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Magnitude of Non-alcoholic Fatty Liver Disease in South East Asia Region

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ABSTRACT

Background: Non-alcoholic Fatty Liver Disease (NAFLD) is a recognised public health problem in the developed world. The prevalence of NAFLDis escalating in developing countries along with increased prevalence of metabolic syndrome. Limited medical literature on NAFLD is contributed by American and European countries which may not be generalizable to Asians. Hence, it is important to study the Asian experience, particularly South-East Asian region (SEAR) with respect to NAFLD for better understanding. **Methods:** All published articles in the MEDLINE database on NAFLD in South-East Asia were included. The important findings were summarized and critically analysed. **Results**: Prevalence of NAFLD in the SEAR region ranges from 8.0% to 77.0%. NAFLD in South east Asia was associated with metabolic syndrome particularly obesity and insulin resistance. 'Lean NAFLD' is a novel concept that describes NAFLD among non-obese individuals. **Conclusion:** NAFLD is an emerging problem in South-east Asia. This review summarizes the prevalence of NAFLD in SEAR region and discusses the implications of these findings. Further population-based studies on prevalence and incidence are required on obese and lean NAFLD to quantify the magnitude of the disease in SEAR for better management of the condition.

Keywords: *NAFLD; NASH; Asia; South-East Asia; India; Sri Lanka, Bangladesh; Indonesia*

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a broad-umbrella term to describe a spectrum of conditions ranging from hepatic steatosis to steatohepatitis either identified by imaging or histological analysis [1].The definition of NAFLD also includes the elimination of other secondary causes of hepatic steatosis including viral hepatitis (e.g., Hepatitis C), various inborn errors of metabolism (e.g., lecithin-cholesterol acyltransferase deficiency, cholesterol ester storage disease, Wolman's disease), auto-immune disorders (e.g., Wilson's disease), parenteral nutrition, chronic use of steatogenic medications (e.g., mipomersen, lomitapide, amiodarone, methotrexate, tamoxifen, corticosteroids) and significant alcohol consumption (daily intake of alcohol up to ≥30 g for men and ≥20 g for women) [1–3].

NAFLD majorly includes two pathologically distinct states with different prognoses- non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). NAFL is a condition characterised by the presence of ≥5.0% hepatic steatosis in absence of any evidence of hepatocellular injury whereas NASH is characterised as inflammation with hepatocyte injury with or without fibrosis in addition to ≥5.0% hepatic steatosis [1-3]. NASH is described to consist of various disease conditions ranging from mild-stage fibrosis to end-stage conditions like cirrhosis and hepatocellular carcinoma (HCC) [3].

The natural history of NAFLD is under active investigation. Few groups of researchers suggest that the progression from steatosis to NASH is not following a linear curve rather it is more dynamic and exponential as the stage of fibrosis increases. The fibrosis progression rate in NAFL is estimated to be 14 years per stage of fibrosis whereas in NASH it is estimated to be 7 years per stage of fibrosis. The fibrosis progression rates varies from person to person indicating NAFLD being a complex disorder affected by interactions of environmental and genetic factors [4-6]. The heritable component of this hepatic disease, has a heritability ranging from 22.0% to 38.0% [7-9]. Despite NAFLD having genetic predisposition, environmental factors like dietary habits, physical activity, ethnicity, locality and metabolic risk factors of

the various regions can't be overlooked [19].

Both the genetic and environmental factors vary across the globe, so as the prevalence of the disease. The epidemiology of NAFLD varies between regions and within regions. The western countries have considered NAFLD as one of the growing epidemics in their regions and are formulating effective policies and population-level measures to address them whereas Asian countries are yet to recognise NAFLD epidemic in their regions, despite having similar prevalence [11].

It is important to recognise, though there is emerging importance of NAFLD in Asia but most of the medical literature on hepatic disease is contributed by the data on patients of American and European descents. These Western literatures may very well explain few traditional risk factors in Asian counterparts but different clinical profiles and outcomes of the disease are expected based on their regional variability. Hence, it is important to study the prevalence of modifiable and non-modifiable risk factors specifically metabolic risk factors, including obesity, diabetes, and metabolic syndrome among NAFLD patients in Asia. Furthermore, recent studies have also suggested that NAFLD can also affect apparently non-obese Asians commonly referred as the 'Asian Paradox' [12-13].

In this review, we look specifically at South-East Asians affected with NAFLD. South-East Asia region (SEAR) comprises of approximately 25.0% of world's total population and is a growing epicentre for NAFLD. The SEAR encompasses of 11 countries - India, Nepal, Bhutan, Bangladesh, Sri Lanka, Maldives, Thailand, Myanmar, Indonesia, Timor Leste and Democratic People's Republic of Korea (DPRK). The available data from these countries remains limited. Hence, the importance of gaining a better and complete understanding of NAFLD in this region is essentially important in view of its growing population and migration to Western nations. In this review, we describe the prevalence of NAFLD in SEAR and further describe the NAFLD phenotype with respect to 'lean NAFLD in the region..

Method

Article search in the online Medline database (Medical Literature Analysis and Retrieval System) was performed using MeSH (Medical Subject Headings) terms: 'Non-alcoholic Fatty Liver Disease'. The search was limited to English language. The above results were further narrowed down by adding the names of each country in the SEAR region (India, Nepal, Bhutan, Bangladesh, Sri Lanka, Maldives, Thailand, Myanmar, Indonesia, Timor Leste and Democratic People's Republic of Korea (DPRK)). Since India had a large number of studies, we further narrowed down the studies by adding the MeSH term 'Epidemiology'. We accessed full text articles of the included studies. We didn't perform a formal systematic analysis due to large variations in study designs. The available data were summarized and presented in the tables categorized by country.

Global magnitude of the problem

NAFLD is highly prevalent in all regions of the world with global prevalence estimated through recent meta-analysis is 25.2% (95%CI=22.1-28.6). There is noticeable variation observed in the prevalence of NAFLD across the regions. The highest prevalence of NAFLD is reported from the Middle East regions (31.7% (95% CI=13.4- 58.2)) and South American regions (30.4% (95% CI=22.7-39.4)) followed by Asia (27.3% (95%CI=23.2-31.88)), North America (24.1%(95%CI=19.7-29.1)) and Europe (23.7% (95%CI=16.1-33.4)). The lowest prevalence is reported from African countries as 13.4% (95%CI=5.6- 28.6) [11-14]. However, these estimates may be underestimation as the Ultrasound was the most common method for diagnosing NAFLD and it has been found that accuracy of ultrasound is inferior to liver biopsies. The liver biopsy being the 'gold standard' for diagnosing the NAFLD is neither feasible nor ethical to use in apparently healthy and asymptomatic people. Absence of simple and non-invasive diagnostic tests are a big hurdle in getting the true epidemiology of the disease.

The global prevalence of NASH is estimated to be 1.5–6.4% in the general population whereas prevalence of NASH among biopsy confirmed NAFLD cases was 59.1% (95%CI= 47.5-69.7). Less inconsistency was seen in the pooled regional NASH prevalence estimates among NAFLD patients with an indication for biopsy. NASH prevalence among NAFLD cases among Asians were 63.4% (95%CI=47.6-76.7), Europeans were 69.2% (95%CI=55.9-79.9) and Americans were 60.6% (95%CI=49.5-70.7) [11, 14].

In contrast to the prevalence data, there is a significantly fewer number of publications describing the incidence of NAFLD in the general population. It has been estimated that the incidence of NAFLD also varies across the world as prevalence estimates, ranging from 28.01 per 1000 person-years (95%CI=19.3-40.5) to 52.34 per 1000 person-years (95%CI=28.3-96.7) [14-16].

Magnitude of the problem in SEAR

The pooled prevalence of NAFLD in Asia was documented as 29·6% (95%CI=28·1–31.1), regardless of diagnostic method used. The prevalence of NAFLD in Asian countries is greatly wavering, ranging from 22.2 % in Japan to 51.0% in Indonesia [17]. A pooled analysis from Mainland China reported a prevalence of 20.0% (95%CI=17.9-22.3) [18]. Several small population-based studies suggested variation in the prevalence estimates of NAFLD South-East Asian nations. The highest prevalence has been reported from Thailand as 76.8% whereas lowest prevalence was reported from Indonesia as 7.9% [19, 20] (Table 1).

Table 1 Prevalence of NAFLD in South-East Asia

Year	Author	Study	Setting	Sample size	Male:Female	Population	Prevalence	Mode of diagnosis
Bangladesh								
2019	Khan et al	Cross-sectional	Hospital-based	334	148/334	Apparently Healthy	44.3	Ultrasound
2019	Khan et al	Cross-sectional	Hospital-based	100	58/42	T2DM	67	Ultrasound
2018	Kabir et al	Cross-sectional	Hospital-based	258	-	T2DM	64.7	Ultrasound
2018	Alam et al	Cross-sectional	Community-based	2782	1694/1088	Apparently Healthy	33.86	Ultrasound
2017	Saha et al	Cross-sectional	Hospital-based	1019	316:703	Apparently Healthy	18.5	Ultrasound
2017	Hossain et al	Cross-sectional	Hospital-based	140	77/63	Pre-diabetic	53.4	Ultrasound
2017	Alam et al	Cross-sectional	Community-based	2621		Apparently Healthy	34.34	Ultrasound
2015	Hossain et al	Cross-sectional	Hospital-based	110	63/47	Pre-diabetic	43.6	Ultrasound
2015	Rahman et al	Cross-sectional	Community-based	789	277/512	Apparently Healthy	18.4	Ultrasound
DPRK								
2009	Lee et al	Cross-sectional	Hospital-based	13621	7221/6400	Apparently Healthy	26.2	Ultrasound
Nepal								
2019	Paudel et al	Cross-sectional	Community-based	573	-	-	70.1	Ultrasound
2018	Mandal et al	Cross-sectional	Hospital-based	210	119/91	T2DM	55.7	Ultrasound
2015	Wang et al	Cross-sectional	Community-based	9360	0/9360	Women	12.8	BAAT/Ultrasound
2011	Mittal et al	Retrospective	Hospital-based	515	-	-	17.08	Raised ALT
Thailand								
2019	Tantanavipas et al	Cross-sectional	Hospital-based	63	0/63	PCOD	49.2	Ultrasound
2017	Saokaew S et al	Cross-sectional	Hospital-based	509	232/277	Metabolic yndrome	76.8	Ultrasound
Sri Lanka								
2019	Niriella et al	Cohort study	Community-based	2985	-	Apparently Healthy	32.6	Ultrasound
2019	Herath et al	Cross-sectional	Hospital-based	573	0/573	Pregnant women	18.2	Ultrasound
2019	Herath et al	Cross-sectional	Hospital-based	233	110/123	T2DM	62.6	Ultrasound
2018	Bulathsinhala et al	Retrospective	Hospital-based	550	473/77	Hepatocellular carcinoma	56	Liver Biopsy
2017	Rajindrajith et al	Cross-sectional	Community-based	499	236/263	Adolescent	8.4	Ultrasound
2017	Niriella et al	Cohort study	Community-based	2985		Apparently Healthy	32.6	Ultrasound
2016	Perara et al	Cross-sectional	Hospital-based	120	75/45	Acute coronary syndrome	46.7	Ultrasound
2015	Kasturiratne et al	Cohort study	Community-based	3002	1343/1659	Apparently Healthy	32.6	Ultrasound
2014	Silva et al	Cross-sectional	Hospital-based	34	25 / 9	Liver Donors	44.8	Ultrasound
2011	Pinidiyapathirage et al	Cross-sectional	Community-based	403	189/212	Rural population	18	Ultrasound
Indonesia								
2019	Hazim et al	Cross-sectional	Community-based	118	-	First Degree relatives of T2DM	22.03	Ultrasound
2013	Cahyono et al	Cross-sectional	Community-based	2105	185/43	Apparently Healthy	7.9	Ultrasound

The systematic review suggested the significant increase in the prevalence of NAFLD during a period of two decades. The prevalence of NAFLD increased form 25·8% (95%CI= 22.4–28.3) between 1999 and 2005 to 33.9% (95%CI=31.74-36.12) between 2012 and 2017 [17]. In contrast to prevalence, there are scanty data on the incidence of new-onset NAFLD in Asia. The pooled annual NAFLD incidence rate were found to be 50.9 cases per 1000 person-years (95%CI=44.8–57.4) [17].

