

Prevalence of Chronic Kidney Disease, Its Risk Factors and Outcome in Nepal: A Systematic Review and Meta-analysis

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ABSTRACT

Background: Hypertension, diabetes, glomerulonephritis, obesity, and family history of kidney diseases are major risk factors for chronic kidney disease. Due to the paucity of data on a national level regarding the prevalence, risk factors, and complications of chronic kidney disease, we performed this meta-analysis.

Methods: We searched online databases from January 2000 till October 2020. Two reviewers screened articles using Covidence software. Comprehensive Meta-Analysis Software version 3 was used for data analysis.

Results: Among chronic kidney disease patients, 35.96% were found to have high LDL, 34.22% had hypercholesterolemia, 39.18% had hypertriglyceridemia, and 42.23% had low HDL. Pigmentary changes were reported in 37.71%, pruritus in 30.96%; and xerosis in 48.55%. Among the reported nail problems, the brown nail was reported in 7.19%, half and half nail in 6.07%, and white nail in 20.65%.

Conclusions: The prevalence of chronic kidney disease among high-risk cohorts in Nepal was significant among risk group with hypertension and diabetes being the most common risk factors. The most common stage of chronic kidney disease was Stage V, and the common complications were skin problems and dyslipidemia.

Keywords: Diabetes mellitus; glomerulonephritis; hypercholesterolemia; hypertension; hypertriglyceridemia; renal insufficiency chronic; risk factors

INTRODUCTION

Chronic kidney disease (CKD) is characterized by the presence of kidney damage or diminished kidney function for three months or more regardless of the cause.¹ The indicators of kidney damage are albuminuria and decreased glomerular filtration rate (GFR).^{1,2} The eGFR is estimated based on the serum creatinine level and used for staging of CKD.³ The staging of CKD is important to formulate management plans, stratifying likely risks for progression and various complications.¹

The major risk factors of CKD are hypertension, diabetes mellitus (DM), glomerulonephritis, etc.⁴ Cardiovascular diseases are major cause of mortality in patients with CKD.⁵ CKD is also associated with anemia, dyslipidemia, and other metabolic derangements.⁶ The global prevalence of CKD was 13.1% with stage 3 being the most common stage.⁷ There is a lack of national database regarding the prevalence, risk factors, and

complications of CKD among high-risk groups in Nepal so, we conducted this systematic review and meta-analysis.

METHODS

We followed the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines for conducting this systematic review and meta-analysis.⁸

Protocol registration

We registered the protocol of our study in PROSPERO ([CRD42020215499](https://doi.org/10.33314/jnhrc.v19i2.3302)).

Data sources and search strategy

We searched in medical databases like Pubmed, PubMed Central, Scopus, and Google scholar to search relevant articles from January 2000 till October 2020 using the appropriate MeSH terms and Boolean operators as: ("chronic kidney disease" OR "chronic renal failure" OR "renal failure") AND "Nepal". We have included the

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detailed search strategy as Supplementary file.

Eligibility criteria

The inclusion criteria for our studies were: (a) Cross-sectional studies, case series reporting more than 50 patients and cohort study (b) Studies reporting the prevalence of CKD and risk factors of CKD, outcome, and outcome predictors in Nepal. (c) Published articles. We excluded (a) Editorials, Comment, Viewpoint articles with no proper data of CKD and lacking adequate data of interest (b) Study conducted outside Nepal.

Study Selection

Two reviewers (YA and AM) screened the title and abstracts of articles using Covidence software based on the inclusion criteria. Any potential conflict was resolved by the third reviewer (SB).

Data Collection Process and Data Items/ Data Extraction

We collected the following data from the studies included in our meta-analysis. (a) Study year (b) Study

design (c) Sample size (d) Study area (e) Prevalence of CKD based on types of CKD (f) Risk factors of CKD that including hypertension, DM, chronic glomerulonephritis, etc (g) Outcomes that included dyslipidemia, thyroid dysfunction, dermatological (pallor, xerosis, pigmentary changes, vascular changes, panniculitis, etc) and nail changes. We independently extracted these data onto a standardized form designed in excel. Finally, we reviewed each other's work to minimize the error of entry.

Data synthesis

We conducted our statistical analysis using the Comprehensive Meta-Analysis Software (CMA) version 3. We used Proportions to estimate the outcome with 95% confidence interval (CI). I-squared (I^2) test was used for the assessment of heterogeneity (0% to 40%- considered as mild; 30% to 60%- as moderate; 50% to 90%- as substantial; and 75% to 100%- as considerable heterogeneity).⁹ Random or fixed effect model were used in accordance with the amount of heterogeneities. A forest plot was created to demonstrate the findings.

