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Original Article **GMSMJ** Greater Mekong Subregion Medical Journal

Efficacy of Fixed-dose Combination of Sofosbuvir and Ledipasvir (SOF/LDV) ± Ribavirin (RBV) in Patients (n=130) Infected with HCV Genotype 6 (Real World Myanmar Experience)

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Abstract:

Background: The prevalence rate of HCV Genotype 6 is estimated to account for 36% of all HCV infections in Myanmar.

Objective: This study is aimed to assess the efficacy of SOF/LDV ± RBV in patients infected with HCV genotype 6.

Methods: We performed the prospective and observational study of 130 patients infected with chronic HCV genotype 6 (both treatment-naïve and treatment-experienced) was performed. The patients were treated with SOF/LDV ± RBV for 12 or 24 weeks.

Results: Overall SVR (sustained virologic response) rate was 77% of patients. Higher SVR rate was noted among the cirrhotic patients (p-value = 0.003) and treatment-experienced patients (p-value = 0.008). Co-infection with HBV was seen in 7 patients and all these patients achieved SVR12. In the study cohort, 104 patients were treatment-naïve and 26 patients were treatment-experienced. SVR rates of treatment-naïve patients with or without cirrhosis treated with SOF/LDV regimen for 12 weeks was 65% (n=47), SOF/LDV/RBV for 12 weeks was 82% (n=9) and SOF/LDV for 24 weeks was 91% (n=19). Twenty-six treatment-experienced patients were treated with SOF/LDV/RBV for 24 weeks and achieved 96% SVR rate.

Conclusion: SOF/LDV ± RBV therapy achieved SVR12 in 77% of all categories of genotype 6 patients demonstrating the unsatisfactory response and efficacy in the era of SVR rates approaching 100% in other genotypes. Therefore, our real-life experience showed genotype 6 as the most difficult to treat genotype. However, it was noted that the addition of RBV or extension of treatment duration can increase the SVR rates significantly.

Keywords: Hepatitis C virus, genotype 6, sofosbuvir, ledipasvir, ribavirin

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Introduction

Globally, an estimated 71 million people have chronic hepatitis C infection. A significant number of those who are chronically infected will develop cirrhosis or liver cancer. Approximately 399,000 people die each year from hepatitis C, mostly from cirrhosis and hepatocellular carcinoma[1]. HCV Genotypes 1, 2 and 3 are widely distributed globally and Genotypes 4 and 5 are found mainly in Africa and Middle East. Genotype 6 is major genotype distribution in Southeast Asia especially in Thailand, Vietnam and Myanmar, detected in 10-60% of all HCV patients[2]. In Myanmar, HCV genotype 6 is the one of the most prevalent accounting 49% of all HCV patients. Regarding genotype distribution in Myanmar, HCV genotype 6 was the most prevalent genotype (49%), followed by HCV genotypes 3 (39%), 1 (11%), and 2 (0.7%)[3]. In Myanmar, HCV genotype 6 was most often found in patients in the northern cities and HCV genotype 3 in the southern and western cities, suggesting that there are regional differences in HCV genotype distribution[3].

In recent years, the development of drugs that directly interfere with HCV replication has changed the landscape of HCV treatment and there are now effective combinations of direct-acting antiviral agents for most patients. Ledipasvir (Gilead Sciences) is a new HCV NS5A inhibitor and Sofosbuvir is a nucleotide analogue inhibitor of the HCV NS5B polymerase approved for the treatment of HCV in combination with NS5A inhibitor such as ledipasvir, and ribavirin.

For the treatment-naïve HCV genotype 6 patients, APASL (Asian Pacific Association for the Study of the Liver) recommend SOF/LDV without ribavirin for 12 weeks in patients with no cirrhosis (evidence level – B1) and SOF/LDV with ribavirin for 12 weeks for those with compensated cirrhosis (evidence level – B1)[4].

According to EASL (The European Association for the Study of the Liver) HCV Guidelines 2016, treatment-naïve patients infected with genotype 6 with or without compensated cirrhosis can be treated with SOF/LDV without ribavirin for 12 weeks (evidence level – B1). And treatment-experienced patients with or without compensated cirrhosis should be treated with SOF/LDV with ribavirin for 12 weeks (evidence level – B1)[5].

AASLD (American Association for the Study of the Liver Diseases) 2016 Guidelines recommend that treatment-naïve patients with or without cirrhosis should be treated with SOF/LDV for 12 weeks (Rating – Class IIA, Level B). For Peg-IFN/SOF-experienced patients with or without cirrhosis should be treated with SOF/LDV 12 weeks (Rating – Class IIA, Level B)[6].

Although HCV Genotype 6 is encountered predominately in Southeast Asia, data on optimal treatment strategy is limited. Fixed-dose combination of sofosbuvir and ledipasvir (SOF/LDV) is the first all-oral DAA (direct acting antiviral) approved for HCV Genotype 6. For the optimal treatment regimen for the patients with genotype 6, the international treatment guidelines such as APASL, AASLD, and EASL guidelines are followed and at the time of this study, SOF/LDV with or without ribavirin is the regimen of choice for the HCV genotype 6. But the evidence grading of these guidelines are not strong enough to adopt the most effective guidelines for the resource-limited country like Myanmar. Therefore, this study is aimed to assess the efficacy of available generic version of fixed-dose combination of Sofosbuvir

(400 mg) and Ledipasvir (90 mg) (SOF/LDV) with or without ribavirin in Myanmar patients infected with HCV genotype 6.

Methods

This is the open-label, real-world prospective non-randomized observational study conducted at a single centre, Yangon GI and Liver Centre, in Yangon, Myanmar from January 2016 to September 2017 as an investigator-initiated study. In this single-centre study, all the patients received a fixed-dose combination tablet containing 400 mg of sofosbuvir and 90 mg of ledipasvir, administered orally once daily. Ribavirin was administered orally twice daily, with the dose determined according to body weight (1000 mg daily in patients with a body weight <75 kg, and 1200 mg daily in patients with a body weight ≥75 kg).

In Myanmar, the available generic versions of SOF/LDV (400mg/90mg) are Ledifos® manufactured by Hetero, LediHep® by Zydus and MyHep LVIR® by Mylan. The monthly cost of generic SOF/LDV/RBV combination therapy varies between 250-300 USD with different manufacturers from India, Pakistan, and Bangladesh. As Myanmar does not have the National Health System nor the medical insurance system, the medications and investigations were paid for by the patients themselves and informed consents were taken from all patients.

SOF/LDV without ribavirin for 12 weeks was given in treatment-naïve patients without cirrhosis. Treatment-naïve patients with compensated cirrhosis were given SOF/LDV with ribavirin for 12 weeks or 24 weeks without ribavirin if ribavirin was ineligible or if patients were intolerant to ribavirin. PEG-IFN/RBV-experienced patients with or without compensated cirrhosis were treated with SOF/LDV with ribavirin for 24 weeks.

Patients

Total 130 patients infected with chronic HCV genotype 6 (both treatment-naïve and treatment-experienced) were enrolled. Eligible patients were men and women who were older than 12 years old, who had serum HCV RNA level > 25 IU/mL with HCV genotype 6, patients with or without compensated cirrhosis, treatment-naïve patients and those who relapsed after PEG-IFN/RBV-containing regimen. Patients with hepatitis B virus (HBV) co-infection and/or human immunodeficiency virus (HIV) co-infection were included in the study. Patients were excluded if they were pregnant, willing to conceive in the near feature, or lactating and if they had chronic kidney disease with creatinine clearance < 30 mL/min as estimated by the Cockcroft-Gault method. Patients with significant medical co-morbidities such as ischemic heart diseases, chronic pulmonary diseases, psychiatric disorders and hepatocellular carcinoma (HCC) were also excluded from the study.

HCV Genotype were analyzed by the use of the Roche® cobas® 4800 system. The presence of cirrhosis or advanced fibrosis (F3/F4) was assessed using Fibroscan® (Echosense, France), abdominal ultrasonography, aspartate aminotransferase: platelet ratio index (APRI), and clinical evaluation. The presence of cirrhosis was defined as a FibroScan score of more than 12.5 kPa (on a scale of 1.5 to 75.0 kPa, with higher scores indicating a greater degree of fibrosis) and/or an APRI of more than 2 (with higher scores indicating a greater likelihood of extensive fibrosis).

Assessments

HCV viral loads were analyzed by Roche® COBAS® HCV quantitative nucleic acid test 4800 system, COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Assay. The lower limits of detection and quantification were 15 IU per milliliter and 25 IU per milliliter, respectively. Serum HCV RNA levels were measured at baseline, week 4, 12, 24 (if applicable) and 12 weeks after the end of treatment.

Patients were evaluated clinically along with laboratory testing, at entry and every 4 weeks during treatment and 12 weeks after the end of treatment to assess safety of treatment. Assessments during treatment included standard laboratory testing, serum HCV RNA, vital signs, electrocardiography, and symptom-directed physical examinations. All adverse events were recorded and graded according to a standardized scale. Anemia was defined as mild (hemoglobin (Hb) values between 10-12 g/dL), moderate (Hb values between 8.5-10 g/dL), or severe (Hb values less than or equal to 8.5 g/dL). Occurrence of anemia during treatment was managed by 200 mg RBV dose reduction, use of erythropoietin, and/or blood transfusions.

Outcomes and endpoints

The primary efficacy end point was the rate of sustained virologic response (SVR), defined as the absence of quantifiable HCV RNA in serum (<25 IU per milliliter), at 12 weeks after the end of therapy (SVR12) among all patients. Virologic relapse was defined as a confirmed HCV RNA level of 25 IU per milliliter or more 12 weeks after receipt of the last dose of drug among patients who completed treatment.

Statistical analyses

Data analysis was done by SPSS software (v.16). The data were described using counts and proportions for categorial data and mean ± standard deviation if the data showed a non-parametric distribution. Categorical data were calculated by Chi-square and Fisher's Exact Test. Continuous data was calculated by ANOVA (Analysis of Variance). The level of statistical significance was set at a two-tailed p-value of < 0.05.

Study oversight

This study received approval from the Institutional Review Board or independent ethics committee to review the data for publication purposes and was conducted in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice guidelines and local regulatory requirements. The investigators agreed to maintain confidentiality of the data and all the authors had access to the data and assume responsibility for the integrity and completeness of the reported data.

Results

Demographics and baseline characteristics

Total of 145 patients were screened for this study and received the fixed-dose combination of sofosbuvir and ledipasvir (SOF/LDV) with or without ribavirin for 12 or 24 weeks according to the cirrhosis status and the treatment history, at Yangon GI and Liver Centre, between January 2016 and September 2017. Among them, 15 patients were excluded because of the

Table 1 Baseline demographic and laboratory characteristics

Characteristics	12-week regimen		24-week regimen		p-value
	SOF/LDV x 12 weeks (n = 72)	SOF/LDV/ RBV x 12 weeks (n = 11)	SOF/LDV x 24 weeks (n = 21)	SOF/LDV/RBV x 24 weeks (n = 26)	
Age – years					
Mean	50.9 (±12.1)	55.8 (±13.2)	54.5 (±11.1)	57.1 (±8.8)	0.88
Range	15 – 76	27 – 72	26 – 69	37 – 79	
Body Mass Index – kg/m²					
Mean	22.6 (±2.9)	21.5 (±2.0)	22.3 (±3.0)	24.6 (±3.0)	**0.007**
Range	18 – 31	19 – 26	19 – 28	20 – 32	
Sex – n (%)					
Male	37 (51)	3 (27)	8 (38)	5 (19)	0.174
Female	35 (49)	8 (83)	13 (62)	21 (81)	
Subtype of Genotype 6 – n (%)					
Subtype 6 n	4 (6)	1 (9)	1 (5)	6 (23)	
Subtype 6 m	8 (11)	2 (18)	-	-	**0.017**
Subtype 6 cL	47 (65)	8 (73)	19 (90)	14 (54)	
Unspecified	13 (18)	-	1 (5)	6 (23)	
HCV RNA (Quantitative Viral Load)					
≥ 800,000 IU/mL	53	9	14	15	0.367
< 800,000 IU/mL	19	2	7	11	
Cirrhosis status – n (%)					**< 0.0001**
No cirrhosis	72 (100)	-	-	5 (20)	
With compensated cirrhosis	-	11 (100)	21 (100)	21 (80)	
HCV/HBV Co-infection	4	1	-	2	0.622
ALT – IU/mL, mean (±SD)	53.8 (±35.1)	59.0 (±35.0)	74.7 (±55.3)	66.3 (±37.0)	0.149
Total Bilirubin – mg/dL, mean (±SD)	0.85 (±0.48)	1.62 (±3.0)	1.07 (±0.64)	1.16 (±1.08)	0.138
Albumin – g/dL, mean (±SD)	5.5 (±0.9)	3.4 (±0.4)	3.5 (±0.4)	3.4 (±0.5)	0.606
Hemoglobin – g/dL, mean (±SD)	13.1 (±1.8)	12.4 (±0.9)	12.6 (±1.3)	12.4 (±2.2)	0.233
Platelets count – 10^9/L, mean (±SD)	226.8 (±72.1)	173.4 (±56.4)	146.4 (±50.6)	187.0 (±126.0)	**0.001**
AFP – IU/mL, mean (±SD)	6.2 (±7.8)	4.6 (±2.3)	6.8 (±4.8)	8.0 (±5.4)	0.499
Creatinine* – mg/dL, mean (±SD)	0.97 (±0.30)	1.00 (±0.71)	0.90 (±0.30)	0.98 (±0.28)	0.961

Data expressed as mean ± SD or number (%)
SOF = Sofosbuvir, LDV = Ledipasvir, RBV = Ribavirin, ALT = Alanine aminotransferase, AFP = Alpha-fetoprotein
*Estimated by the Cockcroft-Gault method

insufficient follow-up and incomplete treatment. Table 1 shows the baseline demographic and laboratory characteristics of the remaining 130 patients classified by the different treatment regimens.

