VOL. 17|NO. 3|ISSUE 67|JULY-SEPT. 2019

Prehypertension and its Risk Factors in Suburban Nepal – Findings from the Dhulikhel Heart Study

Tamrakhar D,[1] Karmacharya BM,[1,2] Shrestha R,[3] Koju R,[4] Fitzpatrick AL,[5] Shrestha A[2]

[1]Department of Community Medicine,
[2]Department of Public Health,
[3]Department of Pharmacology,
[4]Department of Internal Medicine
Kathmandu University School of Medical Sciences,
Dhulikhel, Nepal.
[5]Departments of Family Medicine, Epidemiology, and Global Health, University of Washington, Seattle, WA, USA.

Corresponding Author

Dipesh Tamrakar
Department of Community Medicine,
Kathmandu University School of Medical Sciences,
Dhulikhel, Nepal.
E-mail: dipesht@kusms.edu.np

Citation

Tamrakhar D, Karmacharya BM, Shrestha R, Koju R, Fitzpatrick AL, Shrestha A. Prehypertension and its Risk Factors in Suburban Nepal - Findings from the Dhulikhel Heart Study. *Kathmandu Univ Med J.* 2019;67(3):234-40.

ABSTRACT

Background

Prehypertension, defined as a systolic blood pressure of 120-139 mmHg or a diastolic blood pressure of 80-89 mmHg, leads to higher rates of incident hypertension, and is associated with excess morbidity and deaths from cardiovascular diseases.

Objective

To estimate the prevalence of and examine the factors associated with prehypertension in Dhulikhel.

Method

This cross-sectional study utilized data from the 752 participants of the Dhulikhel Heart Study (DHS). The data collectors interviewed the participants at their home using a tablet based structured pre-tested questionnaire and measured blood pressure using a standard digital blood pressure machine (Microlife, Switzerland). Multivariate analysis was conducted using generalized estimating equations with multivariate logistic regression (with household as cluster) adjusting for age, sex, ethnicity, marital status, income, education, alcohol consumption, smoking, physical activity, body mass index (BMI) and food consumption.

Result

Males had a three-fold higher odds of prehypertension than females (OR:3.17, 95% CI:1.91-5.26). The odds of prehypertension increased with being overweight (OR:2.29, 95% CI:1.42-3.70) and with being obese (OR:5.00, 95% CI:1.81-13.79) compared to normal BMI. Education reduced the odds of developing prehypertension (OR:0.51, 95% CI:0.29-0.91). Those who met the recommended level of physical activity (OR:0.61, 95% CI:0.40-0.95) also were associated with lower prehypertension prevalence.

Conclusion

Obese/overweight and being male increased the odds of prehypertension whereas formal education and recommended level of physical activities were associated with lower prehypertension prevalence. Primordial prevention against cardiovascular risk factors at the community level, especially targeting the young adult male, is imperative.

KEY WORDS

Nepal, Prehypertensoin, Risk factors

INTRODUCTION

Prehypertension, defined as a systolic blood pressure (SBP) of 120-139 mmHg or a diastolic blood pressure (DBP) of 80-89 mmHg, leads to higher rates of incident hypertension and is associated with excess morbidity and deaths from cardiovascular diseases (CVD).[1-4] Mortality from ischemic heart disease and stroke increases from blood pressure (BP) levels as low as 115/75 mmHg and upward.[5] Therefore, from a public health perspective, shifting the distribution of BP by a small amount in the population can have a substantial effect on hypertension-related mortality rates.

