



Glimpse of Metabolic-Associated Steatotic Liver Disease [MASLD] in Myanmar

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Research Article

Volume 9 Issue 2

Received Date: May 29, 2024

Published Date: July 23, 2024

DOI: 10.23880/ghij-16000217

Abstract

The hospital-based retrospective descriptive study was done to determine the characteristic and associated factors of MASLD in 817 patients at Yangon Gastrointestinal and Liver Center, Myanmar from April 2017 to Jun 2022. Male and female patients were 427 [52.3%] and 390 [47.7%], respectively. Their steatosis grades were 39.3% in S0, 11.6% in S1, 16.4 in S2 and 32.7% in S3 groups. For fibrosis, F0F1 patients were 89.4%. Twenty-nine patients were F4 stage Cirrhosis. Their mean age at the time of diagnosis was 46.63 [SD \pm 11.583] years, between 16 to 77 years. Body Mass Index [p<0.001] and Fibroscan-CAP score [p=0.015] were different between sex. Hb A1C, lipid profile, ALT and AST were not statistically different between sex. Steatosis grading [S0, S1, S2 and S3] was associated with BMI [p<0.001] and HbA1C [p=0.003]. Positive correlations were found between Fibroscan-CAP score and age at the time of diagnosis, BMI and HbA1C [p<0.01]. Steatosis grading was associated with HbA1C [p=0.004] and BMI [p<0.001]. Fibrosis staging was associated with HbA1C [p<0.001] and BMI [p=0.007]. Older age patients were more likely to have higher BMI, HbA1C, steatosis grading and fibrosis staging. Overweight and elevated HbA1C patients tend to have higher steatosis grading and fibrosis staging.

Keywords: Fatty Liver; MASLD; Lean MASLD; MASH; Myanmar; Southeast Asia

Introduction

Myanmar is a Southeast Asian country with over 55 million populations, and an epidemic region for viral hepatitis B [1,2]. Although there have been some improvements in universal coverage of hepatitis B 3 doses [HepB3] and birth dose [HepB-BD] vaccination, and the national Hepatitis C elimination goal is in place; the prevalence of chronic hepatitis B and C are still at 6.51% and 2.65% respectively [2,3]. Along the tide of global MASLD, many cases of MASLD and its complications including MASH, are seen in everyday clinical practices in Myanmar. According to a 2014 national survey of non-communicable diseases, the prevalence of diabetes in Myanmar was at 10.2% and dyslipidaemia was at 69.7% of which only 1.2% of survey participants were

aware of their dyslipidaemia [4,5]. However, there is no up-to-date data available in Myanmar regarding the prevalence of MASLD and its complication. The risks of getting MASLD are expected to be high with the increased adoption of sedentary lifestyles and westernized diets with the influx of fast-food chains in the last decade in the country. MASLD and its complications have a large impact on the outlook of patients who already have the cardiovascular risk factors, including metabolic diseases, in addition to chronic viral hepatitis.

The prevalence of metabolic-associated steatotic liver disease is 30 % globally, and it is projected to increase dramatically in the coming years until 2030 [6,7]. Previously, it was thought that MASLD is the disease of the industrialised countries, but the current data showed that MASLD is also an

increasing health issues in less developed countries and, in fact, it impose larger and significant risks to the population in Asian countries [8-12]. Asian countries, including Myanmar, are still struggling to fight against chronic hepatitis B and its complications [2,13]. Like many Asian countries, the rising trend of MASLD in the viral hepatitis epidemic region has put the situation on the verge of breaking down in already saturated healthcare system in a resource constraint setting [13,14].

The uptrend of obesity and its metabolic complications including type 2 diabetes mellitus, dyslipidaemia, weakness in health education about healthy lifestyle, adoption of sedentary lifestyle and dietary westernisation has all together put the situation conducive of MASLD and its complications in the Southeast Asian countries [14]. Although extensive research has conducted in Western countries for MASLD and its complications, data regarding MASLD are limited in Asia [10,15]. According to the latest meta-analysis data available, the overall prevalence of MASLD in Asia is estimated to be 29% and it was found to be highest in Southeast Asia, at 42% [8]. However, in Myanmar, the prevalence of MASLD and its complications remains unknown because of a limited data. In this study, we explored the registry data of Yangon Gastrointestinal Liver Center [YGLC] between April 2017 and Jun 2022 to determine the characteristic of MASLD patients and its associations at YGLC. We can gain insight into the MASLD in Myanmar from this study, and it can be applied for advocacy work to drive MASLD policymaking in Myanmar.

Materials and Methods

Yangon GI-Liver Center [YGLC] is the one stop tertiary care for gastrointestinal and liver diseases in Myanmar and receives patients from all over the country. The hospital-based descriptive retrospective study was done from the registry data at YGLC. The study was conducted in accordance with the Declaration of Helsinki, and institutional ethical approval was obtained from the YGLC. Adult patients who are free of Chronic viral hepatitis including Hepatitis B and C, patients who do not drink or need to comply with the limit of alcohol as in male < 30 g/day and in female <20 g/day and patients who underwent a complete set of investigations, including FibroScan and laboratory work for MASLD, were included in the data analysis. Exclusion criteria including chronic liver disease patients with cirrhosis of viral etiology, alcoholic liver disease, Hepatocellular carcinoma [HCC] and end stage liver disease patients with limited life expediency. The data of laboratory investigation for biochemical parameters were from the first-time visit.

