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PREVALENCE AND ASSOCIATED RISK FACTORS AMONG CHRONIC KIDNEY DISEASE (CKD) PATIENTS IN MIRPUR, AJK

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ABSTRACT

This paper explored chronic kidney disease (CKD) risk factors and their occurrence in patients of all ages who receive treatment in different Hospitals of District Mirpur, AJ&K. The major aims were to determine prevalence of CKD in these hospitals and find the risk factors contributing to kidney failure symptoms in order to manage them. The study adopted a cross-sectional design which was carried out in District Mirpur. All the patients, clinically diagnosed with CKD, Stage 1-5, were participants. The data collection was undertaken in three-parts, through Questionnaire i.e Demographics, duration and laboratory results of kidney disease, Risk factors of CKD. The analysis was done with the help of SPSS-21 (Statistical Package for Social Science). Both male and female estimated glomerular filtration rate (eGFR) was calculated on the GFR calculator Davita kidney care program. The number of patients involved in the study was 385 and several risk factors which are significant in CKD were identified; hypertension was the most common risk factor and it occurred in 76.6 percent of the patients. Diabetes was also a key factor since 42.3 percent of the respondents had it. The percentage on those who have long-term use of NSAIDs was 30.1 of the study population. Herbal medications were used by 30.1%. Out of the total, 51.17% used tap water as their main source of drinking water. The other significant risk factors were: Bone disease (29.3%), Urinary tract infection (22.3%), Hepatitis C (21.5%), History of kidney stones (17.4%), Acute kidney injury (AKI) (10.6%), kidney disease during or after pregnancy (7.53%), Congenital anomalies of the kidney (7.53%).

The researchers determined that the predominant risk factors of CKD were hypertension and diabetes. Also, unnatural and unmanaged cholesterol was discovered to be one of the biggest factors. The history of Hepatitis B, Hepatitis C, AKI, presence of kidney stones and urinary tract infections were also some of the significant risk factors setting the predisposition of CKD progression. CKD was also aided by long term usage of some drugs such as antibiotics, biguanides, thiazide diuretics, and nephrotoxic drugs like NSAIDs. Herbal medicines, the use of tap water, overuse of soft drinks and meat intake and junk food were also mentioned as risk factors in the study. In addition, the new risk factors such as pregnancy abnormalities and chronic bone disease were identified to cause CKD, as well as congenital anomalies of the kidney.

Keywords: *CKD(chronic kidney disease), GFR (glomerular filtration rate), AKI (acute kidney injury), Scr (serum creatinine), BUN (blood urea nitrogen), CAKUT (congenital anomalies of the kidney and urinary tract infection), UTIs(urinary tract infections), DM(diabetes mellitus), SBP(systolic blood pressure).*

INTRODUCTION

Any structural or functional abnormality of the kidneys lasting three months and longer is considered a chronic kidney disease (CKD) where glomerular filtration rate decreases to less than 60ml/min/1.73m2 or albuminuria (>30 mg/24 hours). It is a progressive and majorly a non-communicable disease that occurs in one out of ten individuals in the world. CKD is further described by

National Kidney Foundation (NKF) as the damage to the kidney, either with or without an estimated glomerular filtration rate less than that threshold with the presence of indication like high blood urea nitrogen (BUN) and serum creatinine (Scr), blood/ urine pH abnormalities, or imaging examinations.

According to the Kidney Disease Improving Global Outcome (KDIGO) framework, the degree of albuminuria and GFR is used to classify five stages of CKD. The stages are as follows:

Stage 1: Normal or high GFR (>90ml/min/1.73m2)	**Stage 2:** Mild CKD (60–89ml/min/1.73m2)
Stage 3A: Moderate CKD (45–59ml/min/1.73m2)	**Stage 3B:** Moderate CKD (30–44ml/min/1.73m2)
Stage 4: Severe CKD (15–29ml/min/1.73m2)	**Stage 5:** End-Stage CKD (<15ml/min/1.73m2)

Followed by stating stages GFR, glomerular filtration rate, is usually measured and calculated based on a simple blood test in which creatinine is measured, which is a product of muscle breakdown and filtered by kidney.

Nephron deficiency at birth, nephron loss due to aging, and nephron loss with obesity, hypertension, diabetes, and family history of kidney disease are some of the risk factors associated with the development and progression of chronic kidney disease. It is estimated that globally CKD, chronic kidney disease, prevalence rates stand at 8.6 and 9.6 percent amongst adult males and females respectively. Overall prevalence of CKD among adult persons aged 18 years or above in Pakistan is a horrifying 21.2 percent and the high ends are as frightening as 29.9 percent.

The symptoms of CKD cannot be obvious until the disease has been advanced considerably. Stage-1 (GFR >90) has symptoms that might consist of losing weight, feeling very tired, itching a lot ,swelling in hands or feet and no appetite. Moving into mild CKD (GFR 60 -89) causes the disease to exhibit symptoms of blood in stool or urine, insomnia and bad breath. During the end stages (GFR <45), individuals might be anaemic, have a shortness of breath and hypertension and swelling of ankle and pedal edema.

The pathophysiology of CKD is a complex process, involves progressive loss of kidney function. Damage of the proximal tubules of the kidneys will trigger a vicious inflammation-fibrosis-nephron loss cycle. Since some of the nephrons are destroyed, the rest hypertrophies and this causes an extra work. This ultimately exceeds their oxygen competence, leading to hypoxia, acidosis as well as additional inflammatory reactions.