Nepal is one of the least developed countries in the world experiencing an epidemiologic transition from infectious to chronic diseases, similar to many other low and middle-income countries. Ischemic heart disease is the leading cause of death in Nepal.[6] Sub-optimal and high SBP are the second and third leading risk factors that contribute to death and disability.[6]

Prehypertension is more common than hypertension.[7] Despite being common and associated with excess cardiovascular disease morbidity and mortality, only two studies have assessed its prevalence in the adult population and only two studies have investigated its risk factors in the Nepalese population.[8-10] The aim of this study was to estimate the prevalence and factors associated with prehypertension from a population-based study - The Dhulikhel Heart Study.[11]

METHODS

This cross-sectional study utilized data from the baseline survey of the Dhulikhel Heart Study (DHS). The DHS is a population-based observational cohort study designed to investigate cardiovascular disease and its conventional risk factors in a suburban Nepalese population in central Nepal. The study design has been published elsewhere.[11] A third of the households (n=735) in the town of Dhulikhel were randomly selected and all eligible residents were recruited from the sampled household. Inclusion criteria were: adults 18 years or older; a permanent resident of Dhulikhel; having lived in Dhulikhel for at least six months; non-pregnant at the time of data collection; and able to communicate in Nepali or Newari language. A total of 1,372 eligible participants were enumerated, out of which the data collectors were able to contact 1,103 (80%) participants. Eligible subjects who provided informed consent (n=1,073, 78%) were recruited in the study. Data collected occurred between November 2013 and February 2015.

This study analyzed the data of 752 participants excluding 298 hypertensive individuals (SBP ≥ 140 mmHg, DBP ≥ 90 mmHg or person taking anti-hypertensive medications) identified during the baseline survey. The institutional review boards of the University of Washington and the Nepal Health Research Council approved the study.

Trained data collectors visited participant's household and measured systolic and diastolic blood pressure three times in a sitting posture on the right arm over loose clothes using a standard digital blood pressure machine (Microlife, Switzerland). The mean of the three measurements was used for the analysis. Prehypertension was defined as a systolic blood pressure (SBP) of 120 mmHg to 139 mmHg and/or diastolic blood pressure (DBP) of 80 to 89 mmHg.[12]

The data collectors interviewed the participants at their home using a tablet based structured pre-tested questionnaire. Sociodemographic characteristics included self-reported age (years), sex (male/female), marital status (married / not married), ethnicity (Newar / Brahmin Chhetri / other), education (the number of formal years), household income (converted to USD) and lifestyle factors including smoking (never / former / current) and alcohol consumption (never, low, moderate, high) Physical activity was assessed using the Global Physical Activity Questionnaire.[13] A weekly MET equivalent of 600 reflects approximately 30 minutes brisk walking five times per week or 15 min running five times per week. The activity level of 600 metabolic equivalent minutes per week was categorized as having adequate physical activity as per the WHO recommendation. (WHO Guide) Dietary intake (whole grains, refined grains, lentils, fruits, vegetables and salty food) were collected using a validated food frequency questionnaire.[14]

Weight was measured without shoes wearing minimal clothing using an Omron Model HBF-400 scale and recorded to the nearest of 0.1 pounds. Height was measured without shoes using a standard tape measure with participants standing against a wall for measurement and recorded to the nearest of 0.1 cm. Body Mass Index (BMI) was calculated as weight in kilograms divided by height in meters squared. Overweight was defined as a BMI of 25 kg/m^2 or higher and obesity was defined as BMI of 30 kg/m^2 or higher based on international cut off points.[15]

Sample characteristics were described for males and females using means and standard deviations for continuous variables and percentages for categorical variables. The main models utilized generalized estimating equations (GEE) with multivariate logistic regression, exchangeable working correlation and robust variance. In Nepal, households generally consume food together and eating norms are shared by all of its members. We thus expected that the outcomes among individuals in the same household would be correlated. GEE corrects for correlation of responses for participants from a common household (clustered within household), and robust variance estimators provide assurance for valid inference under possibly mis-specified correlation structure.[16] The association of prehypertension with demographic characteristics (age, sex, ethnicity, marital status, income and education); lifestyle factors (smoking, alcohol intake, physical activity) and body mass index was measured in univariate and multivariate models. The odds ratios are reported with 95% confidence interval.

RESULTS

Of 752 participants included in this analysis, 64% were women (Table 1). The mean age was 36 ± 15 years. Majority of the participants were of Newar ethnicity. Men were found to have higher education and income than women in the study.

