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RESEARCH ARTICLE

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Determining the Risk Factors of Chronic Kidney Disease: A Case Study of Swat, Khyber Pakhtunkhwa

Shahana Niaz [a] Robina Karim [b] Bilal Durrani [c] Muhammad Idrees [d] Muhammad Ismail [e]

Corresponding Author: Muhammad Idrees; muhammad.idrees@aup.edu.pk

Abstract: This study examined factors associated with chronic kidney disease (CKD) among patients attending Nawaz Sharif Kidney Hospital in Swat, Khyber Pakhtunkhwa, Pakistan. Data were obtained from 516 hospital attendees using a structured questionnaire and clinical assessment. Recorded characteristics included age, sex, education, residence, employment, household income, marital status, family history, physical activity, smoking, non-steroidal anti-inflammatory drug (NSAID) use, body-size measures, and coexisting conditions, including hypertension, diabetes, ischemic heart disease, stroke, hypercholesterolemia, and peripheral vascular disease. Associations were assessed using chi-square tests and logistic regression with backward elimination. Logistic regression and four classification approaches—k-nearest neighbours (k-NN), classification and regression trees (CART), random forest, and support vector machines (SVM)—were evaluated for binary CKD classification. Analyses were conducted in R. Among the 516 participants, 319 (61.8%) were classified as CKD-positive and 197 (38.2%) as CKD-negative. There were 343 women (66.5%) and 173 men (33.5%). Chi-square analyzes revealed significant associations of CKD status with household income, abdominal obesity, diabetes, hypertension, anemia, prior ischemic heart disease, stroke, hypercholesterolemia, peripheral vascular disease, kidney stones, use of NSAIDs, blood-pressure status, and exercise ($p < 0.05$). Several demographic and clinical predictors were also retained in the backward-selected logistic model. Random forest and CART classification were generally similar (51, 52, 127, 137) across the train-test split and feature set splits used by the authors.

Keywords: Chronic Kidney Disease, Associated Factors, Logistic Regression, Backward Elimination, Machine-Learning Classification

Introduction

Chronic kidney disease (CKD) is a significant cause of morbidity and mortality and can lead to end-stage renal disease (ESRD) with the need for dialysis or transplantation. The clinical burden of CKD is on the rise due to population ageing and the rising prevalence of diabetes and hypertension. It is estimated that diabetes and hypertension play a major role in the etiology of CKD and ESRD, though these estimates differ among populations and health systems. Increased demand for renal replacement therapy is also putting a strain on health care resources, especially in places where treatment can be costly or difficult to obtain in the long term. Maintain and document the sources for these estimates.

[a] PhD Scholar, Department of Statistics, Abdul Wali Khan University, Mardan, Khyber Pakhtunkhwa, Pakistan.
[b] Assistant Professor, Department of Agricultural and Applied Economics, the University of Agriculture Peshawar, AMK Campus Mardan, Khyber Pakhtunkhwa, Pakistan.
[c] Assistant Professor, Department of Management Science, the University of Agriculture Peshawar, AMK Campus Mardan, Khyber Pakhtunkhwa, Pakistan.
[d] Assistant Professor, Department of Computer Science, IBMS, The University of Agriculture, Peshawar, Khyber Pakhtunkhwa, Pakistan.
[e] Research Scholar, Department of Epidemiology and Biostatistics, College of Public Health, Zhengzhou University, Henan, PR, China.

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Resources used by kidney failure patients for dialysis and other renal replacement therapies (RRT) are an indicator of the burden of kidney disease. While a relatively small fraction of the population might require this treatment, European reports indicate a large number of patients undergoing such treatment. These patterns represent the significant expense and service requirements of complicated chronic kidney disease.

