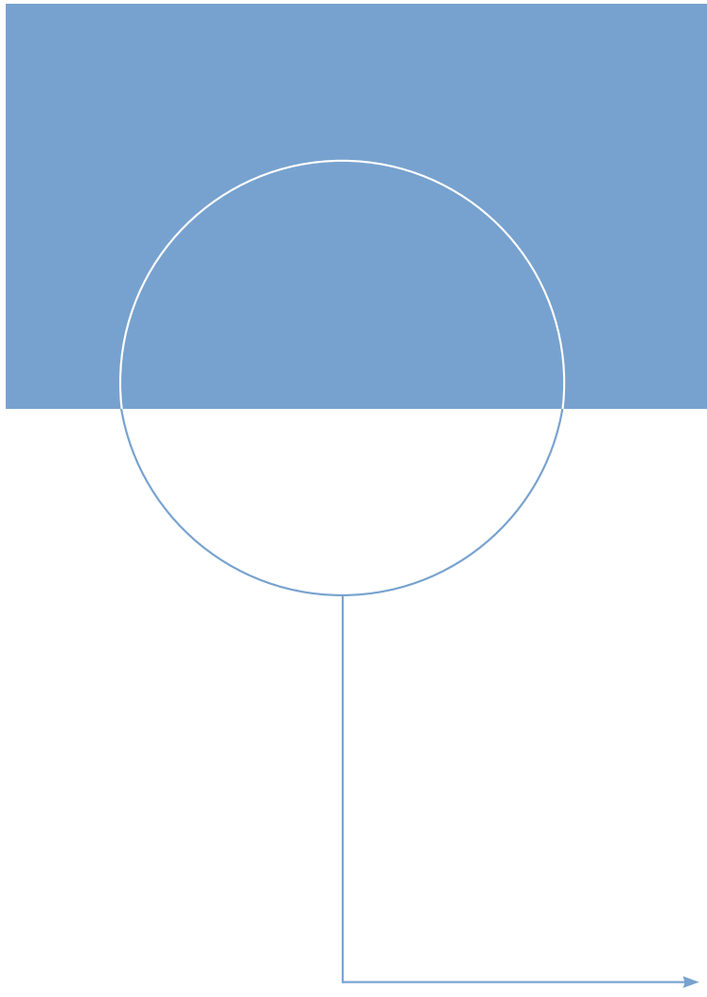

Master's thesis

2021

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ABSTRACT

Introduction: Metabolic syndrome (MetS) is a constellation of conditions including hypertension, hyperglycemia, central obesity and dyslipidemia, known to increase the risk for diabetes type 2 (T2D) and cardiovascular diseases (CVDs), the leading cause of death worldwide. MetS has become a global epidemic, affecting ≈ 25% of the world's population. The burden of MetS is increasing, especially among South Asians. Several studies have reported a higher prevalence of MetS among women. Given that very few studies have addressed MetS in rural women in Nepal, we sought to estimate the prevalence of MetS and its risk factors among women in a rural district.

Methods: This cross-sectional sub-study is part of a larger study conducted in Bolde village of Nepal, including 743 women. The participants were recruited from a study conducted in 2013, where married, non-pregnant women age 15-81 years were included. The same inclusion criteria were applied in the present study. The Joint Interim Statement (JIS) definition of MetS was used for assessment of prevalence, which defines MetS as presence of any three of the following: waist circumference (WC) ≥ 80 cm, triglycerides (TG) ≥ 1.7 mmol/L, high-density lipoprotein cholesterol (HDL-C) < 1.29 mmol/L, or on treatment for these dyslipidemias, systolic blood pressure (SBP) ≥130 mm Hg and/or diastolic blood pressure (DBP) ≥ 85 mm Hg, or on treatment for hypertension; and fasting plasma glucose (FPG) ≥ 5.6 mmol/L, previously diagnosed T2D, or on treatment for T2D. HbA1c was used as criterion for hyperglycemia instead of FPG. For comparison with previous studies, prevalence was also estimated according to the Adult Treatment Panel III (ATP III) and International Diabetes Federation (IDF) definitions of MetS. Fasting blood samples were collected, and height, weight, WC, and BP were measured. Asian cut-offs were used for BMI and WC. A questionnaire addressing among others socio-demographic, dietary factors, smoking, alcohol consumption and physical activity was filled in. Hemoglobin A1c (HbA1c) measurements were performed consecutively. Sera were stored at -80C until analyses of lipid profile. All analyses were performed at Dhulikhel hospital.

Results: Altogether, 716 women aged 48.3 ± 11.7 years were included, based on the access to all parameters of the MetS. The prevalence of MetS according to JIS was 37.7%, and 27.4 and 30.3% according to ATP III and IDF definitions, respectively. Low HDL-C was the most prevalent component (57.0%), followed by high WC (45.3%). The prevalence of MetS increased steadily

with age, the age group ≥ 61 years being about five times more likely to have MetS than those of 21-30 years (crude OR= 4.8, 95% CI = 1.87, 12.37). MetS was also frequent in younger age groups. In addition to age, high BMI, postmenopausal status and Dalit ethnicity were risk factors for MetS.

Conclusion: The prevalence of MetS among women of rural Nepal was high even at young ages and increased steadily with age. Low HDL-C and abdominal obesity were the most frequent components. Given the increased risk of CVDs and T2D in subjects with MetS, our findings are of concern, and efforts to prevent these abnormalities through awareness campaigns and lifestyle modification should be commenced, encouraged and sustained in order to reduce complications.

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ABBREVIATIONS

ATP III	Adult treatment panel III
BP	Blood pressure
CAD	Coronary artery disease
CVDs	Cardiovascular diseases
DALY	Disability adjusted life year
DBP	Diastolic blood pressure
FPG	Fasting plasma glucose
HbA1c	Glycated hemoglobin
HDL-C	High density lipoprotein-cholesterol
IDF	International Diabetes Federation
JIS	Joint interim statement
LDL-C	Low density lipoprotein-cholesterol
MetS	Metabolic syndrome
NCDs	Noncommunicable diseases
SBP	Systolic blood pressure
TC	Total cholesterol
TG	Triglycerides
T1D	Type 1 diabetes
T2D	Type 2 diabetes
WC	Waist circumference
WHO	World Health Organization

1. INTRODUCTION

The advancement in the medical field has provided us the power to control and win over many infectious communicable diseases. However, noncommunicable diseases (NCDs) have emerged as a major cause of morbidity and mortality in both developed and developing countries, accounting for 71% of all deaths globally. About 15 million people die from NCDs between the ages of 30-69 years, low- and middle-income countries being mostly affected with over 85% of these "premature" deaths (1). Most NCDs deaths are due to cardiovascular diseases (CVDs), accounting for about 17.9 million deaths annually (2). Metabolic syndrome (MetS) is a growing problem globally, and is a contributor to NCDs such as type 2 diabetes (T2D) and CVDs. In order to reduce the burden of CVDs, it is mandatory to identify potential risk factors that can be modified.

1.1 Metabolic Syndrome - definition

MetS, also known as insulin resistance syndrome, syndrome X, dysmetabolic syndrome, and Reaven syndrome, comprises a series of conditions known to increase the risk for T2D and CVDs. Conditions such as hypertension, hyperglycemia, central obesity, abnormal cholesterol, and hypertriglyceridemia are included. There has been some disagreement on the definition of MetS (3-5). In 2009, a Joint Interim Statement (JIS) on the definition of MetS was issued by International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity (4). It is defined as having any three of the following: central obesity (waist circumference (WC) $\geq$ 90 cm in men and $\geq$80 cm in women for Asian population); triglycerides (TG) $\geq$ 1.7 mmol/L; high-density lipoprotein cholesterol (HDL-C) < 1.03 mmol/L in males, < 1.29 mmol/L in females, or on treatment for these dyslipidemias; systolic blood pressure (SBP) $\geq$ 130 mm Hg and/or diastolic blood pressure (DBP) $\geq$ 85 mm Hg, or on treatment for hypertension; and fasting plasma glucose (FPG) $\geq$ 5.6 mmol/L, previously diagnosed T2D, or on treatment for T2D (4). The definitions by other international bodies are included in Annex I.

1.2 Prevalence of MetS

1.2.1 Global prevalence of MetS

Data from WHO suggest that most of the world's population live in countries where overweight and obesity kill more people than underweight (6). Development of MetS is largely attributed to poor nutrition, sedentary lifestyle, and smoking (7, 8). Also, diabetes prevalence has been rising, and 1.6 million estimated deaths were caused by diabetes (preferentially T2D) each year (9). Due to variation in its diagnostic criteria and definition, studies assessing the prevalence of MetS do not provide consistent results. However, despite the inconsistent results with the application of different criteria, it is a well-known fact that the prevalence of MetS in both developing and developed parts of the world is increasing in epidemic proportion (10). MetS is considered to be three times more common than diabetes. The International Diabetes Federation (IDF) estimated that MetS affected about one-quarter of the world's adult population (5, 11). The estimated prevalence from large prevalence studies and systematic reviews in various geographical regions are presented in Table 1. Most of the prevalence estimates in the geographic regions mentioned below were made on the basis of National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III, hereafter referred to as ATP III) and IDF criteria. Apart from these two, various other definitions were also used, making comparison between studies difficult.

Table 1. *Estimated Prevalence of metabolic syndrome in different geographical regions of the world*

Geographical region	Year of publication	Estimated MetS prevalence (%)
Asia-Pacific (12)	2017	11.9 – 37.1
Africa (13)	2012	12.5–62.5
Central America (14)	2015	23.0–35.1
Europe (15)	2014	11.6–26.3
Middle East (16)	2012	13.6–36.3
South America (17)	2011	18.8–43.3
South Asia (18)	2016	26.1

1.2.2 Prevalence of MetS in South Asia

Different definitions applied in the various studies in South Asia make comparison difficult. The weighted mean prevalence has been estimated to be 29.8% by IDF criteria, and 32.5% by modified ATP III criteria (18). The majority of the studies included in the systematic reviews were from India, with only one or two from other South Asian countries. The real burden of MetS in South Asia is still unknown because of lack of nationally representative surveys in other countries than India. The prevalence of MetS in the female population was higher compared to the male population in South Asian countries in several studies (18-20). This sex difference was more pronounced in one study in Pakistan which reported a difference of 37% according to IDF criteria (male 13% vs. 50% female) (21). Additionally, a follow-up study reported that South Asians in the UK had higher prevalence of the various components of MetS, as well as higher prevalence of diabetes (19% vs. 4%), higher fasting and post-glucose serum insulin concentrations, than Europeans (22).

1.2.3 Prevalence of MetS in Nepal

In a cross-sectional study conducted in Eastern Nepal, including 2191 participants, the weighted mean prevalence of MetS was 20.7% and 22.5% according to ATP III and IDF criteria, respectively. MetS was more frequent in females compared to males according to both ATP III (21.9% vs. 18.6%) and IDF (25.7% vs. 17.1%) criteria (23). The presence of abnormal lipids (high TG and low HDL-C) was more frequent than other components of MetS according to the ATP III criteria.

In a secondary analysis of data sets from a stepwise approach to surveillance (STEPS) including 4200 individuals aged 15 to 69 years, the prevalence of MetS was estimated to be 15% and 16% according to the ATP III and IDF criteria (24). The odds of MetS was higher in females (AOR: 1.44; 95% CI: 1.05–1.97) as opposed to their male counterparts according to IDF criteria (24). Among the five components of MetS, low HDL-C (71%) was found to be the most predominant, followed by high BP (26%) and raised TG (25%).

1.3 Consequences of MetS and their burden

MetS comprises several conditions that enhance the risk of NCDs, such as T2D and CVDs. It has been predicted that people with MetS have a triple risk of having a heart attack and stroke and a double risk of dying compared to those without MetS (5). In a 12-year follow-up study conducted in middle-aged Finnish men, men with MetS were 2.9-4.2 times more likely to die from CVDs than those without MetS (25). In addition, MetS increased the risk of developing T2D by five-fold (5, 26). It is evident that the prevalence of MetS has been increasing globally, and around 20-25 % of the adult population have MetS (5).

Globally, deaths owing to CVDs grew by roughly 21% from 2007 to 2017 (2). In 2017, an estimated 4 million people died as a result of diabetes and its complications, with nearly half (46%) of the deaths occurring in people under the age of 60. On a global scale, the mortality rate for type 1 diabetes (T1D) has decreased by 11% from the year 2007 to 2017, whereas the mortality rate for T2D has increased by 5.9% (2). In addition, diabetes-related mortality was even higher in women (2.3 million) than in males (1.9 million) (27). Women without diabetes have a lower risk of acquiring CVDs than men without diabetes at the same age. However, it is worth noting that women with T2D have a 25-50% greater risk of CVD events in comparison to men (28).

