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GMSMJ

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Manuscript Types

1. Special Article

These articles are invited by Editor-in-Chief, written in English, and structured as follows: Introduction, Main text, Conclusion and References.

2. Original Article

Original article reveals the research results regarding of basic and advanced clinical research in medicine and related health sciences, as well as medical education.

3. Community Medicine Article

Community medicine is topic related to community in the countries of Greater Mekong Subregion and also the health issues of people along the border of Thailand.

4. Review Article

Review article aggregates knowledge from the journals or books.

5. Short Report

Short report may be a preliminary study, short communication, case report or new emerging diseases.

6. Letter to the editor

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The manuscript should provide an English abstract which includes introduction, methodology, results and conclusion. It should be written concisely (should not exceed 300 words).

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Includes Introduction, Methodology which should detail materials or participants, ethical approval, clinical trial registration number (if any), methods, and statistical and data analysis, results, review contents, discussion and criticism, conclusion, acknowledgements (if any) and references. Total length of the body from abstract to conclusion does not exceed 4,000 words for original and review article and do not exceed 2,000 words for others.

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The journal publishes 3 issues a year: Issue 1 (January - April), Issue 2 (May - August) and Issue 3 (September -December). All submitted research articles and review articles will be evaluated by a double blinded peer-review process and reviewed by 2 experts who have knowledge, expertise, and experience in the field of medicine and related health sciences prior to publication. The journal encloses the information of authors and reviewers. In case of a difference of evaluation, the article evaluation will be considered and given a final decision.

Greater Mekong Subregion Medical Journal establishes the roles and duties for three different groups in the process of article publication: author (s), editor, and reviewers. The following information is given to the three groups of people so that they will strictly abide by its benefits of those concerns, including readers and others in academia.

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Contents

Original Article

Comparison of Characteristics and Outcome of The Patients with DRESS Who Received Culprit Drugs as Inpatient and Outpatient Basis

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Abstract:

Background: Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous adverse reaction (SCAR), life-threatening with multiple internal organs involvement. The difference between inpatient and outpatient cases have not been reported.

Objective: To compare the characteristics and outcome of the patient with DRESS who received culprit drugs as inpatient and outpatient basis.

Materials and Method: This was a prospective study in a total of 64 patients visiting the division, who were diagnosed with DRESS according to the RegiSCAR criteria (score ≥ 4). We compared the results of demographic data, clinical presentation, laboratory, and mortality rate between inpatient and outpatient cases.

Results: Among the 64 patients, the inpatient cases were 47% and outpatient cases were 53%. The most common culprit drugs were antibiotic drugs in inpatient cases and anti-epileptic drugs in the outpatient cases. Time interval to detect DRESS of inpatient cases were shorter than that of outpatient cases (13 days versus 22 days); *P*-value = 0.001. Antibiotic drugs were significantly higher in inpatient cases (*P*-value = 0.005). Allopurinol, facial edema, lymphadenopathy, atypical lymphocytes and RegiSCAR score were significantly higher in outpatient cases (*P*-value = 0.005, 0.001, 0.021, 0.031, and 0.047 respectively). Mortality rate was not significantly different in both cases.

Conclusion: The difference between inpatient and outpatient cases were time interval to detect DRESS, facial edema, lymphadenopathy, atypical lymphocytes and RegiSCAR score. This data can be useful to manage the patients with DRESS.

Keywords: Drug reaction, Eosinophilia, Systemic symptoms, Inpatient, Outpatient

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Introduction

Drug reaction with eosinophilia and systemic symptoms (DRESS) is a severe cutaneous drug reaction (SCAR).[1,2] Severe cutaneous adverse reactions are composed of drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), generalized bullous fixed drug eruptions (GBFDE), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN).[3,4] DRESS is life-threatening with multiple internal organs involvement.[4,5] The incidence is about 1:1,000 - 1:10,000 of the patients who receive culprit drugs.[5,6] The common culprit drugs are anti-epileptic drugs, allopurinol, antibiotic drugs, NSAIDs, dapsone and antidepressant.[5-14]

The time interval of DRESS after the culprit drugs administration is 2-6 weeks.[5,7] Clinical manifestations are fever, morbilliform eruption, lymphadenopathy, facial swelling, eosinophilia, and multiple internal organs involvement such as liver, heart, lung, and etc.[8,11,16,17] The RegiSCAR scoring system is the most used diagnostic criteria for diagnosing DRESS syndrome. They comprised of fever, lymphadenopathy, eosinophilia, atypical lymphocytosis, skin rash, skin biopsy, internal organs involvement, rash resolution and excluding other causes.[5,13]

Management of DRESS are withdrawal the culprit drugs, supportive treatments, systemic and topical corticosteroids.[18,19] The mortality rate is about 10%.[18,20] Long-term sequelae of DRESS are end stage renal disease (ESRD) and autoimmune disease such as autoimmune thyroid disease (Graves' disease and Hashimoto thyroiditis), autoimmune hemolytic anemia (AIHA), type 1 diabetes mellitus and alopecia areata.[21,22] To the best of our knowledge, no previous study of the difference between inpatient and outpatient cases have ever been reported.

Material and Methods

Study design

We conducted a prospective study from January 2013 to December 2019 including 64 patients who were diagnosed with DRESS by dermatologist at the dermatology unit of Phramongkutklao Hospital, Bangkok, Thailand.

Inclusion and exclusion criteria

The inclusion criteria included the patients over the age of 18 years old and the patients who were diagnosed with DRESS according to the RegiSCAR criteria. We enrolled the patients who had RegiSCAR scores 4-5 (probable DRESS) and RegiSCAR scores > 5 (definite DRESS). We excluded patients who declined to participate in the research. This study was approved by the Research Ethic Committee of Phramongkutklao College of Medicine.

Definition and data collection

IPD cases were defined as patients who received culprit drugs as inpatient basis and OPD cases were defined as patients who received culprit drugs as outpatient basis. After the DRESS patients were enrolled, we collected demographic data, clinical manifestations, laboratory, electrocardiogram, echocardiogram and mortality rate. Coronary angiogram was done in some patients who were suspected of having coronary artery disease.

Primary and secondary outcome

The primary outcome was the comparison of characteristic and outcome of the patients with DRESS who received culprit drugs as inpatient and outpatient basis. The secondary outcome was the prevalence of DRESS in Phramongkutklao Hospital, Bangkok, Thailand.

Statistical analysis

The demographic data were presented as number, percentage, range and mean ± SD. We compared the difference between IPD cases and OPD cases by independent t test or Mann-Whitney test and Fisher's exact test. P-value ≤ 0.05 was considered statistically significant.

Results

We enrolled a total of 64 patients who were diagnosed with DRESS due to the RegiSCAR criteria (RegiSCAR score ≥ 4). The mean age of participants were 53.3 years old. Males were slightly more than females. A nearly equal ratio of inpatient and outpatient were found. The RegiSCAR score 4-5 and > 5 were 78.1% and 21.9%, respectively. The demographic data were shown in Table 1.

Table 1 Demographic data of 64 DRESS patients

Characteristics	
Number of patients	64
Age in years (mean ± SD), (range)	53.3 ± 21.84 (18-91)
Sex (Male: Female)	36 : 28
Tine interval to detect DRESS in days, (mean ± SD), (range)	19.0 ± 11.95 (1-60)
Status of patients (Inpatient: Outpatient)	1 : 1.13
RegiSCAR score	
RegiSCAR score = 4-5, number (%)	50 (78.1%)
RegiSCAR score > 5, number (%)	14 (21.9%)

The most common culprit drugs were antibiotics. The second and the third common culprit drugs were anti-epileptic drugs and allopurinol, respectively. The other culprit drugs were shown in Table 2.

The comparison data were shown in Table 3. The antibiotic drugs were significantly higher in IPD cases (P-value = 0.005) and allopurinol were significantly higher in OPD cases, (P-value = 0.005). The time interval to detect DRESS of IPD cases were shorter than outpatient cases (13 days versus 22 days); (P-value = 0.001). The Average RegiSCAR score of OPD cases were significantly higher than IPD cases (5.21 versus 4.53); (P-value = 0.047). About clinical manifestations, facial edema and lymphadenopathy were significantly higher in OPD cases (P-value = 0.001, 0.021 respectively). Mean atypical lymphocytes count were significantly higher in outpatient cases (P-value = 0.031). The liver and heart were mostly common internal organs involvement but no significant internal organs involvement was found between both cases. The 30 days mortality rates were 16.7% in IPD cases and 14.7% in OPD cases and the 90 days mortality rates were 26.7% in IPD cases and 14.7% in OPD cases but the mortality rate was not significantly different.

Discussion

To the best of our knowledge, this study was the first prospective study to compare the characteristics and outcome of the patients with DRESS who received culprit drugs as inpatient and outpatient basis.

The demographic data of our study were similar to previous studies. The previous studies showed mean age of patients with DRESS at about 40-60 years old.[6,9,11,14] The most common culprit drugs in our study were antibiotic drugs but anti-epileptic drugs were the most common culprit drug in many previous studies.[6,8,9,11] The most common internal organ involvement was the liver which were similar to many previous reports.[5,7,8,12,15]

From our study, antibiotic drugs were significantly higher in IPD cases. In our opinion, we believe that IPD patients had higher chance to receive the antibiotic drugs due to serious infection or nosocomial infection. The significant parameter. In OPD cases, the parameter composed of drugs, diagnostic data and clinical manifestations. Allopurinol, time interval to detect DRESS, RegiSCAR score, facial edema, lymphadenopathy, and atypical lymphocytes were significantly higher in OPD cases.

Table 2 Culprit drugs

Culprit drugs	
Antibitotic drugs, number (%)	34 (51.5%)
Imipenem	5 (7.7%)
Isoniazid + Rifampicin + Pyrazinamide + Ethambutol	4 (6.1%)
Ceftriaxone	4 (6.1%)
Trimethoprim-Sulfamethoxazole	4 (6.1%)
Vancomycin*	3 (4.5%)
Clindamycin	2 (3.0%)
Meropenem*	2 (3.0%)
Ciprofloxacin*	2 (3.0%)
Ethionamide + Levofloxacin + Cycloserine	2 (3.0%)
Amoxicillin-clavulanic acid	1 (1.5%)
Colistin	1 (1.5%)
Abacavir	1 (1.5%)
Dapsone	1 (1.5%)
Piperacillin/tazobactam*	1 (1.5%)
Azithromycin	1 (1.5%)
Anti-epileptic drugs, number (%)	18 (27.3%)
Phenytoin	11 (16.8%)
Carbamazepine	3 (4.5%)
Lamotrigine	3 (4.5%)
Levetiracetam	1 (1.5%)

*2 patients received 2 suspected culprit drugs such as meropenem with vancomycin and piperacillin/tazobactam with ciprofloxacin.

Table 2 Culprit drugs (con.)

Culprit drugs	
Allopurinol	8 (12.1%)
NSAIDs, number (%)	3 (4.5%)
Ibuprofen	1 (1.5%)
Diclofenac	1 (1.5%)
Indomethacin	1 (1.5%)
Others, number (%)	3 (4.5%)
Antispasmodic drug	1 (1.5%)
Contrast media	1 (1.5%)
Methimazole	1 (1.5%)

IPD patients had shorter time interval to detect DRESS compared to OPD patients. In our opinion, we believe that the causes of shorter time interval in IPD cases were early detection of rashes and close monitor of the abnormal laboratory results by health care worker. Late detection by the patients or relatives in OPD cases resulted in higher clinical manifestations such as facial edema, lymphadenopathy, higher level of mean atypical lymphocytes count, and RegiSCAR score.

Table 3 Comparison of characteristics of DRESS between OPD cases and IPD cases

	OPD	IPD	*P*-value
Age in years (mean ± SD)	52.5 ± 22.72	54.13 ± 21.15	0.768
Male sex, number (%)	18 (52.9%)	18 (60%)	0.620
Culprit drugs			
Antibiotic drugs, number (%)	11 (32.4%)	21 (70.%)	0.005*
Anti-epileptic drugs, number (%)	11 (32.4%)	7 (23.3%)	0.579
Allopurinol, number (%)	8 (23.5%)	0 (0%)	0.005*
NSAIDs, number (%)	2 (5.9%)	1 (3.3%)	1.000
Others, number (%)	2 (5.9%)	1 (3.3%)	1.000
Time interval to detect DRESS in days,			
Median	22	13	<0.001*
Average RegiSCAR score (mean ± SD)	5.21 ± 1.57	4.53 ± 0.97	0.047*
Probable (score = 4-5), number (%)	24 (70.6%)	26 (86.7%)	0.142
Definite (score > 5), number (%)	10 (29.4%)	4 (13.3%)	0.142

Table 3 Comparison of characteristics of DRESS between OPD cases and IPD cases (con.)

