ORIGINAL ARTICLE

COMORBIDITY BURDEN IN END STAGE RENAL DISEASE PATIENTS ON MAINTENANCE HEMODIALYSIS

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ABSTRACT

Objective: To perform an assessment of comorbidities of our hemodialysis dependent patients.

Material & Methods: This was a cross-sectional descriptive study conducted in the Institute of Kidney Diseases Hayatabad, Peshawar and Khyber Teaching Hospital, Peshawar, Pakistan. The study included 177 patients and the study duration was 04 months (December 2015 to March 2016). ESRD patients on maintenance hemodialysis were asked about their comorbid conditions. This information was recorded on a questionnaire.

Results: A total of 177 patients responded to a specially designed questionnaire asking questions about their comorbidity status. Out of these 177 patients 111 (62.7%) were male (M:F 1.7:1). The mean age for male patients was 43.1 years (SD ±14.8 and range from 18 to 70 years). While the mean age for females was 42.3 years (SD ±15.2 and range from 18 to 80 years). About 79% patients were on hemodialysis for duration of less than 03 years. Only 7.3% patients were undergoing hemodialysis at the recommended frequency of 03 or more sessions per week. All but 24.3% patients reported no emergency visits to hospital and all except 33.9% patients had no hospital admission in the previous 06 months. Around 34% patients had more than 5 emergency visits, while 37.8% patients had more than 5 admissions in the previous 06 months. Around 55.3% of patients were taking more than 5 types of drugs in a single day, while 76.7% were taking more than 3 drugs per day. Hypertension was the commonest comorbidity found in about 93.8% of patients. This was followed by cardiac diseases (46.9%) and diabetes (40.6%). Viral hepatitis was found in 21.4% patients, Infections in 12.4%, pulmonary diseases in 9.0%, and strokes were reported by 4.0% patients. Off the male patients, 67.5% (n=75) had two or more co-morbidities while 37.8% (n=42) had both Diabetes and hypertension. Off the female patients 89.3% (n=59) had two or more comorbidities while 45.4% (n=30) had both Diabetes and Hypertension.

Conclusion: Comorbidities are common in our ESRD patients. Hypertension is the most common comorbidity followed by Diabetes Mellitus and cardiac diseases. The frequency of these comorbidities is higher in our patients when compared to the international data. This could explain the higher morbidity and mortality of our ESRD patients.

Key Words: End stage renal disease, ESRD, Chronic Kidney disease, co-morbidity, Hemodialysis, CKD stage 5-D.

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INTRODUCTION

End Stage Renal Disease (ESRD) is the final stage of chronic kidney disease (CKD). End stage renal disease (ESRD) patients have multiple comorbid conditions that play an important role in determining the higher mortality rate and poor survival of Hemodialysis dependent patients. This study aimed to assess the comorbidity burden in our ESRD patients. Despite advances in the management of ESRD patients and improvements in renal replacement therapies, dialysis dependent patients have reduced life expectancy when compared to the normal general populations. The mortality rate of End-stage renal disease (ESRD) patients reported by international studies is in order of around 20% per year with a 5 year survival rate of only 33%. Cardiovascular diseases and infections are the major contributors to this high mortality.[1] The mortality rate of ESRD patients in Pakistan is reported to be around 35% in the first year.[2]

ESRD patients have multiple comorbidities which are thought to result in the increased mortality observed in this group of patients. These comorbidities include

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Diabetes Mellitus, Hypertension, Cardiovascular diseases, strokes, infections especially those of arterio-venous access, liver diseases and malnutrition.[3]

Mahmud et al in their study from Karachi, Pakistan revealed that 42.8% of their Hemodialysis patients had both Diabetes Mellitus and Hypertension at the time of initiation of Hemodialysis. It is well known that such patients are at an increased risk of having atherosclerotic vascular disease and its complications.[4] In an another study Ahmad and colleagues found that around 30% of their Hemodialysis cohort had more than one comorbidity and that these patients were most likely to have adverse events.[5]

Thus a very high percentage of our ESRD patients are expected to have multiple comorbidities and that these comorbidities contribute to the higher mortality of our ESRD patients. Better management of these comorbidities can result in significant reduction in mortality and improvement in the quality of life of ESRD patients. There is no formal record of ESRD patients in our setup. The cause of very high mortality of our ESRD patients is still not exactly known, although it can be speculated that multiple comorbidities contribute to this end. This study aimed to assess the comorbidity status of our ESRD patients. Based on the results of this study we can also comment on the general health status of our patients and the complexities of their medical management.

