

A STUDY ON THE CLINICO-AETIOLOGICAL PROFILE OF PATIENTS WITH CHRONIC KIDNEY DISEASE IN NORTH-EAST INDIA: A HOSPITAL BASED STUDY

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ABSTRACT

BACKGROUND

The exact prevalence of CKD in India is not known due to lack of regular national registry data and is provided only by small observational studies or personal experiences, and the quality of data is quite uneven. This study was undertaken with a view to throw some light on the present clinical and aetiological profile of CKD in this part of the country. We tried to find out, retrospectively, the possible aetiology and special emphasis on the history of intake of indigenous medicines in this part of the country.

METHODS

This study is cross-sectional, retrospective and hospital based. The study was conducted at Medicine and Nephrology Departments of Assam Medical College and Hospital, Dibrugarh, Assam for one year starting from 1st September 2014 to 31st August 2015. Patients below 13 years, renal transplant recipients, pregnant women, patients with acute kidney injury (AKI) were excluded from the study. Informed consent was taken from all the patients. The patients were evaluated from detailed history and clinical examination. The history also included enquiry for use of herbal medications. All relevant lab and imaging investigations were recorded.

RESULTS

A total of 105 cases were taken up randomly for the study. The study showed male preponderance M:F ratio 1.6:1. The age of the cases ranged from 15 years to 78 years and the mean age was 47.70±17.58. The most common symptom was easy fatigability, with 93 cases (88.57%) and pallor (91 cases, 86.67%) was the most common clinical finding. Anaemia was found in all the patients. The aetiological incidence in the present study was highest for Diabetic Nephropathy (36.2%) followed by the Idiopathic group (16.8%), Chronic Glomerulonephritis (CGN) (15.2%), Hypertensive Nephropathy (11.4%) and Chronic Interstitial Nephritis (CIN) was found in 8.6%, obstructive uropathy in 4.9% of cases while Lupus Nephritis was found in 3.8% of cases. Polycystic Kidney Disease (PKD) was found in 3 patients (3.1%). 30.5% patients had history of intake of indigenous medicine at some point of time. Category wise, the prevalence of indigenous medications use was highest among the patients with chronic interstitial nephritis (80%).

CONCLUSION

In the present study, Diabetic nephropathy emerged as the commonest cause of chronic kidney disease (CKD) in this part of India, followed by the Idiopathic group of patients. This is in line with the latest Indian CKD registry data (2012). From this small study of only 105 patients, it is difficult to draw a definite conclusion regarding the aetiological profile. However, a larger longitudinal study will be required to substantiate the above findings. In this study, quite a significant number of patients had history of indigenous or herbal medications.

KEYWORDS

Aetiological Profile, CKD, Herbal Medication Use.

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INTRODUCTION: Chronic Kidney Disease [CKD] is a worldwide health problem. According to the WHO Global Burden of Disease Project, diseases of the kidney and the urinary tract contribute to global burden with approximately 850,000 deaths every year and 115,010,107 disability adjusted life years [DALYs], at present is the 12th leading cause of death.^[1]

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Chronic Kidney Disease is defined by the National Kidney Foundation as either kidney damage or a GFR less than 60 mL/minute/1.73 m² for 3 months or more.^[2] Kidney damage is defined by pathological abnormalities or markers of kidney. The exact prevalence of CKD in India is not known due to lack of regular national registry data and is provided only by small observational studies or personal experiences, and the quality of data is quite uneven.^[3] There is definite lack of information available on prevalence, incidence and outcome of CKD in India. However, the creation of CKD registry by Indian Society of Nephrology (ISN) in 2005 has contributed to some of the data.^[4]

There are only three population based studies in India- Mani MK [2005], Agarwal SK, Dash SC [2005] and Modi GK, Jha V [2006].^[5-7] The prevalence rate of CKD according to Mani MK [2005] and Agarwal SK [2005] were 0.86% and 0.79% respectively. According to Modi GK and Jha V [2006], the average crude and age adjusted incidence rate of ESRD ranged from 151 to 232 per million population respectively. The uses of alternative and indigenous systems of medicine are popular amongst the poorer sections of society in the developing world since time immemorial. Their use in the developed world has also increased in recent times. A study conducted by Guh_JY et al in Taiwan showed that the use of herbal medications was associated with risk of CKD.^[8]

This study was undertaken with a view to throw some light on the present clinical and aetiological profile of CKD in this part of the country. We tried to find out, retrospectively, the possible aetiology and special emphasis on the history of intake of indigenous medicines in this part of the country.