The mean age at the time of treatment initiation was 53.2 years (SD = 11.6) and 43% of patients were male (n=56) and 57% were female (n=74). The majority of patients were treatment-naïve (80%, n=104) and 26 patients (20%) had a history of previous PEG-IFN/RBV therapy. About 40% (n=53) of patients had cirrhosis at the time of treatment initiation. The median BMI (Body Mass Index) of the entire group was 22.9 kg/m^2 (SD = 3.0). The mean baseline viral load prior to start of treatment was 3.3 million IU/mL (range 11,000 to 22,322,717) with 61 patients (48%) who had HCV RNA ≥ 800,000 IU/mL.

Regarding the pre-treatment liver functions assessment, the pretreatment mean albumin level was 4.0 g/dL (SD = 0.4), the mean total bilirubin was 1.0 mg/dL (SD = 1.1), and the mean platelet count was 201 x 10^9/L (SD = 86.9). The mean serum creatinine level was 0.97 mg/dL (SD = 0.3), and the mean AFP (Alpha-Feto Protein) level was 6.5 IU/mL (SD = 6.6).

Among all the patients, 7 patients were co-infected with chronic hepatitis B infection. of these HCV/HBV co-infected patients, 5 were treatment-naïve and 2 had the history of previous PEG-IFN/RBV therapy. All 7 patients co-infected with HCV/HBV achieved SVR12.

Efficacy

Overall SVR rates of entire group was 77% (n = 100). Among the patients who reached SVR 12, males were 43% (n = 43/100) and females were 57% (n = 57/100). The higher SVR rate (90%) was noted among the cirrhotic patients (n = 48/53) than cirrhotic patients (68%, n = 52/77). Among the treatment-naïve patients (n = 104), 75 patients (72%) achieved SVR whereas 25 out of 26 treatment-experienced patients (96%) achieved SVR 12. The patients with baseline HCV RNA viral load < 800,000 IU/mL achieved SVR rate of 59% (n = 59/100) whereas among those with viral load ≥ 800,000 IU/mL, there were 41% of patients (n = 41/100) who achieved SVR 12. Table 2 shows the overall treatment outcomes of patients infected with HCV genotype 6.

Moreover, SVR rates were analyzed according to the treatment regimens. Of the entire group, 72 treatment-naïve patients without cirrhosis received SOF/LDV for 12 weeks, resulting in 65% SVR rate (n = 47). Remaining 32 treatment-naïve patients with compensated cirrhosis received SOF/LDV for 24 weeks (n = 21) (if they are ribavirin-ineligible or ribavirin-intolerant) and SOF/LDV with ribavirin for 12 weeks (n = 11). 91% of patients (n = 19) achieved SVR 12 among those who received SOF/LDV without ribavirin for 24 weeks and 82% (n = 9) achieved SVR 12 in patients who received SOF/LDV with ribavirin for 12 weeks. For the participants who had a treatment history with PEG-IFN/RBV, SOF/LDV with ribavirin for 24 weeks was adopted. Among these 26 treatment-experienced patients, 25 patients (96%) achieved SVR 12 and only one patient relapsed. Table 3 and Figure 1 show the SVR rates according to the different treatment regimens.

Safety

The patients were well-tolerated to drugs and no one discontinued the treatment through the study. There were no incidents of serious adverse events and no discontinuation of treatment due to adverse events during the course of this study. The most frequently reported side effects were fatigue (20%) and anemia (17%). Majority of these side effects were reported by patients who received the treatment regimen containing ribavirin. Among the entire group, the dose of ribavirin had to be reduced in 16 patients (12%) and only 6 patients needed the erythropoietin-stimulating agents for the correction of anemia but no blood transfusions were necessary.

Discussion

This study of efficacy of generic version of SOF/LDV with or without ribavirin in the treatment of patients with chronic HCV genotype 6 is one of the largest real-world studies. Higher SVR rates of have been reported with the all oral combination of SOF/LED for 12 weeks in a clinical trial and real-world Vietnamese study[7,8]. However, in our study, treatment with the once-daily, interferon-free, single-tablet regimen of SOF/LDV ± RBV resulted in a sustained virologic response in 77% of patients with HCV genotype 6. Therefore, the SVR rates in our study were somewhat lower than those reported.

Table 2 Overall outcomes of HCV genotype 6 patients

		SVR 12 Achieved		SVR 12 Not achieved		p-value
		Number	%	Number	%	
Overall		**100**	**77**	**30**	**23**	
Sex	Male	57	57	13	43	1.000
	Female	43	43	17	57	
Cirrhosis status	Cirrhosis	48	48	5	17	**0.003**
	No cirrhosis	52	52	25	83	
Treatment History	Treatment-naïve	75	75	29	97	0.008
	Treatment-experienced	25	25	1	3	
0.831BMI	BMI < 25	74	74	24	80	0.684
	BMI ≥ 25	26	26	6	20	
Subtype of HCV genotype 6	Subtype 6 n	8	8	4	13	0.831
	Subtype 6 m	8	8	2	7	
	Subtype 6 cL	68	68	20	67	
	Unspecified	16	16	4	13	
HCV RNA	< 800,000 IU/mL	59	59	2	7	**0.000**
	≥ 800,000 IU/mL	41	41	28	93	

Data expressed as n and %
SVR12 = sustained virologic response at 12 weeks after the end of therapy

Throughout the development of HCV therapy, cirrhosis remains to indicate low rates of response in regimens that include SOF, LDV or DCV[9]. But, one of the important findings of our study was that cirrhotic patients achieved about 90% SVR with SOF/LDV/RBV for 12 weeks or SOF/LDV for 24 weeks regimens. Prior studies revealed that treatment-experienced patients reached lower SVR rates[10]. However, in our study, patients who had the previous treatment history had greater SVR rates (96%, n=26/25) compared to treatment-naïve patients (72%, n=75/104). These study results could be justified by the addition of ribavirin and the extension of treatment duration up to 24 weeks in treatment-experienced patients.

There were a significant association between SVR and each treatment regimen (p =0.004). But no conclusion regarding the superiority of the treatment regimen containing ribavirin over the regimen without ribavirin could be made due to the observational nature of our study. Our study results suggested that the addition of ribavirin improved the efficacy of SOF/LDV in the treatment of HCV genotype 6 patients. Also, treatment-experienced patients with or without compensated cirrhosis received SOF/LDV/RBV for 24 weeks, so groups that received 12 or 24 weeks of SOF/LDV/RBV were not comparable. Therefore, assessment between treatment duration could not be done. However, according to our real world Myanmar experiences, the addition of ribavirin to regimen of SOF/LDV and/or

Table 3 SVR rates by treatment regimens of patients with HCV genotype 6

	Regimens								p-value
	SOF/LDV x 12 weeks		SOF/LDV/RBV x 12 weeks		SOF/LDV x 24 weeks		SOF/LDV/RBV x 24 weeks		
	No.	%	No.	%	No.	%	No.	%	
SVR Achieved	47	65	9	82	19	91	25	96	**0.004**
Virologic Failure	25	35	2	18	2	9	1	4	

Data expressed as n and %

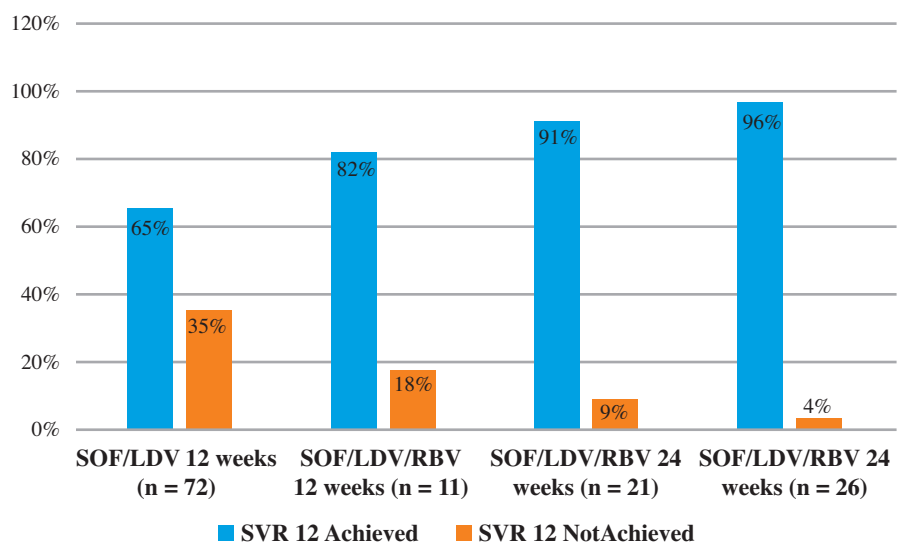

Figure 1 SVR rates by treatment regimens of patients with HCV genotype 6

extension of treatment duration may increase the SVR rates and this should be applied for the guidance of management of HCV genotype 6 patients.

When the data were analyzed by the subtypes of HCV genotype 6, there were 67% (n=20/30) of subtype 6-cL patients who had virologic failures. Thus, another finding of our study is that subtype 6-cL is the most common and difficult to treat subtype in Myanmar although this is not statistically significant.

The most common adverse effects in our study were fatigue, insomnia, and headache. While 17% of patients experienced adverse effects that led to modification and/or interruption of ribavirin, no one discontinued treatment suggesting that ribavirin was tolerable in most patients. Therefore, SOF/LDV ± RBV was safe and well-tolerated with the safety profile consistent with the known effects of ribavirin.

This study has the limitations related to its open-label, non-randomized and observational nature and real-world design including potential physician prescribing bias, local practice discrepancies, and data entry errors. Another limitation of our study is that we do not have analysis of virologic failures but we expected that treatment failures would be predominantly associated with resistance-associated variants.