Table 1. Demographic characteristics of 752 non-hypertensive participants of the Dhulikhel Heart Study

Study	No of cases	Sampling error	Interpretation error
Characteristics	Men (n=270)	Women (n = 482)	Total (n=752)
Age, mean(SD), (years)	35.5 (14.8)	36.4 (14.8)	36.0 (14.8)
Ethnicity(n,%)			
Newar	99 (36.7)	212 (44.0)	311 (41.4)
Brahmin/ Chhetri	96 (35.6)	143 (29.7)	239 (31.8)
Other	75 (27.8)	127 (26.3)	202 (26.9)
Religion(n,%)			
Hindu	221 (81.9)	405 (84.0)	626 (83.2)
Non-Hindu	49 (18.1)	77 (16.0)	126 (16.8)
Education(n,%)			
No formal education	44 (16.3)	170 (35.3)	214 (28.4)
Formal education	226 (83.7)	312 (64.7)	538 (71.6)
Annual income (USD), mean (SD)	1090.6 (3323.1)	469.9 (2814.6)	692.8 (3019.6)
Marital Status, n(%)			
Married	187 (69.3)	339 (70.3)	526 (69.9)
Not married	83 (30.7)	340 (29.7)	226 (30.1)

More men were smokers, drinkers and were less physically active (Table 2). The prevalence of obesity was higher in women. The mean intake of fruits and vegetables per day was only 3.4±2 servings per day. Whole grain consumption was very low compared to refined grains

Almost half (48.4%) of the participants had pre-hypertension (Figure 1). The prevalence of prehypertension was higher (62%) in men as well as among the overweight (60%) and obese (78%).

The odds of prehypertension increased with year of age (OR: 1.01, 95% CI: 1.00-1.02) in univariate analysis but no association was observed after controlling for other factors (OR: 1.01, 95% CI: 0.99-1.03) (Table 3). Both univariate (OR: 2.42, 95% CI: 1.79-3.28) and multivariate analysis (OR: 3.17, 95% CI: 1.91-5.26) showed that males had a three-fold higher odds of prehypertension than females. No

Table 2. Lifestyle factors of 752 non-hypertensive participants of the Dhulikhel Heart Study

Characteristics	Men n=270)	Women (n=482)	Total (n=752)
Smoking, n (%)			
Non Smoker	153 (56.7)	399 (82.8)	552 (73..4)
Former Smoker	20 (7.4)	16 (3.3)	36 (4.8)
Current Smoker	97 (35.9)	67 (13.9)	164 (21.8)
Alcohol, n (%)			
Non drinkers	147 (54.4)	395 (81.9)	542 (72.0)
Low (Less than 1 glass per week)	22(8.2)	36 (7.5)	58 (7.7)
Moderate (1-3 glass per week)	26 (9.6)	16 (3.3)	42 (5.6)
High (> 3 glass per week)	75 (27..8)	35 (7.3)	110 (14.6)
Physical activity,n(%)			
Less than recom-mended level			
(<600 MET min utes per week)	85 (31.5)	193 (40.4)	278 (37.0)
Met recommend ed level			
(>=600 MET minutes per week)	185 (68.5)	289 (59.9)	474 (63.0)
Body Mass Index (BMI), n(%)			
Normal (18.5 - 24.9 kg/m^2)	180 (66.7)	305 (63.3)	485 (64.5)
Underweight (< 18.5 kg/m^2)	22 (8.2)	31 (6.4)	53 &.1)
Overweight (25.0 -29.9 kg/m^2)	63 (23.3)	123 (25.5)	186 (24.&)
Obese (>= 30 kg/m^2)	5 (1.9)	23 (4.8)	28 (3.7)
Intake (servings per day)			
Fruits and Veg etables (mean, SD)	3.5 (2.01)	3.2 (1.9)	3.4 (2.0)
Whole grains (mean, SD)	0.4 (0.34)	0.4 (0.4)	0.4 (0.4)
Refined grains (mean, SD)	3.4 (1.23)	3.7 (1.1)	3.5 (1.2)
Lentils (mean, SD)	1.5 (1.02)	1.5 (1.0)	1.5 (1.0)
Salty snacks (mean, SD)	0.4 (0.58)	0.4 (0.6)	0.4 (0.6)