Bangladesh

A study on apparently healthy population with mean age 40.1 ± 12.2 years reported that the prevalence of NAFLD is 44.3%. The prevalence was found to be highest in the age group 40-60 years (59.3%). Though the prevalence of metabolic syndrome was 27.2% in general population but higher prevalence was reported in NAFLD group (61.5%) [21]. In comparison to this, study from rural Bangladesh displayed overall prevalence of NAFLD to be around 18.4% [22]. This

variation in the prevalence of the disease can either be underestimation of the disease in the rural setting or an overestimation in tertiary clinic due to referral bias. A community-based study, one of the largest studies on NAFLD from Bangladesh, reported the prevalence to be 34.0% and the common age of presentation of NAFLD was found to be 30-50 years. Furthermore, NAFLD was also noted to be more common in people having known metabolic risk factors, with a highest prevalence of NAFLD in diabetics as 71.0% and among hypertensives was 62.8% [23]. A study on Bangladeshi immigrants in London showed an increased susceptibility to developing NAFLD as compared to Caucasians [24]. Other studies from the region mentioned the prevalence of the disease ranges from 18.4 % to 44.3% [22-26]. Further future population-based studies are needed to understand the risk of NAFLD to the country.

Bhutan

To the best of our knowledge, there are no studies from Bhutan describing the epidemiology of NAFLD. A country with 8 lakh population reported low levels of physical activity in 52.3% of the general population and 65.3% among diabetics. Moreover, self-reported prevalence of hypertension was 17.4% in general population and 44.7% among diabetics [27]. Approximately, 65.0% of the female population was found to be overweight and obese and about 69.0% of the women had a waist circumference >80 cm indicating abdominal obesity [28]. Though, there is limited data from the country but increased prevalence of obesity, diabetes, hypertension and reduced physical activity can contribute to high prevalence of NAFLD when investigated.

DPRK

A single but large hospital-based study is available from the nation. The prevalence of hepatic steatosis diagnosed by ultrasonography in absence of alcohol consumption was 26.2% in Korea among who visited a health check-up centre. The prevalence of metabolic syndrome in the same population was found to be approximately 18.0% with 35.0% of population having BMI above 25kg/m^2. The study also reported the risk of NAFLD to be 1.8 times higher in males (35.0%) as compared with females (16.3%) [29].

India

India contributes approximately 72% of the population in the SEAR region and hence has the ability to manipulate the prevalence of the SEAR region accordingly. Several but small studies including hospital, community as well as rural and urban regions are available from India (Table 2).

Year	Author	Type of Study	Region	Location	Setting	Sample size	Study population	Prevalence	Mode of diagnosis
2019	Duseja A	Cross-sectional	Chandigarh	Urban	Hospital/Clinic OPD	986	Male Healthy Blood Donors	55.1	Liver ultrasonography
2019	Rajput R	Cross-sectional	Rohtak, Haryana	Urban	Hospital/Clinic OPD	200	Pre-diabetic	Prediabetics (59%) Vs controls (26%)	Liver ultrasonography and biochemical parameters
2019	Varma S	Cross-sectional	South India		Hospital/Clinic OPD	60	PCOS	38.3	Liver ultrasonography
2019	Bhatt SP	Cross-sectional	New Delhi	Urban	Hospital/Clinic OPD	240	Overweight /Obese	70	Liver ultrasonography
2018	Jain V	Cross-sectional	New Delhi	Urban	School based	218	Adolescent (10-16 years)	62.5	Liver ultrasonography
2018	Vanjiappan S	Cross-sectional	Pondicherry	Urban	Hospital/Clinic OPD	300	T2DM	61	Liver ultrasonography
2017	Choudhary NS	Retrospectively analysed from a prospective database.	New Delhi	Urban	Hospital/Clinic OPD	573	Prospective donors (307 females)	49.2	Liver ultrasonography and Liver attenuation index values
2016	Pawar SV	Cross-sectional	Mumbai	Urban	School based	616	Adolescent (11-15 years)	62	Liver ultrasonography, elevated serum transaminases, fibroscan
2016	Majumdar A	Cross-sectional	Ballabhgarh, Haryana	Rural	Community	216	Apparently Healthy and asymptomatic subjects	30.7	Liver ultrasonography
2015	Anurag L	Cross-sectional	Maharashtra	Rural	Hospital/Clinic OPD	410	Apparently Healthy and asymptomatic subjects	28.1	Liver ultrasonography
2015	Praveenraj P	Cross-sectional	Coimbatore, Tamil Nadu	Urban	Hospital/Clinic OPD	134	Overweight /Obese	65.7	Liver Biopsy
2014	Vendhan R	Cross-sectional	Chennai, Tamil Nadu	Urban	Hospital/Clinic OPD	736	T1DM patients	27.7	Liver ultrasonography
2014	Ajmal MR	Cross-sectional	Aligarh, Uttar Pradesh	Urban	Hospital/Clinic OPD	104	Patients of coronary artery disease and hypertensive heart disease.	69.2	Liver ultrasonography
2013	Kalra S	Cross-sectional	101 cities in India	Urban	Hospital/Clinic OPD	924	T2DM	56.5	Elevated aminotransferase levels
2012	Madanagobalane S	Case-Control	Chennai, Tamil Nadu	Urban	Hospital/Clinic OPD	663	Psoriatic patient and non-psoriatic population	17.4	Liver ultrasonography
2011	Agarwal A	Cross-sectional	New Delhi	Urban	Hospital/Clinic OPD	124	T2DM	57.2	Liver ultrasonography

2010	Das K	Nested case-control study	West Bengal	Rural	Community	1911	Apparently Healthy and asymptomatic subjects	8.7	Liver ultrasonography and blood sampling
2009	Mohan V	Cross-sectional	Chennai, Tamil Nadu	Urban	Community	541	Apparently Healthy and asymptomatic subjects	32	Liver ultrasonography
2007	Amarapurkar D	Cross-sectional	Mumbai, Maharashtra	Urban	Community	1168	Apparently Healthy and asymptomatic subjects	14.6	Liver ultrasonography
2004	Singh SP	Cross-sectional	Coastal eastern India	Urban	Hospital/Clinic OPD	159	Apparently Healthy and asymptomatic subjects	24.5	Liver ultrasonography

Though there are several small-scale studies at community level in India from across the country. The community prevalence of NAFLD in India varies from 8.0% to 32.0%. The most common age of presentation is described to be 30 to 50 years in India [30]. Studies from rural India indicate the prevalence in apparently healthy people to range from 8.7% to 30.7%, whereas in urban areas it is ranging from 14.6% to 32.0% [30-33]. A study on apparently asymptomatic adults ranged between 24.0% -28.0% in few studies whereas a study on male blood donors depicted the prevalence to be 55.1% [34-36]. Moreover, the high prevalence in the later can be attributable to metabolic syndrome and its components [36]. Hence, it is difficult to estimate the true prevalence in the country based on the existing data.

Indian studies have shown that prevalence of NAFLD coincides with the prevalence of metabolic syndrome because most of the metabolic covariates of NAFLD are highly prevalent in Indians. The prevalence of metabolic syndrome in India based on prior study is 11.0% - 41.0% [37, 38]. Studies from hospitals or tertiary care units have reported the prevalence as low as 17.4% to as high as 70.0% in the country [39, 40]. These studies were conducted in high-risk groups like pre-diabetics, diabetics, females with PCOS, obese, hypertensives and psoriatic population. The highest prevalence was observed in obese population as 70.0% followed by patients of cardiovascular disease (69.2%) [40, 41]. A study conducted in New Delhi, documented NAFLD cases had significantly higher obesity parameters (BMI, waist circumference and hip circumference), fasting hyperglycemia, fasting hyperinsulinemia, hypercholesterolemia, and hypertriglyceridemia [42]. Another study demonstrated the strong association of NAFLD with high-sensitive C-reactive protein (hs-CRP), hypertension, and Metabolic syndrome in addition to other factors mentioned above [43]. There is paucity of longitudinal studies on the natural history of NAFLD and NASH in Indian patients, hence incidence of NAFLD can't be estimated.

In contrast to this, prevalence of NAFLD among Paediatric population is well explained. The prevalence in apparently healthy children including adolescents is 7.6% [44]. However, few regional studies across the country in obese population (approximately 60.0%) have shown approximately twice the prevalence of NAFLD when compared to the global obese paediatric population (approximately 34.0%) [45-49]. This is almost 8-folds more than the prevalence in apparently healthy children. Moreover, there is absence of NAFLD among underweight children but a presence of NALFD among large proportion of normal-weight children [49]. As these data indicate, it is important to recognize that NAFLD may also occur in normal-weight children, though less frequently than in overweight and obese group. The prevalence of NAFLD among urban pre-adolescents (children aged 5-10 years) is 22.4% .The prevalence of NAFLD increases as the child progresses from childhood to adulthood via adolescence [49].

Indonesia

According to the Global Health Estimates-2015, NAFLD and other causes accounted for 17.4% of all deaths due to chronic liver diseases including NAFLD, and for 20·9% of those due to liver cancer [50]. Data on the prevalence of NAFLD have been rare in Indonesia (7.9%). The study demonstrated males are predominantly (81.1%) affected by NAFLD as compared to opposite sex. The average age of NAFLD patients were 43.38 ± 9.26 years as compared to non-NAFLD patients (39.73 ± 9.94) (p-value=0.005) [20]. However, risk factors for NAFLD, specifically individual components of metabolic syndrome are prevalent and increasing in the country [51, 52].

Age-standardised estimates for non-communicable risk factors in Indonesian adults have shown a drastic increase from 1975 to 2014, particularly obesity and T2DM irrespective of the gender [51, 52]. Moreover, age-standardised estimates for obesity in paediatric and adolescent population have considerably increased from 0.1% to 7.1% in four decades. These children and adolescents are more susceptible to NAFLD in the future [53].

Maldives

No studies from the country was found on NAFLD. The data on prevalence of NAFLD needs to be investigated in the county.

Myanmar

No studies in general population was found from the region. One of the study characterizing liver disease suggested a 20.0% share of fatty liver in all liver etiologies [54].

Nepal

Limited studies are available from the country. A study by Mittal et al reported the prevalence of NAFLD to be 17.0%. The study used non-invasive markers like AST and ALT to estimate the prevalence

retrospectively [55]. Data collected from 9360 adult females reported the prevalence of NAFLD as 12.8%. Furthermore, the women appearing menopause or reached menopause showed unfavourable risk factor indicating protective nature of estrogen towards NAFLD [56]. However, another community-based study with 573 subjects documented an exceptional high prevalence of 70.0%. The higher prevalence rate can be attributed to higher prevalence of metabolic syndrome in the population [57].

Sri Lanka

Several studies have been reported from Sri Lankan island. Prevalence of NAFLD among urban community dwellers is reported to be approximately 33.0%, which is higher than mean prevalence of Asia [58, 59]. In the same community, the incidence of NAFLD was found to be 6.2% and the incidence rate were influenced by general and central obesity, raised triglycerides and diabetes [60]. Some small hospital-based studies on pregnant females and liver donors stated a prevalence of 18.0% and 45.0% respectively [61, 62]. Studies in high-risk groups like diabetics and patients of acute coronary syndrome showed much higher prevalence of NAFLD indicating its association with metabolic derangements [63, 64]. Moreover, NAFLD induced cirrhosis is the most common and aggressive cause of hepatocellular carcinomas (56.0%) in a large Sri Lankan cohort [65]. The higher prevalence rates can be attributable to increased industrialization and reduced physical activity. However, a study on rural community which are more physically active depicted a prevalence of 18.0%, pointing a tendency of association with PNPLA3 gene polymorphisms [66]. Significant association of PNPLA3 (rs738409) polymorphism with susceptibility to NAFLD (OR=1.25; 95%CI=1.08-1.44) has been established in Sri Lankans [59].

Furthermore, the NAFLD is not only restricted to adults but also affect adolescents of the island. Prevalence of NAFLD was high in Lankan teenagers (8.4%) as compare to global prevalence of NAFLD in adolescents. Metabolic derangements particularly obesity and insulin resistance and early cessation of breast feeding are few factors attributable to high prevalence of NAFLD among adolescents [67].