Table 1. Risk of bias assessment based on the JBI critical appraisal checklist.

Study	Was the sample frame appropriate to address the target population?	Were study participants sampled in an appropriate way?	Was the sample size adequate?	Were the study subjects and the setting described in detail?	Was the data analysis conducted with sufficient coverage of the identified sample?	Were valid methods used for the identification of the condition?	Was the condition measured in a standard, reliable way for all participants?	Was there appropriate statistical analysis?	Was the response rate adequate, and if not, was the low response rate managed appropriately?	RESULT (Overall appraisal: Include <input type="checkbox"/> Exclude <input type="checkbox"/> Seek further info <input type="checkbox"/>)
Dhimal et al. ¹¹	YES	YES	YES	YES	YES	NA	YES	YES	YES	INCLUDE
Sah et al. ¹²	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Poudel et al. ¹³	YES	YES	YES	YES	YES	NA	YES	YES	YES	INCLUDE
Chhetri et al. ¹⁴	YES	YES	YES	YES	YES	YES	YES	NO	YES	INCLUDE
Shah et al. ¹⁵	YES	YES	YES	YES	YES	UNCLEAR	YES	YES	YES	INCLUDE
Amatya et al. ¹⁶	YES	YES	YES	YES	YES	UNCLEAR	YES	YES	YES	INCLUDE
Khatiwada et al. ¹⁷	YES	YES	YES	YES	NO	YES	YES	YES	YES	INCLUDE
Khakurel et al. ¹⁸	YES	YES	YES	YES	YES	YES	UNCLEAR	YES	YES	INCLUDE
Sharma et al. ¹⁹	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Poudel et al. ²⁰	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Paudel et al. ²¹	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Devkota et al. ²²	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE

Khadka et al. ²³	YES	YES	YES	YES	YES	YES	UNCLEAR	YES	YES	INCLUDE
Poudel et al. ²⁴	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Singh et al. ²⁵	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Bartaula et al. ²⁶	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Sigdel et al. ²⁷	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Pokhrel et al. ²⁸	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE
Anand et al. ²⁹	YES	YES	YES	YES	YES	YES	YES	YES	YES	INCLUDE

Risk of bias assessment based on the critical appraisal checklist

We used the Joanna Briggs Institute (JBI) critical appraisal tool for qualitative assessment of the included studies.¹⁰ The bias assessment of the included studies is presented in Table 1.

Subgroup analysis

Subgroup analysis was performed among outcomes, namely stage of CKD, dyslipidemia, skin changes, and nail changes.

Sensitivity analysis

We excluded individual studies to determine the likely effect on the result after exclusion for sensitivity analysis.

RESULTS

We identified a total of 1346 records after database searching. After the removal of 283 duplicates, we screened the title and abstract of 1083 records, and 978 records were excluded. A total of 86 articles were excluded with definite reasons. Finally, we included 19 studies in our qualitative and quantitative analysis (Figure 1). The qualitative analysis of included studies

are discussed in Table 2.

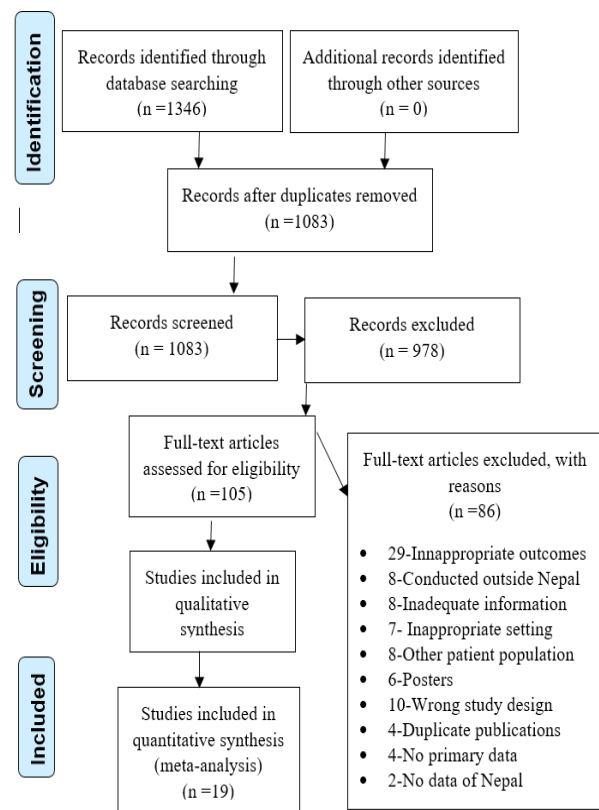


Figure 1. PRISMA flow diagram.

Table 2. Qualitative analysis of included studies.

