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Examination of Antibiotic Response of *Staphylococcus aureus* in Human Saliva for Personal Identification in Forensic Science: A Preliminary Study

Intasin Kitpatanasombat[1], **Parinya Seelanan[1]**, **Thongchai Taechowisan[2]** and **Pasuk Mahakkanukrauh[3,4,5]**

[1]Faculty of Forensic Science, Royal Police cadet Academy; [2]Department of Microbiology, Faculty of Science, Silpakorn University, Nakhon Pathom; [3]Forensic Osteology Research Center; [4]Department of Anatomy, Faculty of Medicine; [5]Research Cluster in Osteology Research and Training Center (ORTC), Chiang Mai University, Chiang Mai, Thailand

ABSTRACT

OBJECTIVE To study the relationship among antibiotic response profiles and to compare differences in antibiotic response profiles of *Staphylococcus aureus* (*S. aureus*).

METHODS Saliva samples were collected from 33 donors after which *S. aureus* in the samples was identified and isolated for morphological and biochemical testing. The antibiotic response was analyzed by disk diffusion and the patterns of antibiotic response from the individual saliva samples were compared to identify the differences in antibiotic response profiles.

RESULTS All 33 saliva samples tested positive for *S. aureus.* The antibiotic responses were analyzed by disk diffusion, with test values being classified as Sensitive (S) Intermediate (I) or Resistant (R). The antibiotic response profiles showed only four matching pairs with each pair dissimilar from the other profiles. The antibiotic response profiles had a high incidence of differentiation of up to 93.94%.

CONCLUSIONS In this study, *S. aureus* in saliva samples was identified by morphological and biochemical testing. Antibiotic response profiles can be analyzed by disk diffusion and the results can be used to aid in the identi-fication of individuals with a high level of differentiation of up to 93.94%. Our proof-of-concept study shows that antibiotic response profiles of saliva samples can be used in forensic science to identify individuals.

KEYWORDS saliva, *Staphylococcus aureus*, disk diffusion method, biochemical testing, antibiotic response profiles, personal identification

INTRODUCTION

Crime in every country is an important social phenomenon. Whether it is a misdemeanor or a felony, crime has an impact on the physical and mental health of the victim. In addition, the number of crimes and the severity of crimes committed in a society are indicative of the level of safety of people's lives and property. In Thailand, violence related to sexual har-assment is one of the four major categories of crimes in the country, and it appears to be in-creasing. According to the information system of the Royal Thai Police, there were 1,341 rape cases in 2020; 1,210 offenders were arrested, representing 90.19% of the cases. The province with the most unsolved rape cases was Nakhon Ratchasima, showing that there are still some areas where the perpetrators have not yet been found to be punished. How to identify offenders is a very important feature of police investiga-tions, requiring the accumulation of solid evi-dence to clearly confirm the identity of the per-petrator as well as to provide evidence of guilt. To that end, forensic science has been brought

in to help provide evidence at the crime scene (1). In most sexual harassment cases, evidence is regularly left by the offender on the victim's body or at the scene of the crime. One of the most important types of evidence is saliva, which is vital evidence that can help identify the perpetrator (2,3). Saliva contains proteins, fats, carbohydrates, salts and non-protein nitrogenous compounds as well as endemic microorganisms (4). Those microorganisms live in various parts of the body, e.g., the inner skin, the oral cavity, the respiratory tract, the intestines, the excretory system, and the reproductive organs, and can be used to distinguish individual differences (5). However, how the court judges evaluates this evidence depends on such the most important thing as evidence that is the evidence being reliable enough to be admissible in a court of law. Whether the evidence is personal testimony of witnesses, documentary evidence, or objects, forensic examination results have come to play an increasingly important role in the judicial process (6,7). Such evidence is also potentially very important as proof of innocence of an accused individual. At present, forensic science agencies have applied various techniques to prove personal identity, e.g., fingerprints, genetic material (DNA), and dental history (8,9). These techniques are all important aids in solving other types of important matters involving identification of individuals. Unfortunately, there are still a number of crimes that have yet to be closed, especially in the case of rape, where the offender cannot be brought to justice because the existing evidence is incomplete or insufficient to detect identify the perpetrator (10).

The researcher had the idea that samples of saliva might be contaminated with host microorganisms and studied which could potentially identify differences among individuals. The study focused on *Staphylococcus aureus* (*S. aureus*), a gram-positive bacterium in the groups of Staphylococci, which are endemic bacteria found in the human body (11). It seemed likely that *S. aureus* in different individuals might possesses different traits and respond differently to various antibiotics. This study aimed to evaluate the feasibility of identifying individuals by analyzing differences in antibiotic response profiles. Specifically, this preliminary study investigated whether antibiotic response profiles can be used as a forensic science tool to help identify individuals (12).

METHODS
Saliva sample collection
Ethical permission for this study was obtained from the ethics committee of the Royal Police Cadet Academy (Certificate No.: 621108-022). An informed consent agreement was signed by all participants and personal information was kept confidential. Saliva samples from 33 healthy donors were obtained using sterile cotton swabs which were preserved in 10 mL of sample collection buffer at 4°C (137 mM NaCl, 2.68 mM KCl, 10.1 mM Na_2HPO_4 and 1.76 mM KH_2PO_4, pH 7.4 and 0.01% (w/v) agar) for further analysis.

Isolation and characterization of *Staphylococcus aureus*
The saliva samples were isolated in mannitol salt agar (HiMedia, India) then incubated at 37°C for 18-24 h. After incubation, the cultured mannitol salt agar turned yellow, and the bacterial colonies in cultured plates were subjected to further study. The resulting colonies were confirmed by gram staining, a catalase test involving 3% hydrogen peroxide and using BBL TM coagulase plasma, rabbit plasma with EDTA for a coagulase test (Becton Dickinson and Co., USA).

Antibiotic susceptibility test
The isolated bacteria were cultured in nutrient agar (HiMedia, India) and then incubated at 37°C for 24 h. Then the resulting colonies were resuspended with 0.85% NaCl and concentration was adjusted to reach 0.5 McFarland Standard (10^8 CFU). The bacterial suspension was spread onto Mueller-Hinton Agar (HiMedia, India) +2% NaCl to analyze the antibiotic susceptibility. Antibiotic disks (HiMedia, India) used in this study included ampicillin (AMP) (10 μg), cefazolin (CZ30) (30 μg), cefoxitin (FOX) (30 μg), chloramphenicol (C30) (30 μg), ciprofloxacin (CP) (5 μg), clindamycin (CD2) (2 μg), erythromycin (ERY) (15 μg), linezolid (LZD30) (30 μg), penicillin (P10) (10 μg), rifampicin

(RA) (5 µg), sulfamethoxazole/trimethoprim (SXT25) (25 µg) and tetracycline (TE) (30 µg). The cultured plates were incubated at 37°C for 24 h and the diameter of the zones of inhibition zones were measured and compared with the standard tables of the Clinical and Laboratory Standard Institute (13). Then, the patterns of the multidrug responses from the isolated bacteria were compared to investigate the develop response profiles. Differentiation, measured as a percentage, was calculated using the formula below.

$$\text{Percent differentiation} = 100 - \left(\frac{\text{Total number of pairs of similar multidrug response profiles}}{\text{Total number of multidrug response profiles}} \times 100\right)$$

RESULTS

Isolation and characterization of *S. aureus*

In this study, the experiment was performed under the permission of ethics committee of Royal Police Cadet Academy. The saliva samples form 33 donors were collected and kept in an appropriated buffer to preserve the bacteria for the analytical study.

The saliva samples were cultured in mannitol salt agar which was used as a selective medium to isolate the *S. aureus*. The medium consisted of mannitol which is a fermentable carbohydrate. *S. aureus* consumed the mannitol and produced acid, after which the phenol red indicator in the medium changed to yellow. The results showed that the bacterial colonies could grow on the plate and could change the color of the medium from red to yellow (Figure 1). The bacterial colonies were then used for further biochemical testing and gram staining.

For gram staining, the isolated bacterial colonies were stained and imaged under an scanning electron microscope. The stained bacteria had a purple appearance which indicates a gram-positive bacterium; the bacteria had roughly spherical shaped cells with a smooth surface and a diameter of 0.5 to 1.0 µM (Figure 2).
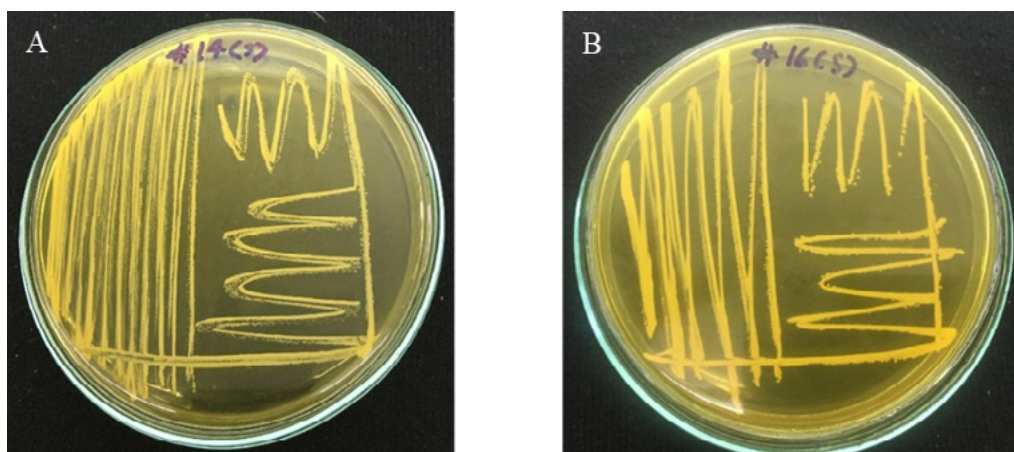
Figure 1. Mannitol salt agar for the isolation of *Staphylococcus aureus* in saliva samples from donors No. 14 (A) and No. 16 (B).
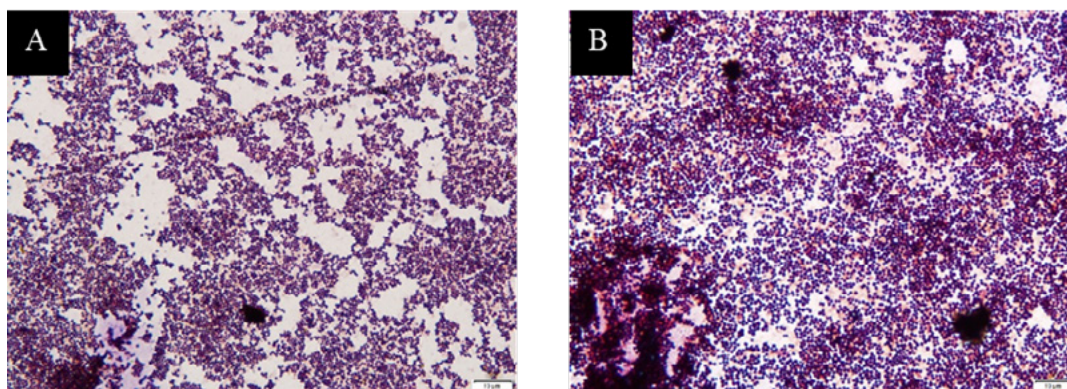
Figure 2. Gram staining for characterization of the morphology of isolated *Staphylococcus aureus* bacteria in the saliva sample of donors No. 14 (A) and No. 16 (B).
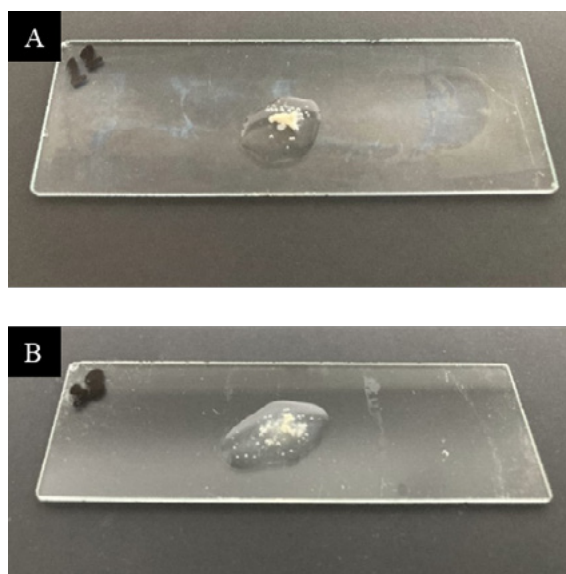
Figure 3. Catalase test for *Staphylococcus aureus* identification in the saliva samples from donors No. 22 (A) and No. 38 (B).