There are variations in prevalence, progression, and the need for treatment of CKD across populations and settings, as evidenced in different countries. Previous estimates in the US had shown a large population that was at increased risk or had CKD. Differences between age and sex, pregnancy-related risk, and the changes in the number of renal replacement therapy patients have been studied in Iran, Japan, Norway and Canada. Combined, these reports suggest that CKD is a multifactorial disease whose occurrence and impact are influenced by demographic, clinical, and health-system characteristics.

Diabetes and hypertension have been shown repeatedly in international studies to be significant factors in ESRD. There has been increasing prevalence of diabetic nephropathy reported through time in Egypt, and analyses from both Saudi Arabia and Kuwait have shown diabetes and hypertension to be major risk factors. Association of kidney-stone history with CKD has also been reported in the United States, but these associations have varied in strength and type across studies. Other factors, such as glomerular disease and obstructive uropathy, have been reported in studies in Saudi Arabia, Egypt and Jordan and are also recognized causes of ESRD. These estimates should be used within the framework of the populations, time periods, and study design of each of these studies.

Several interacting factors can contribute to renal-function decline, such as diabetes, hypertension, primary renal diseases, dietary influences, potentially nephrotoxic medications and environmental exposures. The multiple-hit view acknowledges that various insults can cause nephron loss, and the compensatory filtration of the remaining nephrons can raise intraglomerular pressure and then further damage renal tissue.

Candidates for predicting progression to ESRD have been investigated in longitudinal studies, and proteinuria and obesity are often considered clinically relevant. The significance may be variable depending on the underlying renal disease and group to be studied.

There have been conflicting results in studies regarding obesity, lipid abnormalities, and smoking. In a few studies, overweight and obesity were found to be independent risk factors for chronic renal impairment, with other cardiovascular risk factors reported to contribute to the findings. These disparities emphasize the importance of evaluating candidate factors in the targeted population being studied.

The effect of dietary protein has also been evaluated in CKD. Protein restriction was formerly a routine part of clinical practice to diminish the uraemic symptoms, and experiments indicated that high protein load can enhance renal blood flow and filtration. The advantage of protein restriction is not consistent throughout disease stages, and trial results have been inconsistent. There's some evidence that it may help with moderate to severe CKD, but findings have been more mixed for earlier-stage CKD.

In Asian countries, a rise in chronic disorders like diabetes, hypertension, and metabolic disorders has raised the alarm about CKD and its comorbidities. The incidence of CKD in adults in Asia has been reported to be a significant proportion of the adult population, and this has varied between different countries and different study populations. The overall burden and economic cost are difficult to quantify in many settings because surveillance and access to diagnostic services are incomplete.

Untreated, CKD can develop into ESRD (end-stage renal disease), which leads to dialysis or kidney transplant, thus making CKD a major public-health challenge in Pakistan. These interventions come with significant financial burden and may not be available because of limited resources and services.

The burden of CKD in Pakistan has been attributed to various factors, such as high prevalence of diabetes and hypertension, poor primary health care services, lack of knowledge about health and hygiene, and lack of funding for health care. In previous studies, a national estimate of the prevalence of CKD was reported to

be about 12.5%, but this should be interpreted in the context of the population and methodology used in the source study.

The reported estimates have varied between provinces in Pakistan and CKD stages. The estimates provided in the region are also suggestive of geographic differences, which are not easily comparable because they rely on different sampling frames, diagnostic criteria, and survey periods. Further population-based studies using standard methodologies are required to provide more reliable provincial and national estimates.

Swat is a district of the Khyber Pakhtunkhwa province of Pakistan having a significant and varied population. The size of the population and its composition are important factors to consider when interpreting local health research, but the hospital-based sample used in this study should not be interpreted as representative of the entire population of Swat without a population-based sampling design.