MATERIALS AND METHODS: The design of this study is cross-sectional, retrospective and hospital based. A total of 105 cases were taken up for the study by random sampling. The study was conducted at Medicine and Nephrology Departments of Assam Medical College and Hospital for one year starting from 1st September 2014 to 31st August 2015. Patients below 13 years, renal transplant recipients, pregnant women, patients with acute kidney injury (AKI) were excluded from the study. Informed consent was taken from all the patients. The patients were evaluated from detailed history and clinical examination. The history also included enquiry for use of herbal medications. A detailed clinical examination of all the patients was done. Past medical records were reviewed whenever available. All routine investigations to detect pathological abnormalities in blood, urine, biochemistry, imaging studies along with 24-hour urinary protein were done. Special investigations for immunology and serum protein electrophoresis etc. were done according to the requirement.

Chronic glomerulonephritis (CGN) and Chronic interstitial nephritis (CIN) were to be differentiated based on the 24-hour urinary protein.^[9] If it was >1.5 g, then it was considered as CGN. The ultrasound findings of bumpy kidney contours or scarred kidneys were also suggestive of CIN. Hypertensive Nephropathy was diagnosed in patients who had history of longstanding hypertension (more than a decade) with evidence of end-organ damage like left ventricular hypertrophy (LVH) on ECG or Echocardiography, CVA (past or present), abnormal renal function test and anaemia.

Lupus nephritis was diagnosed clinically in known SLE cases with evidence of proteinuria, hypoalbuminemia, oedema, and elevated serum creatinine levels. Diabetic Nephropathy was diagnosed in diagnosed cases of Diabetes Mellitus with albuminuria, unremarkable urinary sediment, and the presence of retinopathy. Other urinary tract diseases were excluded in these patients. Body Surface Area (BSA) was calculated using Mosteller's formula.^[10]

$$BSA = \sqrt{[\text{Height}(\text{cm}) \times \text{Weight}(\text{Kg})]/3600}$$

Estimation of GFR was by using Cockcroft-Gault equation and then, it was adjusted for BSA, to give eGFR per 1.73 m².

COCKCROFT-GAULT EQUATION
Cr Clearance = $[\text{140} - \text{age}(\text{y})] \times \text{Body weight}(\text{Kg}) \times 0.85$ (If female) $72 \times \text{S. creatinine}(\text{mg/dL})$

Data analysis was done using Microsoft Office Excel 2007.

RESULTS AND OBSERVATIONS: The present study was conducted at the Medicine and Nephrology Departments of Assam Medical College and Hospital, Dibrugarh, for a period of one year from 1st September, 2014 to 31st August, 2015. A total of 105 cases were taken up randomly for the study. The sex ratio in the present study revealed that males were more affected than the females. There were 65 males and 40 females. The ratio of male: female was 1.62:1. (Table 1 & Figure 1). The age of the cases ranged from 15 years to 78 years and the mean age was 47.70±17.58.

As shown in Table 3, the most common symptom is easy fatigability, with 93 cases (88.57%) followed by reduced urine output (76 cases, 72.38%). Swelling (of legs, face and abdomen) and GI symptoms (anorexia, nausea vomiting and hiccups) were found in equal frequency with 75 cases each. Pallor (91 cases, 86.67%) was the most common clinical finding in the present study, followed by pedal oedema (82 cases, 78%) and Hypertension (71 cases, 67.6%) (Table 4; Fig. 4). In the present study, anaemia was present in all the cases. The haemoglobin level ranged from 3 g/dL to 10.2 g/dL with a mean of 6.85±1.6 g/dL. As shown in the Table 6, majority (50.5%) of the cases had haemoglobin level in between 6 and 8 g/dL. A total of 28 cases (26.7%) had haemoglobin level below 6 g/dL. One case had haemoglobin level above 10 g/dL (Table 5).