	OPD	IPD	*P*-value
Facial edema, number (%)	23 (67.6%)	8 (26.7%)	0.001*
Lymphadenopathy, number (%)	12 (35.3%)	3 (10%)	0.021*
Eosinophils count (cells/μl), (mean ± SD)	1810.5 ± 2234.92	1189.59 ± 1351.79	0.191
Atypical lymphocytes count (cells/μl), (mean ± SD)	88.51 ± 147.28	26.83 ± 63.07	0.031*
Internal organ involvement			
Liver, number (%)	22 (64.7%)	20 (66.7%)	1.000
Heart, number (%)	14 (41.2%)	17 (56.7%)	1.000
Kidney, number (%)	1 (2.9%)	0 (0%)	1.000
Pancreas, number (%)	2 (5.9%)	2 (6.7%)	1.000
Chest, number (%)	1 (2.9%)	1 (3.3%)	1.000
30 days mortality, number (%)	5 (14.7%)	5 (16.7%)	1.000
90 days mortality, number (%)	5 (14.7%)	8 (26.7%)	0.352

P-value ≤ 0.05 was considered statistically significant

The limitations of our study included too small sample size and the data of underlying diseases was not collected.

Conclusion

Our study showed the common culprit drugs were antibiotic drugs, anti-epileptic drugs and allopurinol. The difference between inpatient and outpatient cases were time interval to detect DRESS, facial edema, lymphadenopathy, atypical lymphocytes and RegiSCAR score. This data can be useful to management the patient with DRESS.

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Comparison between "Rokprachamtua Khong Chan (My Underlying Diseases)" Web Application and Human-based Conventional Method to Stratify Military Personnel's Health Status and Report Results Effectively

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Abstract:

Background: Fort Nawamintharachini hospital developed the "5 colors ball tool" innovation to promote health concerns among military personnel after health checkups. However, this process resulted in time consumption, a high misdiagnosis rate, resource waste, expenses, and healthcare worker burnout. Consequently, a web application was developed to automate health checkup stratification and reporting.

Objective: The aim of this study is to evaluate the effectiveness of the "Rokprachamtua Khong Chan" web application in stratifying and reporting health results compared to human based conventional method.

Methods: This is an observational study which sampled 130 checkup results from 2,285 health results of military personnel who underwent medical checkups with Fort Nawamintharachini Hospital in 2023. The study compared misdiagnosis rate of web application with human-based process by using the same health results and stratified by specialist as a gold standard. Furthermore, the study also measured the time to report heath results.

Results: 2,285 checkup results were stratified into the following groups: green group 510 (22.32%), yellow group 482 (21.09%), orange group 759 (33.22%), pink group 232 (10.15%), and red group 302 (13.22%). The misdiagnosis rate of web application was lower than human-based conventional method which were 5.38% and 10.77% respectively (p=0.05). The web application reduced the time it took to stratify and report results from three months to seven days.

Conclusion: The "Rokprachamtua Khong Chan" web application is a useful tool that utilizes computer-based processing and technology to stratify the health status of military personnel. The application offers several advantages, including preventing human error, shortening the time required to report health results, and streamlining the process.

Keywords: Web application, Stratification, Checkup results, Effectiveness, Military personnel

Introduction

Fort Nawamintharachini Hospital is a military secondary care unit that offers health promotion, health prevention, and medical care to military personnel and their families. One of our services is an annual health checkup. To promote health concern in military service members, we created the "5 Colors Ball Tool," which is adapted from the "7 Colors Ball Tool" that contributes to health concern, severity perception, and leads to positive behavioral change.[1,2] Our 5 Colors Ball comprises green for good health, yellow for an increased chance of developing a disease, orange for a possible new diagnosis, pink for a well-controlled status of chronic diseases, which consist of hypertension, diabetes, or hyperlipidemia, and red for a poorly controlled status of chronic diseases.

The workflow of health checkup consisted of the following steps: (1) Military personnel underwent medical history taking, blood pressure measurement, weight and height assessment, waist circumference measurement, chest X-ray, and blood sample collection. (2) All checkup results were printed. (3) Two nurses stratified checkup results into the 5 colors groups. (4) Nurses sent checkup reports to military personnel in each military unit and provided advice.

After using the 5 Colors Ball Tool, we expected a decrease in the number of military personnel in the orange and red groups. However, we found that the number of personnel in the orange group increased from 14.45% in 2021 to 15.46% in 2022. Moreover, we encountered several issues,

including a misdiagnosed rate of 18.75%, lengthy reporting period which took three months to send health reports, loss of documents, waste of time and resources, and healthcare worker burnout.

Nowadays, technologies have been developed so far that healthcare professionals apply technology devices and applications for many purposes. It has been revealed that technology provides many benefits, such as a lower error rate, a rapid process, improved quality of data management and accessibility, and, most importantly, a positive effect on patient care outcomes.[3-7] Therefore, Fort Nawamintharachini Hospital decided to create an application that stratifies and reports results automatically with effectively, which was measured by reducing misdiagnosed rate and shorten the time to report health results.

Methods

In 2022, we developed a web application called "Rokprachamtua Khong Chan," which we first implemented in the recent health checkup from January to March 2023. Military personnel can access their checkup results through various devices, such as mobile phones, computers, laptops, and iPads.

Workflow

In 2023, a total of 2,285 military personnel underwent health checkups. Their data, which included blood pressure (BP), body mass index (BMI), waist circumference, blood test results, urine test results, stool test results, and ICD10-

diagnosis codes, were used to categorize them into five colors, which were then displayed in the web application alongside their lab results, medical information, and health advice. Those who were categorized as orange were appointed by the nurse for medical treatment, and the appointment date was displayed in the web application. The new workflow process is shown in Figure 1.
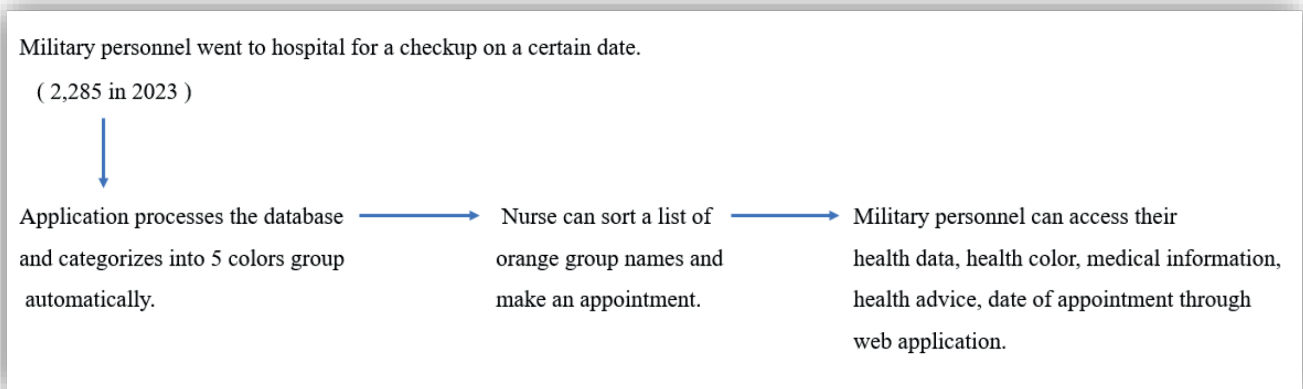
Figure 1 Workflow of health checkup with "Rokprachamtua Khong Chan" web application

User Interface

We developed a user-friendly interface (Figure 2) in the web application.[8-11] To log in, users need to fill in their ID number and password, which they created during registration. The application provides various functions, such as displaying personal data, health status, health colors, medical illnesses, medications, laboratory results, referral documents, appointment dates, medical information, and health advice. Moreover, a supportive channel was created for users to change their appointment date or inquire about their health through Line Official Account.
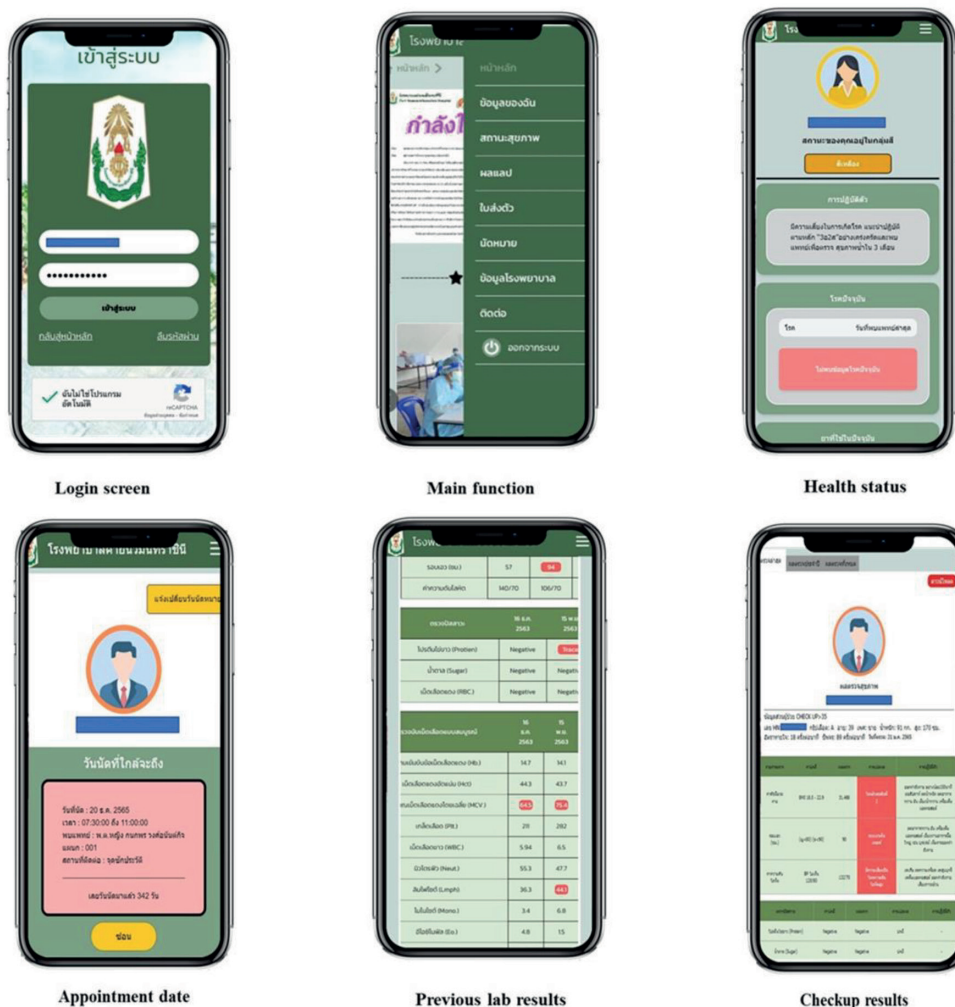
Figure 2 User interface

Apart from the user interface, the nurse interface can monitor users in each group and track those in the orange and red groups for treatment.

Stratification Algorithm

The "Rokprachamtua Khong Chan" web application categorizes health checkup results into five color-coded groups (Table 1) to identify health concerns and promote positive behaviors for preventing noncommunicable diseases (NCDs), which are the leading cause of death in Thailand.[12] The green group represents healthy individuals with blood pressure (BP) < 120/80 mmHg, body mass index (BMI) < 23 kg/m^2, waist circumference < 80 cm (female) or < 90 cm (male), and all laboratory results within the normal range. The yellow group represents individuals at risk with one or more of the following: BP 120-139/80-89 mmHg, BMI 23-39 kg/m^2, waist circumference ≥ 80 cm (female) or ≥ 90 cm (male), fasting blood sugar 100-125 mg/dL, serum uric acid > 8.4 mg/dL. The orange group represents individuals with suspected disease, with one or more of the following: BP ≥ 140/90 mmHg, BMI ≥ 40 kg/m^2, fasting blood sugar ≥ 126 mg/dL, serum cholesterol > 200 mg/dL, serum triglyceride > 150 mg/dL, etc. The pink and red groups are identified using ICD-10 codes. Users diagnosed with ICD-10 codes I10, E10, E11, or E78 are categorized as either pink or red. Users with I10 recorded with BP ≥ 140/90 mmHg, E10 or E11 recorded with fasting blood sugar ≥ 130 mg/dL, or E78 recorded with serum cholesterol ≥ 200 mg/dL or serum triglyceride ≥ 150

mg/dL, are categorized as red. Users who do not meet these criteria are categorized as pink (Figure 3). Our algorithm is based on guidelines from sources such as the Division of Non-Communicable Diseases, WHO criteria for diagnosing polycythemia vera, The Thai Society of Hematology, etc.