For biochemical testing, the catalase test was conducted to identify *S. aureus*. The isolated colonies were introduced into 3% H_2O_2 (Figure 3). The result was a rapid production of bubbles due to the reaction with catalase which breaks down hydrogen peroxide into oxygen and water. The coagulase test was also performed to verify the presence of *S. aureus*. The isolated colonies were subjected to rabbit plasma. The rabbit plasma solution caused clotting because the coagulase changed the fibrinogen in the plasma to fibrin (Figure 4).

The results of these tests demonstrated that all 33 saliva samples from donors were positive for *S. aureus*.
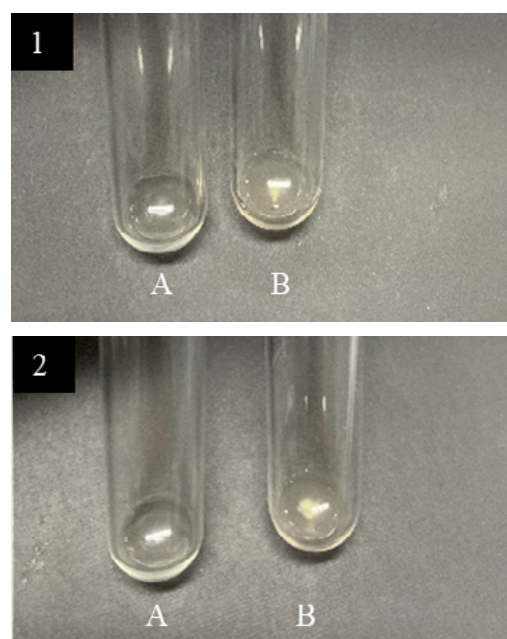
Figure 4. Coagulase test for *Staphylococcus aureus* identification: (A) negative control and (B) isolated bacteria in the saliva samples from donors No. 22 (1) and No. 38 (2).

Antibiotic response profile

To study antibiotic susceptibility, the *S. aureus* isolates were incubated in Mueller–Hinton agar and were then used in the disk diffusion test (Figure 5). After obtaining a clear zone on the culture plates, the diameter of the zone was measured and compared to the standard table. The results showed that all 33 isolates (100%) were resistant to penicillin, 18 (54.55%) to ampicillin, 6 (18.18%) to cefazolin, 24 (72.73%) to cefoxitin, 25 (75.76%) to chloramphenicol, 1 (3.03%) to ciprofloxacin, 10 (30.30%) to clindamycin, 20 (60.61%) to erythromycin, 17 (51.52%) to linezolid, rifampicin (5 μg), 1 (3.03%)
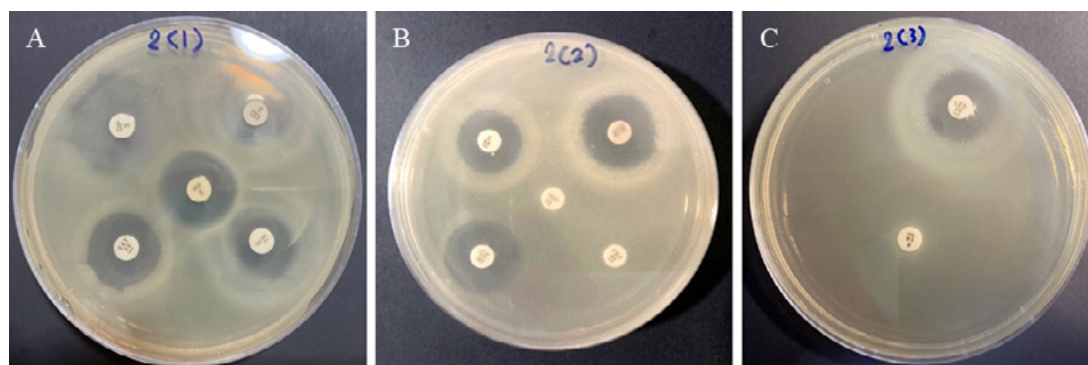
Figure 5. Disk diffusion and antibiotic susceptibility tests of *Staphylococcus aureus* of the saliva samples from donor No. 2. Disc diffusion susceptibility was tested using several antibiotics including (A) ciprofloxacin, clindamycin, erythromycin, rifampicin, sulfamethoxazole/trimethoprim, (B) ampicillin, cefazolin, cefoxitin, chloramphenicol, tetracycline, and (C) linezolid, penicillin.
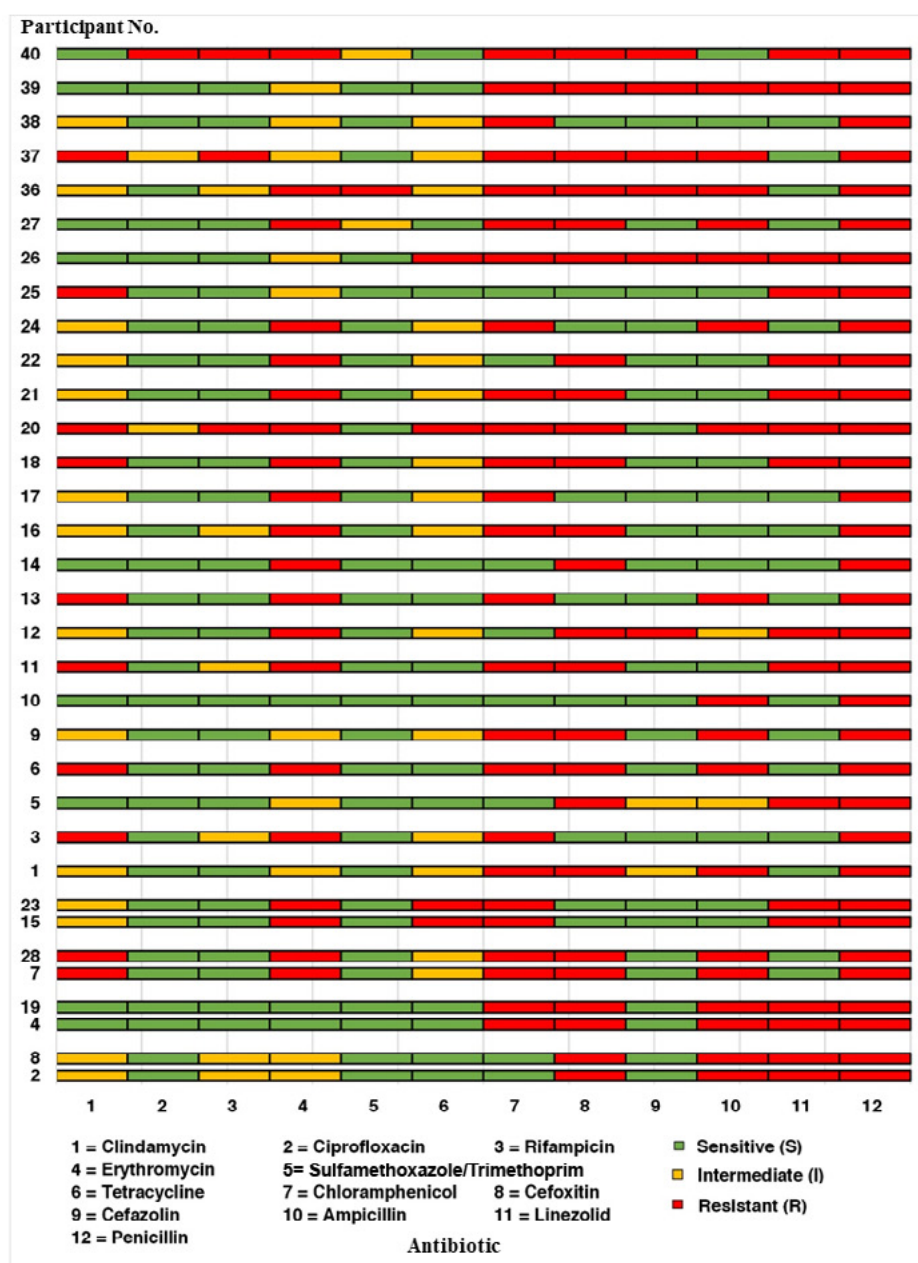
Figure 6. Multidrug response profiles of *Staphylococcus aureus* isolates from the different saliva samples

to sulfamethoxazole/trimethoprim and 4 (12.12%) to tetracycline.

The patterns of multidrug responses among the 33 isolates were compared to determine the level of ability to differentiate donors (Figure 6). The results indicated that only four pairs of isolates had similar patterns, while the multidrug response profiles showed a high percentage of differentiation of up to 94%.

DISCUSSION

Saliva is a form of forensic evidence that may be able to be collected at a crime scene, especially in cases of sex crimes. This biological evidence can be used for identification purposes (4,5). Saliva contains several biochemical components which can be used in fingerprint profiling of saliva (14) and including identification of a variety of microorganisms (normal flora) (15). Although saliva contains various microorganisms, the one that was selected for testing is *S. aureus* (16,17). This study aimed to evaluate the ability to differentiate individuals by analyzing the antibiotic response of *S. aureus* in their saliva (18).

Saliva samples were collected from 33 donors using a sterile cotton swab to swab in the mouth around both cheeks five times. The collected

sample was placed in the appropriate solution to preserve *S. aureus* for testing. *S. aureus* was isolated from the collected samples using mannitol salt agar, which contains a high salt concentration that allows *S. aureus* to grow while inhibiting other bacteria (19). *S. aureus* can also ferment mannitol into acidic, acting as an indicator that alters the color of the medium from red to yellow. The isolated bacterial colonies were also identified by morphological study and biomedical testing (20).

Gram stains of all 33 bacterial samples with crystal violet were blue, indicating that the bacterial samples were gram positive. Gram-positive bacterial cell walls are thick and contain a small amount of lipids. The cell wall can be stained by crystal violet and iodine solution to form a crystal violation complex. On the other hand, gram-negative bacterial cell walls contain a large amount of lipid and the crystal violet and the lipid can be dissolved with 95% ethyl alcohol. Subsequently, the red dye safranin O was used to counterstain the cell walls of gram-negative bacteria (21). The bacteria had roughly spherical shaped cells with a smooth surface and a diameter of 0.5 to 1.0 μM which is characteristic of *S. aureus* (22).