According to criteria set by the American Association for the study of Liver Disease, MASLD is defined by the presence of hepatic steatosis and the presence of any cardiometabolic

risk factors [CMRF] as follow, after excluding the other causes of hepatic steatosis. The following liver and its associated CMRF are used to define MASLD in this study [16].

- Hypertension as the systolic blood pressure of >130 mmHg and diastolic blood pressure of >85 mmHg or taking antihypertensive medication [16].
- Type II diabetes mellitus as a fasting serum glucose >5.6 mmol/l or a 2-hour post-load glucose level >7.8 mmol/l or HbA1C >5.7 mmol/l or taking treatment for Type II diabetes mellitus [16].
- Dyslipidaemia as an LDL level of >200 mmol/L, HDL < 50 mmol/L for male and HDL<40 mmol/L for females, triglyceride level of >150 mmol/L on fasting lipid profile, or anti-lipid medication to control their dyslipidaemia [16].
- Obesity is defined as the BMI > 23 * [Asian reference value] and having the waist circumference of > 80 cm for female and >94 cm for male patient [16].
- Steatosis is defined as a FibroScan controlled attenuation parameter [CAP] score of 238-260 decibels/meter [dB/m] for S1, > 260– 290 dB/m for S2 and > 290 -400 dB/m for S3 [17].
- Fibrosis is defined as the FibroScan Metavir score of 2-7 Kilopascal for F0F1, 7.5 – 10 kPa for F2, 10-14 kPa for F3 and >14 kPa for F4 [17].
- MASLD patients with elevated liver enzymes including Alanine aminotransferase M>33 IU/L and F> 25 IU/L and Aspartate aminotransferase >30 IU/L are categorised as metabolic dysfunction-associated steatohepatitis [MASH] [16,18,19].

Statistical Analysis

Collected data was entered in the Excel file and data cleaning was done by looking up total frequencies and frequency distribution. Data analysis was done by [SPSS version 21.0; IBM, Inc., New York; USA]. A total of 817 patients were available for analysis between April 2017 and Jun 2022. The demographic characteristics, and biochemical measurements of the patients were described using mean, standard deviation [SD] for continuous variables, and frequency and percentage [%] for categorical variables. Independent t test and one-way ANOVA test was run to determine differences in demographic characteristics and biochemical measurements. Pearson correlation was done between age at time of diagnosis and BMI, HbA1C and fibroscan score. Its significant level was set at p value <0.01. Pearson Chi square test was done to determine association between steatosis grading and Body mass index [BMI], gender, and HbA1C. Steatosis grading S0 and S1 were categorized into low steatosis [amount of liver with fatty change 11-33%], S2 was medium steatosis [amount of liver with fatty change 34-66%] and S3 was high steatosis

[amount of liver with fatty change >67%]. Fibrosis staging F0F1 was categorized into minimal fibrosis, F2 as significant fibrosis, and F3 and F4 was grouped to advance fibrosis and cirrhosis changes. Significant level was set at p value <0.05.

Results

Out of 817 patients, 427 [52.3%] were male and 390 [47.7%] were female. Almost all the patients were non-drinker [96.9%] and non-smoker [93.6%]. Regarding previous medical history, vast majority of the patients did not have known diabetes [93.1%], hypertension [95.8%],

dyslipidemia [97.4%] and Hypertriglyceridemia [99.6%]. The percentage of patients with steatosis were 39.3% in S0, 11.6% in S1, 16.4 in S2 and 32.7% in S3 groups. In detection of fibrosis, 89.4% of patients were F0F1. The rest were 3.8% in F2, 3.3% in F3 and 3.5% in F4. More female had elevated ALT, higher than their reference value, compared to male [58.5% vs 20.4%]. Very few patients had elevated AST [9.8%]. Anti-HBc antibodies positive patients were 2.08%. Only one patient was developed hepatocellular carcinoma after five years of diagnosed MASLD, Table 1.

Characteristics	Frequency	[%]
Sex		
Male	427	[52.3]
Female	390	[47.7]
Drinking alcohol status		
Non-drinker	792	[96.9]
Current drinker	10	[1.2]
Ex-drinker	15	[1.8]
Smoking status		
Non-smoker	765	[93.6]
Current smoker	16	[2.0]
Ex-smoker	36	[4.4]
Diabetes history		
Yes	56	[6.9]
Hypertension history		
Yes	34	[4.2]
No	783	[95.8]
Dyslipidemia history		
Yes	21	[2.6]
No	796	[97.4]
Hypertriglyceridemia history		
Yes	3	[0.4]
No	814	[99.6]
Steatosis grade		
S0	321	[39.3]
S1	95	[11.6]
S2	134	[16.4]
S3	267	[32.7]
Fibrosis		
F0F1	730	[89.4]
F2	31	[3.8]