Table 1 Criteria for risk stratification

		Green	Yellow	Orange	Red	Pink
Blood pressure (mmHg)	Systolic	< 120	120 - 139	≥ 140	≥ 140	
	Diastolic	< 80	80 - 89	≥ 90	≥ 90	
Heart rate (bpm)				<50, >120		
Body mass index (kg/m²)		< 23	≥ 23 - < 40	≥ 40		
Waist circumference (cm)	Female	< 80	≥ 80			
	Male	< 90	≥ 90			
Fasting blood sugar (mg/dL)		< 100	100 – 125	≥ 126	≥ 130	
Hb (g/dL)	Male	13-16.5		<13, > 16.5		
	Female	12-16		<12, > 16		
Hct (%)	Male	39-49		<39, > 49		
	Female	36-48		<36, > 48		
Platelet (10³cell/cu.mm.)		140-400		<140, > 450		
WBC (10³cell/cu.mm.)		4-11		< 4, > 11		
Uric acid (mg/dL)		2.47-8.4	> 8.4			
BUN (mg/dL)		6-20		> 20		
Creatinine (mg/dL)		0.5-1.2		> 1.2		
eGFR (ml/min/1.73mm³)		> 90		< 60		
Cholesterol (mg/dL)		≤ 200		> 200	≥ 200	
Triglyceride (mg/dL)		≤ 150		> 150	≥ 150	
SGOT /AST(U/L)		0-37		>37		
SGPT/ALT (U/L)		0-41		> 41		
Alkaline phosphatase (U/L)		40-129		> 129		
Stool occult blood				positive		
Urine				Sugar1+, RBC 1+, Protein 1+		

Application Security

During the development of this application, cybersecurity policies were a top priority, especially when handling medical data. We designed the application to restrict access to healthcare workers and only permitted authorized personnel to access the data. Users are required to register with the application manager before using the program, and the user's details must be
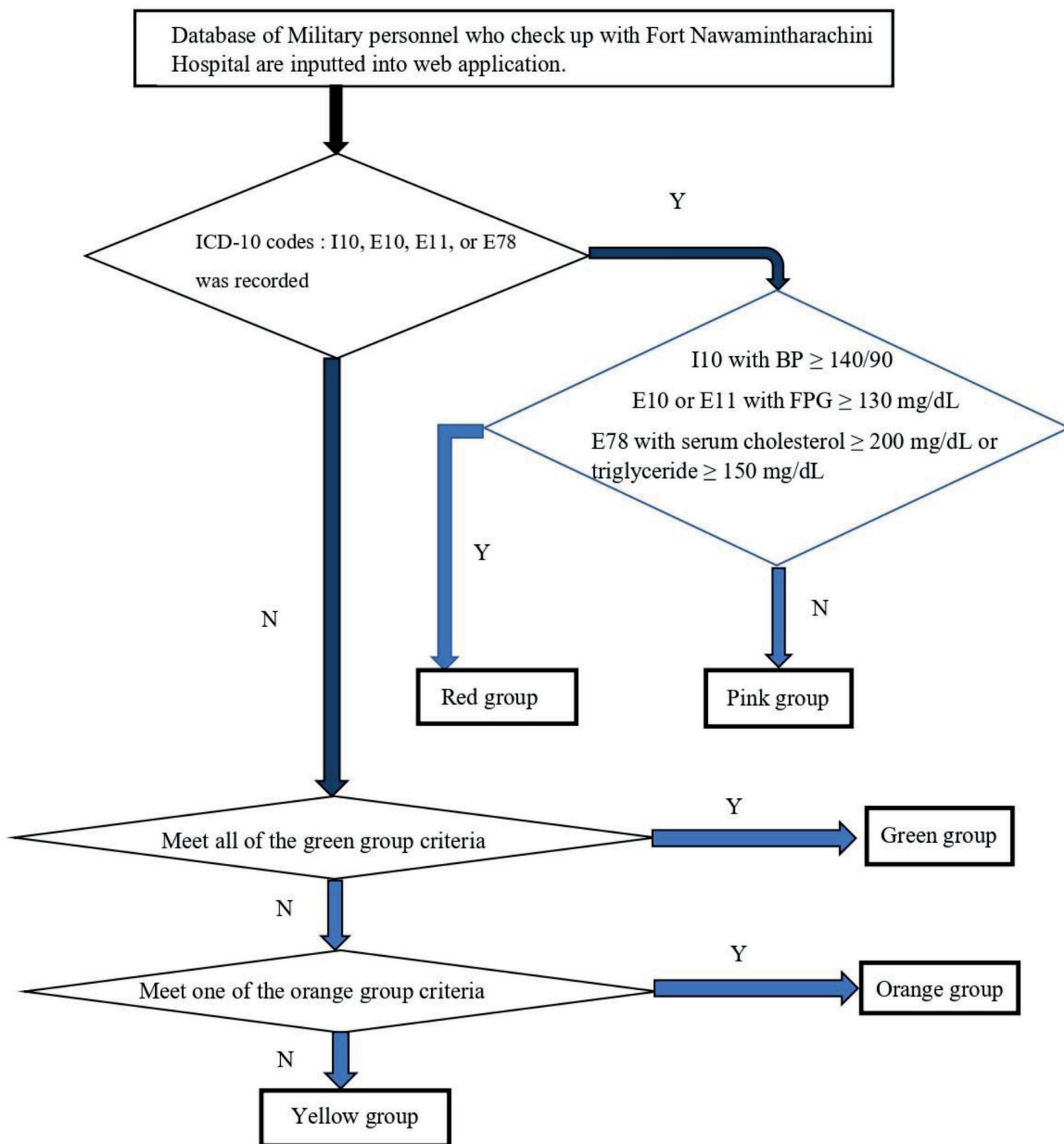
Figure 3 Workflow of algorithm stratification

registered and identified in the hospital's database before being granted access. Moreover, if the user remains inactive for 15 minutes, the application will log out automatically. According to the Personal Data Protection Act (2019), users must be informed of the purpose of collecting, using, or disclosing their Personal Data and be requested to provide their consent before starting to use the application.

Because it's a pilot study, authors calculated sample size from the misdiagnosed data in 2022 which was 9 misdiagnosed results from the sampling of 48 results (18.75%). The calculated sample size was 40. The authors sampled 130 results from the health reports of 2,285 military personnel who underwent health checkups with Fort Nawamintharachini Hospital in 2023 by simple randomization and compared misdiagnosed rate of web application stratification with nurse stratification.

Results

In 2023, 2,285 military personnel underwent medical checkups, all of them were male. The average age was approximately 33 years and ranged from 20 to 58 years. All 2,285 health reports were stratified into five color groups: green (510, 22.32%), yellow (482, 21.09%), orange (759, 33.22%), pink (232, 10.15%), and red (302, 13.22%). The misdiagnosed rate in the stratification process using the web application was 5.38% compare with nurse stratification was 10.77% ($p= 0.05$) as shown in Figure 4. The application reduced the time to stratify and report results from three months to seven days. The Lean process also reduced costs of transportation, paper, ink which were 23,220 baht, more importantly, web application saved 462 hours of nurse working hours, reduced nurse workload, and prevented burnout in healthcare professionals.
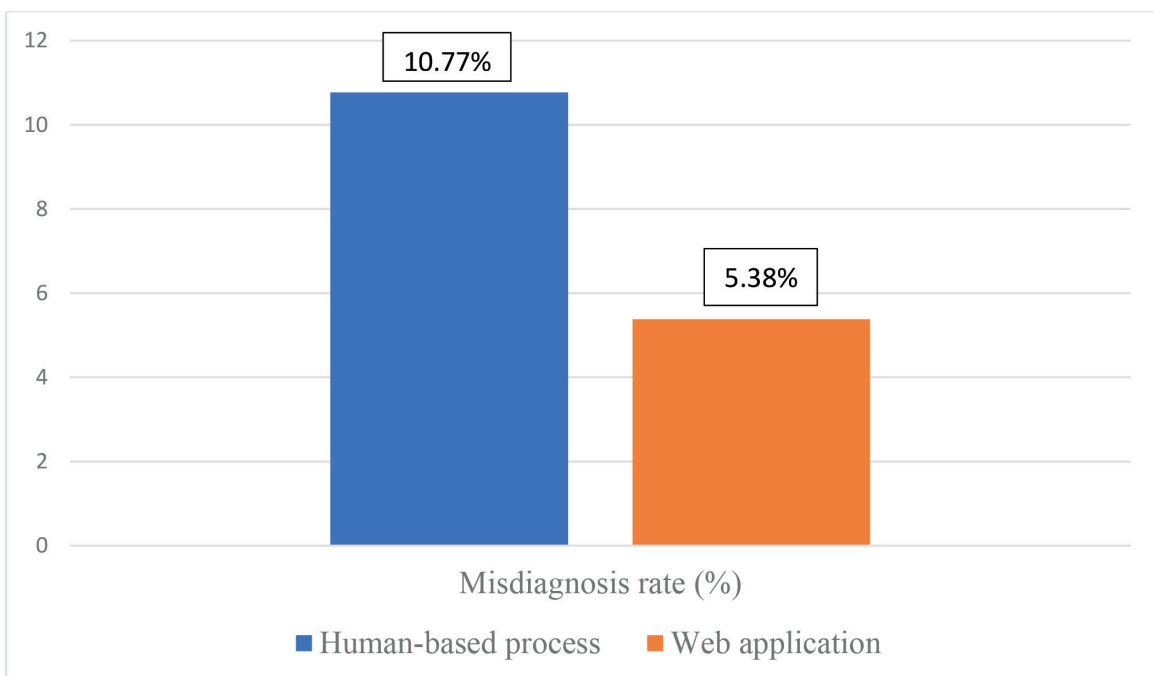
Figure 4 Comparison the misdiagnosis rate of stratification between human-based process and web application

Discussion

The "Rokprachamtua Khong Chan" application is the first application in Thailand that uses color to stratify checkup results for promoting health concern in military personnel. Using colors will contribute to visual perception, perceived severity, health motivation leading to positive behavioral change according to the concept of the health belief model theory. Previous studies[1,2,4] have also shown the effectiveness of reduction in disease severity with the provision of health behavior modification programs. The study in Bangladesh[4] also suggested that using both technology and color stratification in health checkups is an effective tool in the social healthcare system in developing countries.

Because the military unit in Chachoengsao province was transferred to take responsibilities by Fort Chakrapong Hospital, the number of military personnel who had checkups with Fort Nawamintharachini Hospital declined in 2023. The number of military personnel in the orange group increased from 15.46% in 2022 to 33.22% in 2023 because the stratification criteria were defined more specifically, such as hemoglobin of male < 13 mg/dL, creatinine > 1.2 mg/dL, instead of the "lab abnormality" in previous criteria, which we can't ensure that sorter used all laboratory results to determine. As well as, we interviewed nurses who stratified checkup results, they said that sometimes they used their opinions to stratify colors. If the lab was slight abnormality like AST 40 mg/dL, they didn't stratify to orange group. Furthermore, the stratification with the web application is more effective than human, as it is more precise, accurate, and faster, which is demonstrated by the lessened misdiagnosed rate and the shortened time to stratify and report. Besides, web application has a channel for military personnel to ask about their health problems and healthcare workers

gives recommendations such as exercise, healthy dietary pattern, and individual lifestyle counseling. The authors identified the cause of misdiagnosed rate and found that one of problems was inadequate input of ICD-10 diagnosed history data. Therefore, data of ICD-10 diagnosed history for at least 5 years were inputted to solve this problem. Moreover, some health information such as blood pressure, heart rate, BMI, waist circumference must be filled by healthcare workers which can cause human error and lead to the wrong stratification.

There were some limitations in the process of health checkup. Firstly, there was still a human process such as filling in the data about BMI, waist circumference, and vital signs because there was no automatic machine. Secondly, limited resources both in healthcare workers and medical equipment caused screening hustle. The healthcare workers had to screen about 120-300 military personnel per day, so sometimes there was not enough time to repeat blood pressure measurement which might affect the blood pressure result.

The authors plan to create health behavior modification interventions that are specified in each group and measure the health outcomes. We not only want to survey user satisfaction to improve the application but also want to validate our stratification algorithm and create the best version to maximize health benefits. Furthermore, we want to use the data to create projects and determine the hospital policy for improving the process of care in military personnel and their families.

Conclusion

The "Rokprachamtua Khong Chan" application is a helpful web application that categorizes the checkup results of military personnel into five color groups to raise health concerns. We used computer-based processing and technology to avoid human

error, shorten the time to report health results, use a Lean process, prevent document loss, facilitate two-way communication, and proactively care for military personnel.

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Bloodless Treatment in Jehovah's Witnesses with Acute Myeloid Leukemia

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Abstract: Jehovah's Witnesses are a millenarian Christian faith with approximately 8.5 million adherents worldwide involved in evangelism and a much larger number (nearly 20 million) who associate with them.[1] In Thailand, there are more than 5,000 Jehovah's Witnesses. They value life and accept the vast majority of medical treatments. However, they do not accept allogeneic blood transfusion therapy because of their understanding of Biblical statements to abstain from blood. We report the case of a Thai woman who presented with pruritus for 6 weeks and was diagnosed acute myeloid leukemia (AML). She received treatment without any blood component transfusion and achieved complete remission. We also used measures and drugs that alleviated anemia and bleeding problems in order to avoid blood transfusion. Because the number of Jehovah's Witnesses is increasing, growing numbers of non-Witness patients prefer treatment without blood transfusion, and because blood inventory shortages, safety, and blood costs continue to be of concern in many countries, this is a relevant topic for clinicians. Management of patients without allogeneic blood is a medical and ethical challenge for medical practitioners in Thailand, but it can be met as we show in this case report.

