7
Serum potassium (in meq/l)	4.2±1.1	4.5±0.9
Serum sodium (in meq/l)	136.2±6.7	134.8±8.2
Fasting serum glucose (in mg/dl)	134.2±61.7	126.8±65.2
Serum urea (in mg/dl)	100.8±53.2	91.9±44.1
Serum creatinine (in mg/dl)	4.7±2.5	5.5±2.7

[Table/Fig-2]: Differences in the clinico-demographic and laboratory parameters in subjects ≥60 yrs of age and ≤60 yrs



[Table/Fig-3]: Age distribution of the subjects

DISCUSSION

The present study shows that the patients with end stage renal disease (ESRD) had a mean age of 53.5±14.5 yrs. The age distribution is depicted in [Table/Fig-3]. There are more subjects in the 51-60 yrs age group in this study. In countries like Nigeria there are more subjects in the 41-50 yr age group [7]. The elderly were the ones affected with CKD in developed countries probably because of improved life expectancy [2]. More males were affected than females in this study. Females were on an average 2 years younger than males (52.6 years vs. 55.2 years). These values are similar to a study done by Rajapurkar et al., which reported the mean age as 50.1±14.6 yrs and males were older to females (50.9 ±14.6 vs. 48.3 ± 14.4 years) [8]. More males were affected according to the screening and early evaluation of kidney disease (SEEK) study in India [3]. The SEEK study reported 55.1% males and 44.9% females which is similar to our study where males were 54.3% and females were 45.7% . The SEEK study also showed that the incidence of CKD was highest in Visakhapatnam, Andhra Pradesh (48%) compared to Bangalore (4%) [3].

The most common cause of CKD in the developing and developed countries was diabetes mellitus (DM) [2]. The present study shows that 43 subjects out of 140 were hypertensive and 20 were subjects with only DM and 31 had a diagnosis of both DM and hypertension. The SEEK study also reported a higher incidence of hypertension in CKD patients when compared to DM (64.5% had hypertension and 31.6% had DM) [3]. Our findings are in consonance with the SEEK study and the number of patients with hypertension is higher than DM. Both high systolic and diastolic blood pressure have been linked to the development of ESRD. A study by Tozawa et al., has reported that high blood pressure is an independent risk factor for both diabetic and non diabetic ESRD [9].

The mean serum urea and creatinine values were high; being 95.6±48 mg/dl (normal-15-40 mg/dl) and 5.2±2.8 mg/dl (normal-0.5-1.5mg/dl) respectively and the difference in these values between males and females was statistically significant, the values being higher in males than in females [Table/Fig-1]. These values are indicative of CKD [1]. All the subjects had moderate anaemia (anaemia classified based on WHO classification), with a mean haemoglobin (Hb) concentration being around 9.0±2 g/dl [10]. The KDOQI-NKF 2012 guidelines suggest that Hb levels should be corrected to 11 g/dl or above to prevent secondary complications due to anaemia [11]. The complications that arise due to anaemia are left ventricular hypertrophy (LVH), cardiac failure, exercise intolerance and defective cognitive functions [5,12]. It has been reported in a study that for every 1 g/dl fall in haemoglobin, the mortality rises by 18-25% and the risk of LVH increases by 50% [13]. Another study reported that an increase in mean Hb of 2.7 g/dl was accompanied by a decreased left ventricular mass index in almost all the patients. This occurs even in the absence of blood pressure control [14]. The cause of anaemia in CKD is multi factorial. Early studies on CKD found decreased erythropoietin as a cause of anemia. Later several factors were identified that included, haemolysis due to uremic toxins, disordered iron homeostasis due to increased hepcidin (a protein- regulating iron levels), frequent phlebotomies and trapping of blood in the dialysis apparatus [12].