Problem Statement: Chronic kidney disease is a significant health issue, and it causes morbidity and death to worldwide population. The study contributes to the absence of details regarding CKD's prevalence and risk factors in Mirpur, AJK. Knowledge of these risk factors in the early stages is important in devising effective prevention measures of end-stage renal disease.

Rationale: CKD is an expensive burden on healthcare systems and has a poor influence on the quality of life of a patient, and it is necessary to research the issue of contributing factors to its occurrence. In the whole world, its prevalence lies in the range of 11-13% and most cases are at Stage-3. Given the fact that the prevalence and associated risk factors of CKD has not been published yet, this cross-sectional study was carried out, which will serve as a basic evaluation of any focus group-based subsequent research that is intended to postpone the development of the disease.

Significance: This is the first research of its type in Mirpur region. In determining the causes and risk factors of CKD, the study will help the general population to be aware of the disease and risks and as a result, identify it earlier so that interventions can be carried out.

Objectives: The primary goals of this study were to:

- Assess the effectiveness and rate of chronic kidney disease in different hospitals in District Mirpur AJK.
- Determine what are the particular risk factors of the disease's pathogenesis.
- Help to reduce the risk factors and treatment of the symptoms of kidney failure.

LITERATURE REVIEW:

A risk factor can be explained as any of the characteristics that are linked with having an upsurged probability of a given outcome. When it

comes to chronic kidney disease (CKD), the factors are classified into four types:

- Proneness factors: These add susceptibility of a person to damage his or her kidneys, which include: old age and family history of CKD.
- Initiation factors: The kidney damage including hypertension, diabetes mellitus, urinary tract infections (UTIs), kidney stones is directly caused by the initiation factors.
- Progression factors: They worsen the kidney damage that already exists and this reduces the kidney activity after the original damage such as non-controlled blood pressure and a bad glycemic control.
- End-stage renal disease factors: These finally result in the failure of the kidney, as an illustration, anemia, proteinuria, as well as untreated acute kidney injury (AKI).

Key Risk Factors for Chronic Kidney Disease:

Some of the major risk factors to CKD as identified in the literature are substantiated by the research studies conducted in differing populations.

Gender:

According to the multiple cross-sectional studies, women are reported to have a higher prevalence of CKD than men. For instance:

A 2020 study of the Ilorin Renal Study Group (IRSG) composed of 1353 people (758 females and 595 males) reported an overall prevalence of CKD to be at 12 percent but much higher in women, 14.1 percent than in men, 9.5 percent.

In a Mashhad study in 2018, 2,976 respondents were included; the study found that 64.9 percent (1,931) of them were women and 35.1 percent (1,045) were men, indicating that CKD was mostly prevalent in women.

On the United States, the Chronic Renal Insufficiency Cohort (CRIC) Study of 5,500 adults with CKD also argued that women would likely decline in kidney promptness rapidly because of variables such as low socioeconomic status, rising rates of obesity, reduced bodily activity and counterproductive levels of cholesterol. Nevertheless, women are less prone to kidney failure, perhaps because of the endogenous estrogens protective effects.

In Yopougon (Africa) and Qingdao (China) higher prevalence rates of CKD and worse renal functioning in women were observed as well, with obesity playing a crucial mediating role in the latter one.

On the other hand, a 2017 Luxembourg study found that CKD prevalence was much higher in males and lipid disorders predominated as a high-risk factor in both sexes. A different study conducted in Egypt, in E-Sharkia, revealed that there is a higher incidence of End-Stage Renal Disease (ESRD) among male (62.2%) than females (37.8%). Although there are certain differences, higher CKD prevalence in women was reported in a study conducted by Bezmialam Vakif University in Turkey and that which took place in Karachi, Pakistan in 2014.

Age:

The age is always named as one of the significant contributors to the development of CKD:

A study conducted at a university in Gondar in 2016 in the hospital revealed that as age advances, there is a progressive loss of nephrons and diminished renal blood flow. Patients aged above 65 years were more likely (2.5 times) to develop renal failure (decreased in renal superfluous gland functioning (eGFR <60ml/min/1.73m2) and albuminuria.

Qingdao (2016), Mashhad (2018), Luxembourg (2017) studies all confirmed the age as a risk factor that leads to a significant increase in the prevalence of decreased kidney function in older correct age groups in both genders. The Luxembourg study revealed the risk with more than 2-fold higher risk among participants that were between 50-69 years.

A population-based study carried out in Nepal showed that people above the age of 60 years had an almost triple chance of developing CKD than those between 20 and 39 years.

A study by Bezmialam Vakif University (2015) suggests that kidney health diminishes with age in the case of both men and women and usually leads to CKD stages 3-5.

Hypertension

Hypertension is a critical risk factor for CKD:

According to the study conducted at the University of Gondar Hospital (2016), hypertension was found to be itself associated with CKD. The risk of CKD in patients meeting the criteria of blood pressure level (>140mmHg) was 3.633 times greater in patients with blood pressure levels equal to systolic blood pressure (SBP) than in other patients with lower blood pressure values (SBP <140mmHg).

In a study conducted in Qingdao, 34,588 subjects were enrolled in a study and concluded with 70.6 percent of them having hypertension which was

statistically confirmed as independently related to CKD after multivariate analysis.

The IRSG research has raised the issue of low levels of awareness and control of hypertension as a factor contributing to an increased state of CKD in middle-income countries.

CRIC Study confirmed that SBP >130mmHg is associated with increased risk of kidney failure as in the American Health Association, which suggests a blood pressure target <130/80mmHg in CKD patients.