Keywords: Jehovah's Witnesses, Acute myeloid leukemia, Optimal Patient Blood Management

Introduction

Jehovah's Witnesses are a Christian faith that had its modern beginnings in the 1870s in the US. In their latest report from 2022, there were approximately 8.5 million Jehovah's Witnesses worldwide[1], including more than 5,000 in Thailand. Jehovah's Witnesses believe that life is sacred and accept the vast majority of medical treatments. However, they do not accept transfusions of allogeneic (donor) whole blood, red blood cells, white blood cells, platelets, and plasma.[2] Neither do they accept preoperative autologous blood donation for later reinfusion. Although the risks associated

with allogeneic blood are well established, the Witnesses' primary reason for declining blood transfusion is religious. Both the Old and New Testaments clearly command them to abstain from blood. (Genesis 9:4; Leviticus 17:10; Deuteronomy 12:23; Acts 15:28, 29). Also, God views blood as representing life. (Leviticus 17:14). So, they avoid taking blood not only in obedience to God but also out of respect for him as the Giver of life.[3] At one time, the medical community generally viewed strategies for avoiding transfusions, so-called bloodless medicine, as extreme, even suicidal, but this has changed in recent years. For example, in 2004, an article published in a medical education journal stated that "many of the techniques developed for use in Jehovah's Witness patients will become standard practice in years to come."[3] More recently, in 2021 the World Health Organization urged all nations to make wider use of so-called Patient Blood Management (PBM) strategies to conserve and manage patients' own blood in order to preempt the use of allogeneic blood transfusion to improve patient outcomes, reduce costs, and respect patient autonomy. In the past, blood component transfusion has been viewed as a routine or standard treatment. However, the management of patients who are Jehovah's Witnesses can be a medical and ethical challenge for some physicians and health-related personnel. Here, we report successful treatment of newly diagnosed acute myeloid leukemia presenting with pruritus. This can be an example of bloodless management for Jehovah's Witnesses in medical practice of Thailand.

Case Presentation

A 73-year-old housewife Jehovah's Witnesses with underlying diseases of hypertension, DM type 2 and ischemic heart disease, living in Bangkok presented with six weeks of pruritus. Before her symptom, she stated having COVID-19 vaccination and had pruritus with some response to topical corticosteroid. She then developed skin lesion on both forearms and anorexia. She went to see medical attention and was found to have anemia, leukopenia and thrombocytopenia. Because of being Jehovah's Witnesses, she was referred to another hospital for bone marrow examination to get definite diagnosis. Her current medication was novomix, isosorbide dinitrate, bisoprolol, aspirin, azilsartan, atorvastatin, hydrochlorothiazide, amlodipine, tibolone, omeprazole, vitamin C, nicergoline, piracetam, betahistine, vitamin B12, clobazam, clonazepam and dimenhydrinate. She had 2 healthy children; both were also Jehovah's Witnesses. At hematology clinic, physical examination revealed an obese old woman, looked fatigue and moderate anemia without jaundice or palpable lymph nodes. She had no palpable liver and spleen. Multiple well defined erythematous scaly papules and thin plaques were seen on both forearms (Figure 1). She also had pitting edema 2+ on both legs. CBC showed Hct 27%, WBC 2.93 x 10^9/L, PMN 27%, L 35%, M 36%, B 2%, platelet 49 x 10^9/L, NRBC 4%, MCV 91 fL. Bone marrow examination (Figure 2) revealed blast cells 50% and dyserythropoiesis of erythroid cells. Immunohistochemistry (IHC) of blast cells showed CD34+, CD117+, CD33+, MPO+, CD68-, lysozyme+, CD3-, PAX5- findings were consistent with acute myeloid leukemia (Figure 3). Bone marrow cytogenetics revealed 46, XX.
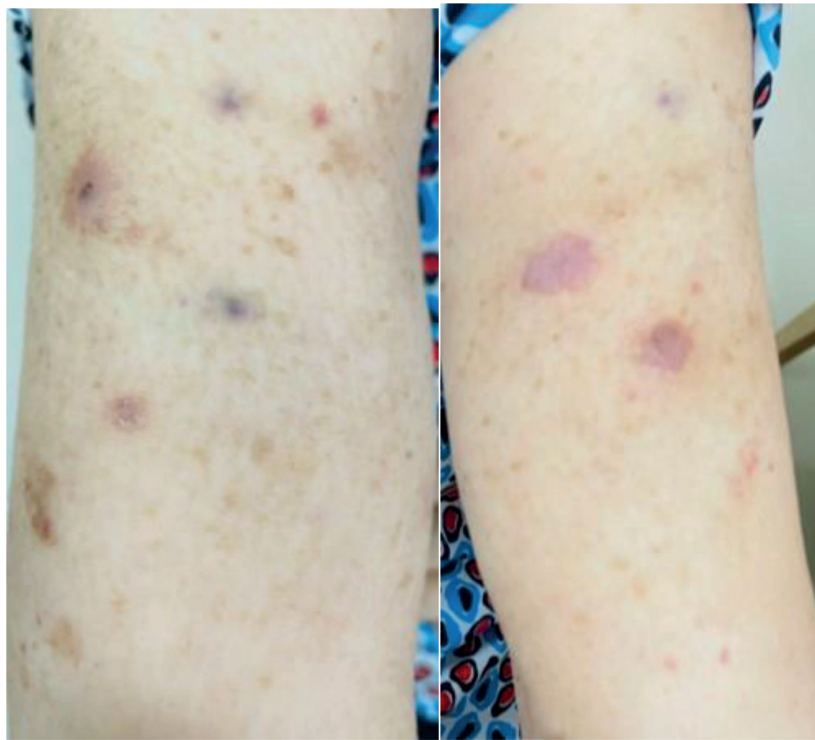
Figure 1 Skin lesions on both forearms
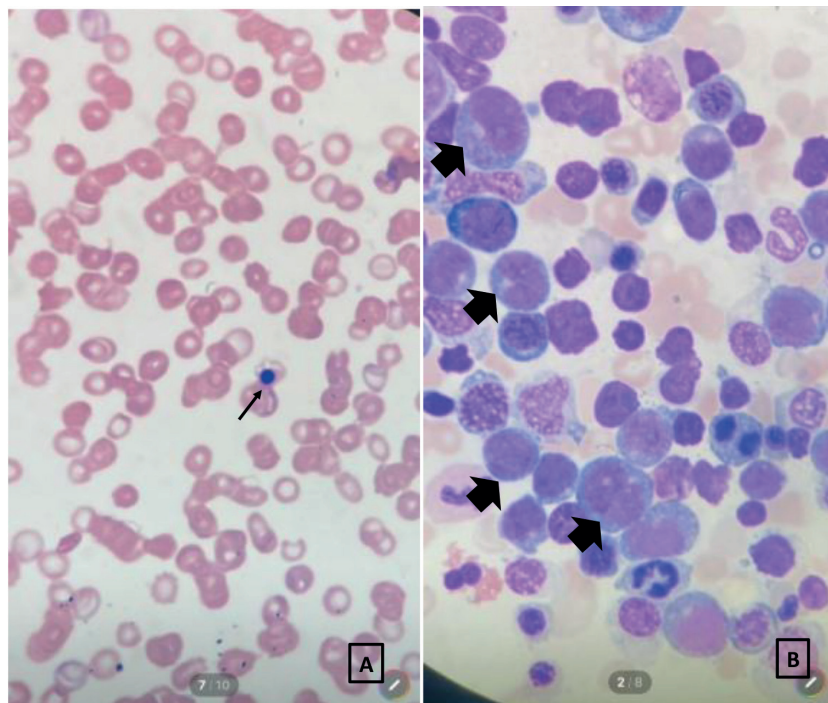
Figure 2 Peripheral blood smear (A) shows pancytopenia with nucleated red cell (arrow). Bone marrow smear (B) shows dyserythropoiesis with blast cells (arrowhead).
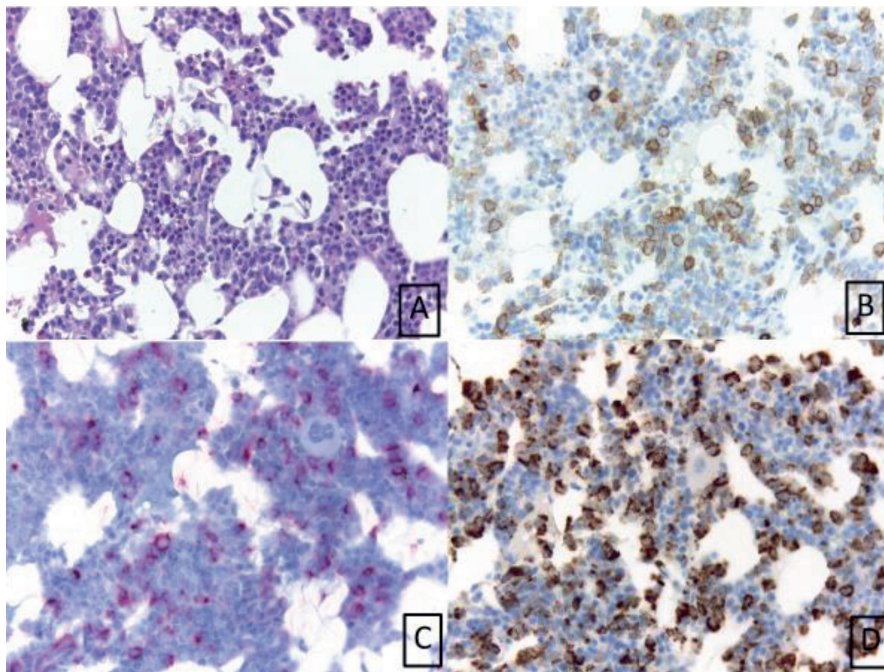
Figure 3 Bone marrow biopsy (H&E) (A) shows hypercellular marrow with mildly increased mononuclear cell infiltrate. Immunohistochemistry for CD34 (B), CD117 (C) and MPO (D) highlights increased myeloblasts.

Patient received azacytidine 12 cycles for treatment of acute myeloid leukemia with complete response but unfortunately had relapsed disease and so, venetoclax was added with causing lowing platelet from 15×10^9/L to 7×10^9/L. Patient subsequently received romiplostim injection and platelet was up to 26×10^9/L. She had never received any blood component during treatment which was accepted by her belief. She did not have any serious bleeding from treatment. She also received erythropoietin injection for anemia.

Discussion

This patient presented with pruritus and fatigue for 6 weeks. She had history of COVID-19 vaccination before this illness which we did not know this illness was vaccine related or co-incidence. She had pancytopenia and bone marrow examination was diagnostic. Because, the patient was Jehovah's Witnesses, this could be more complicated during treatment. Most patients who received induction chemotherapy for acute myeloid leukemia usually experienced infection, bleeding and anemia which most of them required blood component therapy. The patient refused any blood component transfusion. So, if patient needed transfusion, what should be the suitable management? We had to critically planned for the best treatment and prepared for complication management before treatment initiation. Because of the aggressiveness of disease, we had not much time. Treatment should be started as soon as possible.

Management of patients with Jehovah's Witnesses should begin with awareness and open-minded attitude to patients' beliefs. We have to accept the truth that there are many patients with this denomination and they don't accept blood component treatment in all circumstances. We have to respect their rights and decision. This is such a medical challenge of physician capability and teamwork to flexible using alternative therapy in case that patients need it. With advanced knowledge and technology in medicine, we can use MIS (minimally invasive surgery)

e.g., laparoscopic, limited surgery, if patients need surgery or may use radiation therapy instead of surgery if possible. Intervention radiology such as embolization or surgical clipping can help to stop bleeding during surgical procedure. For perioperative blood management, optimization of hemoglobin levels preoperatively, attention to blood-salvaging methods intraoperatively, and minimization of blood draws postoperatively should be applied.[4] Hemostatic agents such as fibrin glue, recombinant activated factor VII, prothrombin complex concentrate (PCC) can be used by patients' permission. Tranexamic acid and DDAVP can also be applied for minor bleeding. We also have drugs activating production of blood cells[5-6] such as erythropoietin (Epoetin) for red cells, G-CSF (granulocyte-colony stimulating factor) for white blood cells and thrombopoietin receptor agonists such as eltrombopag and romiplostim for platelet production. These measurements can alleviate the need for blood component requirement. Hematology consultation can be helpful in management of patients undergoing surgery.[7] For specific treatment of cancer, we should avoid any aggressive chemotherapy, if possible, by using alternative such as azacytidine, decitabine venetoclax for acute myeloid leukemia. All-trans retinoic acid (ATRA) and arsenic trioxide should be considered for acute promyelocytic leukemia treatment. At present, we have many targeted therapy and immunotherapy for cancer treatment such as gefitinib and erlotinib in lung cancer with EGFR mutation. So, the role of aggressive chemotherapy should be less, and this brings less complication which resulted in less requirement for blood component.

Conclusion

We reported case of acute myeloid leukemia in Jehovah's Witnesses Thai patient. Although this was serious hematologic malignancy and had potentially required blood component during treatment, we successfully used bloodless management in this case which was accepted by the patient and relatives. This was such a challenge in medical and ethical issue and could be an example for physician and teamwork to coping with their illness in the future.

Conflict of interest

The authors declare no conflict of interest in this case report.