Study	Study date	Type of Study	Sample Size	Study Location	Key Study Findings
Khatriwada et al. ¹⁷	2015	Cross-Sectional	360	BPKIHS	CKD 3 144/360, CKD 4 156/360 and CKD 5 60/360 Hypercholesterolemia 124/360, Hypertriglyceridemia 132/360, Low HDL 123/360 and High LDL 126/360
Chhetri et al. ¹⁴	2006-2007	Prospective Cross sectional Study	100	Nepal Medical College Teaching Hospital	HTN 54/100, DM 18/100, Chronic GN 18/100 and Others (Obstructive Uropathy) 9/100
Dhimal et al. ¹¹	2016-2018	Cross-Sectional	13200	Nationwide	Prevalence of CKD 792/13200

Poudel et al. ¹³	2008-2009	Cross-sectional study	160	Institute of Medicine, TUTH	HTN 112/160, DM 36/160 Hypertriglyceridemia 74/160 and Low HDL 98/160
Sharma et al. ¹⁹	2003-2005	Cross-sectional	3218	Dharan*	Prevalence of CKD 1458/3218 HTN 1243/3218, DM 242/3218
Poudel et al. ²⁰	2008-2010	Cross-section study	212	TUTH	Prevalence of CKD 78/212 CKD 1 10/78, CKD 2 35/78, CKD 3 31/78 and CKD 4 2/78 HTN 212/212
Amatya et al. ¹⁶	2003-2004	Case-control study	104	BPKIHS	Xerosis 23/104, Pigmentary changes 17/104, Pruritus 12/104. Half and half nail 4/104, White nail 65/104, Brown nail 9/104
Bartaula et al. ²⁶	2019	Cross-sectional study	228	BPKIHS	HTN 70/228, DM 87/228, Chronic Glomerulonephritis 61/228 and Others (Obstructive uropathy) 10/228
Shah et al. ¹⁵	2008-2009	Cross-sectional study	83	Bir hospital and Shree Birendra Hospital	Pallor 76/83, Xerosis 63/83, Pigmentation 54/83, Pruritus 50/83, Vascular 14/83, Gynecomastia 4/83 and Panniculitis 1/83
Sah et al. ¹²	2016-2017	Cross-sectional study	136	Kathmandu medical college and teaching hospital	HTN 47/136, DM 107/136
Sigdel et al. ²⁷	2018	Cross-sectional study	401	Institute of Medicine, TUTH	CKD 3 18/401, CKD 4 51/401 and CKD 5 332/401 HTN 87/401, DM 128/401, Chronic GN 145/401 and Others (Obstructive uropathy, ADPCKD) 41/401
Pokhrel et al. ²⁸	2017	Cross-sectional study	100	Nepal Medical College and Teaching Hospital	HTN 93/100, DM 29/100 and history of smoking 40/100
Anand et al. ²⁹	2006-2011	Cross-sectional study	21809	Nationwide	Prevalence of CKD 4558/21809
Singh et al. ²⁵	2014-2015	Cross-sectional study	103	Kist Medical College	HTN 24/103, DM 46/103, Chronic GN 27/103 and Others (Obstructive uropathy, ADPCKD) 6/103
Khadka et al. ²³	2015-2016	Cross-sectional study (hospital based)	57	Bir Hospital	HTN 15/57, DM 2/57, HTN + DM 6/57, Smoking 2/57 and Smoking + HTN 18/57
Poudel et al. ²⁴	2008-2010	Cross-sectional study	326	TUTH	CKD 1 34/326, CKD 2 36/326, CKD 3 31/326, CKD 3 32/326, CKD 4 30/326 and CKD 5 163/326 Hypercholesterolemia 55/163, Hypertriglyceridemia 58/163, Low HDL 53/163 and High LDL 62/163
Khakurel S ¹⁸ et al.	2001-2006	Retrospective cross sectional study	802	Bir hospital	CKD 5 802/802 HTN 110/802, DM 135/802, Chronic GN 326/802, Idiopathic 144/802 and Others 32/802
Paudel K ²¹ et al.	2011	Cross sectional study	64	Gandaki Medical College Teaching Hospital	CKD 5 64/64 Low TSH 2/64, High TSH 17/64
Devkota K ²² e al.	2015-2016	Cross sectional study	62	BPKIHS	HTN 36/62, DM 3/62, Chronic GN 2/62 and HTN + DM 14/62 and Idiopathic 7/62

Note: * Study denoted by Sharma SK¹⁹ et al. was community-based study conducted in Dharan. Abbreviations: ADPCKD- Autosomal dominant polycystic kidney disease, BPKIHS- B P Koirala Institute of Health Sciences, CKD- Chronic kidney disease, DM- Diabetes mellitus, GN- Glomerulonephritis, HDL-High Density Lipoprotein, HTN- Hypertension, LDL-Low Density Lipoprotein, TSH- Thyroid stimulating hormone, Tribhuvan University Teaching Hospital

Quantitative result

CKD prevalence: Five studies reporting prevalence of CKD among different patient populations showed a 27.6% rate of CKD among specific risk groups (Proportion: 0.27; CI, 0.13-0.48; $I^2=99.85$) (Figure 2.). Sensitivity analysis by excluding individual studies did not show significant changes (Supplementary file Figure 1.)