The impact of it is further supported by the researches in Yopougon (47.1% prevalence of hypertension among CKD patients; Luxembourg (three times greater likelihood of CKD in a population with hypertension).

A research conducted in Nepal (2018) revealed that hypertension is an independent factor in creating the risk of CKD development, which was raised by two times.

According to a study conducted by Bezmialam Vakif University (2015), uncontrolled hypertension may cause intra-glomerular capillary pressure which results in glomerulosclerosis and lose of kidney functional abilities.

In one such study in Egypt (2016) carried out in dialysis centers, hypertension, was shown as a major risk factor in causing ESRD contributing to 30.4 percent of all causes of ESRD.

Diabetes:

Diabetes is a leading cause of CKD globally:

In Lome, Togo, a study conducted in 2022 revealed that diabetic patients are at a higher risk of developing kidney disease, therefore, early risk screening on the renal is recommended to determine the presence of risk factors that can impact the development of CKD, such as hyperglycemia, hypertension, proteinuria, etc.

According to the 2016 study in Qingdao, diabetes emerged as one of the greatest risk factors since it is becoming very quick to increase in China.

According to a 2020 systematic review in Nigeria, diabetes four times more puts the risk of CKD at the peak. The prevalence of diabetes has been on the rise in Nigeria as it has risen age-adjusted prevalence of diabetes in Nigeria has risen up to 5.7 percent in 2015, compared to 2 percent in 1990, and this is more so in women. Diabetes constitutes a major cause of CKD worldwide and especially in high-income countries and the burden of diabetes is expected to increase by 50 percent between the years 2011 and 2030, especially in low- and middle- income countries.

A 2020 Ethopian-based study has attributed CKD to longer duration of diabetes and family history of kidney disease in many cases, caused by poorly managed diabetes.

The Turkish Society of Nephrology (2015) highlighted Diabetes Mellitus (DM) as the primary cause of CKD and ESRD in both developed and developing nations, with about half of new ESRD patients in the US having diabetic nephropathy. Mechanisms include hyper-filtration injury and advanced glycosylation end products

Obesity:

Obesity is also a growing risk factor for CKD:

A 2019 study conducted in Qingdao showed that both men and women have a higher prevalence of CKD than before with obesity being a leading factor towards induction. Obesity and central obesity were significantly higher in females.

The Nigerian study conducted in 2020 also revealed that obesity prevalence was 8.7 percent, but it was higher among females (11.8 percent) than males (5.2 percent).

A 2014 US retrospective study carried out on 320 000 people over 15 years showed that as Body Mass Index (BMI) increases there is a clear association between the increased relative risk of kidney dysfunction.

Use of Herbal and Other Medications

Certain medications can contribute to CKD:

Drug addiction, especially habitual use of lead-contaminated opium, was found to be high-risk factor of CKD in 2018 Mashhad study especially in adolescents who used the ubiquitous drug.

According to a 2017 study conducted by the American Journal of Medicine, the negative effects of large quantities of NSAID consumption on GFR were found to be linear in nature, and it is particularly dangerous in older individuals and should be avoided as much as possible.

Thiazide diuretics interfere insidiously with kidney function and damages the patient situation, especially in acute kidney injury accompanied by hypertension (2017 study).

A diabetes medicine by the name metformin can hasten CKD when being administered over a long period in patients with renal dysfunction since it is disposed of through the kidneys (2022 research).

A 2017 Chinese cohort study of 1.9 million individuals established a correlation of high dose of

NSAIDs to reduce GFR to less than 60ml/min/1.73m 2and decline by up to 30%, thus correlating it with CKD progression.

Hepatitis:

Hepatitis B and C are risk factors of CKD:

Another prospective cohort study carried out in Taiwan in 2014 demonstrated that the risk of CKD was much higher in individuals with hepatitis. In the absence of hepatitis, CKD risk was 38.4 but in the presence of hepatitis, it increased to 52.6.

Kidney Stones:

Recurrent kidney stones can lead to CKD progression:

A 2020 Taiwan study based on a national health insurance database also reported that the risk of CKD progression was much higher in those with kidney stones.

A cross-sectional assessment underlined that frequent kidney stones must be prevented because of their not only short-term, but also long-term predisposition to the development of CKD.

Acute Kidney Injury (AKI)

Excessive cases of urinary incontinence left untreated are a major cause of future CKD:

The 2018 book on both basic research and clinical practice and 2018 US study both noted that AKI, even with subsequent kidney recovery, predisposes the individual to future development of CKD.

Metabolic Factors:

Metabolic imbalances can contribute to CKD:

Bone Disorder: In a study conducted in 2018 in the US, it was established that the mineral and bone disorder constitute a significant problem in CKD. High concentrations of fibroblast growth factor 23 (FGF23), a protein that controls vitamin D and phosphate regulation, were also found to be one of the key problems to developing CKD.

Urinary Oxalate: A high level of 24 hours of urinary oxalate excretion was associated with an increase in the risk of kidney failure by 45 percent. Sources include hepatic synthesis, ascorbic acid breakdown, and diet. Oxalate nephropathy occurs because of the accumulation of calcium oxalate crystals that cause tissue damage and inflammation in renal parenchyma.

Behavioral Factors

Lifestyle choices play a crucial role in CKD prevention:

Among the findings of the study named Healthy Lifestyles: The CRIC Study (2018) are that healthy habits, such as a lack of smoking, healthy diet, physical activity, and bodyweight help to avoid CKD development. The most significant factor that was associated to the lower risk was smoking cessation.