South Asia is one of the most densely populated geographical regions in the world, providing a home to about one-fourth of the world's population (29). Each year, 8.5 million deaths are estimated to be caused by NCDs in the South-East Asia Region (SEAR). One-third of these deaths occur among economically productive individuals of age less than 70 years (1). CVDs and diabetes, preferentially T2D, are estimated to account for 27% and 4% deaths, respectively, in this region, with the risk of such diseases manifesting 5-10 years earlier than in Europeans (30).

Nepal, a developing country, has faced a rapid increase in the burden of NCDs, with estimated 66% of deaths in 2018 compared to 50% of deaths in 2011 caused by NCDs. In the same period, the number of deaths due to CVDs and diabetes increased from 25% to 30% and 2% to 4%, respectively (31, 32). These estimates show that the prevalence of CVDs and diabetes are increasing and hence are the major causes of mortality in Nepal. In addition, ischemic heart disease was ranked first in 2017 compared to being number 10 in 1990. Similarly, T2D was ranked 10th in 2017 versus 41st in 1990 in Nepal's top causes of disability adjusted life years (DALYs). High

SBP, short gestation, smoking, high FPG, and low birth weight are the top five risk factors contributing to DALYs (33).

Maternal hyperglycemia has been linked to obesity and impaired glucose tolerance in the offspring in adulthood (34). The fetus is exposed to higher quantities of glucose, free fatty acids, and amino acids during pregnancies with gestational diabetes, resulting in increased fetal insulin production. Hyperglycemia and fetal hyperinsulinism are thought to predispose to metabolic diseases later in life (35). It is now evident that excess gestational weight gain has a short- and long-term impact on offspring obesity (36). This may be attributed to affection of organogenesis by the intrauterine environment, resulting in long-term detrimental effects on organ morphology and physiology (37). Another probable mechanism can be persistent change in gene regulation and pathways caused by environmentally induced epigenetic changes (38). The recent meta-analysis by Irakoze et al. concluded that offspring of parents with MetS exhibit a high risk of MetS in adulthood (39). This vicious cycle may accelerate the epidemic of metabolic disease in near future.

Apart from CVDs and T2D, subjects with MetS are susceptible to other conditions, notably polycystic ovary syndrome among women (40), nonalcoholic fatty liver disease, cholesterol gallstones, asthma, and some forms of cancer (41).

1.4 Components of MetS

1.4.1 Hypertension

Hypertension in adults has been defined as SBP $\geq$ 140 mm Hg and/or DBP $\geq$ 90 mm Hg in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) Guideline (42). The systematic review by Aryal & Wasti (18) revealed that hypertension was the most common component of MetS in South Asian men (42%) and the third most common in South Asian women (38%), which was similar to the NHANES study where 41% of the men (most common) and 37% of the women (third most common) were hypertensive (43).

WHO has stated hypertension as the major cause of premature death, with an estimated 1.13 billion globally having hypertension, with two-third of such cases being in low and middle-income countries. They have also estimated that 1 in 4 men and 1 in 5 women globally have hypertension

(44). The Center for Cardio-metabolic Risk Reduction in South Asia (CARRS) study conducted in an adult cohort of India estimated that one in three men and one in four women had hypertension, with a higher incidence among older women than men. The study showed alarmingly high incidence, with one in six adults developing hypertension over the two years (45).

1.4.2 Obesity

According to WHO, overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health (6). Obesity has tripled globally between 1975 and 2016, according to WHO estimates, with 39 % of individuals over 18 years being overweight, and 13% obese in 2016 (6). Globally more women are overweight and obese than men (46). A similar scenario was seen in urban India, where central obesity among women was significantly more prevalent than in men (48.3% vs. 33%) (47). Many studies have used BMI to define obesity. It is, however, an imperfect marker of adiposity as it does not differentiate between muscle and fat mass and gives no information about fat distribution (48, 49). BMI differs according to ethnicity. In South Asians, central adiposity is higher for a given body weight than in other ethnic groups, making them more susceptible to metabolic diseases (5, 50). WC has been identified as better metabolic marker, for development of CVDs and T2D, than BMI (5, 48, 51). Specific thresholds for WC as a marker of central obesity have been recommended in Asians (Men ≥ 90 cm; Women ≥ 80 cm) (4, 5).

1.4.3 Hyperglycemia

Hyperglycemia is a condition caused by insulin deficiency (T1D) or low insulin/insulin resistance (T2D). For diagnosis of MetS, FPG ≥ 5.6 mmol/L (≥ 100 mg/dL) is set as cut-off point by JIS (4), which includes both prediabetic (FPG ≥ 5.6 -7.0 mmol (100-125 mg/dL)) and diabetic (FPG ≥ 7 mmol/L (126 mg/dL)), as defined by American Diabetes Association (ADA) (52).

Glycated Hemoglobin, or hemoglobin A1c (HbA1c), is the chronic marker (average plasma glucose concentration over 2-3 months) of hyperglycemia, and its measurement can be done at any time without any pre-requirements such as fasting. HbA1c has lower biological variation in comparison to FPG (52, 53). Because of these properties, it is regarded as the gold standard for assessing glycemic control in people with diabetes and is used to diagnose diabetes (52). The American Diabetes Association has set the cut-off point for diagnosis of prediabetes and diabetes

as HbA1c ≥ 5.7-6.49% (39-47 mmol/mol) and ≥ 6.5% (48 mmol/mol), respectively. For diagnosis of MetS, a threshold of ≥ 5.7% (39 mmol/mol) is used (52). Hence, HbA1c may be used as a proxy of FPG.

1.4.4 Dyslipidemia

Dyslipidemia is characterized by elevated levels of total cholesterol (TC) and TG, and reduced HDL-C concentration (54). Lipid abnormalities contribute to development of arteriosclerotic CVD. Moreover, reduced HDL-C is highly associated with coronary artery disease (CAD) (3, 55, 56), with a 13% increase in the risk of CAD by every 10% reduction in HDL-C level as seen in the Quebec cardiovascular study (57). Different cut-off points are used for HDL-C for men and women to define MetS (4), as sex-difference is observed with women having higher levels of HDL-C than men (58).

Studies regarding dyslipidemia in South Asians are limited. Vascular protective effects were reported with increasing HDL-C levels in European adults (55, 56). In contrast, the protective effect of increased HDL-C level was weaker in South Asians (59). Rashid et al. (60) found more pronounced dyslipidemia among South Asians compared to Europeans; mean levels of TG and HDL-C were 136 mg/dL (1.54 mmol/L) vs. 174 mg/dL (1.97 mmol/L), and 46 mg/dl (1.2 mmol/L) vs. 39 mg/dL (1.01 mmol/L) among Europeans and South Asian adults, respectively.

1.5 MetS and sex differences

Sex-specific cut-off points are used for the assessment of abdominal obesity by WC. That is also the case for HDL-C, with a lower threshold in men since the first definition of MetS by WHO (61). The clear distinction of cut-off levels for these two cardio-metabolic parameters in men and women has been maintained by every other definition, except for the American Association of Clinical Endocrinologist (AACE) criteria. They have used BMI ≥ 25 kg/m^2 (both sexes) to define the obesity component instead of WC (62). In the Third National Health and Nutrition Examination Survey (NHANES III, 198-94), a US-based nationally representative survey, MetS prevalence was shown to increase acutely after 30 years of age in men and women. The rise in age-adjusted prevalence was associated with an increase in obesity in both sexes, and with high levels of TG and FPG in women alone (63). Similarly, in the SPECT-China study, a Chinese population-based

cross-sectional survey among 10,441 individuals, the overall prevalence was similar in men and women. The prevalence of MetS increased steeply after the age of 45 years in women, with the most pronounced rise, in abdominal obesity. However, MetS and abdominal obesity prevalence remained stable across the different age groups in males ≥ 45 years (64). Other studies have also confirmed the change in prevalence of MetS with aging in both sexes, and they have reported a steeper increase in the prevalence of MetS and its components after menopause in women (20, 63-65). In the MORGAM project, a prospective cohort study of 69094 individuals in European countries, the prevalence of MetS increased five-fold in women and two-fold in men from age group 19-39 years to 60-78 years (65).

MetS and its components increase after menopause and thus partly explain CVDs risk in postmenopausal women due to changes in the secretion of cytokines and sex steroids (66). The Study of Women's Health Across the Nation, a multi-center, multi-ethnic longitudinal study conducted in 949 premenopausal women without MetS, reported that postmenopausal women had higher odds (OR =1.24, CI =1.18, 1.3) of developing MetS than premenopausal women. The odds were even higher in peri-menopausal (< 1 year after menopause) women (OR = 1.45, CI = 1.35, 1.56). The author concluded that the decreased estrogen level in the menopausal transition was related to increased MetS prevalence irrespective of age and other covariates (67). Experimental studies have confirmed that due to the influence of estrogen in women, they have a high level of HDL-C on average, augmented glucose disposal in skeletal muscle, and fat distribution more towards the hip and gluteal regions, rather than in the abdomen as in men (68, 69). Because of changes in hormonal homeostasis and estrogen decline after menopause, alterations in fat distribution occur with an increase in visceral obesity irrespective of age and baseline total adiposity (70). This accumulation of visceral fat, usually followed by insulin resistance, and a rise in hepatic lipase activity and free fatty acid concentration, contributes to adverse changes in blood lipid concentrations (hypertriglyceridemia) (70, 71). Therefore, physiological changes during menopause beyond individual predisposition can contribute to increased incidence and prevalence of MetS.

There is inconsistency in the data regarding the gender differences, with most studies showing higher overall prevalence in women compared to men (12-14, 16-20, 23, 72-74), whereas some researchers report the opposite (75, 76). These conflicting results can partly be attributed to

difference in age, ethnicity, population studied, and various definitions used to diagnose MetS. For instance, when both IDF and ATP III criteria are applied to the Asian Indian population, more pronounced gender difference was found when using ATP III criteria than IDF criteria (77).

1.6 Rationale

1.6.1 Rationale for the study

There has been a dramatic rise in the burden of obesity, especially in Asia, and in parallel with that, MetS (12). Almost all studies conducted in Nepal to assess the prevalence of MetS are hospital-based or limited to urban settings. Few studies have been performed in rural settings where more than three-fourth of the total population live and no study have addressed women specifically. Given that MetS is a risk factor for CVDs and T2D, resulting in excess morbidity and mortality, it is crucial to assess the size of the problem in Nepal and identify risk factors that may be modified. In the current study, we chose to address women as the prevalence of MetS is reported to be higher in females than in their male counterparts in South Asia (18, 20). Moreover, women may be more prone to develop disease due to poverty and malnutrition. The offspring of mothers with T2D and obesity have increased risk of T2D and obesity later in life (34). Notably women are the principal care givers in almost every household in rural Nepal and has major impact on the welfare of the family. Our study may facilitate lifestyle changes and preventive approaches and access to clinical intervention, contributing to the improvement of public health.

1.6.2 Objectives of the research

1.6.2.1 Main Objective

To determine the prevalence of MetS and its risk factors among women in a rural community of Nepal to provide new knowledge and competence that may be applied to develop interventional strategies and health policies targeted to reduce the burden of MetS.

1.6.2.2 Specific objectives

1. To estimate the prevalence of MetS
    a. the JIS definition will be applied as the main definition to determine prevalence
    b. the ATP III and IDF definitions will be applied for comparison with previous studies

2. To estimate the prevalence of individual components of MetS
3. To assess risk factors for MetS

2. MATERIALS AND METHODS

2.1 Study design, study population & data collection

This cross-sectional sub-study is a part of a large, prospective cohort study entitled "Early-onset and increasing burden of DM in Nepalese women. Risk factors, complications, and relation with vitamin A and D. A prospective cohort study in rural Nepal" (78). The participants were recruited from women (n=1498 age 15-86 years) who initially took part in a study in 2012-13 addressing sexually transmitted diseases and NCDs. Inclusion criteria for the original study were: non-pregnant, married women ≥15 years old. The exclusion criteria were physical and mental conditions that made it challenging to participate. The same inclusion and exclusion criteria were applied for the current project. During October-December 2019, 813 women accepted the invitation to participate in the study, age 21-80 years. Ten women did not participate in the interview, and 27 women refused to provide enough blood samples. Finally, women in whom all parameters of MetS had been successfully measured were included in the study. A flowchart on the study population is presented in Figure 1.