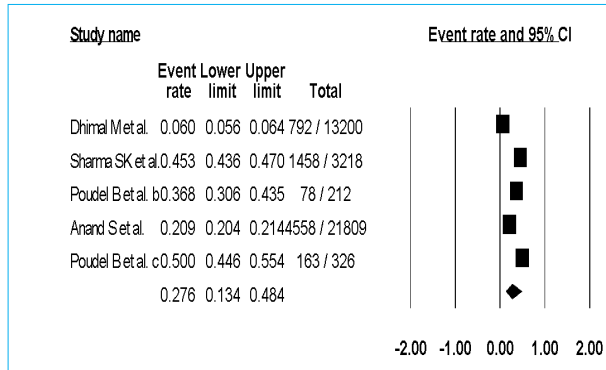


Figure 2. Prevalence of CKD among at risk population

CKD staging among reported studies: Among CKD cases, CKD stage-1 was reported in 10.9% (CI: 8.23-14.36); CKD stage-2 in 24.01% (CI: 4.77-66.62%); CKD stage-3 in 17.84% (CI: 5.73-43.69); CKD stage-4 in 13.05% (CI: 4.31-33.34); CKD stage-5 in 81.02% (CI: 34.86-97.14) (Figure 3).

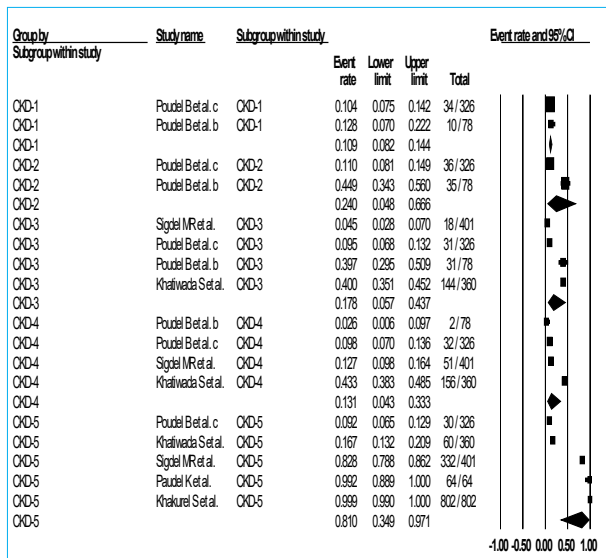


Figure 3. CKD staging among reported studies

Risk factors of CKD among CKD patients

Hypertension: Twelve studies reported hypertensive status among CKD patients. 45.07% of CKD patients had hypertension (Proportion: 0.45; CI, 0.33-0.57; $I^2=97.16$) (Figure 4). Sensitivity analysis carried by excluding individual studies did not show any significant differences (Supplementary file, Figure 2).

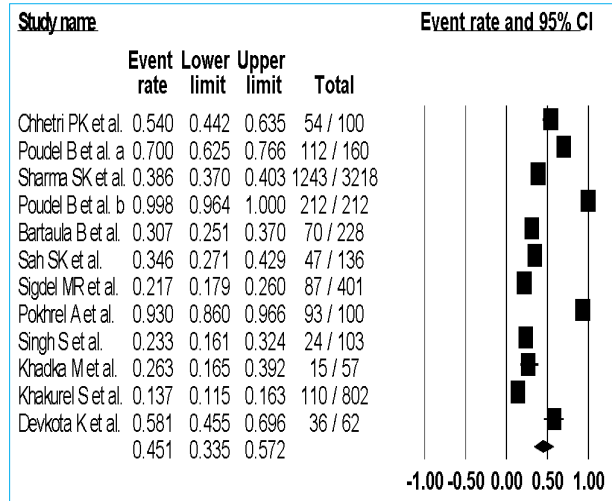


Figure 4. Hypertension among CKD patients among reported studies

DM among CKD: Among CKD patients, 23% had DM (Proportion: 0.23; CI, 0.13-0.37; $I^2=98.26$) (Figure 5.). Sensitivity analysis for DM after excluding individual studies did not show significant changes (Supplementary file Figure 3).