F3	27	[3.3]
F4	29	[3.5]
ALT for male		
Not elevated [≤ 33 U/L]	340	[79.6]
Elevated [> 33 U/L]	87	[20.4]
ALT for female		
Not elevated [≤ 25 U/L]	162	[41.5]
Elevated [> 25 U/L]	228	[58.5]
AST		
Not elevated [≤ 30 U/L]	737	[90.2]
Elevated [> 30 U/L]	80	[9.8]
BMI > 30 kg/m ²	38	[4.7]
Developed Cirrhosis	21	[4.1]
Developed HCC	1	[0.12]
Anti-HBc Antibodies positive	17	[2.08]

ALT -Alanine aminotransferase, AST- Aspartate aminotransferase, BMI- Body Mass Index, HCC – Hepatocellular carcinoma
Table 1: Characteristics of patients registered at Yangon GI-Liver Center [YGLC] [n=817].

Mean age at the time of diagnosis of the studied patients was 46.63 [SD ± 11.583] years, between the range from 16 to 77 years. Results showed that that women were older age [p=0.002], smaller waist circumference [p=0.021] and lighter weight [p=0.015] as compared to men. However, Body Mass Index [BMI] of female patients was higher than that of male [p<0.001]. Hb A1C of both groups were not different statistically [p=0.941]. In addition, lipid profile of male and

female was nearly the same and they were not statistically and significantly different between sex [total cholesterol p=0.9, HDL p=0.462, LDL p=0.211 and triglyceride p=0.062]. Both Alanine aminotransferase [ALT] and Aspartate aminotransferase [AST] were not different between sex [ALT p=0.809, AST p=0.101]. Fibroscan CAP score of females was less than that of male and it was statistically significant [p=0.015] (Table 2).

Parameter [unit]	Men [n=427]	Women [n=390]	Total [n=817]	Min-Max
Age [years]	44.71 \pm 13.525	47.43 \pm 11.581*	46.63 \pm 11.583	16-77
Waist circumference [cm]	89.18 \pm 6.081	88.08 \pm 7.329*	88.66 \pm 6.724	62-120
Weight [kg]	66.162 \pm 6.150	64.88 \pm 8.481*	65.55 \pm 7.379	44.5-127.2
Body Mass Index [kg/m ²]	22.22 \pm 2.498	24.95 \pm 3.377*	23.53 \pm 3.249	14.81-46.72
Hb A1C [mmol/L]	5.16 \pm 0.611	5.15 \pm 0.736	5.15 \pm 0.673	4-10
Total cholesterol [mmol/L]	130.48 \pm 20.754	130.30 \pm 18.442	130.39 \pm 19.673	84-281
HDL [mmol/L]	39.88 \pm 3.960	40.09 \pm 4.018	39.98 \pm 3.987	27.5-58
LDL [mmol/L]	123.62 \pm 15.470	122.26 \pm 15.216	122.97 \pm 15.499	46-180
Triglyceride [mmol/L]	131.45 \pm 23.629	128.78 \pm 16.132	130.17 \pm 20.423	61-459
Fibroscan CAP [dB/m]	264.29 \pm 58.730	254.31 \pm 58.189*	259.63 \pm 58.649	25-546
ALT [U/L]	28 \pm 7.423	27.88 \pm 7.020	27.94 \pm 7.229	11-62
AST [U/L]	23.7 \pm 5.192	24.30 \pm 5.273	23.99 \pm 5.236	10-47

*p values significant at 0.05.

Table 2: Anthropometric and biochemical measurements of patients [mean \pm SD] Parameters.

A one-way ANOVA was performed to evaluate the relationship between steatosis grading [S0, S1, S2 and S3], BMI and HbA1C. The means and standard deviations are presented in Table 3 below. The ANOVA was significant at the 0.05 level. For BMI, $F[3,813]=29.055$, $p<0.001$. A post hoc LSD test revealed that mean BMI of steatosis grade S0 patients was significantly lighter than that of steatosis grade steatosis grade S3 [$p<0.001$] patients. In addition, there was significantly lower mean BMI in steatosis grade S0 patients, steatosis grade S1 patients and steatosis grade S2 patients

when comparing to steatosis grade S3 patients, [$p<0.001$]. For HbA1C, $F[3, 813] = 4.6240$, $p = 0.003$. A post hoc LSD test indicated that the mean HbA1C of the steatosis grade S0 was significantly lower than that of the steatosis grade 3 [$p<0.001$]. However, there were no significant differences between the mean HbA1C of the steatosis grade S0 and steatosis grade S2 [$p = 0.115$] nor between the steatosis grade S2 and steatosis grade S3 [$p = 0.170$]. Steatosis grade S1 and S3 were not statistically significant either [$p=0.145$].

Steatosis Grading	BMI		HbA1C	
S0	22.6013	±3.181	5.0578	±0.494
S1	23.1684	±2.643	5.1472	±0.661
S2	23.1883	±2.687	5.1663	±0.612
S3	24.9379	±3.317	5.2637	±0.856

Table 3: Descriptive statistics for steatosis grading and HbA1C [mean ± SD].

