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Aetiology of end-stage renal disease at the National Referral Hospital of Bhutan

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ABSTRACT

Introduction: End stage renal disease (ESRD) is a late stage of chronic kidney disease (CKD) requiring chronic dialysis or renal transplant to survive. End stage renal disease is a growing problem worldwide. In Bhutan too, there are anecdotal evidence showing increasing number of ESRD patients every year, which has become a cause of serious concern for the country. **Methods:** This retrospective descriptive study was conducted at the National Referral Hospital of Bhutan, from 2019 to 2020 to find out the aetiology of ESRD in the country. The demographic information and aetiology of ESRD were collected from the past record of the patients. A total of 202 eligible ESRD patients were enrolled in this study. **Results:** The study showed that the mean age of patients was 47.3 ±13.20 years. The majority of the patients 139 (68.8%) were in the age group 24-60 years. Of the total patients, 107 (53.0%) were females. The common aetiologies of ESRD were hypertension (HTN), chronic glomerulonephritis (CGN) and Diabetes Mellitus (DM) constituting 20.8%, 12.9%, and 8.9% of the total patients respectively. In 50.0% of the patients, the aetiology of ESRD were unexplained. **Conclusions:** The most common aetiologies of ESRD were HTN (20.8%), CGN (12.9%) and DM (8.9%); in 50.0% of the patients, the aetiologies remained unexplained. The majority of ESRD patients (68.8%) in this study were from middle age group, with female predominance (53.0%).

Keywords: Aetiology; DM; ESRD; HTN; Herbal nephropathy; Unexplained aetiology.

INTRODUCTION

CKD is an irreversible, usually progressive kidney disease defined as kidney damage for 3 or more months, with structural or functional abnormality of the kidney with or without decreased glomerular filtration rate (GFR); or, GFR less than 60ml/minute/1.73m² for 3 or more months[1].Over a period of time, CKD may progress further to a point, where life is incompatible without treatment with long term dialysis or kidney transplantation called ESRD[2].

Though there are several causes of CKD/ESRD, the leading causes worldwide are DM, HTN and CGN[2,3]. The disease burden of chronic kidney disease CKD and ESRD have become a major public health problem worldwide, and continues to increase at an alarming rate[4-6]. Increasing number of affluent people all over world, contributes greatly to increasing number of life style related diseases like obesity, diabetes mellitus and hypertension, which are risk factors for CKD/ESRD[2]. This would mean that the number of people with CKD/ESRD is only going to grow further with time.

Ever growing burden of CKD/ESRD would mean increase adverse consequences associated with it, such as compromised quality of life, increased morbidity and mortality of the patients and a huge adverse socio-economic burden to patients, their family, Government and society at larg[7-9]. The brunt of the ever increasing burden of CKD/ ESRD is most felt in poor developing countries where resources are scarce and priorities many[10].

The key strategies to mitigate problems associated with CKD/ESRD are its prevention, early diagnosis, timely and appropriate treatment. This would require the baseline information on demography, and aetiologies of CKD/ESRD, which are very scarce in poor developing countries with no proper CKD/ESRD registry, including in Bhutan.

Any attempt to mitigate the problem of CKD/ESRD and its adverse impact would require a sound policy and effective intervention strategies. Adequate and complete information is indispensable for effective, appropriate policy and planning, which is currently lacking in Bhutan.

Therefore, this study was undertaken to determine the aetiologies of CKD/ESRD in the country. The findings from this study would support policy makers and planners to develop relevant policies, strategies and program realignment to effectively address the problem of ever-growing CKD/ESRD patients in the country.

