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# Clinical Profile of End Stage Renal Disease Patients Undergoing Hemodialysis in Chitwan, Nepal

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## ABSTRACT

**Background:** There are very few researches from Nepal that have evaluated clinical profile of end stage renal disease patients. Our main objective was to study the clinical profile of end stage renal disease patients, who were under maintenance hemodialysis for at least three months duration in two dialysis centers located in Chitwan Nepal.

**Methods:** This was a descriptive, cross-sectional study conducted among 138 end stage renal disease patients, who were undergoing maintenance hemodialysis at two government centers located in Chitwan, Nepal.

**Results:** Among 138 patients in our study, 42 (30.4%) patients had diabetic nephropathy and 11 (8%) patients had hypertensive nephropathy as the leading causes of end stage renal disease; however the cause could not be ascertained in 63 (45.7%) patients. 47 (34.1%) patients had started hemodialysis within one month of diagnosis of their kidney disease. Fatigue and musculoskeletal pain were the commonest symptoms found in 78 (56.6%) patients, whereas hypotension and fever were the two most common intra-dialytic complications found in 73 (52.9%) and 61 (44.2%) patients respectively. Anemia was present in 127 (92%) patients, 41 (29.7%) had hyperkalemia, 54 (39.1%) had hypocalcemia, 116 (84.1%) had hyperphosphatemia and 43 (31.2%) had hyperuricemia. Regular use of erythropoietin analogs was significantly associated with higher hemoglobin levels (p value- 0.000) and lesser frequency of blood transfusions (p value- 0.000) in our study.

**Conclusions:** Diabetic nephropathy was the leading cause of end stage renal disease in our study. Cause of ESRD could not be ascertained in nearly half of the total patients.

**Keywords:** Chronic renal failure; end stage renal disease; hemodialysis; Nepal

## INTRODUCTION

The prevalence of chronic kidney disease has progressively increased in low and middle income countries worldwide.[1] According to existing literature, one to four out of ten individuals in South Asia, are suffering from chronic kidney disease [2] and, the prevalence in urban Nepal is estimated to be 10.6%.[3] It has been estimated that both the incidence and prevalence of end stage renal disease patients in Nepal, is 100 to 200 per million population.[4]

Nephrology services, which started forty years ago in Nepal, has gained momentum since 2016 A.D, with the introduction of free lifetime hemodialysis service by the Government of Nepal.[5] There are very few researches from Nepal that has studied the profile of end stage renal disease patients. This research intends to study clinical profile of end stage renal disease patients undergoing maintenance hemodialysis at two government centers, located in Chitwan district of central Nepal.

## METHODS

This was a descriptive, cross-sectional study, conducted among 138 ESRD patients, undergoing maintenance hemodialysis at dialysis centers of Bharatpur Hospital and Bakulahar Ratnanagar Hospital, located in Chitwan district of Nepal. The Institutional Review Committee (IRC) of Bharatpur Hospital had approved our protocol prior to starting the study (IRC no: 08/076/77). All ESRD patients of 16 years and above, undergoing maintenance hemodialysis for at least three months duration in these two centers, who gave written consent to participate in this study, were included. Patients with diagnosis of acute kidney injury, patients who were under maintenance

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hemodialysis for less than three months duration and, patients who refused to give written consent, were excluded from this study.

Data collection was completed in three months duration from 1st June, 2020 till 30th August, 2020. A single interview session was done during routine dialysis procedure. Data was collected on a structured questionnaire, which included questions related to demographic variables and relevant clinical history. Pre-dialysis blood pressure was taken and recorded. Blood pressure was categorized as normal (systolic blood pressure <120mmHg, diastolic blood pressure <80mmHg), elevated blood pressure (SBP 120-129mmHg, DBP 80-89mmHg), stage 1 hypertension (SBP 130-139, DBP 90-99mmHg) and stage 2 hypertension (SBP ≥140mmHg, DBP ≥100mmHg). History was taken regarding cause of CKD, symptomatology related to each organ system due to CKD, the frequency of hemodialysis and intra-dialytic complications. Cause of CKD was ascertained after reviewing history and past medical records including renal biopsy reports, wherever available. Diagnosis of hypertensive nephropathy was made based on long history of systemic hypertension of atleast more than ten years duration prior to diagnosis of kidney disease, with ultrasound finding of small contracted kidneys and relatively normal urine sediments. Diagnosis of diabetic nephropathy was based on the history of diabetes mellitus (atleast ten years prior to diagnosis of kidney disease in case of Type 1 diabetes mellitus/ any duration of Type 2 diabetes mellitus prior to diagnosis of kidney disease) with persistent proteinuria in urine routine examination. Two past urine routine examination atleast three months apart were reviewed to confirm persistent proteinuria in patients with diabetes mellitus. Reports of ultrasound abdomen were also reviewed to rule out alternative causes in patients speculated to have diabetic nephropathy. Patients who had diabetes and hypertension concomitantly of more than ten years duration with persistent proteinuria in urine routine examination were speculated to have diabetic nephropathy in our study.