Thailand

There is lack of data on epidemiology of NAFLD in general population. However, few studies are available in special groups. A study on PCOS diagnosed women described the overall prevalence of NAFLD as 49.2% [68]. Another study showed a higher prevalence of NAFLD as 76.8% [19]. It is mainly attributable to population studied were diagnosed with metabolic syndrome. A study in another high-risk group estimated the prevalence of NAFLD as 60.7% in diabetics [69]. Significant liver fibrosis was found in 11.0% of psoriatics. Moreover, waist circumference, diabetes, and AST level were the independent predictors for development of NAFLD [70]. A community-based study among asymptomatic Thai population with predominately females in the study suggested a prevalence of 18.0%. Among NAFLD diagnosed cases, 18.4% demonstrated significant liver fibrosis and 2.6% has cirrhosis. In this study, male gender and history of dyslipidemia were identified as predictors of significant liver fibrosis in NAFLD [71]. Based on a baseline survey conducted in the north-eastern region of Thailand the prevalence of NAFLD in females was 22.9% (95%CI=22.5-23.5), whereas it was only 18.3% (95%CI=17.4-19.2) in males [72]. However, further studies in general population are required to estimate the accurate prevalence of NAFLD in the country.

Timor Leste

No studies for the nation could be extracted. Low prevalence of obesity suggests a lower prevalence of NAFLD in the nation but lean NASH may be more popular. To address the true prevalence, studies are to be undertaken in this country [73].

Table 3 Prevalence of Lean NAFLD in South-East Asia

Year	Author	Country	Study	Setting	Sample size	Male : Female	Population	Prevalence	Mode of diagnosis
2010	Das K et al	India	Nested case-control study	Community based	1911		Apparently Healthy and Asymptomatic subjects	8.7	Liver ultrasonography and blood sampling
2019	Niriella et al	Sri Lanka	Cohort study	Community based	2985		Asymptomatic	4	Ultrasound
2014	Alam et al	Bangladesh	Cross-sectional	Hospital-based	119	62/57	Obese/Non-obese	25.6	Liver Biopsy

Prevalence of "Lean NAFLD"

Despite the strong relationship with obesity, NAFLD is known to affect non-obese individuals and the condition is commonly termed as 'Lean NAFLD' [74]. The prevalence of lean NAFLD varies from 7.0% in western countries to as high as 19.0% in Asian countries [74, 75]. Despite appearing to have lower BMI and obesity, significant prevalence of NAFLD is seen in the South Asians, this observation is known as the 'Asian Paradox'. This phenomenon is further hypothesized to be associated with ethnic disparities in distribution of visceral fat. The study further mentioned the blacks generally have more lean mass and less fat mass when compared to whites [76, 77]. Furthermore, fat distribution in both subcutaneous and total adipose tissues are found to be correlated with pathological severity of NAFLDin South Asians [78, 79]. Hence, screening obese people for NAFLD may not provide

the accurate estimates. Studies have shown that Asian people with lower BMI are also at increased risk of cardiovascular and metabolic diseases and are susceptible to develop insulin resistance as compared to individuals from Western countries [80].

It is important to note that there is no increased mortality in lean (or overweight) people with NAFLD as compared to age and sex-matched controls. However, prior studies in western countries have identified three prognostic indicators associated with mortality in lean NAFLD- older age, fibrosis stage, and hypertension [74]. However, these findings may not be generalizable to Asian descent because of different risk profile.

Limited evidences are available for describing the prevalence of Lean NAFLD in South-east Asia. However, based on available data, community prevalence of lean NAFLD ranges from 4.0% to 21.3% [81, 82] (Table 3). A study by Kumar et al in India reported that diabetes was less common among the lean NAFLD cases as compare to obese NAFLD cases (3.7% vs 26.0% respectively). Insulin resistance (HOMA-IR) is following the similar pattern among lean and obese NAFLD cases (7.4% vs 60.0% respectively). The mean age of presentation of NAFLD was almost similar between the obese and lean NAFLD cases. A noticeable point about the study includes disparity in degree of necro-inflammatory activity and stage of fibrosis, despite having similar incidence of dyslipidemia, steatohepatitis, and advanced fibrosis among lean and obese NAFLD cases [82]. A study from Bangladesh documented lean NAFLD cases are metabolically similar to obese, except they are non-obese by BMI grade [83]. A Sri Lankan study described the prevalence as 4.0% in a cohort study. The study demonstrated the risk of developing diabetes within 3 years of diagnosis of NAFLD increases 3 to 4 times, even among lean individuals [81].

Way Forward

NAFLD represents only the tip of iceberg, what we see, whereas it reflects the ongoing devastating process inside the body, i.e., occurrence of Metabolic syndrome or increased risk for its occurrence in body with time if not properly managed at an early stage, which is essentially a preventable condition.

This review highlights the fact that the South-East Asians are at increased risk of having NAFLD and NASH. Further presence of the disease should be investigated even in non-obese individuals, as they are relatively more metabolically obese (Asian Paradox) and more prone to develop NAFLD as compared to other ethnic groups.

Therefore, the hepatic problem due to NAFLD needs to be addressed by each country in the region. Hence, understanding the magnitude of the problem is the first step towards the resolution of the problem which is at present, not available from almost all countries in the region. Therefore, ultrasound of abdomen or other cost-effective non-invasive diagnostic tools should be included in the list of tests provided in government setup for early diagnosis of NAFLD. This will result in addressing the problem with necessary measures at an early stage in resource-constraint SEAR. Furthermore, early management of the disease will not only reduce the hepatic diseases but will also reduce the other metabolic disease in future.

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Validation of Global Mental Health Assessment Tool in Western Development Region, Nepal: A Cross Sectional Study

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ABSTRACT

Introduction: Global Mental Health Assessment Tool Primary Care Version (GMHAT/PC) is comprehensive tool that can encompass wide array of mental health problems. This can be used by health professionals in detecting and managing mental disorders in primary care and general health settings. **Objective:** This Study aim to Validate and examine Feasibility of Global Mental Health Assessment Tool Primary Care Version in Primary Healthcare Setting of Nepal. **Methods:** We Conducted a Cross sectional study in the regional hospital of Western Development Region, Nepal. The GMHAT/PC tool and semi structured questionnaire were used to collect data. Interview was taken by the paramedical person with Proficiency Certificate Level (PCL) in General medicine qualification. Data were analyzed using SPSS-16 version. Sensitivity and specificity were calculated to measure the validity of GMHAT/PC. Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of tool, positive and negative likelihood ratio were calculated. Cohen's Kappa statistics was calculated to determine inter-rater reliability for the tool. Average time taken for the interview, patient satisfaction and completion of interview by the patient was taken as an indicator of feasibility. **Results:** The tool had good sensitivity 0.79 (95% CI: 0.73-0.85) and excellent specificity 0.94 (95% CI: 0.83 – 1). Overall there was a good level of agreement between psychiatrist and GMHAT/PC tool 0.76 (95% CI: 0.67 – 0.84). Likewise, overall Positive Predictive Value (PPV) of the test was excellent 0.98 (95% CI: 0.94 – 0.99) while Negative Predictive Value (NPV was fair 0.40 (95% CI: 0.24 – 0.56). And Likelihood Ratio Positive (LR+ve) of diagnostic agreement of the GMHAT/PC tool was 13.17 (95% CI: 2.01 – 90.67) and Likelihood Ratio Negative (LR –ve) was 0.22 (95% CI: 0.15 – 0.31). **Conclusion:** This study provides proven evidence to use Global Mental Health Assessment Tool Primary Care Version in specialist limited healthcare setting of Nepal. Findings of this study also support mid-level health workers and possibly others health workers having some training, can use the computer assisted programme GMHAT/PC to make a valid assessment and diagnosis for early detection and management of mental health related problem.

Keywords: *Mental Health, GMHAT-PC, Primary healthcare, Nepal*

Introduction

Mental illness is considered as medical condition that lead to disrupt a person's daily normal functioning, feeling, thinking and behavior or combination of these all condition. Most mental health problems are not very severe or long lasting. However, proper support asks for help and visit doctors are important factor to early diagnosis and treatment of mental health problems. "Mental health is a state of well-being in which individuals realize their potential, can cope with the normal stresses of life, can work productively and make contributions to their community" [1].

Mental health problems are serious threats for current medical and public health sector, these are leading causes of disability in the present world. Mental health problem alone is responsible for about 14% of global burden of disease [2]. It is estimated that about 25% of global population are affected from mental health related problems [2]. "Mental disorders make a substantial independent contribution to the burden of disease worldwide" [3].

Problem related with psychiatric disorders are common but many disorder among them are under-recognized and under-treated in the population because of few reasons such as shortage of health manpower specially psychiatrist, less concern from government, and shortage of appropriate instrument and facilities for treatment and diagnosis of mental health illnesses [4].

There are so many myths and faiths which are a barrier for the treatment of the mental disorders predominantly in the South East Asia Region of World Health Organization (WHO). Psychotic illnesses are considered a "curse from Gods" or manifestations of evil spirits or punishment for immoralities in the past life. In Nepal, there is an increasing access-gap in mental health care, especially in rural areas. Although the Government of Nepal committed to integrating mental health services into the health system through a national mental health policy in 1997, its translation into practice remains fraught with challenges. The country's 60 psychiatrists remain concentrated in urban areas, while less than ten district hospitals out of its 75 erstwhile districts offered mental health services (largely limited to psychotropic medication), and primary care providers (PCPs) have limited training and experience with mental health. Many times, patients are ignored, isolated or taken faith healers and treated with rituals rather than seeking appropriate healthcare center and proper medications in resource limited settings of Nepal [5].

Very less documented literature is available regarding validation of mental health tools in Nepal. Few mental health tools like: Beck anxiety inventory, Depression self-rating scale, Edinburgh Postpartum Depression Scale are validated in Nepal, but they are not comprehensive in nature as they can screen single mental health disorder like anxiety.

Depression, while GMHAT/PC is comprehensive tool that can encompass wide array of mental health problems [6][7][8]. Available literature shows that the tools which are validated in Nepal are not specifically for primary level setting but Primary version of GMHAT/PC is designed to use at primary level health care. The GMHAT/PC is a tool which can be used by grassroot level healthcare provider for detecting and managing mental health disorders in primary healthcare level setting and other health settings. GMHAT/PC covers detection and management of a wide range of mental health disorders, including psychosis and organic disorders. The tool is proved itself useful for early and accurate mental health problem detection and management. The tool consists of various questions on the mental state symptoms or problems. For each of the major clinical disorders, there are significant screening questions with their cutoff points which serve for shortening the interview [9]. The result from screening questions then proceeds to a summary report of symptoms, their scores and presents the GMHAT/PC diagnosis [10].

The GMHAT/PC focuses on mental illness related symptoms or problems such as; depressed mood, suicidal risk, sleep disorder, lack of appetite, eating disorders, hypochondriasis, obsessions and compulsions, disorientation, memory impairment, alcohol misuse, drug misuse, worries, anxiety and panic attacks, concentration, phobia, mania/hypomania, thought disorder, psychotic symptoms (delusions and hallucinations), , personality disorder and stressors [11]. The tools main computer diagnosis is resulting using a ranked model and designed with International Classification of Diseases, tenth revision (ICD-10) [12][13].

The GMHAT/PC English version was developed by Dr. Sharma and Prof. Copeland, the package is an innovational itself to address mental health problem. This method object to improve the detection of mental illness in primary care and early initiation of appropriate treatments by proper skilling up of primary healthcare professionals. The tool took approximately 10 years to develop its all aspect. The Sharma and Copeland involved in epidemiological research in large population samples, funded by Welcome Trust, the Medical Research Council UK and The Department of Health of UK [14]. We used GMHAT/PC English version to assess the feasibility of tool in resource limited primary healthcare settings of Nepal. To ensure its reliability, we translated English version questionnaire in Nepali language and back translated to English language with consultation of Psychiatrist.