The biochemical testing approach consisted of catalase and coagulase tests that can be used to examine the enzyme production in *S. aureus*. The catalase test was conducted by adding 3% H_2O_2 to the isolated bacterial colonies. Positive results were evidenced by the rapid production of oxygen bubbles due to the action of the catalase enzyme which can breakdown hydrogen peroxide into oxygen and water (22). The coagulase test was also performed by introducing the isolated colonies to rabbit plasma containing EDTA (Ethylene Diamine Tetra Acetic Acid), an anticoagulant. The result was that the rabbit plasma solution clotted because coagulase enzyme can change fibrinogen to fibrin (22). The isolation and the characterization showed positive results for *S. aureus* in saliva samples from both the morphology tests and the biochemical tests (23).

To identify the pattern of the antibiotic responses, the disk diffusion method was used to test the inhibition of a total of 12 antibiotics and to categorize the response as Sensitive (S), Intermediate (I) or Resistant (R) based on the measurement of the clear zone using a standard table (13,24). Comparison of the antibiotic response patterns of 33 donors found that only four pairs of isolates had similar patterns, while the multidrug response profiles showed a high percentage of differentiation of up to 94%. This preliminary study demonstrates that *S. aureus* from saliva is appropriate for use in forensic science to help with individual identification.

CONCLUSIONS

The presence of *S. aureus* in saliva samples can be identified by morphological and biochemical testing. Antibiotic response profiles can be analyzed by disk diffusion, and the results can be used for personal identification with a high percentage of differentiation of up to 93.94%. Our proof-of-concept study shows that antibiotic response profiles can be used to support forensic science efforts to identify individuals.

ACKNOWLEDGEMENTS

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by ethics committee of the Royal Police Cadet Academy (Certificate No.: 621108-022).

CONFLICTS OF INTERESTS

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

All authors designed all the experiments, analyzed the data, and contributed to the manuscript preparation.

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A Survey of Clinicians' Preferences Regarding Style and Content of Abdominal Computed Tomography Radiology Reports

Teeravut Tubtawee, **Rawiporn Roma,** **Wiwatana Tanomkiat** **and Keerati Hongsakul**

Department of Radiology Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand

Correspondence: Teeravut Tubtawee, MD, Department of Radiology, Faculty of Medicine, Prince of Songkla University, 15 Karnjanavanij Road, Korhong, Hat Yai, Songkhla 90110, Thailand. E-mail: Ttubtawee@gmail.com

ABSTRACT

OBJECTIVE Radiology reports should be readable and understandable, while ensuring there is sufficient pertinent information. This study was conducted to survey the preferred style and content of radiology reports of referring clinicians.

METHODS One hundred and forty questionnaires were sent to clinicians working in departments that frequently request abdominal CT examinations in Songklanagarind Hospital. The participants were asked to rank a set of four radiology reports each with different styles and content (report types A, B, C and D). They were also asked about valued features which should be included in a radiology report. Data were analyzed by normal rank score for the most preferred and using the Kemeny-Young method for preference order. Statistical significance was determined by Kruskal Wallis rank sum tests. $P < 0.05$ were considered statistically significant.

RESULTS Eighty-nine responses were received. The most significant preference was for a structured style with more detail (report type C) (69.7%). Clinical information, quality of examination, measurement of the normal organs and recommendations were statistically significant factors considered appropriate to be included in the radiology report ($p < 0.05$). Route of administration, dose and name of contrast media were considered statistically inappropriate with statistically significant ($p < 0.05$).

CONCLUSIONS The preferred report style was structured and included more detail and included clinical information, quality of the examination, measurements of normal organ and recommendations.

KEYWORDS radiology report style, radiologist, preference, computed tomography

INTRODUCTION

The radiology report is the most important tool for communication between radiologists and referring physicians (1). The advancement of medical imaging has increased over the past few decades, resulting in a larger number of images for radiologists to interpret, resulting in changes in the style and format of radiology reports (2). A number of guidelines have been devised for radiology report patterns, e.g., the American College of Radiology guidelines of 1 October 2005 (3) and the December 2010 guidelines of the Royal Australian and New Zealand College of Radiologists (4). However, the style and content of the radiology report has remained controversial for many years.

A wealth of literature has described report style preferences of referring clinicians and radiologists. An early study by Neak et al. (5) found that prose reports fostered a lack of standardization of content among different radiologists. Itemized reports facilitated com-

plete documentation of information and measurements and were more popular with both radiologists and referring clinicians (5). In a later study, Schwartz et al. found that the preference of referring clinicians and radiologists was for structured reports which had better content and greater clarity than free-form reports (2). Although a shorter and easy to follow structure is helpful, content is also important. Plumb et al. (6) found that detailed reports which included radiologists' comments were preferred to briefer reports, even for normal examinations (6). The level of experience of the radiologist and clinician were also found to be important factors in the efficiency of the radiology report (7).

However, to our knowledge there have been few studies of radiology reports from Asia, including Thailand. Most reports in the Songklanagarind Hospital are in prose style; however, that style is a more changing structure highly variable. The upshot is that it is not clear what type of report referring clinicians prefer. This study was conducted to survey the style and content of radiology reports preferred by referring clinicians in various experiences circumstances.

METHODS
Population

Our study was performed in Songklanagarind Hospital , Songkla Province between April 2016 and April 2017. A questionnaire was sent to 140 clinicians of different grades and specialties who frequently referred patients to the hospital radiology department for abdominal computed tomography (CT). This study was approved by the Research Ethics Committee of the Faculty of Medicine, Prince of Songkla University (IRB no. 59-057-07-4).

Survey questionnaire contents

The questionnaire was composed of three sections. The first component was information about the responding clinician including grade, department, specialty and number of years practicing. The second component concerned features which should be included in a radiology report including clinical scenario, examination technique, route of administration, dose and name of contrast media used, quality of the examination, measurement of the normal organ and recommendations. The third component included four different styles of radiology reports which the clinicians were asked to rank. The four report styles were: A = structured style with brief detail, B = prose style with brief detail, C = structured style with more detail and D = prose style with more detail (Figures 1 and 2). A space for comments was included at the end of each scenario.

Statistical analysis

Categorical variables and features which should be included in a radiology report are presented as counts and percentages; significance evaluation was performed using Fisher's exact test and the chi-square test. Identification and presentation of the most preferred choice was determined by normal rank and Kemeny-Young score, and significance evaluation was made by Kruskal Wallis rank sum test score.

RESULTS
Demographics and general information

Of the 140 questionnaires distributed, 89 completed questionnaires were returned (63% response rate). The grades of the respondents varied: 16 staff members (18%), 10 fellows (11.2%) and 63 residents (70.8%). Medical specialties included 34 surgeons (38.2%), 24 internists (27%), 19 obstetrician-gynecologists (21.3%), 9 emergency physicians (10.1%) and 3 radio-oncologists (3.4%). Among the responders, 63 (70.8%) were general practitioners while 22 (24.7%) were abdominal-related subspecialists (gastrointestinal, hepatobiliary, urogenital, oncology, obstetrics, gynecology and reproduction) and 4 (4.5%) were other subspecialists (chest and neurology). The duration of clinical experience ranged from 1 to 35 years with a mean of 4.2 years (Table 1).

Report components

Clinical information ($p < 0.001$), quality of examination ($p = 0.014$), measurement of the normal organ ($p < 0.001$), and recommendation ($p < 0.001$), were rated as statistically significantly appropriate to be included in the radiol-

Figure 1. (A) Report type A. Structured style with brief details. (B) Report type B. Prose style with brief details.

Figure 2. (A) Report type C. Structured style with more detail. (B) Report type D. Prose style with more detail

ogy report. Route of administration, dose and name of contrast media were, however, not found to be statistically significant for inclusion (p = 0.014) (Table 2).

Report style and content preferences

The most highly ranked report for style and content was report C (structured with more detail) (Figure 3a). The preference order of the reports (most preferred to least preferred) by

Table 1. Clinician demographics and general information (n=89)

Category	Number (%)
Grade	
Fellow	10 (11.2)
Resident	63 (70.8)
Staff	16 (18.0)
Specialty	
ER	9 (10.1)
Internal medicine	24 (27)
OB-GYN	19 (21.3)
Radiotherapy	3 (3.4)
Surgery	34 (38.2)
Subspecialty	
General	63 (70.8)
Gastrointestinal	2 (2.2)
Hepatobiliary	2 (2.2)
Nephrology	3 (3.4)
Urogenital	3 (3.4)
Oncology	4 (4.5)
Gynecology	6 (6.7)
Obstetric	1 (1.1)
Reproductive	1 (1.1)
Others	4 (4.5)

the Kemeny-Young method were C, A, D and B (Figure 3b). Similarly, report C was statistically significantly preferred for style and content both by normal ranking and by the Kemeny-Young method by residents and fellows. However, among staff, the most preferred report by normal ranking was report C, while the preference by the Kemeny-Young method was report D, but the difference was not statistically significant (Figure 4). There was no statistically significant difference in report preferences between abdominal-related subspecialists and other specialists, with report C the most preferred report (Figure 4).

Respondent comments

Four referring clinicians included comments. The first comment suggested that the first paragraph of the impression should relate to the clinical question. For example, in a report on clinical indications of metastasis, the first paragraph of impression should indicate whether there is evidence of metastasis or not.

The other three comments were that they liked structured reports very much because this type of report is easy to understand and to determine the results. Another mentioned that it is necessary to include recommendations in the report.

Table 2. Components which should be including in a radiology report (n=89)

Component	Yes N (%)	No N (%)	p-value
Clinical information	62 (69.7)	27 (30.3)	< 0.001*
Examination technique	46 (61.7)	43 (48.3)	0.75
Route, dose and name of contrast media	33 (37.1)	56 (62.9)	0.014*
Quality of examination	56 (62.9)	33 (37.1)	0.014*
Measurement of normal organ	71 (79.8)	18 (20.2)	< 0.001*
Recommendation	84 (94.4)	5 (5.6)	< 0.001*
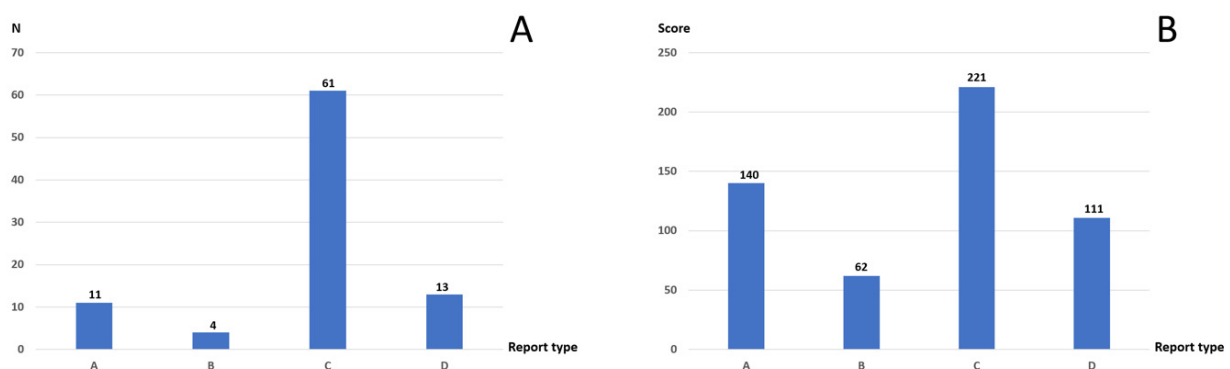
Figure 3. (A) Frequency of ranking of report styles by all responders (N). (B) Order (most to least preferred) of each report style by Kemeny-Young score. (A= report type A, B= report type B, C= report type C, D= report type D).
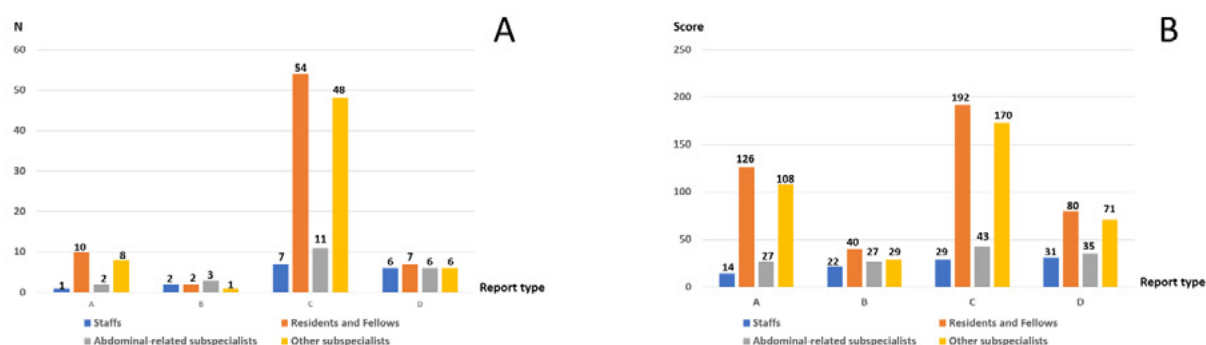
Figure 4. (A) Frequency of ranking of report styles by level and subspecialty. (B) Rank order (most preferred to least preferred) of each style by Kemeny–Young score by level of experience and subspecialty.