Patients' charts of last three months duration, which were routinely maintained in dialysis units, were also reviewed. Data related to hematological parameters like hemoglobin, serum sodium, potassium, calcium, uric acid, phosphorus, pre-dialysis and post-dialysis urea, were duly recorded. The mean of three monthly readings were taken. Serum potassium levels were categorized as normal (3.5 to 5.4mg/dl), hypokalemia (<3.5mg/dl) and hyperkalemia (≥5.5mg/dl). Serum sodium levels were categorized as normal (135-149mg/dl), hyponatremia (<134mg/dl) and hypernatremia (≥150mg/dl). Serum calcium levels were categorized as normal (8.5mg/dl to 10.4mg/dl), hypocalcemia (<8.5mg/dl) and hypercalcemia (≥10.5mg/dl). Serum uric acid levels were categorized as normal (3.5 to 7mg/dl), hypouricemia (<3.5mg/dl) and hyperuricemia (>7mg/dl).

Data was entered in Microsoft Excel and converted into Statistical Package for Social Sciences (SPSS) version 21 for statistical analysis. Descriptive statistics were calculated using frequency and percentage for qualitative variables, and mean and standard deviation for quantitative variables. Bivariate analyses were done using Chi-square and Fischer's exact test, wherever appropriate. P value of < 0.05 was considered to be statistically significant.

## RESULTS

A total of 138 ESRD patients were included in this study, out of which 94 patients were from Bharatpur hospital and 44 patients were from Bakulahar Ratnanagar Hospital. 91 (65.9%) patients were males and 47 (34.1%) were females with male:female ratio of 1.9:1. 86 (62.4%) patients were of age group 45-74 years, 37 (26.8%) patients were of age group 25-44 years, 10 (7.2%) patients were of age group 15-24 years, and 5 (3.6%) patients had age more than 74 years. 83 (60.1%) patients, who came for hemodialysis in these two centers, resided in Chitwan district. However, rest of the patients came from various other districts of Nepal like Nawalpur (18.1%), Gorkha (3.6%), Makwanpur (3.6%), Lamjung (2.9%), Tanahun (2.9%), Parsa (2.2%), Sarlahi (2.2%), Baglung (0.7%), Bara (0.7%), Bardiya (0.7%), Dhading (0.7%), Kaski (0.7%) and Palpa (0.7%). 73 (53.6%) patients said that their monthly family income was below NPR 20,000/ USD166 (1USD=NPR120.15) (Table 1).

Table 1. Baseline characteristics of ESRD patients (N=138).

| Baseline Characteristics | | Frequency n (%) |
|---|---|---|
| Gender | Male | 91 (65.9) |
| | Female | 47 (34.1) |
| Age group | 15 - 24 years | 10 (7.2) |
| | 25 - 44 years | 37 (26.8) |
| | 45 - 74 years | 86 (62.4) |
| | ≥ 75 years | 5 (3.6) |
| Monthly family income | < Nrs.20,000 | 74 (53.6) |
| | Nrs.20,000 - Nrs.50,000 | 49 (35.5) |
| | > Nrs.50,000 | 15 (10.9) |