The 24-hour urinary protein level ranged from 300 mg to 3000 mg with a mean of 1045.71±797.14 mg. Majority of the cases had 24-hour urinary protein excretion between 1001 and 1500 mg (42.86%) [Table 6]. In the present study, the mean sizes of the right and left kidneys were 9.15±1.81 cm (range 5.6-12.3) and 9.07±1.78 cm (range 6.1-12.3) respectively. The mean kidney sizes were greater amongst the diabetic cases (mean sizes 11.0±0.65 cm and 10.9±0.58 cm for the right and left kidneys respectively) (Table 7).

The aetiological incidence in the present study was highest for Diabetic Nephropathy (36.2%) followed by the Idiopathic group (16.8%), Chronic Glomerulonephritis (CGN) (15.2%), Hypertensive Nephropathy (11.4%) and Chronic Interstitial Nephritis (CIN) was found in 8.6%, obstructive uropathy in 4.9% of cases while Lupus Nephritis was found in 3.8% of cases. Polycystic Kidney Disease (PKD) was found in 3 patients (3.1%) (Table 8, Figure 5). From Table 9, it can be seen that Diabetic nephropathy is the commonest cause in both male and female cases accounting with 21 and 17 cases respectively. All the causes of CKD were more in the male cases except for Lupus Nephritis.

Diabetic Nephropathy was the commonest cause of CKD in this study. All the cases had Type 2 Diabetes mellitus. DN

was most common in the age group of 43-52 years with 11 out of 38 cases (Table 10). Males (55.3%) outnumbered females (44.7%). Idiopathic cases and patients with CGN were commonly found in the younger age groups (<32 years). Hypertensive nephropathy was commonly found in the older age groups (>52 years). Chronic Interstitial Nephritis was almost equally distributed among the age groups (Table 10). Patients with obstructive uropathy were mainly in the middle age group (43–62 years). Lupus nephritis was found in 4 cases. All of them were females. The age ranged from 15 to 36 years. The duration from diagnosis of SLE to development of nephropathy ranged from 1 to 3 years. Three cases of Polycystic Kidney Disease (ADPKD) were seen in the study.

The eGFR in the present study ranged from 5.4 to 51.5 mL/min/1.73m² of BSA with a mean of 20.24±11.35 mL/min/1.73m² BSA. Majority (41%) of patients were in Stage 5 CKD, 34.2% patients were in Stage 4 CKD and 22.9% patients in CKD stage 3. Only 2 patients were found in CKD stage 2 (Table 12; Fig. 7). As shown in Table 13 and Figure 8, a total of 32 out of 105 cases, i.e. 30.5% had history of intake of indigenous medicine at some point of time. Category wise, the prevalence of indigenous medications use was highest among the patients with chronic interstitial nephritis (80%). The prevalence of indigenous medication use was almost equal in the Hypertensive Nephropathy and CGN groups, with 43.5% and 45.5% respectively, of cases giving positive history. In the Diabetic Nephropathy group, 26.31% had history indigenous medications.

Sex	No. of Cases	Percentage (%)
Male	65	62%
Female	40	38%
Total	105	100%

Table 1: Showing Sex Distribution

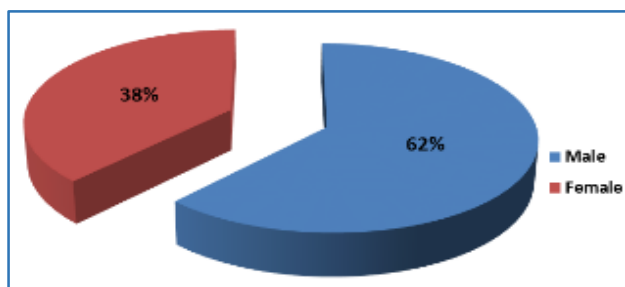


Fig. 1: Pie Diagram Showing Sex Distribution

Age-Groups (Y)	No. of Cases	Percentage (%)
13-22	12	11.43%
23-32	17	16.2%
33-42	22	20.9%
43-52	16	15.24%
53-62	18	17.14%
63-72	13	12.38%
>72	7	6.7%
Total	105	100%