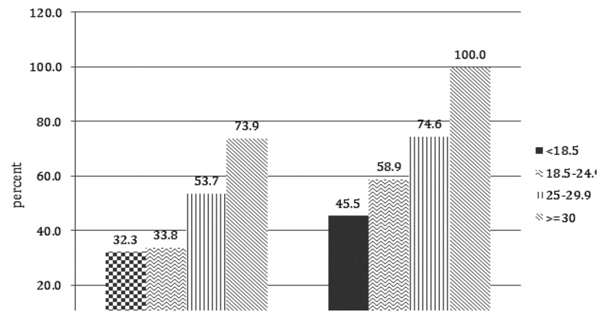

Figure 1. Bar Diagram Showing Prevalence of Pre-hypertension Among Non-hypertensive Participants of Dhulikhel Heart Study According to BMI and Sex

Table 3. **Factors associated with pre-hypertension among non-hypertensive participants of the Dhulikhel Heart Study**

Characteristics	N(%), N=752		Univariate Analysis				Multivariate Analysis*		
		OR	95 % CI	p value	OR	95% CI	p value		
Age (mean, SD)	37.4(15.0)	1.01	1.00	1.02	0.01	1.01	0.99	1.03	0.35
Gender									
Female	196(40.6)	Ref							
Male	168(62.2)	2.42	1.79	3.28	0.00	3.17	1.91	5.26	0.00
Ethnicity									
Newar	171((54.9)	Ref							
Brahmin/Chhetri	95(39.7)	0.54	0.38	0.76	0.00	0.73	0.45	1.18	0.20
Other	98(48.5)	0.77	0.54	1.09	0.14	0.71	0.42	1.18	0.18
Marital Status									
Unmarried	106(46.9)								
Married	258(49.0)	0.92	0.67	1.25	0.59	1.39	0.80	2.43	0.24
Annual income (USD), mean(SD)	1124.3(1403.7)	1.00	1.00	1.00	0.75	1.00	1.00	1.00	0.43
Education									
No formal education	107(50.0)	Ref							
formal education	257(47.7)	0.91	0.67	1.25	0.58	0.51	0.29	0.91	0.02
Smoking									
Non Smoker	261(47.2)								
Former Smoker	25(69.4)	2.54	1.23	5.27	0.01	2.02	0.68	6.03	0.21
Current Smoker	78(47.5)	1.01	0.71	1.44	0.94	0.73	0.39	1.34	0.31
Alcohol intake									
Non drinker	238(43.9)	Ref							
Less than 1 glass per week	37(63.7)	2.25	1.28	3.96	0.01	2.07	0.96	4.50	0.07
1-3 glasses per week	24(57.1)	1.73	0.92	3.26	0.09	1.56	0.63	3.82	0.33
More than 3 glass per week	65(59.0)	1.88	1.24	2.85	0.00	1.16	0.57	2.38	0.68
Physical activity									
less than recommended	153(55.0)	Ref							
Met recommended level	211(44.5)	0.66	0.49	0.88	0.01	0.61	0.40	0.95	0.03
BMI, kg/m^2									
Normal (18.5 to 24.9)	209(43.1)	Ref							
Underweight (< 18.5)	20(37.7)	0.78	0.44	1.40	0.41	0.61	0.23	1.63	0.32
Overweight (25.0 -29.9)	113(60.7)	2.07	1.46	2.92	0.00	2.29	1.42	3.70	0.00
Obese (>= 30)	22(78.5)	4.92	1.95	12.36	0.00	5.00	1.81	13.79	0.00
Food Intake (servings per week)									
Fruits and Vegetables (mean, SD)	25.8(15.0)	1.15	1.07	1.24	0.00	1.12	0.97	1.29	0.12
Whole grains (mean, SD)	2.87(2.65)	1.24	0.84	1.82	0.28	0.89	0.50	1.59	0.70
Refined grains (mean, SD)	25.7(8.78)	1.17	1.03	1.32	0.01	1.04	0.86	1.25	0.69
Lentils (mean, SD)	11.8(7.72)	1.37	1.18	1.58	0.00	1.14	0.88	1.49	0.32
Salty snacks (mean, SD)	3.12(4.49)	1.26	0.98	1.62	0.07	1.09	0.65	1.83	0.74

*adjusted for all other factors in model

associations were observed with marital status, ethnicity and annual income.