Conclusion

Among a large cohort study of chronic HCV genotype 6, treatment with all-oral SOF/LDV achieved SVR 12 in 77% of patients, demonstrating the unsatisfactory response and efficacy of this treatment regimen in Myanmar. Therefore, it can be concluded that according to Myanmar experience of 130 patients, genotype 6 was found to be most difficult

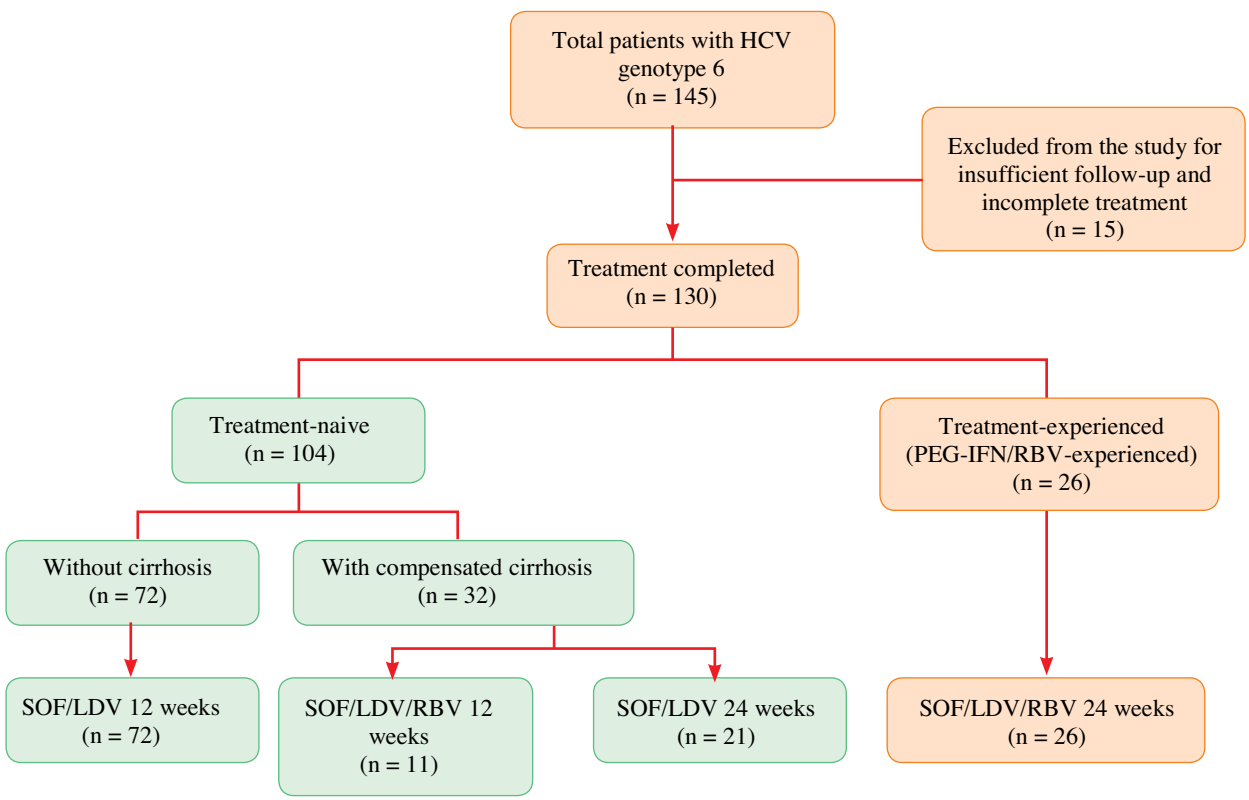

Figure 2 Flow Chart – Outline of the study treatment scheme for patients

to treat genotype. The increased efficacy will be achieved with addition of RBV to SOF/LDV and/or extension of treatment duration or more effective and pan-genotypic regimen such as sofosbuvir and velpatasvir.

Conflict of interest

All authors do not have any conflict of interest.

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Prevalence and Associated Factors of Underweight Status among Children Aged 2-4 Years at Child-Care Centers of Wiang Subdistrict, Chiang Khong District, Chiang Rai Province

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Abstract:

Background: Underweight is an important problem among preschool age children and mostly related to undernutrition. Because nutritional problems among children living along the border of Thailand may differ from those living in the city, a survey to identify the prevalence and associated factors is needed.

Objective: The study aimed to determine the prevalence and factors associated with underweight status among children aged 2-4 years living in Chiang Khong District of Chiang Rai Province

Methods: We conducted a cross-sectional study among children attending six child-care centers in Wiang Subdistrict, Chiang Khong District, Chiang Rai Province. The child's current weight and height were reviewed from a growth record program. Parents responded to a questionnaire about nutritional knowledge and practices.

Statistical analysis: Descriptive statistics was used to analyse population characteristics. Comparison between groups were analysed using Chi-Square test or Fisher's Exact as appropriate.

Results: One hundred and seventy children were enrolled. In all, 52 (30.59%), 112 (65.88%) and 6 (3.53%) children were categorized as underweight, normal and overweight, respectively. Hill tribe was the only factor associated with underweight children. Parents of normal or overweight children had better knowledge than those of underweight children including the importance of daily breakfast, consuming milk daily, meat and eggs diet and having seasonal fruits instead of sweets or snacks. Accordingly, normal or overweight children received more appropriate daily nutrition compared with underweight children including daily breakfast, fruit, meat, eggs and iron-rich foods.

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Conclusion: Nutritional knowledge and practices are important factors related to growth among children living at Chiang Khong District, Chiang Rai Province.

Keywords: underweight, day care center

Background

Currently, a report on the nutritional situation of Thai children described a double increase of undernutrition status children under 5 years (stunted 11% and wasted 5%)[1]. Undernutrition is an important factor affecting a child's physical and mental development. In addition, undernutrition status children are more vulnerable to disease and death[2]. For those reasons, good nutrition should be started from infancy to early childhood (1 to 5 years of age)[3]. Nutritional status of children aged 1 to 5 years is an important indicator of overall health and a fundamental influence to reach their full potential of child development.

Wiang Subdistrict of Chiang Khong District, Chiang Rai Province is an area of multinational populations living both in town and hill tribe areas. Although many child-care centers are located in this area, the nutritional status of children has not been well studied. The study aimed to determine the prevalence and associated factors of underweight status among children aged 2 to 4 years living in Wiang Subdistrict, Chiang Khong District of Chiang Rai Province. The result may be useful for planning guidelines to solve the underweight problem of children living in this area.

Methods

We conducted a cross-sectional study at six child-care centers in Wiang Subdistrict, Chiang Khong District, Chiang Rai Province. After obtaining parental consent, we reviewed the data collected of children aged 2 to 4 years from the INMU-Thai Growth Program including the child's age, sex, height, and weight. We categorized children's status in three groups, underweight, normal and overweight, based on weight index for age and height references of the Department of Health[4]. Parents or caregivers responded to the questionnaire about nutrition knowledge and food handling practices for their child. Levels of nutrition knowledge were classified as good, average and poor using total scores of 6 to 8, 3 to 5 and 0 to 2, respectively. Levels of food handling practices were classified as very good, good, average and need improvement using average scores of 3.25 to 4.00, 2.50 to 3.24, 1.75 to 2.49 and 1.00 to 1.74, respectively.

Statistical analysis

Descriptive statistics was used to analyse population characteristics. Comparison between groups were analysed by using Chi-Square test or Fisher's exact test as appropriate.

Results

In all, 170 children and caregivers were recruited from six child-care centers. Thirty-five (20.59%) and 135 (79.41%) were town and hill tribe populations, respectively. Children were categorized in three groups, 52 (30.59%), 112 (65.88%) and 6 (3.53%) as underweight, normal and overweight, respectively (Table 1).

Table 1 Data of normal/overweight and underweight children

Data	Normal/overweight n (%)	Underweight n (%)	P value*
Total children	118	52	
Caregiver			0.700
Parents	97 (82.2)	44 (84.6)	
Relatives or others	21 (17.8)	8 (15.4)	
Age of caregiver (year)			0.578
< 30	49 (41.5)	21 (40.4)	
30-39	39 (33.1)	16 (30.8)	
40-49	16 (13.6)	11 (21.2)	
≥ 50	14 (8.3)	4 (7.7)	
Education of caregiver			0.289
High school or lower	58 (49.2)	30 (57.7)	
Above high school	56 (47.5)	22 (42.3)	
No data	4 (3.4)	0 (0.0)	
Sibling number			0.630
1	25 (21.2)	10(19.2)	
2-4	79 (66.9)	33 (63.5)	
< 4	14 (11.9)	9 (17.3)	
Family income (Baht/month)			0.394
< 5,000	38 (32.2)	13 (25.0)	
5,000-10,000	53 (44.9)	30 (57.7)	
> 10,000	25 (21.2)	9 (17.3)	
No data	2 (1.7)	0 (0.0)	
Population			< 0.001
Town	35 (29.7)	0 (0.0)	
Hill tribe	83 (70.3)	52 (100.0)	
Gender	54 (45.8)	25 (48.1)	0.868
Male			
Birth weight (gram)			0.813
< 2,500	8 (6.8)	5 (9.6)	
2,500 – 3,500	98 (83.1)	42 (80.8)	
> 3,500	12 (10.2)	5 (9.6)	

* *Chi-square test*

No differences of family and child history were found between the normal/overweight and underweight groups. However, all underweight children were hill tribe people (Table 1).

The overall levels of knowledge did not differ between the normal/overweight and underweight groups. However, caregivers of underweight children exhibited significantly poorer knowledge on some items i.e. importance of daily breakfast and daily milk and protein intake for children and providing seasonal fruits instead of sweets or snack food (Table 2).

The overall levels of food handling practices did not differ between the two groups. However, caregivers of normal/overweight children followed nutrition principles significantly better than those of underweight infants especially providing everyday breakfast, fruit, meat, eggs and iron-rich foods (Table 3).

When we compared nutrition knowledge between caregivers living in town and hill tribes, no difference was found between the two groups. However, differences in food handling practices comprised eating breakfast and fruit daily (data not presented).

Discussion

Although related studies described the influence of family characteristics and child history on the nutritional status[5-14], we found no differences of those factors between the normal/overweight and underweight groups in this study. However, one noticeable factor was all underweight children were hill tribe people, e.g., Hmong, Yao and Tai Lue, living in

Table 2 Caregiver's nutrition knowledge of normal/overweight and underweight children

Nutrition knowledge	Normal/overweight n (%)	Underweight n (%)	P value*
Total caregivers	118	52	
Fat and vegetable or animal oils are not necessary for children	69 (58.5)	32 (61.5)	0.738
Vegetables provide energy for the body	22 (18.6)	12 (23.1)	0.506
Flour, rice and sugar help to repair the worn parts of the body	32 (27.1)	16 (30.8)	0.626
Breakfast is an important meal	116 (98.3)	47 (90.4)	0.017
Daily milk intake is suitable for the growth of children	117 (99.2)	47 (90.4)	0.004
Meat and eggs are essential food for children	118 (100.0)	47 (90.4)	0.001
Children should have seasonal fruits instead of sweets or snacks	115 (97.5)	45 (86.5)	0.005
Eating fruit and vegetable is better for the digestive system	117 (99.2)	49 (94.2)	0.051
Levels of nutrition knowledge			0.592
- Very good	75 (63.6)	30 (57.7)	
- Good	41 (34.7)	20 (38.5)	
- Poor	2 (1.7)	2 (3.8)	

* *Chi-square test*

the hills. These tribes had different family characteristics and lifestyle from people living in town. They often had many children and low incomes. In addition, living in the hills may present a limitation in providing adequate nutrients for their children.

This study demonstrated the effect of caregivers' nutrition knowledge on food handling practices for children which corresponded to the results of related studies[6,13]. From that result, some issues should be emphasized, i.e., providing five main food groups of nutrients is essential for child growth and development and the importance of daily breakfast.

From the above, we realized that providing nutrition knowledge for caregivers is the key success factor to modify food practice behavior and finally to solve the underweight problem. However, poverty and language barriers are challenging problems among hill tribes. Providing education using local language and monitoring food handling practices at home may provide solutions. In addition, nutritional support including daily breakfast and adequate food supplement should be provided at child-care centers.

Currently, there are some efforts to improve growth and nutritional status of children at these child-care centers, e.g., monitoring serial growth, supporting nutritional practices and providing education. Our study could not demonstrate any outcome of the activities performed due to the study design and time limitation. However, we believe that the result of this study will be the starting point revealing the underweight problem among children especially hill tribes living along the Thai border. Such evidence may lead to creating policies or guidelines to improve nutritional status and overall health of hill tribe children and those living along the Thai border in the future.

Table 3 Caregiver's food handling practice for normal/overweight and underweight children

Food handling practice	Normal/overweight n (%)	Underweight n (%)	P value*
Total caregivers	118	52	
The child eats 3 meals every day	96 (81.4)	36 (69.2)	0.063
The child eats breakfast every day	88 (74.6)	28 (53.8)	0.006
The child eats at least 3 scoops of rice or flour a day	64 (54.2)	24 (46.2)	0.322
The child eats vegetable every day	65 (55.1)	22 (42.3)	0.134
The child eats fruit every day	74 (63.7)	22 (42.3)	0.012
The child eats meat every day	79 (66.9)	26 (50.0)	0.030
The child drinks at least 1 glass or box of milk a day	97 (82.2)	37 (71.2)	0.082
The child eats at least 1 egg every day	69 (58.5)	17 (32.7)	0.003
The child eats foods containing iron e.g. liver, blood, etc.	28 (23.7)	5 (9.6)	0.030
Levels of food handling practice			0.174
- Good-very good	116 (98.3)	50 (96.2)	
- Average-need improvement	2 (1.7)	2 (3.8)	

* *Chi-square test*

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Comparison of Perinatal Complications between Thai and Foreign Pregnant Women at Chiang Khong Crown Prince Hospital, Chiang Rai Province

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Abstract:

Background: The number of foreign pregnant women living at the border of Thailand is increasing. Maternal and neonatal problems of this group may differ from those of Thai pregnant women. Therefore, a study of their perinatal problems may lead to better understanding and improve maternal and child health of foreign women in Thailand.