| | | |
|---|---|---|
| Literacy status | illiterate | 53 (38.4) |
| | literate | 85 (61.6) |
| Duration of diabetes mellitus prior to diagnosis of CKD | < 5 years | 15 (10.8) |
| | 5 to 10 years | 10 (7.2) |
| | > 10 years | 17 (12.3) |
| Duration of hypertension prior to diagnosis of CKD | < 5 years | 41 (29.7) |
| | 5 to 10 years | 17 (12.3) |
| | > 10 years | 25 (18.1) |
| Diagnosis of CKD while working abroad | Yes | 17 (12.3) |
| | No | 121 (87.7) |
| Duration of conservative management before dialysis | < 1 month | 47 (34.1) |
| | 1 month to < 1 year | 42 (30.4) |
| | 1 to 5 years | 33 (23.9) |
| | > 5 years | 16 (11.6) |
| Duration of hemodialysis | < 1 year | 47 (34.1) |
| | 1 to < 3 years | 71 (51.4) |
| | 3 to < 5 years | 17 (12.3) |
| | ≥ 5 years | 3 (2.2) |
| Hours of dialysis per week | 4 hours | 17 (12.3) |
| | 8 hours | 116 (84.1) |
| | 12 hours | 5 (3.6) |
| Regular use of erythropoietin analogs | Yes | 78 (43.5) |
| | No | 60 (56.5) |

**Table 2. Etiology of Chronic kidney disease (N=138).**

| Etiology of Chronic kidney disease | Frequency n (%) |
|---|---|
| Unknown | 63 (45.7) |
| Diabetic nephropathy | 42 (30.4) |
| Hypertensive nephropathy | 11 (8.0) |
| Obstructive uropathy | 6 (4.3) |
| IgA nephropathy | 6 (4.3) |
| Polycystic kidney disease | 3 (2.3) |
| Focal segmental glomerulosclerosis | 2 (1.4) |
| Membranoproliferative glomerulonephritis | 1 (0.7) |
| Thrombotic microangiopathy | 1 (0.7) |
| Pauci-immune RPGN (Type III) | 1 (0.7) |
| IgA nepropathy superimposed on DKD | 1 (0.7) |
| Acute cortical necrosis | 1 (0.7) |

Cause of ESRD could not be ascertained in 63 (45.7%) patients. Among those patients, where cause of ESRD could be ascertained, the commonest cause was speculated to be diabetic nephropathy (30.4%) followed by hypertensive nephropathy (8.0%). Out of 138 patients, 15 had undergone renal biopsy procedure. Out of these 15 patients, only 13 patients had their renal biopsy reports with them. The most common cause of kidney disease among biopsied patients was IgA nephropathy (4.3%) followed by focal segmental glomerulosclerosis (1.4%). One diabetic patient was biopsied in our study where the cause of kidney disease was found to be IgA nephropathy superimposed on diabetic kidney disease. One patient had developed acute cortical necrosis following the complication of intraoperative hypotension during a major elective surgical procedure. The patient was under hemodialysis for more than three months duration without any improvement in renal function (Table 2).

**Table 3. Symptoms/signs in ESRD patients (N=138).**

| Symptoms/ Signs | | Frequency n (%) |
|---|---|---|
| Musculoskeletal pain and fatigue | | 78 (56.6) |
| Anorexia, nausea or vomiting | | 70 (50.7) |
| Tingling, numbness or burning sensation | | 63 (45.7) |
| Hypertension | Elevated BP | 6 (4.3) |
| | Stage 1 HTN | 16 (11.6) |
| | Stage 2 HTN | 40 (28.9) |
| Pedal edema or orthopnea or ascites | | 58 (42) |
| Dryness of skin and pruritus | | 57 (41.3) |
| Epistaxis or bleeding from any sites | | 14 (10.1) |
| Oliguria (< 300ml urine output per day) | | 72 (52.2) |

**Table 4. Intra-dialytic complications in ESRD patients (N=138).**

| Complications | Frequency n (%) |
|---|---|
| Hypotension | 73 (52.9) |
| Fever | 61 (44.2) |
| Muscle cramps | 52 (37.7) |
| Hypoglycemia | 36 (26.1) |
| Backache and chest pain | 35 (25.4) |
| Altered sensorium | 10 (7.2) |
| Bleeding from access site | 5 (3.6) |