Compared to non-smokers, there was an increased risk of prehypertension among former smokers in univariate analysis (OR: 2.42, 95% CI:1.79-3.28) but it was not significant after adjustment for other factors (OR:2.02, 95% CI:0.68-6.03). Compared to non-drinkers, there was an increased risk of prehypertension among those who drink alcohol in univariate analysis (non- drinker vs < 1 glass/week OR: 2.25, 95% CI:1.28-3.96, non-drinker vs < 1-3 glasses/week OR: 1.73, 95% CI:0.92-3.26, non-drinker vs > 3 glasses/week OR: 1.88, 95% CI:1.24-2.85) but not in multivariate analysis.

Having any formal education was protective for prehypertension (OR: 0.51, 95% CI: 0.29-0.91) in multivariate analysis. People who met recommended physical activity levels had a one third lower chance of developing prehypertension as shown by both univariate (OR:0.66, 95% CI: 0.49-0.88) and multivariate analysis (OR:0.61, 95% CI: 0.40-0.95). In terms of the BMI, the chance of prehypertension was higher among the overweight in comparison to normal BMI in univariate (OR: 2.07, 95% CI: 1.46-2.92) as well as multivariate analysis (OR: 2.29, 95% CI: 1.42-3.70). The odds of prehypertension were even higher among the obese than normal BMI in univariate (OR: 4.92, 95% CI: 1.95-12.36) as well as multivariate analysis (OR: 5.00, 95% CI: 1.81-13.79).

The risk of prehypertension was seen among those who consumed refined grains (OR: 1.17, 95% CI: 1.03-1.32) as well as lentils (OR: 1.37, 95% CI: 1.18-1.58) but the association was not significant after adjustment for other factors.

DISCUSSION

In a suburban population of Nepal, almost half of the non-hypertensive adults had prehypertension. Those who were male, overweight or obese had a higher chance of having prehypertension; and those with formal education and met recommended levels of physical activity had lower odds of prehypertension.

The prevalence of prehypertension was higher in this study (48%) compared to the national survey adults (26%), mothers of young children (32%) and adolescent population (21%) in Nepal.[8,17,18] Koju et al. reported a 29% prevalence of prehypertension among adults in Dhulikhel five years previous to this study.[9] The rise of prehypertension prevalence might be attributable to the epidemiological transition in Nepal which may have affected an increase in CVD risk factors such as obesity, increased intake of salt and low fruits and vegetable consumption.[19-21]

In our study, males had a higher prevalence of prehypertension compared with females even after adjusting age, education, smoking, physical activity, body mass index, and fruits and vegetables intake. This finding is consistent with other studies from Nepal and the US.[8,10,22] This may be attributed to biological differences such as sex hormones, chromosomal differences, and other biological sex differences that are protective against high blood pressure in women.[23-25]

Having formal education was inversely associated with prehypertension prevalence in our population, similar to another study from China.[26] However, the nation-wide study from Nepal did not show significant association between higher education and prehypertension.[8] This study compared prehypertension prevalence among primary and secondary-level educated adults with those who did not have any formal education. It is likely that our adults with formal education have a higher level of health literacy and a healthier lifestyle, which could have contributed to the inverse relation.