Objective: The study aimed to compare the rate of perinatal problems between foreign and Thai pregnant women at Chiang Khong Crown Prince Hospital, Chiang Rai Province.

Study design: Cross-sectional study

Methods: We retrospectively reviewed medical records of foreign and Thai pregnant women attending Chiang Khong Crown Prince Hospital between October 1, 2018 and September 30, 2019. The review included maternal factors, perinatal and natal complications, infants' gestational age and birth weight.

Results: In all, 501 pregnant women were enrolled of which 328 (65.45%) and 173 (34.53%) were Thai and foreign, respectively. Maternal age more than 35 years among Thai pregnant women (10.67%) was more frequent than those in the foreign group (4.62%). The rates of anemia, hepatitis B carrier and history of abortion more than 2 times among foreign pregnant women (19.65, 6.36 and 5.20%, respectively) were significantly higher than those of Thai pregnant women (11.59, 2.74 and 1.83%, respectively). The rate of low birth weight (less than 2,500 gm) of infants born to foreign pregnant women (12.14%) was significantly higher than that of Thai pregnant women (6.71%).

Conclusion: The rates of perinatal problems and low birth weight infants among foreign women were higher than those of Thai pregnant women. Good antenatal care should be encouraged to improve maternal and child health among this group of women.

Keywords: pregnant women, ethnic minority, complication

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Background

Maternal and infant mortality are one of the most important indicators of population health[1-6]. In Thailand, policies and programs have been continuously implemented with a goal to decrease the maternal and infant mortality rate including safe childbirth, safe mother program and good antenatal care. Statistics report of maternal and infant mortality in Thailand (2011-2015) have varied from region to region and ranged from 28.38 to 34.42 per 100,000 live birth and 10.36 to 12.21 per 1,000 live birth, respectively[7]. A previous study at Rajavithi Hospital reported no difference of pregnancy outcomes between immigrant and Thai pregnant women. However, the incidence of low birth weight was higher among immigrant pregnant women[8].

Chiang Khong District of Chiang Rai Province is located on the bank of the Mekong River opposite the Lao People's Democratic Republic. Therefore, many patients attending Chiang Khong Crown Prince Hospital are Laos, ethnic minorities and Burmese. Health information of foreign and ethnic minority group of pregnant women and infants living along the Thai border remains limited. The study aimed to compare the rate of perinatal problems between foreign and Thai pregnant women at Chiang Khong Crown Prince Hospital of Chiang Rai Province.

Methods

We conducted a cross-sectional study by retrospectively reviewing medical records of pregnant women attending Chiang Khong Crown Prince Hospital between October 1, 2018 and September 30, 2019. Pregnant women were divided into two groups based on races, i.e. Thai and foreign people. Independent variables were compared between the two groups including maternal characteristics, mode of delivery, pregnancy complications, infants' gestational age and birth weight.

Statistical analysis

Comparison between the groups was analyzed by using independent t-test for continuous data and Chi-square or Fisher's exact for categorical data as appropriate. Statistically significant difference between groups was assigned at p value less than 0.05.

Results

In all, 501 pregnant women were enrolled in the study. Three hundred and twenty-eight (65.45%) and 173 (34.53%) were Thai and foreigner, respectively. The ethnicities of Laos, hill tribe and Burmese were 180 (35.92%), 136 (27.15%) and 2 (0.40%), respectively. Maternal age more than 35 years among Thai pregnant women (10.67%) was more frequent than that of the foreigner group (4.62%). No difference was found in height, body mass index and underlying diseases between groups. The rates of anemia, hepatitis B carrier and history of abortion more than 2 times among foreign pregnant women (19.65, 6.36 and 5.20%) were significantly higher than those of Thai pregnant women (11.59, 2.74 and 1.83%), respectively (Table 1). Mode of delivery and complications did not differ between groups (Table 2). Rate of low birth weight (less than 2,500 gm) of infants born to foreign pregnant women (12.14%) was significantly higher than that of Thai pregnant women (6.71%) (Table 3).

Discussion

This study showed a higher rate of pregnant women aged more than 35 years in a Thai population. In contrast to foreign women[9], Thai women tended to have higher education levels resulting in getting married late and having children at older age.

The higher rate of anemia among foreign pregnant women corresponded to related studies[10-12]. The common cause of anemia was iron deficiency which was probably due to poor antenatal care and compliance with iron treatment. Therefore, an educational program for pregnant women with anemia should be implemented using teaching materials in both Thai and foreign languages with an emphasis on having proper nutrition and iron supplement.

Table 1 Characteristics of Thai and foreign pregnant women

Data	Thai n (%)	Foreign n (%)	P-value
Total pregnant women	328	173	
Age, mean±SD	26.06±6.56	25.51±5.40	0.342
≤ 16 years of age	15 (4.57)	3 (1.73)	0.132
> 35 years of age	35 (10.67)	8 (4.62)	0.028
Parity ≥ 4	18 (5.49)	7 (4.05)	0.523
Abort ≥ 2 times	6 (1.83)	9 (5.20)	0.035
Height (cm.) mean±SD	153.85±6.35	153.54±5.77	0.582
< 145 cm.	18 (5.47)	12 (6.94)	0.534
BMI (kg/m^2), mean±SD	24.07±5.55	23.21±5.18	0.092
< 5 kg/m^2	20 (6.10)	11 (6.36)	0.973
Underlying diseases			
Diabetic mellitus	9 (2.74)	2 (1.16)	0.342
Hypertension	2 (0.61)	0	0.544
Epilepsy	1 (0.30)	0	0.464
Thyrotoxicosis	1 (0.30)	0	0.464
Poor antenatal care (< 4 times)	148 (45.12)	90 (52.02)	0.150
Laboratory test			
HIV positive	1 (0.30)	1(0.58)	1.000
VDRL positive	1 (0.30)	0	1.000
HBsAg positive	9 (2.74)	11 (6.36)	0.049*
DCIP positive	2 (0.61)	4(2.31)	0.096
Hct < 33%	38 (11.59)	34 (19.65)	0.016*
Abnormal Hemoglobin typing	15/20 (71.4)	32/45 (71.1)	0.719
Alpha trait	1/20 (4.80)	8/45 (17.80)	0.255

BMI = Body mass index, HIV = Human Immunodeficiency Virus, VDRL = Venereal disease research laboratory, HBsAg = Hepatitis B surface antigen, DCIP = Dichlorophenol Indophenol Precipitation test
** Chi-square test*

Table 2 Delivery and complications of Thai and foreign pregnant women

Data	Thai n (%)	Foreign n (%)	P-value
Total pregnant women	328	173	
Mode of delivery			
Vaginal	260 (79.27)	142(82.08)	0.481
Cesarean	67 (20.43)	31(17.92)	0.554
Vacuum extraction	1 (0.30)	0	1.000
Maternal complications			
Cephalopelvic disproportion	24 (7.32)	9 (5.20)	0.450
Gestational diabetes mellitus	22 (6.71)	10 (5.88)	0.848
Pregnancy induced hypertension	5 (1.52)	1 (0.58)	0.669
Twin pregnancy	1 (0.30)	2 (1.16)	0.275
Preterm labour	21 (6.40)	17 (9.83)	0.213
Meconium-stained amniotic fluid	0	1 (0.58)	0.345
PROM > 12 hours	1 (0.30)	0	0.170
Breech presentation	9 (2.74)	7 (4.09)	0.433
Nuchal cord	8 (2.44)	5 (2.89)	0.773
Syphilis	3(0.91)	0	0.555
Condyloma acuminata	2 (0.61)	2 (1.16)	0.611
Birth before arrival	1 (0.30)	2 (1.16)	0.275
Postpartum hemorrhage	3 (0.91)	3 (1.73)	0.420
Fetal death	2 (0.30)	2 (1.16)	0.611

PROM: Premature rupture of membrane

Table 3 Neonatal data of infants born to Thai and foreign women

Data	Thai n (%)	Foreign n (%)	P-value
Total infants	328	173	
Gestational age, mean±SD	38.61±1.53	38.58±1.78	0.838
< 37 weeks	21 (6.40)	17 (9.83)	0.213
> 42 weeks	4 (1.22)	2(1.16)	1.000
Birth weight, mean±SD	3,113.45±415.08	3,028.91±470.58	0.039*
< 2,500 grams	22 (6.71)	21 (12.14)	0.045**
> 4,000 grams	8 (2.44)	3 (1.73)	0.755

* *Unpaired t-test*
** *Chi-square test*

The higher rate of hepatitis B carrier among foreign pregnant women corresponded to a related study reporting a higher prevalence of positive hepatitis A, B and C infections among foreign workers in Thailand.[13] Hepatitis B vaccine should be provided to all foreign infants within 12 hours after birth as the same routine practice for Thai infants.

Birth weights of infants born to foreign and Thai pregnant women did not differ. However, foreign pregnant women delivered infants with low birth weight (less than 2,500 gm) more frequently. Although the rate of poor antenatal care did not differ between the two groups, the cause of low birth weight was probably from inadequate maternal nutrition[14, 15] and self-care due to low socioeconomic levels and language barrier. The limitation of this study was retrospective study in design; therefore, we were unable to review infant's complications after birth.

Conclusion

Anemia, hepatitis B carrier and low birth weight were more common among foreign pregnant women compared with a Thai population. Good antenatal care should be encouraged to improve maternal and child health among this group of women.

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Review Article **GMSMJ** **Greater Mekong Subregion Medical Journal**

Nutritional Values of the Gelatinous Substance in Bamboo Internodes

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Abstract:

Background: During the rainy and cool seasons, internodes of bamboo *(Dendrocalamus strictus)* contain a clear light brown gelatinous substance with a pale bamboo odor. This gelatinous substance is traditionally called "Piang" and has long been used as a food by northern Thai people. However, there have been no reports regarding nutritional values to support the promotion of this local wisdom usage.

Objective: Thus study aimed to evaluate the nutritional values and anti-oxidant properties of this gelatinous substance.

Methods: Bamboo gelatinous substance was collected from local markets in Chiang Rai, freeze dried and subjected to nutritional analysis and anti-oxidant assay.

Results: The results showed that 1.0 gram of dried gelatinous substance contains 0.79 g of insoluble dietary fiber and 0.11 g of soluble dietary fiber. There was 0.16 g of protein in 100 grams of fresh gelatinous substance and no fats or sugars were detected. Silicon was the most predominant mineral found in the bamboo gelatinous substance. Its content was 20 mg/100 g fresh gelatinous weight. Other minerals found in 100 g fresh gelatinous substance were potassium (104 mg), sodium (2 mg), magnesium (1.78 mg), calcium (4 mg), phosphorus (8 mg), iron (0.14 mg), zinc (0.04 mg) and chloride (4.40 mg). Total polyphenols at small concentrations were found but no anti-oxidant properties were detected.

Conclusion: All of these findings suggested that bamboo gelatinous substance contains almost zero calories but is rich in dietary fibre and silicon, both of which are beneficial to health. This natural product could be developed as a potential dietary supplement.

Keywords: Gelatinous substance, *Dendrocalamus strictus,* Nutritional values

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Introduction

Bamboos are evergreen perennial flowering plants that are part of the true grass family Poaceae. Most bamboo species are found in tropical, subtropical and mild temperate climates, particularly in the Indian subcontinent, East and Southeast Asia and islands of the Indian and Pacific oceans. Bamboo is considered a multipurpose plant since all of its parts can be used. People in the countryside of the Greater Mekong Subregion (GMS) have their houses built from bamboo wood and bamboo shoots are still a mainstay delicacy of their diet in the rainy season. Bamboo shoots contain amino acids, carbohydrates, minerals, vitamins and nutrient fibers but virtually no fat. It has been demonstrated that there are 6-8 grams of nutrient fibers per 100 grams of fresh weight of bamboo shoot[1]. Nutrient fibers are known to possess cholesterol lowering effects and delay sugar absorption, both which are good for diabetes treatment and weight management[2, 3].

In Thailand, there are 13 genera and 60 species of bamboos recorded[4]. Bamboo shoots from all species are edible. However, bamboo shoot is not the sole source of food material from bamboo. During the late rainy and early cool seasons. another edible material can be collected from the bamboo of a certain species *(Dendrocalamus strictus)*. On the inside of some internodes of some bamboo branches there is found a clear light brown gelatinous substance, with a pale bamboo odor. The internodes in which the gelatinous substance is found are shorter than others in the same clump. The gelatinous substance collected from 3-4 internodes is enough for 1-2 servings. Vendors selling bamboo gelatinous substance are commonly seen in the local markets of Chiang Rai, Thailand, particularly during the months of September to December.