Methodology

Analytical cross-sectional study was conducted at western regional hospital of Kaski district Nepal. This hospital covers 16 districts of western region, and it provides wide range of preventive, curative and rehabilitative services. It provides psychiatric Outpatient Department (OPD) and eight bedded psychiatric indoor services. Data from the Patients visiting the Psychiatric OPD of Western Regional Hospital were collected from July 2014 to December 2014. Patient with severe psychiatric problems who did not participate in the interview were excluded for the study process.

Data collection Tools

A semi structured questionnaire was used to assess the socio demographic information of respondents and a computer assisted GMHAT/PC version was used to assess the mental health problem of the respondent. The Global Mental Health Assessment Tool Primary Care Version has been designed to support primary healthcare professionals to make a quick and comprehensive standardized mental health assessment in primary healthcare setting [14].

Data collection technique & process

Face to face Interview was conducted to collect the information from the patients. Census sampling was done for all the cases visiting psychiatric OPD from July 2014 to December 2014. We applied Interview in two phase, first interview was conducted by Certificate level (PCL) in General Medicine Health professional before patient being diagnosed by the psychiatrist. Then same respondent was examined by the psychiatrist for clinical diagnosis of mental disorder using ICD 10 classification. Both the interviewer and psychiatrist were blinded to each other diagnosis.

Finally, the diagnosis by Certificate Level (PCL) general Medicine Health Professional using the tool and psychiatrist diagnosis was recorded. The season for selecting these health professionals for data collection was that; these are the human resource working in primary level of health system in Nepal, hence this can also assess whether these human resources can adopt with this tool or not.

Data processing and Analysis

The collected data was entered and analyzed using the software SPSS version 16. Sociodemographic distribution of all participant was calculated. Sensitivity and specificity were calculated to measure its validity. Positive Predictive Value (PPV) and Negative Predictive Value (NPV) as well as Positive likelihood and negative likelihood ratio was also calculated. Cohen's Kappa statistics was calculated to determine the inter-rater reliability for the tool. Average time taken for the interview, patient satisfaction and completion of interview by the patient was taken as an indicator of feasibility.

Validity and Reliability

Sensitivity and specificity were calculated for the validity of the tool and Kappa statistics was calculated to assess the reliability of the tool.

Pre-testing of the tool

Pre-testing of the tool was done among the 10 patients in Western Regional Hospital to make the interviewer verse with the software and to identify the problems during data collection.

Ethical consideration

Ethical approval was obtained from Nepal Health Research Council (IRB No:182-2014). Written informed consent was taken from all the participants of the study. Information of the participants was maintained confidential and data were used only for research purpose.

Results

Highest age group of participants was recorded in the age group of 30-39 years and which accounts 32.1 Percent of total sample. Lowest age group was 60 years and above, which accounts 6.7% of the total participants. Age of the participants varies between 6 years to 68 years. Consent from immediate caretaker was granted for participants having age less than 18 years. The mean age of the participants was 38 years and age range were too wide (38+13.57; Mean+ SD). More than half (56.7%) of the participants were female and rest of them were male. Regarding the religious information of the participants, more than three fourth (85.8%) of the participants were Hindu, while least percentage (0.7%) were Muslim. Regarding the socio caste information, Majority were brahmin (32.8%) followed by (31.3%) Janajati caste,18.7 % Dalit, 16.4% Chhetri and minority were terai caste which were 0.7% of total respondents.

Table 1 Distribution of participants according to age, sex, religion and caste (n=134)

Variables	N (%)
Age	37.54±13.57
0-9 years	12 (9)
20-29 years	23 (17.2)
30-39 years	43 (32.1)
40-49 years	26 (19.4)
50-59 years	21(15.7)
60 and above years	9 (6.7)
Sex	
Male	58 (43.3)
Female	76 (56.7)
Religion	
Hindu	115 (85.5)
Muslim	1 (0.7)
Christian	5 (3.7)
Buddhist	13 (9.7)
Caste	
Brahmin	44 (32.8)
Chhetri	22 (16.4)
Dalit	25 (18.7)
Janajati	42 (31.3)
Terai	1 (0.7)

Table 2 reveals that, among total participants about one third (32.85%) of participants had non-formal education, similarly 18.75% of participants were illiterate. Only 12.7% of the participants had higher education. Most of the participants (67.2%) were from rural area and 32.8% were from urban areas.

Table 2 Distribution of participants according to education and place of residence (n=134)

Variables	N (%)
Education	
Illiterate	25 (18.7)
Non-formal	44 (32.8)
Primary	14 (10.4)
Lower secondary	21 (15.7)
Secondary	13 (9.7)
Higher education	17 (12.7)
Place of residence	
Rural	90 (67.2)
Urban	44 (32.8)

Table 3 reveals that,117 participants were diagnosed as having mental disorder by psychiatrist, among them 93 were correctly diagnosed by GMHAT/PC tool.17 cases were diagnosed by psychiatrist as not having mental disorder, and among them 16 were correctly diagnosed by GMHAT/PC tool

as not having mental disorder(2). All the disorders were categorized in seven major categories according to ICD-10 classification by an independent psychiatrist. There were total 24 participants having organic disorder by psychiatrist among them 16 were correctly diagnosed by GMHAT/PC tool. Of the 5 cases of substance related disorder diagnosed by psychiatrist, 4 were correctly diagnosed by GMHAT/PC. Likewise, 5 participants were diagnosed with schizophrenia and other psychotic disorder by psychiatrist among whose 5 cases were correctly diagnosed by GMHAT/PC tool. Similarly, 43 cases of mood disorder diagnosed by psychiatrist, 41 were correctly diagnosed by GMHAT/PC tool. Among 38 cases of neurotic stress and somatoform disorder diagnosed by psychiatrist 26 were correctly diagnosed by GMHAT/PC tool. There was 1 case of personality disorder diagnosed by both psychiatrist and GMHAT/PC tool.

Table 3 Cross-tabulation of the number of participants diagnosed by the psychiatrist and by the Global Mental Health Assessment Tool – Primary Care version (GMHAT/PC)

Psychiatrist Diagnosis	GMHAT/PC								
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**Total**
A	16	0	0	3	0	0	0	5	24
B	0	4	0	1	0	0	0	0	5
C	0	0	5	0	0	0	0	0	5
D	0	0	0	41	2	0	0	0	43
E	1	0	1	3	26	0	0	7	38
F	0	0	0	0	0	0	0	1	1
G	0	0	0	0	0	0	1	0	1
H	0	0	0	0	0	1	0	16	17
Total	17	4	6	48	28	1	1	29	134

A - Organic mental disorder B - Substance related disorder
C - Schizophrenia and other psychotic disorder D - Mood disorder
E - Neurotic, stress and somatoform disorder F - Eating disorder
G - Personality disorder H - No mental illness

Table 4 Sensitivity and specification of GMHAT/PC

Variable	Sensitivity (95% CI)	Specificity (95% CI)
Overall	0.97 (0.73 – 0.85)	0.94 (0.83 – 1)
Organic mental disorder	0.66 (0.47 – 0.85)	0.98 (0.89 – 1)
Substance related disorder	0.80 (0.45 –1)	1 (1 – 1)
Schizophrenia and other psychotic disorder	1 (1 – 1)	0.99 (0.97 – 1)
Mood disorder	0.95 (0.89 – 1)	0.92 (0.86 – 0.97)
Neurotic, stress and somatoform disorder	0.68 (0.53 – 0.83)	0.97 (0.94 –1)
Personality disorder	1 (1 – 1)	1 (1 – 1)

Table 4 shows the sensitivity and specificity of GMHAT/PC tool. The tool had good sensitivity 0.79 (95% CI: 0.73-0.85) and excellent specificity 0.94 (95% CI: 0.83 – 1). For organic mental disorder the sensitivity of the tool was found to be 0.66 (95% CI: 0.47 – 0.85) and specificity was 0.98 (95% CI: 0.89 – 1). For the substance related disorder, the sensitivity was 0.80 (95% CI: 0.45 – 1) and specificity was (95% CI: 1 – 1). For the mood disorder the sensitivity of the tool was found to be 0.95 (95% CI: 0.89 – 1) and specificity was 0.92 (95% CI: 0.86 – 0.97). For another category, Neurotic, stress and somatoform disorder the sensitivity of the tool was 0.68 (95% CI: 0.53 – 0.83) and specificity was 0.97 (95% CI: 0.94 – 1). The sensitivity and specificity of personality was excellent which may be due to only one case which was correctly diagnosed by both psychiatrist and GMHAT/PC.

Table 5 Level of agreement between psychiatrist diagnosis and GMHAT/PC tool diagnosis

Variable	Kappa (95% CI)
Overall	0.76 (0.67 – 0.84)
Organic mental disorder	0.74 (0.58 – 0.90)
Substance related disorder	0.88 (0.66 – 1)
Schizophrenia and other psychotic disorder	0.90 (0.72 – 1)
Mood disorder	0.85 (0.76 – 0.94)
Neurotic, stress and somatoform disorder	0.70 (0.57 – 0.84)
Personality disorder	1 (1 – 1)

Table 5 shows the level of agreement between psychiatrist diagnosis and GMHAT/PC tool. In general, there was a good level of agreement between psychiatrist and GMHAT/PC 0.76 (95% CI: 0.67 – 0.84). For the organic disorder the diagnostic agreement of kappa value was 0.74 (0.58 – 0.90). Likewise, for substance related disorder it was found to be 0.88 (95% CI: 0.66 – 1). For schizophrenia & other psychotic disorder kappa value was found to be very good 0.90 (95% CI: 0.72 – 1). The level of agreement for mood disorder was also good 0.85 (95% CI: 0.76 – 0.94). For another category Neurotic, stress and somatoform disorder the kappa value was 0.70 (95% CI: 0.57 – 0.84).

Table 6 Positive and negative predictive values of GMHAT/PC tool

Variable	PPV (95% CI)	NPV (95% CI)
Overall	0.98 (0.94 – 0.99)	0.40 (0.24 – 0.56)
Organic mental disorder	0.94 (0.71 – 0.99)	0.93 (0.86 – 0.96)
Substance related disorder	1 (0.40 – 1)	0.99 (0.95 – 0.99)
Schizophrenia and other psychotic disorder	0.83 (0.36 – 0.97)	1 (0.97 – 1)
Mood disorder	0.85 (0.72 – 0.93)	0.97 (0.91 – 0.99)
Neurotic, stress and somatoform disorder	0.92 (0.76 – 0.98)	0.88 (0.81 – 0.94)
Personality disorder	1 (0.16 – 1)	1 (0.97 –1)

The above table 6 shows positive and negative predictive value of GMHAT/PC tool. Overall PPV of the test was found to be excellent 0.98 (95% CI: 0.94 – 0.99) while NPV was found to be fair 0.40 (95% CI: 0.24 – 0.56). For organic mental disorder PPV was 0.94 (95% CI: 0.71 – 0.99) and NPV was 0.93 (95% CI: 0.86 – 0.96). Likewise, for substance related disorder PPV was 1 (95% CI: 0.40 – 1) and NPV was 0.93 (95% CI: 0.86 – 0.96) and both was found to be excellent. For another category, Schizophrenia and

other psychotic disorder PPV was found to be 0.83 (95% CI: 0.36 – 0.97), and NPV was 1 (95% CI: 0.97 – 1). The PPV of diagnostic agreement for mood disorder was 0.85 (95% CI: 0.72 – 0.93) and NPV was 0.97 (95% CI: 0.91 – 0.99). For another category, Neurotic, stress and somatoform disorder PPV was found to be 0.92(95% CI: 0.76 – 0.98) and NPV was 0.88 (95% CI: 0.81 – 0.94).