METHODS

This retrospective descriptive study through record review was conducted at the National Referral Hospital of Bhutan, from

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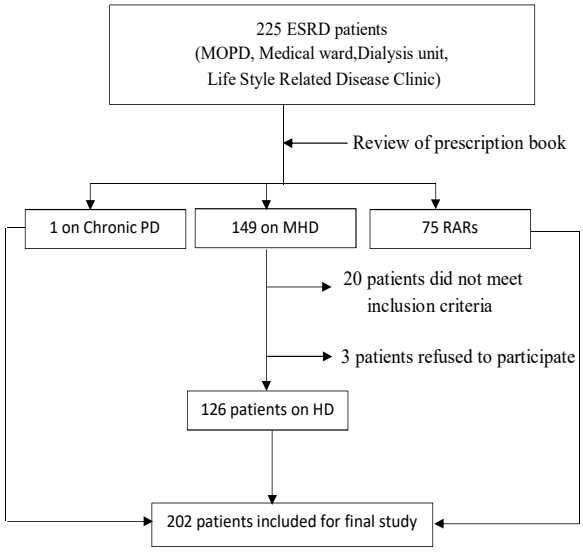
August 2019 to August 2020, to determine the aetiologies of ESRD in the country. The study population consisted of 225 patients who visited Medical Outpatient Department (MOPD), Life Style Related Disease Clinic, admitted in medical ward and undergoing Dialysis in dialysis unit. There were 149 patients on maintenance haemodialysis (MHD), 1 on chronic peritoneal dialysis (PD), and 75 renal allograft recipients (RARs). Out of 225 ESRD patients, 20 patients on haemodialysis for less than 3 months and 3 patients who refused to participate were not included in the study. Therefore a total of 202 patient were recruited for the study.The detailed patient's recruitment plan is mentioned in Figure 1 below.



PD=Peritoneal dialysis
HD=Haemodialysis
RARs= Renal allograft recipients
MOPD=Medical Outpatient Department

Figure 1. Flow chart for recruitment of patients for the study

Prior approval was obtained from Research Ethics Board of Health via Ref. No. REBH/Approval/2019/095 dated 12th may 2019. The demographic characteristics and aetiologies of ESRD, as documented in their prescription books by their treating physician, were collected and entered into EPI data version 3.1, free software. Statistical Package for Social Science (SPSS version 20.0) was used to calculate frequencies and percentages and to create statistical diagram.

RESULTS

The study enrolled 202 patients aged 15 to 85 years with mean age of 47.3 ± 13.20 years. When disaggregated by different age groups, 68.8% of them were in the 24-60 years age group, while 24.8% were above 60 years and the remaining 6.4% below 24 years age group. Of the 202 patients, 107 (53.0%) were females while 95 (47.0%) were males. The male to female ratio of ESRD patients in the study was 0.89:1 (Table 1).

Table 1. Age & Sex distribution of ESRD* patients at JDWNRH†, 2019-2020 (*n*=202)

Characteristics	Percentages (%)(*n*)
Age category(years)	
<24	6.4(13)
24-60	68.8(139)
>60	24.8(50)
Total	**100(202)**
Sex	
Male	47.0(95)
Female	53.0(107)
Total	**100(202)**

**End stage renal disease*
†Jigme Dorji Wangchuck National Referral Hospital

The study revealed that among the ESRD patients, the most common aetiology was found to be HTN (20.8%), followed by CGN (12.9%), and DM (8.9%). Other less common were herbal nephropathy (4.0%), heredofamilial (1.5%), and obstructive nephropathy (1.0%). In 50.0% of the cases, the aetiologies of ESRD was unexplained (Figure 2).

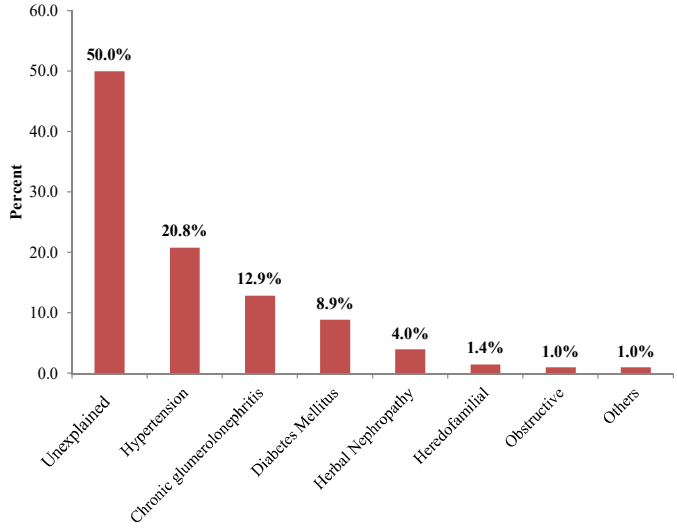


Figure 2. Distribution of aetiology of end-stage renal disease at the National Referral Hospital of Bhutan from 2019 to 2020