Materials and Methods

The participants were selected using structured interview protocol at Nawaz Sharif Kidney Hospital, Swat. Physicians completed a 31-item questionnaire and conducted physical exams. A total of 516 hospital visitors were identified as either CKD-positive or CKD-negative, based on their diagnostic status. Demographic and socioeconomic factors, family history, exercise, smoking, NSAID use, body-size measurements, and comorbidities (such as hypertension, ischemic heart disease, stroke, hypercholesterolemia, and peripheral vascular disease) were recorded. Data were analysed in R and chi-square tests for unadjusted associations and logistic regression with backward elimination to generate a multivariable model. The classifiers—CART, random forest, k-NN, and SVM classifiers—were also fitted to evaluate the binary classification performance. The proportion of CKD observed is not population-based, as recruitment was conducted within a hospital setting, where individuals were enrolled while they were presenting symptoms.

Binary logistic regression was used to model the presence of CKD as a function of candidate explanatory variables. The model is based on the log-odds of the outcome, and supports categorical and continuous covariates. The treatment of the variables in the backward elimination started with the set of candidate predictors, and variables were eliminated sequentially based on their contribution to model fit, following the references cited above. Table 2 shows the variables that remained in the model and the estimated coefficients. The selection of variables and the interpretation of the results should take into account the possibility of unstable estimates, confounding and multiple testing.

Classification and Regression Trees (CART)

Classification and regression trees (CART) classify observations by repeatedly splitting them in dichotomous ways. The algorithm chooses a predictor in each step and a cut point to split the observations into increasingly homogeneous child nodes. Terminal nodes are assigned classes after splitting stops due to a stopping rule. A new observation can then be sorted into the terminal node it falls in.

Random Forest

Random forest is an ensemble classifier, which is composed of multiple decision trees. Each tree is fitted on a bootstrap sample, and candidate predictors are included in the construction of the tree. The majority vote over the trees is used to predict the class for classification.

Support Vector Machine (SVM)

A support vector machine (SVM) finds a decision boundary that classifies a number of classes, aiming to ensure that the boundary is as far away as possible from the nearest observations in the training set, called support vectors. When using nonlinear SVMs, a nonlinear boundary is used; when using linear SVMs, a linear boundary is used.

K-Nearest Neighbours (k-NN)

The k-nearest neighbours (k-NN) method categorises an observation based on the k most similar training observations, measured by some distance function. The new observation is the most common class among the neighbours. The results may vary depending on the metric used for k (distance) and predictor scaling.

Classification Accuracy

Classification accuracy is the proportion of observations assigned to the correct class. It can be calculated from a confusion matrix that cross-tabulates observed status against predicted status.

Table 1

	True Status	
Prediction	**Positive**	**Negative**
Positive	TP (n_{11})	FP (n_{12})
Negative	FN (n_{21})	TN (n_{22})

$$Sensitivity = \frac{n_{11}}{n_{11} + n_{21}} \qquad Specificity = \frac{n_{22}}{n_{12} + n_{22}}$$

In the confusion matrix, true positives (TP) are CKD-positive observations correctly classified as positive; false positives (FP) are CKD-negative observations classified as positive; false negatives (FN) are CKD-positive observations classified as negative; and true negatives (TN) are CKD-negative observations correctly classified as negative. Accuracy is calculated as (TP + TN)/(TP + FP + FN + TN).

$$Accuracy = \frac{TP + TN}{TP + FP + TN + FN}$$

Sensitivity

Sensitivity, also termed the true-positive rate or recall, is the proportion of observed CKD-positive cases that the classifier correctly identifies. It is calculated as TP/(TP + FN).

$$Sensitivity = \frac{TP}{TP + FN}$$

Cohen's Kappa Statistic

Cohen's kappa measures agreement between predicted and observed classes after accounting for the agreement expected by chance. Larger values indicate stronger agreement beyond chance; interpretation should follow the stated reference convention and the context of the classification task.

$$Kappa = \frac{observed\ accuracy - expected\ accuracy}{1 - expected\ accuracy}.$$