MATERIAL AND METHODS

This was a descriptive cross-sectional study, conducted at department of Nephrology, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar, Pakistan and Department of Nephrology, Khyber Teaching Hospital, Peshawar, Pakistan. Data for this study was collected over a period of 04 months (December 2015-March 2016) after the approval of synopsis.

The Sample size was taken to be a minimum of 177, keeping 50% proportion of frequency of Hemodialysis dependent patients (empirical value), with 95% confidence interval and 5% margin of error. The population size was taken as 325, which is approximately the total number of hemodialysis patients in these two hemodialysis centers. Consecutive, non-probability sampling technique was utilized.

All patients above the age of 18 years and both genders, being managed on maintenance Hemodialysis at these centers were included in this study. Maintenance hemodialysis was defined as hemodialysis dependency for at least three months.

Approval was obtained from the hospital research and ethical committee. All patients were counseled regarding the procedure of study and informed consent was obtained. All patients were asked to fill the prescribed proforma asking questions about different comorbidities they had in addition to hemodialysis dependent ESRD. Where ever any patient had difficulty in reading and understanding the proforma, the research assistant was available to read and explain the questions to the patient.

RESULTS

A total of 177 ESRD patients on maintenance Hemodialysis were studied in the two centers of which 111 (62.7%) patients were male. The mean age for male patients was 43.1 years (SD ±14.8 and range from 18 to 70 years). The mean age for females was 42.3 years (SD ±15.2 and range from 18 to 80 years). Comparison comorbodity burden with other regions is shown in Table 1

The duration for which individual patients were on maintenance hemodialysis was asked as an indicator of long term survival of patients (Figure 1). About 79% patients were on hemodialysis for duration of less than

Table 1: Comparison of comorbidity burden with other regions

Comorbidity	Our patients %	Europe[8] %	Japan 8 %	US 8 %
Hypertension		72.7	55.9	83.2
Cardiac diseases	46.9	CAD 29.4	19.2	49.8
		CHF 25.0	6.1	45.8
Hepatitis	21.4	15.6	15.6	9.8
Diabetes	40.6	20.1	25.6	45.7
Strokes	4	13.7	12.5	18.4
Pulmonary diseases	9	10.7	1.4	13.0

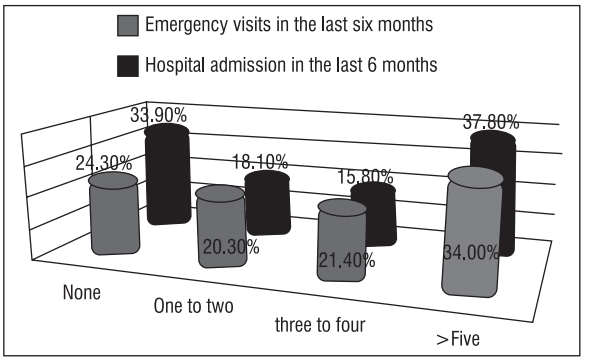

Figure 1: Medical consultations

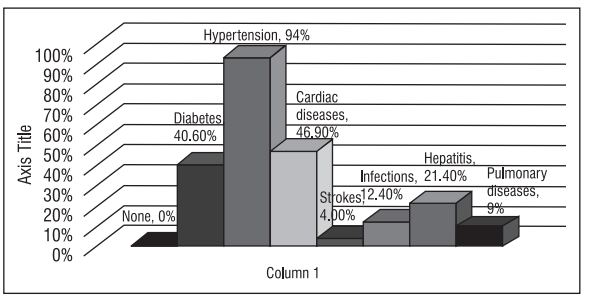

Figure 2: Comorbidities

03 years. The number of hemodialysis sessions that the patients underwent was also recorded as a measure of dialysis adequacy. The percentage of patients undergoing 03, or more than 03 sessions per week was 5.6% and 1.7% respectively. The majority (75.7%) of patients were undergoing 02 session of hemodialysis per week. For 16.9% patients the weekly hemodialysis frequency was 01 or less per week. Thus only 7.3% patients were undergoing hemodialysis at the recommended frequency of 03 or more sessions per week.

The number of emergency visits and hospital admissions in the past six months can indicate the brittleness of health and indicate complex comorbidity status of these patients. Only 24.3% patients had no emergency visits and 33.9% patients had no hospital admissions in the past 6 months. (Figure 1) The number of different types of drugs taken by a patient was taken as an indirect estimate of comorbidity status of the patients. Only 8.5% patients were not taking any additional drug. Around 14.7% patients were taking 1-2 drugs, 21.4% patients were taking 3-4 drugs, and 55.3% of patients were taking more than 5 types of drugs in a single day.