Pearson correlation analysis was conducted to examine the relationship between Fibroscan CAP score and age at the time of diagnosis, BMI and HbA1C. The results revealed that age at the time of diagnosis was significantly and positively correlated with BMI $r[806]=0.13$, $p<0.01$, HbA1C $r[806]=0.14$, $p<0.01$ and Fibroscan CAP score $r[806]=0.22$, $p<0.01$.

This indicates that older patients tended to have higher BMI, HbA1C values and Fibroscan CAP scores. In addition, there were significantly and positive correlation between BMI and Fibroscan CAP scores $r[817]=0.30$, $p<0.01$, and HbA1C and Fibroscan CAP scores $r[817]=0.16$, $p<0.01$. There was no significant correlation between BMI and HbA1C (Table 4).

Indicators	Coefficient [r]	P value	N
age at the time of diagnosis vs BMI	0.13	<0.001	806
age at the time of diagnosis vs HbA1C	0.14	<0.001	806
age at the time of diagnosis vs Fibroscan CAP score	0.22	<0.001	806
BMI vs Fibroscan CAP score	0.3	<0.001	817
HbA1C vs Fibroscan CAP score	0.16	<0.001	817

P value significant at 0.01.

Table 4: Correlation between age at the time of diagnosis and clinical and biochemical parameters.

Chi-Square Test of Independence was performed to evaluate the association between steatosis grading and three variables [sex, HbA1C, and BMI]. Chi square test revealed that there was a significant relationship between HbA1C and steatosis grade [$p=0.004$], and BMI and steatosis grade [$p<0.001$]. The result concluded that overweight patients and higher HbA1C patients were more likely to have higher steatosis grade, (Table 5). Similarly, Chi square test was

done between fibrosis staging and three variables [sex, HbA1C, and BMI]. The result showed that fibrosis staging was significantly associated with HbA1C [$p<0.001$] and BMI [$p=0.007$]. Overweight patients and higher HbA1C patients were more likely to have higher fibrosis stage, (Table 6). Both steatosis grading and fibrosis stage were not found differences between male and female patients.

Variables	Steatosis grade						P value
	Low		Medium		High		
Sex	Frequency	[%]	Frequency	[%]	Frequency	[%]	
Male	198	46.4	59	13.8	170	39.8	0.074
Female	212	54.4	46	11.8	132	33.8	
HbA1C*							
<5.7 mmol/L	367	52.2	92	13.1	244	34.7	0.004
≥5.7 mmol/L	43	37.7	13	11.4	58	50.9	
BMI*							
<23 kg/m ²	253	61.7	58	14.1	99	24.1	<0.001
≥23 kg/m ²	157	38.6	47	11.5	203	49.9	

*p value significant < 0.05.

Table 5: Association between steatosis grading and sex, HbA1C and body mass index [BMI] of patients.

Variables	Fibrosis stage						P value
	Low risk		At risk Cirrhosis		Cirrhosis		
Sex	Frequency	[%]	Frequency	[%]	Frequency	[%]	
Male	383	89.7	19	4.4	25	5.9	0.312
Female	347	89	12	3.1	31	7.9	
HbA1C*							
<5.7 mmol/L	651	92.6	26	3.7	26	3.7	<0.001
≥5.7 mmol/L	79	69.3	5	4.4	30	26.3	
BMI*							
<23 kg/m ²	380	92.7	12	2.9	18	4.4	0.007
≥23 kg/m ²	350	86	19	4.7	38	9.3	

*p value significant < 0.05.

Table 6: Association between fibrosis stage and sex, HbA1C and body mass index [BMI] of patients.

Discussion

MASLD and its Associated Factors

MASLD acts as an open access to more serious complications of spectrum of steatotic liver diseases, including metabolic associated steatohepatitis [MASH], with a rise in transaminases which reflect the inflammation of hepatocytes, followed by fibrosis, cirrhosis, and hepatocellular carcinoma [20,21]. MASLD is strongly associated with metabolic diseases and considerably increases the risk of hepatocellular carcinoma [22]. A meta-analysis by Yi et al. has highlighted that patients with MASLD are at increased risk of not only liver-related mortality and morbidities but also multiple cardiovascular morbidities, extrahepatic cancer, chronic kidney disease and diabetes mellitus [23]. There is also a bidirectional relationship between type 2 Diabetes mellitus and MASLD and metabolic

syndrome and this fact already reflected to our study finding as well [12,24-26]. It is also evident in many literatures that the risk of HCC is increases in patients with diabetes [13,22]. Increased levels of pro-inflammatory cytokines in obesity have also contributed to the development of HCC [27]. In our study, we noticed that almost half of the patients are having Fibroscan CAP score of S2-S3 401 [49.1%] and 87 [10.6%] patients are having clinically significant fibrosis [F2-F4] measured by Fibroscan. Among them 315 [38.6 %] patients are having elevated ALT level, i.e. already suffering from the MASH which shows the potential of serious disease complication including cirrhosis and HCC.