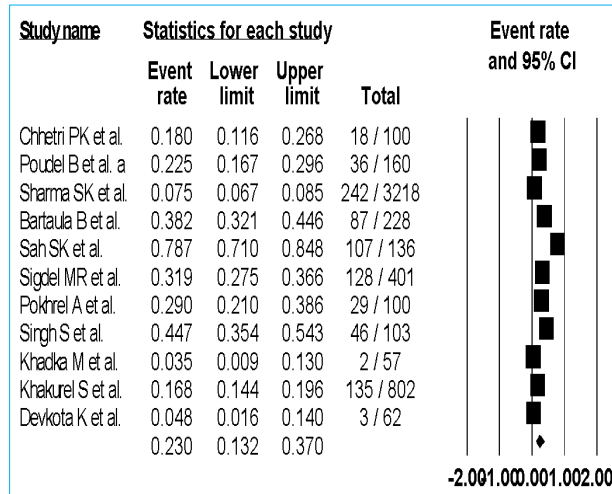


Figure 5. DM among CKD patients among reported studies

Glomerulonephritis among CKD patients: Six studies reported glomerulonephritis among CKD patients and it showed 23.46% were having glomerulonephritis (Proportion: 0.23; CI, 0.16-0.33; $I^2=91.94$) (Figure 6.). Sensitivity analysis for glomerulonephritis after excluding individual studies did not show significant changes (Supplementary file, Figure 4).

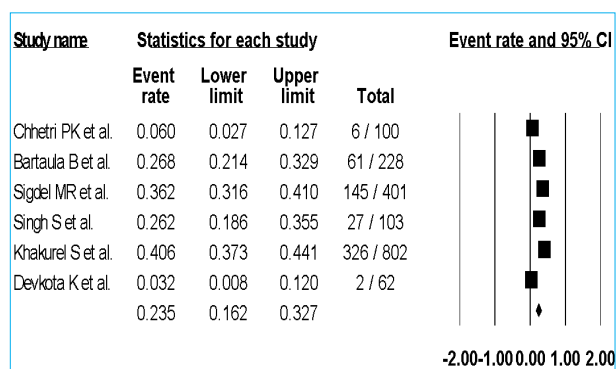


Figure 6. Glomerulonephritis among CKD patients among reported studies.

Obstructive Uropathy among CKD patients: Six studies reported obstructive uropathy among CKD patients and it showed 6.29% were having obstructive uropathy (Proportion: 0.06; CI, 0.04- 0.01; $I^2=79.84$) (Supplementary file. Figure 5.). Sensitivity analysis for obstructive uropathy after excluding individual studies did not show significant changes (Supplementary file, Figure 6).

Associated adverse Outcomes:

Dyslipidemia: Among CKD patients, two study reported high LDL in 35.96% (Proportion: 0.36; CI, 0.32-0.40); two study reported hypercholesterolemia in 34.22% (Proportion: 0.34; CI, 0.30-0.38); three studies reported hypertriglyceridemia in 39.18% (Proportion: 0.39; CI, 0.33-0.45); three studies reported low HDL in 42.23% (Proportion: 0.42; CI, 0.26-0.60) (Supplementary file, Figure 7).

Skin problems: Pooling result of two studies showed pigmentary changes in 37.71% (Proportion: 0.38; CI, 0.06- 0.84); pruritus in 30.96% (Proportion: 0.31 CI, 0.04-0.83); and xerosis in 48.55% (Proportion: 0.49; CI, 0.08-0.91) of CKD patients (Supplementary file, Figure 8).

Nail problems: Pooling result of two studies showed brown nail in 7.19% (CI: 4.19- 12.08); half and half in 6.07% (CI, 2.80-12.66); and white nail in 20.65% (CI, 6.28-91.46) of CKD patients (Supplementary file, Figure 9).

DISCUSSION

The prevalence of CKD in Nepal was found to be 27.6% among specific risk groups for developing CKD (95% CI, 13.39%-48.37%). Estimation of CKD prevalence at the national level in the general population is difficult because most of the available studies are done among high-risk

populations. An international cross-sectional study done in six different regions of the world including Nepal had estimated a CKD prevalence of 20.1% in Nepal, which is lower than the result of the present analysis.³⁰ This can be explained by the inclusion of high-risk population in our study. The same study reported prevalence of CKD in India to be 16.8% and in China to be around 29.9% in the general population. In Bangladesh, among high-risk cohorts, the prevalence of CKD was 49.3% which is much higher than in Nepal.³⁰ As per the CDC, the prevalence of CKD in the US is estimated to be 15% while in the UK, the prevalence is 6.76%.^{31,32} Overall the prevalence is found to be 15% higher in low and middle income countries compared to high income countries.^{7,33} Estimation of prevalence of CKD is important because most of the patients are unaware of their kidney problems due to the paucity of symptoms at the early stage. These prevalence data on CKD in countries like ours helps to direct the appropriate screening programs for CKD in the general population and high-risk groups in addition to continue follow up and treatment.