**Table 5. Hematological profile of ESRD patients (N=138).**

| Hematological parameter (mean of three readings over last three months) | | Frequency (%) |
|---|---|---|
| Hemoglobin | ≤6gm/dL | 12 (8.7) |
| | >6 to 10gm/dL | 115 (83.3) |
| | >10gm/dL | 11 (8.0) |

| | | |
|---|---|---|
| Serum sodium | 125 to 134meq/dL | 5 (3.6) |
| | 135 to 149meq/dL | 130 (94.2) |
| | ≥ 150meq/dL | 3 (2.2) |
| Serum potassium | <3.5meq/dL | 2 (1.4) |
| | 3.5 to 5.4meq/dL | 95 (68.8) |
| | ≥5.5meq/dL | 41 (29.7) |
| Serum calcium | < 8.5mg/dL | 54 (39.1) |
| | 8.5 to 10.4mg/dL | 80 (58) |
| | ≥10.5mg/dL | 4 (2.9) |
| Serum phosphorus | < 2.5mg/dL | 1 (0.7) |
| | 2.5 to 4.4mg/dL | 21 (15.2) |
| | ≥4.5mg/dL | 116 (84.1) |
| Serum uric acid | <3.5mg/dL | 10 (7.2) |
| | 3.5 to 7mg/dL | 85 (61.6) |
| | >7mg/dL | 43 (31.2) |
| Pre-dialysis urea | <100mg/dL | 2 (1.4) |
| | 100 to 200mg/dL | 106 (76.8) |
| | >200mg/dL | 30 (21.7) |
| Post-dialysis urea | <50mg/dL | 55 (39.9) |
| | 50 to 100mg/dL | 81 (58.7) |
| | >100mg/dL | 2 (1.4) |

Table 6. Use of Erythropoietin analogues in ESRD patients (N=138).

| Hemoglobin levels | Regular use of erythropoietin analogues | | p value* |
|---|---|---|---|
| | Yes | No | |
| ≤ 6gm/dL | 1 | 11 | 0.000* |
| > 6gm/dL | 77 | 49 | |
| Frequency of blood transfusion | Yes | No | |
| ≤ 2 tranfusions in last 3 months | 67 | 35 | 0.000* |
| > 2 transfusions in last 3 months | 11 | 25 | |

**p value < 0.05 - statistically significant.*

Table 3 enlists the frequency of system-wise clinical manifestations, due to kidney disease, in our patients. The most common symptoms were fatigue and musculoskeletal pain, followed by gastrointestinal complaints, and neuropathic pain found in 78 (56.6%), 70 (50.7%), and 63 (45.7%) patients respectively (Table 3). The most common procedural complication during hemodialysis was hypotension, fever, and muscle cramps found in 73 (52.9%), 61 (44.2%), and 52 (37.7%) patients respectively (Table 4). Anemia was present in 127 (92%) patients, 41 (29.7%) had hyperkalemia, 54 (39.1%) had hypocalcaemia, 116 (84.1%) had hyperphosphatemia and 43 (31.2%) had hyperuricaemia in our study (Table 5). 78 (43.5%) patients were using erythropoietin (EPO) analogs regularly and the use of EPO analogs was significantly associated with higher hemoglobin levels (p value - 0.000) and lesser frequency of blood transfusions (p value - 0.000) (Table 6). On questioning about the cause for not using EPO analogs among the patients who didn't use it, 27 (19.5%) patients said that they couldn't afford the cost of weekly or twice weekly doses, 17 (12.3%) patients gave history of non-response to treatment following which they had stopped using the medication, 11 (7.9%) said that they didn't know about such compounds and 4 (2.8%) patients said that their hemoglobin levels were mostly more than 10gm/dL; thus never used it. However, those patients who were not using erythropoietin analogs were transfusing blood more frequently as compared to those who were using such analogs (Table 6).

## DISCUSSION

End stage renal disease is the stage of chronic kidney disease that necessitates renal replacement therapy in form of dialysis or kidney transplantation. Anand et al. states that renal replacement therapy is provided to less than 25% of patients who are projected to develop ESRD in developing countries.[6] In the early 1980s, intermittent peritoneal dialysis and renal biopsies were started for the first time in Nepal, followed by the initiation of hemodialysis at Bir Hospital, Kathmandu in 1986 AD.[5] According to latest publication in 2018 AD, there has been tremendous increase in hemodialysis services in Nepal, with more than 200% growth in dialysis centers as compared to that in 2010.[4] National Kidney Center, the nonprofit non-government organization, has set up dialysis facility in Ratnanagar Bakulahar government hospital since 2015 AD with six dialysis machines. Likewise, Bharatpur hospital, the central level government hospital , initiated hemodialysis service in the year 2018 AD, with operation of 12 dialysis machines.