The participants answered a comprehensive questionnaire addressing socio-economic factors, physical activity, dietary factors, alcohol consumption, and smoking (see questionnaire). Height was measured in centimeters with a Stadiometer attached vertically to the wall surface. For weight measurement, participants were requested to stand barefoot on the digital weighing scale, and measurement was made in kilograms. WC was measured in a separate room by a female health worker with a non-stretchable measuring tape after removing the clothing and accessories, in standing position, at the end of a natural expiration, holding the arms relaxed at the sides. The measurement was made at the midpoint between the lower margin of the last palpable rib (12^{th} rib) in the midaxillary line and the top of the iliac crest (hip bone). The measurement was recorded in centimeters. BP was measured using automatic digital blood pressure monitor (Omron). BP was measured twice; one after 15-30 minutes of the interview and another at the end of the interview, and mean BP was included in the analysis. Fasting blood samples were collected. Measurement of HbA1c was performed consecutively. The remaining blood was centrifuged, and sera were kept on ice under transport, stored at -80°C until analysis. HbA1c and serum lipid profile (TC, TG, low-density lipoprotein cholesterol (LDL-C), and HDL-C) were analyzed at the Dhulikhel Hospital

(DH) in Nepal. HbA1c was analyzed by Hb-Vario-For Glycosylated Hemoglobin (HbA1c) test, based on High Performance Liquid Chromatography (HPLC) by Erba Diagnostic Mannhheim GmbH, Germany. Serum lipid profile was measured by enzymatic spectrophotometric method using BA 400- full automatic analyzer, BioSystems S.A.Spain.

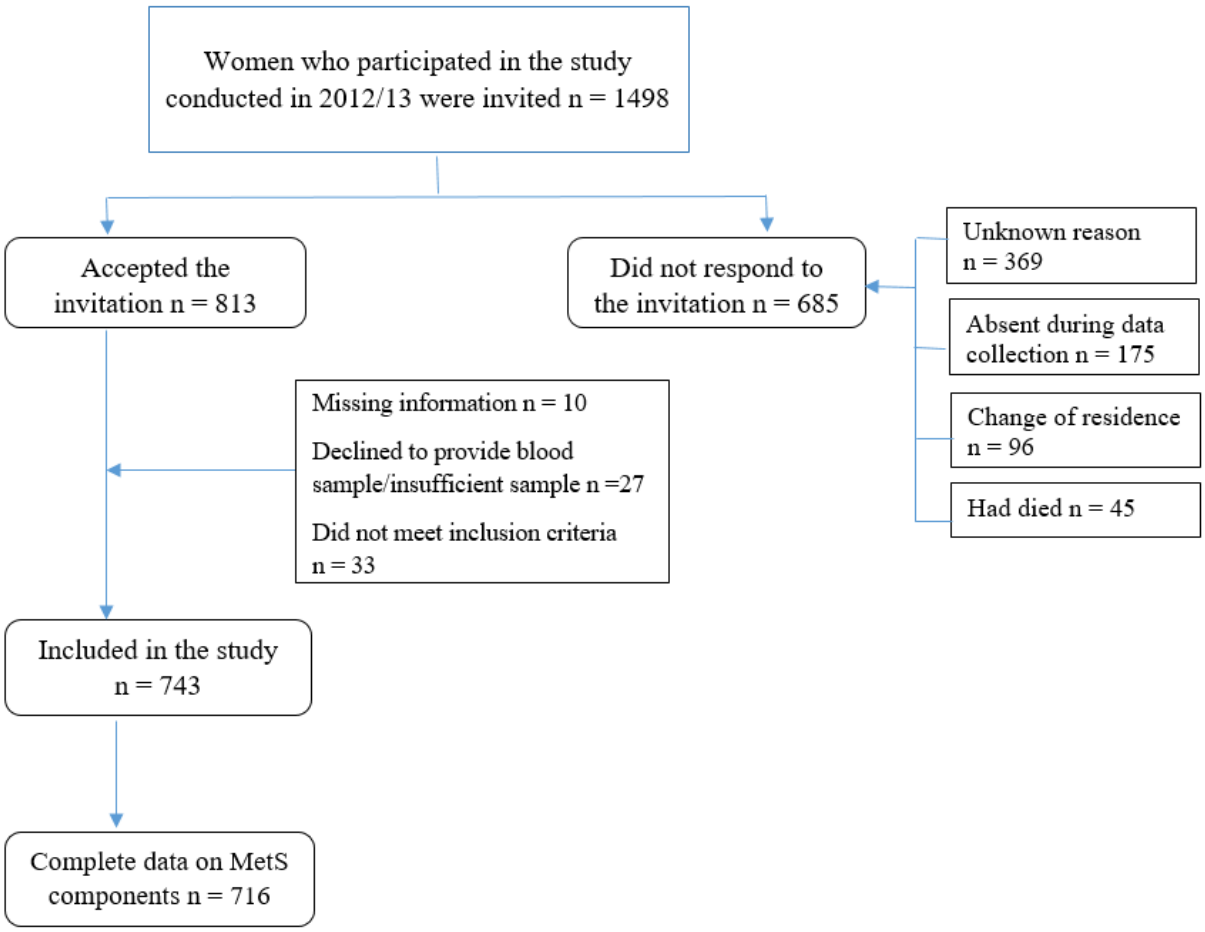

***Figure 1**. Selection of study population. MetS = Metabolic Syndrome*

2.2 Study variables, outcomes, and categorization

2.2.1 Metabolic Syndrome

For estimating the prevalence of MetS in the women, the definition according to the JIS (2009) was used (4). It defines MetS as having any three of the following:

1. Central obesity (WC ≥ 80 cm, Asian cut-off);
2. TG ≥ 1.7 mmol/L, or on treatment for elevated TG;
3. HDL-C < 1.29 mmol/L, or on treatment for reduced HDL-C;
4. SBP ≥ 130 mm Hg, DBP ≥ 85 mm Hg, or on treatment for hypertension;
5. FPG ≥ 5.6 mmol/L, or previously diagnosed T2D, or on treatment for T2D. (HbA1c ≥ 5.7% was used).

For comparison with previous studies, the prevalence of MetS was also calculated according to the ATP III and IDF definitions. The definitions for latter criteria are presented in Annex I.

2.2.2 HbA1c

HbA1c was used as a proxy for FPG. Several studies support the use of HbA1c in defining individuals with MetS (79-82). The American Diabetes Association recommends using HbA1c to diagnose prediabetes and diabetes (52). The cut-offs for MetS, prediabetes and diabetes are presented in Table 2.

Table 2. *Classification of hyperglycemia according to HbA1c*

Classification	Cut-off
Prediabetes	≥ 5.7-6.4 % (39-47 mmol/mol)
Diabetes mellitus	≥ 6.5 % (48 mmol/mol)
Metabolic syndrome	≥ 5.7 % (39 mmol/mol)

2.2.3 Covariates

Covariates included in our study are presented in figure 2.

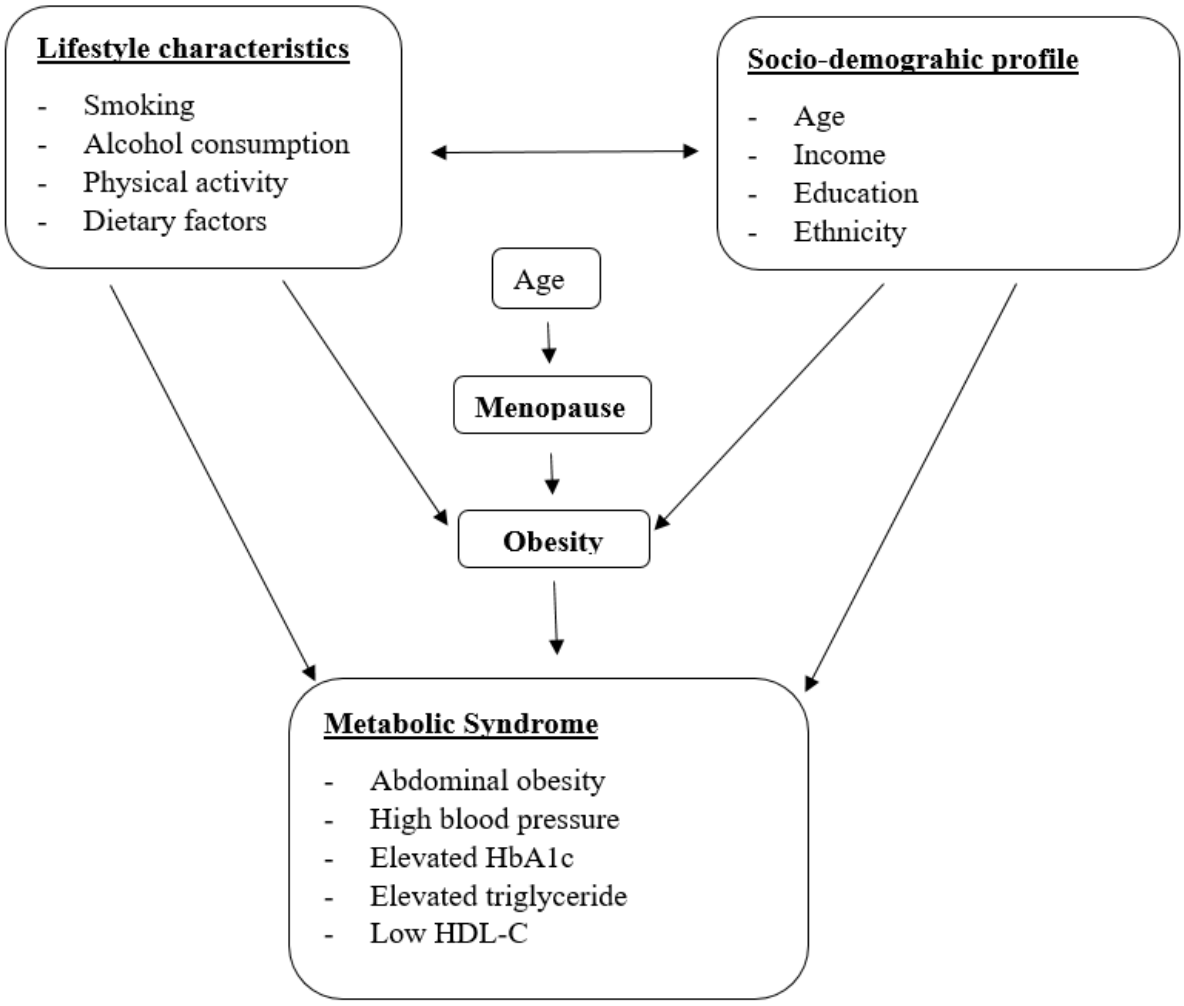

Figure 2. *A conceptual framework of proposed links between lifestyle, socio-demographic characteristics, and metabolic syndrome*

Women were asked, "Do you have regular menstrual bleedings?" and "Have you had your menopause?" to evaluate the menopausal status. "Pre-menopause" was defined as having regular menstrual bleedings, while "Post-menopause" was defined as cessation of regular menstrual bleedings. Table 3 presents the WHO definition for the classification of obesity in an Asian population, which was used to classify obesity in our study (83). BMI was calculated by dividing the participants' weight (in kilograms) by their height in meters squared.

Table 3. *Classification of overweight and obesity according to BMI*

Classification	WHO Asian BMI classification (kg/m^2)	WHO general populations BMI classifications (kg/m^2)
Underweight	< 18.5	< 18.5
Normal weight	18.5 - 22.9	18.5 - 24.9
Overweight	23.0 - 27.5	25.0 - 29.9
Obese	≥ 27.5	≥ 30.0

We collected information on covariates using questionnaires and categorized them in this manner: age (≤ 30, 31-40, 41-50, 51-60, and ≥ 60 years), education (no formal education, school level, college and above), ethnicity (Brahmin/Chhetri, Newar/Tamang, and Dalits), smoking status (current, past and never), alcohol consumption (current, past and never), physical activity (high, moderate and low), and average household income (< NPR 24,000 and ≥ 24,000). Global Physical Activity Questionnaire (GPAQ) version 2 was used to collect information about physical activity (84). Out of three domains, namely, work, travel, and recreational time, data for the recreational time were not available, and therefore not included in the calculation of physical activity level. GPAQ analysis guide was followed for cleaning and analyzing the data (85). After converting the responses of each domain to metabolic equivalent to task-minutes/week, physical activity level was classified as high, moderate, and low based on different combination criteria. Consumption of various food was categorized as yes or no based on the frequency of consumption (≥ 2 times a week and < 2 times a week).

In Nepal, the caste system is organized into hierarchical levels, and Dalits are considered to be the lowest caste. In Nepal, there have been numerous movements to end caste-based discrimination and untouchability. However, discrimination based on caste are still in practice. Dalits are more inferior in education and health, and face high degree of poverty as a result of their social exclusion. For instance, with the national literacy rate of 54%, the literacy rate for Dalits was only 38% according to 2001 census (86). They lie lowest in all indicators of human development index such as life expectancy.