These patients were also specifically asked about different comorbid diseases. Off the male patients, 67.5% (n=75) had two or more co-morbidities while 37.8% (n=42) had both Diabetes and hypertension. Off the female patients 89.3% (n=59) had two or more comorbidities while 45.4% (n=30) had both Diabetes and Hypertension. Figure 2.

DISCUSSION

In our study the mean age for male and female patients was 43.1 years and 42.3 years respectively. Other studies in Indo-Pak subcontinent have reported similar mean age.[6,7] This age is significantly younger than that reported for western populations' i.e. 60.2 years for Europe and 60.5 years for USA.[8] Thus our patients are landing into Dialysis dependency at a much younger age as compared to the patients from more developed countries.

A great majority (79%) of patients were on HD for duration of less than 3 years. This suggests poor long term survival of our dialysis dependent patients. Goodkin et al reported the mean duration of Hemodialysis of 5.1 years for Europeans, 7.4 years for Japanese, and 3.8 years for Americans.[8]

A great majority (92.7%) of patients were undergoing hemodialysis at a frequency of two or less hemodialysis sessions per week. The usual duration of hemodialysis is kept under 03 hours. These statistics highlight the common practice of rationing of hemodialysis in our centers. Kidney Disease Outcome Quality Initiative (KDOQI) guidelines 2015 update, recommend either short (less than 3 hours) duration frequent HD (5-7 sessions per week), OR Long (more than 5-8 hours) 3-6 sessions per week as alternative to Conventional regimen (in-center, thrice weekly sessions, a minimum of 03 hours per session).[9] Thus majority of our patients are under dialyzed. Chandrashekar et al in their study found that patients undergoing twice weekly HD had a lesser chance of survival as compared to those with 03 sessions a week.7 This inadequate hemodialysis could be the most important factor responsible for increased number of comorbidities and higher mortality of our patients.

Questions regarding emergency visits and hospital admissions in the recent past were asked as surrogate markers for additional health related issues. All but 24.3% patients reported no emergency visits to hospital in the past 06 months. Similarly all except 33.9% patients had no hospital admission in the previous 06 months. Moreover 34% patients had more than 5 emergency visits, while 37.8% patients had more than 5 admissions in the previous 06 months. Thus around one third of our dialysis dependent patients were in a

very friable condition. It can be assumed that these patients have the highest short term mortality and very poor long term survival.

Frequent hospital admissions, especially the unplanned emergency hospitalizations represent the overall poor condition of the patients with multiple comorbidities. Such friable patients are likely ones to have poor quality of life and prognosis.[10] The common causes of frequent admissions include dialysis access issues, cardiovascular diseases including myocardial infarction and cardiac failure, infections, volume overload and stroke.[11,12]

Mathew and colleagues in their literature review found the readmission rate, ranging from 12% to 90% in different studies.[12] In another study the rate of hospitalization among ESRD patients was around 2 admissions per patient year, while one-third patients had more than one admission per year.[13] Frequent hospitalizations predispose to malnutrition and acquisition of hospital acquired infections that can poorly affect mortality of already malnourished and immuno suppressed patients. Frequent hospitalizations also have cost effects especially in our society where patients directly bear all the cost of admission. Preventing frequent hospitalizations is expected to improve health outcomes and reduce the cost. The measures that are thought to reduce frequent hospitalizations in ESRD patients include frequent home visits by physicians[10], correction of anemia to hemoglobin of more than 10gm/dl by addition of or increasing the dose of EPO, administration of Vitamin D, modification of target dry weight after index hospitalization, improvement of nutritional status, and avoidance of central catheters.[13]

Only 8.5% patients were not taking any additional drugs. 55.3% patients reported taking 5 or more drugs each day. This higher number of drug intake suggests the presence of multiple co-morbidities. In an interesting study the average types of medications taken each day by ESRD patients was found to be 4.7 $\pm$ 1.8. The same group found that higher number of drugs was related with poor outcome and probably reflected advanced ESRD and higher comorbidities.[14]

When asked specifically about the co-morbidities, the commonest comorbidity was Hypertension which was present in 94% of patients. This was followed by cardiac diseases (46.9%) and Diabetes (40.6%). Viral Hepatitis was also common in our patients and was reported by 21.4% of patients. A comparison with patients from other regions is given in the Table 1.