The mean serum calcium levels were 8.1±0.7 mg/dl (normal value 9-11 mg/dl) and mean serum phosphorus levels were 3.9±0.4mg/dl (normal value-2.5-4 mg/dl). A study by Miller et al., showed that a low serum calcium <9 mg/dl along with a high serum phosphorus of >3.5 mg/dl was associated with greater mortality [15]. Hypocalcaemia occurs as a consequence of hyperphosphatemia and decreased calcitriol. A disordered kidney in ESRD is incapable of excreting phosphate and synthesizing calcitriol. Hyperphosphatemia leads to stimulation of parathyroid gland causing parathormone (PTH) release. It also increases the production of fibroblast growth factor 23 (FGF 23 secreted mainly by osteocytes), which has an inhibitory effect on 1-α hydroxylase enzyme. This leads to decreased calcitriol and decreased absorption of calcium from the intestine. The increased phosphate causes hypocalcemia by precipitating with calcium and forming calcium hydroxyapatite ($CaHPO_4$) crystals. The down-regulation of calcitriol receptors on the parathyroid gland leads to vitamin D resistance. The loss of negative feedback on the parathyroid gland causes increased PTH. Parathormone stimulation causes increased osteoclastic activity, which in turn leads to increased calcium phosphate product and precipitation of $CaHPO_4$ extra skeletally. This further reduces serum calcium. The secondary hyperparathyroidism so produced leads to renal osteodystrophy [16]. Hypocalcaemia states can precipitate adverse cardiac outcomes like cardiomyopathy, congestive cardiac failure, ventricular tachycardia and other arrhythmias [15]. These arrhythmias may lead to sudden death which is a common cause of mortality in haemodialysis patients. The KDOQI guidelines recommend a target value for serum calcium between 8.4 to 9.5 mg/dl. A study by Kestenbaum et al., has revealed an association between high serum phosphorus level and increased risk of mortality. Higher serum phosphorus levels were also associated with female gender, DM, lower GFR and low Hb [17]. They also found a linear relationship between serum phosphate level and mortality for each 0.5 mg/dl rise in serum phosphate, with the highest mortality being observed with values above 3.5 mg/dl [16]. Our study did not show any relation between high serum phosphorus and female gender, DM or Hb. Kovesdy et al., also showed an increased risk of mortality with a serum phosphate value of >4 mg/dl [18]. Abnormal mineral metabolism occurs early in the course of CKD and ESRD. Hyperphosphatemia is associated with a greater cardiovascular morbidity and mortality [18].

The mean serum sodium and potassium levels were 135.7±7.1 meq/l and 4.4±0.9 meq/l respectively. The mean values of serum sodium were slightly lower in females when compared to males being 134.7±7.9 versus 136.5±6.8 meq/l, but there was no significant difference. A study by Mandai et al., has reported that low serum sodium is an independent predictor of a higher risk of infection in maintenance hemodialysis patients [19]. The mean serum sodium levels in females were not very low being 134.7meq/l (normal range 135-145 meq/l). Korgaonkar et al., in a study have reported that low or low normal serum potassium levels of 3.5-4.0 meq/l are associated with a greater risk of mortality [20]. The patients in the present study had a mean serum potassium value of 4.4 meq/l (normal range 3.5-5 meq/l). The only way to reduce the risk of mortality in CKD patients is regular assessment of laboratory parameters as has been suggested in KDOQI guidelines on CKD and correcting abnormalities as indicated. Anaemia should be assessed depending on clinical indicators in patients with GFR >60 ml/mt/1.73m^2, yearly in patients with GFR between 30-59 ml/mt/1.73 m^2 and twice a year in those with GFR <30 ml/mt/1.73 m^2 [1]. Patients should be given either erythropoietin stimulating agents (ESA) or iron therapy depending on the staging of CKD and whether they are on maintenance hemodialysis or not [21]. It is recommended to monitor serum calcium, phosphorus, alkaline phosphatase and PTH at least yearly in patients with GFR <45 ml/mt/1.73m^2. When intact serum PTH levels are above the normal range in this group of patients, they should be monitored for hyperphosphatemia, hypocalcaemia and vitamin D deficiency. Vitamin D should be prescribed in those patients having a documented deficiency [1]. Dietary restriction of phosphorus is advised and use of phosphate binders as indicated to reduce hyperphosphatemia [22]. Calcium supplements are not advised in stages 3 and 4 of CKD and even in stage 5 it should be given judiciously as the risk of coronary calcification should be kept in mind [23]. All these precautions only help in delaying cardiac complications. Dysnatremias have to be detected by regular laboratory investigations as indicated [1]. Hyperkalemia in dialysis patients can be prevented by dietary potassium restriction to 1.5-2 g/day [24].

LIMITATIONS

The inherent limitations of the study are a lack of follow up of these subjects to study the effects of anaemia, hypocalcaemia and increased serum phosphorus on mortality. As this was a descriptive study, the effects of the number of dialysis sessions, duration of CKD, drugs used and diet taken were not recorded. These also have a bearing on the laboratory values. The role of the above mentioned factors will be addressed during the follow up of these patients. We also plan to study the effect of improving anaemia on mortality.

CONCLUSION

The present study is the first such study in this rural area and shows evidence of moderate anaemia, low calcium and increased phosphorus levels in these subjects. These subjects are relatively younger and hypertensive as in the SEEK study. As the number of subjects on hemodialysis is high we plan to follow up these patients, to study the causes of mortality and the risk of adverse cardiovascular outcomes. It can be seen from this study that diabetes and hypertension are the primary causes of CKD. A change in the food habits and lifestyle of Indians is responsible for the high prevalence of lifestyle disorders like DM and hypertension leading to CKD. There should be increased awareness of this common complication of these lifestyle disorders so that we can aim at prevention or early intervention in CKD.

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