2.3 Ethical considerations

Written informed consent was obtained from all the participants before data collection. Data obtained were anonymized and kept confidential. The ethical committees in Norway (REK Midt-Norge (13003), May 2019), and Nepal (The National Health Research Council, Nepal (2715) May 2019, and Kathmandu University School of Medical Sciences (124/19), May 2019) have approved the main project with sub-studies.

2.4 Statistical analysis

Continuous variables are presented as mean with standard deviation (SD) or median with inter quartile range (IQR), and categorical variables as counts and percentage. For group comparisons, a two-tailed independent sample t-test was applied for normally distributed data, and Mann–Whitney U-test for non-normally distributed data and $\chi 2$ tests when appropriate. The normality test (using the Shapiro-Wilk test) was performed, and the Q-Q plot was plotted to test for the normal distribution of the continuous variable.

Binary logistic regression was performed to analyze the association between the outcome variable (MetS) and covariates. The results are presented as odds ratios (OR) with 95% confidence intervals (CI). P-value < 0.05 was considered as statistically significant. All statistical analyses were conducted using the IBM SPSS Statistics Version 26 (SPSS, Inc., Chicago, USA).

3. RESULTS

3.1 Socio-demographic and lifestyle characteristics of the study population

A total of 716 women with a mean age 48.3 ± 11.7 years were included in this study based on all components of MetS being measured. Table 4 presents the characteristics of the study population. The majority were in the age group 41-50 years (30.7%), followed by 51-60 years (25.6%). Most of the women did not have formal education (84.4%), were from Newar/Tamang ethnicity (83.7%), and had monthly household income less than NPR 24,000 (66.8%). We observed that 19.4% of the participants were current smokers, 15.8% had smoked previously, 24.2% consumed alcohol, and around 83% had high physical activity levels.

Table 4. *Characteristics of the study population*

Characteristics	**Overall**
	N (%) or mean ± S.D. or median (IQR)
Overall	716 (100)
Age (years)	48.2 ± 11.7
Age groups (years)	
21-30	43 (6.0)
31-40	165 (23.0)
41-50	220 (30.7)
51-60	183 (25.6)
≥ 61	105 (14.7)
Ethnicity	
Brahmin/Chhetri	83 (11.6)
Newar/Tamang	599 (83.7)
Dalit	34 (4.7)
Educational status (n=707)*	
No formal education	597 (84.4)
Secondary or lower	85 (12.0)
College and above	25 (3.5)
Monthly household income	
< NPR 24000	478 (66.8)
≥ NPR 24000	238 (33.2)
Smoking	
Current	139 (19.4)
Past	113 (15.8)

Never	464 (64.8)
Alcohol consumption (n=714)**	
Current	173 (24.2)
Past	32 (4.5)
Never	509 (71.3)
Physical activity level (n=685)**	
High	568 (82.9)
Moderate	99 (14.5)
Low	18 (2.6)
Dietary intakes (≥ 2 times a week)	
Rice	691 (96.5)
Instant noodles	221 (30.9)
Milk	267 (37.3)
Cold beverages	176 (24.6)
WC (cm)	78.4 ± 10.1
BMI (kg/m^2)	24.8 ± 4.9
SBP (mm Hg)	126.0 ± 19.3
DBP (mm Hg)	81.7 ± 10.8
HbA1C (%)	5.6 ± 0.8
TC (mg/dL)	178.2 ± 41.8
HDL-C (mg/dL)	49.3 ± 14.4
TG (mg/dL)***	113 (77)
LDL-C (mg/dL)***	100 (42)

Abbreviations: NPR, Nepalese rupees (24,000 NPR = approx. 204 USD); WC, waist circumference; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, hemoglobin A1C; TC, total cholesterol TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

** Number not equal to n=716 as 9 participants refused to answer*

*** Number not equal to n=716 due to no answer/ missing data*

**** Data are presented as median (IQR)*

3.2 Prevalence of MetS and its individual components

The overall prevalence of MetS was 37.7% according to the JIF criteria. Table 5 shows the overall prevalence of MetS and the prevalence in different age groups. The prevalence of MetS increased significantly with age, and there was about 30% increase in the prevalence from the lowest age group (21-30 years) to the highest (≥ 51 years). However, the prevalence was high in younger age groups as well, with MetS affecting 30.3% of the women between 31-40 years and 40.5% of women in the age group 41-50 years. When applying the ATP III and IDF criteria the prevalence was somewhat lower, 27.4% and 30.3%, respectively.

Table 5. *Prevalence of metabolic syndrome stratified by age*

Characteristics	**Total**	**N**	**Prevalence of MetS % (95% CI)**
Overall	716	270	37.7 (34.2, 41.2)
Age groups (years)			
21-30	43	6	14.0 (3.6, 24.4)
31-40	165	50	30.3 (23.3, 37.3)
41-50	220	89	40.5 (34.0, 46.9)
51-60	183	79	43.2 (36.0, 50.4)
≥ 61	105	46	43.8 (34.3, 53.2)

Metabolic syndrome is defined as presence of any three of following: waist circumference ≥ 80 cm, systolic and diastolic blood pressure ≥ 130 mm Hg/ 85 mm Hg, HbA1c ≥ 5.7%, Triglyceride level ≥ 1.7 mmol/L and high-density lipoprotein cholesterol level < 1.29 mmol/L.

Table 6 shows characteristics of the study population according to MetS status. The prevalence of MetS was slightly higher among current and previous smokers (38.8% and 44.2%, respectively) than among non-smokers (35.8%), although not significant. The prevalence did not differ between participants who never drank alcohol, and current and previous drinkers. Additionally, the prevalence was significantly higher among women of Dalit ethnicity, and among women without formal education. There were no significant difference in prevalence of MetS with respect to physical activity level.

Table 6. *Characteristics of study population according to metabolic syndrome status.*

Characteristics	N (%)	Metabolic Syndrome		p-value
		Yes	No	
Overall	716 (100)	270 (37.7)	446 (62.3)	
Ethnicity				**0.001**
Brahmin/Chhetri	83 (11.6)	39 (47.0)	44 (53.0)	
Newar/Tamang	599 (83.7)	210 (35.1)	389 (64.9)	
Dalit	34 (4.7)	21 (61.8)	13 (38.2)	
Educational status (n=707)*				**0.012**
No formal education	597 (84.4)	241 (40.4)	356 (59.6)	
Secondary or lower	85 (12.0)	21 (24.7)	64 (75.3)	
College and above	25 (3.5)	7 (28.0)	18 (72.0)	
Monthly household income				0.437
< NPR 24000	478 (66.8)	185 (38.7)	293 (61.3)	
≥ NPR 24000	238 (33.2)	85 (35.7)	153 (64.3)	
Smoking				0.238
Current	139 (19.4)	54 (38.8)	85 (61.2)	
Past	113 (15.8)	50 (44.2)	63 (55.8)	
Never	464 (64.8)	166 (35.8)	298 (64.2)	
Alcohol consumption (n=714)**				0.935
Current	173 (24.2)	66 (38.2)	107 (61.8)	
Past	32 (4.5)	13 (40.6)	19 (59.4)	
Never	509 (71.3)	191 (37.5)	318 (62.5)	
Physical activity level (n=685)**				0.440
High	568 (82.9)	214 (37.7)	354 (62.3)	
Moderate	99 (14.5)	42 (42.4)	57 (57.6)	
Low	18 (2.6)	5 (27.8)	13 (72.2)	
Dietary intakes (≥ 2 times a week)				
Rice	691 (96.5)	264 (38.2)	427 (61.8)	0.150
Instant noodles	221 (30.9)	80 (36.2)	141 (63.8)	0.577
Milk	267 (37.3)	96 (36.0)	171 (64.0)	0.455
Cold beverages	176 (24.6)	65 (36.9)	111 (63.1)	0.806

Data are presented as number (percentage).
Abbreviations: NPR, Nepalese rupees. 24,000 NPR = approx. 204 USD
P-value was calculated using the chi-square test.
** Number not equal to n=716 as 9 participants refused to answer*
*** Number not equal to n=716 due to no answer/missing data*

Table 7 depicts the overall prevalence of components of MetS and the prevalence in different age groups. Low HDL-C was the most frequently observed component of MetS (57%), followed by high WC (45.3%) and elevated BP (44.7%). A high prevalence of low HDL-C was observed in the age groups ≤ 50 years, whereas the prevalence of elevated BP, elevated HbA1c, and elevated TG increased with age.

Table 7. *Prevalence of components of metabolic syndrome stratified by age*

Characteristics	**Total**	**N**	**Prevalence of high BP % (95% CI)**	**N**	**Prevalence of high WC % (95% CI)**	**N**	**Prevalence of elevated HbA1c % (95% CI)**	**N**	**Prevalence of elevated TG % (95% CI)**	**N**	**Prevalence of reduced HDL-C % (95% CI)**
Overall	716	320	44.7 (41.0, 48.3)	324	45.3 (41.7, 48.9)	278	38.8 (35.2, 42.4)	201	28.1 (24.8, 31.4)	408	57 (53.4, 60.6)
Age groups (years)											
21-30	43	3	7 (-0.6, 14.6)	14	32.6 (18.6, 46.6)	10	23.3 (10.7, 35.9)	4	9.3 (0.6, 17.9)	31	72.1 (58.7, 85.5)
31-40	165	59	35.8 (28.4, 43.1)	79	47.9 (40.3, 55.5)	32	19.4 (13.4, 25.4)	29	17.6 (11.8, 23.4)	109	66.1 (58.9, 73.3)
41-50	220	100	45.5 (38.9, 52.1)	106	48.2 (41.6, 54.8)	86	39.1 (32.7, 45.5)	65	29.5 (23.5, 35.5)	134	60.9 (54.5, 67.3)
51-60	183	90	49.2 (42.0, 56.4)	85	46.4 (39.2, 53.6)	85	46.4 (39.2, 53.6)	65	35.5 (28.6, 42.4)	90	49.2 (42.0, 56.4)
≥ 61	105	68	64.8 (55.7, 73.9)	40	38.1 (28.8, 47.4)	65	61.9 (52.6, 71.2)	38	36.2 (27.0, 45.4)	44	41.9 (32.5, 51.3)

Abbreviations: BP, blood pressure; WC, waist circumference; HbA1c, hemoglobin A1C; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol.

Only 10.3% of the participants did not display any components of MetS, while 4.9% had all five components.

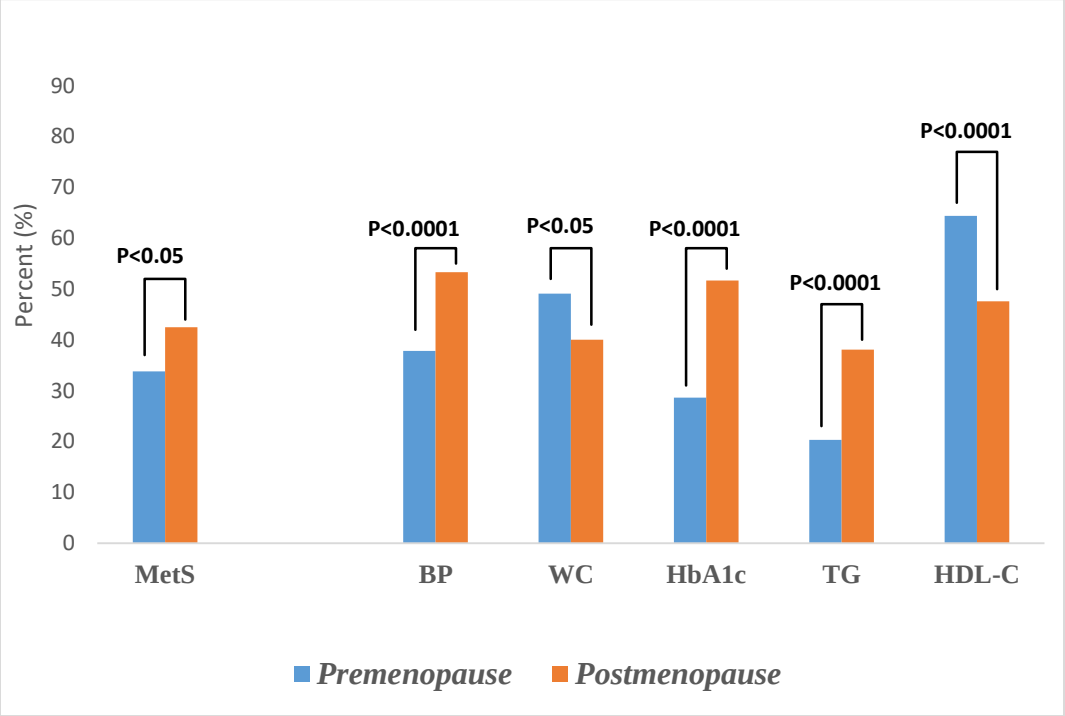

Figure 3. *Prevalence of metabolic syndrome and its individual components by menopausal status*

Abbreviations: MetS, Metabolic Syndrome; BP, blood pressure; WC, waist circumference; HbA1c, hemoglobin A1C; TG, triglycerides; HDL-c, high-density lipoprotein cholesterol.