Diet: A cross-sectional study in the US indicated that poor diet consumption is a source of CKD. It was also found that intake of high sodium and low potassium were associated with hypertension. Greater intake of low-fat milk and less intake of 100 percent fruit juice and whole fat milk predicted reduced CKD.

Pregnancy-Associated CKD

Pregnancy complications can lead to CKD:

A Swedish study conducted in 2020, stated that preeclampsia or preeclampsia with pregnancy obesity is the single most important cause of later CKD during pregnancy, therefore, women with the hypertensive disorders during the pregnancy may be at an advantage to have systematic renal surveillance to allow them to avoid future CKD.

A 2017 study in Mexico stated that CKD or AKI remains under-diagnosed during pregnancy or is placed when the disease has intensified to CKD in pregnant women in developing countries and this is one of the reasons why indicators on CKD in women are high in countries in developing nations.

Congenital Anomalies:

Congenital Anomalies of Kidney and Urinary Tract (CAKUT) are serious contributors to CKD, particularly to pediatric and adolescent population:

As a German study involving 405 children with CKD patients conducted in 2020 has concluded, 44 percent of cases were associated with CAKUT, an issue that can present symptoms as mild as the absence of symptoms up to as maxim hints at UTIs, hypertension, and abdominal swelling. Factors like premature birth and family history increase susceptibility.

A 2018 Indian study on CAKUT in children reported that a large number of them presented with UTIs as their parental awareness was poor.

In a study conducted in Italy (2009), it is stressed that the cause of adult-onset illnesses such as hypertension and chronic renal failure is CAKUT, congenital anomalies of kidney and urinary tract, that causes a decrease in nephron mass.

Global Prevalence of Chronic Kidney Disease

The prevalence rate of CKD in the globe since it was estimated varies with different regions:

According to Clarivate research reports, CKD cases are below the world cases with a higher situation in countries such as Spain (27.9%), Netherlands (28%), the UK (31%), Mediterranean region (34.1%), USA (39.6%), and Japan (42.3%). The differences are also explained by differences in patient population (e.g., Type 1 and Type 2 DM), the respective methods used to determine both creatinine and albumin, sample sizes as well as ethnicity.

In most cases, the prevalence of CKD is found in the low- and middle-income nations rather than in high-income nations. An example relates to the prevalence which remains at 3.3% in the United States but in Norway it stands at 17%.

The worldwide prevalence of CKD stands at 13.4 per cent.

Global and Regional Prevalence of Chronic Kidney Disease:

CKD imposes a substantial burden on the health of the population worldwide in terms of morbidity and mortality. It is estimated that 13.4 percent of the population have CKD, and 4.9 to 7.0 million patients are experiencing end-stage renal disease (Zhang et al., 2019). Although there are reports of lower global prevalence rates, there are major differences within countries numbers. A cross-sectional study demonstrated the prevalence in particular countries, i.e., in Spain (27.9%), Netherlands (28%), in the UK (31%), in the Mediterranean area (34.1%), in the USA (39.6%), and in Japan (42.3%). Such differences can be explained by the different qualities of patients (Type 1 diabetes vs. Type 2 diabetes), modalities, sample size, and ethnicity. The prevalence of KD is usually greater in low middle-income countries than in high-income ones; in the United States, the prevalence is 3.3 percent, in Norway, 17 per cent (Coresh et al., 2017).

Prevalence in Pakistan:

Prevalence of CKD in all Pakistani adults was 21.2 percent. The best studies find a rate of 29.9 percent and the lowest rate is found in 12.5 percent. Such differences could be due to different equations applied in determining CKD even in studies that deal with a similar age group.

Prevalence in Pakistan by age indicates that the rates are highest amongst the eligible participants (those who are over 50) with 43.6 percent of the group participants and 10.5 percent of the ineligible group (those under 30). The gender-specific prevalence rates were mentioned somewhat differently, with certain studies pointing at higher CKD rates in males and high-quality study using country-specific equation showing even a slightly higher proportion in females (13.3%) in comparison to males (11.6%) (Saleem Jessani et al., 2014). It is advised that screening and determination of the risk factors should be done early and in urban settings where the prevalence of CKD has been shown to be higher among the studied persons between the ages of 30-80 years in 2015 (Sehyr Imran et al., 2015).

Prevalence in AJK (Azad Jammu and Kashmir)

Data on CKD prevalence in AJK remains limited. The available study by 109 patients was carried out in DHQ Mirpur. Among them, 58 (53.2 percent) were males and 51 (46.7 percent) were females implying that CKD in Mirpur, AJK affects more men in comparison to women (Sohail Riaz et al., 2021).

METHODOLOGY:

The research was conducted using a cross-sectional design to determine the prevalence and risk factors of chronic kidney disease (CKD) using different age groups in Mirpur, AJK.

The study was done in the hospital sector along three hospitals in the area of Mirpur, AJK, namely: Divisional Headquarters (DHQ), Riasat, and Riaz hospitals, Mirpur. Data collection occurred over a four-month period.

Study Population and Sampling:

The subjects in the study were all patients with confirmed clinical diagnosis of CKD Stage 1-5 including those undergoing haemodialysis or non-haemodialysis. Patients of both sexes and with co-morbidities in the long-term were admitted. A convenience sampling method was utilized. The sample size has been calculated via Rao soft calculator which records a margin of error of 5 percent at a 95 percent confidence level and provides the sample with 385 patients with CKD to participate in the research.