MASLD Related Hepatocellular Carcinoma

According to global cancer observatory 2022 data, hepatocellular carcinoma is the fifth most common cancer and second leading cause of cancer mortality in Myanmar,

with the estimated prevalence of 5.3% and age-standardised incidence rate of 10% [28]. However, data on the prevalence of MASLD-related HCC and its consequences in the country are still lacking. We have found in our study that 31 [4.1%] patients developed cirrhosis as a liver related morbidity at the last follow up of the study with one patient developed HCC [0.12%]. According to the available literatures, approximately 2% of MASH cases progress to MASH-HCC per year [29]. In a systematic review and meta-analysis by Tan et al., the proportion of HCC secondary to MASLD in Southeast Asia was >20% [30]. Therefore, it is very crucial to follow up the high-risk patients with recommended HCC surveillance.

HCC is the most serious complication of chronic liver disease, which is usually arise from the cirrhotic liver, but a rule of deviation of this disease spectrum, MASLD-related HCC can also occur without advanced fibrosis or cirrhosis [12,13,22,31]. In patients with cirrhosis, many guidelines have recommended 6 monthly ultrasonography [USG] with or without alpha-fetoprotein for HCC surveillance [11,18]. HCC surveillance in at-risk MASH-related cirrhosis patients is associated with earlier disease detection and improved survival [29]. However, since MASLD-related HCC can also occur in non-cirrhotic livers, and this has made the HCC surveillance less aggressive for patients with MASLD. Moreover, the obesity of MASLD patients interfere with visual field limitation for ultrasound scans, and some suggest using abbreviated MRI [aMRI] would be a suitable choice of investigation of obese and high-risk MASLD patients for HCC surveillance, albeit it is challenging to implement in the limited healthcare resource setting [32,33]. However, in our study, only 38 patients [4.7%] had BMI >30 or obesity.

MASH-HCC also has unique features in both pathogenesis and treatment outcomes, although the approach to the treatment of MASLD-related HCC is the same as that of other etiologies [29]. Patients with MASLD-related HCC tended to be older and larger and multifocal tumours and are associated with more cardiovascular and renal comorbidities which would prevent them from benefitting from the curative treatment of HCC [21,29,30,34]. Moreover, Patients with MASLD-related HCC are also underrepresented in the systemic treatment of advanced HCC trials, including immunotherapy [35]. According to the latest data available concerning MASLD-HCC treatment outcome, we acknowledge that the tumour microenvironment [TME] of MASLD-related HCC has resulted in limited response to immunotherapy, and toxicity of immunotherapy, including cardiac and thyroid toxicities, is more common in patients with MASLD-related HCC [22,29,35]. These factors including the demographic of the MASLD patients has put these patients on the edge.

Lean MASLD, Asian Body Fat Composition and Consequence of PNPLA3 Polymorphism in Asian MASLD

Recently, there has been a popular concept of lean MASLD which is prevalent among Asian patients with a body mass index <25 [9,36,37]. In our study, 410 [50.2%] patients had found out to be lean MASLD. This type of lean MASLD is more common in Asia partly due to the increase prevalence of the G allele at patatin-like phospholipase domain-containing protein 3 gene [PNPLA3 rs738409] polymorphism in Asian patients which is contributing to the aberrant fat storage and metabolism leading to MASLD and its complications even in lean patients without metabolic disease [37,38]. The germline PNPLA 3 mutation is also a well-recognised genetic mutation for the development of MASH-related HCC [29].

Some data suggest that the consequence and associated morbidities of lean MASLD is less severe than those of MASLD in patients with a higher body mass index [36,37,39]. Conflictingly to this claim, In the largest biopsy proven International MASLD registry in nine Asian countries between 2006 and 2019, 22% of MASLD patients are non-obese and among the non-obese MASLD, 50% of patients have steatohepatitis and 14% have significant fibrosis [40]. According to Wei et al., although the risk of steatohepatitis and advanced fibrosis is lower in non-obese MASLD patients, they are found to be more insulin resistant, even in normoglycaemic patients [37]. It has also found that the PNPLA 3 genetic variants are more common in lean MASLD patients which is associated with a high risk of HCC development in this patient group [9,37]. This shows that the disease burden of lean MASLD is not benign, and actions including lifestyle modification are the cornerstone to prevent serious consequences and complications of lean MASLD [8,9,41,42].

MASLD in Viral Hepatitis Epidemic Region and MASLD Related HCC with Infected Liver

The prospect of the patients with chronic viral hepatitis especially Hepatitis B with MASLD, is detrimental [13]. The presence of hepatic steatosis favours the development of advanced fibrosis in patients with chronic hepatitis B and increases the risk of HCC development, even in patients who have achieved effective viral suppression with antiviral therapy [43,44]. This bidirectional inverse association between CHB and MASLD highlights the danger and burden of the Asian's MASLD population and the active management of MASLD in CHB patients to prevent further deleterious complications [13]. Although we have screen out the viral hepatitis patients for our study, it was found out that 17 patients [2.08%] had occult hepatitis B detected by having

hepatitis B core antibodies among the study population which highlighted the importance of risk of concurrent viral hepatitis in MASLD patients in our country.