Figure 5 shows the prevalence of MetS and its components among premenopausal (mean age 40.5 ± 8.02 years) and postmenopausal women (mean age 58.03 ± 7.76 years). The prevalence of MetS, and its components with the exception of high WC and low HDL-C, was significantly higher among postmenopausal women.

3.3 Anthropometric measures, clinical measures, and biomarkers of the study population

Mean values of anthropometric measures, clinical measures, and biomarkers of the study population stratified by MetS are presented in Table 8. Significant differences between those with and without MetS were observed for all variables, except height.

Table 8. *Characteristics of the study population according to metabolic syndrome status.*

Characteristics, mean ± SD or median (IQR)	**Overall**	**Metabolic syndrome**		**P-value**
		Yes	**No**	
Age (in years)*	48.2 ± 11.7	50.3 ± 10.9	47.1 ± 12.1	< **0.0001**
Anthropometry				
Height (cm)*	148.7 ± 6.6	148.6 ± 6.8	148.7 ± 6.6	0.894
Weight (kg)*	54.6 ± 10.4	59.9 ± 10.8	51.5 ± 8.7	< **0.0001**
BMI (kg/m^2)*	24.8 ± 4.9	27.2 ± 5.6	23.3 ± 3.6	< **0.0001**
WC (cm)*	78.4 ± 10.1	85.2 ± 9.3	74.4 ± 8.1	< **0.0001**
Blood pressure				
SBP (mm Hg)*	126.0 ± 19.3	135.3 ± 19.9	120.3 ± 16.5	< **0.0001**
DBP (mm Hg)*	81.7 ± 10.8	86.3 ± 10.5	79.0 ± 10.0	< **0.0001**
Biomarkers				
HbA1C (%)*	5.6 ± 0.8	5.9 ± 0.8	5.4 ± 0.7	< **0.0001**
TC (mg/dL)*	178.2 ± 41.8	188.4 ± 45.5	172.0 ± 38.1	< **0.0001**
HDL-C (mg/dL)*	49.3 ± 14.4	43.7 ± 12.2	52.7 ± 14.6	< **0.0001**
TG (mg/dL)**	113 (77)	162 (88)	96 (51)	< **0.0001**
LDL-C (mg/dL)**	100 (42)	105 (46)	97.5 (42)	< **0.0001**

** Data are presented as mean ± S.D.*

*** Data are presented as median (IQR).*

Abbreviations: BMI, body mass index; WC, waist circumference, SBP, systolic blood pressure, DBP, diastolic blood pressure; HbA1c, hemoglobin A1c, TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol

3.4 Factors associated with MetS

The association of MetS with socio-demographic characteristics and BMI were assessed with logistic regression and presented in Table 9. A strong association of MetS was found with being older or being overweight and obese. The odds of having MetS was 13.6 times higher among the obese groups (OR 13.6, 95% C.I: 8.33, 22.18) in comparison to groups of normal weight (reference group).

Table 9. *Risk factor associated with metabolic syndrome in study population*

	n (%), N=716	**OR (95% CI) [a]**	**AOR (95%CI) [b]**
Age (in years)			
21-30	43 (6.0)	1	-
31-40	165 (23.0)	**2.7 (1.06, 6.76)***	-
41-50	220 (30.7)	**4.2 (1.70, 10.34)***	-
51-60	183 (25.6)	**4.7 (1.88, 11.65)***	-
≥ 61	105 (14.7)	**4.8 (1.87, 12.37)***	-
Ethnicity			
Brahmin/Chhetri	83 (11.6)	1	1
Newar/Tamang	599 (83.7)	**0.6 (0.38, 0.97)***	**0.6 (0.37, 0.95)***
Dalit	34 (4.7)	1.8 (0.81, 4.11)	1.8 (0.78, 4.03)
Educational status (n=707)[c]			
No formal education	597 (84.4)	1.7 (0.72, 4.23)	1.3 (0.50, 3.18)
Secondary or lower	85 (12.0)	0.8 (0.31, 2.30)	0.8 (0.29, 2.16)
College and above	25 (3.5)	1	1
Monthly household income			
< NPR 24000	478 (66.8)	1.1 (0.82, 1.57)	1.1 (0.78,1.50)
≥ NPR 24000	238 (33.2)	1	1
Smoking			
Current	139 (19.4)	1.1 (0.77, 1.69)	1.0 (0.67, 1.50)
Past	113 (15.8)	1.4 (0.93, 2.16)	1.2 (0.76, 1.80)
Never	464 (64.8)	1	1
Alcohol consumption (n=714)[d]			
Current	173 (24.2)	1.0 (0.72, 1.46)	1.0 (0.72, 1.47)
Past	32 (4.5)	1.1 (0.56, 2.36)	1.1 (0.53, 2.29)
Never	509 (71.3)	1	1
Dietary intakes (≥ 2 times a week)			
Rice (Yes)	691 (96.5)	1.96 (0.77, 4.97)	2.4 (0.92, 6.01)
Milk (No)	449 (62.7)	1.12 (0.82, 1.54)	1.08 (0.78, 1.48)
Instant noodles (Yes)	221 (30.9)	0.91 (0.65, 1.26)	0.97 (0.69, 1.35)
Cold beverages (Yes)	176 (24.6)	0.95 (0.67, 1.36)	0.99 (0.70, 1.42)
BMI (kg/m^2) Asian cut-off (n=715)[d]			
Normal weight (18.5-23.0)	223 (31.1)	1	1
Underweight (< 18.5)	43 (6.0)	0.9 (0.34, 2.22)	0.7 (0.27, 1.84)
Overweight (23.0-27.5)	276 (38.5)	**3.2 (2.10, 5.01)****	**4.0 (2.52, 6.32)****
Obesity (≥ 27.5)	173 (24.2)	**13.6 (8.33, 22.18)****	**21.4 (12.46, 46.74)****
Menopause (n=714)[d]			
No	399 (55.9)	1	1
Yes	315 (44.1)	**1.4 (1.06, 1.96)***	0.9 (0.59, 1.45)

Abbreviations: NPR, Nepalese rupees (NPR 24,000 = approx. 204 USD); OR, odds ratio; BMI, body mass index.
a: Unadjusted
b: Adjusted for age
c: Number not equal to n=716 as 9 participants refused to answer
d: Number not equal to n=716 due to no answer/ missing data
** P-value ≤ 0.05*
*** P-value < 0.0001*

4. DISCUSSION

4.1 Main findings

To our knowledge, this is the first study addressing the prevalence of MetS and its risk factors among women specifically from a rural district of Nepal. We used the JIF criteria as recommended and we observed a prevalence of MetS by 37.7%. When applying the ATP III and IDF criteria the prevalence was somewhat lower, 27.4% and 30.3%, respectively. The prevalence of MetS increased by age, but was high even among young women, 30.3 and 40.5% accordingly, in the age groups 31-40 and 41-50 years. A significant difference was observed between ethnic groups, with almost two-thirds of Dalit ethnicity (61.8%) having MetS, followed by Brahmin ethnicity (47.0%). Low HDL-C (57.0%) was the most prevalent component, followed by increased WC (45.3%), high BP (44.7%), and elevated levels of HbA1c (38.8%), and TG (28.1%). With the exception of low HDL-C and high WC, all other components increased significantly with age. The same pattern was seen in premenopausal women and postmenopausal women. In addition to age, postmenopausal status, high BMI and Dalit ethnicity were risk factors for MetS, although not significant for latter.

4.2 Comparison with previous studies

4.2.1 Prevalence of MetS and its components

We observed a higher prevalence of MetS than in previous studies in Nepal (23, 24). This may be attributed to several factors, including the diagnostic criteria for MetS. Firstly, we used the JIS criteria, whereas previous studies in Nepal have applied the ATP III and IDF definitions. Secondly, HbA1c was used instead of FPG as a measure of hyperglycemia. A nationally representative cross-sectional survey reported that 15 and 18% of women had MetS according to the ATP III and IDF definitions, respectively (24). A cross-sectional study in Eastern Nepal, observed a prevalence among females of 21.9% when applying ATP III and 25.7% according to the IDF definitions (23). When applying these criteria in our study population, the prevalence of MetS was still higher than in the previous studies in Nepal, namely, 27.4% (ATP III) and 30.3% (IDF). However, the prevalence was similar to prevalence in South Asia (ATP III 26.1% and IDF 29.8%), reported by

a systematic review (18). Our data are in accordance with several studies that have shown a higher prevalence of MetS when using the JIS definition (19, 73, 87), and recommended it as a more preferred diagnostic criterion, as it can identify a large number of individuals with MetS and at risk of CVDs (73, 87).

In the present study, HbA1c was applied instead of FPG in the diagnosis of MetS. This could also contribute to the high prevalence as a 2-4% increase in the prevalence of MetS has been reported when using HbA1c as a criterion (79-82).

The high occurrence of low HDL-C observed in our study population was consistent with previous studies conducted in Nepal (23, 24), India (20), and other South Asian populations (18). In line with that, the INTERHEART study revealed that a high percentage of South Asians exhibited low HDL-C compared to the rest of Asia (82.3% vs. 57.4% cases; 81% vs. 51.6% controls) (88). This corresponds with the high frequency of dyslipidemia present in South Asians, as Rashid et al. (60) pointed out.

High WC and high BP were observed in nearly half of our study population. This is in line with a recent hospital-based cross-sectional study in Nepal, among 2,256 outpatients of age 40-69 years, showing a very high prevalence of high WC (77.46%) and hypertension (74.11%) in female participants (89). In contrast, a study by Mehata et al. (24) reported a lower prevalence of abdominal obesity and hypertension among the female participants compared to our study (AO: 36.5% vs. 45.8%; high BP: 20.2% vs. 43.0%). Similarly, a systematic review and meta-analysis by Huang et al. (90) including 99,792 subjects in Nepal, reported a prevalence of prehypertension and hypertension of 40.4% and 24.4%, respectively, in rural areas of Nepal.

4.2.2 Factors associated with MetS

Age, menopause, BMI, and ethnicity were significantly associated with the MetS.

4.2.2.1 Age and menopause

The odds of having MetS increased steadily with age, and women over 60 years of age were about five times more likely to have MetS compared to those 21-30 years of age. This result was in concordance with other studies in Nepal (24) and India (91). In the study in Nepal (24), the age group 45-69 years were 4.5 times more likely to have MetS compared to the age group of 15-29

years (ref. group). A similar result of increasing prevalence with age was reported in studies conducted in other parts of the world (87, 92). As age advances, blood vessels lose their elasticity gradually, which increases resistance. Because of poor circulation, lipids are piled up in the abdomen and release free fatty acids, which as a consequence increases insulin resistance and elevates serum TG (93). Also, the biological changes with aging impede healthy lifestyle factors which are associated with MetS. Thus the biological and physiological changes, together with increased adiposity, may predispose to greater risk of MetS with increased age. Menopause also explain the increase in prevalence with age, as hormonal changes increase the susceptibility to MetS (66, 67).

In line with several studies (67, 94, 95) we observed a higher prevalence of MetS among postmenopausal compared to premenopausal women (42.5 % vs. 33.8%). The prevalence of MetS among postmenopausal women was, however lower than reported by other studies in Nepal (57.8%) and India (48.6%) (94, 95). Our observation of higher percentage of women with high WC in premenopausal women than postmenopausal women is contradictory to previous evidence showing that postmenopausal women are predisposed to increased abdominal obesity (66, 67).

Menopause is regarded as a predictor of MetS independent of women's age (96). Insulin resistance and obesity (visceral adiposity) are detrimental to metabolic health when occurring simultaneously. These two conditions are also associated with postmenopausal modifications in adipokine production, inflammatory and prothrombotic processes, and oxidative stress. (96). In women with MetS, lower adiponectin levels have been shown to be significantly related to low HDL-C and high TG levels (97).

4.2.2.2 BMI

Higher BMI significantly predicted MetS, with odds of having MetS in obese women about 21 times more than normal-weight women. Adipose cells in obese individuals release free fatty acids and cytokines, which reduce glucose uptake in skeletal muscles and the liver. To maintain glucose homeostasis, β-cells of the pancreas release compensatory insulin, leading to hyperinsulinemia (10). A similar observation was made in the IRApen study, a bi-ethnic survey in the Iranian population, which reported a strong association of MetS with overweight and obesity (74).