Data Collection Tools:

Data was gathered using a comprehensive seven-section questionnaire:

1) Demographical variables: Gender, age, marital status, employment, status, and household income.
2) Kidney disease and laboratory result: Serum cholesterol, uric acid, C-reactive protein, estimated glomerular filtration rate (eGFR), and albuminuria.
3) Risk factors reported in the case of CKD: Hypertension, diabetes, history of many different diseases, and nephrotoxic medication usage.
4) Dietary intake.
5) History of bone disease.
6) Kidney damage during or after pregnancy.
7) Congenital factors for kidney disease.

Statistical Analysis:
The data was analysed by means of Statistical Package Social Science (SPSS) software. Men and women were categorised by eGFR distribution on Davita Kidney Care eGFR calculator with serum creatinine, age and gender data typed in. Descriptive statistics was used to establish the significance of demographic characteristics of people and the disease variables.

RESULTS:
In this study, demographic, clinical, and lifestyle aspects of 385 CKD patients residing in Mirpur, AJK, were discussed with the view to determine their important features, and the possible risk factors.

Patient Demographics and Kidney Disease Profile:
Out of the cohort, 53.5 percent belonged to males and 46.5 percent belonged to females with the age range of 41-60 years forming the highest proportion (40.0 percent) followed by 21-40 years (35.8 percent). One of the most remarkable findings was the level of unemployment that is quite high (57.4% of the participants state they are not currently employed). All the 385 were confirmed patients with CKD and most of them (50.9 percent) were diagnosed between 1-5 years past.

Clinical and Laboratory Findings:
Assessment of key clinical parameters revealed widespread abnormalities:
1) Serum Cholesterol: More than 37.7 percent had no cholesterol result. They had borderline high levels of cholesterol (200-239mg/dl) in 25.5 percent of the individuals tested and high cholesterol (>240mg/dl) in 21.3 percent individuals tested.
2) Uric Acid: Uric acid levels exceeding normal were encountered in more than a half of the participants (53.8%).
3) Albuminuria: It was found that a huge percentage (86.0%) of them had albuminuria exhibiting extensive kidney damage varying between 30-300 mg/g.
4) Serum Creatinine: The majority of the participants (99.2%) displayed increased levels of serum creatinine.
5) eGFR (Kidney Function): The research reported that severe kidney dysfunction was found in participants with 56.4 percent of patients experiencing eGFR less than 15ml/min/1.73m 2 (Stage 5 CKD), 42.6 percent with eGFR 15-29ml/min/1.73m 2 (Stage 4 CKD). Remarkably, none of such people were detected to have Stage 1 or 2 CKD.
6) Common Comorbidities and Risk Factors
7) Several comorbidities and lifestyle factors were highly prevalent:
8) Hypertension: Highly common, affecting 76.6% of patients. Majority of hypertensive individuals (50.6 percent) said that they had high blood pressure of more than 140/90 mmHg most of the time.
9) Diabetes: Overall, 42.3 percent of the subjects had diabetes, many of them (21.3 percent) with a long-running history of diagnosis (greater than ten years).
10) Infections: Commonly reported were hepatitis C (21.6 percent), recurrent UTIs (22.3 percent), and kidney stones (17.4 percent). Ten and a half percent of the participants had a history of Acute Kidney Injury (AKI).
11) Use of Medications: It was found that almost all patients (99.2%) took a long-term treatment of different medicines such as thiazide diuretics (76.1%), biguanides (42.9%), antibiotics (23.5%), and NSAIDs (30.1%). Herbal medications were used by 19.5%.
12) Lifestyle: Most of the respondents (51.2%) used tap water to drink. Bone disease was present in 29.4% of patients.
13) Specific Factors: Only a low proportion of females (7.5%) had onset of CKD during or after pregnancy, 7.5 percent of the entire cohort had congenital factors.

Gender-Specific Observations
Males (53.5%) were also slightly more than that of the females (46.5%) overall. Hypertension was much more frequent in men (166 males vs. 40 female sufferers).
1) There were greater incidences of diabetes (113 females had diabetes compared to 93 in males),

UTIs (57 definition of females compared to 29 definition in males), kidney stones (218 females compared to 39 males), and bone diseases (67 females compared to 46 males).

2) The proportion of very low eGFR (<15 ml/min/1.73m 2) was slightly high in males.

Age-Specific Observations

High prevalence of most of the CKD parameters was constantly observed in the 41-60 age group such as: high cholesterol, most serious categories of kidney eGFR, high albuminuria, hypertension, diabetes, and those on long-term medication.

Major frequencies of most severe conditions were also observed in the >60 years age group with high cholesterol and long-duration hypertension and diabetes leading the pack.

Specific results that were found to be quite prevalent among younger age groups (1-20 and 21-40 years) included above-normal uric acid (especially 21-40 years), UTIs, and congenital factors. The age group that showed pregnancy-related CKD was the 21-40 years age group.

Work Status and CKD

The unemployed had the highest numbers in nearly all of the poor CKD indicators such as increased disease duration, worse eGFR, better hypertension rates, diabetes, infections (Hepatitis C, UTI, kidney stones), long-term use of medications etc. This implies that unemployment has a close connection with the burden of CKD and its comorbidities.

Chi-Square Test Results:

Chi-square test is used to determine the relationship between different demographic, clinical, and lifestyle riskfactors with chronic kidney disease (CKD) in this study. The output determines that a variable has a substantial relationship in the case that its p-value is below the marker of 0.05 ($p<0.05$) that is the estimated relationship is not likely to have resulted due to chance occurrence. The opposite is applicable, a p-value bigger than 0.05 ($p>0.05$) indicates no significant relationship.