The bamboo gelatinous substance is likely an exudate from bamboo but its origin is still in question. Indigenous people call it “Piang” and it has long been eaten it as a food. This gelatinous substance is usually eaten raw by mixing it with salt, chili, coriander and onion chive. Approximately one serving consists of at least 100 grams of the gelatinous substance. It can also be cooked, making a clear soup with the addition of meat and vegetables. Despite the long known culinary uses of the bamboo gelatinous substance, there have been no reports regarding its nutritional value and no one knows whether consuming this food is beneficial to health.

To shed light on this matter, this study aimed to evaluate the nutritional values and anti-oxidant properties of bamboo gelatinous substance. The findings may also reveal the potential of this material to be developed as a food supplement.

Materials and Methods

Collection of bamboo gelatinous substance

Bamboo gelatinous substance was collected from local markets in Mae Chan, Mae Fah Luang, Chiang Khong and Chiang Saen districts in Chiang Rai province during November - December 2018. Approximately 60 kg of the Bamboo gelatinous substance was obtained.

Sample preparation

Fresh gelatinous substance was weighed and lyophilized and ground for further analysis. From 53.5 kg of fresh gelatinous substance, 1.070 kg of dried gelatinous substance was obtained. Therefore one 100 grams serving of the fresh gelatinous substance is equivalent to 2 grams of dried powder.

Analyses of nutrient contents and antioxidant activities

The test sample for nutrient and mineral content analysis was prepared by mixing 1.0 g of dried gelatinous substance with 100 ml of deionized water. Analyses of Protein, Fat/Total lipid, Ash, Insoluble dietary fiber, Soluble dietary fiber, Total sugar, Calcium, Phosphorus, Sodium, Potassium, Chloride, Magnesium, Iron, Zinc, Copper, Silicon and total polyphenols was performed. Antioxidant activities were assayed using the ferric reducing ability of plasma (FRAP) and α, α-diphenyl-β-picrylhydrazyl (DPPH), this analysis was carried out at the Food and Nutrition Laboratory, Institute of Nutrition, Mahidol University, certified according to ISO/IEC 17025: 2005. All of the assays except phosphorus, total polyphenol and antioxidant activities were performed according to the official methods of analysis[5]. Phosphorus content was determined by spectrophotometric method[6]. Total polyphenol content was determined according to the Folin-Ciocalteu spectrophotometric method[7]. FRAP was estimated spectrophotometrically following the procedure of Benzie and Strain[8] and DPPH radical scavenging activity was determined according to the method of Katsube et al.[9] Silicon content was measured by β-Silicomolybdenum blue method using the test kit visocolor® *HE* Silicon

Polysaccharide extraction.

The crude polysaccharide fraction was obtained using a hot-water extraction method[10]. Five grams of dried gelatinous substance was mixed with 300 ml hot deionized water. The resulting solution was mixed with four times its volume of anhydrous ethanol for precipitation for 24 h at 4°C. The extraction solutions were separated by centrifugation at 10,000 g for 20 min[11]. After the water supernatant was poured away, the precipitate was washed repeatedly with acetone. The crude polysaccharides were then lyophilized and weighed. The yield (%) of the polysaccharides was calculated as follows:

$$\text{Extraction yield (\%)} = (PS/GS) \times 100$$

Where PS is the dried crude polysaccharide weight and GS is the dried gelatinous substance weight.

Results and Discussion

Macronutrient and mineral content of the bamboo gelatinous substance

Macronutrient and mineral content were expressed in terms of weight per 100 g of fresh bamboo gelatinous substance and reported in Table 1. The amounts of protein, total fat, calcium, phosphorus, sodium, potassium, magnesium, iron, zinc, copper and chloride in

one serving (100 g fresh weight) were far lower than the daily requirements recommended for Thai people[12]. Potassium was the most predominant mineral. Its content in 100 g fresh gelatinous substance was 104 mg. However, in comparison with the level of potassium intake suggested by WHO, at least 3510 mg/day for adult[13], this is still more than thirty times less than the recommended daily intake.

Of all the mineral contents reported here, the most notable value was that of silicon. Silicon content was 20 mg/100 g fresh gelatinous substance. There has been no recommended daily dose of silicon intake for Thais but it was reported that dietary intake of silicon for most Western populations is between 20-50 mg /day[14-16]. Plants in the grass family, including bamboo, are termed "silicon accumulators" because they take up and accumulate silicon from soil to make up a structural component conferring strength and rigidity to stalks[17]. Studies in experimental animals suggested that silicon may be essential for the formation of bone and connective tissues in higher animals and humans[18-20]. Findings from both animal and human experiments suggested that an intake of silicon of near 25 mg/d would ensure nutritional benefits[21].

The results indicate that consuming fresh gelatinous substance from bamboo is safe, even when consumed several times a day and may well have beneficial effects, particularly related to skeletal health.

Phenolic compounds and antioxidant activities

The total polyphenol content of the bamboo gelatinous substance, as measured with Folin-Ciocalteu reagent, was 4.6 mg eq GA/ 100 g fresh weight gelatinous substance while

Table 1 Macronutrient and mineral content of the bamboo gelatinous substance

Components		Reference methods
Protein (g)	0.16	AOAC (2016) 992.23
Total fat (g)	0	AOAC (2016) 948.15, 945.16
Total sugar	ND	AOAC (2016) 982.14
Calcium (mg)	4	AOAC (2016) 985.35
Phosphorus (mg)	8	Kolthoff et al. 1969
Sodium (mg)	2	AOAC (2016) 985.35
Potassium (mg)	104	AOAC (2016) 985.35
Magnesium (mg)	1.78	AOAC (2016) 984.27
Iron (mg)	0.14	AOAC (2016) 984.27
Zinc (mg)	0.04	AOAC (2016) 984.27
Copper	ND	AOAC (2016) 984.27
Chloride (mg)	4.4	AOAC (2016) 971.27
Dietary fibre (g)	1.8	AOAC (2016) 991.42
Si concentration (mg)	20	Test kit visocolor® HE Silicon

Values were expressed in terms of weight per 100 grams of fresh bamboo gelatinous substance, ND = not detected

its total antioxidant properties, as measured with ferric reducing ability of plasma (FRAP) and α, α-diphenyl-β-picrylhydrazyl (DPPH) methods, were undetectable. Since different phenolic compounds made considerable different contributions to different antioxidant activity assays[7], this finding suggested that phenolic compounds in the bamboo gelatinous substance have no anti-oxidant activity.

Polysaccharide and dietary fibre analysis

It was found that 1.0 grams of dried gelatinous substance yielded 0.98 grams of crude polysaccharide. The percentage of crude polysaccharide, soluble dietary fibre and insoluble dietary fibre in dried gelatinous substance were 98, 11 and 79 respectively as shown in Table 2. Therefore, one serving of the fresh gelatinous substance (2 grams of dried powders) should contain nearly 2 grams of dietary fibre. It is noteworthy that the recommended daily intake of dietary for Thais is 25-38 grams[12].

Table 2 Polysaccharide and dietary fiber content of the bamboo gelatinous substance (values were expressed in terms of weight per 1.0 gram of dried bamboo gelatinous substance)

Polysaccharide	Content (g)	%	Reference methods
Crude polysaccharide	0.98	98	Lai and Yang, 2007
Soluble dietary fiber	0.11	11	AOAC (2016) 991.42, 991.43
Insoluble dietary fiber	0.79	79	AOAC (2016) 991.42

Polysaccharides are polymers made up of sugar subunits and can be classified nutritionally into starches and non-starch polysaccharides[22]. The non-starch polysaccharides are included in dietary fibre and not digested by human digestive enzymes[23]. Degradation of these polysaccharides in the human gastrointestinal tract results from the action of enzymes secreted by the intestinal microflora[24].

Dietary fibre is not a nutrient but still plays an important role in maintaining good health[3]. Diets rich in dietary fibre have been associated with beneficial effects on human health and are sometimes considered to be useful for the prevention of obesity[25]. On the basis of solubility, dietary fibre can be classified into two major components. Insoluble fiber adds bulk to the stools and speeds up the passage of stools through the colon while soluble fiber helps in keeping blood sugar levels stable, and creates a feel of satiety and prevents overeating[3].

Conclusion

Gelatinous substance from bamboo contains dietary fibre and minerals that are beneficial to health. The most predominant mineral found in the Gelatinous substance was silicon which has an important role to play in the formation of healthy bone and connective tissues.

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Conflict of Interest

The research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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The Study of Peer-Assisted Learning and Self-Regulated Learning through Clinical-Years Medical Students' Perspectives

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Abstract:

Background: Clinical-years learning is a part of undergraduate medical training that shifted from lectured-based learning to outcome-based education focusing on authentic situation. There are several learning methods which clinical-years medical students can use for academic achievement such as peer-assisted learning (PAL) and self-regulated learning (SRL).

Objective: This study aimed to assess effectiveness of PAL and SRL in clinical medical students' perspectives.

Methods: A total of 142 medical students responded to standardized 5-rating scale questionnaire including 6 aspects of perspectives; knowledge acquired, accuracy of information given, clinical skills acquired, active learning stimulation, comfortable learning environment and time consumption. Exploratory factor analysis (EFA) demonstrating component matrix of perspective on PAL and SRL effectiveness were analyzed.

Results: SRL had higher factor loadings (λ) on perspectives toward knowledge acquired, active learning stimulation and comfortable learning environment than PAL (λ_{SRL} = 0.799, 0.781 and 0.809 respectively and λPAL = 0.707, 0.658 and 0.632 respectively); however, PAL yielded greater factor loadings on clinical skills learning and time consumption (λ_{PAL} = 0.717 and 0.858 respectively) in comparison with SRL (λ_{SRL} = 0.521 and 0.703 respectively). There were almost an equal factor loading when regard to the perspectives toward accuracy of information given (λ_{PAL} = 0.784 and λ_{SRL} = 0.783).

Conclusion: PAL had high impact on clinical skills learning because peer-learners could interact with peer-teachers. SRL provided much knowledge acquired because researching and summarizing information individually would promote long-term memories and stimulated active learning in many medical students. Both methods should be encouraged simultaneously in order to promote successful learning outcomes.

Keywords: Medical students, Peer-assisted learning, Self-regulated learning

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Introduction

During the course of six-year medical training program in Thailand, clinical-year is an important step that transfer from traditional lecture-based learning toward outcome-based and authentic education. Several learning modes during pre-clinical years, especially case-based learning, play important roles in orientating and enhancing medical students' ability to apply their basic science knowledge to social and medical sciences as well as preparing them for workplace situations[1,2]. Although being well prepared, the prompt shift into new environments could resulted in stress which likely to affect their performances and educational outcomes[3]. In this tumultuous situation, medical students must adapt to new forms of clinical education by finding their suitable methods of learning and strategies. In this digital era, there are several methods, learning resources and resource persons which clinical-years medical students can access according to their favor such as staffs, residents and seniors' teaching and modeling, discussion and tutoring with peers and self-learning from several available resources[4-6].

Peer-assisted learning (PAL) is gaining momentum in clinical education. PAL is an umbrella term covering peer teaching, peer learning, peer mentoring, peer assessment and peer leadership[7]. Peer teaching is beneficial for medical students to develop valuable clinical skills and gain experience in teaching as well as mentoring relationship between peers[8,9].

In clinical context, it is undeniable that students must take control of their own learning. This learning method is defined as self-regulated learning (SRL)[10]. This learning method has always been used in medical education as it promoted students' cognitive and psychomotor skills[11, 12]. However, SRL in clinical settings was highly attributed to environments and was influenced by several other persons in these environments such as instructors, residents and peers[10, 13]. Thus, SRL is the learning method which required some degrees of guidance, facilitation and supports, as similar to problem-oriented learning[13, 14].

At Phramongkutklao College of Medicine, transforming to clinical years is a great leap of medical students. They must adapt themselves to new learning styles, environments and social processes. This study aimed to evaluate effectiveness of PAL and SRL in clinical medical students' perspectives in order to address benefits of each learning methods for developing clinical curriculum which is suitable for the students.

Methods

Study design

This study is a part of the curriculum development which engaged clinical-years medical students' perspectives and opinions toward clinical learning methods for management of the curriculum. In this study, the descriptive cross-sectional study was conducted during October 2017 at Phramongkutklao College of Medicine and Phramongkutklao Hospital, the college's teaching hospital.

Study population

The targeted population of this study was clinical-years medical students. This study was preliminary study, as such, the sample size was total population of clinical-years medical students at Phramongkutklao College of Medicine which were fourth, fifth and sixth years. Excluded from this study were sixth year medical students who – during the time this study was conducted – were rotating outside of Phramongkutklao Hospital which made contacts

and collection of responses difficult.