Of the 202 ESRD patients, 14 had undergone prior renal biopsy. Based on the biopsy report, 11(78.7) cases were diagnosed as IgA nephropathy (IgAN), one (7.1) case each for focal segmental glomerulosclerosis (FSGS), diffuse glomerulosclerosis and C3 glomerulopathy (Figure 3).

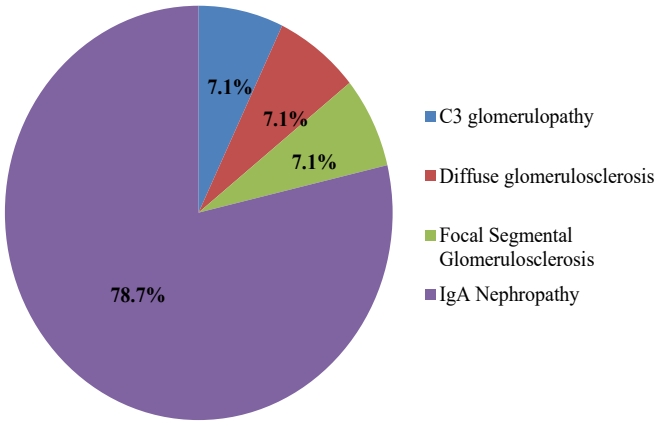


Figure 3. Distribution of aetiology of end-stage renal disease according to renal biopsy report at the National Referral Hospital of Bhutan from 2019 to 2020

DISCUSSIONS

The aetiologies of ESRD recorded in this study were those recorded by treating physicians at the time of presentation based on his/her clinical judgement supported by investigation findings. However, those aetiologies which were not mentioned by the treating physicians, were recorded as ESRD of unexplained aetiology.

The result of this study revealed that ESRD in Bhutan was almost equally distributed among males and female with slightly higher predominance in females. These findings indicate that female population in Bhutan may be at increased risk of ESRD than her male counterpart. A similar findings were reported from many studies conducted in the region[13,15,16] whereas in Bangladesh[14], the findings were opposite with male predominance. However, in one study no differences in sex was found[14]. The effect of sex on ESRD still remains a topic of controversy as there is lack of convincing data supporting a single best answer[6]. But one author explained that sex hormones may mediate the effects of gender on ESRD through alterations in the renin-angiotensin system, reduction in mesangial collagen synthesis, modification of collagen degradation, and upregulation of nitric oxide synthesis[5].

Regarding the age distribution of ESRD in the population, the mean age of the patients were found similar to that of previous studies conducted in the regions[12-16]. Prevalence of high ESRD in middle age population was linked to the fact that overall renal function deteriorates with advancing age[11]. Similarly, other insults that the patient got exposed with duration, needed a firm consideration in relating the age with ESRD[4,5]. A small minority of ESRD patients were also found in younger age group. A similar findings were also reported from Nepal[13], Bangladesh[14] and Iran[15]. The aetiologies of ESRD in younger age groups were mostly unexplained, which warrant further studies[6,8].