1. Demographic Characteristics

In the analysis of the demographic factors, demographic factors on gender have no significant association with CKD; however, age is a highly significant factor.

Gender: The Chi-Square analysis revealed that gender is not connected to chronic kidney disease significantly (p=0.169), which means that the CKD is not overly represented in either male or female patients in this cohort.

Age: Conversely, a very strong relationship between age and chronic kidney disease was observed in the analysis (p=0.000). The finding highlights the fact that age is a key demographic parameter in the expression of CKD in the observable population. The most frequent number of patients stood at the ages of 41- 60 years and 21- 40 years as well which implies a strong correlation of ageing progress and CKD diagnosis.

2. Clinical and Laboratory Findings: They established a strong, significant correlation between all main laboratory findings regarding those with CKD and thus, those markers cannot be ignored as strong indicators of the disease in the present population base.

Serum Cholesterol Level: The result indicated that there was a very great association between the level of serum cholesterol and CKD (p=0.000). As the data indicate, a large part of the patients had borderline high cholesterol levels, which points to dyslipidemia as a significant comorbid condition.

Uric Acid Level: There was also an extremely strong correlation with uric acid level and CKD (p=0.000). Uric acid was elevated in the majority of patients (53.8 percent), and this suggests the emergence of hyperuricemia as a common characteristic of the illness in the studied group.

eGFR (Estimated Glomerular Filtration Rate): eGFR as anticipated was a key test of kidney malfunction and it demonstrated a very strong correlation with CKD (p=0.000). Most of the participants were in the worst stages, including 56.4 in Stage 5 (<15ml/min/1.73m2), and 42.6 in Stage 4 (15-29ml/min/1.73m2). This substantiates the fact that the study population has an advanced CKD.

Albuminuria: CKD was also significantly and strongly associated with the presence of albuminuria, which is a damage indicator of the kidneys (p=0.000). Most of the patients (86.0%) experienced albuminuria between 30 and 300 mg/g, which further confirms that the patient suffered serious kidney damage.

Serum Creatinine: The level of serum creatinine had a very significant relationship with CKD (p=0.000). With 99.2 percent of patients, the value of the creatinine above-normal, this fact reveals the almost

universal inability of the kidney to perform the filtration process in the given cohort.

3. Comorbidities and Infections:
The Chi-Square test established that there is an important relationship between CKD and prevailing comorbidities and history of infections.
1. Hypertension: In the analysis a very significant association with the presence of hypertension and presence of CKD was observed (p=0.000). This is one of the most serious findings because 76.6 percent of the patients had hypertension. Length of hypertension and the rate at which the blood pressure was reported greater than 140/90 mmHg also had significant correlation (p=0.000 in both cases) and this implies that severity and the duration of high blood pressure is directly related to CKD.
2. Diabetes: Completely like in hypertension, existence of diabetes was discovered to be significantly and remarkably related to CKD (p=0.000). The presence of diabetes (p=0.000) and using herbal medicine in treating diabetes (p=0.000) also had significant relationships with CKD.

History of Infections: The study identified a very strong relationship between CKD and history of various infections such as:
a) Hepatitis C virus (p=0.000) with an incidence of 21.6 percent of the cohort.
b) Acute Kidney Injury (AKI) (p=0.000) is reported in 10.6 percent of the patients.
c) Urinary Tract Infection (UTI) (p=0.000) which occurs on 22.3 percent of the patients.
d) Kidney stones (p=0.000), 17.4 percent of the cohort.
e) Hepatitis B (2.3%) history was also associated with CKD significantly (p=0.000).

4. Medication Usage
The Chi-Square analysis indicated an important connection between CKD and long-term application of the wide range of medications, especially those recognized as nephrotoxic or most widely applied to address related comorbidities.

Long-Term Drug Usage: A very large correlation was found between CKD and long-term usage of drugs (p=0.000), where close to all patients (99.2) responded that they used a long-term medication.
Nephrotoxic and Related Drugs: The administration of certain groups of medications also turned out to be closely interconnected with CKD: Result Relationship between non-steroidal anti-inflammatory drugs (NSAIDs) and CKD NSAID use had a significantly high relationship with CKD (p=0.000) with 30.1 percentage of patients using NSAID.

Herbal Medications: A strong association was also observed with herbal medications (p=0.000) and herbal medications were used by 19.5 of the cohort.
Antibiotics: These were also followed by a long-term usage of antibiotics with a significant association with CKD (p=0.000) with 23.4 patients reported to have used it.

Biguanides: Biguanides, a category of diabetes medicine had a great correlation with CKD (p=0.005) and were used by no less than 42.9 percent of patients.

Thiazide Diuretics: Use of thiazide diuretics was extremely significant (p=0.000) which included 76.1 percent of the patients who have actually used it, signifying its role in treatment of hypertension, one of the major comorbidities.

5. Dietary and Lifestyle Factors:
Lifestyle and diet choice were significantly associated with CKD, hence, it was suspected that they could influence CKD or cause it.
Drinking Water Source: The quality of drinking water that was predominantly used was closely related to CKD (p=0.000), whereby majority of the patients (51.2%) used tap water.
- Intake of Soft Drinks and Junk Food: The occurrence of not only soft drinks (p=0.000) but also that of junk food (p=0.000) had a very significant relationship with CKD. This implies that unhealthy diet can be one of the causes.
- Bone Disease: The past medical history of being affected by bone diseases, including osteoporosis, osteopenia, brittle, thin or weak bones was also found to be a significant factor of CKD (p=0.000), where 29.4 per cent of patients were found to have experienced bone diseases. This finding is in line with the recognized CKD complications, which comprise the mineral and bone disorders.