DISCUSSION

We believe that effective reports increase the effectiveness of the diagnosis process and lead to more effective treatment. Many studies have reported on the effect of reporting structure on physicians' interpretation of radiology reports (2,8–13). For example, based on a survey of 104 clinicians, Lafortune et al. (14) concluded that "the written radiology report should be clear, respond directly to the clinical questions, contain a description of findings and a conclusion."

Clinical information, quality of the examination, measurement of the normal organ, and recommendations should be included in the report, i.e., similar to a prior study conducted by Plumb et al. (6).

Many studies have attempted to determine the most preferred style and the necessary details of a radiology report. Most have made suggestions related to structured style and more detail (2,5–7). Similarly, in our study most referring clinicians, as well as most residents and fellows, preferred a structured style with more details. Among the staff, the preferred report was also a structured style with more detail; however, the most preferred order was not significantly different. Even abdominal-related subspecialists as well as generalists and other subspecialists preferred a structured format with more detail.

This study found that route of administration, dose, and type of contrast media were not considered to be essential for clinicians. However, in the opinion of radiologists, this information is appropriate for inclusion in the report because these data help with decision making, e.g., which type of study and which kind of contrast material should be used in the next study. This is particularly important for patients who are determined to be allergic to a certain type of contrast so the next study will not use that same type of contrast or will use it with caution. Additionally, the route of administration and the radiologic study technique of were also felt to be important information for the next technologist. The American College of Radiology committee further recommend that notification of physicians about emergent findings should be appropriate and timely (15).

Strengths of this study include the high questionnaire response rate as well as the variety of experience and subspecialties of the participating clinicians. Limitations of this study include the relatively small number of questionnaires distributed and the fact that only physicians in one tertiary (medical school) hospital participated. Additionally, we did not collect data about the scenario of a single disease with multiple organ involvement, an area which would be a suitable for future studies.

CONCLUSIONS

We conclude that the preferred report is one that is structured and includes more detail, including the clinical scenario, quality of the examination, measurements of the normal organ and recommendations. To develop more universal recommendations, questionnaires should be distributed at additional primary and secondary care hospitals, including both government and private hospitals.

FUNDING

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CONFLICTS OF INTEREST

None.

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Original Article   **Open Access**

Universal COVID-19 Testing Among Hospitalized Pregnant Women during the Initial COVID-19 Period in Thailand

Keerati Chiengthong[1], Wilasinee Areeruk[1], Somsook Santibenchakul[1,2], Shina Oranratanaphan[1] and Tarinee Manchana[1]

[1]*Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, [2]Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand*

ABSTRACT

OBJECTIVE To determine the prevalence of COVID-19 infection among hospitalized pregnant women during the initial COVID-19 period in Thailand.

METHODS Before admission, symptoms and risks of COVID-19 infection of pregnant women were assessed by using a self-administered questionnaire. Nasopharyngeal and oropharyngeal swab tests were collected by trained obstetrics and gynecology residents and analyzed using the real-time fluorescence reverse transcription-polymerase chain reaction technique (RT-PCR). Electronic medical records of the patients were extracted for this study.

RESULTS Among 570 women admitted to the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital from April 16 to June 6, 2020, most (99.6%, 568/570) had a negative COVID-19 test. Results of the other two women (0.4%, 2/570) were missing. Eleven women (1.9%, 11/570) had traveled to or from COVID-19 endemic regions. Thirteen women (2.3%, 13/570) were healthcare personnel. None of the women reported signs or symptoms of COVID-19 infection at admission. Their maternal and neonatal outcomes were comparable to the pre-COVID-19 period, i.e., the incidence of preterm delivery was 27.4% (156/570), and the cesarean section rate was 51.1% (271/530). Eighteen newborns (3.2%, 18/567) had 5-minute Apgar scores of less than 7. Twenty-four (4.2%, 24/567) newborns required neonatal intensive care due to very low or extremely low birth weight, low Apgar scores, or multiple fetal anomalies.

CONCLUSIONS Pre-admission universal testing for COVID-19 infection in asymptomatic pregnant women with a history of low risk for COVID-19 infection during the low prevalence period in Thailand showed negative results. Consideration of implementing universal testing should be adapted to based on the epidemiological situation.

KEYWORDS asymptomatic, COVID-19, pregnancy, SAR-COV-2, screening

INTRODUCTION

In December 2019, the novel coronavirus 2019 (2019-nCoV) outbreak emerged in Wuhan, China and had begun to spread rapidly across the globe by the beginning of 2020. The World Health Organization (WHO) declared the novel coronavirus 2019 a global pandemic on 11 March

2020 (1). The novel coronavirus was named SARS-CoV-2 or COVID-19, and is an enveloped RNA virus (2). The virus attaches to the angiotensin-converting enzyme 2 (ACE2) receptor in the respiratory tract causing symptoms of fever, dry cough and shortness of breath (3,4). In severe cases, pneumonia, respiratory distress syndrome and septic shock can develop. However, one-fifth of patients show no symptoms at the time of hospital admission (5). The primary diagnostic testing method for COVID-19 is nucleic acid detection using real-time fluorescence reverse transcription-polymerase chain reaction (RT-PCR) with biological specimens such as nasal or throat swab or feces (6).

The first COVID-19 case in Thailand was reported on 12 January 2020. The number of infected cases rapidly increased from 42 on March 1 to 3,081 by the end of May 2020 (7). In order to control the disease, the Thai government imposed an emergency decree that consisted of numerous regulations including the closure of many public areas where people congregate.

King Chulalongkorn Memorial Hospital, a tertiary referral hospital in Bangkok, established a special COVID-19 unit which implemented patient care protocols to minimize the risk of infection among both patients and healthcare workers. Before admission, all patients were evaluated for their risk of COVID-19 infection and assessed for symptoms of COVID-19. RT-PCR testing of all at-risk patients using nasopharynx and oropharynx swabs began in March 2020.

Physiologic changes in respiratory, cardiovascular and immune systems make pregnant women more susceptible to severe COVID-19 symptoms. Higher adverse perinatal outcomes have been reported in COVID-19-infected mothers including preterm birth, preeclampsia and fetal intrauterine growth restriction (8,9). Risk of postoperative venous thromboembolism has also been reported to increase in infected cases (10). However, the clinical manifestations in pregnant women are similar to non-pregnant women and the evidence of vertical transmission from mother to fetus is still limited (11,12). The US Centers for Disease Control and Prevention (CDC) recommends COVID-19 testing in both symptomatic and asymptomatic patients if there has been contact with COVID-19 cases (13). In asymptomatic pregnant women who are at low risk of infection, COVID-19 testing is not recommended as routine practice. However, in high prevalence countries, there have been reports of positive COVID-19 test results in asymptomatic pregnant women. In New York City at the height of the early COVID transmission in April 2020, a clinical review found 13.5% of asymptomatic pregnant women tested positive for COVID-19 (14). A study in California, a state with a much lower COVID rate than New York City, showed only 0.43% of patients with a positive COVID-19 test were asymptomatic at the time of admission (15).

The Royal Thai College of Obstetricians and Gynecologists (RTCOG) is responsible for ensuring that clinical practice guidelines for management of COVID-19 infection in pregnancy are followed. The guidelines define individuals requiring COVID-19 testing as those having a fever with one of the following symptoms: cough, runny nose, sore throat, or shortness of breath (16).

This study was conducted to determine the prevalence of COVID-19 infection during the initial COVID-19 period among hospitalized pregnant women at a tertiary hospital in Bangkok, Thailand. In addition, we reported maternal and neonatal outcomes among this cohort of pregnant women.

METHODS

This is descriptive study. After obtaining approval from the Institutional Review Board of Chulalongkorn University, we enrolled all pregnant women at 22 weeks or more of gestation admitted to the Department of Obstetrics and Gynecology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand, from April 16 to June 6, 2020. The multi-step pre-admission COVID-19 screening process was performed by residents trained in obstetrics and gynecology. All residents were coached on how to collect nasopharynx and oropharynx swabs by an emerging infectious diseases team. A questionnaire covering self-reports of symptoms in the 5 days prior to admission and risk exposure to COVID-19 infection within 1 month pri-

or to admission were administered to all newly admitted patients. The risk of COVID-19 infection was assessed based on potential exposure in various settings including contact with an infected person, frequent stays in crowded areas, travel from countries with a high prevalence of COVID-19, and working in a healthcare setting. Reports of any suggested COVID-19 symptoms including cough, runny nose, sore throat, anosmia and shortness of breath were recorded. The temperature of each woman was measured. Nasopharynx and oropharynx swabs were then collected in a negative pressure room. The RT-PCR for COVID-19 was processed by the Chulalongkorn microbiology laboratory using the Cobas® SARS-COV-2 test (Roche Diagnostics, Indianapolis, IN, USA). RT-PCR test results were interpreted as either positive or negative.

Data on patients were retrieved from electronic medical records including age, pre-pregnancy body mass index, ethnicity, gravidas (1 or ≥ 2), parity (nulliparous or multiparous), gestational age, medical diseases and pregnancy risks, mode of delivery, intrapartum complications, postpartum complications, duration of hospital stay and neonatal outcomes.

Categorical variables are reported as frequencies and percentages. Continuous variables are presented as means and standard deviations (SD) or medians and interquartile ranges (IQR). Statistical analyses were conducted using IBM SPSS Statistics software, version 22.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 570 pregnant women hospitalized during the study period were enrolled. Baseline characteristics are shown in Table 1. Almost all (95.0%) were Thai. The mean (SD.) age was 31.4 (5.5) years. The mean (SD.) gestational age at the date of admission was 37.6 (2.6) weeks. Six of the patients had a history of cardiovascular diseases, including three prior cardiovascular accidents, two arrhythmias and one dilated cardiomyopathy. There were 145/570 (25.4%) patients diagnosed with anemia, including 102/570 (17.9%) with the thalassemia trait, 33/570 (5.8%) with iron deficiency anemia, and 9/570 (1.6%) with thalassemia disease. One patient had systemic lupus erythematosus with autoimmune hemolytic anemia.