This study revealed that among the ESRD patients, the most common aetiology was found to be hypertension followed by chronic glomerulonephritis and diabetes mellitus. The other less common aetiologies were herbal nephropathy, heredofamilial and obstructive nephropathy. Surprisingly, half of the aetiology of ESRD remained unexplained. A similar findings were reported from previous studies[3,11-16]. In all those studies hypertension was the top non-communicable disease leading to ESRD. The pathological cascade responsible for hypertension in ESRD patients include increased extracellular volume, increased sympathetic and renin-angiotens in-aldosterone system (RAAS) activation, abnormalities in properties of the vasculature such as endothelial cell dysfunction, increased oxidative stress, arterial stiffness, and exposure to exogenous mediators such as erythropoiesis-stimulating agents (ESA) and dialysate[7,8]. Hence major efforts were directed towards controlling hypertension, prevention of hypertension and health education in general[3,6,7].

Herbal nephropathy causing ESRD was also reported in some studies[12,14] which were also found in our studies too. But the mechanism of herbal treatment causing ESRD was not explored in our study and cannot exactly put it as aetiology. But it was included, as it was the diagnosis of the treating physicians as mentioned/labelled in their prescription books. We concluded that only with proper history taking, clinical examination and thorough investigation, the diagnosis had been made. This could be an interesting and controversial topic that would require further research.

Kidney biopsy is commonly done in adult patients with massive protein leakage in urine, low blood albumin and body swelling termed nephrotic syndrome[7,10]. It is also done in children with similar presentation but resistant to steroid treatment, isolated protein and blood leakage in urine from kidney amongst others[10]. It can also be done in early stages of CKD, mostly stage[1-3], where its cause remain unexplained[10]. In our study, according to renal biopsy report, the most common aetiology of ESRD was IgA nephropathy. Few of the aetiologies were focal segmental glomerulosclerosis, diffuse glumerulo sclerosis and C3 glumerulopathy as well. Our findings were similar to other studies conducted in the region[11-15] but the number of patients who underwent renal biopsy remained significantly low in our study as the procedure was only recently started in the hospital . In half of the study patients, the aetiologies of ESRD remained unexplained. This high unexplained aetiology could likely reflect lack of diagnostic facilities, including kidney biopsy which was only started recently. A study in Brazil also found the most common aetiology of ESRD was unexplained[19], similar to the findings of our study with unexplained aetiology of ESRD exceeding any known cause. Interestingly, Stanifer and group in a study found that in most low and middle income countries, specific aetiology of ESRD is not established or unexplained[19].

This study, being the first of its kind till date in the country, an evidence based scientific data for aetiology of ESRD at the national referral hospital were generated. This data can be used for future reference, planning and policy making at all levels of administration, resource allocation, prioritization of human

resource investment, training and upgradation of knowledge and skills which would ultimately lead to better patient care and treatment.

However, this study had also some limitations too. The retrospective nature of the study prevented us from getting many important information which were not recorded in the patient's prescription book, leading to selection bias of aetiologies. As conducted at a single center, the findings may not necessarily reflect the demographic and aetiologic picture of ESRD patients of the country as a whole. Also the cause of ESRD in this study was based on diagnosis given by treating physician, in most cases without tissue diagnosis, which may have compromised the accuracy of the findings in the study. Therefore, a well-planned, prospective and multi-center study covering whole population of the country is needed in future to generate the true scientific data for the country.

CONCLUSIONS

In our conclusion we report that the most common aetiology of ESRD was hypertension affecting majority of middle aged people in the country. The burden of ESRD on patients and the government is enormous. For patients, the mental trauma, social and financial burden wears down the health more rapidly than the disease itself. For the government, the financial, human resources and other services were drained more quickly than expected. Therefore, the emphasis should be first put in place to prevent the disease taking its toll on everybody. Aggressive lifestyle related diseases advocacy and awareness programme in the country can be one solution, while prevention and timely treatment of hypertension at personal level can be another solution. Together, the measures were expected to provide some relief to already overcrowded dialysis facilities in the country, and also lessen economic impact and financial burden for the Government and the society.

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AUTHORS CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

MD: Concept, design, data collection and analysis, manuscript writing and review.

YP: Concept, design, data collection and analysis, manuscript writing and review

TT: Concept, design, data collection and analysis, manuscript writing and review

GD: Concept, design, data collection and analysis, manuscript writing and review

Author agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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None