In another study Chae described Diabetes with complications to be the most common comorbidity found in 51.1% of their patients. This was followed by Cardiac diseases at 18%.[15] Thus a higher percentage of our patients have comorbid conditions when compared to other registries. Hypertension, Diabetes Mellitus and Hepatitis being much more prevalent in our patients than other regions.

Hypertension in ESRD patients is mainly dependent on the persistently Hyper-volumic status of ESRD patients. This volume control cannot be achieved without adequate and timely hemodialysis. Since it is common practice in our setup to prescribe twice weekly Hemodialysis instead of the recommended thrice weekly sessions, most of our patients are in a persistently volume overloaded state and this can be the explanation of the very high prevalence of hypertension in our ESRD patients.

It is well known that Diabetes Mellitus is much more common in South-east Asia as compared to the rest of the world. The body habitus and diet of our population predisposes to development of Diabetes. Due to poor control, many diabetics develop CKD and therefore Diabetes Mellitus is one of the major causes of ESRD in our population. This explains the higher prevalence of diabetes in our patients.

Viral hepatitis is more prevalent in our general population than in the western world. Likewise the prevalence of viral hepatitis in our ESRD patients is also higher than other ESRD populations. However not all the risk is due to the increased prevalence in the general population. Frequent blood transfusions, repeated use of injections, poor sanitation and sterilization practices at dialysis units are also responsible for this higher prevalence of viral hepatitis in our ESRD patients.

In our study around 67.5% (n=75) of the male patients had two or more co-morbidities while 37.8% (n=42) had both Diabetes and hypertension. Of the female patients 89.3% (n=59) had two or more co-morbidities while 45.4% (n=30) had both Diabetes and Hypertension. In a study on CKD patients, Tonelli et al found that around 25% of their patients had 3 or more comorbidities while 7% of their patients had 5 or more comorbid diseases. This clarifies the multiple comorbidities found in ESRD patients contributing together to a poor prognosis.

In another study by Gomez et al, around 47.6% ESRD patients had Diabetes Mellitus, 52.9% patients

had cardiovascular diseases, 16.7% patients had chronic lung diseases, and 12.1% patients had suffered strokes. Additional 20% patients had peripheral vascular disease and 6.5% patients had neoplastic diseases.[16] We did not study these last two diseases in our patients.

Clearly apart from a reduced prevalence of strokes, our ESRD patients have a high prevalence of all the other major co-morbidities as compared to other regions. This may be due to higher prevalence of Diabetes and Hypertension in our general sub-continental population, inappropriate management of the risk factors, inadequate hemodialysis dose and poor compliance and lack of affordability. The higher burden of co-morbid conditions is associated with poor outcome and a high mortality in CKD and ESRD patients.[17,18] The high prevalence of these co-morbidities in our patients reflects into poor long term survival of our patients and is expected to contribute significantly to health cost of our patients.

It is important to note that these comorbidities do not appear only in advanced CKD stage of ESRD. In fact the high comorbidity burden is found in all stages of CKD. In a study by Fraser et al, CKD stage 3 patients were assessed for the presence of comorbid conditions. Only 04% of the total 1741 patients were found to have no co-morbidities while nearly 70% patients had 2 or more comorbidities.[19] Thus the strategies aimed at minimizing mortality, improving the prognosis and survival of CKD patients should be initiated in the initial CKD stages. This will ultimately translate into lesser comorbidity burden in ESRD patients and thus better survival of these patients.

Multiple comorbidity indices have been developed to assess, quantify and compare the effects of co-morbid conditions. These indices include The Charlson Comorbidity Index (CCI)[20] and End-Stage Renal Disease Comorbidity Index (ESRD-CI)[21]. These indices can and should be utilized to quantify the comorbidity burden, predict and compare mortality and implement strategies to minimize these comorbidities.

CONCLUSION

Hypertension is the commonest comorbidity followed by Diabetes Mellitus and cardiovascular diseases. These comorbid conditions are expected to contribute significantly to the poor survival of our hemodialysis patients.

LIMITATIONS

The major limitation of our study is that it is a questionnaire based data collection rather than scrutiny of hard data provided by the medical records. It involved asking the questions from the patients about other diseases that they had. This is always subject to reporting bias.

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AUTHOR'S CONTRIBUTION

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

Mahmood MBUR: Concept, design, data collection.

Khan AZ: Bibliography and overall supervision.

Ikram T: Tabulation and designing.

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