Importance of Early Identification of High-Risk Patients

In 2022, American Association of Clinical Endocrinology published an algorithm for risk stratification of fibrosis in MASLD that can be adopted in the primary care level using non-invasive test FIB-4 and elastography to categorise the patients into low- and high-risk groups. Primary care physicians are taking care of low-risk patients, whereas high-risk patients for cirrhosis will be referred to the hepatologist [45]. This guidance also has highlighted the importance of the endocrinologists and primary care physicians for early identification of patients at risk to take action to prevent further development of cirrhosis and comorbidities [45]. Primary care physicians, who will be the first contact point of patients and their important role in providing health education, risk stratification for cirrhosis, and the development of effective referral network, will have a positive impact on the outcome of MASLD patients. A small study from diabetic clinic at Yangon General Hospital by Ni et al showed that a significant portion of patients with diabetes had abnormal liver function tests along with hepatic steatosis examined by ultrasonography [46]. Which showed that the referral network between the primary care physicians, endocrinologists, hepatologists and cardiologists etc. still have many rooms to developed and patients with cardiovascular and metabolic disease are receiving fragmented care in the country.

Future Direction of MASLD Management

Metabolic-associated steatohepatitis [MASH] has become the one of the major causes of cirrhosis and hepatocellular carcinoma in the United States, the United Kingdom and in some Western countries [47]. There are also rigorous research ongoing on the pathophysiology and pharmacological treatment of MASH-HCC globally [22,48]. Although, there was no available treatment for MASH previously, Resmetirom, an oral liver directed, thyroid hormone receptor beta agonist, was recently approved by US FDA as a first-ever treatment of MASH with fibrosis [49,50]. However, it is still very early to predict the effects of this new medication on the outcomes of this growing public health concern globally.

Limitation of the Study

Yangon Gastrointestinal and Liver Center [YGLC] is a specialist urban liver centre which receives mixed patients

from urban and rural populations. Since the earlier stage MASLD patients are mostly asymptomatic and left out unscreened in the community [18]. The data we retrieved from YGLC only represents hospital-based setting which is liable for getting referred patients or symptomatic MASLD patients. Also, we cannot differentiate between the urban-rural domicile for the patients which we can leverage on geographic distribution of the disease within the country. All the diagnosis of MASLD were based on the imaging including ultrasound and fibroscan and none of the patients had undergone liver biopsy. Biochemical investigations were only done at first time visit.

Conclusion

Proportion of male patients was higher in this study. At the time of diagnosis, minimum age of patients was 16 years. Out of 817 patients, 267 patients were steatosis S3 and 29 patients were fibrosis F4. The study shown positive correlation between Fibroscan-CAP score and BMI, and Fibroscan-CAP and HbA1C. Such correlation was consistent not only steatosis grading and BMI but also steatosis grading and HbA1C. Fibrosis staging was also associated with BMI and HbA1C. Patient with higher BMI and elevated HbA1C was more likely to have higher steatosis and fibrosis level.

Because of the rising trend of MASLD in Southeast Asia and MASLD-related HCC, there is an urgent need for measures to control the MASLD and its outcomes [8,15]. Like most Southeast Asian countries, there is no national strategy to tackle the MASLD and its complications in Myanmar [15]. MASLD in Southeast Asia are younger than in other regions and the western world and the disease burden is also bigger because of the concurrent high prevalence of chronic hepatitis B and genetic susceptibility of the PNPLA3 polymorphism [13,37,38,42,51]. Moreover, Asians are underrepresented in most drug research and this will have an impact on the outcomes of MASLD in Asian patients since the Asians have a stronger genetic risk of MASLD [9,13,37,38,42]. Subsequently, it is imperative to take actions at the national level to educate the public regarding a healthy lifestyle, healthy eating, regular exercise, maintaining healthy body weight, taking proper and regular treatment for type II diabetes and dyslipidaemia and building a proper referral network between the primary care physicians, endocrinologists and hepatologists to prevent and treat MASLD and its complications. In conclusion, the vulnerability of the liver outcomes due to the high prevalence of chronic viral hepatitis, it is imperative that efforts need to apply to prevent or treat the MASLD and its complications in its earlier stage to reduce the disease burden as well as the healthcare burden.