Results

The analytic sample comprised 516 hospital attendees: 319 (61.8%) were classified as CKD-positive and 197 (38.2%) as CKD-negative. There were 343 women (66.5%) and 173 men (33.5%). In the CKD-positive group, 212 participants were women and 107 were men. Most participants were recorded as illiterate (422; 81.8%), lived in rural areas (447; 86.6%), and were married (385; 74.6%). A total of 190 participants (36.8%) were in the lower-income category, 277 (53.7%) in the middle-income category, and 49 (9.5%) in the higher-income category. Hypertension was recorded for 275 participants (53.3%), diabetes for 120 (23.3%), abdominal obesity for 88 (17.1%), anemia for 476 (92.2%), and a history of kidney stones for 240 (46.5%). Physical activity was reported by 51 participants (9.9%), while 313 (60.7%) reported NSAID use. These are descriptive results for the recruited sample, not estimates of population prevalence.

The chi-square results in Table 1 indicate evidence of association between CKD status and income, abdominal obesity, diabetes, hypertension, anemia, ischemic heart disease, stroke, hypercholesterolemia, peripheral vascular disease, kidney-stone history, NSAID use, blood-pressure status, and exercise (reported p-values below 0.05). Age, sex, education, residence, employment, marital status, smoking, weight category, and family history did not show statistically significant associations at the 5% level in the displayed table. Backward-elimination logistic regression retained age, income, smoking, diabetes, anemia, kidney-stone history, CKD family/history variable, NSAID use, blood pressure, haemoglobin (HB), and serum creatinine (SC) as reported in Table 2. The direction and interpretation of coefficients depend on outcome coding and reference categories, which should be explicitly verified before submission.

The final logistic-regression specification is summarised below. Please verify that the displayed equation, variable coding, and coefficient labels match the fitted model and Table 2 before submission.$\text{Logit}(p) = -0.344 - 0.650\text{age} - 0.114\text{income} + 1.354\text{smoking} - 1.460\text{diabetes} - 1.517\text{anemia} - 0.806\text{kidney}_{\text{stone}} + 0.637\ \text{history}_{\text{CKD}} - 1.108\ \text{NSAIDS} - 0.852\text{BP} - 0.242\text{HB} - 0.352\text{SC}$

Discussion

Of the 516 participants, 61.8% (n=319) were identified as having CKD based on this hospital-based analysis. This proportion is that of the study sample and should not be interpreted as the prevalence of CKD in Swat, as the sample was selected from the people visiting the kidney hospital as opposed to a community probability sample.

The results emphasize the importance of enhancing awareness, diagnosis and follow-up on the common comorbidities and CKD. Some individuals may not be screened or receive routine primary care services, resulting in the potential for undiagnosed or untreated individuals in settings where screening and primary care services are not commonly provided. Community education and easy access to risk assessment can be used to identify those who require a clinical evaluation, but the influence of risk assessment interventions was not directly measured in the present study.

Limited access to renal replacement therapy may be due to the cost of therapy, availability of dialysis services, and access to transplant centres. In resource-challenged environments, these barriers are especially significant and should be taken into account when planning kidney-health services.

The burden of CKD is difficult to precisely quantify in Pakistan due to differences in sampling, diagnostic criteria and geographic coverage of available studies. The current study gives evidence from hospital on the characteristics associated with the CKD condition of the patients attending a kidney hospital in Swat, which is not a community prevalence survey.

For this sample, hypertension and diabetes were significantly related to CKD, as expected because they are well-known clinical risk factors for CKD. The results corroborate the importance of preventing and controlling these conditions, but the cross-sectional hospital-based study design is unable to prove causation or quantify the risk levels in the broader population. Long-term strategies should involve early clinical screening, effective treatment and evidence-based public health planning.

Early recognition and management of advanced CKD will be important priorities in the context of the potential clinical and financial consequences. Regional policy recommendations should be based on population representative surveillance and evidence of availability, effectiveness and cost of interventions.