Table 1. Baseline characteristics of hospitalized pregnant women (N=570)

	N (%)
Maternal age	
< 35 years	393 (68.9)
≥ 35 years	177 (31.1)
Pre-pregnancy BMI (kg/m²)	
Underweight (less than 18.5)	76 (13.3)
Normal weight (18.5-24.9)	342 (60.0)
Overweight (25-30)	92 (16.1)
Obese (greater than 30)	47 (8.3)
Missing	13 (2.3)
Ethnicity	
Thai	540 (94.7)
Lao	10 (1.8)
Burmese	8 (1.4)
Cambodian	3 (0.5)
Unidentified	5 (0.9)
Other[a]	4 (0.7)
Gravidities	
1	252 (44.2)
≥ 2	317 (55.6)
Missing	1 (0.2)
Parity	
Nulliparous	308 (54.0)
Multiparous	261 (45.8)
Missing	1 (0.2)
Maternal comorbidities	
Gestational diabetes	37 (6.5)
Pregnancy induced hypertension	41 (7.3)
Asthma	6 (1.1)
Cardiovascular disease	6 (1.1)
Anemia	144 (25.3)

[a]Filipino, Guinean, Malin, Pakistani

Table 2. Risk of COVID-19 infection of hospitalized pregnant women (N=570)

	N (%)
Risk-based screening	
Recent travel from COVID-19 endemic regions	11 (1.9)
Contact with known infected persons	0
Healthcare providers	13 (2.3)
Symptom-based screening	
Fever (BT > 37.5 °C)	0
Cough	3 (0.5)
Nasal symptoms	0
Sore throat	2 (0.4)
Anosmia	0
Shortness of breath	0

The risk of COVID-19 infection 1 month prior to admission and symptoms of COVID-19 infection 5 days prior to admission are displayed in Table 2. All patients were afebrile, including 13/570 (2.3%) patients who were healthcare

Table 3. Maternal outcomes (N=530)

Maternal outcomes	N (%)
Mode of delivery	
Spontaneous vertex delivery	250 (47.2)
Operative vaginal delivery	9 (1.7)
Elective cesarean delivery	124 (23.4)
Emergency cesarean delivery	147 (27.7)
Gestational age at delivery	
< 37 weeks, n (%)	119 (22.5)
≥ 37 weeks, n (%)	411 (77.5)
Postpartum complications	
None	491 (92.6)
Postpartum hemorrhage (EBL > 1,000 mL)	11 (2.1)
Wound infection	6 (1.1)
Breast complications	1 (0.2)
Others[a]	3 (0.6)
Missing	18 (3.4)

[a]Fourth-degree perineal tear, wound separation, heart failure

Table 4. Neonatal outcome (N=567)[a]

Neonatal outcome	N (%)
Birthweight, n (%)	
Normal birthweight (≥ 2,500 g)	463 (81.6)
Low birthweight (< 2,500 g)	85 (15.0)
Very low birthweight (< 1,500 g)	13 (2.3)
Extremely low birthweight (< 1,000 g)	6 (1.1)
Apgar scores at 1 min, mean (SD.)	8.7 (1.2)
Apgar scores at 5 min, mean (SD.)	9.8 (1.0)

[a]496 were singleton neonates, 62 were twin neonates, and 9 were triple neonates.

providers. RT-PCR tests were interpreted as negative in 568/570 (99.6%) patients with the results of 2/570 (0.4%) patients missing.

Maternal outcomes are shown in Table 3. Six patients had intrapartum fever without specific causes which resolved after delivery. One patient had a prolonged rupture of membranes and developed chorioamnionitis. Non-reassuring fetal heart rate was detected in 14/530 (2.6%) patients. The median (interquartile range) duration of hospital stay was 4 (3-5) days. None of the women developed signs or symptoms of COVID-19 infection during admission and 40/570 (7.0%) patients were undelivered. Among those who delivered (93.0%, 530/570), 496 were singleton neonates, 62 were twin neonates, and 9 were triple neonates. Mean (SD.) gestational age at delivery was 37.8 (2.3) weeks with a mean (SD.) birthweight of 2,897.0 (587.8) grams. Eighteen (18/567, 3.2%) newborns had 5-minute Apgar scores of less than 7. Twenty-four (24/567, 4.2%) newborns required neonatal intensive care, including 5 preterm births with low birthweight and low Apgar scores. There were 11 with very low birth weight, 5 with extremely low birth weight and 3 with multiple fetal anomalies (Table 4).

DISCUSSION

Universal testing of COVID-19 infection found negative results in all asymptomatic pregnant women and there were no reports of COVID-19 related symptoms during admission. These results mirror the very low prevalence of COVID-19 infection during the initial infection period in Thailand (1 in 23,000) and help explain the differences from studies in other countries. The prevalence of COVID-19 infection in asymptomatic pregnant women was reported as 13.7% in New York City (14), 3.3% in London (17), 0.5% in Madrid (18) and 0.43% in California (15). Differential prevalence of COVID-19 infection in each country might be a plausible cause. In Thailand, a total of 2,672 confirmed cases of COVID-19 infection had been recorded by April 16, 2020 when the universal testing protocol began. The total increased to 3,104 cases by the end of the study period on 6 June 2020 (7). On July 28, 2020, the Global COVID-19 Index (GCI) ranked Thailand as first in the Global COVID-19 recovery index with an index score of 82.06 (19).

The policy of King Chulalongkorn Memorial Hospital during the early phase of the outbreak period aimed to reduce the number of routine antenatal visits to limit potential exposure risk. Additionally, the universal RT-PCR test was applied to all pregnant women who required hospitalization. None of the pregnant women in this study had a positive screening test result for COVID-19. All pregnant women were afebrile prior to admission, with cough and sore throat only presenting in 3 (0.5%) and 2 (0.4%) women, respectively. Our study findings support previous CDC recommendations that COVID-19 testing should not be performed routinely (13). According to the RTCOG guidelines, testing for COVID-19 was suggested only for women who have fever with one of the following symptoms: cough, runny nose, sore throat, shortness

of breath, or a diagnosis of pneumonia. Differences in screening protocols might be necessary among countries due to differences in prevalence of the disease.

The incidence of preterm delivery (27.4%), cesarean section (51.1%) and NICU admission (4.2%) are comparable to the pre-COVID period figures of 28.7% (20), 51.6% (21) and 5.7% (22), respectively. This study represents a large cohort involving universal testing for COVID-19 infection among pregnant women in Thailand. While testing by the standard RT-PCR technique can yield false negative rates in asymptomatic patients (23), this study found no patients developed symptoms related to COVID-19 infection during the postpartum period.

CONCLUSIONS

Pre-admission universal testing for COVID-19 infection in asymptomatic pregnant women with a history of low risk for COVID-19 infection during a low prevalence period like the initial phase of COVID-19 in Thailand showed negative results. However, the result of our study might not be applicable in high prevalence settings such as the current COVID situation in Thailand. Consideration of implementation of universal testing should be based on the epidemiological situation.

STRENGTH

Nasopharynx and oropharynx swab tests were collected by well-trained residents and evaluated using reliable assays for qualitative detection of COVID-19 (24).

LIMITATION

During the initial pandemic, diarrhea and nausea were considered to be atypical COVID-19 symptoms (25). The hospital protocol did not include those symptoms in symptom-based screening for risk of COVID-19 infection. The data was collected for only a short period of time. For further information, the longer period is needed.

DATA AVAILABILITY

All data generated and analyzed during this study are included in this published article.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest regarding the publication of this paper.

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Original Article   **Open Access**

Medication Errors in Ready-to-Administer Injectable Admixtures Compounded by Pharmacy Personnel: A Study of Hospitals in Northern Thailand

Pitchayut Rattanatanyapat[1], Chutima Chaiwut[2], Ong-art Maneemai[3,4], Kridsana Karnman[3], Jiraprapa Decha[3], Sudthida Takongkaew[3], Muntana Duangmon[3] and Kunwara Ob-un[5]

[1]University of Phayao Hospital, School of Medicine, University of Phayao, Phayao; [2]Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Chiang Mai; [3]Department of Pharmaceutical Care, School of Pharmaceutical Sciences, University of Phayao, Phayao; [4]Pharmacoepidemiology, Social and Administrative Pharmacy (P-SAP) Research Unit, School of Pharmaceutical Sciences, University of Phayao, Phayao; [5]Chemotherapy Ward, Chiang Rai Prachanukroh Hospital, Chiang Rai, Thailand

ABSTRACT

OBJECTIVE To determine the number, types, and severity of medication errors in ready-to-administer injectable admixtures compounded by pharmacy personnel in northern Thai hospitals.

METHODS This retrospective descriptive study was conducted in six hospitals in northern Thailand. Data were gathered from hospital incidence reports over the three-year period 2017-2019. The following data were extracted from each report: stage of error, medication involved, care setting, and severity of error. The National Coordinating Council for Medication Error Reporting and Prevention index was used to categorize the severity of the medication errors. Results are presented as number and percentage.

RESULTS The total number of medication error events in the six hospitals was 405, classified as transcribing (n=59, 14.5%), pre-dispensing (n=217, 53.6%) and dispensing errors (n=129, 31.9%). The most frequent type of pre-dispensing errors was inappropriate techniques in medication compounding (n= 54, 13.3%). Almost all the medication errors were of severity level B (errors resulting in no harm to patients) (n=398, 98.3%). The most frequent errors were reported in antineoplastic agents (n=373, 92.1%).

CONCLUSIONS The great majority of medication errors were pre-dispensing errors with a low level of severity. The provision of strategies to prevent medication errors is necessary for patient safety.

KEYWORDS medication errors, ready-to-administer injection, pharmacist

INTRODUCTION

Injectable therapies are complex, potentially dangerous, and are susceptible to errors. Injection medications have been associated with higher rates of medication administration errors compared to orally administered medications (1). Several studies have reported medication errors which occurred during the injectable medication preparation process, e.g., wrong drug (2,3), wrong diluent (2-7), wrong amount of diluent volume (2,3,5,6), expired medication, preparations which became unstable after dilution (2,5), wrong concentration (3,8,9), wrong

labelling (3), omissions of drugs (9), and inappropriate storage (4). In some cases, medical personnel did not follow a standardized drug preparation process, e.g., not washing the device (8), not sterilizing the vial with alcohol (2), not cleaning the drug preparation area before preparing the medication (2), using an inappropriate drug preparation area and not wearing gloves during preparation and administration of the drug (2,5).

Ready-to-administer medications are recommended as standard practice by the Joint Commission International (10). One category of the ready-to-administer medications is ready-to-administer injectable products. The compounding of medications is a fundamental skill of pharmacy practice. All compounding personnel, including pharmacists and pharmacy technicians, are responsible for compounding and dispensing sterile products. Previous studies (11-13) have demonstrated that preparation of injectable medications by pharmacists results in fewer medication errors.

In some areas of Thailand, hospital pharmacists are responsible for compounding sterile injectable products. Most of these are chemotherapy products and parenteral nutrition admixtures. Due to human resources limitations, injection products are frequently prepared by medical personnel other than pharmacists, especially nurses. One study (14) in Thailand showed that the cost of the ready-to-use system over a 10-year period was about 18 million baht lower than the traditional compounding system by a saving of about 2%. Moreover, the study reported that the ready-to-use system also decreased nurses' workload (14). However, the impacts on medication errors were questionable. Little is known about the rate of medication errors in ready-to-administer injection medications prepared by pharmacists. To the best of our knowledge, there have been no studies of ready-to-administer injectable medications prepared by pharmacists conducted in Thailand. More evidence is needed, especially studies with a sample size large enough to identify appropriate approaches to preventing errors. In this study, we investigated the incidence of medication errors in ready-to-administer injectable admixtures

prepared by pharmacists in northern Thai hospitals.