Table 7 Positive and negative likelihood ratios of GMHAT/PC tool

Variable	L.R.+ve (95% CI)	L.R.-ve (95% CI)
Overall	13.17 (2.01 – 90.67)	0.22 (0.15 – 0.31)
Organic mental disorder	73.33 (10.21 – 526.63)	0.35 (0.19 – 0.59)
Substance related disorder	-	0.20 (0.03 – 1.15)
Schizophrenia and other psychotic disorder	129 (18.31 – 908.87)	0
Mood disorder	12 (6.06 – 25.33)	0.05 (0.01 – 0.20)
Neurotic, stress and somatoform disorder	32.84 (8.19 – 131.64)	0.32 (0.20 – 0.52)
Personality disorder	-	0

Table 7 reveals that, the overall LR +ve of diagnostic agreement of the GMHAT/PC tool was found to be 13.17 (95% CI: 2.01 – 90.67) and LR –ve was 0.22 (95% CI: 0.15 – 0.31). For organic mental disorder LR +ve was 73.33 (95% CI: 10.21 – 526.63), and LR –ve was 0.35 (95% CI: 0.19 – 0.59). Another category was substance related disorder and LR –ve for substance related disorder was 0.20 (95% CI: 0.03 – 1.15). Likewise, for Schizophrenia and other psychotic disorder LR +ve was 129 (95% CI: 18.31 – 908.87) and LR –ve was 0. For another category, mood disorder LR +ve was 12 (95% CI: 6.06 – 25.33) and LR – ve was 0.05 (95% CI: 0.01 – 0.20). And for neurotic, stress and somatoform disorder LR +ve was 32.84 (95% CI: 8.19 – 131.64) and LR –ve was 0.32 (95% CI: 0.20 – 0.52).

Table 8 Distribution of participants according to feasibility indicators (n=134)

Variables	N (%)
Average time taken	16.95±2.69
Satisfaction	
Satisfaction	131 (97.8)
Unsatisfaction	3 (2.2)
Understand question	
Yes	129 (96.3)
No	5 (3.7)
Completion of interview	
Yes	134 (100)

Table 8 show average time taken to deal out GMHAT/PC was 16.95 minutes with standard deviation 2.69. Minimum time taken for interview was 10 minute and maximum were 28 minutes. Among the total 134 participants, most of all responded positive feedback regarding interview and most of them expressed satisfaction that the interview covered all aspects of their mental health using GMHAT/PC. More than ninety six percent (96.3%) of the participants understood question clearly. None of the participant declined to participate in the study. Hundred percent of the participants completed the interview.

Discussion

In this study over all sensitivity and specificity of the tool was found to be 76% and 94% respectively. Similarly, the study conducted in Wrexham Maelor Hospital, UK, entitled Epidemiological and clinical use of GMHAT/PC in cardiac patients found that 73% sensitivity and 98% specificity [15].Another study showed that good sensitivity 77% and excellent specificity 96%[16]. Another study found excellent sensitivity 97% which was higher than our study but specificity (94%) was similar to our study [17].The study was conducted in North West of England and North Wales, aimed to assure validity and feasibility of Global Mental health diagnosis tool by nursing professionals, found to be 84% sensitivity and 92% specificity[10].We found that the sensitivity and specificity of our study was consistent with other similar studies that have been carried out in various countries, this is because we have conducted our study in primary healthcare setting with diagnosis verification of Psychiatrist with PCL general medicine health professionals.

In this study we found good kappa value that is similar with other studies. In this study the overall kappa values was 76% which is also similar with the study conducted in North West of England and North Wales [10]. Another study reported 72% kappa value, which was slightly less than our study [16].Likewise another study conducted in United Arab found 0.91% level of agreement[17].

Another similar study found 76% kappa value which was similar to the our study [15].The overall positive predictive value (PPV) was 98% and negative predictive value (NPV) was 40%, similarly positive predictive value for Schizophrenia and other psychotic disorder was found to be very good i.e. 83% and negative predictive value was found to be excellent i.e. 100%. For another category mood disorder, positive and negative predictive value was found as 85% and 97% respectively. In this study we found that positive likelihood ratio was 13.7 and negative likelihood ratio was 0.22.

In our study the average time taken to complete interview was 16.95 minutes with standard deviation 2.69. And minimum time taken to complete interview was 10 minutes and maximum time was 28 minutes. Similar study was conducted in three different psychiatric day hospital of UK, which aimed to ensure validation and feasibility of the Primary Care Version of Global Mental Health Assessment Tool in older

adults and result revealed that the mean time taken to administer GMHAT/PC was 14 min with standard deviation 6.38[18][16].Another study conducted in Jaipur, India, found that the mean time taken for the interview was around 16 minutes [14].

In this study most of the participants expressed their gratification on researcher's questionnaire pattern and coverage of all aspect and dimensions of mental health and participant friendly questionnaire pattern. and express friendly. All participants (100% of sample size) completed their interview, which is similar as the study conducted in Jaipur, India [14]. Another study conducted in three different psychiatric day hospital of UK, which aimed to ensure validation and feasibility of the Primary Care Version of Global Mental Health Assessment Tool in older adults also revealed the similar finding i.e. No participants declined and responded any negative feedback regarding the tool and questionnaire pattern [18]. Almost all participants expressed their satisfaction on researchers coverage of all aspects and dimensions of mental health using Global Mental Health Assessment Tool Primary Care Version (GMHAT/PC) [16].

Strength and limitation of the study

The Study had good sample size and varying degree of psychopathology in different healthcare settings. All the Clinical diagnosis were made by well-trained consultant psychiatrists using ICD-10 criteria to compare with the GMHAT/PC diagnosis. Both consultant psychiatrist and health worker doing the assessment in this study were blind to each other's diagnoses. The interviewers were not provided knowledge of the patients before the assessment. We used Consultant Psychiatrists' diagnoses as a gold standard rather than a criterion standard. Although this is fewer desirable, in routine clinical care, the diagnosis by a consultant psychiatrist is considered as an adequate gold standard. We did not attempt to examine the inter-rater reliability between the health worker who implemented the GMHAT/PC. The relatively small number of subjects in this study limited from carrying out sub-group analysis. There is no comparative group without detection of mental illness. The absence of follow up and outcomes did not allow proving changes in clinical management and outcomes.

Conclusion

This study provides proven evidence to use Global Mental Health Assessment Tool-Primary Care Version (GMHAT/PC) in specialist limited healthcare setting of Nepal. Findings of this study also support mid-level health workers and possibly others health workers having some training and the tool would be can used by mid-level health workers with the computer-assisted programme GMHAT/PC to make a valid assessment and diagnosis for early detection and management of mental health related around 16.95 minutes makes it feasible in routine assessments in primary care and general health settings. The authors accept that Medical Officer may not have enough time in their routine primary care clinics, but they can utilize other health professionals in assessing the mental health of their patients using the GMHAT/PC. In some cases, it took longer to complete the interview, mainly because the patients wanted to report their emotional problems and the mid-level health workers felt it was necessary to listen to them. Both the patients and health worker found the GMHAT/PC not only acceptable, but useful in making a quick, yet comprehensive, mental health assessment.

Availability of data and material

Due to privacy reason, data are not publicly available, the datasets used and analyzed during the current study are available from the corresponding author on reasonable request. Authors can provide study protocol, data and materials under the request. Please redirect the email laxmanbhattbph@gmail.com for data and study protocols.

Competing Interests

Authors declares that they have no competing interests.

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Author contributions

All the authors had equal contribution on this study. Task were separated to all authors according to their expertise on specific topic. Shankar Singh Dhami (SSD) generated the research topic for this study and reviewed relevant literatures. Laxman Datt Bhatt (LDB)was the designer for the study. He designed methodology and analysis plan for the study and analyzed all the outcomes of the study and he also contributed on overall writeup. SSD and Laxman both compiled and drafted the manuscript.

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Prevalence and Factors Associated with Depression among Elderly in San Ton Kok Village, Chiang Rai, Thailand

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ABSTRACT

Introduction: Depression is an important public health concern due to its devastating morbidity and mortality among elderly. **Objectives:** The study aimed to estimate the prevalence of and factors associated with depression among elderly in San Ton Kok Village, Chiang Rai Province, Thailand. **Methods:** An analytic cross-sectional study was conducted at San Ton Kok village, Chiang Rai Province, during the period of September to November in 2018. People aged 60 years or above were randomly selected into the study. A validated questionnaire and the PHQ-9 were used to collect information from participants and to assess a depressive symptoms. Logistic regression was used to determine the associations between variables at α=0.05. **Results:** A total of 72 participants were recruited into the study; 62.5% were female, and 61.1% were aged 60-69 years. The prevalence of depression was 16.6%. The multivariable logistic regression model revealed that marital status (AOR = 5.33; 95%CI = 1.20-23.61) was found to be associated with depression among elderly. **Conclusion:** Elderly without partner needs to be regularly screened and provided a proper care to reduce the sufferring from depression.

Keywords: *Depression, Elderly, Prevalence, factors, Thailand*

Introduction

Depression is a common and serious mental illness that effects negative impact on how people feel, the way people think and how people act, but it can be treatable. Depression may cause feelings of sadness and loss of interest in activities. It can lead to a variety of emotional problems and can decrease a person's ability to function. Symptoms of depression includes feeling sad or having a depressed mood, loss of interest, trouble sleeping, feeling worthless, difficult thinking, and people who have severe symptom may think of death or suicide. The symptoms must be presented for at least two weeks before being diagnosis of depression [1]. At a global level, there were estimated over 300 million people who lived with depression, or equal 4.4% of the world's population in 2017. Depression was the leading cause of disability worldwide, and contributes to the global burden of disease. The prevalence of depression was greater among females than males. At its severe impact, depression can lead to suicide and there are almost 800,000 people died due to suicide every year [2].

The prevalence of depression is increasing every year, particularly in lower-income countries. In 2017, depressive symptom was found the highest in Southeast Asia (SEA) Region for 27.0% or about 85.67 million people. In the region of SEA, Thailand was the second rank of the high prevalence of depression which accounted for 4.4% or 2.88 million of the population [3], and the rate of completed suicide was reported at 6.03 per 100,000 population [3]. The northern part of Thailand was reported the highest rate of suicide which was 10.88 per 100,000 population. Mae Hong Son, Lampang, Chiang Mai, Nan, and Chiang Rai Provinces were reported from the highest to the lowest rates of suicide, respectively. Moreover, 60.0% of completed suicide was led by depression [4].

Depression is one of a key public mental health concerns among the elderly population in the community. In a study conducted in Chiang Rai Province, it was found that the prevalence of depression at 38.9% among 1,049 participants [5]. In 2013, San Ton Kok village was reported 2 cases the elderly who completed suicide [6]. The study aimed to estimate the prevalence of and identify the factors associated with depression among elderly in San Ton Kok Village, Chiang Rai Province, Thailand.

Methodology

Study design

Analytic cross-sectional study design was conducted to estimate the prevalence and to identify

the factors associated with depression among the elderly people. The duration of the study was 2 months, between 18 September and 18 November 2018.

Study setting

The study was conducted at San Ton Kok Village, Chiang Rai Chiang Rai Province, Thailand.

Study population

All the elderly who aged 60 years and over, and lived in the study setting at least 12 months prior the survey date were met the inclusion criteria for the study.

Study sample

Elderly who were diagnosed by a physician as having severe cognitive impairment, experiencing psychotic disorder, and unable to communicate were excluded from the study. There were 132 elderly aged 60 years or over in San Ton Kok Village in 2018. The sample size was calculated by the Krejcie and Morgan formula [7], it needed at least 70 samples for the analysis.

Research instruments

Questionnaire was developed and used to collect information from the participants such as age, sex, marital status, education, having chronic illness, employment status, smoking and alcohol use behaviors. The questionnaire was tested for its reliability and validity by piloting among 10 subjects who had similar characteristics with the study population. The Cronbach's alpha coefficient was found at 0.84.

Detection of depression of the participants was assessed by using PHQ-2 and PHQ-9. The PHQ-2 is the first 2 questions to assess the possibility of having depression problem, and followed by the PHQ-9. Using the two tools for assessing depression has effectively screening depression particularly the elderly population.

Participants answered "yes" in one of the two questions in PHQ-2, were re-assessed by PHQ-9. The PHQ 9 is a high validated questionnaire to review the 9-key symptoms of depression based on the DSM diagnostic criteria for the major depression. This tool has contained 9-items, and each items is possible to be scored 4-scale (0=symptom absent to 3=severe symptoms). Then, those who scored > 7 or higher were defined as depression [8]. The Thai version of the PHQ-9 has been detected its internal consistency (Cronbach's alpha = 0.79)[9].

Data collection

Data were collected by door-to-door survey and verbal consent was obtained from all participants after completly description about the purpose and process of the study. Each interview lasted 10 minutes.