Table 2: Showing Age Distribution of the Patients

Symptoms	No. of Cases	Percentage
Easy fatigability	93	88.75%
Reduced urine output	76	72.38%
GI symptoms (Anorexia, nausea, vomiting & hiccups)	75	71.42%
Swelling (Face, legs or abdomen)	75	71.42%
Body ache	44	41.90%
Difficulty in breathing	22	20.95%
Easy bruising	13	12.38%
Altered sensorium	11	10.47%
Seizure	4	3.8%
Haematuria	2	1.9%

Table 3: Showing the Symptoms

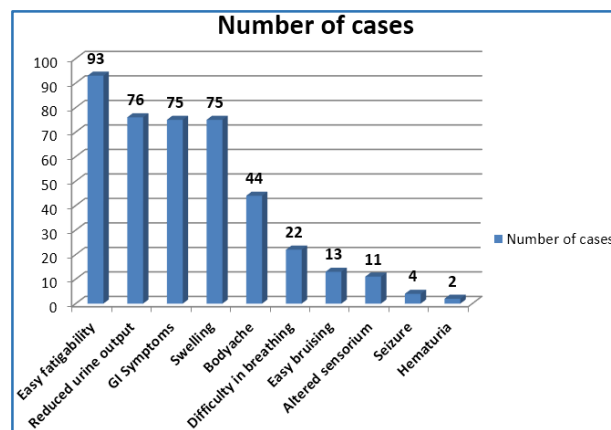


Fig. 2: Showing the Symptoms

Clinical Findings	No. of cases	Percentage
Pallor	91	86.67%
Pedal oedema	82	78%
Hypertension	71	67.61%
Peripheral Neuropathy	33	31.42%
Ascites	27	25.71%
Dermatological changes (hyperpigmentation, petechiae, ecchymosis)	26	24.76%
Acidotic breathing	19	10.09%
Chest creps/rales	17	16.19%
Pericardial rub	9	8.57%
Pleural rub	7	6.67%
Cyanosis	7	6.67%

Table 4: Showing the Clinical Findings

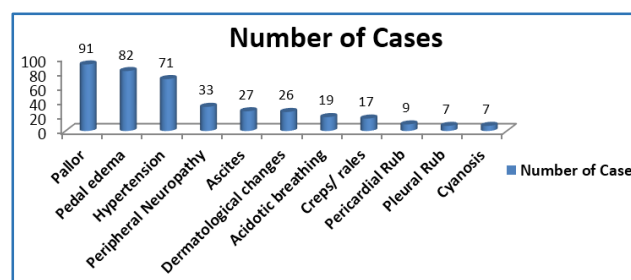


Fig. 3: Showing the Clinical Findings

Haemoglobin level (g/dL)	No. of Cases	%
<6	28	26.7%
6-8	53	50.5%
8.1-10	23	21.90%
>10	1	0.9%
Total	105	100%

Table 5: Showing the Haemoglobin Levels

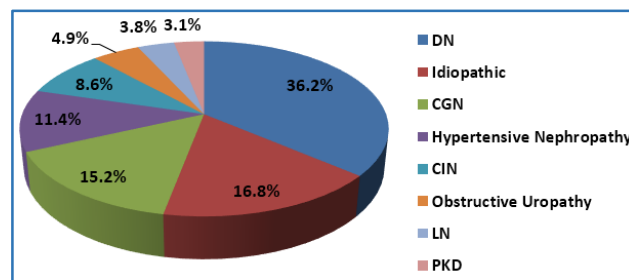


Fig. 4: Showing aetiological Diagnosis

24-Hour Urinary Protein (mg)	No. of Cases	%
<500	23	21.90%
500-1000	12	11.43%
1001-1500	45	42.86%
1501-2000	18	17.14%
>2000	7	6.67%
Total	105	100%

Table 6: Showing 24 hours Urinary Protein Levels

Etiological Diagnosis	Male		Female		Total
	No. of Cases	%	No. of Cases	%	
Diabetic Nephropathy	21	55.3%	17	44.7%	38
Idiopathic	13	72.2%	5	27.8%	18
Chronic Glomerulonephritis	10	62.5%	6	37.5%	16
Hypertensive Nephropathy	9	75.0%	3	25.0%	12
Chronic Interstitial Nephritis	7	77.8%	2	22.2%	9
Obstructive Uropathy	3	60.0%	2	40.0%	5
Lupus Nephritis	0	0.0%	4	100.0%	4
Polycystic Kidney Disease	2	66.7%	1	33.3%	3
Total	65	61.9%	40	38.1%	105