Our study found that CKD stage 5 (81.02%) was the most common stage of CKD in Nepal followed by stage 2 (24.01 %), stage 3 (17.84%), stage 4 (13.05%) and stage 1 (10.9%). Our findings of Grade 5 being the most common stage of CKD in Nepal was in contrast to the published global data and UK where CKD stage 3 was the most common among patients with CKD.^{7,32} This might be explained by the fact that almost all of the studies included in this analysis were hospital based and there is paucity of data on the prevalence of CKD in the community level. Moreover, due to the lack of awareness and easy accessibility of health services, people tend to wait till the development of symptoms, which occur only in the advanced stages of the disease. We found that around 45.07% of patients with CKD had hypertension, 23% each had DM and chronic GN. The least common finding in CKD patients was obstructive uropathy which accounted for 6.29% of CKD. An increased association of CKD was found with hypertension and DM globally, especially in low and middle-income countries which is in agreement with our findings.¹⁹ Hypertension and DM are both risk factors for progression to chronic kidney disease. Especially in developing countries like ours, there is a low level of awareness about these conditions and their possible complications. Various studies in Nepal have found that people with hypertension and DM do not take medications regularly, have poorly controlled blood pressure and blood sugar due to poor knowledge and inaccessibility to health services.³⁴⁻³⁷ These factors are important because they contribute to the progression of CKD. It is thus necessary to screen high-risk cohorts

including patients with hypertension, DM and other risk factors in compliance with Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, especially in developing country like Nepal.²

The most commonly reported complications in our analysis were skin problems (37.71%), dyslipidemia (35.96%), and nail problems (7.19%). Dyslipidemia in CKD has been shown to be due to abnormalities of lipoproteins resulting in increased cholesterol, increased triglycerides, and decreased HDL.³⁸ Lipoprotein lipase function has been shown to be diminished in patients with chronic kidney disease.³⁹ There was an increase in dyslipidemia from 45.5% in Stage I to 67.8 % in CKD Stage IV as NHANES (National Health and Nutritional Examination Survey) data of US from 2001-2020. Our findings of dyslipidemia were slightly lower than the US but still remain significant.⁴⁰ It is important to manage dyslipidemia in patients with CKD owing to increased risks of cardiovascular morbidity and mortality. Skin changes in CKD like pruritus is considered to be due to systemic inflammatory process rather than local skin problem.⁴¹

Our study had several limitations. Firstly, we could not estimate the prevalence of CKD among the general population due to the lack of nationwide databases. Secondly, sub-group analysis comparing the prevalence of CKD based on gender, age and race could not be performed due to lack of relevant data. Although cardiovascular diseases are common causes of mortality and morbidity in CKD, we did not study this due to lack of data. Each study had their own inherent limitations, like small sample size, observational nature, high drop outs rate, etc. The heterogeneities in our study are explained by diverse patient populations, different study designs and locations.

CONCLUSIONS

The prevalence of chronic kidney disease among high-risk cohorts in Nepal was 27.6% with hypertension and DM being the most common risk factors in patients. The most common stage of CKD was Stage V and common complications were skin problems and dyslipidemia. Further studies involving the general population are needed for the estimation of CKD among the general population and at-risk population to prevent or timely treat it.

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REFERENCES

1. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J kidney Dis Off J Natl Kidney Found.* 2002;39(2 Suppl 1):S1-266. [\[PubMed\]](#)[\[Article\]](#)
2. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: A position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int.* 2005;67(6):2089-2100. [\[PubMed\]](#) | [\[Article\]](#)[\[DOI\]](#)
3. Miller WG, Jones GRD. Estimated Glomerular Filtration Rate; Laboratory Implementation and Current Global Status. *Adv Chronic Kidney Dis.* 2018;25(1):7-13. [\[PubMed\]](#)[\[Article\]](#) | [\[DOI\]](#)
4. Kazancioğlu R. Risk factors for chronic kidney disease: An update. In: *Kidney International Supplements.* Vol 3. Nature Publishing Group; 2013:368-371. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
5. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic Kidney Disease and the Risks of Death, Cardiovascular Events, and Hospitalization. *N Engl J Med.* 2004;351(13):1296-1305. [\[PubMed\]](#) [\[Full Text\]](#)[\[DOI\]](#)
6. Thomas R, Kanso A, Sedor JR. Chronic Kidney Disease and Its Complications. *Prim Care.* 2008;35(2):329-344. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
7. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA,

- Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis. Remuzzi G, ed. PLoS One. 2016;11(7):e0158765. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
8. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. JAMA. 2000;283(15):2008-2012. [\[PubMed\]](#) [\[Full Text\]](#)[\[DOI\]](#)
 9. Cochrane Handbook for Systematic Reviews of Interventions | Cochrane Training. [Internet]. [Accessed December 6, 2020]. Available from: <https://training.cochrane.org/cochrane-handbook-systematic-reviews-interventions>.
 10. critical-appraisal-tools - Critical Appraisal Tools | Joanna Briggs Institute. [Internet]. [Accessed December 6, 2020]. Available from: <https://joannabriggs.org/critical-appraisal-tools>.
 11. Dhimal M, Karki KB, Sharma SK, Aryal KK, Shrestha N, Poudyal A, et al. Prevalence of Selected Chronic Non-Communicable Diseases in Nepal. J Nepal Health Res Counc. 2019;17(3):394-401. [\[PubMed\]](#) [\[Full Text\]](#) [\[DOI\]](#)
 12. Sah SK, Adhikary LP. Association between Dyslipidemia and Serum Level of 25-Hydroxyvitamin-D in Early Chronic Kidney Disease, Not on Dialysis: An Observational Cross-Sectional Study from the Himalayan Country. Int J Nephrol Renovasc Dis. 2020; 13:211-218. [\[PubMed\]](#)[\[Full Text\]](#)[\[DOI\]](#)
 13. Poudel B, Yadav BK, Jha B, Raut KB. Dyslipidaemia in chronic kidney disease in Nepalese population. Mymensingh Med J. 2013;22(1):157-163. [\[PubMed\]](#) [\[Article\]](#)
 14. Chhetri PK, Manandhar DN, Bhattarai SP, Pahari LR, Shrestha R. Chronic kidney disease 5 on hemodialysis in Nepal Medical College Teaching Hospital. Nepal Med Coll J. 2008;10(1):8-10. [\[PubMed\]](#)[\[Article\]](#)
 15. Shah A, Hada R, Kayastha BMM. Dermatological Disorders in Chronic Kidney Disease. J Nepal Med Assoc. 2013;52(190):365-71. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
 16. Amatya B, Agrawal S, Dhali T, Sharma S, Pandey SS. Pattern of skin and nail changes in chronic renal failure in Nepal: A hospital-based study. J Dermatol. 2008;35(3):140-145. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
 17. Khatiwada S, Rajendra KC, Gautam S, Lamsal M, Baral N. Thyroid dysfunction and dyslipidemia in chronic kidney disease patients. BMC Endocr Disord. 2015;15(1). [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
 18. Khakurel S, Agrawal RK, Hada R. Pattern of end stage renal disease in a tertiary care center. J Nepal Med Assoc. 2009;48(174):126-130. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
 19. Sharma SK, Dhakal S, Thapa L, et al. Community-Based Screening for Chronic Kidney Disease, Hypertension and Diabetes in Dharan. J Nepal Med Assoc. 2013;52. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
 20. Mahato RV, Jha B, Raut KB, Gyawali P, Yadav BK, Nepal AK. Prevalence of metabolic syndrome in chronic kidney disease: a hospital based cross-sectional study. Journal of Nepal Health Research Council. 2013 May 27. [\[PubMed\]](#) [\[Full Text\]](#) [\[DOI\]](#)
 21. Paudel K. Prevalence and clinical characteristics of hypothyroidism in a population undergoing maintenance hemodialysis. J Clin Diagnostic Res. 2014;8(4):MC01. [\[PubMed\]](#)[\[Article\]](#) [\[DOI\]](#)
 22. Devkota K, Gupta MK, Pant AR, Karki P. Correlation of Duplex Ultrasonographic Parameters with Glomerular Filtration Rate in Chronic Kidney Disease. J Nepal Health Res Counc. 2019;17(1):32-37. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
 23. Khadka M, Pantha B, Karki L. Correlation of uric acid with glomerular filtration rate in chronic kidney disease. J Nepal Med Assoc. 2018;56(212):724-727. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
 24. Poudel B, Yadav BK, Shrestha R, Mittal A, Jha B, Raut KB. Assessment of chronic kidney disease in Nepalese people with hypertension. Nepal Med Coll J. 2012;14(1):25-30. [\[PubMed\]](#) [\[Article\]](#)
 25. Singh S, Verma A, Aryal G, Thapa S, Khakurel S, Shrestha K. Thyroid hormone profile in patients with chronic kidney disease: a single centre study. J Nepal Health Res Counc. 2016;14(34):197-201. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
 26. Bartaula B, Subedi M, Kumar MM, Shrestha M, Bichha N, Mudbhari B. Spectrum of complications in chronic kidney disease patients undergoing maintenance hemodialysis: An experience of a tertiary care center in Nepal. Saudi J Kidney Dis Transpl. 2019;30(1):208-214. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
 27. Sigdel MR, Pradhan RR. Chronic Kidney Disease in a Tertiary Care Hospital in Nepal. Journal of Institute of Medicine. 2018;40(2):104-111. [\[Download PDF\]](#)
 28. Pokhrel A, Gyawali P, Pokhrel BR, Khanal MP, Manandhar DN, Bwititi P, Nwose EU. Prevalence of cardiovascular risk factors among chronic kidney disease patients undergoing hemodialysis in a tertiary care center, Kathmandu, Nepal. Nepal Medical College Journal. 2019;21(4):313-8. [\[Article\]](#)[\[DOI\]](#)
 29. Anand S, Zheng Y, Montez-Rath ME, Wei WJ, Perico N,