References

1. Worldometer (2024) Myanmar Population.
2. World Health Organization (2024) Myanmar National Action plan for Viral Hepatitis response 2017-2020.
3. Sandhu HS, Roesel S, Sharifuzzaman M, Chunsuttiwat S, Tohme RA (2020) Progress Toward Hepatitis B Control - South-East Asia Region, 2016-2019. *MMWR Morb Mortal Wkly Rep* 69(30): 988-992.
4. Aung WP, Bjertness E, Htet AS, Stigum H, Kjøllesdal MKR (2019) Trends in Diabetes Prevalence, Awareness, Treatment and Control in Yangon Region, Myanmar, Between 2004 and 2014, Two Cross-Sectional Studies. *Int J Environ Res Public* 16(18): 3461.
5. Pengpid S (2023) High prevalence of dyslipidemia and associated factors among adults in a national survey in Myanmar. *International Journal on Disability and Human Development* 22(2): 139-144.
6. Younossi ZM, Golabi P, Paik JM, Henry A, Dongen CV, et al. (2023) The global epidemiology of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH): a systematic review. *Hepatology* 77(4): 1335-1347.
7. Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ (2018) Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. *Hepatology* 67(1): 123-133.
8. Li J, Zou B, Yeo YH, Feng Y, Xie X, et al. (2019) Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999–2019: a systematic review and meta-analysis. *lancet Gastroenterology & hepatology* 4(5): 389-398.
9. Fan J-G, Kim S-U, Wong VW-S (2017) New trends on obesity and NAFLD in Asia. *Journal of Hepatology* 67(4): 862-873.
10. Josol VJD, Salvador PBU, Cruz LLA, Ornos EDB, Tantengco OAG (2024) Trends of nonalcoholic fatty liver research in Southeast Asia from 2004 to 2022: A bibliometric analysis. *Obesity Medicine* 45: 100527.
11. Eslam M, Sarin SK, Wong VW-S, Fan J-G, Kawaguchi T, et al. (2020) The Asian Pacific Association for the Study of the Liver clinical practice guidelines for the diagnosis and management of metabolic associated fatty liver disease. *Hepatology International* 14(6): 889-919.
12. Wong SW, Chan WK (2020) Epidemiology of non-alcoholic fatty liver disease in Asia. *Indian J Gastroenterol* 39(1): 1-8.
13. Yip TCF, Lee HW, Chan WK, Wong GLH, Wong VWS (2022) Asian perspective on NAFLD-associated HCC. *J Hepatol* 76(3): 726-734.
14. Pati GK, Singh SP (2016) Nonalcoholic Fatty Liver Disease in South Asia. *Euroasian J Hepatogastroenterol* 6(2): 154-162.
15. Ong J, Alswat K, Hamid S, El-Kassas M (2023) Nonalcoholic Fatty Liver Disease in Asia, Africa, and Middle East Region. *Clin Liver Dis* 27(2): 287-299.
16. Kanwal F, Neuschwander-Tetri BA, Loomba R, Rinella ME (2024) Metabolic dysfunction-associated steatotic liver disease: Update and impact of new nomenclature on the American Association for the Study of Liver Diseases practice guidance on nonalcoholic fatty liver disease. *Hepatology* 79(5): 1212-1219.
17. Memorial Sloan Kettering Cancer Center (2024) Understanding Your Liver Elastography (FibroScan®) Results.
18. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, et al. (2023) AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. *Hepatology* 77(5): 1797-1835.
19. Kwo PY, Cohen SM, Lim JK (2017) ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. *Am J Gastroenterol* 112(1): 18-35.
20. Jou J, Choi SS, Diehl AM (2008) Mechanisms of disease progression in nonalcoholic fatty liver disease. *Semin Liver Dis* 28(4): 370-379.
21. Piscaglia F, Svegliati-Baroni G, Barchetti A, Pecorelli A, Marinelli S, et al. (2016) Clinical patterns of hepatocellular carcinoma in nonalcoholic fatty liver disease: a multicenter prospective study. *Hepatology* 63(3): 827-838.
22. Anstee QM, Reeves HL, Kotsiliti E, Govaere O, Heikenwalder M (2019) From NASH to HCC: current concepts and future challenges. *Nat Rev Gastroenterol Hepatol* 16(7): 411-428.
23. Yi M, Peng W, Feng X, Teng F, Tang Y, et al. (2022) Extrahepatic morbidities and mortality of NAFLD: an umbrella review of meta-analyses. *Alimentary Pharmacology and Therapeutics* 56(7): 1119-1130.
24. Younossi Z, Tacke F, Arrese M, Sharma BC, Mostafa I, et al. (2019) Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. *Hepatology*