Questionnaire and data collection

A 5-Likert scale questionnaire was developed. Score of 5 was defined as highly agree, while score of 1 meant highly disagree. The questionnaire included questionnaire regarding perspectives of clinical-years medical students toward PAL and SRL in six aspects which were knowledge acquired, accuracy of information, clinical skills acquired, active learning stimulation, learning environment and time consumption. The questionnaire was examined by 3 experts on medical education and tested for reliability by alpha-coefficient which used 0.70 as the threshold of reliability of the questionnaire. From all items, it yielded the alpha-coefficient of 0.75. Thus, the questionnaire was deemed reliable and valid. The questionnaire was made online and distributed to all clinical-years medical students. Students' responses were stored in online datasheet.

Statistical analysis

Statistical analysis was performed on IBM SPSS 22.0 (Armonk, New York, US). Descriptive statistics were used for describe general characteristics of samples. Exploratory analysis was used for evaluate impact factors of students' perspectives of each aspect toward PAL and SRL. Factor loadings of 0.5 or greater[15] were indicated that students' perspectives were likely to be more clustered and oriented toward the same direction than perspectives with lower factor loadings.

Ethical consideration

This study was medical education research which was exempted from ethical approval by Institutional Review Board of Royal Thai Army Medical Department. The exemption number was CodeR218q/60_Exp.

Results

From 200 students, 142 (71.000%) responded. Most (63, 44.366%) were fourth-year medical students. Fifth- and sixth-year students were 59 (41.549%) and 20 (14.085%) respectively. Male students were 73 (51.408%). Students with grade point average (GPA) of 3.00-3.49 (B) shared highest proportion in fourth- and fifth-year (36, 25.352% and 22, 15.493% respectively). Most sixth-year students (8, 5.634%) had GPA of 3.50 and above (B+ and A). The baseline characteristics classified by clinical years were displayed in Table 1. Mean score of students' perspectives toward PAL and SRL were shown in Table 2.

Exploratory factor analysis

EFA revealed students' perspectives toward PAL and SRL. Statistical analysis showed that SRL had high factor loadings (λ) of clinical-years medical students' perspectives toward knowledge acquired, active learning stimulation and learning environment ($\lambda_{SRL} = 0.799, 0.781$ and 0.809, respectively). There were high factor loadings of students' perspectives on clinical skills acquired and time consumption toward PAL (λ_{PAL} = 0.717 and 0.858, respectively). The EFA results were shown in Table 2.

Discussion

This study addressed perspectives of clinical-years medical students toward PAL and SRL. It should be noted that EFA was used for addressing important issues from PAL

and SRL in students' perspectives rather than for comparison between PAL and SRL.

Clinical staffs and residents were positive toward teaching medical students and perceived this task as one of their major responsibilities; however, due to lack of teaching skills and time constraint limited them from this task[16]. On the other hand, some staffs and especially some residents perceived themselves as more a clinician than teacher; thus, teaching medical students fall to lower priorities[17]. As a result, medical students have to adapt their learning style, social behavior and environment in order to be successful in education and professionalism in clinical settings.

Table 1 General characteristics of clinical-years medical students of Phramongkutklao College of Medicine according to their clinical years

Characteristics	Clinical year		
	Fourth n (%)	**Fifth n (%)**	**Sixth n (%)**
Genders			
Male	32 (22.535%)	30 (21.127%)	11 (7.746%)
Female	31 (21.831%)	29 (20.423%)	9 (6.338%)
GPA			
2.00-2.49 (C)	1 (0.704%)	1 (0.704%)	1 (0.704%)
2.50-2.99 (C+)	11 (7.746%)	18 (12.676%)	5 (3.521%)
3.00-3.49 (B)	36 (25.352%)	22 (15.493%)	6 (4.225%)
Above 3.50 (B+ and A)	15 (10.563%)	18 (12.676%)	8 (5.634%)

Table 2 Mean score and factor loadings of each aspect of perspective toward PAL and SRL

Students' perspectives	Learning methods	Mean ± SD	Factor loadings (λ)
Perspectives toward knowledge acquired	PAL	3.585 ± 0.969	0.707
	SRL	3.923 ± 0.859	0.799
Perspectives toward active learning stimulation	PAL	3.669 ± 1.009	0.658
	SRL	4.120 ± 1.028	0.781
Perspectives toward learning environment	PAL	3.366 ± 1.307	0.632
	SRL	3.148 ± 1.321	0.809
Perspectives toward clinical skills acquired	PAL	3.592 ± 0.976	0.717
	SRL	3.401 ± 1.045	0.521
Perspectives toward time consumption	PAL	3.078 ± 1.130	0.858
	SRL	2.197 ± 1.279	0.703
Perspectives toward accuracy of information	PAL	3.268 ± 0.883	0.784
	SRL	3.711 ± 0.822	0.783

In earlier studies, learner-centered curriculum, which students have to manage their own learning strategies, enhanced psychomotor, cognitive and metacognitive awareness as well as self-regulated learning skills[11, 12, 18]. SRL also developed critical thinking skill, elaborating learning strategies and task value[19]. Moreover, SRL is a learning method that required active students to take charge of their own learning strategies[10] and clinical context education is a complex, flexible and authentic situations, as a result, active learning is a required quality of clinical-years medical students[20]. This approach of learning method always supports the goal for 'lifelong learning' and thus, SRL was valued by medical students.

There was an interesting point in which most students' perspectives focused on learning environment in SRL. It can be implied that in this context, learning environment was more comfortable and favorable for individual learning although previous study indicated that in PAL, students help each other to learn and feeling more relaxed and comfortable[21, 22]. In previous study in medical schools in Thailand, one of the major stressors to Thai medical students was learning competition[23]. Thus, it could be concluded that in this setting, underneath the friendly and helpful learning environment among peers, many students felt inferior or superior to others and competition was inevitable. It is suggested that gaps between grading systems should be decreased and empathy as well as respect toward peers should be implemented.

In the aspect of clinical skills learning, students' attitudes toward PAL was high which could be interpreted that students were highly concern about this aspect in PAL. This could be attributed to the fact that clinical skills required audiovisual interactions in order to practice the procedures from others[4]. Learning clinical skills with peers were perceived as comfortable and also developing confidence among peer-learners[22]. In addition, peer-teachers can benefit in deeper level of understanding from PAL[22]. From these evidences, this study suggested a concept of senior peers teaching clinical skills to junior peers under supervision from staffs or residents in order to enhance confidence and agility to senior and develop clinical skills to junior peers as well as fostering good relationship between seniors and juniors. On the other hand, PAL was seemed to had greater effect to time consumption than SRL. This might be due to different levels of knowledge between peer-learners of which peer-teachers might have to slowly tutoring in order to allow everyone in the group to catch up with the lesson. Also, discussion occurs in PAL[24], as a result, discussion among peers could prolong the tutoring, thus, consuming more time than learning individually.

Both SRL and PAL had high impact factors toward perspectives regarding accuracy of information. In a previous study, among peer-learners, they felt that information form peer-teachers were valuable because the information was believable, relevant and useful[21]. However, in this study, the similar results could be resulted from their perception that both peer-teachers and peer-learners were in the same level and the information acquired from peers were not different from learning by their own.

There was a limitation of this study as most sixth-year students were absence from data collection due to rotating outside of Phramongkutklao Hospital. As, the data of this study were used for further quantitative studies, there were constraint time for collecting responses from all sixth-year students. Perceptions of sixth-year students could be different

from their juniors due to their work, responsibilities and experiences. Other means of assessing outcomes from Peer-teaching and self-learning other than using perspectives could be done in order to yielded results from various aspects for promotion of peer-teaching and self-learning effectiveness.

Recommendations for further studies were explorations into aspects with high impact factors. Focus groups interview and mean comparison were recommended for comparing students' perspectives toward PAL and SRL.

It was concluded that both PAL and SRL were beneficial in different aspects. Both methods should be encouraged simultaneously with traditional clinical learning in order to promote successful learning outcomes for medical students.

Acknowledgement

We would like to thanks all participants for contributing this valuable information for further development of the curriculum. We must also thank the crews of Medical Education Unit, Phramongkutklao College of Medicine for facilitate the processes of this study.

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Case Report GMSMJ Greater Mekong Subregion Medical Journal

A Middle-aged Man with High-grade Fever, Non-productive Cough, Weight Loss for 2 Weeks.

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Abstract:

A 55-year-old man, a carpenter in northeastern Thailand with no underlying disease presented with acute onset of fever with chills, non-productive cough, weight loss of 3 kilograms in 2 weeks. He also experienced easily fatigue and tiredness for 1 month. He went to local hospital and was diagnosed pancytopenia. He received 3 units of packed red cells and 1 unit of platelet concentrate without significant improvement. Then he was referred to another hospital for investigation. After blood smear review, there were many abnormal white blood cells with numerous small cytoplasmic granules. The bone marrow examination and cytogenetics revealed diagnosis of acute promyelocytic leukemia. So, in case of pancytopenia without apparent causes, blood smear and bone marrow examination can be helpful in definite diagnosis.

Keywords: Pancytopenia, promyelocytic leukemia, high-grade fever

Introduction

Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML) with distinctive biologic and clinical features that is now highly curable. Most patients are young, present with leukopenia or pancytopenia and exhibit a life-threatening coagulopathy because of procoagulant released from cytoplasmic granules. The leukemic promyelocytes cells from almost all patients have a balanced reciprocal translocation[1] between chromosomes 15 and 17 which generates a fusion transcript joining the PML (promyelocyte) and RAR-α (retinoic acid receptor-α) genes[2]. They have the unique ability to undergo differentiation with exposure to retinoic acid and both differentiation and apoptosis with exposure to arsenic trioxide (ATO)[3]. Because APL patients can be cured up to 80-90% according to risk classification with ATRA (all trans retinoic acid), ATO (arsenic trioxide) and chemotherapy, so definite diagnosis is required and, in the patients suspected APL, treatment with ATRA should be started without delay because bleeding from coagulopathy is serious and major cause of death. There are 2 variants of APL, hypergranular and microgranular. Multiple Auer rods were common in hypergranular promyelocytes but in microgranular variant,

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the leukemic promyelocytes were characterized by striking nuclear folding, and the nuclei frequently appeared bilobed or reniform. However, the granularity of the leukemic cells may show considerable variation, even within the same patient[4]. The definite diagnosis of APL requires demonstration of balanced reciprocal translocation between chromosome 15 and 17 by cytogenetic study or FISH (Fluorescence in situ hybridization).

Case Presentation

A 55-year-old man, a carpenter in north-eastern Thailand, presented with high-grade fever with chills for 2 weeks. He also experienced non-productive cough, easily tiredness and weight loss of 3 kilograms in the past 2 weeks. He had anorexia, normal bowel movement and urination. At the local hospital, the complete blood count showed pancytopenia with promyelocytes and myelocytes. Then antibiotics, along with packed red cell and platelet transfusion was administered without significant improvement. He was subsequently referred to another medical center hospital for investigation and further management. On admission at this hospital, vital signs showed body temperature of 39.4^{o}C, heart rate 100/minute, blood pressure 141/83 mmHg, respiration 26/min and oxygen saturation of 97%. He had no palpable lymphadenopathy, liver and spleen was also impalpable. No skin bleeding was detected. Investigation revealed Hct 26%, WBC 2.32 x 10^{9}/L, PMN 15%, L 44%, M 30%, promyelocyte 10%, platelet 22.0 x 10^{9}/L, MCV 87.6 fL, MCH 30.9 pg, LDH 467 U/L (120-246), PT 13.4 second, INR 1.18, APTT 28.9 second, C 25.3, TT 8.6 second, C 7.1, fibrinogen 217.4 mg/dL, uric 1.9 mg/dL, anti-HIV negative, chest x-ray: borderline cardiomegaly, no pulmonary infiltration, bilateral paratracheal shadowing (Figure 1), ultrasound abdomen showed multiple gall stones with evidence of chronic cholecystitis. Review of blood smear found many abnormal white blood cells having bilobed nuclei with numerous cytoplasmic granules. (Figure 2A and 2B) Then bone marrow aspiration and biopsy with cytogenetic study was performed. The finding revealed hypercellular bone marrow 3+ with decreased erythroid cells, many abnormal cells with numerous fine granules similar seen in blood smear and rarely seen Auer's rod (Figure 3A, 3B and 4) These abnormal cells were consistent with abnormal promyelocytes and so the diagnosis of acute promyelocytic leukemia, microgranular variant was made. Because of low initial white blood cells and platelet count, the patient was classified intermediate risk group. ATRA was started on the following day without delay.