4.2.2.3 Ethnicity

The majority of women in the study population belonged to the Newar/Tamang ethnicity. They appeared to have a reduced risk for MetS, whereas Dalits displayed an increased risk, although non-significant. The reliability of the data is, however, uncertain due to the small number of participants from this ethnic group.

Dalits are the underprivileged caste group that belong to the lowest level in the hierarchical caste system of Nepal. Although many policies and laws are in place to eradicate inequality and caste-based untouchability, Dalits are still facing discrimination and are socially excluded at the ground level. Because of social exclusion, they are denied resources and a better livelihood. Hence they are poorer in terms of education, economic status, and health (98). Although insignificant, the interplay of these factors might have resulted in a higher risk of MetS among Dalit ethnicity compared to other ethnicities.

4.2.2.4 Lifestyle factors

Unhealthy diet, physical inactivity, tobacco use and harmful use of alcohol are proposed to be risk factors for MetS. Our study site had a location that made it possible to visit neighboring cities by bus in the course of a day. This may impact the eating habits and facilitate a more semi-urban lifestyle. Accordingly, our study sites have witnessed a nutritional transition, as exemplified by a high intake of instant noodles.

Consumption of instant noodles and sugar sweetened beverages (SSB) such as Coca-Cola and Pepsi is high in Nepal. Consuming such foods is considered as symbol of status. Because of its availability they are consumed by many people in both rural and urban districts. In contrast to other studies, instant noodles and cold beverages consumption showed inverse association with MetS in our study population. A study among 10,711 Korean adults aged 19-64 years showed a higher prevalence of MetS among women who reported instant noodle intake $\geq$2 times weekly (OR = 1.68, CI: 1.10, 2.55) (99). Various prospective studies has concluded that high consumption of SSB was positively associated with development of MetS (100, 101). A follow-up study which included 1868 subjects aged 55-80 years without MetS at baseline, reported 43% higher risk of development of MetS among those who consumed > 5 servings a week of SSB compared to those who rarely consumed it (100). Further a meta-analysis by Malik et al. which included prospective cohort studies from 1966 to 2010 showed a positive association of high consumption of SSBs and of MetS and T2D (101).

Rice, mainly white rice, is still the main constituent of the diet, and is consumed nearly universally at least one to two times a day in Nepal. The carbohydrate content of white rice is high, resulting in a higher dietary glycemic load particularly among populations who eat rice as a staple food. It has been suggested that rice consumption is associated with increased risk of T2D and MetS because of its high glycemic load and glycemic index (102, 103). Although non-significant, rice consumption $\geq$ 2 times a week showed about twice the odds of having MetS compared to consumption $\leq$ 2 times a week in our study population. A longitudinal study conducted in Tehran among 1476 adults aged 19-70 years, reported increased risk of MetS in the highest quartile of rice consumption compared to the lowest quartile (OR = 1.66, CI: 1.04, 2.66) (102). A meta-analysis by Guo et al., which included 61,431 subjects from 2004 to 2020 found the refined grain consumption such as white rice was positively associated with MetS (RR = 1.37, CI: 1.02, 1.84) (104).

The majority of the literature point towards increasing risk of the MetS with lifestyle factors such as low physical activity, smoking, and alcohol consumption (105, 106). In contrast to this evidence, we observed no significant association of these lifestyle factors and MetS. Given that the information relies on self-report, this may have impacted the results. Epidemiological studies have suggested that high and moderate physical activity reduces the risk of developing MetS, and therefore is an important component in CVD prevention. The majority of the women in our study reported moderate/high physical activity level and only a few women had low physical activity. We found no significant difference between physical activity and prevalence of MetS. Likewise, a higher proportion of women without MetS reported moderate physical activity, compared to those with MetS, 57 and 42%, respectively. Major occupation in rural areas of Nepal is traditional farming, which involves strenuous activity and use of manual force. Similarly, no association was observed between MetS with current smoking and alcohol consumption. There are several studies showing that high consumptions of alcohol increases the risk of Mets, whereas occasional low to moderate consumption has been linked with reduced risk of CVDs and diabetes (107, 108). A systematic review by Ronksley et al., reported that consumption of 2.5-14.9 g alcohol (about $\leq$ 1 drink) per day reduced the risk for CVD outcomes. On the other hand, consumption of > 60 g alcohol per day significantly increased the risk of CVDs (107). Our study population included women from the Brahmin/Chhetri ethnic group, who follow the religious norm of abstinence from

alcohol, while consumption of alcohol among Dalits and Newar/Tamang is high due to cultural influence.

4.3 Strengths and limitations

To our knowledge, this is the first study to assess the prevalence of MetS among married women of the rural Nepalese population. This study might help to assess the burden of MetS in rural Nepal. The large sample in our study strengthened the stratified analysis.

Being a cross-sectional study design, it has a limitation to establish a causal relationship between risk factors and MetS. To explore the causal relationship, further longitudinal studies are needed. The findings of our study may not be generalizable to other populations or to men. However, our results may be representative for rural district in Nepal. The use of HbA1c as a criterion for MetS may make comparisons with other studies that use FPG for MetS diagnosis challenging. However, previous studies have provided evidence that using HbA1c instead of FPG identifies more individuals with MetS (79-81). Recall bias and social desirability bias on self-reported behavioral risk factors might have led to under or over reporting. Social desirability bias is highly possible when reporting smoking and alcohol consumption. Certain cultural and religious norms and roles in the Nepalese society, may have persuaded women to underreport such behaviors. In contrast, physical activity may have been over reported.

4.4 Public health implication

Our study provides new data on overall prevalence of MetS and its components in rural Nepal. The high prevalence of MetS in our study shows the importance of interventional strategies and health policies to reduce the associated risk factors and prevent future complications of the MetS. For instance, creating an encouraging environment for healthy diet and awareness on risk reduction behavior could reduce the prevalence of risk factors. Our findings may facilitate policy makers to take evidence-based decisions. Furthermore, the high prevalence of MetS among women of child-bearing age is worrisome as it increases risk for metabolic diseases and CVDs in both mother and offspring in later life. This highlights the urgency to intervene the growing tide of MetS prevalence and the looming epidemic of T2DM and CVD. Therefore, timely recognition, diagnosis and the

management of the MetS components in women of childbearing age can reduce the threat of CVDs and T2D epidemic.

5. CONCLUSION

In summary, the prevalence of MetS in our study area was very high, with a steady increase of prevalence with age. The high prevalence even among young women aged 31-40 years is of concern. Low HDL-C and high WC were most frequent components. The prevalence of MetS was higher in postmenopausal women compared to premenopausal women. Our findings point to a higher risk of CVD and T2D, and underscores the urgency to stem these abnormalities through lifestyle modification, and awareness campaigns.

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ANNEXES

ANNEX I

Table 10. *Definition of metabolic syndrome*

Various definition of Metabolic Syndrome				
Components	**NCEP-ATP III (2001)** (3)	**IDF (2005)** (5)	**Modified NCEP-ATP III (2005) (41)**	**JIS (2009) (4)**
BP	SBP ≥ 130 and/or DBP ≥ 85 mmHg	SBP ≥ 130 and/or DBP ≥ 85 mmHg or on treatment for HPT	SBP ≥ 130 and/or DBP ≥ 85 mmHg or on treatment for HPT	SBP ≥ 130 and/or DBP ≥ 85 mmHg or on treatment for HPT
WC	M ≥ 102 cm F ≥ 88 cm (Caucasian cut-points)	M ≥ 90 cm F ≥ 80 cm (South Asian cut-points)	M ≥ 90 cm F ≥ 80 cm (Asian cut-points)	M ≥ 90 cm F ≥ 80 cm (South Asian cut-points)
FPG	≥6.1 mmol/L	≥5.6 mmol/L or previously diagnosed T2DM	≥5.6 mmol/L or on treatment for elevated glucose	≥5.6 mmol/L or on treatment for elevated glucose
TG	≥1.7 mmol/L	≥1.7 mmol/L or on treatment for TG	≥1.7 mmol/L or on treatment for TG	≥1.7 mmol/L or on treatment for TG
HDL-C	M < 1.03 mmol/L F < 1.29 mmol/L	M < 1.03 mmol/L F < 1.29 mmol/L or on treatment for HDL-C	M < 1.03 mmol/L F < 1.29 mmol/L or on treatment for HDL-C	M < 1.0 mmol/L F < 1.3 mmol/L or on treatment for HDL-C
MetS definition	**≥ 3 components**	**High WC + ≥ 2 components**	**≥ 3 components**	**≥ 3 components**

Abbreviations: NCEP-ATP III, National Cholesterol Education Program Adult Treatment Panel III; IDF, International Diabetes Federation; JIS, Joint Interim Statement; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; WC, waist circumference; FPG, fasting plasma glucose; TG, triglyceride level; HDL-c, high-density lipoprotein cholesterol; HPT, hypertension;

ANNEX II

Diabetes among women in rural Nepal; risk factors, complication and relation with vitamin A and D. A prospective cohort study.

Location and date		**Response**	**Code**
1.	Name of village		
2.	Ward No.		
3.	Local Place Name		
4.	Interviewer ID		

Participants ID					**number**	
Consent, interview language and name			**Response**			**Code**
5.	Consents has been read and obtained		1. Yes **2. No (If No, End)**			
6.	Interview language		1. Nepali 2. Tamang 3. Newari			
7.	Time of interview					
8.	Family Surname					
9.	First name					
10.	Husband Name					
11.	Contact phone number where possible					

A. Personal information				Code	
1.	How old are you?	Year	Mention complete year	P1	
2.	What is your ethnicity? 1. Brahmin/Cheetri 2. Newar/Tamang 3. Dalit/lower cast 4. Others		Mention if others	P2	
3.	What is your religion? 1. Hindu 2. Buddhist 3. Christina 4. Muslim		Mention if others	P3	
4.	What is your highest education level you have completed? 1. Illiterate 2. Primary education 3. Secondary 4. Higher /SLC 5. College 6. Refuse			P4	
5.	Are you involved in income generating group/activities? A. Yes 2. No If Yes, Since how many years ……			P5	
6.	Which of the following best describes your main work status over the past 12 months? 1. Employee (gov/non gov) 2. Self-employee … 3. Retried 4. Housewife 5. Others (specify)……			P6	
7.	What is your average income (NRS)…….			P7	

B. Household Information				
1.	How many family members do you live with?	Number	H1	
2.	What is the average family income per month? (NPR)		H2	
3.	Your husband education? a. Uneducated c. Primary education b. Secondary d. Higher e. University education f. No response	Escape for widow and divorce women	H3	
4.	Your husband occupation a. Employee (gov/non-gov) d. Self-employee c. Homemaker b. Retired e. Others		H4	
5.	Did anyone from your family go abroad for work? 1. Yes 2. No If Yes, How many months…….	If No go to H6	H5 H5a	
6.	What are the most common energy source for cooking ? a. LPG c . Traditional b. Improved cooking stove d. Others (specify)..		H5	
7.	How long time do you spend for cooking daily ?	Hours ……. Min…..	H7	

C. Marital and reproductive information

1.	What is your current marital status? 1. Married living with husband 2. Married husband is not with me 3. Widow 4. Divorced	Mention if others	MR1	
2.	What was the age when you were married?	Years	MR2	
3.	How many children do you have? a. Son b. Daughter c. Total	If Null go to Q.D	MR3a MR3b MR3c	
4.	What was the birth weight of your last-born child?	…… (Kg)	MR4	
5.	When was your last child born?	Years …….	MR5	
6.	How old were you when you had your first baby?	Years	MR6	
7.	Where did you give birth your last baby? a. House b. Health institution c. Others specify		MR7	
8.	How many days did you have on an average for postnatal care?	Days	MR8	
9.	How long did you exclusively breastfeed your last baby? a. < 2 weeks b. 2-6 weeks c. 6 weeks -3 months d. 3-6 month e. 6-12 months f. >12 months		MR9	
10.	In the first 5 months after delivery of your last baby, did your baby get anything to eat or drink other than breast milk?	a. Yes b. No	MR10	
11.	What was the extra food and fluid given to your baby? a. Formula b. Water c. Cerelac d. Lito e. Buffalo /cow Milk f. Others		MR11	
12.	Generally, how many times did you breastfeed your baby per day?	Frequency……	MR12	
13.	For how many months did you breastfeed your baby?	Number of days	MR13	
14.	Do you have regular menstrual bleedings?	Yes No	MR14	
15.	Have you had your menopause? (**If women age > 40 years)**	Yes , Mention age …… No	MR15	

D. Family planning and gynecological related

Do you currently use any family planning methods? 1. Yes 2. No			If No…… Why	FP1	
FP devices	Used past	Currently using	Never used		
a. Depo (inj)				FP1a	
b. Oral contraceptives				FP1b	
c. Norplant				FP1c	

E. Pelvic Organ Prolapse symptom score (POP-SS)							
How often during the last 4 weeks have you had the following symptoms		0	1	2	3	4	
1.	A feeling of something coming down from or in your vagina?						UP1
2.	An uncomfortable feeling or pain your vagina which is worse when standing?						UP2
3.	A heaviness or dragging feeling in your lower abdomen/tummy ?						UP3
4.	A heaviness or dragging feeling in your lower back?						UP4
5.	A need to strain (push) to empty your bladder?						UP5
6.	A feeling that your bladder has not emptied completely?						UP6
7.	A feeling that your bowel has not emptied completely?						UP7
8.	Which of the symptoms above (1-7) causes you most bother?						