Table 9: Showing aetiological Incidence in Male and Female

Kidney Size (cm)	Right Kidney		Left Kidney	
	No. of cases	%	No. of cases	%
5-7.5	21	20%	24	22.84%
7.6-8.5	29	27.6%	26	24.8%
8.6-9.5	13	12.3%	16	15.24%
9.6-10.5	11	10.5%	8	7.62%
10.6-11.5	24	22.9%	25	23.8%
>11.5	7	6.7%	6	5.7%
Total	105	100%	105	100%

Table 7: Showing the Ultrasound Kidney Size (Length)

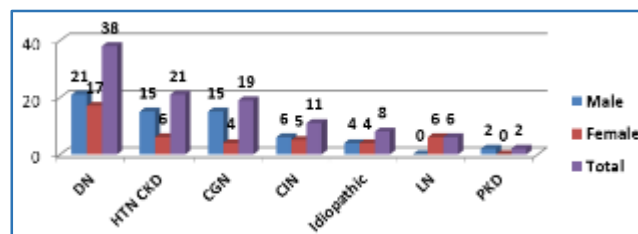


Fig. 5: Showing Etiology in Male and Female

Aetiological Diagnosis	No. of cases	%
Diabetic Nephropathy	38	36.2%
Idiopathic	18	16.8%
Chronic Glomerulonephritis	16	15.2%
Hypertensive Nephropathy	12	11.4%
Chronic Interstitial Nephritis	9	8.6%
Obstructive Uropathy	5	4.9%
Lupus Nephritis	4	3.8%
Polycystic Kidney Disease	3	3.1%
Total	105	100%

Table 8: Showing aetiological Incidence

Age Group	DN	Idiopathic	CGN	Hypertensive Nephropathy	CIN	Obstructive Uropathy	LN	PKD
13-22	0	3	6	0	1	0	2	0
23-32	1	8	6	0	1	0	1	0
33-42	8	7	4	0	2	0	1	0
43-52	11	0	0	1	1	3	0	0
53-62	8	0	0	5	1	2	0	2
63-72	6	0	0	4	2	0	0	1
>72	4	0	0	2	1	0	0	0
Total	38	18	16	12	9	5	4	3

Table 10: Showing Aetiology in Different Age Groups

Age Group	DN	Idiopathic	CGN	Hypertensive Nephropathy	CIN	Obstructive Uropathy	LN	PKD
13-22	0	3	6	0	1	0	2	0
23-32	1	8	6	0	1	0	1	0
33-42	8	7	4	0	2	0	1	0
43-52	11	0	0	1	1	3	0	0
53-62	8	0	0	5	1	2	0	2
63-72	6	0	0	4	2	0	0	1
>72	4	0	0	2	1	0	0	0
Total	38	18	16	12	9	5	4	3

Table 11: Showing Aetiology in Different Age Groups

Stage of CKD	eGFR (mL/min/1.73 m ² of BSA)	No. of Cases	Percentage %
Stage 1	≥ 90	0	0
Stage 2	60-89	2	1.8%
Stage 3	30-59	24	22.9%
Stage 4	15-29	36	34.2%
Stage 5	<15	43	41.0%
Total		105	100%