6. Specific Factors:
Lastly, two other conditions were asked and tested and proved to be significantly associated with CKD.
- Pregnancy-Associated CKD: It was shown in our female patients that a history of pregnancy-

associated kidney disease was a strong predictor of the development of CKD (p=0.000) with a prevalence of 7.5% in the total cohort of this study.

- Congenital Factors: Congenital factors or birth abnormality exhibited a P value of 0.000 in connection to CKD and also 7.5 percent of the cohort were associated with it.

DISCUSSION:

The discussion section summarizes the results of a cross-sectional study to find out about the prevalence and the risk factors of chronic kidney disease (CKD) in Mirpur, Azad Jammu and Kashmir (AJK). The rationale behind the study is that the cases of dialysis have increased significantly at the Divisional Headquarter Teaching Hospital in Mirpur between 2005 and 2021, which indicates that there is a growing problem in the field of public health in the light of a population of around 125,000 people. The study, which is the first in the region, gives important baseline information about the local CKD situation.

Key Biomarkers and Clinical Indicators:

The research thoroughly explored some of the key indicators of kidney damage such as the estimated Glomerular Filtration Rate (eGFR), serum creatinine, uric acid, and albuminuria. These findings indicate that the participants of the study had a very serious case of kidney dysfunction. Stunningly, 99.2 percent of the population of 385 subjects showed a serum creatinine value that lies above the normal range, which the extensive indicator of an impaired normal kidney. Similarly, 86.0 of the patients showed albuminuria that is associated with an impairment of renal barriers. Also the most convincing was the fact that 100 % of the respondents had eGFR of below 60 ml/min/1.73m2 which was one of the initial presumptive signs of CKD. Moreover, the average of such a large population 53.8 percent had a high uric acid condition. With all such significant biomarkers that have a p-value=0.000, the correlation with the CKD is strongly emphasized. The GFR calculator Davita kidney care software proved to be an accurate way of estimating GFR which is an important step in substantiating the claim of existence of the disease according to earlier works (Salini & Sajeeth, 2013).

Demographic and Classical Risk Factors

The research found that the onset of CKD in certain demographic groups was high, which is also in line with trends across the world.

Gender: Out of the total number of 385 participants, 206 (53.5 percent) were male and 179 (46.5 percent) female. This observation reveals the more significant percentage of men affected with CKD, which agrees with those concluded in cross-sectional studies carried out in Luxembourg and El-Sharkia, Egypt. These studies also indicated higher cases of CKD among men, which is an indicator of the gender susceptibility that should be investigated deeply.

Age: It was found that the progression of CKD has a strong relationship with age. Fifty percent of the subjects were aged more than 40. This observation is adequately supported by previous studies which have established that renal insufficiency and albuminuria was more common among the older people. Advanced age is a significant risk factor with the natural decrease in the anatomy and physiology of kidneys with age.

Hypertension: Hypertension turned out to be the most common risk factor among all the causes. The paper mentions the vicious physiologic process in which the high blood pressure then destroys and constrains blood vessels in every part of the body, including the kidneys. This constriction hinders the flow of blood and therefore the kidneys filtering of waste. The resulting fluid retention works further to add pressure to blood hence escalating the damage and speeding up the breakdown of kidney failure. The status of the blood pressure level exceeding 140 mmHg as a significant risk factor of CKD progression is well confirmed by the data of the previous studies, one of which was conducted in Gondar Hospital. A study on Youpogon led to the conclusion that systolic BP of 130mmHg or more predisposes the sufferer to kidney failure and therefore control is paramount.

Another traditional risk factor was the presence of diabetes in 42.3 percent of individuals in the population. The co-morbidity that is prevalent in CKD is prolonged diabetes. This result correlates with the study findings that the Sylvanus Olympio Hospital in Togo and Qingdao University identified the definite and statistically significant relationship between complications of diabetes and the development of kidney disease.

Other Contributing Risk Factors:

What is additionally important is that, beyond the standard risk factors, there are a number of other important contributors to CKD that the study identified.

Obesity and Cholesterol: It has been found that obesity due to a p-value of 0.000, is an important factor, which contributes to the development of kidney disease. Moreover, 21.3 % of the respondents showed their cholesterol level normalized with serum levels being high which was also a significant finding. These findings are corroborated by those of Qingdao University and the University of Ilorin Teaching Hospital in Nigeria, which observed that obesity was a major contributor to the induction and the development of CKD.

Infections: A comprehensive connection between different infections and CKD was established in the study. Urinary tract infection (UTI) was found in 22.34 percent of the respondents, whereas Hepatitis C and Hepatitis B were discovered to be 21.56 percent. Also, 17.4 percent had a history of kidney stones, and 10.6 percent had Acute Kidney Injury (AKI) history. The existence of such infections and conditions was closely linked to the CKD progression.

Poor Use of Medications: This paper emphasized that the inappropriate use of various medications is one of the greatest threats. Their personal use of the NSAIDs and antibiotics, especially patients with the bone illness in an attempt to alleviate pain, was recorded to be a major cause of CKD. Another risk factor was the use of herbal medications, as some patients took them in order to treat hypertension, diabetes, or even the symptoms of weakness when trying to recover their own energies, which, unintentionally, led to kidney damage and failure. This finding has been reinforced by findings made by a group of researchers in the University of Ilorin and also in the Mashhad University stating that herbal remedies can be a risk to kidney disease. Another study conducted in the American Journal of Medicine also found a connection between high NSAID use and progression of a kidney disease.