0= Never, 1= occasionally, 2= sometimes, 3= most of the time, 4= all of the time

F. International Consultation on Incontinence Questionnaire –Urinary Incontinence Short-Form (ICIQ-UI SF)				
1.	Do you have urine incontinence problem If No Go to **H section**	No	0	
		Yes	1	
2.	How often do you leak urine?	Never	0	UI10
		About once a week or less often	1	UI11
		Two/ three times a week	2	UI12
		about once a day	3	UI13
		Several times a day	4	UI14
		All the time	5	UI15
3.	We would like to know how much urine <u>you think</u> leaks. How much urine do you <u>usually</u> leak *(whether you wear protection or not)*?	None	0	UI20
		A small amount	2	UI22
		A moderate amount	4	UI24
		A large amount	6	UI26
4.	Overall, how much does leaking urine interfere with your everyday life? *Please ring a number between 0 (not at all) and 10 (a great deal)* 0 1 2 3 4 5 6 7 8 9 10 Not at all a great deal			UI3
5.	When does urine leak? (*Please tick all that apply to you)*	never – urine does not leak	UI41	
		leaks before you can get to the toilet	UI42	
		leaks when you cough or sneeze	UI43	
		leaks when you are asleep	UI44	
		leaks when you are physically active/exercising	UI45	
		leaks when you have finished urinating and are dressed	UI46	
		leaks for no obvious reason	UI47	
		leaks all the time	UI48	

G. St. Mark's score

1.	During last four weeks, how often have you experienced	Never	Rarely	Sometimes	Weekly	Daily	
2.	Incontinence for sold stool	0	1	2	3	4	
3.	Incontinence for liquid stool	0	1	2	3	4	
4.	Incontinence for gas	0	1	2	3	4	
5.	Alteration in lifestyle	0	1	2	3	4	
6.	Need to wear a pad or plug	No		Yes			
		0		2			
7.	Taking constipating medicines	0		2			
8.	Lack of ability to defer defecation for 15 minutes	0		4			

Never, no episodes in the past four weeks, **Rarely**, 1 episode in the past four weeks, **Sometimes**, >1 episode in the past four weeks but < 1 a week , **Weekly** , 1 or more episodes a week but < a day, **Daily**, 1 or more episodes a day

Add one score from each row: minimum score = 0 = perfect continence, maximum score= 24= totally incontinent.

H. Well-being index

S.No	Question	All of the time	Most of the time	More than half of time	Less than half of time	Some of the time	At no the time
1.	I have felt cheerful and in good spirits	5	4	3	2	1	0
2.	I have felt calm and relaxed	5	4	3	2	1	0
3.	I felt active and vigorous	5	4	3	2	1	0
4.	I woke up fresh and rested	5	4	3	2	1	0
5.	My daily life has been filled with things that interest me	5	4	3	2	1	0

I. Tobacco and alcohol use				
Tobacco use				
1.	Do you smoke?	a. Yes b. No	If yes, go to T8	T1
2.	Do you currently smoke and use any tobacco products, such as cigarettes, bidis, hukhs or tamakhus?	a. Yes b. No	If No go to T8	T2
3.	Do you smoke tobacco products daily?	a. Yes b. No		T3
4.	How old were you when you started smoking ?	Years		T4
		Don't know		
		Weeks		
5.	How many cigarettes do you smoke daily?	Number……..		T5
6.	During any visit to a doctor or other health worker in the past 12 months, were you advised to quit smoking tobacco?	a. Yes b. No c. No visit during last 12 months	If T2 = yes, go to T12, if T2=NO, go to c9) If T2 = yes, go to T12, , if T2=NO, go to c9) If T2 = yes, go to T12, , if T2=NO, go to c9)	T6
7.	In the past, did you ever smoke daily ?	a. Yes b. No	If No, go to C12	T8
8.	How old you were you when you stopped smoking?	Years		T9
		Don't know		
9.	How long ago did you stop smoking (**Record only 1, not all 3**)	Years		T10a
		Months		T10b
		Weeks		T10c
10.	Do you currently use any smoke-less tobacco products such as (snuff, chewing tobacco, khaaini surti, gutak)	a. Yes b. No		T11
11.	Do you currently use smokeless tobacco products daily?	a. Yes b. No	If no go to T15	T12
12.	On average, how many times a day/week do you use.		Daily / Weeks	
		Chewing tobacco		T14a
		Betel		T14b
		Other		T14c
		Don't know		T14d
13.	In the past, did you ever use smokeless tobacco products such as (snuff, chewing tobacco, nasal snuff, Khaini, surti, gutka) daily	a .Yes b .No		T15

14.	In the past , did you ever use smokeless tobacco products such as (snuff, chewing tobacco, nasal snuff, Khaini, surti, gutka) daily	a. Yes b. No		T16

J. Alcohol consumption

1.	Have you ever consumed an alcoholic drink such as beer, wine, spiritis, fermented cider or (jaad, raksi, tungba) ?	a. Yes b . No	If no, go to K	A1
2.	Have you consumed an alcoholic drink within the past 12 month ?	a. Yes b . No	if no, go to K (other section)	A2
3.	During the past 12 months, how frequently have you had at least one alcoholic drink ?	Daily 5-6 days per week 1-4 days per week 1-3 days per month Less than once a month		A3
4.	Have you consumed alcohol in the past 30 days	a. Yes b. No	if no, go to K	A4
5.	If yes a. How often did you drink	Daily 5-6 days per week 1-4 days per week 1-3 days per month Less than once a month		A5
	b. How many standard drinks did you have on each occasion **(show card)**			
	c. How often did you have meals together with the drink ?(**do not count snacks**)			
	d. During the last week, how many standard drinks did you have each day?			
6.	During each of the past 7 days, how many standard alcoholic drinks did you have each day? **(Use Showcard)**	Sunday		A8a
		Monday		A8b
		Tuesday		A8c
		Wednesday		A8d
		Thursday		A8e
		Friday		A8f
		Saturday		A8g
		Donot know		77

K. Diet			
SNO	Questionnaire	Response	Code
1.	In a typical week, on how many days do you eat fruit**?** **(Show card)** Number of days…….	if zero days , go to D3	D1
		Don't know	
2.	How many servings of fruit do you eat on one of those days ? (**Show card**)	number of servings	D2
		Don't know	
3.	In typical week, on how many days do you eat vegetables?	Number of servings	D3
		Don't know	
4.	How many serving of vegetables do you eat on one of those days?	Number of servings	D4
		Don't know	
5.	What type of oil or fat is most often used for meal preparation in your household?	Mustard oil	D5a
		Refined vegetable oil	D5b
		lard or suet	D5c
		Butter or ghee	D5d
		noodles oil	D5e
		None used	D5f
		don't know	d77
		Others (specify)	D5g

Show portion size picture to for estimating portion size

		Frequency of eating								Portion size			
	Food name	2-4 times a day	Once a day	2-4 times a week	Once a week	2-4 times a month	Once a month	Once every 4 months	less than 1 every four	Average size	Less	Average	More
1.	Cereal												
1.1	Rice	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.2	Beaten rice	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.3	Whole wheat flour	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.4	Maize/corn	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.5	Choumin	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.6	Sooji	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
1.7	Other like kodo, fapar, bajra	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
2.	Legumes												
2.1	Sprouts	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
2.2	Cheakpeas, dry peas, dry beans	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐
2.3	Soyabean	☐	☐	☐	☐	☐	☐	☐	☐	1 cup	☐	☐	☐

3.	Vegetables (in season)												
3.1	Broccoli, Cauliflower	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.2	Radish, Turnip	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.3	Cabbage/Kohlrabi	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.4	Watercress	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.5	Spinach	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.6	Pumpkin	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.7	green beans, peas	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.8	Eggplant	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.9	Tomato	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.10	Garlic	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.11	Onion/ Shallot	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.12	Carrot	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.13	Cucumber	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.14	Potato	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.15	Yam	□	□	□	□	□	□	□	□	1 cup	□	□	□
3.16	Sweet potato	□	□	□	□	□	□	□	□	1 cup	□	□	□
4.	Eggs and Milk Product												
4.1	Eggs	□	□	□	□	□	□	□	□				
4.2	Milk	□	□	□	□	□	□	□	□	1 cup	□	□	□
4.3	Consensed milk	□	□	□	□	□	□	□	□	1 cup	□	□	□
4.4	Curd	□	□	□	□	□	□	□	□	1 cup	□	□	□
4.4	Chees, panner etc	□	□	□	□	□	□	□	□				
5.0	Junk Food												
5.1	Instance noodles	□	□	□	□	□	□	□	□				
5.2	Fruit juices/carbonated drinks (coca cola, pepsi etc)	□	□	□	□	□	□	□	□				
5.3	Cookies (biscuit)	□	□	□	□	□	□	□	□				

L. Physical activity

SNO	Questionnaire	Response		Code
1.	Does your work involve vigorous-intensity activity that causes large increase in breathing or heart rate like carrying or lifting heavy loads, digging or construction work, etc.. for at least 10 minutes continuously	1. Yes 2. No	if no go toP4	P1
2.	In a typical week, on how many days do you do vigorous- intensity activities as part of your work?	No of days …		P2
3.	How much time do you spend doing vigorous-intensity activities at work on a typical day	Hours ____	Minu_ ____	P3
4.	In a typical year, how many months are you involved in this activity	Months ____		P4
5.	Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking [or carrying light loads] for at least 10 minutes continuously?	Yes No	if no go to P7	P5
6.	In a typical week, on how many days do you do moderate- intensity activities as part of your work?	Days_____		P6
7.	How much time do you spend doing moderate-intensity activities at work on a typical day?	Hours_____	Mins_ _	P7
8.	Do you walk for at least 10 minutes continuously to get to and from places	Yes No		P8
9.	In a typical week, on how many days do you walk for at least 10 minutes continuously to get to and from places?	number of days ___		P9
10	How much time do you spend or walking for travel on a typical day ?	Hours_____	Mins	10
Sedentary behavior				
	How much time do you usually spend sitting or reclining on a typical day?	Hours_____	Mins___ __	

Recreational activities *NA sports fitness, cycling swimming volleyball etc as recreational activities

M. Pesticide use

SNO	Questionnaire	Response		Code
1.	Do you use pesticide in your agriculture field?	Yes	If No (Go to food frequency section)	
2.	If Yes, what is the purpose of pesticide use ?			

SN	Purpose	Yes (1)	No (0)	code
1.	To prevent vegetables from pest			
2.	To kill the pest			
3.	To increase the productivity			

3.	For how long have you used pesticides?		Months		Years	
4.	What kind of footwear do you have during pesticide use?	Sandals	Close shoes	Barefoot		
5.	Are you the one in your family who mainly use pesticides?		Yes (1)	No (0)		

6.	How do you determine amount (concentration) of pesticide to use?	
	1. According to the information given in label	
	2. Self judgement	
	3. As per advice from expert (authorized person)	
	4. Not committed with specific concentration	
7.	What do you typically wear while applying pesticides	
	1. Shoes — Yes (1) — No (0)	
	2. Hat/head cover	
	3. Glasses	
	4. Full sleeves/shirt	
	5. Gloves	
	6. Mask	
	7. Others	
8.	Do you think pesticide have any adverse human health effects?	
9.	How do the pesticide enter in human body	
	1. Inhalation — Yes (1) — No (0)	
	2. Skin	
	3. Mouth	
	4. Others	
10.	What are the most three common health effects you have experienced? 1……. 2…… 3……	
11.	Have you had any adverse effect after use of pesticides? 1……. 2…… 3……	

N. Medical History – Blood pressure (BP)

Questionnaire		Response		Code
	Any chronic diseases you are suffering from? If Yes, What ……..	Yes No		H0
1.	Have you ever had your BP measured by a doctor or other health worker?	1. Yes 2. No if no, go to Diabetes section		H1
2.	Have you been told that you have raised BP or hypertension?	1. Yes 2. No if no, go to Diabetes section		H2a
3.	Have you been told in the past 12 months?	1. Yes 2. No		H2b

4. Are you currently receiving any of the following treatment/advice for high BP prescribed by a doctor or other health workers?