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Lactose intolerance: Biochemistry Perspective

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Abstract: Lactose is disaccharide that found mainly in dairy products derived from mammary glands except in sea lions and walruses due to low milk production. It also contains fatty lactose-free milk. β-galactosyl-1,4 glucose.[1] Lactose is an essential sugar for a newborn. Since there randomized comparative studies.[2,3] They gathered breastfed newborns or receiving lactose-containing milk is compared with newborns fed lactose-free milk, the first group of newborns had higher blood sugar levels, nutrients and amino acids than the second group. Studies in adults have found that 14% of their energy intake comes from dairy products, figures from Europe and North America. while the People's Republic of China and developing countries account for only 4%, but the overall consumption of dairy products in all regions is on an upward trend.[4]

Keywords: Lactose intolerance, Lactase deficiency, Malabsorption

Introduction

There is 5 g of lactose in 100 ml of cow's milk, which is equivalent to 12.5 g of lactose in 250 ml of cow's milk, which is more commonly sold in packaged quantities than 100 ml. Others include yogurt and cheese, which are the second largest fermentation industry after alcohol.[4] Yogurt contains half of the unprocessed lactose. Compared to cheese, cheese has less lactose and sugar content. There is even less lactose available if cooked. Lactose has also been found to be produced in powdered form to be used as a common additive in processed foods to add texture and taste to foods such as: sausage, gravy, margarine, bread. In addition, the content of lactose in various foods is shown in Table 1.

Table 1 shows the content of lactose in various food products

Food type	Lactose content per 100 grams of food (grams)	Lactose content per 1 serving (grams)
Soft ice cream	6.4	5.7
Full milk	4.7	15
Goat's milk	4.5	13
Latte macchiato	4.3	8.6
Biological yogurt	4.0	9.5
Ready sauces	3.6	4.5
Pudding/ custard	3.6	4.5

The digestion and absorption of lactose occurs in the small intestine. The enzyme lactase is coded from the LCT gene located on the second pair of chromosomes consisting of 17 exons. The lactase-phlorizin hydrolase [3.2.1.23] is found in the brush border of the small intestine and is most abundant in the mid-jejunum covering the epithelium of matured enterocytes and contains two identical 160 kDa extracellular polypeptide chains with alpha-glucosidase and beta-galactosidase activity. Part of this enzyme cleaves sugars into monosaccharides, glucose and galactose. These sugars then enter the enterocyte via sodium-glucose cotransporter 1 (SGLT1), is digested in large quantities and enters the enterocyte via glucose transporter 2 (GLUT2) as well.[5-7]

The definition of a condition of lactose deficiency, depletion, or abnormal absorption of lactose can be categorized as shown in Table 2.

Table 2 shows disease or condition related to lactose intolerance

Disease or condition	Definition
Congenital lactase deficiency	A very rare genetic disorder is a frameshift mutation that leads to an inability to produce the enzyme lactase. The symptoms are often severe immediately after birth.
Lactase non-persistence	Reduced intestinal lactase expression in the first 20 years of life. This phenotype is found worldwide.
Lactase persistence	The persistent expression of intestinal lactase enzyme beyond infancy, the phenotype was found to be more common in western countries.
Lactase deficiency	An inability to digest large amounts of lactose due to low activity of the enzyme lactase in the small intestine.
Lactose malabsorption	Conditions with the passage of lactose into the colon as a result of lactase deficiency or other pathologies.
Primary lactose malabsorption	Abnormal lactose malabsorption caused by lactase non-persistence.

Disease or condition	Definition
Secondary lactose malabsorption	Abnormal absorption of lactose caused by decreased lactase expression is commonly caused by acute enteritis, which can be reversible.
Lactose intolerance	Typical gastrointestinal symptoms such as abdominal pain, flatulence, and diarrhea in people with lactose malabsorption after testing by eating lactose sugar
Functional lactose intolerance	Symptoms of lactose intolerance without lactose malabsorption
Self-reported lactose intolerance	Based on the history of symptoms of lactose intolerance without the diagnosis of lactose intolerance or lactose malabsorption.

Lactose malabsorption and Lactose intolerance

Lactose malabsorption is often a condition that leads to lactose intolerance. However, these two conditions require careful diagnosis as they are confusing, and the cause of the condition must be considered separately. It was found that a small number of patients with lactose malabsorption did not experience any abnormalities after consuming standard dairy products. While some people experience symptoms such as borborygmi (a feeling of shaking in the stomach) and flatulence after consuming lactose-containing products. The onset of disease was also found to be strongly associated with the production of hydrogen gas during the breath test. In addition, the digestible sugar lactose in the small intestine caused osmotic trapping and excessive fermentation[8] times the amount of lactose converted to short-chain fatty acids (SCFA).[5] Diarrhea will occur if the associated lactose content exceeds the capacity of the colonic microbiota due to fermentation or excessive amounts of SCFA in the colon as shown in Figure 1.
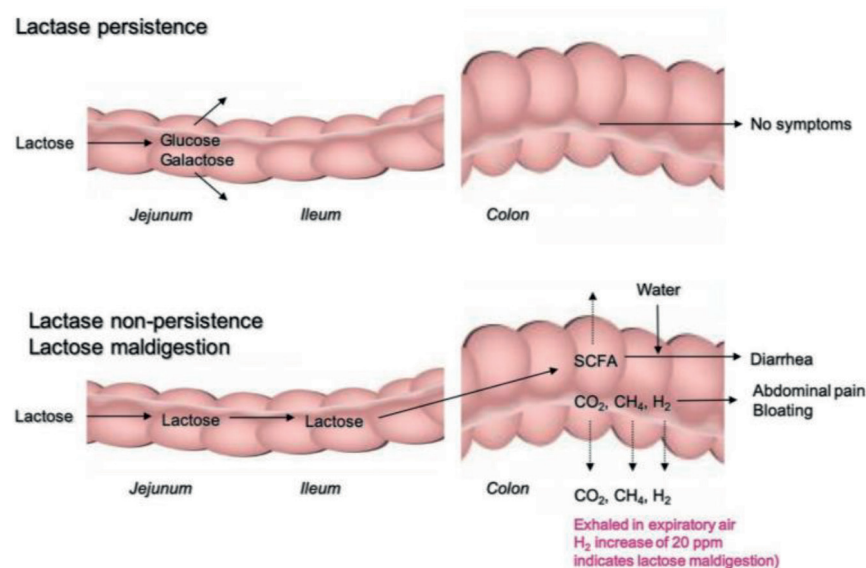
Figure 1 shows the pathophysiology of the enzyme lactase production leading to the fermentation of lactose to short-chain fatty acids, methane, and carbon dioxide. and hydrogen gas, which can lead to diarrhea, abdominal pain, and flatulence.[9]

Fermentation that occurs in the large intestine is caused by the normal state of decreased oxygen in the large intestine. These bacteria transport electrons via NADH to the organic compound resulting from their inability to digest lactose to produce lactose into NAD+, which will have a variety of microbial fermentation forms. But all of these require electron transport receptor generated during the oxidation reaction. Therefore, fermentation requires many organic compounds to accept electrons as mentioned, e.g., short-chain fatty acids, lactic acid, alcohol, etc.[8,10]

There are many factors that can induce lactose intolerance or are classified as lactose intolerance that are multifactorial. It consists of extrinsic factors and intrinsic factors as shown in Figure 2. Examples of extrinsic factors that trigger such as the amount of lactose consumed affects its movement into the small intestine and increases the rate of transport of indigestible lactose into the large intestine. Intrinsic factors that drive the expression of genes that play a role in the production of enzymes responsible for digestion and absorption of diglycerides at the brush border of the small intestine, or the history of abnormal gastrointestinal anatomy. including abnormal intestinal microbiota.[10,11]

Signs and symptoms of lactose intolerance usually appear 30 minutes to 1 to 2 hours after eating foods containing lactose, such as dairy products. The severity of symptoms depends on the amount of lactose consumed and the severity of the disease as mentioned above. The symptoms that can occur include diarrhea, flatulence, abdominal pain, nausea, vomiting, a lot of wind in the stomach, or there may be more than usual burping.[12]
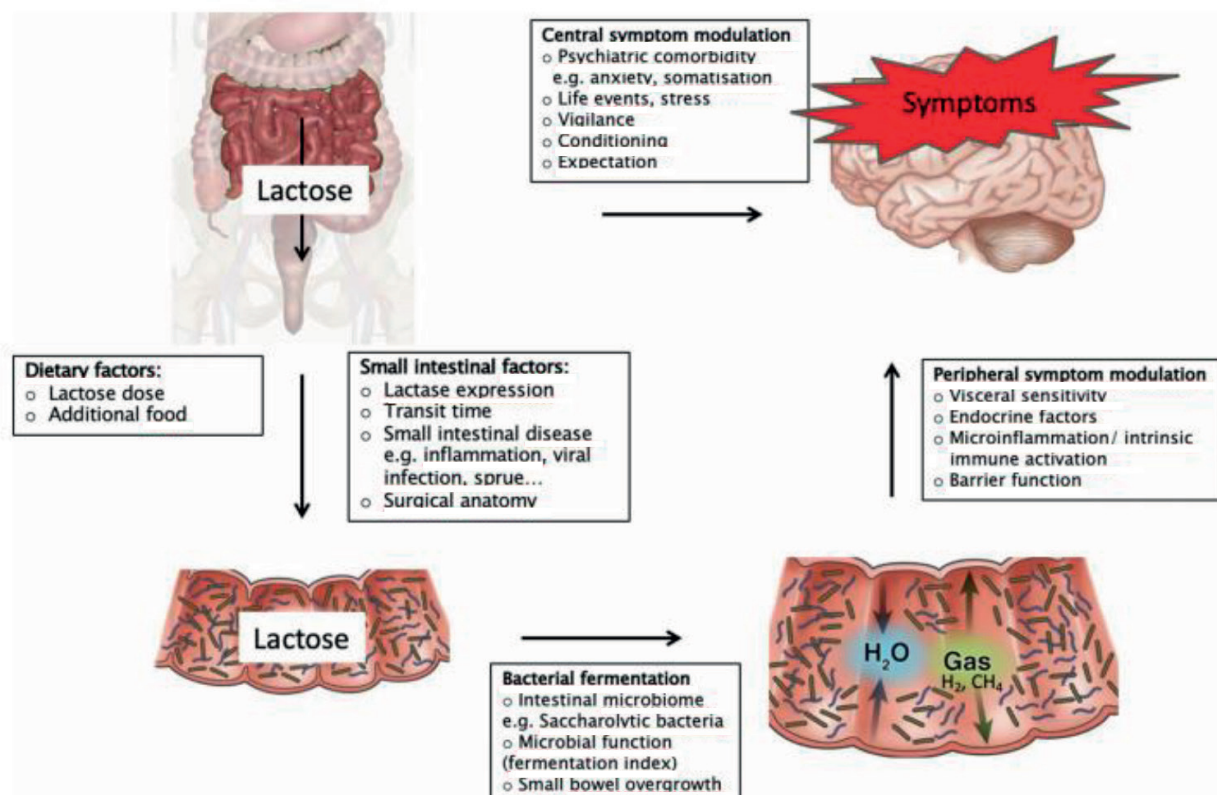

Figure 2 shows the factors inducing lactose intolerance and the pathophysiology

Secondary Lactose Intolerance

Certain conditions or environmental conditions can trigger lactase enzyme deficiency. Rotavirus infection, which is a pathology on the epithelium of the small intestine that is common in children under 5 years of age.[13] The rotavirus can invade the cells of the mature small intestinal epithelium, meaning that the cells are already able to produce the enzyme lactase fully and detachment of the villi, causing villi atrophy, thereby inducing crypt cell hyperplasia. In which these cells are not fully developed so they are unable to produce lactase, even if they can produce it in small amounts in addition to rotavirus infection, other conditions can cause secondary lactose intolerance, such as inflammation of the intestinal mucosa caused by bacterial infection. Infants with cow milk protein allergy (CMPA) are another common cause. Others are patients with small bowel resection or stomach surgery, receiving chemotherapy, opportunistic infections in HIV-infected patients. However, if the trigger or underlying condition is treated, lactose intolerance is also resolved.

Investigation in Lactose Intolerance

Although lactose intolerance can be diagnosed by history taking especially nutritional history, eating history, physical examination but there are cases where history taking physical examination still cannot be clearly identified. Therefore, additional diagnostic tests were sent to confirm it.

Genetic testing using Real-time PCR, in which genomic DNA is extracted from a patient's blood or collected from the buccal area. This method is appropriate in areas where there is a high prevalence of genetic predisposition or in epidemiological studies.

In Caucasians, the LCT-13910:C/T polymorphism results in persistent lactase and genetic testing can also identify lactase non-persistent syndrome. However, genetic testing is more complex and genetically heterogeneous in patients of African or Asian descent, where genetic testing is currently considered unsuitable in this population. Additionally, genetic testing cannot be used to diagnose secondary lactose intolerance.

Lactase activity by intestinal biopsy can diagnose both primary and secondary lactose malabsorption. Anesthetized endoscopic examination is not an indication of this test. However, it is important to collect biopsies in patches and check for lactase enzyme activity rather than collecting single biopsies because it will provide more accurate results.[14]

The Hydrogen breath test (HBT) measures the excretion of hydrogen in the respiratory tract after a challenge with a standard dose of lactose (20-25 g of lactose).[15, 16] Since hydrogen cannot be produced by mammalian enzymes, hydrogenation can indicate the presence of sugars in contact with bacteria, which indicates lactose malabsorption. The stool acidity test is based on the principle that unabsorbed lactose is fermented by colonic bacteria into lactic acid, which lowers the pH of the stool.