Figure 1 Chest x-ray shows bilateral paratracheal shadowing

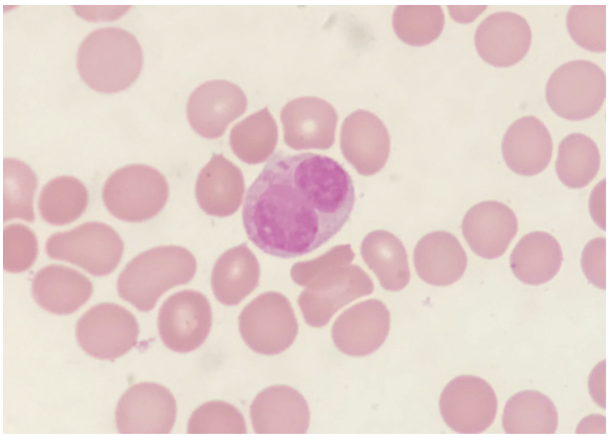

Figure 2A Blood smear shows immature myeloid cell with binucleated nucleus and cytoplasmic granules consistent with abnormal promyelocyte (x100)

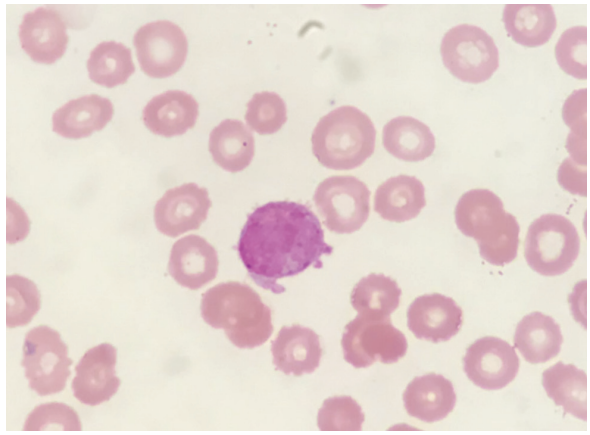

Figure 2B Blood smear shows abnormal promyelocyte with numerous cytoplasmic granules (x100)

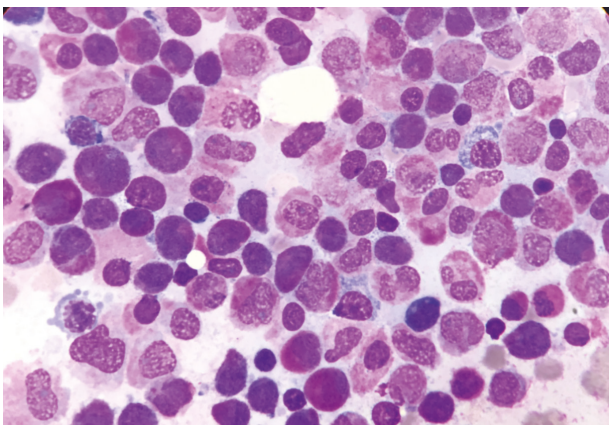

Figure 3A Bone marrow smear shows hypercellular marrow with increased promyelocytes (x100)

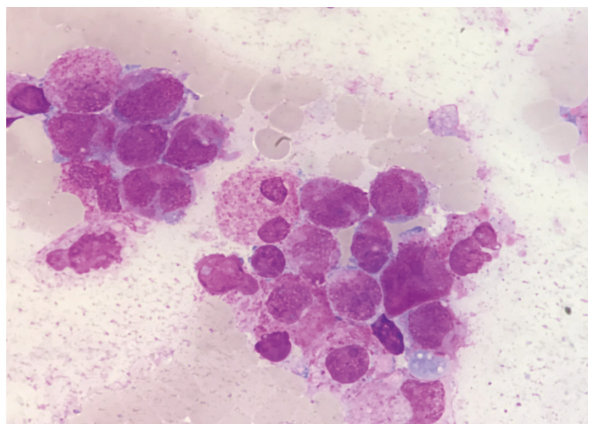

Figure 3B Bone marrow smear shows abnormal promyelocytes with binucleated and numerous granules (x100)

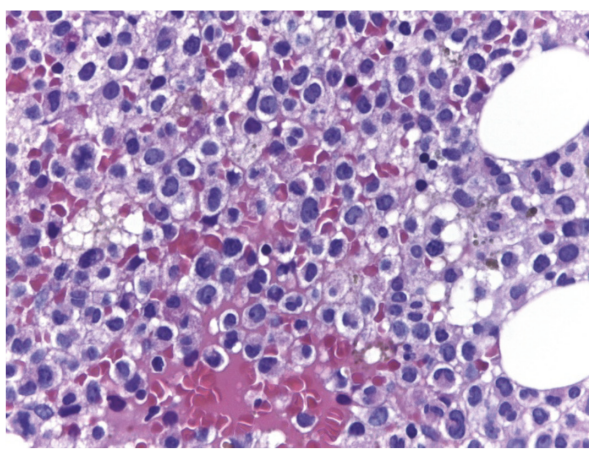

Figure 4 The bone marrow core biopsy shows markedly hypercellular marrow with numerous blastoid cells with moderate amount of eosinophilic cytoplasm (x40)

Discussion

This patient was a 55-year-old man with acute illness. He had intermittent high-grade fever, cough, easily tiredness, anorexia and weight loss. He had no organomegaly or significant bleeding lesion. CBC showed pancytopenia, so differential diagnosis should be bone marrow failure by myelophthisis from abnormal cells, infection, marrow necrosis, drug-related effect or destruction of hematopoietic precursors in the bone marrow such as hemophagocytosis. Because his clinical, blood and bone marrow aspirate cytology were suspicious of acute promyelocytic leukemia, so ATRA should be initiated without delay for cytogenetic or FISH study. Finally, on day 5 after admission, bone marrow cytogenetics revealed t (15;17) (q24; q21) which is characteristic of acute promyelocytic leukemia. This patient had no clinical bleeding, which is common in typical APL, because of early transfusion from the local hospital.

Conclusion

The authors reported case of APL which was able to make early diagnosis from blood and bone marrow smear. In case suspected APL, early initiation of ATRA should be done before definite diagnosis by cytogenetic or FISH study.

Conflict of interest

The author has declared no conflict of interest.

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Mobile Application (DMemo) for Gathering Data from Diabetic Patients and Caregivers

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Abstract:

Background: Currently the device which everyone takes everywhere with him is a smartphone. Data collection via mobile applications can conveniently help patients gather their health information. In addition, the users can view the information from the database in graph or chart for easy interpretation.

Objective: The aim of this study is to help diabetic patients record their data easily, to see the trends of each data set and to improve theircompliance, by developing a mobile application for self-gathering of their glucose data.

Methods: A total of fifteen subjects, five physicians and ten diabetic patients, tested this application and used this application for both collecting data and other functions. After a week of using this application, the users completed a satisfaction questionnaire so that their suggestions could be used to improve this application performance.

Results: After a week of testing this application, the overall efficiency of this application was good (more than 3.41/5.00). The patients found recording their data on this application was easy. In addition, showing the trend of each patient data had benefit for both patients and physicians. However, some functions were too complicated to use without assistance from staff.

Conclusions: This mobile application was useful for patients and physicians to gather data and see the trends of each data. Future enhancement could include adding some beneficial features such as notification, adding others relevant data, or connection to the health care system. Importantly, this application should be able to be run on every operating system and be displayed in other languages. Therefore, using technology is helpful for long-term data gathering and analysis.

Keywords: Diabetes self-management, compliance of diabetic patients, glucose monitoring, mobile applications

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Introduction

Diabetes mellitus is one of the non-communicable diseases (NCDs) which is increasing in incidence worldwide. Over 60% of global diabetic patients live in Asia, with the prevalence across these countries ranging from 3% to 47.3%. The prevalence of diabetes in Thailand, one of the Asian countries, has become very high[1]. The overall prevalence of diabetes in Thai adults, aged ≥ 20 years, was 9.9% (95% CI: 9.4%, 10.4%)[2]. The American Diabetes Association has confirmed that effective self-management, leading to improved clinical outcomes, health status, and quality of life, are key goals of diabetes self-management education and supports that these parameters should be measured and monitored as part of routine care[3]. Therefore, physicians should provide education and self-monitoring to persons with diabetes.

Self-monitoring requires that diabetic patients should record data on blood glucose in their notebooks. But sometimes the patients may forget to take notes or bring their notebooks when they attend hospital. Moreover, patients must maintain good compliance with medication therapy and lifestyle modifications. According to the International Diabetes Federation, consistently high blood glucose levels can lead to disease-related complications affecting the heart and blood vessels, eyes, kidneys, nerves, and teeth. In addition, people with diabetes also have a higher risk of developing infections[4]. Therefore, diabetic patients who show good compliance, usually have a greatly improved prognosis.

At present, the increase of smartphone use leads to increased and more convenient access to relevant information. *"Hootsuite"*, the most ubiquitous social media management platform, and *"We Are Social"*, the global conversation agency from the United Kingdom, reported that there were 55.56 million mobile users (80%) in Thailand[5]. Using a smartphone to record data in an application can make data collection easier compared with taking notes in a notebook; moreover, collecting data using a smartphone reduces paper use. Applications that help data collection, such as blood glucose levels, blood pressure, body weight, meal times, medication times and exercise participation, can help the patients and their physicians know the trends of each data. Furthermore, this application assists physicians to adjust medications, tailored to each patient.

Objective

The research study aimed to develop a mobile application and test this application system, for gathering data of diabetic patients, which help them to record their data easily, see the trends of each data set and improve their compliance.

Methods

2.1 User Involvement

The study protocol was ethically approved by the Ethics in Human Research Committee of Mae Fah Luang University (REH-62012) in 2018. A total of fifteen subjects, five physicians and ten diabetic patients, tested this application. The subjects were recruited using the following inclusion and exclusion criteria. In addition, all study participants agreed to follow the study protocol and provided written consent. After the subjects had used this

application for a week, they completed a satisfaction questionnaire, as detailed in Appendix B for the patients and Appendix D for the physicians.

Patient Inclusion Criteria

1. Type 2 Diabetic patient between the ages of 30 and 70 years.
2. Patient undergoing treatment at Mae Fah Luang University Medical Center Hospital and Mae Fah Luang University Hospital from January 1, to March 31, 2019.
3. Patient who was able to use an Android smartphone and access the internet.
4. Patient who was able to read and understand Thai language proficiently.

Patient Exclusion criteria

1. Patient having a significant past medical history or other co-existing serious diseases (including coronary artery disease, stroke, or chronic obstructive pulmonary disease).
2. Patient having dementia or any other similar conditions (including drug abuse, alcohol abuse, or psychiatric disorder)

Physician Inclusion Criteria

Subjects were physicians at Mae Fah Luang University Medical Center Hospital and Mae Fah Luang University Hospital between the January 1, and March 31, 2019.

2.2 System Architecture

This application was created with the Ionic framework. Ionic framework is an HTML5 mobile application development framework, targeted at building cross-platform applications, which can be exported and run on every operating system. Figure 1 indicates that all data is stored on a secure database server. The users are patients who can add their data and physicians who can access the data via this application. The following overview figure summarizes the integration of the application and database server:

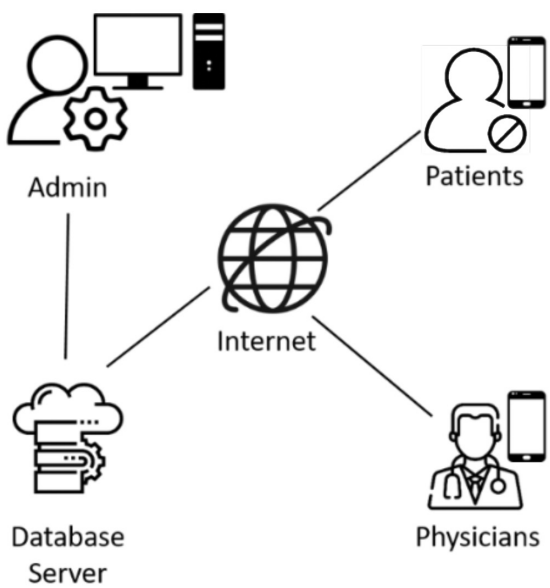


Figure 1 System Architecture of this application

2.3 User Case Diagram

This user case diagram indicates users and subsystems of this application. The features for the patients are log in, edit personal profile, see the trend of the data, add daily data, and edit daily data. In addition, the features of the physicians are search patients' name, see daily data, and see the trend of the data as shown in Figure 2.