METHOD
Study settings, design and data collection
To publicize the project, invitation letters and copies of the research proposal were sent to all 143 hospitals located in northern Thailand including a discussion of the study's purpose, expected benefits, and risks. Hospitals which agreed to participate in the study and sent acceptance letters to the researcher within one month after the invitation were included in the study.

This retrospective descriptive study gathered data from hospital incidence reports over the three-year period 2017-2019. Reports were drawn from the hospital safety reporting systems, a voluntary system used by healthcare professionals to report many types of safety incidents including medication errors. Medication error reports about ready-to-administer injection preparations by pharmacists were included in the study. The following data were extracted from each report: stage of error (i.e., transcribing, pre-dispensing, or dispensing error), medication involved, care setting, and severity of the error.

The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) index was used to categorize the severity of the medication errors (Table 1) (15). Final confirmation of the data was performed by pharmacists at the study hospitals.

Measures
The primary outcome was medication errors which had been reported through the hospital safety reporting system. Errors were categorized into three types: transcribing, pre-dispensing, and dispensing errors. A transcribing error is a mistake in the identification of a specific type of medication which occurred due to a data entry error. A pre-dispensing error is an error that happened in the process of drug refilling or drug preparation. This type of error can be detected at the pharmacy unit before the drug is dispensed to the patient or before delivery to wards. A dispensing error is defined as a deviation from a prescription that occurs

Table 1. The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) index (15)

Level	Description
A	Events that have the capacity to cause error
B	An error occurred, but the medication did not reach the patient
C	An error occurred that reached the patient but did not cause the patient harm
D	An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm
E	An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
F	An error occurred that may have contributed to or resulted in temporary harm to the patient and prolonged hospitalization
G	An error occurred that may have contributed to or resulted in permanent harm to the patient
H	An error occurs that required intervention necessary to sustain the life of the patient
I	An error occurred that have contributed to or resulted in the patient's death

Table 2. Definition of categories of medical errors in the study (16–18)

Types of medication errors	Definitions
Omission of drug	The prescribed medication(s) was/were not prepared or did reach the patient.
Preparation without prescription	The medication(s) was/were prepared without a physician's prescription.
Wrong diluent	The prescribed medication(s) was/were not reconstituted or diluted with the correct type of diluent or solution or did not follow the physician's prescription.
Wrong amount of diluent volume	The prescribed medication(s) was/were not reconstituted or diluted with the correct volume of diluent or solution or did not follow the physician's prescription.
Wrong drug	The prescribed medication(s) was/were not prepared or dispensed correctly according to the physician's prescription.
Wrong concentration	The prescribed medication(s) was/were prepared in a dose or concentration higher than or lower than the amount prescribed by the physician.
Wrong label	The label of prescribed medication(s) was/were incomplete, incorrect or did not follow the physician's prescription.
Wrong quantity	The amount of the prescribed medication(s) dispensed was/were incorrect or did not follow the physician's prescription.
Wrong preparation technique	The preparation of the prescribed medication(s) was done using inappropriate procedures or improper techniques.
Wrong storage	The prescribed medication(s) was/were kept or stored incorrectly.

during the dispensing process, e.g., a dose/item error, incorrect labelling, and identification of the wrong patient. Detailed definitions of each type of medication error are presented in Table 2.

Data analysis

Data were analyzed using statistical software. Types of medication errors and the NCC MERP medication error index were analyzed using descriptive statistics. The results are presented as number and percentage.

Ethical considerations

The study protocol and ethical principles were reviewed and approved by the University of Phayao Human Ethics Committee (Ref. No. 2/193/62). The research protocol was approved by the individual hospitals as necessary. Before the initial data collection, the eligible hospitals signed an informed consent. Anonymity and confidentiality of all participants was assured. As the data was collected, neither the names nor personal details of the patients or of the data reporters were recorded at any stage of the data collection process.

RESULTS
Hospital characteristics

Of the 143 hospitals in the northern region of Thailand, nineteen (13.3%) responded, of which six (4.2%) met the inclusion criteria. Thirteen hospitals were excluded due to an

incomplete hospital safety reporting system and ethical review process. The participating hospitals included five government hospitals and one private hospital. The hospitals were located in Phayao (n=1), Phrae (n=1), Chiang Mai (n=3), and Chiang Rai (n=1) provinces. Five were general hospitals with 30-500 beds and one was a teaching hospital with more than 1,000 beds. The ready-to-administer injection preparations were prepared in a variety of settings in two hospitals, and in chemotherapy and parenteral nutrition departments in four hospitals.

Types of medication errors

The number of medication error reports in ready-to-administer injection preparations by pharmacists in 2017, 2018 and 2019 were, respectively, 185 (45.7%), 118 (29.1%), and 102 (25.1%), a total of 405 events. Those events included 59 transcription errors (14.5%), 217 pre-dispensing errors (53.6%) and 129 dispensing errors (31.9%). The types of medication errors in ready-to-administer injection preparations by pharmacists are presented in Table 3.

The transcribing errors involved incorrect entry of physician's orders into the computer system and included wrong diluents (n=22, 5.4%), wrong drugs or items (n=20, 4.9%), wrong patients (n=13, 3.2%), and wrong volume of diluents (n=4, 1.0%). The majority of pre-dispensing errors occurred in the process of production (n=89, 22.0%); the most frequent pre-dispensing errors were preparing using the wrong preparation techniques (n=54; 13.3%), using the wrong diluent (n=30, 7.4%) and using the wrong dose or strength of

Table 3. Types of medication errors in ready-to-administer injection preparations prepared by pharmacists [n (%)]

Types of medication errors	Overall (n=405)	2017 (n=185)	2018 (n=118)	2019 (n=102)
1. Transcribing errors	59 (14.5)	38 (20.5)	6 (5.1)	15 (14.7)
Wrong diluent	22 (5.4)	15 (8.1)	0 (0.0)	7 (6.9)
Wrong patient	13 (3.2)	6 (3.2)	5 (4.2)	2 (1.9)
Wrong dose	11 (2.7)	9 (4.9)	1 (0.9)	1 (1.0)
Wrong drug	9 (2.2)	8 (4.3)	0 (0.0)	1 (1.0)
Wrong volume of diluent	4 (1.0)	0 (0.0)	0 (0.0)	4 (3.9)
2. Pre-dispensing errors	217 (53.6)	89 (48.1)	76 (64.4)	52 (51.0)
2.1 Pre-preparation errors				
Omission of drug	27 (6.7)	13 (7.0)	7 (5.9)	7 (6.9)
Wrong diluent	18 (4.4)	7 (3.8)	8 (6.8)	3 (2.9)
Wrong drug	8 (2.0)	3 (1.6)	4 (3.4)	1 (1.0)
Preparation without prescription	3 (0.7)	2 (1.1)	0 (0.0)	1 (1.0)
2.2 In-process errors				
Wrong preparation techniques	54 (13.3)	21 (11.4)	23 (19.5)	10 (9.8)
Wrong diluent	30 (7.4)	13 (7.0)	9 (7.6)	8 (7.8)
Wrong volume of diluent	3 (0.7)	1 (0.5)	0 (0.0)	2 (2.0)
Wrong concentration	2 (0.5)	0 (0.0)	0 (0.0)	2 (2.0)
2.3 Post-preparation errors				
Wrong concentration	29 (7.1)	11 (5.9)	14 (11.9)	4 (3.9)
Wrong diluent	15 (3.7)	7 (3.8)	3 (2.5)	5 (4.9)
Wrong drug	15 (3.7)	7 (3.8)	4 (3.4)	4 (3.9)
Wrong label	10 (2.5)	4 (2.2)	2 (1.7)	4 (3.9)
Wrong storage	3 (0.7)	0 (0.0)	2 (1.7)	1 (1.0)
3. Dispensing errors	129 (31.9)	58 (31.4)	36 (30.5)	35 (34.3)
Omission of drug	61 (15.1)	34 (18.4)	13 (11.1)	14 (13.7)
Wrong concentration	18 (4.4)	6 (3.2)	6 (5.1)	6 (5.9)
Wrong quantity	17 (4.2)	7 (3.8)	3 (2.5)	7 (6.9)
Wrong label	14 (3.5)	0 (0.0)	11 (9.3)	3 (2.9)
Wrong storage	10 (2.5)	9 (4.9)	0 (0.0)	1 (1.0)
Wrong drug	7 (1.7)	2 (1.1)	2 (1.7)	3 (2.9)
Wrong diluent	2 (0.5)	0 (0.0)	1 (0.8)	1 (1.0)

Table 4. Severity of medication errors and medications involved (n=405)

Categories	Number of errors (%)			Total
	B	C	D	
Medication errors				
1. Transcribing errors	59 (14.8)	0 (0.0)	0 (0.0)	59 (14.5)
2. Pre-dispensing errors	217 (54.5)	0 (0.0)	0 (0.0)	217 (53.6)
3. Dispensing errors	122 (30.7)	3 (100.0)	4 (100.0)	129 (31.9)
Drug classes				
1. Antineoplastic agents	370 (92.9)	2 (66.7)	1 (25.0)	373 (92.0)
2. Antibiotics	12 (3.0)	0 (0.0)	0 (0.0)	12 (2.9)
3. Antidotes	7 (1.7)	0 (0.0)	0 (0.0)	7 (1.7)
4. NSAIDs	3 (0.7)	0 (0.0)	1 (25.0)	4 (0.9)
5. Vasopressors	1 (0.3)	0 (0.0)	1 (25.0)	2 (0.5)
6. Vitamins	2 (0.5)	0 (0.0)	0 (0.0)	2 (0.5)
7. Antipsychotics	0 (0.0)	0 (0.0)	1 (25.0)	1 (0.3)
8. Anticholinergic agents	0 (0.0)	1 (33.3)	0 (0.0)	1 (0.3)
9. Loop diuretics	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
10. Neurotrophic agents	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
11. Electrolyte supplements	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)

NSAIDs; non-steroidal anti-inflammatory drugs

intravenous products (n=29, 7.1%). The most frequent dispensing errors were omission of prescribed medications (n=61, 15.1%), wrong dose/strength (n=18, 4.4%) and wrong amount of drug dispensing (n=17; 4.2%), respectively.

Severities of medication errors and medication involved.

The NCC MERP index for categorizing medication errors is shown in Table 4. None of the reported errors resulted in harm to patients. Of the reported errors, in 398 cases the medication did not reach the patients (B level), in 7 cases the medication reached the patient of which 3 did not cause patient harm (C level), and 4 errors resulted in the need for increased patient monitoring but did no harm (D level). Most of the events involved antineoplastic agents (n=373, 92.1%). Most of the reported medication errors involved fluorouracil (n=73), methotrexate (n=31) or cisplatin (n=27) (data not shown). The three in C level errors involved fluorouracil (n=1), gemcitabine (n=1) and hyoscine (n=1). The errors in D level involved cyclophosphamide (n=1), haloperidol (n=1), norepinephrine (n=1), and parecoxib (n=1).