The lactose tolerance assay measures plasma glucose levels at different times: 0, 30, 60 and 120 minutes after consuming 50 g of lactose. But it is inconvenient for the patients because the blood must be collected several times. Capillary measurement with a portable glucose meter is more convenient and less painful for the test subject but may not be as accurate in diagnosis as venous collecting.[17]
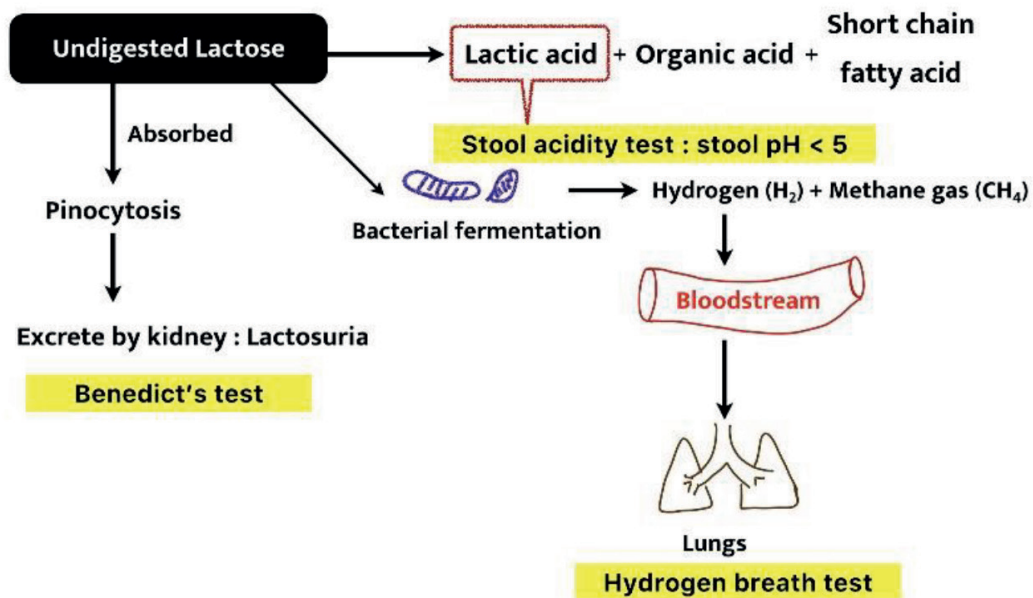
Figure 3 shows the correlation of additional diagnostic tests with the pathophysiology that occurred in patients with lactose intolerance. (Courtesy by Dr. Yutthana Pansuwan)

Management Lactose Intolerance

Management of patients with lactose intolerance aims to maintain the patient's condition and to avoid the risk of long-term malnutrition or malnutrition. There are 4 main points:

(1) Reduce or limit the amount of lactose intake.

(2) Replace lactose with other nutrients.

(3) Substitute enzymes or substances that can digest lactose.

(4) Take calcium and vitamin D supplements.

It is generally recommended that patients follow a diet low in lactose. However, in contrast to the maintenance of this condition, a strict lactose-free diet may not be necessary, as patients with lactose intolerance often tolerate up to 250 ml (12 g of lactose) of milk[16], no symptoms and others when taken with other foods as well the foods high in lactose that should be avoided include: dairy products, soft cheese, butter, ice cream, yogurt, margarine, custard, mashed potatoes, pancakes.

Prebiotics can also be given, which play a role in the management of the colonic microbiota. A randomized, placebo-controlled study in which 85 patients with lactose intolerance was administered orally administered short-chain galactooligosaccharides (GOS, RP-G28), a type of prebiotics, has been found to reduce hydrogen gas production and relieve stomach pain. Additional microbiological examination in the patients studied found that there was an increase in *Bifidobacterium spp.*, which is a bacterium capable of producing lactase enzyme.[18,19]

There are now more and more lactose-free dairy products on the market that are considered safe, although some allergic reactions have been reported.[20] These products also reduce lactose crystallization (decrease lactose crystallization) and increase sweetness.[21] Lactase enzymatic treatment in tablet form can both treat lactose digestion leading to reduced hydrogen gas production and alleviate symptoms.[22]

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Fabrication and Characterization of Ready-Use Artificial Skull

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Abstract:

Background: At present, medical care in Thailand is far advanced in all specialties. With this, we have to import large amount of high-cost medical equipment from other countries. However, there are many animal and plant products which can be modified and used for medical care.

Objective: This research aims to add value to Thailand's agricultural products, including rice starch, rubber, and animal bones in Thailand by transforming these products into medical devices, namely artificial skull for the Thai people.

Materials and method: By using green technology, which is to use chemicals that are not toxic to the environment and humans to prepare pure medical cow bone implants in the human body. Heating to remove contaminants and crushing, casting, and sintering. Increasing toughness by coating with rice starch and additives. Artificial skull prototype fabricated based on fresh cow bone in Thailand was made.

Result: Artificial skull was made which consists of 75% by weight cow bone powder and binder which is composed of 80% by weight rice starch and 20% by weight filler, representing 25% for forming. Biocompatibility with the living body and highly responsive to the growth of human bone tissue. The samples had a maximum degree of swelling in the water of 23% after 2 hours becoming stable.

Conclusion: This simple green technology was friendly to the environment and human. This method could make value-added agricultural products for medical material. For this reason, trade deficit to the country could be decreased.

Keywords: Artificial skull, Hydroxyapatite, Cow bone, Plastic skull.

Introduction

Currently, Thailand still has to import medical equipment worth about one hundred thousand million baht per year from abroad. Exports, on the other hand, amount to about ten thousand million baht. The research team aims to add value to Thailand's agricultural products, including rice starch, rubber, and animal bones. They will be processed into medical devices, especially artificial skulls for the Thai people. This is the development of agricultural products, and we will manage the knowledge from research to expand the results to the community by bringing it to the production and export industries.[1-3]

Hydroxyapatite (HA) is generally a compound of calcium phosphate. It can be synthesized by chemical methods such as co-precipitation[4,5], sol-gel synthesis[6,7], hydrothermal[8], and thermal deposition.[9] The problem with these methods is that the reactant cost to produce hydroxyapatite is high. In addition, the yield is low. Therefore, the increasing demand for HA has led to the processing of HA from natural sources such as edible animal bones, eggshells, and cockle shells[6,10] as attractive alternatives in the future.[11] If researchers want to use HA powder for medicinal purposes, the powder must be shaped to be convenient and easy to use, depending on the research objective. The molding must be mixed with binder to obtain the desired shape. Pharmaceutical grade rice starch, such as Era-Tab[12], was used as a tablet ingredient, as was medical grade PVA, a water-soluble polymer.[13]

The research project is to produce a dense and porous prefabricated artificial skull from cow bones mixed with rice starch and PVA. This will be used to repair broken and damaged human skulls after accidents or serious diseases in Thailand. The precursor from Thai cow bones, a material of natural origin, is physically and chemically processed, so that it is pure without organic substances. It is then introduced into the synthesis process and processed into a fine powder that is formed into a human skull prosthesis, aiming for commercial expansion. Therefore, there is joint research funding with academic departments of universities to urgently advance concrete results. This research will start with laboratory trials. Then, further trials are conducted with human subjects from various disciplines, such as general surgery, neurosurgery, orthopedics, etc.[14]

Materials and method

Materials

The cow bone was prepared according to the American Society for Testing and Materials (ASTM) designation F1581-99, 2016.[15] The concentration of trace elements had to be as follows: Arsenic < 3 ppm, cadmium < 5 ppm, mercury < 5 ppm, lead < 30 ppm and total heavy metals < 50 ppm. Then the bovine bone particles were crushed by high-speed grinding for 3 hours. Era-Tab was supplied by Erawan Research and Laboratory, Thailand. PVA was purchased from Sigma-Aldrich, USA.

Specimen preparation

Calcined cow bones were prepared, dried, and wet ground using 95% ethanol as a suspension medium. Grinding through a ball mill with a grinding pot and grinding ball (pot mill) for 70 hours, drying at 80°C, then filtering the powder through a 400 mesh sieve (size less than 37 microns) until obtained. The obtained powder is mixed with rice starch powder (Era-Tab) and a PVA binder. Then it is pressed into the mold for an artificial skull. Finally, it is dried at 150°C for 14 hours.

Characterization of samples

A scanning electron microscope (SEM-EDS, JEOL, JSM-IT800, Japan) was used to study the morphology of the cross section of the samples. The degree of swelling and volume expansion were determined as follows.[16] All quantitative data were analyzed with origin 8.0 (Origin Lab Corporation, USA) and presented as the mean ± standard deviation. Statistical comparisons were carried out using analysis of variance (ANOVA, Origin 8.0). A value of $p < 0.05$ was considered to be statistically significant.

Result and discussion

Figure 1 shows the prototype of the artificial bone, and Figure 2 shows the SEM (Scanning Electron Microscope) results of the cow bone surface after being calcined at 900°C to remove all organic matter and visible white spots less than 1 μm in size uniformly distributed on the surface of the cow bone. This was caused by the growth of new calcium phosphate crystals, and the chemical composition on the surface of cow bone was analyzed at spectrum No. 1 (Figure 3) by the EDS (Energy Dispersive Spectroscopy) technique. The main minerals were calcium (Ca) and phosphorus (P). Nitrogen as a component of protein was not found, indicating that there was no organic matter in the cow bone. The average value of Ca:P was 1.68 ± 0.34, which is close to the pure HA of 1.67 (Figure 4).

Figure 1 shows prototype of an artificial skull
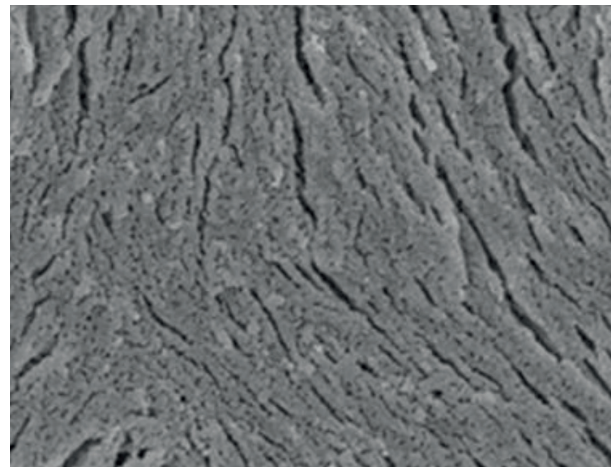
Figure 2 shows scanning electron microscope (SEM) of cow bone surface at 900⁰C (3,000 x)
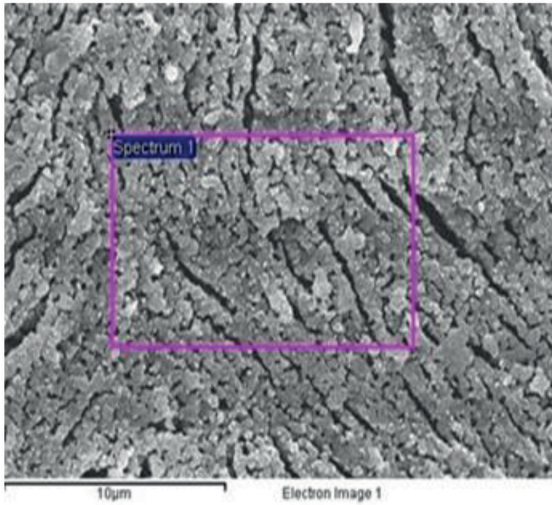
Figure 3 shows energy dispersive spectros-copy (EDS) of cow bone surface of spectrum 1

Element	Weight%	Atomic%
C K	6.51	12.62
N K	-	-
O K	43.31	59.80
P K	15.28	8.7
Ca K	34.90	18.88
Totals	100.00	Ca/P = 1.68

Figure 4 Chemical composition spectrum 1 by EDS technique

The sample of an artificial skull consists of 75 wt% cow bone powder, and 80 wt% rice starch and, 20 wt% filler, corresponding to 25 wt% of the binder for moulding.