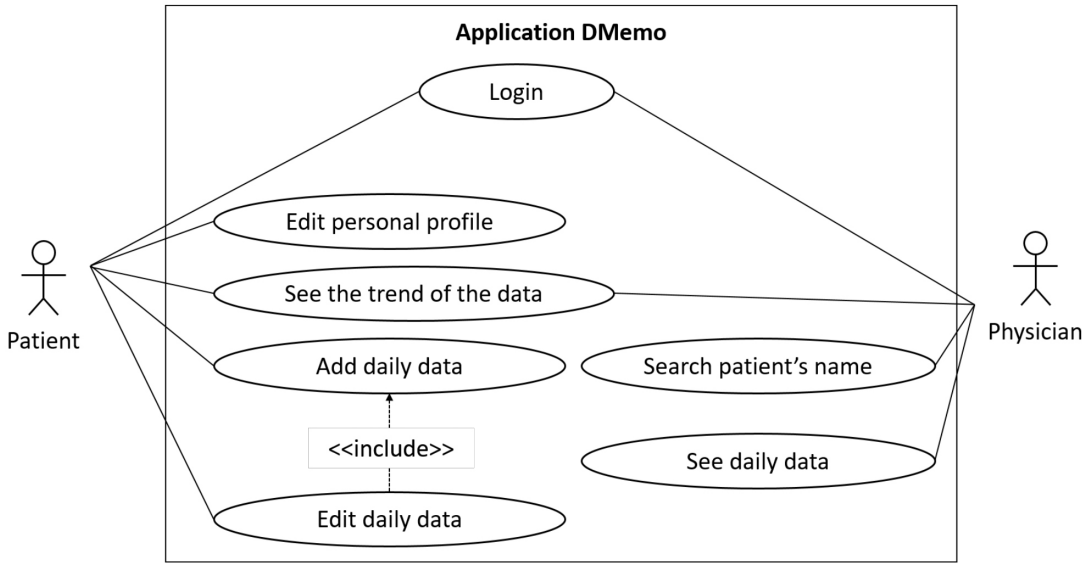


Figure 2 User Case Diagram of this application

2.4 Assessment

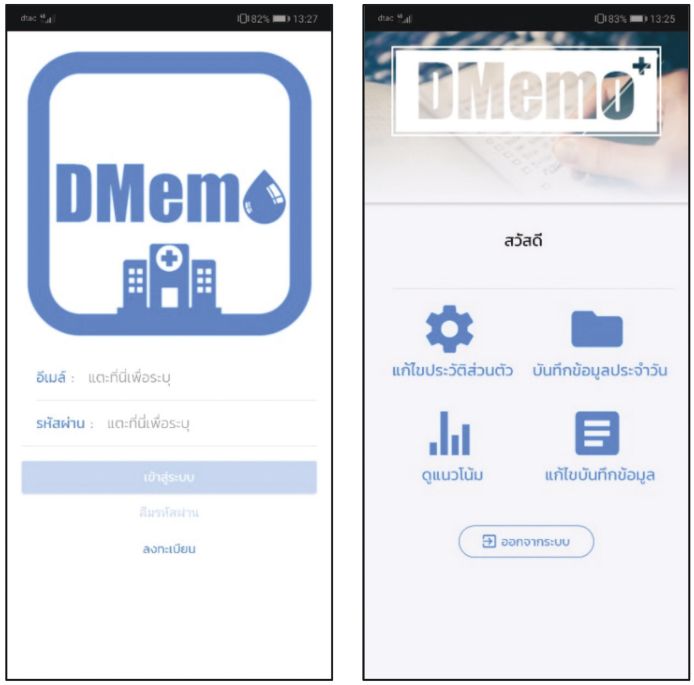
The questionnaire is divided into three parts, comprising information about patients or physicians by checklist, the satisfaction of this application based on Likert Scale[6], and recommendations for this application. In the satisfaction part, there are 8 questions, scored from 1 to 5 (1: strongly agree, 2: agree, 3: neutral, 4: disagree, and 5: strongly disagree). In addition, the summation points of each question were calculated and the mean of the satisfaction displayed as a graph using Microsoft Excel 2016.

Results

3.1 Implementation system

3.1.1 Patient user interface

The patient has to input their email and password for login as shown in Figure 3a. After that, this application showed the patients' home page, as shown in Figure 3b. There are four basic patient features which consist of Edit personal profile, Add daily data, See the trend of the data, and Edit daily data.



(a) (b)

Figure 3 Login page (a) and Patient home page (b)

Then the patient has to put the personal profile include name, date of birth, gender, age, height, weight, e-mail, and telephone number. The medicine name list and the drug names included medication administration route (tablet or injection), dosage, and directions. Then daily data which consists of blood glucose level, blood pressure, weight, waist circumference, medication time, meal time, and exercise participation. Blood glucose level, measured time duration of the measurement, blood pressure feature and weight, waist circumference is added. Then medication time, including the drug name and dosage time is added. Exercise intensity, exercise time, the length of exercise, and kind of sport is then added. The line graph of blood glucose, blood pressure is plotted with time. Furthermore, meal time and medication time are also displayed below this blood glucose level graph.

3.1.2 Physician user interface

Logging onto the physician account shows the list of patient's names which can be searched using the text box. The profile, the trends of each data, and the daily data of the patient chosen can be accessed. In addition, the instructions of each feature in this home page are the same as the patient feature.

3.2 Questionnaire Results

This application was tested by five physicians and ten patients. The demographics of the patients and the physicians are shown in Table 1 and 2. They used this application for collecting data and used the other features. After a week of using this application, the users completed satisfaction questionnaires so that their suggestions can be used to fine tune this application.

Table 1 shows the information about the patients who completed the patient questionnaire. A total of 10 patients treated at Mae Fah Luang University Medical Center Hospital and Mae Fah Luang University Hospital 80% where male 20% were female. The number of patients aged 40–49 years, 50–59 years, and 60–70 years were 20%, 20%, and 60% respectively. 80% of informants were patients, and 20% of informants were caregivers. The number of users who used this application less than two times/week, 2 to 4 times/week, and more than four times/week was 70 %, 20, and 10% respectively.

Table 2 shows information about the physicians who completed the physician questionnaire. A total of 5 physicians at Mae Fah Luang University Medical Center Hospital and Mae Fah Luang University Hospital were male 100%. The number of physicians whose age 20–29 years, 30–39 years, 40–49 years, and 60–65 years are 40%, 20%, and 20% and 20% respectively. The participating physicians included general practitioners (40%), anesthesiology (20%), surgery (20%), and internal medicine(20%). All of these physicians used this application less than two times/week.

Table 1 Information about the patients who completed the patient questionnaire

Variables	%
Gender	
Male	80
Female	20
Age	
40 - 49 years	20
50 - 59 years	20
60 - 70 years	60
Informant	
Patient	80
Caregiver	20
Frequency of using this application	
Less than 2 times/week	70
2 to 4 times/week	20
More than 4 times/week	10

Table 2 Information about the physicians who completed the physician questionnaire

Variables	%
Gender	
Male	100
Age	
20 - 29 years	40
30 - 39 years	20
40 - 49 years	20
60 - 65 years	20
Specialty	
General practitioner	40
Anesthesiology	20
Surgery	20
Internal medicine	20
Frequency of using this application	
Less than 2 times/week	100

The results of patient satisfaction and physician satisfaction are shown in Figure 4 and Figure 5 respectively.

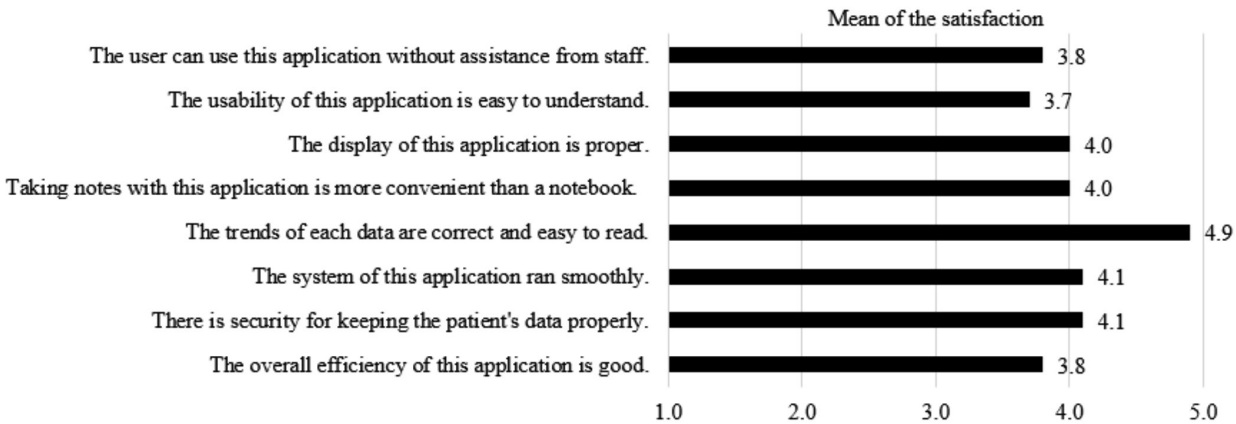


Figure 4 The result of the questionnaire about the patient satisfaction for this application (N = 10)

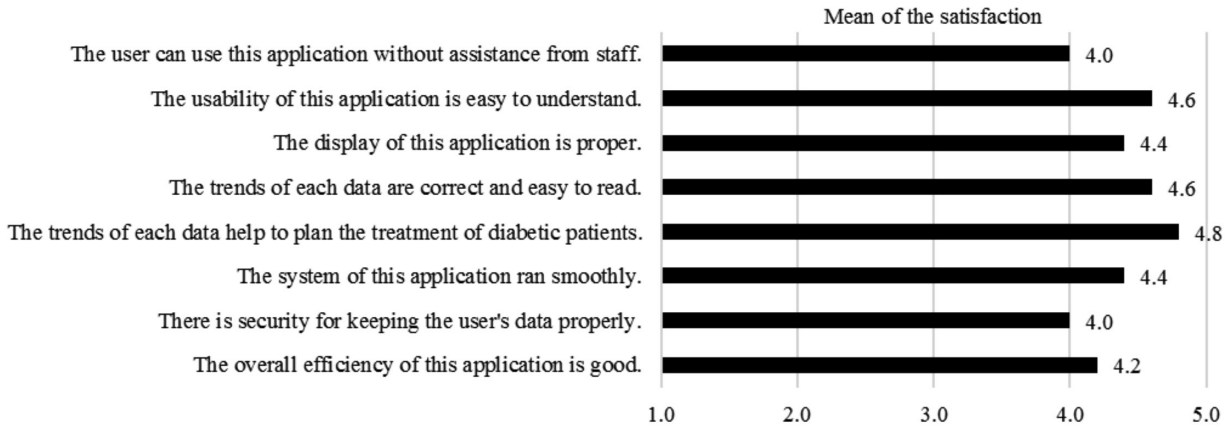


Figure 5 The result of the questionnaire about the physician satisfaction for this application (N = 5)

Discussion

All questions of the patient and physician satisfaction questionnaires received good score (more than 3.41/5.00). This application helped these diabetic patients to record and see the trend of their data with real-time data from the database server, in the same way as *Diamate*, a popular application for diabetic patients in Thailand[7]. In addition, the strength of this application is the display of the graph of blood glucose level, as well as the graph of blood pressure with meal times and medication times, to highlight possible causes of ineffective blood glucose control. Some applications merely list data or graphs of blood glucose levels and so correlation is difficult[8, 9]. The trends of each data set in this application help the physicians to monitor behavior and plan optimal treatment schedules for their patients. However, there are some limitations of this application. For example, some users cannot use this application properly by themselves because some features are too complicated. For instance, the user has to select the start date and end date before seeing the trends of each data set, by clicking on the date above each graph. Also, some functions might be forgotten, such as seeing the details by clicking on a plot or bar on the graph. In addition, this application is an Android-based mobile application so that it can be run on Android smartphones only, and not iphone or web based platforms.

Conclusion

In this project, this mobile application was developed and used smoothly. The results have shown that using information technology for gathering data is good for both patients and physicians. This application is also useful for other hospitals or diabetic clinics as it helps to collect data at the expert level. Further studies should add some additional beneficial features, such as notifications for recording data, adding other relevant data, which can help to prevent diabetic complications, connection of this application to health care systems so that data can be checked and confirmed by physicians or staff, show edited history, use one account for one physician, export the data in a file for opening on other operating systems.

In addition, this application should be run on every operating system such as Apple iOS and Microsoft's Windows Phone OS, because this application was developed with the Ionic framework which is a program for developing cross-platform applications. Furthermore, this application should be displayed in other languages such as English and French. Furthermore, hospitals, which have diabetic clinics or collection of diabetic patients, should publicize this application in both website and poster

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