Majority of the patients in our study were of age group 45 to 74 years with the minimum age of 16 years and maximum age of 82 years. The male: female ratio was 1.9:1 which was consistent to findings in other studies from South Asia.[7,8] Male predominant profile could be explained due to treatment seeking behavior of male gender in the patriarchal society of Nepal. 38.4% patients were illiterate and 53.6% patients had monthly family income less than 20,000 NPR. In a study by Sigdel and Pradhan, 35% CKD patients were illiterate and 72.5% had annual income of less than 5,00,000 NPR.[7] Poor socioeconomic status can be both

the cause and effect of kidney diseases. Poverty, lack of awareness and inequitable health care has led low and middle income countries to become hotspots of chronic kidney diseases. Except these, increasing prevalence of diabetes and hypertension, environmental factors, infectious diseases, and intrauterine growth retardation are also the predisposing factors for CKD in developing countries of South Asia.[9]

The most common cause of kidney disease in our study was speculated to be diabetic nephropathy (30.4%) followed by hypertensive nephropathy (8%). In a study done in eastern Nepal by Bartaula et al., 38.2% ESRD patients had diabetic nephropathy and 30.6% had hypertensive nephropathy.[10] A study from India, by Modi and Jha, reported diabetic nephropathy in 44% ESRD patients.[11] These findings are consistent with the worldwide trend of evolving pandemic of diabetic kidney disease.[12] IgA nephropathy (4.3%) followed by focal segmental glomerulosclerosis (1.4%) were the commonest causes of ESRD in patients who underwent renal biopsy. In a study by Subedi et al., the most common primary glomerular disease was found to be IgA nephropathy (17%), followed by membranous nephropathy (14.6%) and focal segmental glomerulosclerosis (14.6%) in the biopsied samples.[13] Though, our findings are consistent to other studies related to glomerular pattern in renal biopsies, the number of patients who underwent renal biopsy in our study was too small to give a statistically significant value.

The cause of kidney disease was not known in 63 (45.6%) patients in our study. Likewise, 47 (34.1%) patients in our study said that hemodialysis was initiated within one month of diagnosis of their kidney disease. These findings highlight the facts regarding inaccessibility of diagnostic facilities and late presentation of patients to healthcare providers with established kidney disease and uremic manifestations, warranting for urgent dialysis. Chronic kidney disease passes silently through different stages to result in ESRD.[14] Early CKD can be diagnosed with active screening programs, which could prevent progression to renal failure.[14] However, lack of healthcare seeking behaviors and lack of health infrastructures in developing countries like Nepal, has resulted kidney diseases to be diagnosed in stages when renal replacement therapies are the only options.

Around 17 (12.3%) patients in our study gave history of working abroad, mostly in the Middle East countries, and were diagnosed of kidney disease while working abroad. Cause of CKD was not known in 13 (9.4%) of those patients. Such unexplained renal failure could be equivalent to mesoamerican nephropathy or chronic kidney disease of unknown cause (CKDu), primarily seen in young agricultural workers in Central America.[15] Poor occupational conditions with dehydration, heat stress, nutritional deficiencies, repeated infections and chemical exposures have been hypothesized to cause kidney injury in these group of patients.[15] However, these findings need further evaluation.

Fatigue and musculoskeletal pain were the commonest complaints (56.6%) followed by gastrointestinal complaints like nausea, vomiting and anorexia (50.7%) in our study. The prevalence of fatigue in advanced kidney diseases has been reported to range from 42% to as high as 89%, which has adversely affected quality of life in patients.[16] Fatigue in CKD has not been widely studied, but multiple factors like anemia, raised inflammatory cytokines and altered metabolic pathways including changes in tryptophan catabolism have been implicated in the pathogenesis of fatigue in patients of CKD.[17] Likewise, anorexia has been reported to be present in 40 to 50% patients under maintenance hemodialysis.[18] Uremia, pleotrophic effect of proinflammatory cytokines and concomitant depression have been implicated to cause anorexia in patients of advanced kidney diseases.[19] Activation of renal angiotensin aldosterone system, over activity of sympathetic nervous system, sodium retention, endothelial dysfunction and increased intracellular calcium levels are the different mechanisms resulting in hypertension in patients of CKD.[20] Around 44.8% patients had raised blood pressure in our study, despite being on antihypertensive medications. Under dosing of medications, insufficient dialysis hours, non-compliance and dietary indiscretion could be the causes for inadequately controlled hypertension in this group of patients.