Consistent with other study, the physical activity level of 600 MET minutes per week or more was found to be inversely related with prehypertension.[27] The exact mechanism how physical activities reduces the blood pressure and prevent hypertension is still unclear. The animal studies suggest that aerobic exercise may prevent increases in BP through beneficial alterations in insulin sensitivity and autonomic nervous system function, while resistance training may prevent increases in BP through beneficial alterations in vasoconstriction regulation. However, epidemiological evidence has demonstrated the consistent, temporal and dose-response relationship between physical activity and high blood pressure which is supported by interventional studies which confirmed favorable effect of exercise on blood pressure reduction.[28-32]

The relation of obesity and hypertension is well established.[33,34] A meta-analysis from Asia reported that being overweight increased the risk for hypertension by 61%.[35] In this study, overweight individuals had about a two times higher odds and obesity individuals had five times higher odds of having prehypertension compared to normal weight individuals. These results are similar to other studies from Nepal and globally.[8,10,36-38] The consistent relationship between being overweight or obese on both prehypertension and hypertension might indicate that these conditions have the same impact on blood pressure. Overweight and obesity are rapidly increasing among adult population in Nepal, which indicates that the burden of prehypertension and subsequently high blood pressure will continue to rise.[19,21] Clinical studies have shown that weight loss among overweight individuals can significantly reduce blood pressure.[39] JNC-7 also recommends lifestyle modifications such as weight loss, physical activity, and adoption of a healthy diet for all people with prehypertension.[12] Targeting prehypertensive subjects early and encouraging lifestyle modifications to reduce weight may result in long-term health and economic benefits, especially in resource-poor setting like Nepal, where blood pressure control among individuals with hypertension is a serious problem.[40]

There are notable strengths of the study. To our knowledge it is one of the first studies in Nepal to find the association of traditional behavioral risk factors with prehypertension in a community setting. This study investigated the association of prehypertension with a wide variety of risk factors including socio-demographic (age, gender, ethnicity, education, income) behavioral (smoking, alcohol, diet, physical activity) and body mass index; compared to previous prehypertension studies from Nepal that reported on demographic and body mass index.[8,10] The random sampling of study participants, use of standard validated methods, skilled researchers to measure blood pressure, and extensive information on possible confounders and effective statistical models were also major strength of the study.

There are several limitations in our study. First, we cannot establish the temporal association between the study factors and prehypertension due to the cross-sectional study design. Second, we assessed blood pressure with an automated device on a single day which may have over-diagnosed prehypertension. However, this measurement error will be non-differential resulting in the underestimation of effect size.[41] Third, this study was conducted in a suburban population of Dhulikhel and generalizability is limited as Nepal has diverse in ethnic, geographic and dietary habits. Fourth, we could not adjust for other confounding factors such as dyslipidemia, concomitant diabetes and objectively measured salt intake.

CONCLUSION

In conclusion, prehypertension is common in the general population residing in suburban central Nepal. Three modifiable risk factors, overweight/obesity, low education and lower level of physical activities, along with one non-modifiable risk factor i.e., male gender, was related with higher prehypertension prevalence. These results indicate the need for programs to modify lifestyle targeting weight reduction and increased physical activity to prevent prehypertension and subsequently reduce high blood pressure and associated cardiovascular diseases in Nepal.

ACKNOWLEDGEMENTS

We would like to thank all the research participants for their valuable time and expressing their views and opinions. We would also like to thank all the data enumerator for their contribution on data collections.