DISCUSSION

Proper utilization and analysis of medication error reports can provide valuable insights into system-based pitfalls regardless of the care setting. In the present study, half of the medication errors were pre-dispensing errors (53.6%). This result is similar to previous studies which have reported 88.6% of pre-dispensing errors in out-patient pharmacy service (19), 50% in in-patient pharmacy services(20), and 51% in community pharmacies (21). Prior studies have demonstrated that systematic rechecking by a pharmacist can help prevent and correct medication errors. In one study, 88.6% of pre-dispensing errors were detected by pharmacists (19). Another study confirmed that pharmacists can have an important role in preventing, detecting and correcting medication errors (21).

The majority of pre-dispensing errors in the current study involved inappropriate techniques in medication compounding (n=54, 13.3%). A disguised observation study of intravenous preparations by nurses in two hospitals in the UK found that errors related to improper technique occurred in 13.3% of intravenous doses (22). A study in two Vietnamese hospitals reported 34.4% of errors were related to improper technique (18). Errors in the preparation phase can have serious consequences as that is the last step before administration. The inappropriate technique errors in our study were reported to have occurred in the pre-dis-

pensing process and the medications did not reach the patient. However, the evidence base for evaluating the accuracy of intravenous admixture units prepared by pharmacy personnel appeared to be weak. The second and third most frequent types of pre-dispensing error were "wrong diluent" (detected during the process of compounding) and "wrong concentration" (detected after the dilution process). Wrong concentration errors in intravenous therapy were reported to account for 148 of 799 errors (18.5%) in the neonatal intensive care unit in one study (16). The most frequent types of errors in intravenous admixtures reported from five hospitals in the US were wrong dose (70.0%) and wrong based solution (16.0%) (wrong volume 6% and wrong content 10%) (23).

This study found 31.9% of the errors were dispensing errors, significantly higher than the 1.1% reported in other medication error studies in Thailand (20) and the 3.88% in studies in Mexico (16). Most dispensing errors in our study involved drug omission (15.1%). Previous studies have reported drug omission error rates of 3% in US (23) and 5% in Vietnam (24). A possible cause of this type of error could be an imbalance between the workload and the number of pharmacy personnel. Four of the six participating hospitals in this study had only two pharmacists on staff preparing the intravenous admixtures. The other two hospitals had 3 and 6 pharmacists on staff.

Our finding of 98.3% NCC MERP medication index level B errors is similar to a previous study which reported 97.3% level B errors (20). Although the errors in this study resulted in no harm to patients, possible causes of the errors should be analyzed. A regular review of risk management procedures should be implemented to reduce the incidence of near miss events and to help protect against medication errors which could cause harm.

This study found that injectable chemotherapy was the most common type of medication error (92.1%) and that the most frequent errors involved fluorouracil, methotrexate, and cisplatin. Previous studies have reported findings similar to the present study, e.g. the highest rate of errors involved methotrexate,

fluorouracil, and vincristine (25). The high error rate in this study may be due to the participating hospitals providing significant levels of chemotherapy preparation services.

This is the first study focused on medication errors among ready-to-administer injection preparations done by hospital pharmacists in Thailand. The issue of injection preparation has received only limited systematic investigation by researchers, and is recognized as an area that requires attention. The results of this study may be used as empirical evidence that can help emphasize the need to design and implement improved strategies, for example, increasing the number of pharmacists to match the workload and implementing continuous error-prevention training programs.

This study has some limitations. First, it is likely that not all medication errors which occurred during the study period were recorded or reported under the hospital safety reporting system, and therefore were not included in this study. Second, this study analyzed only voluntary reports from 2017 to 2019. Potential sources of negative impact on the study findings include under-reporting, bias and internal validity problems. Third, this study does not detail of the incidents or the rates of the different types of medication errors. As some participating hospitals did not have a complete record of medication errors, the analysis was incomplete and the results might not reflect the actual annual incidence of medication errors. Despite these limitations, results of this study should be beneficial for the further development of intravenous medication safety processes. Further study focusing on the etiology of medication errors and the economic impact of those errors is needed.

CONCLUSIONS

This study of medication errors presents the number and characteristic of medication errors in ready-to-administer injection preparations by pharmacists in northern Thai hospitals. A large number of the medication errors were pre-dispensing errors with a low level of severity. This study highlights the importance of complete and accurate reporting of medication errors, patient medication safety and the need

for effective guidelines to help prevent medication errors in hospitals.

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AUTHOR CONTRIBUTIONS

PR drafted the first manuscript. OM conducted the analysis, interpreted parts of the data and revised the manuscript. CC contributed to the data collection and conception of the analysis. KK, JD, ST, and MD conducted the data collection at the study sites. KO assisted with the analysis. All authors contributed toward the study design, data analysis, drafting and critical revision of the manuscript. The final draft manuscript was approved by all authors prior to submission for publication.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

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Original Article   **Open Access**

Symptom Burden and Health-Related Quality of Life among Patients Undergoing Hemodialysis in China

Jie Yuan[1], Chomphoonut Srirat[2], Chiraporn Tachaudomdach[2] ⊙

[1]Master Degree Student, Faculty of Nursing, [2]Faculty of Nursing, Chiang Mai University, Chiang Mai, Thailand

ABSTRACT

OBJECTIVE This descriptive correlational study aimed to identify the top three contributors to symptom burden and health-related quality of life (HRQOL) and to examine the relationship between the top three symptom burdens and HRQOL among patients undergoing hemodialysis (HD) in the People's Republic of China.

METHODS Purposive sampling of 142 patients from 2 hospitals receiving HD was done. Instruments included demographic data form, Dialysis Frequency Severity, Symptom Burden Index, and Kidney Disease Quality of Life-36. Data were analyzed using descriptive statistics and Spearman rank-order.

RESULTS The top three symptom burden items were feeling tired, itching, and having trouble staying asleep. The mean scores were 8.80 ± 2.67, 6.42 ± 3.17, and 5.94 ± 4.20, respectively. The mean score for five subscales of HRQOL were symptoms/problems with kidney disease 77.27 (SD = 10.37), impact of kidney disease 59.62 (SD = 11.18), burden of kidney disease 15.67 (SD = 15.29), physical component summary 30.15 (SD = 5.98), and mental component summary 40.29 (SD = 7.91). There was a negative relationship among the top three symptom burdens and HRQOL (rs = -0.26 -0.52, *p* < 0.01).

CONCLUSIONS The findings provide clinical nurses in China with information to develop more effective symptom management strategies which may help improve patients' HRQOL.

KEYWORDS symptoms burden, health-related quality of life, hemodialysis, end-stage renal disease

INTRODUCTION

End-stage renal disease (ESRD) is a common disease that seriously endangers human health and life (1). Hemodialysis (HD) is the main treatment for patients with ESRD (2). In China, the number of patients undergoing HD increased from 234,000 in 2011 to 511,000 in 2017 (3). Although HD can prolong the life of patients with ESRD, it can replace only a small portion of normal physiological renal function. For that reason, patients undergoing HD frequently suffer from a high symptom burden which may cause numerous negative impacts on their quality of life (4). Compared to the general population, patients undergoing HD have a poorer health-related quality of life (5). A previous study found that symptom burden was an important independent predictor for health-related quality of life (HRQOL) (5). However, no studies have been conducted to document the relationship in Honghe city,

Yunnan Province, the People's Republic of China. In this study, the top three symptom burdens and the subjective state of HRQOL among patients in Honghe city undergoing HD were identified and the relationship to HRQOL was examined.

Symptom burden is defined as the patient's perception of inconvenience caused by the occurrence, frequency, severity, and distress of chronic disease (6). A review of the literature found the most common symptom burdens among patients undergoing HD were fatigue, insomnia, and pruritus (4,5,7). HRQOL is defined as an individual's perceived physical and mental health and how a chronic disease interferes with their day-to-day life (8).

Any bothersome burden from symptoms not controlled by the patient or healthcare professionals can negatively affect the patient's health (4). Fatigue affects 60% to 97% of patients receiving HD (9) which mainly affects their physical and psychological states. Fatigue affects the patient's ability to manage their daily activities, requiring more time to complete those activities (10). It also has a negative impact on the patient's memory and ability to focus on conversations and what is happening around them (11). Approximately 50% to 75% of patients undergoing HD complained of insomnia (12). Insomnia has many harmful effects on behavior, health, happiness, enjoyment of interpersonal relationships, and personal safety (13). Severe insomnia can impair daytime functions, increase accidents and reduce the overall quality of life (14). The incidence of pruritus among patients undergoing HD has been estimated to be between 40% and 90% (15). Pruritus affects a patient's quality of life in many ways, including limiting activities of daily living, being closely related to physical and mental limitations and insomnia, causing lesion scratching and secondary skin changes, making patients feel discomfort, anger, or anxiety (16) which can contribute to low quality of life in patients undergoing HD (17).

As for the relationship between symptom burden and HRQOL or general quality of life (QOL) among patients undergoing HD, several studies have been conducted. In Canada, Davison

and Jhangri found that symptom burden was a significant independent predictor for HRQOL (5). In Australia, Raj et al. found a strong relationship between symptom burden and general QOL. The top three symptom burdens were fatigue, trouble staying asleep, and trouble falling asleep (18). In Switzerland, Delmas et al. reported a significant negative relationship between symptom burden and general QOL. They found decreased interest in sex, difficulty becoming sexually aroused, and trouble falling asleep were the greatest burden for patients (4). In China, researchers found a significant negative correlation between symptom burden and general QOL among patients undergoing HD in Chongqing, Guangdong and Zhejiang Province (7,19,20). In Chongqing Province, patients reported that the three most burdensome symptoms were trouble falling asleep, decreased interest in sex, and trouble staying asleep (20). In Guangdong Province, the top three symptom burden items were itching, trouble staying asleep, and dry skin (7).

A literature review found the three most common symptom burden items complained about by patients vary in different countries and even in different provinces in China. Previous studies have focused on the correlation between symptom burden and general QOL and have used a generic instrument to assess the QOL. However, the generic instrument used to measure QOL in those studies is intended for all populations, not specifically the population undergoing HD. HRQL is the key element in identifying changes in health status, describing disease progression, guiding treatment decisions and nursing interventions, and evaluating clinical trial results (21). Therefore, it is important to study the top three symptom burdens and the subjective state of HRQOL among patients undergoing HD in Honghe city.

OBJECTIVES

This study aimed to identify the top three contributors to symptom burden and the HRQOL and examine the relationship between each symptom burden item and HRQOL among patients undergoing HD in Honghe city, Yunnan Province, the People's Republic of China.

METHODS

A descriptive correlation study design was used. The participants included 142 patients undergoing HD in two tertiary hospitals in Honghe city, Yunnan Province, the People's Republic of China. The inclusion criteria were as follows: 1) age 18 years or older; 2) receiving regular hemodialysis two or three times per week for at least six months; 3) no severe complications such as malignant tumors, severe infections, or persistent heart failure; 4) able to communicate in the Chinese language; 5) willing to participate in the study; 6) Montreal cognitive assessment score of more than 26 points. The exclusion criterion was a previous or current history of mental illness or depression as identified in the patient's medical record.

The study was approved by the Research Ethics Committee of the Faculty of Nursing, Chiang Mai University, Thailand (Study code: 2020-EXP025). Permission for data collection from each hospital included in this study was also obtained. The researcher informed participants that their human rights would be protected. Participants were free to decide whether to participate in the study and to withdraw from the study at any time without repercussions. Refusal to participate in this study did not affect the patients' future treatment. Participants signed an informed consent form.

The research instruments included a Demographic Data Form, the Dialysis Frequency Severity and Symptom Burden Index (DFSSBI), and the Kidney Disease Quality of Life-36 (KDQOL-36).