5.				
	Drugs (medication) that you have taken in the past two weeks	Yes	No	H3a
	Advice to reduce salt intake			H3b
	Advice or treatment to decrease weight			H3c
	Advice or treatment to stop smoking			H3d
	Advice to start or do more exercise			H3e

6.	Have you ever seen a traditional healer for raised BP or hypertension?			H4
7.	Are you currently taking any herbal or traditional remedy for your raised BP?			H5
8.	Has anyone in your family suffered from high BP?			H6
9.	Who---			H7
10.	Since how long			H8
11.	Any medication			H9

O. Knowledge on Diabetes

S.No	Questionnaire	Response		Code
1.	Do you have diabetes?	1. Yes 2. No		DK1
2.	If Yes, what type	Type 1 Type 2 Don't know		DK1a
3.	Have you ever had your blood sugar measured?	1. Yes 2. No		DK1b
4.	What was the result?	1. Normal 2. Elevated 3. Don't know		DK1c
5.	Where the test was done?	1. Hospital 2. Primary health center 3. Others		DK1d
6.	Do you think, in general, more and more people are getting affected with diabetes ?	1. Yes 2. No 3. Don't know		DK2
7.	Do you think occurrence of diabetes is increasing?	1. Yes 2. No 3. Donot know		
8.	Which factors do you think contribute to diabetes? 1. Obesity 2. Decreased physical activity 3. Family history of diabetes 4. Mental stress 5. Consuming more sweets 6. Others			DK3
9.	Do you know that diabetes can cause complications in other organs? 1. Yes 2. No 3. Don't know			DK4
10.	If yes, what are they?	_____	1	Dk4a
		_____	2	Dk4b
		_____	3	Dk4c
11.	Can diabetes be prevented	1. Yes 2. No 3. Don't know		
12.	Is anyone in your family suffering from diabetes? If **Yes,**	1. Yes 2. No		Dk7
	Who			Dk71
	Since how long			Dk7b
	What type			Dk7c

Bone fragility				
Questionnaire		Response		Code
A.	Have you heared about osteoporosis? Did you ever experience any fractures?	Yes No if no, go to Night blindness section		F1
B.	If yes, at which age ……			
C.	When was the last fracture? ……			
D.	What type of fracture? (hip, pelvis, elbow, wrist, spine etc)	_____		F2
E.	Was it low energy fracture? (fall from low height or less) nepali version			
F.	Where did you go for the treatment?	_____		F3
G.	How long did it take to recover? (in months)	_____		F4
H.	Any long-term complications	Yes No		F5
I.	Did your parents ever break after age of 40?	Yes No If Yes, , Mother Father Others		F6
J.	Are you on any medication for osteoporosis a. Vitamin D b. Calcium c. Alendronate (*widely used in Nepal as well)*	Yes No		F7
K.	Do you take any supplementation of calcium and vitamin D?	Yes No		F8

Night Blindness				
Questionnaire		Response		Code
1.	Do you have any difficulty in vision?	Yes No if no, go to Section V(oral health)		NB1
2.	If yes, since how long do you have this problem ……			NB2
3.	Is your vision dim during night?	Yes No		NB3
4.	If yes, does it affect in day also?	Yes No		NB4
5.	Did you have any treatment for this problem?	Yes No		NB5
6.	If yes, what are these ….			NB6

L. Oral Health				
SNO	Questionnaire	Response		Code

1.	How many natural teeth do you have ?	No natural teeth	if no natural teeth, go to O4	OH1
		1 to 9 teeth		
		10 to 19 teeth		
		20 teeth above		
		Don't know		
2.	How would you describe the State of Your teeth?	Excellent		OH2
		Very good		
		Good		
		Average		
		Poor		
		Very poor		
		Don't know		
3.	How would you describe the state of your gums	Excellent		OH3
		Very good		
		Good		
		Average		
		Poor		
		Very poor		
		Don't know		
4.	Do you have any removable dentures	Yes	if no go to O6	OH4
		No		
5.	Which of the following removable dentures do you have			
	An Upper jaw denture	Yes		OH5a
		No		
	A lower jaw denture	Yes		OH5b
		No		
6.	During the past 12 months, did your eeth or moth cause any pain or discomfort?	Yes		OH6
		No		
7.	How long has it been since you last saw a health worker?	Less than 6 months		OH7
		6-12 months		
		less than 2 years		
		2 or more years		
		Never received dental care	if never, go to O9	
8.	What was the main reason for your last visit to the health worker	Consultation/advice		OH8
		Pain or trouble with teeth, gums or mouth		
		Treatment/follow-up treatment		
		routine check up		
		other (specific)		
9.	How often do you clean/brush your teeth?	Never		OH9
		2-3 times a month		
		once a week		
		2-6 times a week		
		once a day		
		twice or more a day		

10.	Do you use toothpaste to clean your teeth?	Yes No	If no, go to O12a	OH10
11.	Do you use toothpaste containing fluoridate?	Yes No Don't know		
12.	Do you use any of the following to Clean your teeth?			OH12

	Yes (1)	No (0)		
Toothbrush				OH12a
Wooden toothpick				OH12b
Plastic toothpick				OH12c
Thread (dental Floss)				OH12d
Charcoal				OH12e
Chewstick/ miswak				OH12f
Others (specify)				OH12g

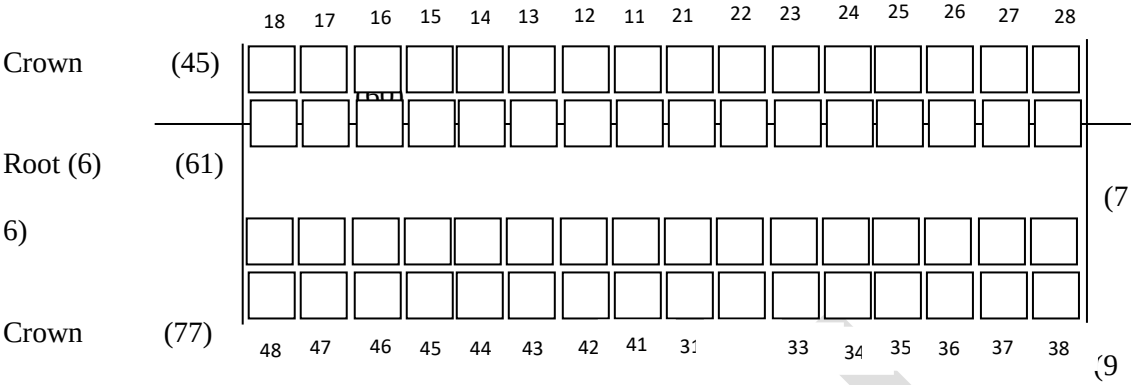
13. Have you experienced any of the following problems during the past 12 months because of the state of your teeth?

Oral Problem	Yes (1)	No (0)		
Difficulty in chewing food				OH13a
Difficulty with speech/trouble pronouncing words				OH13b
Felt tense because of problem with teeth or mouth				OH13c
Embarrassed about appearance of teeth				OH13d
Avoided smiling because of teeth				OH13e
Sleep is often interrupted				OH13f
Days not at work because of teeth or mouth				OH13g
Difficulty doing usual activities				OH13h
Less tolerant of spouse or people close to you				OH13i
Reduced participation in social activities				OH13j
Are you currently suffering dental carries				OH14

B. Physical measurement			
Height	in centimeter		
Weight	in Kilogram		
Waist	in centimeter		
Hip Circumference	In Centimeter		
Blood pressure 1	Systolic mmHg		
	Diastolic mmHg		
Blood pressure 2	Systolic mmHg		
	Diastolic mmHg		

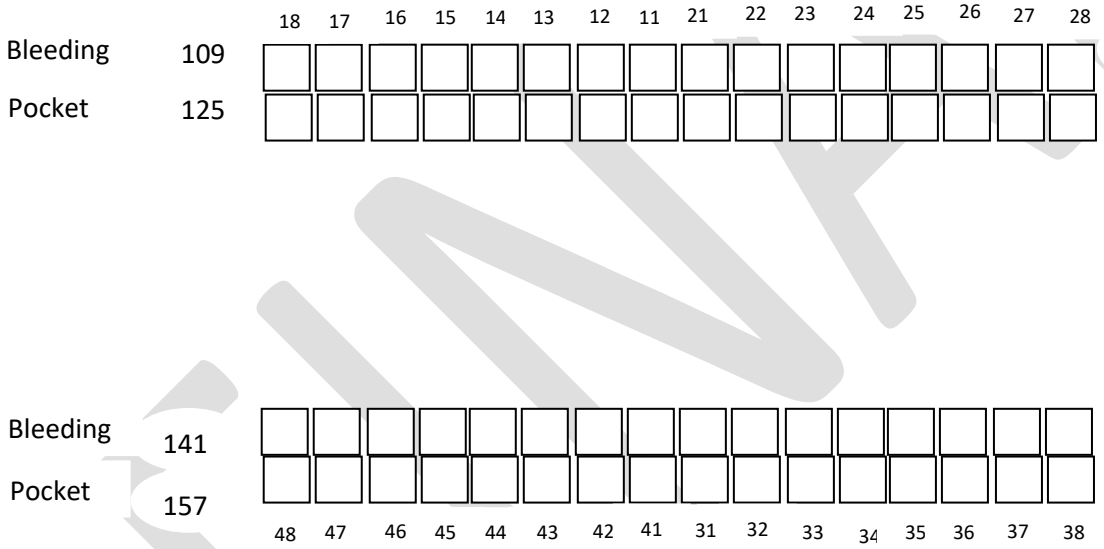
WHO- Oral Health Assessment form for adults

Dentition status



Permanent teeth Status
0= sound
1=carries
2= filled w/carries
3=filled, no carrries
4=missing due to carries
5= missing for any another reason
6= fissure seatant
7=fixed dental prosthesis/crown abutment, veneer, plant
unerpuptd
9= not recodered

Periodontal status (CPI Modified)



Gingival bleeding

Score
Absence of
ition
- presence of condition
9=Tooth excluded
X= tooth not present

Pocket
0= Absence of condition
ocket 4-5mm
Pocket 6mm or
e
9=Tooth excluded
X=Tooth not present

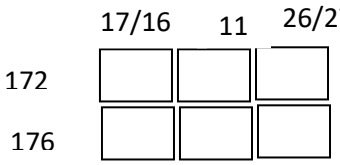
Loss of attachment

Severity
0 = 0-3mm

1 = 4-5mm cemento- enamel junction (CEJ) within black band
2 = 6-8 mm CEJ between upper limit of black band and 8.5 mm ring
3 = 9-11mm CEJ between 8.5mm and 11.5 mm ring
4 = 12mm or more CEJ beyond 11.5mm ring
X = Excluded sextant
9 = Not recorded

*Not recorded under 15 years of age

Index teeth



Enamel fluorosis

Severity
0 = Normal
1 = Questionable
2 = Very Mild
3 = Mild
4 = Moderate
5 = Severe
8 = Excluded (crown, restoration, *bracket*)
9 = Not recorded (unerupted tooth)

Dental erosion

Severity ☐ (180)

0 = No sign of erosion
1 = Enamel lesion
2 = Dentinal lesion
3 = Pulp involvement

Number of teeth affected

☐☐

Dental trauma

Status ☐ (183)

0 = No sign of ovary
1 = Treated injury
2 = Enamel fracture only
3 = Enamel and dentine fracture
4 = Pulp involvement
5 = Missing tooth due to trauma
6 = Other damage
9 = Excluded tooth

Oral Mucosal lesion

☐ ☐ ☐

Condition

0 = No abnormal condition
1= Malignant tumour (oral cancer)
2= Leukoplakia
3= Lichen Planus
4= Ulceration (aphthous, herpetic traumatic)
5= Acute necrotizing ulceration gingivitis (ANUG)
6= Candidiasis
7= Abscess
8= Other condition (specifiy if possible)
9= Not recorded

☐ ☐ ☐

Location

0 =Vermillion border
1= Commissures
2= Lips
3= Sulci
4= Buccal mucosa
5= Floor of the mouth
6= Tonuge
7= Hard and /or soft palate
8= Alvelorar ridgs/gingiva
9=Not recorded

Dentures (s)

Upper ☐ Lower ☐

Status
0= No denture
1= Partial denture
2= Complete denture
9= Not recoded

Intervention urgency

0= No treatment needed
1 = Preventive or routine treatment needed
2 = Prompt treatment (including scaling) needed
3= Immediate (urgent) treatment needed due to pain or infection of dental and/or oral origin
4= Referred for comprehensive evaluation or medical/dental treatment (systemic condition)

Thank you