Newly Recognized Risk Factors: The Mirpur study was the first to identify some of the risk factors that had a high prevalence.
Tap Water: A considerable 51.17 of respondents answered that they use tap water to drink it. The researchers hypothesize that even tap water pollutants may be the cause of both CKD and kidney stones.

Bone Disease: Binomial proportion: It was recorded that about 29.35 percent of the respondents had history of bone disease. It was also observed that the frequency of use of medications as a result of these conditions, i.e. calcium and vitamin D supplements and NSAIDs to deal with any pain, was also a risk factor in regards to CKD. This has been in line with the results of a 2018 study on US soil which associated mineral and bone disorder and control of related proteins (FGF23) to CKD development.

Pregnancy-Related Anomalies: Of the female subjects, 29 had stated that either at the point of pregnancy or delivery, they developed kidney disease or the problem was traced to pregnancy problems or complications associated with delivery. A research conducted by the Department of Obstetrics and Gynaecology, Karolinska University Hospital supports this finding because it explained that CKD is one of the major complications of pregnancy obesity that can lead to pre-eclampsia among others.
Congenital Factors: The research identified 7.53 percent of the patients to have CKD as a result of congenital factors, meaning the disease was the case since birth, and it could be caused by improper nephron development or improper genetic makeup. This gets vindicated through research in India which concluded that congenital anomalies of the kidney and urinary tract is a significant risk factor of CKD.

CONCLUSION:

On the basis of findings of this cross-sectional study some important conclusions can be made about prevalence and risk factors of chronic kidney disease (CKD) in Mirpur AJK. The research has achieved its goal of creating a base knowledge of CKD in the area because of the little knowledge that is out there, and also due to the increasing number of cases of dialysis.
The study rectifies the fact that the leading risk factors of CKD are associated with hypertension and diabetes. The incidence rate of such conditions within the study group was disconcertingly high, and it was a direct connection to kidneys damage and progression. Another classic risk factor lying at the heart of kidney damage was also identified by the study, as it is obesity and unchecked cholesterol levels.
And to add more to this analysis, the analysis has discovered that the risk factor to the progression of CKD is the history of a variety of infections, including hepatitis B and C, acute kidney injury, kidney stones, and urinary tract infections. Prolonged and, in most instances, misused use of medications, especially nephrotoxic drugs, such as NSAIDs,

antibiotics, and certain herbal medications were also found to be a significant cause of kidney damage as well as kidney failure.

Last but not least, the research found a number of minor risk factors that yet are crucial, such as the habit to drink tap water on a regular basis, the existence of long-term bone disease, and fetal abnormalities. The occurrence of congenital anomalies of the kidney was also validated as a factor contributing to CKD in a group of the patients. Such an in-depth knowledge of many risk factors is essential in coming up with specific strategies in trying to prevent something.

Ethical Considerations

Ethical guidelines were followed in the study with necessary permissions obtained by the study team of Akson College of Pharmacy in joint venture with Mirpur University of Science and Technology (MUST) Mirpur, AJ&K (reference numbers 310/11/Ex/ACP/22, 311/11/Ex/ACP/22, 312/11/Ex/ACP/22). Moreover, permission was granted by the medical superintendents and executive directors of the participating hospitals before the study took off.

RECOMMENDATIONS:

Based on the conclusions and findings of the study, the following is recommended in the Mirpur, AJK area as a way of curbing the health care burden of CKD:

Education and Awareness Plans and Screening:

Education of the patients and public on CKD is paramount. The findings of the study show that most individuals are not aware of the risk factors and silent and progressive aspect of the disease. As such community sensitization ought to be launched to enlighten the people about the causes, symptoms, and prevention of CKD.

Targeted Screening: Screening of CKD ought to be given precedence to at-risk populations. These are people with diagnosed hypertension, diabetes and individuals above the age of 40. Early detection is beneficial in the early identification of CKD before it progresses to permanent loss of kidney functions.

Education on Risk of Medication: The risk of medications, particularly with misuse and self-use of NSAIDs, antibiotics as well as herbal remedies should be taught in the communities through educational campaigns. It is recommended that Patients should always contact a healthcare expert before proceeding to use any new medication especially in cases where they intend to use a medication on a long term basis.

Lifestyle and Diet Education: Education that raises awareness to the lifestyles of positive diet should be encouraged such as a balanced diet, physical exercise and being able to maintain a healthy body weight. The risks of consuming soft drinks, junk food, and meat in excess should be mentioned particularly, and there is the risk of contaminants in tap water.

Progressive Studies and Treatments

Since this is the first study in this area of the whole region, further research with a wider scope would be important to increase the understandings of these results.

Longitudinal Studies: Future studies ought to entail longitudinal studies that can then be used to keep track on the progression of CKD and the progress of interventions.

Intervention Evaluation: Research on the evaluation of interventions should be done to evaluate the effects of intervention developed and available to slow the progression of CKD and enhance the quality of life of patients.

Further Data Wide Collection: In further research, they should include more details on data to understand more on the risk factors including which type of herbal drugs and tap water contaminants are involved in causing the disease.

The recommendations suggested will help the healthcare providers and the public health officials in taking proactive measures to eliminate risk factors that could eventually lead to CKD, they will help in regulating the process of CKD and eventually they will help in easing the burden on the population of Mirpur, AJK.

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