- Carminati S, et al. Do attributes of persons with chronic kidney disease differ in low-income and middle-income countries compared with high-income countries? Evidence from population-based data in six countries. *BMJ Glob Heal.* 2017;2(4):e000453. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
30. Ene-Iordache B, Perico N, Bikbov B, Carminati S, Remuzzi A, Perna A, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. *The Lancet Global Health.* 2016 May 1;4(5):e307-19. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
31. Chronic Kidney Disease in the United States, 2019. [Internet]. [Accessed December 6, 2020]. Available from: <https://www.cdc.gov/kidneydisease/publications-resources/2019-national-facts.html>.
32. De Lusignan S, Tomson C, Harris K, van Vlymen J, Gallagher H. UK Prevalence of Chronic Kidney Disease for the Adult Population Is 6.76% Based on Two Creatinine Readings. *Nephron Clin Pract.* 2012;120(2):107-107. [\[Article\]](#)[\[DOI\]](#)
33. Mills KT, Xu Y, Zhang W, Bundy JD, Chen CS, Kelly TN, et al. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. *Kidney Int.* 2015;88(5):950-957. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
34. Neupane D, Shrestha A, Mishra SR, Bloch J, Christensen B, McLachlan CS, et al. Awareness, Prevalence, Treatment, and Control of Hypertension in Western Nepal. *Am J Hypertens.* 2017;30(9):907-913. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
35. Maharjan B. Prevalence and Awareness of Hypertension among Adults and its Related Risk Factors. *J Nepal Health Res Counc.* 2017;15(3):242-246. [\[PubMed\]](#)[\[JNHRC\]](#)[\[DOI\]](#)
36. Devkota S, Dhungana RR, Pandey AR, Bista B, Panthi S, Thakur KK, et al. Barriers to Treatment and Control of Hypertension among Hypertensive Participants: A Community-Based Cross-sectional Mixed Method Study in Municipalities of Kathmandu, Nepal. *Front Cardiovasc Med.* 2016;3. [\[PubMed\]](#) [\[Article\]](#)[\[DOI\]](#)
37. Gyawali B, Hansen MR, Povlsen MB, Neupane D, Andersen PK, McLachlan CS, et al. Awareness, prevalence, treatment, and control of type 2 diabetes in a semi-urban area of Nepal: Findings from a cross-sectional study conducted as a part of COBIN-D trial. Soundy A, ed. *PLoS One.* 2018;13(11):e0206491. [\[PubMed\]](#)[\[Article\]](#) [\[DOI\]](#)
38. Tsimihodimos V, Mitrogianni Z, Elisaf M. Dyslipidemia Associated with Chronic Kidney Disease. *Open Cardiovasc Med J.* 2011;5(1):41-48. [\[PubMed\]](#) [\[Full Text\]](#)[\[DOI\]](#)
39. Vaziri ND, Liang K. Down-regulation of tissue lipoprotein lipase expression in experimental chronic renal failure. *Kidney Int.* 1996;50(6):1928-1935. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
40. Kuznik A, Mardekian J, Tarasenko L. Evaluation of cardiovascular disease burden and therapeutic goal attainment in US adults with chronic kidney disease: An analysis of national health and nutritional examination survey data, 2001-2010. *BMC Nephrol.* 2013;14(1):132. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)
41. Kuypers DRJ. Skin problems in chronic kidney disease. *Nat Clin Pract Nephrol.* 2009;5(3):157-170. [\[PubMed\]](#)[\[Article\]](#)[\[DOI\]](#)