Data analysis

Data were double-entered into excel spreadsheet. All analyses were operated by using the statistical package of the social science (SPSS) version 20 (IBM, Armonk, NY). Descriptive statistics were used for explaining the general characteristics of the participants. The associations between variables were detected by logistic regression at the signifincance level of $\alpha = 0.05$.

Ethical consideration

All study tools and procedures were followed the Declaration of Helsinki. Verbal consent for all participants was obtained before the study commenced, after explaining to them in all aspects of the study. All participants were assured that their participation was fully voluntary, that they could stop participating the study in anytime without any adversed consequences. Data obtained were treated as confidential.

Results

Table 1 General characteristics of participants (n = 72)

Characteristics	n	%
Sex		
Male	27	37.5
Female	45	62.5
Age (years)		
60-69	44	61.1
70-79	19	26.4
≥ 80	9	12.5
Marital status		
Married	45	62.5
Widowed	17	23.6
Divorce	8	11.1
Separated	2	2.8
Education		
Illiterate	21	29.2
Primary education	51	71.8
Chornic illness		
Yes	57	79.1
No	15	20.9
Employment status		
Employed	28	38.9
Unemployed	44	61.1
Smoking		
Yes	7	9.7
No	65	90.3
Alcohol use		
Yes	20	27.8
No	52	72.2
Depression (PHQ9)		
Yes	12	16.6
No	60	83.4

A total of 72 elderly were enrolled into this study; 62.5% were female, 61.1% were aged 60-69 years, 62.5% were married or live with their partners, 70.8% graduated in the primary school, and 61.1% were unemployed. 79.1% had one or more chronic diseases, 9.7%smoked, and 27.8% used alcohol. The prevalence of depression was 16.6% (Table 1).

In the univariate analysis, only marital status was found to be associated with depression (OR = 4.3; 95% CI = 1.16-16.12). While other factors such as sex, age, education level, having underlying disease, employment status, smoking and drinking behaviors were not found to be significantly associated with depression.

Table 2 Univariate analysis of factors associated depression among elderly.

Factors	Depression n (%)	Non-depression n (%)	Total	Crude OR (95% CI)	p-value
Gender					
Male	5 (6.9%)	22 (30.6%)	27	1.23 (0.35-4.36)	0.744
Female	7 (9.7%)	38 (52.8%)	45	1.00	
Age (years)					
< 80	10 (13.9%)	53 (73.6%)	63	1.51 (0.27-8.38)	0.634
≥ 80	2 (2.8%)	7 (9.7%)	9	1.00	
Marital status					
No partner	8 (11.1%)	19 (26.4%)	27	4.32 (1.16-16.12)	0.030*
With partner	4 (5.6%)	41 (56.9%)	45	1.00	
Education level					
Illiterate	3 (4.2%)	18 (25.0%)	25	0.78 (0.19-3.21)	0.728
Primary education	9 (12.5%)	42 (58.3%)	51	1.00	
Underlying disease					
Yes	10 (13.9%)	47 (65.2%)	57	1.138 (0.27-7.11)	0.698
No	2 (2.8%)	13 (18.1%)	15	1.00	
Employment status					
Employed	4 (5.6%)	24 (33.3%)	28	0.75 (0.20-2.77)	0.666
Unemployed	8 (11.1%)	36 (50.0%)	44	1.00	
Smoking					
Yes	2 (2.8%)	5 (6.9%)	7	2.20 (0.37-12.95)	0.383
No	10 (13.9%)	55 (76.4%)	65	1.00	
Alcohol drinking					
Yes	5 (6.9%)	15 (20.9%)	20	2.14 (0.59-7.77)	0.246
No	7 (9.7%)	45 (62.5%)	52	1.00	

* Significant level at $\alpha \leq 0.05$

After controlling for all potential confouder variables such as sex, age, education level, having underling disease, amoking and alchol use behaviors, marital status was only a factor to be found statistical associated with depression. In the other words, elderly who were in the stage of widowed, divorced, separated, or did not live with their partners had a greater chance to develop depression than those married status with 5.33 times (95% CI = 1.2-23.61) (Tabel 3).

Table 3 Multivariate analysis of factors associated with depression among elderly

Factor	Depression n (%)	Non-depression n (%)	Total	Adjusted OR (95% CI)	p-value
Sex					
Male	5 (6.9%)	22 (30.6%)	27	0.30 (0.02-5.64)	0.744
Female	7 (9.7%)	38 (52.8%)	45	1.00	
Age (years)					
< 80	10 (13.9%)	53 (73.6%)	63	0.42 (0.56-3.36)	0.422
≥ 80	2 (2.8%)	7 (9.7%)	9	1.00	
Marital status					
No partner	8 (11.1%)	19 (26.4%)	27	5.33 (1.20-23.61)	0.028*
With partner	4 (5.6%)	41 (56.9%)	45	1.00	
Educational					

Factor	Depression n (%)	Non-depression n (%)	Total	Adjusted OR (95% CI)	p-value
Illiterate	3 (4.2%)	18 (25.0%)	21	0.10 (0.19-4.30)	0.902
Primary education	9 (12.5%)	42 (58.3%)	51	1.00	
Underlying disease					
Yes	10 (13.9%)	47 (65.2%)	57	1.30 (0.22-7.78)	0.771
No	2 (2.8%)	13 (18.1%)	15	1.00	
Employment status					
Employed	4 (5.6%)	24 (33.3%)	28	0.75 (0.20-2.77)	0.307
Unemployed	8 (11.1%)	36 (50.0%)	44	1.00	
Smoking					
Yes	2 (2.8%)	5 (6.9%)	7	1.07 (0.11-10.88)	0.956
No	10 (13.9%)	55 (76.4%)	65	1.00	
Alcohol drinking					
Yes	5 (6.9%)	15 (20.9%)	20	14.56 (0.55-383.59)	0.109
No	7 (9.7%)	45 (62.5%)	52	1.00	

* Significant level at $\alpha \leq 0.05$

Discussion

Several studies have reported that the prevalence of depression among the elderly living in a community in Thailand were vary from 12.0% to 43%. A study conducted in Bangkok, presented that the prevalence was 43.1% [10], while 25.6% were reported from the urban of Prachuap Khiri Khan Province [11], 14.39% in the urban of Chiang Mai Province [12], 21.6% in a southern population of Thailand [13]], and 12.5% in the rural of Phra Nakhon Si Ayutthaya Province[14]. The differences of the prevalence from different studies could be led by the tool used [15].

Regarding the multiple model, marital status is only the factor that found to be associated with depression among the elderly. Some previous studies showed the similar finding, the elderly with disturbed marital life were susceptible to depression compared to those elderly who lived with their partners. This migh be they lost the supported person in their life and lost the skill to cope the problem then become depression.

Dependence of the elderly on their spouse increases as they age. Death of a spouse renders them vulnerable to mental stress. Indeed, widowhood has been found to be strongly associated with depression in several instances [16]. Loneliness and depression [17] [18] [19]. This may be attributed to sensation of loneliness and lack of social support. Loneliness as a natural part of aging was tied to loss of friends and family, usually through death or abandonment and loneliness as a precursor to depression [20]. However, there were also some studies found no association between marital status and depression [21]. This may be the difference of social context, population characteristic and measurement tools [15].

The results show no association between gender and depression. This agrees with the study of Kokler and Heun[22] which reported that the atypical or the somatic subtype of depression between male and female elderly were not influenced by gender difference like younger population because the perception or the expression of depression might be influenced by biological or psychological factors like gender role or coping style.

The results show no association between age and depression. This similar with the study of [22] which reported that advanced age among the elderly were not a risk factor for depression because many factors can be prevented the depression in elderly such as decrease income, physical disability, and social support.

This study found that there was no association between employment status and depression. Some studies showed the similar results that no association between employment status and depression [23] [24] while some studies found the depression higher in elderly who were unemployed [17] [16] because the activities could improve the spirit, mood and had positive effect on mental well-being and social relation.

Conclusion

The elderly people in San Ton Kok village are facing depression problem particularly those who are living alone. With the conditions of poor economic and low education including a high rate in use some kind of susbtances, then the elderly in the rural area of Thailand are needed to be screended for depression and given a proper method to address depression. This should be concerned in all steakholders both goverment and non-goverment agencies to cooperate for reducing the problem effectively.

Limitations

There are some limitations in this study. Samples were collected from one community which might not be generalized for all elderly populations, it provides a snapshot of the risk profile of those with depression. The participants may incur some recall and reporting bias. However, the participants were requested to think carefully and answer as honestly as possible. Some variables such as income, family history of depression,

and social support were not considered in this analysis. It should be included in the next study.

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Readiness in Response the Epidemic of Coronavirus Disease-2019 (COVID-19) among Young Adults in Chiang Rai Province, Thailand

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) is currently recognized as the greatest threat to human life, with a large number of deaths. It is rapidly spreading, including to people living in rural areas, through several mechanisms, including population movement. Chiang Rai Province is located in rural northernmost Thailand and has a long border with neighboring countries. This study aimed to assess the readiness of young adult people living in Chiang Rai Province to the epidemic of COVID-19. **Methods:** A cross-sectional study was used to collect data from the participants. The study setting was Chiang Rai Province, Thailand. People aged 18-23 years living in selected villages and individuals at a university were invited to participate in the study. A validated questionnaire was used to collect data from the participants. A chi-square test was used to detect the associations between the variables at the significance level of α=0.05. **Results:** A total of 315 participants were recruited into the study; 65.7% were female, and 54.0% were aged 20-21 years. One-third had a chronic disease (34.6%) and had been immunized with the flu vaccine in 2019 (32.1%). A few people were diagnosed with flu in 2019 (2.9%) and 2020 (1.6%). The majority received information related to COVID-19 through television (51.7%) and the Internet (41.3%); however, only 31.1% responded that they had sufficient information. The majority had a poor level of knowledge regarding COVID-19 prevention and control (67.9%), while a few people had good perceptions of COVID-19 prevention and control (1.6%). Only 29.5% had good skills for COVID-19 prevention and control. **Conclusion:** Young adult people in Chiang Rai Province are living with poor knowledge, perception and skills to prevent and control COVID-19. Effective prevention and control measures are required to prevent people in rural areas, such as people living in Chiang Rai Province, from infection by COVID-19.

Keywords: *COVID-19, Readiness, Knowledge, Perception, Young adult*

Introduction

Since the first unknown-cause pneumonia case was detected in China and officially reported to the World Health Organization (WHO) in December 2019, there have been 509,164 confirmed cases and 23,335 deaths reported globally (as of 27 March 2020) [1]. A total of 2,932 cases were reported from the South-East Asia Region (SEAR), among which 105 cases died [1]. Thailand has been reported to rank first among the countries in the SEAR [1]. On March 28, 2020, the Department of Disease Control, Ministry of Public Health, Thailand, reported that the number of cumulative confirmed cases of COVID-19 was 1,245 cases and 6 deaths [2].

Currently, COVID-19 is identified as the major human threat and has killed a number of people around the world [3]. People of older age and those with previous health conditions are most vulnerable to infection and death. With the high capability of the disease to spread and the severity of its pathogenesis, humankind is facing serious problems, especially in countries with scarce resources in their health care systems to save victims' lives, particularly during the crisis period of the disease. It is clear that the most effective measure is to prevent infection from the disease. Several control and prevention measures have been implemented in different countries [4, 5]. The government of Thailand, which is led by the Ministry of Public Health, is intervening with various methods to reduce the possibility of spreading the disease from infected persons to others, particularly by stopping the movement of the population living in large cities to

rural areas in an attempt to avoid spreading the disease to people living in remote areas far from good health care facilities [6].

The northern region of Thailand, especially Chiang Rai Province [7], is one of the most critical areas for the epidemic of COVID-19 due to its long border with neighboring countries such as Myanmar, Lao, and southern China [8]. Due to its geographic condition of long borders, a large number of people move across the borders every day. Moreover, most people who live in poor economic and educational conditions have increased vulnerability to the infection. Many young adults who work in large cities, such as Bangkok, return to their villages on occasions such as the Songkran Festival. Many prevention and control measures have been launched in Thailand by the Thai government to prevent infection of people living in rural areas. With the movement of population who lived in high risk areas to their home villages where were lower risk of the disease. This might be increasing the possibility to get infection among those people living in the village particularly among the greatest vulnerable for the disease infection such as elderly population and also other people who had underlying disease. Therefore, this study aimed to assess the readiness among young adults who are the most valuable for contribution to respond to the COVID-19 epidemic in Chiang Rai Province particularly in the strengthening in contribution of control and prevention measures in their village, which has a long border and a high population movement rate.