Table 12: Showing the Stages of CKD

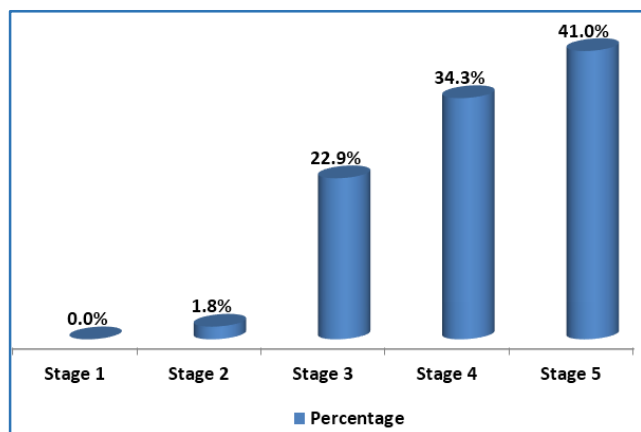


Fig. 6: Showing the Stages of CKD

Diagnosis	Indigenous Medication Present	Total Cases	Percentage
DN	10	38	26.3%
Idiopathic	0	18	0.0%
CGN	7	16	43.8%
Hypertensive Nephropathy	8	12	45.5%
CIN	5	9	80.0%
Obstructive Uropathy	2	5	40.0%
LN	0	4	0.0%
PKD	0	3	0.0%
Total	32	105	30.5%

Table 13: Showing the Prevalence of Use of Indigenous Medicine among the Different Aetiological Groups

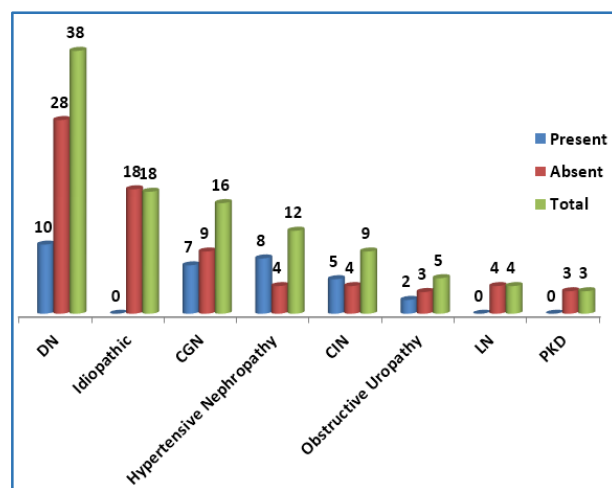


Fig. 7: Showing the Prevalence of Indigenous Medication Use among the Different Aetiological Groups

Studies	Mean Age (Years)
Varma PP et al (1999) ¹¹	41.19
Bhowmick D et al (1999) ¹²	46.4±16.6
Talwar et al (2002) ^[13]	44.6
Agarwal SK et al (2005) ^[6]	42±13
Present Study	47.70±17.58

Table 14: Age Comparison with Other Studies

Studies	Mean Hb level (g/dL)
Varma et al (1999) ¹¹	7.6
Bhowmick et al (1999) ^[12]	6.5±1
Talwar et al (2002) ^[13]	7.1
Present study	6.85±1.6

Table 15: Hb Comparison with Other Studies

DISCUSSION: The age of the cases ranged from 15 years to 78 years and the mean age was 47.70±17.58 years. The present study is comparable to the studies of Bhowmick D et al (1999)^[12] and Talwar et al (2002)^[13] (Table 14). In the present study, 62% were males and 38% were females. The 5th Annual Report of CKD Registry of ISN showed 70.3% preponderance in males. In the present study, anaemia was present in all the cases. The haemoglobin level ranged from 3 g/dL to 10.2 g/dL with a mean of 6.85±1.6 g/dL. Majority (50.5%) of the cases had haemoglobin level in between 6 and 8 g/dL.

This is in concordance with the other studies as shown in Table 15. Among the clinical features, the most common symptom is easy fatigability (88.57%) followed by reduced urine output (72.38%).

Swelling (of legs, face and abdomen) and GI symptoms (anorexia, nausea vomiting, hiccups and melena) were found in equal frequency (71.42%). Talwar et al^[13] found oedema (96%), Dyspnoea (70%), anorexia, nausea and vomiting (63%) and oliguria (55%) as the major symptoms. In the present study, pallor (86.67%), pedal oedema (78%) and hypertension (67.6%) were the most common clinical findings. (Table 4). According to the 5th Annual report of CKD Registry of ISN, 74.7% had hypertension out of 45,885 cases. Anaemia was present in all the cases in this study. The haemoglobin level ranged from 3 g/dL to 10.2 g/dL with a mean of 6.85±1.6 g/dL. Majority (50.5%) of the cases had haemoglobin level in between 6 and 8 g/dL.