The samples had a maximum degree of swelling in water of $23 \pm 0.5\%$, which became constant after 2 hours (Figure 5).
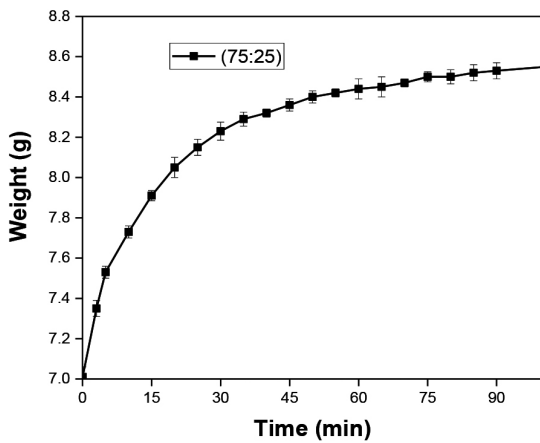
Figure 5 Weight increase of the samples
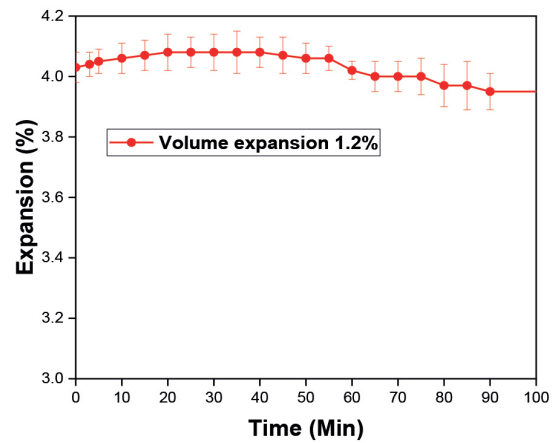
Figure 6 Volume expansion of the samples
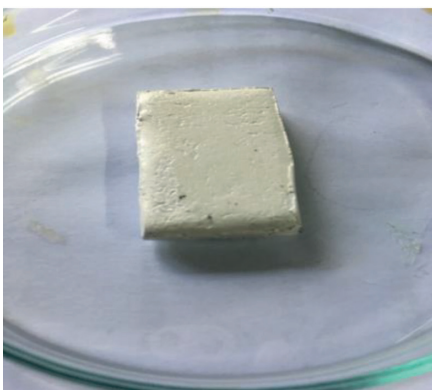
Figure 7 Artificial skull parts before immersion testing

Figure 8 Artificial skull parts after immersion testing

An artificial skull exhibited the greatest volumetric expansion of 1.2%, starting at 20 min to 40 min after the onset of decomposition of the sample surface, until greater decomposition of the bone powder was observed at 60 min. However, the shape of the sample remains 90% intact without complete dissolution or disintegration into small pieces. The image remains intact until after 2 hours (Figure 5) and an expansion of 1.2%, starting at 20 min to 40 min after the onset of decomposition of the sample surface, until greater decomposition of the bone powder is observed at 60 min. However, the shape of the sample remains 90% intact without complete dissolution or disintegration into small pieces. The image remains intact until after 2 hours (Figure 5 and 6). Figure 7 and 8 show the comparison of the surface shapes of the samples. It was found that the skin was normal, smooth, and firm before the test. However, after the immersion test in water, the skin was bubbly and swelled due to the hydrolysis of water, so the surface of the samples absorbed water. Meanwhile, the shape of the specimens is still intact until they are completely broken in a short time. Foreign artificial skulls are made of polymethyl methacrylate plastic, which does not have the properties to stimulate bone growth, although it is light, strong, and durable.[17] Rice starch was the hydrogel state that swelled and was hydrophilic. This leads to natural degradation. PVA, on the other hand, is a synthetic polymer and stable polymer in nature. Therefore, HA in combination with rice and PVA can cause cross linking between the OH groups of rice starch and the hydrogen groups of PVA.

Conclusion

An artificial skull made of cow bone mixed with rice starch and PVA was the dense artificial skull in this study. It has basic physical properties that make it possible to be used as a prosthetic skull made of Thai agricultural materials. Because the theory of an artificial skull is not less than 0.5 mm thick and resistant to impact, skull fixation materials can be used to hold a prosthetic skull made of cow bone powder and rice starch to blend seamlessly into a real human skull with a real human head. After suturing the skull, the size of the skull is comparable to that of a real human skull.

Acknowledgment

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Prevalence and Associated Factors of Sexually Transmitted Diseases in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand

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Abstract:

Background: Sexually transmitted diseases (STDs) are disease which transmitted from one person to another via sexual intercourse through vaginal, anal or oral routes. In Thailand the number of gonococcal infection and syphilis are 14.8 and 13.2 cases per 100,000 population respectively and the number is not lessening down since 2015 despite having proper ways to cope with STDs. There are a few numbers of studies reporting prevalence and associated factors of STDs and conducting one in rural area might reveal a hidden cause why the rate of infection is not yet diminishing.

Objective: The study aimed to identify prevalence and associated factors of sexually transmitted diseases in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand.

Methods: This study recruits the data from 22,477 patients who visited Sanam Chaikhet hospital is retrieved as a secondary data from hospital databases and entered SPSS Version 22 to analyze the prevalence and associated factors of STDs.

Results: The prevalence of sexually transmitted diseases in Sanam Chaikhet Hospital is 0.5%. The associated factors of STDs with statistically significant value were pregnancy and age between fifteen to twenty-nine years old.

Conclusion: Considering health education support to the students and people of age group 15-29 years old might be able to cover both of the problems including STDs and unwanted pregnancy.

Keywords: Sexually transmitted diseases, Prevalence, Chachoengsao Province, Thailand

Background

Sexually transmitted diseases (STDs) are diseases which transmitted from one person to another via sexual intercourse due to body secretion contact which, sometimes, introduced to body through small wound occurred during sexual activity. There are more than 30 species of organism which can cause STDs including bacteria, virus and protozoa. From those over 30 species of organism, most of STDs are majorly caused by only 8 species, 4 of which can be treated nowadays which are syphilis, gonorrhea, chlamydia and trichomoniasis. The other 4 diseases are caused by virus, cannot be completely eradicated. They are hepatitis B virus infection (HBV), human papilloma virus infection (HPV), herpes simplex virus infection (HSV) and human immunodeficiency virus infection (HIV). Though cannot be completely treated, the number of organisms, disease severity and clinical symptom can be lessened through using antiretroviral drugs.[1]

A study in 2016 from World Health Organization (WHO) which accumulated information from more than 205 countries found that the prevalence of non-gonococcal (non-GC) infection in women and men age 15-49 years old is 3.8% and 2.7% respectively. For gonococcal (GC) infection, the prevalence is 0.7% in both male and female. Apart from trichomoniasis, 5.3% in female and 0.6% in male. It is statistically defined that the region which has the largest prevalence of STDs is South Africa especially when talking about male non-GC infection, both sex syphilis and GC infection and lastly, female trichomoniasis. On the other hand, female non-GC infection and male trichomoniasis is mostly found in America.[2] Other studies note that there are more than 124.3 million people worldwide being infected with non-GC, 30.6 million are infected with GC, 110.4 million are infected with trichomonas and 19.9 million are syphilis infection.[3]

Nowadays, more than one million people are sexual transmitted infection daily. A study conducted by WHO in 2016 found that there were more than 376 million people infected with STDs and 80% of which occurred in developing countries including Thailand. The number can be distributed into 4 main diseases which are non-GC, GC, Syphilis and trichomonas infection contributing 127 million, 87 million, 6.3 million and 156 million respectively. The other diseases which caused by virus and cannot be treated also produce aa enormous number which are 500 million cases of HSV infection, 300 million cases of HPV infection and more than 240 million cases of HBV infection currently living with chronic HBV infection.[1]

The current STDs situation in Thailand is gradually worsening. The number has been rising since 2015 through 2019 even though we have been implementing ways to cope with the situation.[5] In Thailand, the highest number of cases goes to GC infection followed by syphilis which account around 14.8 and 13.2 cases per 100,000 population respectively. The rising momentum also goes along with the HIV infection rate which increased 5-9 times during the period.[4] These rising number affect Thailand in many aspects including the expense that the Ministry of Health bear. Center of Disease control and infection of America estimates the expense which is caused by STDs alone to be around 1,600 million dollars yearly.[6]

The complication of STDs depends on each disease individually which cause both short-term and long-term complications such as pelvic inflammatory diseases (PID), ectopic pregnancy, infertility, chronic pelvic pain or even joint pain. Moreover, when the disease progresses while pregnant, the disease can be transmitted through placenta or laboring which can furthermore cause complications. For instance, syphilis can cause complications besides reproductive system such as nervous system, cardiovascular

system, congenital disabilities, preterm labor or even perinatal death.[7] More than million pregnant women with syphilis ended up with more than 200,000 cases of perinatal death and still birth combined. More than 350,000 cases are alive with sequelae of perinatal complication.[8] Another study also found that STDs is directly associated with the increasing number of HIV infection.[9]

By gathering the correlating factors of STDs from studies, it is found that there are numerous risk factors of STDs such as teenage period, refer to population age between 10 and 19[10,11] which have significant probability of getting STDs when comparing with adult period. Other risk factors are people whose parents are farmer, prostitution[12,13] being single parent, having unproper education, those who has history of STDs, smoking, drinking alcohol and substance abusing such as amphetamine, heroine, marijuana.[13,15]

Objective

The study aimed to identify the prevalence and the associated factors of sexually transmitted diseases in Sanam Chaikhet Hospital, Chachoengsao province, Thailand.

Material and Methods

Study design

A quantitative study by cross-sectional study to find the prevalence associated factors of sexually transmitted diseases in the population who came to receive service at Sanam Chaikhet Hospital.

Study population

The information used in the study was retrieved from the people who came to receive service at OPD and ER from 1st January 2020 to 21st June 2021 and STDs which caused by proven or suspected congenital infection and rape must be excluded.

Sample size

Single population proportion formula was used to calculate the sample size by referring to a result of a study "Increase in Sexual Risk Behavior and Prevalence of Chlamydia trachomatis Among Adolescents in Northern Thailand".[25] The study found that the prevalence of non-GC infection of adolescence in the northern part of Thailand was 9.6%.

Considering P = 0.096 (the prevalence of non-GC infection of adolescence in the northern part of Thailand) d = 20 % of P = 0.2 x 0.096 = 0.0192 with a 95% confidential interval, the value of Z = 1.96 (cut-off value of the normal distribution). Hence, the number of samples we need was 906 cases

However, when the researchers arrived at Sanam Chaikhet Hospital and assessing the information mention earlier, it was found that the prevalence of STDs in the area was lower than the ones we referred. Hence, we decided to retrieve the information of everyone who came to receive services since 1st January 2020 to 21st June 2021. More than 184,684 visits information had been retrieved so we managed the data by screening off the information that might interfere our result including outpatient clinic, non-communicable disease clinic and antenatal care clinic visits, patients who revisited within the period, patients age less than 9 years old and more than 59 years old (the age mentioned were not likely to be infected with STDs hence may causing the result bias). After excluded data, the final number was 22,477 cases.

Data collection

The data was gathering by retrieving secondary data from the Department of Statistics of Sanam Chaikhet Hospital. The secondary data included general information and specific data which was considered important in this study, for instance, pregnancy, teenage pregnancy and substance abuse.

Data analysis

The collected data was entered into SPSS Version 22. By using descriptive statistics, the demographic information was interpreted as mean, percentage, standard deviation etc. To calculate the association between STDs and the risk factors, univariate and multivariate logistic regression analysis was used with 95% confidence interval and p-value less than 0.05 was considered statistically significant.

Definition

Teenage was defined as people who aged 10-19 years old.[10,11] Teenage pregnancy was defined as maternal age less than 20 years old considering the date of labor. STDs (Sexually transmitted diseases) was defined as diseases which transmitted from one person to another through sexual activity via vaginal, anal or oral routes.[24]

Ethical consideration

The information was kept secret by not revealing names and detail of everyone. The data was used only for research purposes. The result was shown as a whole data, not exposing each individual information.

Result

There were 22,477 patients in the study, M: F 1:1.2. 72.2% of the patients were between 15-49 years old as in Table 1. Mean age was 35.12 ± 13.91 years. 89.4% were non-alcoholic drinking and 89.4% had never smoked. Most patients about 99% had no dyslipidemia, diabetes mellitus or hypertension. For socioeconomic status, 73.2% were employee, 25.5% and 28.3% had highest education of elementary school and junior high school respectively as in Table 2. The prevalence of sexually transmitted diseases in Sanam Chaikhet Hospital was 103 out of 22,477 patients (0.5%). The associated factors of STDs with statistically significant value were pregnancy and age between 15-29 years old as in Table 3 but only aged 10-19 and 20-29 years had statistically significant association with STDs as in Table 4.

Table 1 Socio-demographic characteristics among patients in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand

Data	n	%
Gender		
Male	10198	45.4
Female	12279	54.6
Age group		
10-19	3630	16.1
20-29	5134	22.8
30-39	4596	20.4
40-49	4514	20.1
50-59	4603	20.5
Age group		
<15	1644	7.3
15-49	16230	72.2
>49	4603	20.5
Body mass index		
Underweight	2481	11
Normal	8254	36.7
Obese I	3514	15.6
Obese II	5524	24.6
Obese III	2704	12
Alcohol drinking		
Non-alcohol drinking	20095	89.4
Alcohol drinking	2235	9.9
Ex-alcohol drinking	147	0.7
Smoking status		
Never	20093	89.4
Current smoker	2236	9.9
Ex-smoker	148	0.7

Table 2 Socio-demographic characteristics among patients in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand

	N	%
Dyslipidemia		
Yes	201	0.9
No	22276	99.1
Diabetes mellitus		
Yes	207	0.9
No	22270	99.1
Hypertension		
Yes	231	1
No	22246	99
Occupation		
Unemployed	715	3.2
Agriculture	1062	4.7
Employee	16460	73.2
Student	3289	14.6
Civil service	626	2.8
Merchant	194	0.9
Other	131	0.6
Education level		
Below elementary school	1298	5.8
Elementary school	5730	25.5
Junior high school	6360	28.3
High school	1299	5.8
High Vocational Certificate	119	0.5
Bachelor degree	580	2.6
Master/doctor degree	54	0.2
Not specified	7037	31.3
Age (years)	35.12 ± 13.91	
Body mass index (kg/m²)	24.04 ± 5.18	

Table 3 Factors associated with sexually transmitted diseases in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand

Variables	Sexually Transmitted Diseases		COR	95% CI	p-value
	No	Yes			
Pregnancy					
Yes	282 (98.6)	4 (1.4)	3.165	1.157-8.66	0.025*
No	22092 (99.6)	99 (0.4)	1		
Age group					
<15	1641 (99.8)	3 (0.2)	0.699	0.197-2.482	0.58
15-49	16142 (99.5)	88 (0.5)	2.086	1.14-3.816	0.017*
>49	4591 (99.7)	12 (0.3)	1		
Age group					
10-19	3600 (99.2)	30 (0.8)	3.188	1.63-6.236	0.001*
20-29	5096 (99.3)	38 (0.7)	2.853	1.489-5.466	0.002*
30-39	4583 (99.7)	13 (0.3)	1.085	0.495-2.381	0.838
40-49	4504 (99.8)	10 (0.2)	0.849	0.367-1.968	0.703
50-59	4591 (99.7)	12 (0.3)	1		
Body mass index					
Underweight	2464 (99.3)	17 (0.7)	2.066	0.919-4.643	0.079
Normal	8216 (99.5)	38 (0.5)	1.385	0.669-2.868	0.381
Obese I	3499 (99.6)	15 (0.4)	1.284	0.561-2.938	0.554
Obese II	5500 (99.6)	24 (0.4)	1.307	0.607-2.815	0.495
Obese III	2695 (99.7)	9 (0.3)	1		

Table 3 Factors associated with sexually transmitted diseases in Sanam Chaikhet Hospital, Chachoengsao Province, Thailand (con.)