REFERENCES

1. Selassie A, Wagner CS, Laken ML, Ferguson ML, Ferdinand KC, Egan BM. Progression is accelerated from prehypertension to hypertension in blacks. *Hypertension.* 2011;58(4):579-87.
2. Conen D, Ridker PM, Buring JE, Glynn RJ. Risk of cardiovascular events among women with high normal blood pressure or blood pressure progression: prospective cohort study. *BMJ.* 2007;335(7617):432.
3. Huang Y, Wang S, Cai X, Mai W, Hu Y, Tang H, et al. Prehypertension and incidence of cardiovascular disease: a meta-analysis. *BMC Med.* 2013;11:177.
4. Huang Y, Su L, Cai X, Mai W, Wang S, Hu Y, et al. Association of all-cause and cardiovascular mortality with prehypertension: a meta-analysis. *Am Heart J.* 2014;167(2):160-8.e1.
5. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R, Prospective Studies C. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet.* 2002;360(9349):1903-13.
6. Nepal Health Research Council. Assessment of Burden of Disease in Nepal, 2009. Kathmandu, Nepal: Nepal Health Research Council; 2018.
7. Huang Y, Guo P, Karmacharya BM, Seeruttun SR, Xu DR, Hao Y. Prevalence of hypertension and prehypertension in Nepal: a systematic review and meta-analysis. *Glob Health Res Policy*. 2019;4:11.
8. Kibria GMA, Swasey K, Sharmeen A, Sakib MN, Burrowes V. Prevalence and associated factors of pre-hypertension and hypertension in Nepal: Analysis of the Nepal Demographic and Health Survey 2016. *Health Sci Rep.* 2018;1(10):e83.
9. Koju R, Manandhar K, Gurung R, Pant P, Bedi TRS. Prevalence of Hypertension in Semi-Urban area of Nepal. *Nepalese Heart Journal*. 2013;7(1):35-9.
10. Agho KE, Osuagwu UL, Ezeh OK, Ghimire PR, Chitekwe S, Ogbo FA. Gender differences in factors associated with prehypertension and hypertension in Nepal: A nationwide survey. *PloS one.* 2018;13(9):e0203278.
11. Shrestha A, Koju RP, Beresford SAA, Gary Chan KC, Karmacharya BM, Fitzpatrick AL. Food patterns measured by principal component analysis and obesity in the Nepalese adult. *Heart Asia.* 2016; 8(1): 46-53.
12. Chobanian AV. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood PressureThe JNC 7 Report. *JAMA*. 2003;289(19):2560.
13. Bull FC, Maslin TS, Armstrong T. Global physical activity questionnaire (GPAQ): nine country reliability and validity study. *J Phys Act Health*. 2009;6(6): 790-804.
14. Shrestha A, Koju RP, Beresford SAA, Chan KCG, Connell FA, Karmacharya BM, et al. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for Nepalese diet. *Int J Food Sci Nutr*. 2017;68(5):605-12.
15. WHO. Expert Consultation. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet.* 2004;363(9403):157-63.
16. Zorn CJW. Generalized Estimating Equation Models for Correlated Data: A Review with Applications. *American Journal of Political Science.* 2001;45(2):470.
17. Vaidya A, Oli N, Krettek A. High prevalence of prehypertension in mothers of young children in peri-urban Nepal. *Journal of Kathmandu Medical College*. 2017;5(2):52-60.
18. Thapa J, Budhathoki SS, Pokharel PK. A11418 A study on prehypertension and its associated factors among higher secondary school students in Eastern Terai, Nepal. *Journal of Hypertension*. 2018;36:e143.
19. Aryal KK, Mehata S, Neupane S, Vaidya A, Dhimal M, Dhakal P, et al. The Burden and Determinants of Non Communicable Diseases Risk Factors in Nepal: Findings from a Nationwide STEPS Survey. *PloS one*. 2015;10(8):e0134834.
20. Vaidya A, Pathak RP, Pandey MR. Prevalence of hypertension in Nepalese community triples in 25 years: a repeat cross-sectional study in rural Kathmandu. *Indian heart journal.* 2012;64(2):128-31.
21. Ministry of Health and Population Government of Nepal, Society for Local Integrated Development Nepal (SOLID Nepal), World Health Organisation (WHO). WHO STEPS Surveillance: Non Communicable Disease Risk Factors Survey. 2008.
22. Wang Y, Wang QJ. The prevalence of prehypertension and hypertension among US adults according to the new joint national committee guidelines: new challenges of the old problem. *Arch Intern Med*. 2004;164(19):2126-34.
23. Vitale C, Mendelsohn ME, Rosano GMC. Gender differences in the cardiovascular effect of sex hormones. *Nature Reviews Cardiology*. 2009;6(8):532-42.
24. Vitale C, Fini M, Speziale G, Chierchia S. Gender differences in the cardiovascular effects of sex hormones. *Fundamental & Clinical Pharmacology.* 2010;24(6):675-85.