Despite being relatively safe procedure, periprocedural complications are common during hemodialysis. Prabhakar et al. reported hypotension (26.1%), vomiting (14.2%), and fever (14.4%) as the commonest intradialytic complications.[21] In our study, hypotension (52.9%), fever (44.2%) and muscle cramps (37.7%) were fairly common occurrence during hemodialysis. Excessive removal of ultrafiltrate, cardiac autonomic neuropathy, and use of antihypertensive medications prior to dialysis usually resulted in intra-dialytic hypotension.[22] It could be avoided by the rational prescription for ultrafiltrate during each hemodialysis session after assessing dry weight and inter-dialytic weight gain of the patient. Dialyzer reactions and frequent blood transfusions result in febrile reactions which could be avoided with single use of dialyzer and proper disinfection techniques during reuse.[10] Rapid shift of extracellular fluid volume,

changes in plasma osmolality and dyselectrolytemia are the proposed mechanisms for muscle cramps, which tend to occur in the later hours of a dialysis session, and are more common in patients with high inter-dialytic weight gains. Dietary counseling is the first step for prevention of muscle cramps as it helps to minimize inter-dialytic weight gains so that rapid osmolar shifts during dialysis could be avoided.

More than 40% patients in our study were using erythropoietin analogs. Erythropoietin analogs were supplied free of cost by the study centers for those who were insured under 'Swasthya Beema Karyakram - Health Insurance Program' by the Government of Nepal. Regular use of erythropoietin analogs was significantly associated with higher hemoglobin levels and less frequent blood transfusions in our study (Table 6). Only 8 percent patients had hemoglobin levels above 10gm/dL. Anemia has been associated with poor quality of life, increased hospitalizations, cognitive impairment, increased cardiovascular morbidity and mortality in patients of CKD.[23] High prevalence of anemia among patients in our study could be due to multiple factors like inability to use or under dosing of erythropoietin analogs, micronutrient deficiencies, deficient iron stores or resistance to erythropoietin stimulating agents. Most of the patients in our study were economically underprivileged and the major hindrance for them to use EPO analogs was cost of treatment; thus they relied on frequent blood transfusions for correction of anemia.

Hyperphosphatemia was noted in 84.1% patients in our study which is an alarming finding, as increased phosphate levels have been linked to cardiovascular calcification, metabolic bone disease and development of secondary hyperparathyroidism in patients of chronic kidney disease.[24] Patients must be counseled regarding dietary restriction of phosphates and use of phosphate binders to correct hyperphosphatemia. Hyperkalemia was found in 29.7% patients despite regular hemodialysis in our study. Hyperkalemia is a potential threat to patient safety as it has been linked to life threatening cardiac arrhythmias and sudden death.[25] Possible causes of this complication could be dietary indiscretion and constipation, which is usually not addressed in patients of ESRD.

Limitation of this study: A major limitation was regarding the etiological diagnosis of ESRD in our study. In absence of renal biopsy, diagnosis of diabetic and hypertensive nephropathy could not be confirmed; rather the speculated diagnosis was based on clinical history of prior diabetes and hypertension with basic urine routine examination and ultrasound findings. Both the disease entity follows a prolonged evolutionary course of kidney damage to have the end result of ESRD. Different glomerular and tubular pathologies could be the reason of renal failure in patients with diabetes and hypertension, but study of those concomitant pathologies was beyond the scope of this study. This might have led to overestimation of diabetes and hypertension as cause of ESRD in our study. Another limitation of our study was that this study included patients from hemodialysis centers of two government hospitals in Chitwan district of central Nepal. However, hemodialysis service is also provided by private medical colleges in the same district, which were not included in this study.

## CONCLUSIONS

Diabetic nephropathy was the leading cause of end stage renal disease in our study. However, the cause of ESRD could not be ascertained in nearly half of the patients. Late presentation of ESRD patients to health care providers was fairly common in our study. This finding highlights the need to aware general population regarding kidney diseases so that they develop early healthcare seeking attitude; and at the same time, it is necessary to strengthen the diagnostic and therapeutic services for kidney disease patients so that they can be adequately and timely managed.

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