Methodology

A cross-sectional study design was used to collect information from the participants. The study setting was Chiang Rai Province, Thailand. People aged 18-23 years who lived in the study area were the study population. People who were unable to provide all essential information regarding the study protocols were excluded from the study. The sample size was calculated by the standard formula [9] for a cross-sectional design. At $Z_{\alpha/2}= 1.96$, $P= 0.26$ (having good knowledge) [8], $Q= 0.73$, and $e= 0.05$, a total of 291 participants were required for the analysis.

Two groups of participants were randomly selected into the study; a) People who lived in five villages in Muang and Mae Chan Districts, Chiang Rai Province; b) student attending in a university were selected by a random method. Young adults aged 18-23 years who lived in selected villages and students aged 18-23 years in 5 programs were selected by a random method from a university and were invited to participate in the study. All participants were requested to complete the questionnaire. Data were collected between 3 March and 5 March, 2020.

A validated questionnaire was used for data collection. It was developed based on all availability information from different sources of information, such as the websites of the World Health Organization (WHO) , The Centers for Disease Control and Prevention (CDC), and the Ministry of Public Health Thailand. The opinions of medical experts and epidemiologists were also used for questionnaire development. The questionnaire had five sections. In Section I, 8 questions were used to collect the general information of the participants, such as age, sex, religion, and education. In Section II, 8 questions were used to collect all medical histories, such as chronic disease, history of receiving the flu vaccine, and history of a diagnosis of flu the previous year. In Section III, 10 questions were used to assess knowledge regarding COVID-19 prevention and control. Each question had three choices; correct, and not correct. If the participants provided the choice correctly, it was scored "1" in that item. In vice versa, if the participant provided the wrong answer, it was scored "0". In total, those participants were scored 0-5, it was defined as "low knowledge". Those participants scored between 6-8 were classified into " moderate knowledge" , and those who scored equal of greater than 9 were classified into "high knowledge".

In Section IV, 10 questions were used to assess perceptions of the measures of COVID-19 prevention and control. There were two groups of the questions in this section; 5 questions were positive direction questions and another 5 questions were negative direction questions. Every question had three answer choices; agree, neutral, disagree. In every positive question, it was scored "3" "2" and "1" while people chose "agree", "neutral", "disagree", respectively. For the questions in negative direction, it was scored in the opposite way from the positive direction questions. It means that it was scored "1" "2" and "3" while people chose in "agree", "neutral", "disagree", respectively. In total, those who had been scored equal or more than 26 were classified into " high perception" , while those scored between 20 to 25, and less than 20 scores, were classified into " moderate" and " low" perceptions, respectively.

In section V, 10 questions were used to assess the skills for COVID-19 prevention and control. The questions were asked on different daily life practices on prevention and control the disease such as frequency of hands washing, frequency on use face mask, etc. Each question had three answer choices; no, sometime, and very often. Anyone chose " no" , "sometime", or "very often", was scored "0", "1", or "2", respectively. In total, those who had been scored 16 and over were classified into "high", and those who had been scored 10-15 and less than 10 were classified into " moderate" , and " low" skill in prevention and control the disease, respectively.

The questionnaire was validated before use by the item objective congruence method (IOC) by three external experts. It was subsequently piloted in 10 similar populations in Muang District, Chiang Rai Province. Cronbach's alpha was 0.73.

All study protocols were approved by the Chiang Rai Public Health Provincial Ethical Committee (No. CRPPHO 12-2563) . All selected participants were

asked to obtain the informed consent form before beginning the questionnaire.

Results

A total of 315 participants participated in the study; 65.7% were female, and 54.0% were aged 20-21 years. The majority were Buddhist (96.5%), single (100.0%), had no income (77.7%), and were studying in a university (83.5%). One-third had a chronic disease (34.6%) and had been immunized with the flu vaccine in 2019 (32.1%). A few people were diagnosed with flu in 2019 (2.9%) and 2020 (1.6%). The majority received information relevant to the disease through television (51.7%) and the Internet (41.3%); however, only 31.1% responded that they had sufficient information (Table 1).

Table 1 General characteristics of the participants

Characteristics	n	%
Total	**315**	**100.0**
Sex		
Male	108	34.3
Female	207	65.7
Age (years)		
18-19	73	23.2
20-21	170	54.0
22-23	72	22.8
Religion		
Buddhist	304	96.5
Other	11	3.5
Marital status		
Single	315	100.0
Education		
Illiterate	6	1.9
Primary school	29	9.2
High school	17	5.4
University	263	83.5
Annual income (baht)		
No income	243	77.2
<30,000	29	9.2
30,001-50,000	23	7.3
50,001-100,000	14	4.4
≥100,001	6	1.9
Number of family members (persons)		
1-3	117	37.1
4-6	182	57.8
≥7	16	5.1
Having a chronic disease		
Yes	109	34.6
No	206	65.4
Having been diagnosed with the flu in 2019		
Yes	9	2.9
No	306	97.1
Having a family member who was diagnosed with the flu in 2019		
Yes	25	7.9
No	290	92.1
Having been diagnosed with the flu in 2020		
Yes	5	1.6
No	310	98.4
Having a family member who was diagnosed with the flu in 2020		
Yes	10	3.2
No	305	96.8
Having been immunized with the flu vaccine in 2019		
Yes	101	32.1
No	214	67.9
Main channel for receiving COVID-19 information		
Television	163	51.7
Internet	130	41.3
Medical staff	22	7.0
Sufficiency of information		
Yes	98	31.1
No	217	68.9

The majority had a poor level of knowledge regarding the disease (67.9%); only 7.3% reported a good level and 24.8% reported a moderate level of knowledge of COVID-19. There were no statistically significant differences in the levels of knowledge by different profiles of participants, such as sex, age, religion, etc. (Table 2).

A few people had good perceptions of COVID-19 prevention and control (1.6%), while 58.1% had poor perceptions. Only the profile of participants with a chronic disease was found to be significantly different in the level of perception of disease prevention and control (p-value=0.002), while the other characteristics were not found to differ (Table 3).

One-third (29.5%) of the participants had good skills for COVID-19 prevention and control. However, in the comparisons of the participants' profiles and the levels of skills for COVID-19 prevention and control, a difference was found only among the different age categories, while other characteristics were not found to be significantly different (Table 4).

Discussion

Young adult people in Chiang Rai Province, Thailand, received information relevant to COVID-19 through television, but only one-third responded that they had sufficient information. These respondents had high vulnerability to disease infection due to their poor level of knowledge, poor perception and poor skills for COVID-19 prevention and control.

COVID-19 has been found to be a new emergent disease with serious pathogenesis for infected patients [10]. It has spread worldwide, and the elderly population is reported to have high morbidity compared to other groups [1,2]. Thailand has established thermal screening for all travelers from China since 3 January 2020, and on 8 January 2020, the first suspected case was reported [11].

Our study found that the young adult population in rural Thailand had poor knowledge, perception, and skills regarding COVID-19 prevention and control. However, a study in China [12] reported that people had high knowledge and personal protective skills for the disease infection. This might be because the Chinese population was exposed to the disease earlier than the Thai population. Given the serious situation in China, most Chinese have developed their knowledge and behaviors to prevent the disease.

Social distancing and isolation are recognized as effective prevention and control measures, particularly between high- and low-risk populations through migration. These methods have been implemented in different countries, including those currently facing problems, such as Thailand [6], and post-exposed countries, such as China [13]. If people in any country do not have sufficient skills in response to the COVID-19 epidemic, the health system would collapse and would not be completely effective in saving lives, as in Italy[14].

Table 2 Comparison of participants' characteristics and knowledge of COVID-19 prevention and control

Characteristics	Knowledge			χ^2	p-value
	Poor n (%)	Moderate n (%)	Good n (%)		
Total	214 (67.9)	78 (24.8)	23 (7.3)	N/A	N/A
Sex					
Male	76(70.4)	25(23.1)	7(6.5)	0.46	0.792
Female	138(66.7)	53(25.6)	16(7.7)		
Age (years)					
18-19	55(75.3)	12(16.4)	6(8.3)	4.30	0.367
20-21	109(64.1)	49(28.8)	12(7.1)		
22-23	50(69.4)	17(23.6)	5(7.0)		
Religion					
Buddhist	209(68.8)	72(23.7)	23(7.5)	4.49	0.105[a]
Christian	5(45.5)	6(54.5)	0(0)		
Annual income (baht)					
No income	160(65.8)	65(26.7)	18(7.5)	5.78	0.215[a]
< 30,000	20(69.0)	5(17.2)	4(13.8)		
≥ 30,001	34(79.0)	8(18.6)	1(2.4)		
Number of family members (persons)					
1-3	74(63.2)	31(26.5)	12(10.3)	4.43	0.322
4-6	126(69.2)	45(24.8)	11(6.0)		
≥ 7	14(87.5)	2(12.5)	0(0)		
Having chronic disease					
Yes	79(72.5)	25(22.9)	5(4.6)	2.41	0.299
No	135(65.5)	53(25.8)	18(8.7)		
Having flu vaccine in 2019					
Yes	67(66.3)	25(24.8)	9(8.9)	0.58	0.747
No	147(68.7)	53(24.8)	14(6.5)		
Main channel for obtaining information					
Facebook/Line/Internet	91(70.0)	33(25.4)	6(4.6)	3.69	0.449
Television	109(66.9)	38(23.3)	16(9.8)		
Medical staff	14(63.6)	7(31.8)	1(4.6)		
Sufficiency of information					
Yes	149(68.6)	52(24.0)	16(7.4)	0.23	0.887
No	65(66.3)	26(26.6)	7(7.1)		

* Significant at α=0.05, [a]Fisher's exact test

Table 3 Comparison of participants' characteristics and perceptions of COVID-19 prevention and control

Characteristics	Perception			χ^2	p-value
	Poor n (%)	Moderate n (%)	Good n (%)		
Total	**183 (58.1)**	**127 (40.3)**	**5 (1.6)**	**N/A**	**N/A**
Sex					
Male	62(57.4)	45(41.7)	1(0.9)	0.42	0.813[a]
Female	121(58.5)	82(39.6)	4(1.9)		
Age (years)					
18-19	43(58.9)	29(39.7)	1(1.4)	2.15	0.714[a]
20-21	103(60.6)	64(37.6)	3(1.8)		
22-23	37(51.4)	34(47.2)	1(1.4)		
Religion					
Buddhist	175(57.6)	124(40.8)	5(1.6)	3.60	0.165[a]
Other	8(75.0)	3(25.0)	0(0)		
Annual income (baht)					
No income	140(57.6)	98(40.3)	5(2.1)	3.42	0.904[a]
< 30,000	15(51.7)	14(48.3)	0(0)		
≥ 30,001	28(65.2)	15(34.8)	0(0)		
Number of family members (persons)					
1-3	64(54.7)	50(42.7)	3(2.6)	6.10	0.192[a]
4-6	112(61.5)	69(37.9)	1(0.6)		
≥ 7	7(43.7)	8(50.0)	1(6.3)		
Having chronic disease					
Yes	51(46.8)	54(49.5)	4(3.7)	11.33	0.002*
No	132(64.1)	73(35.4)	1(0.5)		

* Significant at α=0.05, [a]Fisher's exact test

Table 4 Comparison of participants' characteristics and skills for COVID-19 prevention and control