25. Sandberg K, Ji H. Sex differences in primary hypertension. *Biol Sex Differ.* 2012;3(1):7.

26. Sun Z, Zheng L, Wei Y, Li J, Zhang X, Liu S, et al. Prevalence and risk factors of the rural adult people prehypertension status in Liaoning Province of China. *Circulation journal : official journal of the Japanese Circulation Society.* 2007;71(4):550-3. Epub 2007/03/27.

27. Seow DYB, Haaland B, Jafar TH. The Association of Prehypertension With Meals Eaten Away From Home in Young Adults in Singapore. *Am J Hypertens.* 2015;28(10):1197-200.

28. Lee D-C, Sui X, Church TS, Lavie CJ, Jackson AS, Blair SN. Changes in fitness and fatness on the development of cardiovascular disease risk factors hypertension, metabolic syndrome, and hypercholesterolemia. *J Am Coll Cardiol*. 2012;59(7):665-72.

29. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. *J Am Heart Assoc.* 2013;2(1):e004473.

30. Cornelissen VA, Fagard RH, Coeckelberghs E, Vanhees L. Impact of resistance training on blood pressure and other cardiovascular risk factors: a meta-analysis of randomized, controlled trials. *Hypertension.* 2011;58(5):950-8.

31. Jae SY, Heffernan KS, Yoon ES, Park SH, Carnethon MR, Fernhall B, et al. Temporal changes in cardiorespiratory fitness and the incidence of hypertension in initially normotensive subjects. *Am J Hum Biol.* 2012;24(6):763-7.

32. Diaz KM, Shimbo D. Physical Activity and the Prevention of Hypertension. *Current Hypertension Reports*. 2013;15(6):659-68.

33. Jayedi A, Shab-Bidar S. Nonlinear dose–response association between body mass index and risk of all-cause and cardiovascular mortality in patients with hypertension: A meta-analysis. *Obesity Research & Clinical Practice*. 2018; 12(1): 16-28.

34. Lee M-R, Lim Y-H, Hong Y-C. Causal association of body mass index with hypertension using a Mendelian randomization design. *Medicine.* 2018; 97(30): e11252.

35. Luo L, Luan R-S, Yuan P. Meta-analysis of risk factor on hypertension in China. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2003; 24(1): 50-3.

36. Ishikawa Y, Ishikawa J, Ishikawa S, Kayaba K, Nakamura Y, Shimada K, et al. Prevalence and determinants of prehypertension in a Japanese general population: the Jichi Medical School Cohort Study. *Hypertens Res*. 2008; 31(7): 1323-30.

37. Li Z, Guo X, Zheng L, Sun Z, Yang H, Sun G, et al. Prehypertension in rural northeastern China: results from the northeast China rural cardiovascular health study. *J Clin Hypertens.* 2014; 16(9): 664-70.

38. Li G, Guo G, Wang W, Wang K, Wang H, Dong F, et al. Association of prehypertension and cardiovascular risk factor clustering in Inner Mongolia: a cross-sectional study. *BMJ open.* 2017; 7(6): e015340.

39. Tyson CC, Appel LJ, Vollmer WM, Jerome GJ, Brantley PJ, Hollis JF, et al. Impact of 5-year weight change on blood pressure: results from the Weight Loss Maintenance trial. *J Clin Hypertens.* 2013; 15(7): 458-64.

40. Karmacharya BM, Koju RP, LoGerfo JP, Chan KCG, Mokdad AH, Shrestha A, et al. Awareness, treatment and control of hypertension in Nepal: findings from the Dhulikhel Heart Study. *Heart Asia*. 2017;9(1):1-8.

41. Armstrong BG. Effect of measurement error on epidemiological studies of environmental and occupational exposures. *Occupational and Environmental Medicine.* 1998;55(10):651-6.