Overall, there were more women with CKD than men, and more women than men in total. The chi-square test displayed here was not significant ($p = 0.993$), so the number of samples in each group should not be interpreted as suggesting that women are more likely to have CKD than men. Likewise, socioeconomic and marital status patterns should include reported tests and adjusted estimates, not descriptive counts.

The majority of respondents did not engage in any physical activity. The chi-square analysis showed an association between exercise status and CKD status, but smoking status was not statistically significant, as shown in Table 1. The observational data should not be interpreted as evidence that smoking was protective or that exercise is directly protective of CKD due to the possibility of residual confounding and measurement limitations.

In the unadjusted analysis, CKD status was associated with abdominal obesity. Statistically significant unadjusted associations also were observed for anemia, hypertension, diabetes, ischemic heart disease, hypercholesterolemia, peripheral vascular disease, use of NSAIDs, and blood-pressure status. The chi-square table showed that family history and sex were not statistically significant. These findings should be interpreted as associations of the recruited sample and not as confirmed independent predictors unless these are supported by the final adjusted model.

At the 5% level of significance, the chi-square analysis found clinical and socioeconomic factors to be correlated with CKD, including income, abdominal obesity, diabetes, hypertension, anemia, ischemic heart disease, stroke, hypercholesterolemia, peripheral vascular disease, kidney stones, NSAID use, blood pressure and exercise. Chance findings should be noted as some tests are run. The observational design also hinders any causal inferences.

The majority of the sample had diabetes and hypertension, which were associated with CKD status. Variations between this hospital sample and results from other countries may be related to the differences in recruitment, clinical case mix, diagnostic practice, access to healthcare and distribution of underlying risk factors. Direct comparisons must have comparable study design and case definitions.

The chi-square analysis showed that 313 participants (60.7%) used NSAIDs, which was associated with CKD status. This discovery should be interpreted with caution due to the study design, which would not be able to differentiate whether medication was used prior to the diagnosis of CKD, and the presented data does not confirm medication-dosing errors. While medication safety in CKD is important, it needs to be measured on the basis of prescribing and dosing data specifically collected for the purpose of measuring medication safety.

Trends in smoking, diabetes, hypertension, obesity and other cardiovascular risk factors could impact the burden of CKD in the future. These exposures should be monitored, and the availability of preventive services must be enhanced with reasoned public health priorities, and local projections need suitable longitudinal or population-based data.

The manuscript mentions research findings on varying rates of medication-dose adjustment problems by country. The comparisons can't be made directly to the results in the present study unless similar definitions of medications, dosage, renal function, and patient selection were used. The present data (Methods and tables) do not allow assessment of the prevalence of medication-dosing errors, nor to compare quality of prescribing between countries.

The relationships of diabetes and hypertension to CKD found here are consistent with the general literature. However, there are some differences in published estimates of prevalence in Pakistan and other regions, which may be attributed to different sampling frames and diagnostic criteria. Community-based research is needed to measure the burden of CKD and identify possible causes in the community, including environmental exposures, low birth weight, and kidney-stone disease, by implementing appropriate measures.

Classifier performance was different under different training/testing splits and different numbers of selected features. For the reported results, the random forest and CART algorithms gave comparable accuracy, with the k-NN algorithm giving less accuracy for some settings. A validation strategy, that is, a plan that specifies how the best-performing configuration will be determined, must be prespecified, and the

manuscript should explain whether feature selection took place on the training set only to ensure no information leakage.

Overall, this hospital-based study identified several clinical and socioeconomic factors that were associated with the presence of CKD and compared conventional regression with machine-learning classifiers. Results should be analyzed in the context of the sample-selection process and potential confounding factors, as well as discrepancies that need to be confirmed in source tables. The generalizability of these estimates and the burden of the disease in the community requires larger population-based studies with well-defined criteria for the diagnosis of CKD, validated measurements of the CKD predictors, and external validation of the models.

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