Characteristics	Prevention and control skills			χ^2	p-value
	Poor n (%)	Moderate n (%)	Good n (%)		
Total	34 (10.8)	188 (59.7)	93 (29.5)	N/A	N/A
Sex					
Male	17(15.8)	59(54.6)	32(29.6)	4.33	0.118
Female	17(8.2)	129(62.3)	61(29.5)		
Age (years)					
18-19	3(4.1)	42(57.5)	28(38.4)	10.92	0.027*,[a]
20-21	26(15.3)	97(57.1)	47(27.6)		
22-23	5(6.9)	49(68.1)	18(25.0)		
Religion					
Buddhist	34(11.2)	177(58.2)	93(30.6)	N/A	N/A
Other	0(0)	11(100.0)	0(0.0)		
Annual income (baht)					
No income	27(11.1)	135(55.5)	81(33.4)	12.49	0.094
< 30,000	2(6.9)	22(75.9)	5(17.2)		
≥ 30,001-50,000	5(11.6)	31(72.1)	7(16.3)		
Number of family members (persons)					
1-3	11(9.4)	69(59.0)	37(31.6)	2.14	0.720
4-6	20(11.0)	109(59.9)	53(29.1)		
≥ 7	3(18.8)	10(62.4)	3(18.8)		
Having chronic disease					
Yes	17(15.6)	62(56.9)	30(27.5)	3.90	0.144
No	17(8.2)	126(61.2)	63(30.6)		

* Significant at α=0.05, [a]Fisher's exact test

Conclusion

This study provides proven evidence to use Global Mental Health Assessment Tool-Primary Care Version (GMHAT/PC) in specialist limited healthcare setting of Nepal. Findings of this study also support mid-level health workers and possibly others health workers having some training and the tool would be can used by mid-level health workers with the computer-assisted programme GMHAT/PC to make a valid assessment and diagnosis for early detection and management of mental health related around 16.95 minutes makes it feasible in routine assessments in primary care and general health settings. The authors accept that Medical Officer may not have enough time in their routine primary care clinics, but they can utilize other health professionals in assessing the mental health of their patients using the GMHAT/PC. In some cases, it took longer to complete the interview, mainly because the patients wanted to report their emotional problems and the mid-level health workers felt it was necessary to listen to them. Both the patients and health worker found the GMHAT/PC not only acceptable, but useful in making a quick, yet comprehensive, mental health assessment.

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Dengue Shock Syndrome Case Management and Investigation in Chiang Saen District Hospital, Chiang Rai Province: A case study

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ABSTRACT

An early case of dengue shock syndrome (DSS) was treated and further investigated by a surveillance and rapid response team (SRRT) of Chiang Saen Hospital, Chiang Rai, Thailand. A DSS patient was admitted to the hospital and indicated the need for immediate investigation. The ultimate goal of the study was to understand the effectiveness of case management and identify an effective mechanism for dengue fever (DF) prevention and control in a community. Specific procedures to assess case management and perform standard disease investigations in a community were applied, and information was collected from several sources, such as medical records, laboratory results, and information obtained from interviews with key informants in the community. The surveillance and rapid response team (SRRT), which consisted of public health professionals, medical doctors, nurses, etc., performed disease investigations in the community. A Thai female aged 56 years who was working as a merchant and who lived in San Thon Pao Village, Yo Nok Sub-District, Chiang Saen District Chiang Rai Province, had a high fever on June 16, 2019 and received treatment on June 18, 2019 at the hospital. After completion of the medical investigation, she was diagnosed with DSS, which was the first case in this area in many years and indicated the need for further investigation. The SRRT prepared for further public health actions to respond to the disease properly and started community work on June 20, 2019; the public health actions included mass media education, screening for more cases in the community, and cooperation of people in the community. Finally, an additional 9 cases of DF were detected, the disease was controlled, and no more cases were reported in this area. DSS requires effective medical care, particularly in the critical period, and a rapid response with effective measures, including strong collaboration with people in the community, is key to the success of controlling a disease, and this method could be applied to other severe diseases.

Keywords: *Dengue fever, Dengue shock syndrome, Case management, Investigation, surveillance and rapid response team (SRRT)*

Introduction

Dengue fever (DF) has been recognized as a public health challenge, particularly in tropical countries [1]. Dengue is a mosquito-borne virus that is frequently reported in the rainy season, especially in Southeast Asian countries [2]. The virus has four serotypes (dengue virus (DENV)-1, -2, -3, and -4) and presents similar clinical features among infected persons, but DF presents a wide spectrum of clinical features from an absence of symptoms to severe manifestations, such as shock syndrome [3]. Infection with one serotype of DENV stimulates life-long immunity to that serotype but not to other serotypes [4]. Symptomatic dengue virus infections are grouped into three categories: undeferential fever, DF, and dengue hemorrhagic fever (DHF) [5]. DHF is classified into four severity grades, with grades 3 and 4 being defined as dengue shock syndrome (DSS) [2]. All cases of DHF or DSS need to be cared for properly and intensively by medical staff. DHF is a severe and potentially life-threatening condition [2]. While DSS is a dangerous complication of dengue infection and is associated with high mortality [6], if the condition is detected early and the patient is cared for properly, the

fatality rate is below 1.0% [1].

The World Health Organization (WHO) estimated that 100-400 million cases of DF occurred globally, and most of the severe cases were reported in countries in Asian and Latin America [1]. The Ministry of Public Health in Thailand reported more than 82,00 cases of DF in 2019. The largest proportion of cases was reported among people aged 5-14 years, followed by 15-34 years. The cases peaked between July and August 2019, and the northern region of Thailand reported the highest number of cases of DF from 2018-2019 [7]. In 2018, 103 deaths caused by DHF and DSS were reported, and those who were older had a greater chance of death than those who were younger, especially those who had underlying diseases such as obesity, hypertension, asthma, etc. [8]. In 2018, there were 1,933 cases of DF in Chiang Rai Province, and Chiang Saen District was identified as one of the high-risk areas for DF in Chiang Rai Province due to having a high population density, having long border areas with Myanmar and the Republic of Lao, and people living in poverty and with poor education levels [9]. To respond to DF, including DHF and DSS, the availability of a team to rapidly implement prevention and control measures is important [10]. Environmental management is another factor to reduce the epidemic potential of the disease [11]

The objectives of this study were to understand effective case management, particularly effective care in febrile (dehydration and high fever may cause neurological disturbances and febrile seizures in young children) and critical phases (shock from plasma leakage, severe hemorrhage, and organ impairment) [2], and identify the associated community factors.

Method

The DSS patient was cared for, and a field investigation was conducted in Chiang Saen District, Chiang Rai Province between June 19th and July 31st 2019, by collaborating with the district surveillance and rapid response team (SRRT). The team consisted of an epidemiologist from the Chiang Saen District Public Health Office, a medical doctor and a nurse from Chiang Saen Hospital, a public health professional from Yo Nok Health Promoting Hospital and village health volunteers (VHVs). The investigation aimed to understand the effectiveness of DSS case management, to identify additional DHF cases in the villages and to identify effective prevention and control measures that reduce potential risk factors for the disease at the community level.

The World Health Organization (WHO) criteria were used for probable case identification, which require at least two of the following signs: severe headache, pain behind the eyes, muscle and joint pain, nausea, vomiting, swollen glands, and rash. People with high fever, fatigue, and headache were excluded. The definition of severe dengue required one of the following criteria to be met: a) plasma leakage that may lead to shock (dengue shock), b) fluid accumulation with or without respiratory distress, c) severe bleeding and/or d) severe organ impairment. Moreover, severe dengue can present with severe abdominal pain, persistent vomiting, rapid breathing, bleeding gums, fatigue, restlessness and blood in vomit [1].

Step of investigation

The investigation was initiated by confirming the occurrence of DSS based on medical records, including asking the doctor who handled the case. The laboratory information was also confirmed according to the WHO guidelines. Then, the epidemic activity of the disease was confirmed by comparing data from three years prior, and no DSS was reported in the area. Additional information was obtained from the patient and her relatives regarding the travel history of the patient. Possible risk factors and potentially vulnerable or at-risk populations were also identified.

A case definition was developed and understood among the SRRT team. The roles of the SRRT were elucidated, including the flowchart of the authority and all relevant mechanisms, including the major channels of communication. Hypotheses were developed before field investigation. A cross-sectional design was used to test the hypotheses. Family members and selected community members were interviewed. Quality of sanitation and environmental factors were also assessed.

Results

A total of 34 cases of DF were reported through the surveillance system of Chiang Saen Hospital between January 1st, 2019 and July 15th, 2019 (morbidity rate 87.74 cases per 100,000 people).

A case profile:

A 56-year-old female who lived in village No 6, San Thon Pao Village, Yo Nok Sub-District, Chiang Saen District, Chiang Rai Province visited a doctor at Chiang Saen Hospital with high fever, headache and fatigue on June 18, 2019. Her symptoms began on 16 June 2019. A doctor performed an overall assessment including past and present illness history for her and her family members. She had been fully physically assessed, including both routine and dengue-specific laboratory identifications. Finally, she was preliminarily diagnosed with dengue fever (DF) and treated. However, based on her clinical features, she was not admitted and was asked to follow-up the next day (on June 19, 2019).

Early in the day on June 19, 2019, the patient met a doctor again and was admitted to the inpatient care unit because her clinical signs worsened, particularly fever and headache. On June 20, 2019, the patient presented signs of shock because plasma was leaking out of the cells. On June 21, 2019, a large area of red spots presented on her arms and whole body. On June 22, 2019, she went into shock and was cared for in the

intensive care unit (ICU). On June 23, 2019, the patient's signs improved, and the fever decreased. On June 24, 2019, the patient had largely improved, with no fever or usual symptoms. On 25 June 2019, the patient was discharged from the hospital and was further cared for at home.

According to the patient's illness history and physical examination, the patient had high fever, headache, eye pain, bone or joint pain, red rash, and shock, and the tourniquet test was positive, which was a clinical manifestation of dengue fever. The following are the comparisons of the clinical signs and symptoms with those in the World Health Organization (WHO) guidelines.

Table 1 Clinical characteristic of dengue fever patients

Symptoms	Yes	No	WHO definition [12]
Fever and acute fever	✓		++++
Headache	✓		++++
Vomiting		✓	++
Eye pain	✓		+
Bone and joints pain	✓		
Rash	✓		+
Internal organs bleeding		✓	+
Liver failure		✓	+
Shock	✓		+
Tourniquet test	positive		++

Laboratory results

Several biomarkers were detected from the first day to the last day for monitoring and case management (Table 2).

Community works;

In the villages, several tasks were performed during the investigation. Two major teams were grouped in the SRRT. In the first group, two staff members looked for probable cases in the village to identify the cases of DF and DHF. Finally, 9 cases met the criteria of probable cases. The second group worked on a) identifying and destroying egg-laying habitats, b) emptying and cleaning water storage containers, c) encouraging people to use long-sleeved shirts in the daytime to reduce bites from mosquitoes, d) providing mass media education on DF disease and proper methods to control and prevent DF at the family and community levels, e) spraying with chemicals to kill adult mosquitoes, and f) performing active larval surveillance in households.

Conclusion

Dengue fever is a critical and threatening health problem, even in very remote areas. Most patients need to be cared for carefully by the medical team. Even in remote and small hospitals in Thailand, medical staff should be able to handle DHF cases properly and effectively. This reflects the quality of the health care and health care system. The formation of an SRRT is challenging in the health system, especially in health resource-limited areas. Under these conditions, timing is important to stop the spread of the disease. Regular training and meeting in teams, including a concrete structure of the team or organization, leads to the optimal effective prevention and control of a disease in certain areas. Communication is found to play a critical role in all steps while working in the field. Finally, the cooperation of people in the community and collaboration among the relevant agencies and organization to integrate all resources to address the problem are also identified as keys to success in the context of the disease investigation.

Table 2 Laboratory result

No	Date	WHO DHF Criteria					Temp.
		WBC (<5,000 cell/mm^3)	Platelet <100,000 cell/mm^3)	Hct (increase 10%-20% from original date)	IgM	IgG	
1	June 18, 2019	1,940	135,000	36.6	-	-	35.7
2	June 19, 2019	2,750	109,000	38.8	Neg.	Pos.	38.2
3	June 20, 2019	2,170	51,000	36.1	-	-	38.3
4	June 21, 2019	3,160	34,000	35.4	-	-	37.8
5	June 22, 2019	3,450	25,000	35.1	-	-	37.3
6	June 23, 2019	3,760	29,000	34.5	-	-	37.3
7	June 24, 2019	3,830	84,000	34.5	-	-	37.1

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