Majority of patients in this study were in CKD Stage 5 (41%) almost comparable to the latest Indian CKD Registry Data 2012 Rajapurkar MM et al^[14] where 48% patients were in CKD Stage 5.^[12] Diabetic nephropathy (DN) had the highest incidence at 36.2%. The mean duration of diabetes was 6.97±4.5 years (range 2-20 years) in patients of Diabetic Nephropathy. According to a study conducted by Agarwal, Dash et al in 2005 at Delhi, DN as the commonest cause accounted for 41% of cases.^[6] The 5th Annual report of CKD Registry of ISN showed DN accounting for 31.2% of cases as the commonest cause of CKD.^[11] Previous studies conducted by MK Mani et al (1993)^[15] and Mittal S et al (1997)^[15] showed DN to be the cause in 26.76% and 23.2% cases respectively and was the second commonest cause in their studies. In 16.8% patients, no cause for CKD could be found which were labelled as Idiopathic.

There was also no history of use of any herbal medications in these patients. This is comparable to the data from the Indian CKD Registry (16%).^[12] CGN was the third commonest cause found in 15.2% cases. Studies by Mani MK et al (1993)^[15] and Agarwal, Dash et al (2005)^[6] have also placed CGN as the third commonest cause of CKD accounting for 18.20% and 16% respectively. The 5th Annual Report of CKD Registry of ISN in 2010 also placed CGN in the third position accounting for 13.8% of the cases.^[11] This is also comparable to the Indian CKD Registry.^[12] which is 14%. However, Mittal S et al (1997)^[16] and Reshi AR et al (1999)^[17] have placed CGN as the commonest cause in their studies, accounting for 28.6% and 32.7% respectively.

Hypertensive nephropathy (HN) was the fourth common cause (11.4%). Agarwal, Dash et al (2005)^[6] also found HN as the second commonest cause of CKD in their study, accounting for 22% of the cases. However, studies of MK Mani et al (1993)^[15] and Mittal S et al (1997)^[16] placed HN (benign nephrosclerosis) in the 4th and 5th position accounting for 10.06% and 4.1% respectively. The 5th Annual CKD Registry of ISN report, HN accounted for 12.8% cases.^[11] HN was found in 13% in the latest Indian CKD registry data.^[12] The mean duration of hypertension was 12.62±2.38 years (range 10-20 years). All 12 patients had history of irregular treatment. Chronic interstitial nephritis

was found in 8.6% patients who had chronic history of intake of NSAIDs and also herbal medications (80%).

A study by Mani MK et al (1993)^[15] ranked CIN (27.85%) as the commonest cause of CKD. Mittal S et al (1997)^[16] Sakhuja V et al (1994)^[18] showed the incidence as 14%, 16.5% respectively. However, the studies of Reshi AR et al (1999)^[17] and Agarwal SK, Dash et al (2005)^[6] have shown the incidence rate to be comparatively low with 5.6% and 5.4% respectively. The 5th Annual Report of CKD Registry of ISN showed that Tubulointerstitial diseases and Obstructive Uropathy accounted for 7% and 3.4% respectively.^[11] 4 (3.8%) patients had lupus nephritis and 3 (3.1%) had polycystic kidney disease (ADPKD).

Some 30.5% had history of intake of indigenous medicine at some point of time. Category wise, the prevalence of indigenous medications use was highest among the patients with chronic interstitial nephritis (CIN) (80%). In 2007, Guh JY, Chen HC et al from Taiwan found that herbal therapy was independently and positively associated with CKD.^[3] Another study in China in 2009 by Ming-Nanlai, Jung-Nienlai et al has shown that herbal medications were associated with the development of CKD.^[18]

CONCLUSION: In the present study, diabetic nephropathy emerged as the commonest cause of chronic kidney disease (CKD) in this part of India followed by the Idiopathic group of patients. From this small study of only 105 patients, it is difficult to draw a definite conclusion regarding the aetiological profile. However, a larger longitudinal study will be required to substantiate the above findings. Majority of the patients were in CKD stage 5 indicating the insidious nature of the disease with late presentation and referral. Ingestion of indigenous medicines is likely an important factor, either alone or in combination with other aetiological factors, in the pathogenesis of certain patients with CKD in this region.

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