- 69(6): 2672-2682.
25. Wang M, Zhao Y, He Y, Zhang L, Liu J, et al. (2023) The bidirectional relationship between NAFLD and type 2 diabetes: A prospective population-based cohort study. *Nutrition, Metabolism and Cardiovascular Diseases* 33(8): 1521-1528.
 26. Niriella MA, Ediriweera DS, Withanage MY, Darshika S, De Silva ST, et al. (2023) Prevalence and associated factors for non-alcoholic fatty liver disease among adults in the South Asian Region: a meta-analysis. *Lancet Regional Health Southeast Asia* 15: 100220.
 27. Chen Y, Wang X, Wang J, Yan Z, Luo J (2012) Excess body weight and the risk of primary liver cancer: An updated meta-analysis of prospective studies. *European Journal of Cancer* 48(14): 2137-2145.
 28. International Agency for Research on Cancer (2024) Myanmar Global Cancer Observatory.
 29. Llovet JM, Willoughby CE, Singal AG, Greten TF, Heikenwälder M, et al. (2023) Nonalcoholic steatohepatitis-related hepatocellular carcinoma: pathogenesis and treatment. *Nature Reviews Gastroenterology & Hepatology* 20(8): 487-503.
 30. Tan DJH, Ng CH, Lin SY, Pan XH, Tay P, et al. (2022) Clinical characteristics, surveillance, treatment allocation, and outcomes of non-alcoholic fatty liver disease-related hepatocellular carcinoma: a systematic review and meta-analysis. *The Lancet Oncology* 23(4): 521-530.
 31. Koh JH, Wang M, Suzuki H, Muthiah M, Ng CH, et al. (2024) NAFLD and NAFLD-related HCC in Asia: Burden and Surveillance. *Journal of Clinical and Experimental Hepatology* 14(1): 101213.
 32. Gupta P, Soundararajan R, Patel A, Kumar-M P, Sharma V, et al. (2021) Abbreviated MRI for hepatocellular carcinoma screening: A systematic review and meta-analysis. *Journal of Hepatology* 75(1): 108-119.
 33. Park HJ, Kim SY, Singal AG, Lee SJ, Won HJ, et al. (2022) Abbreviated magnetic resonance imaging vs ultrasound for surveillance of hepatocellular carcinoma in high-risk patients. *Liver International* 42(9): 2080-2092.
 34. Chin KM, Prieto M, Cheong CK, Martino MD, Ielpo B, et al. (2021) Outcomes after curative therapy for hepatocellular carcinoma in patients with non-alcoholic fatty liver disease: a meta-analysis and review of current literature. *HPB* 23(8): 1164-1174.
 35. Sangro B, Chan SL, Meyer T, Reig M, El-Khoueiry A, et al. (2020) Diagnosis and management of toxicities of immune checkpoint inhibitors in hepatocellular carcinoma. *Journal of Hepatology* 72(2): 320-341.
 36. Leung JC-F, Loong TC-W, Wei JL, Wong GL-H, Chan AW-H, et al. (2017) Histological severity and clinical outcomes of nonalcoholic fatty liver disease in nonobese patients. *Hepatology* 65(1): 54-64.
 37. Wei JL, Leung JC-F, Loong TC-W, Wong GL-H, Yeung DK-W, et al. (2015) Prevalence and severity of nonalcoholic fatty liver disease in non-obese patients: a population study using proton-magnetic resonance spectroscopy. *Am J Gastroenterology* 110(9): 1306-1314.
 38. Shen J, Wong GL-H, Chan HL-Y, Chan H-Y, Yeung DK-W, et al. (2014) PNPLA3 gene polymorphism accounts for fatty liver in community subjects without metabolic syndrome. *Alimentary Pharmacology & Therapeutics* 39(5): 532-539.
 39. Tang A, Ng CH, Phang PH, Chan KE, Chin YH, et al. (2023) Comparative Burden of Metabolic Dysfunction in Lean NAFLD vs Non-lean NAFLD - A Systematic Review and Meta-analysis. *Clin Gastroenterol Hepatol* 21(7): 1750-1760.
 40. Tan EX-X, Lee JW-J, Jumat NH, Chan W-K, Treeprasertsuk S, et al. (2022) Non-obese non-alcoholic fatty liver disease (NAFLD) in Asia: an international registry study. *Metabolism* 126: 154911.
 41. Ahadi M, Molooghi K, Masoudifar N, Namdar AB, Vossoughinia H, et al. (2021) A review of non-alcoholic fatty liver disease in non-obese and lean individuals. *J Gastroenterol Hepatol* 36(6): 1497-1507.
 42. Nakatsuka T, Tateishi R, Koike K (2022) Changing clinical management of NAFLD in Asia. *Liver Int* 42(9): 1955-1968.
 43. Chan AWH, Wong GLH, Chan H-Y, Tong JHM, Yu YH, et al. (2017) Concurrent fatty liver increases risk of hepatocellular carcinoma among patients with chronic hepatitis B. *Journal of Gastroenterology and Hepatology* 32(3): 667-676.
 44. Hyeki C, Young C, Jeong-Hoon L, Youn CY, Yeul NJ, et al. (2020) Radiologic Nonalcoholic Fatty Liver Disease Increases the Risk of Hepatocellular Carcinoma in Patients With Suppressed Chronic Hepatitis B. *Clinical Gastroenterology* 54(7): 633-641.
 45. Cusi K, Isaacs S, Barb D, Basu R, Caprio S, et al. (2022) American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and

Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD). *Endocrine Practice* 28(5): 528-562.

46. Ni H, Soe H, Htet A (2012) Determinants of Abnormal Liver Function Tests in Diabetes Patients in Myanmar. *International Journal of Diabetes Research* 1: 36-41.
47. Huang DQ, El-Serag HB, Loomba R (2021) Global epidemiology of NAFLD-related HCC: trends, predictions, risk factors and prevention. *Nat Rev Gastroenterol Hepatol* 18(4): 223-238.
48. Wang Y, Fleishman JS, Li T, Li Y, Ren Z, et al. (2024) Pharmacological therapy of metabolic dysfunction-associated steatotic liver disease-driven hepatocellular carcinoma. *Front Pharmacol* 14: 1336216.
49. Harrison SA, Bedossa P, Guy CD, Schattenberg JM, Loomba R, et al. (2024) A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. *New England Journal of Medicine* 390(6): 497-509.
50. Brett AS (2024) Resmetirom, the First Drug Approved by the U.S. FDA for Treating Patients with Nonalcoholic Steatohepatitis. *NEJM Journal Watch*.
51. Kam LY, Huang DQ, Teng MLP, Takahashi H, Tanaka K, et al. (2022) Clinical Profiles of Asians with NAFLD: A Systematic Review and Meta-Analysis. *Dig Dis* 40(6): 734-744.