Variables	Sexually Transmitted Diseases		COR	95% CI	p-value
	No	Yes			
Smoking status					
Never	20003 (99.6)	90 (0.4)	1		
Current smoker	2224 (99.5)	12 (0.5)	1.199	0.656-2.194	0.555
Ex-smoker	147 (99.3)	1 (0.7)	1.512	0.209-10.923	0.682
Alcohol drinking					
No alcohol drinking	20006 (99.6)	89 (0.4)	1		
Alcohol drinking	2223 (99.5)	12 (0.5)	1.213	0.663-2.221	0.53

Table 4 Multivariate logistic regression analysis to assess relationships between potential factors associated to sexually transmitted diseases in Sanam Chaikhet Hospital, Thailand

Variables	Sexually Transmitted Diseases		AOR	95% CI	p-value
	No	**Yes**			
Pregnancy					
Yes	282 (98.6)	4 (1.4)	2.26	0.82-6.23	0.115
No	22092 (99.6)	99 (0.4)	1		
Age group					
10-19	3600 (99.2)	30 (0.8)	3.119	1.593-6.107	0.001*
20-29	5096 (99.3)	38 (0.7)	2.753	1.432-5.291	0.002*
30-39	4583 (99.7)	13 (0.3)	1.067	0.486-2.341	0.872
40-49	4504 (99.8)	10 (0.2)	0.848	0.366-1.964	0.7
50-59	4591 (99.7)	12 (0.3)	1		

Discussion

The prevalence of STDs infection in this research was slightly below the average of each disease in the STDs group, which might be explained by the current situation that was still affected by COVID-19, which could result in decreased patients going to the hospital. Patients might neglect and overlook those symptoms and chose not to come to the hospital to reduce the risk of COVID-19 infection due to the minor symptom or even asymptomatic presentation of most STDs by the way they could go to pharmacy and received medication by themselves.

In relation to STDs, it was evident that only the age group and pregnancy were statistically significantly correlated. Firstly, the age group was in adolescence, which was reproductive period, resulting in a frequent sexual intercourse and subsequently caused STDs. The second was pregnancy, which was expected to occur in conjunction with STDs from other factors, such as no condom uses in contraception. With reduced prevention, STDs including unwanted and intentional pregnancies were increased.

The factors which were not associated with STDs in this research include teenage pregnancy, drinking alcohol and smoking cigarette. According to other research, these factors should be associated with STDs by, for example, lacking restraint from various compounds in liquor and cigarettes, or the teenage pregnancy which the age group was already a risk factor. This might be due to the insufficient number of case studies. When looking back at the results of this research, no patients had been infected with STDs and getting pregnant in adolescence at the same time so by increasing the number of case studies, this might result in more efficient interpretation of the number.

Limitation

The prevalence of STDs at Sanam Chaikhet Hospital was below the standard average, so we imply some patients came to another hospital or the symptoms were not recognized by themselves. Laboratory investigation at community hospitals could be difficult and slow to conduct, so on many occasions, when doctors saw patients with STDs, they might not test until they have a definite diagnosis. Rather, they would provide an empirical treatment instead. These might affect the prevalence of the disease in this study.

Conclusion

The results of this study showed that factors associated with STDs were the age range between 15-29 years old and pregnancy. If we look at the problem as a whole, we might consider providing health education which support the students and people of that age group, which is expected to be able to cover both of the problems including STIs and unwanted pregnancy.

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Short Communication

Recreational Brackish Water Injury at Mangrove Lagoon Leads to *Vibrio parahaemolyticus* Acute Wound Infection with Peripheral Edema

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Abstract: A wound infection with *Vibrio parahaemolyticus* was seen in a male who injured his right foot during a water leisure activity in Indonesia. It is known that the number of vibrio species in the sea is increasing due to the rise in seawater temperature accompanying global warming. Hand in hand with that rise in vibrio species and seawater temperature is the rise in the number of vibriosis cases. Hence, paying attention to the increase in imported cases of *V. parahaemolyticus* wound infection from tropical regions is necessary. For increased diagnostic accuracy, proper bacterial testing must be conducted based on the patient's epidemiological information. We highlight the innocuous nature of the initial presentation and the importance of rapid testing for an accurate diagnosis to prevent potentially devastating sequela.

Introduction

Vibrio parahaemolyticus is a Gram-negative, comma-shaped, halophilic bacterium which inhabits sea and brackish water.[1] This bacterium is well known as a cause of food poisoning and mainly causes gastroenteritis through the consumption of raw fish or shellfish.[1] It is also a cause of infection in wounds that encounter seawater.[2]

Whereas the incidence of gastrointestinal vibriosis has decreased in past years, the incidence associated with wound infection has increased.[3] People with immunocompromising conditions or chronic disease have a higher risk of severe infection or sepsis.[3] Therefore, it is important to make an early diagnosis based on clinical symptoms, epidemiological information and start

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empiric therapy as soon as possible. Here we report a case of wound infection with *V. parahaemolyticus* caused by injury during a water leisure activity. This case was also characterized as an imported *V. parahaemolyticus* infection from a tropical resort in Indonesia to Japan.

Case

A forty-six-year-old previously healthy male who had traveled to Indonesia in 2021 and been injured between the first and second toe of his right foot (Figure 1). He had fallen from a boat into the brackish water area during a water leisure activity and caught his foot in mangrove branches. At a hospital in Indonesia, his wound had been cleaned and sewed, he had been injected with tetanus toxoid, and was prescribed cefixime and mefenamic acid. Two days after his injury, he returned to Japan and visited Yamagata Prefectural Central Hospital complaining of

Figure 1 The first and second toe wounds of the patient's right foot

Figure 2 *Vibrio parahaemolyticus* blue-green colonies from first and second toe wounds pus swab specimen

redness and swelling from his right ankle joint to the periphery. Laboratory testing revealed his C-reactive protein was elevated to 11.531 mg/dL and white blood cell count was elevated to 14.33×10^9/L with 87.6% neutrophils. The pus on the suture treated by his previous doctor was taken by a sterile swab and stored at 4°C until the next day when a microbiological examination was performed. He was hospitalized and was administrated 2 g/day of ceftriaxone. No bacteria were observed by light microscope in Gram staining of the pus swab specimen. The pus swab specimen was smeared in thiosulphate citrate bile sucrose (TCBS) agar (Eiken Chemical, Tokyo, Japan) in addition to the 5% sheep blood agar (Kyokuto, Tokyo, Japan) and bromothymol blue (BTB) lactate agar (Kyokuto) for ruling out of Vibrio vulnificus infection, and these media were incubated at 35°C for a day. Several irregular-shaped, mucoid, and non-lactose degrading colonies developed on TCBS agar (Figure 2), whereas only a few coagulase-negative Staphylococcus or coryneform bacteria that could be considered skin resident bacteria developed on blood agar and BTB lactate agar. Using MALDI biotyper (Bruker, Texas, USA) and Vitek 2 (BioMérieux, Lyon, France), the bacteria were identified on TCBS agar as *V. parahaemolyticus*. The MALDI score value was 2.378 and the Vitek 2 percent probabilities were 94%, indicating very reliable identification. Susceptibility testing, performed according to Clinical & laboratory standards institute Guidelines[4] using a Dry Plate DP31 (Eiken Chemical), revealed that the bacteria was susceptible to all of the antibiotics tested except for cefazolin (Table 1). His leg recovered rapidly with antibiotic therapy, redness, swelling and pain were improved and the skin lesions did not progress to deep necrotic fasciitis and he was discharged 5 days after hospitalization.

Table 1 Susceptibility testing results of *Vibrio parahaemolyticus*

Antibiotics	Minimum inhibitory concentration (µg/mL)	Interpretation of breakpoint*
Piperacillin	16	S
Sulbactam/Ampicillin	≤2/4	S
Cefazolin	8	R
Cefotaxime	≤0.5	S
Ceftazidime	≤0.5	S
Gentamicin	2	S
Amikacin	8	S
Imipenem	≤0.25	S
Meropenem	≤0.25	S
Levofloxacin	≤0.25	S
Sulfamethoxazole-trimethoprim	≤9.5/0.5	S

* S, susceptible; R, resistant. The breakpoints were interpreted according to the Clinical and Laboratory Standards Institute.[4]

Discussion

V. parahaemolyticus is a common cause of food poisoning[1] and, less commonly, also the cause of wound infection by direct contact with seawater contaminated with this pathogen.[2] The most common vibrio species causing wound infection is V. vulnificus.[2] V. vulnificus infection tends to become severe with necrotic fasciitis, especially in patients with underlying diseases such as liver disease, immunosuppression, or other chronic diseases.[1] Similar to V. vulnificus infection, wound infection with V. parahaemolyticus tends to be serious in persons with chronic underlying diseases such as liver disease, alcoholism, or diabetes.[5] Indeed, several previous cases from different part of the world reported that elderly people or patients with chronic diseases developed necrotic fasciitis by V. parahaemolyticus wound infection.[6-9] Conversely, in the present case and a previous case of a 12-year-old girl in Singapore with a V. parahaemolyticus wound infection[10], the patients had no underlying disease and their infection remained local and relatively mild. Therefore, patients with aged or chronic underlying diseases should monitor the severity of their wound infection with V. parahaemolyticus.

The present case was characterized as an imported V. parahaemolyticus infection from a tropical resort. Vibrio species including V. parahaemolyticus tend to be more common in warmer waters, above 17 to 20°C.[2] In north-eastern Japan including Yamagata Prefecture where our hospital is located, seawater temperature is usually below 20°C from late autumn (November) through early summer (May). On the other hand, seawater temperature remains around 30°C throughout the year in Indonesia where this case had injured. Hence, injury during a water leisure activity in a tropical resort such as Indonesia may be considered a higher risk for infection with V. parahaemolyticus than north-eastern Japan. Moreover, it has been reported that the number of vibrio species in the sea is increasing due to the rise in seawater temperature accompanying global warming[11] and that vibriosis cases are similarly increasing.[12] Therefore, it should be noted if imported cases of V. parahaemolyticus infection from tropical legions increase in the future. However, in the countries where V. parahaemolyticus is mainly considered a cause of food-borne illness such as Japan, imported wound infections with V. parahaemolyticus may be missed or not diagnosed rapidly. Therefore, epidemiological information of patients such as this injury in a tropical resort will help clinicians to suspect imported V. parahaemolyticus infection and prompt treatment with appropriate antimicrobial is essential for the best prognosis.

In the diagnosis of V. parahaemolyticus infection, rapid culture testing is necessary. It is known that low temperature storage at 1-5°C for a day reduces the number of V. parahaemolyticus to less than 1/10 in fish samples.[13] Indeed, in the present case, bacterial culture testing could detect only a few colonies on TCBS agar, which is optimized for selective isolation of vibrio spp. However, V. parahaemolyticus can grow on 5% sheep blood agar in general. This phenomenon can be explained by the facts that the specimen was stored at 4°C for a day because it was taken on holiday in addition to the prior administration of cefixime right after an injury in Indonesia. Therefore, wound cultures should be sent during the early stages of infection for rapid diagnosis. However, many patients have already received antibiotics before admission, which may increase the negative rate of culture and complicate diagnosis. When V. parahaemolyticus infection is suspected by a patient's epidemiological information, sharing information with the laboratory will also expedite the bacterial culture testing with a selective isolation medium for vibrio spp.

Conclusion

We reported the imported case of wound infection with *V. parahaemolyticus* from a foreign tropical resort to Japan. Rapid and proper bacterial testing based on epidemiological information of the patient will help for accurate diagnosis of, and care for, *V. parahaemolyticus* wound infection.

Conflict of interest

None to declare.

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