The demographic data form was developed by the researcher and included age, gender, marital status, education level, occupation, income, dialysis duration, and associated diseases plus blood urea nitrogen, creatinine, and potassium levels.

The Chinese version of the DFSSBI was translated by Zhou et al. (20). It includes 30 items and four domains: presence, frequency, severity, and distress. The presence or absence of symptoms was reported using "yes" or "no". The frequency was measured using a 4-point Likert scale with 1=occasional, 2=sometimes, 3=often, and 4=always. Severity was measured using a 4-point Likert scale with 1=mild, 2=

moderate, 3=severe, and 4=very serious. Distress was measured using a 5-point Likert scale with 0=not at all, 1=a little bit, 2=somewhat, 3=quite a bit, and 4=very much. The maximum total score was 360; the higher the score, the heavier the individual's symptom burden. The content validity was 0.939 (20). Reliability was tested with ten patients undergoing HD and showed a Pearson correlation coefficient of 0.96.

The Chinese version of the KDQOL-36 was translated by Amgen Incorporated and the MAPI Institution (22). It is a 36-item HRQOL survey divided into five subscales: a physical component summary and a mental component summary (items 1-12), the burden of kidney disease (items 13-16), symptoms/problems of kidney disease (items 17-28), and effects of kidney disease (items 29-36). The total transformed score is 100, with a higher score indicating a better HRQOL. The item-level content validity index (I-CVI) and scale-level content validity index (I-CVI) were both 1.0. Reliability was tested with ten patients undergoing HD and showed a Cronbach's alpha coefficient of 0.80.

After receiving the approval of the ethics committees, the researcher screened for cognitive impairment using the Montreal Cognitive Assessment (MoCA). A score of 26 or higher is considered normal (23). The researcher explained the purposes, method, benefits, and potential risks of the study. The researcher conducted the survey with the participants by reading each questionnaire item without explanation in a quiet and private room. The average survey time was approximately 30 to 40 minutes for each participant. The researcher checked the collected questionnaires, and incomplete or non-qualifying questionnaires were excluded. The researcher checked the results of laboratory tests to obtain demographics related to the disease.

The demographic data and the scores of all variables were analyzed using descriptive statistics that consisted of frequency, percentage, mean, and standard deviation. The relationships between the top three symptom burden items and HRQOL were analyzed using Spearman rank-order correlation. The data showed an abnormal distribution ($p > 0.5$) using the Kolmogorov-Smirnov test. The correlation

coefficient (r) value was based on Burns and Grove (24): r < 0.30 = weak; 0.30 ≤ r ≤ 0.50 = moderate; r > 0.50 = strong.

RESULTS

Among the 142 patients undergoing HD, more than half were male (59.20%), and their ages ranged from 23 to 76, with a mean of 49.49 (SD=12.52). The majority of the patients were married (87.30%) and had a middle school education or below (71.80%). Most of them (90.10%) were unemployed, and 60.50% of patients' family per capita monthly income was 300-600 USD. The duration of dialysis of the participants ranged from 0.5-25 years, with a mean duration of 4.58 years (SD=3.75). Most (52.10%) had been undergoing HD for more than three years, while 47.90% had received HD for three years or less. Among the patients, 46.50% had a blood urea nitrogen value of less than 20 mmol/L, and 40.80% had a blood urea nitrogen value between 20 and 30 mmol/L. Nearly half the patients had a creatinine value of 1,000 to 2,000 μmol/L. Regarding potassium, 55.60% of the patients had a value ≥ 5 mmol/L, while 44.40% had a value < 5 mmol/L.

Among the 30 items on the Chinese version of the DFSSBI, the top three symptom burden items among patients undergoing HD were feeling tired (mean = 8.80, SD = 2.67), itching (mean = 6.42, SD = 3.17), and trouble staying asleep (mean=5.94, SD=4.20) (Table 1). For the five subscales of HRQOL, the highest mean score was symptoms/problems of kidney disease

Table 1. Frequency, mean and standard deviation of symptom burden of the samples (orderly ranked by sum of symptom burden) (n = 142)

Symptoms	N	Percent (%)	Frequency $\overline{X}$ (SD)	Severity $\overline{X}$ (SD)	Bother $\overline{X}$ (SD)	Sum symptom burden X (SD)
1. Feeling tired or lack of energy	142	100.00	3.10 (0.82)	2.85 (0.94)	2.85 (1.02)	8.80 (2.67)
2. Itching	128	90.14	2.38 (1.09)	2.05 (1.09)	1.99 (1.14)	6.42 (3.17)
3. Trouble staying asleep	108	76.06	2.07 (1.39)	1.94 (1.43)	1.93 (1.51)	5.94 (4.20)
4. Trouble falling asleep	94	66.20	1.63 (1.38)	1.58 (1.39)	1.53 (1.40)	4.74 (4.04)
5. Dry mouth	136	95.78	2.06 (0.82)	1.46 (0.63)	1.19 (0.72)	4.70 (1.80)
6. Muscle soreness	99	69.72	1.68 (1.25)	1.35 (1.10)	1.30 (1.09)	4.32 (3.33)
7. Dry skin	131	92.25	1.75 (0.85)	1.41 (0.80)	1.04 (0.83)	4.20 (2.26)
8. Bone or joint pain	83	58.45	1.43 (1.36)	1.18 (1.17)	1.12 (1.15)	3.73 (3.59)
9. Worrying	128	90.14	1.57 (0.72)	1.23 (0.62)	0.89 (0.74)	3.69 (1.85)
10. Feeling irritable	88	61.97	1.11 (1.01)	0.92 (0.86)	0.82 (0.89)	2.84 (2.64)
11. Nausea	77	54.23	1.10 (1.17)	0.85 (0.98)	0.70 (0.79)	2.65 (2.80)
12. Constipation	69	48.59	1.08 (1.23)	0.85 (0.97)	0.70 (0.84)	2.63 (2.92)
13. Headache	72	50.70	1.03 (1.13)	0.79 (0.90)	0.76 (0.86)	2.58 (2.81)
14. Muscle cramps	70	49.30	0.96 (1.13)	0.80 (0.96)	0.69 (0.88)	2.46 (2.87)
15. Feeling anxious	89	62.68	0.96 (0.87)	0.77 (0.72)	0.69 (0.74)	2.42 (2.21)
16. Decreased appetite	69	48.59	0.94 (1.09)	0.77 (0.94)	0.70 (0.84)	2.41 (2.78)
17. Swelling in legs	63	44.37	0.89 (1.09)	0.70 (0.89)	0.64 (0.87)	2.23 (2.77)
18. Feeling nervous	92	64.79	0.92 (0.81)	0.74 (0.63)	0.54 (0.72)	2.20 (1.97)
19. Lightheadedness or dizziness	51	35.92	0.74 (1.08)	0.60 (0.91)	0.58 (0.91)	1.92 (2.84)
20. Restless legs or difficulty keeping legs still	56	39.44	0.73 (1.01)	0.63 (0.91)	0.54 (0.81)	1.90 (2.66)
21. Difficulty becoming sexually aroused	59	41.55	0.74 (0.94)	0.63 (0.85)	0.49 (0.81)	1.85 (2.47)
22. Cough	58	40.85	0.74 (1.03)	0.58 (0.80)	0.46 (0.71)	1.78 (2.44)
23. Numbness or tingling in feet	43	30.28	0.67 (1.12)	0.57 (0.98)	0.53 (0.92)	1.77 (2.98)
24. Shortness of breath	45	31.69	0.62 (1.01)	0.54 (0.89)	0.52 (0.86)	1.68 (2.72)
25. Feeling sad	68	47.89	0.73 (0.84)	0.58 (0.69)	0.36 (0.63)	1.66 (2.02)
26. Decreased interest in sex	50	35.21	0.65 (0.94)	0.56 (0.85)	0.44 (0.77)	1.65 (2.45)
27. Difficulty concentrating	42	29.58	0.38 (0.65)	0.35 (0.58)	0.26 (0.58)	0.99 (1.73)
28. Chest pain	22	15.49	0.27 (0.69)	0.23±0.60	0.23 (0.60)	0.73 (1.87)
29. Diarrhea	19	13.38	0.20 (0.54)	0.15 (0.39)	0.15 (0.45)	0.49 (1.33)
30. Vomiting	6	4.23	0.07 (0.35)	0.06 (0.34)	0.05 (0.27)	0.18 (0.94)

(SPKD) (mean = 77.27, SD = 10.37), followed by the effect of kidney disease (EKD) (mean = 59.62, SD = 11.18), while the mean score of the burden of kidney disease (BKD) was the lowest (mean = 15.67, SD = 15.29). The mean score of the physical component summary (PCS) and the mental component summary (MCS) were 30.15 ± 5.98 and 40.29 ± 7.91, respectively (Table 2).

The results of the Spearman rank-order coefficient showed a negative relationship between each symptom burden item and the subscales of HRQOL. There was a moderate negative relationship between feeling tired and the overall subscales (SPKD, EKD, BKD, PCM, and MCS) of HRQOL (rs=−0.41, rs=−0.38, rs = − 0.32, rs = −0.50, and rs = −0.38, $p < 0.01$, respectively). Itching had a strong negative relationship with SPKD (rs = −0.52, $p < 0.01$) and a weak negative relationship with MCS (rs = −0.17 $p < 0.05$). Moreover, the results showed a significant negative relationship between trouble staying asleep and four subscales (SPKD, EKD, PCM, and MCS) of HRQOL (rs = −0.51, rs = −0.34, rs = −0.40, and rs = −0.26, $p < 0.01$, respectively) (Table 3).

DISCUSSION

In this study, the top three symptom burden items among patients undergoing HD were slightly inconsistent with different countries and even from different parts of China.

Firstly, this study did not find decreased interest in sex or difficulty becoming sexually aroused among the highest symptom burden items, which is inconsistent with previous studies done in Switzerland [4] and Chongqin Province, China [20]. One possible explanation of the difference is related to the traditional beliefs of patients and being ashamed to report problems related to decreased interest in sex or difficulty becoming sexually aroused. Due to the influence of thousands of years of traditional feudal thought, people may think that sexual desire is low and dirty, sexual intercourse is harmful, discussing sexual issues is indecent, and that sex is considered the source of all evil [25]. Especially in cities heavily influenced by traditional beliefs and where education levels are low such as Honghe city, people tend to avoid talking about sex. Another more probable explanation is related

Table 2. Range, possible score, mean and standard deviation of each dimension of health-related quality of life of the samples (n = 142)

Health-related quality of life	Possible score	Range	Mean (SD)
Symptom/problem kidney disease	0–100	41.67–95.83	77.27 (10.37)
Effects of kidney disease	0–100	12.50–78.13	59.62 (11.18)
Burden of kidney disease	0–100	0–50	15.67 (15.29)
Physical component summary	0–100	16.48–45.12	30.15 (5.98)
Mental component summary	0–100	27.28–55.61	40.29 (7.91)

Table 3. The relationships between each symptom burden item and the five subscales of health-related quality of life

	Feeling tired		Itching		Trouble staying asleep	
	Spearman rank	*p*-value	Spearman rank	*p*-value	Spearman rank	*p*-value
HRQOL						
SPKD	−.41**	0.00	−.52**	0.00	−.51**	0.00
EKD	−.38**	0.00	−.16	0.05	−.34**	0.00
BKD	−.32**	0.00	−.01	0.91	−.03	0.69
PCS	−.50**	0.00	−.15	0.07	−.40**	0.00
MCS	−.37**	0.00	−.17*	0.04	−.26**	0.00

**p < 0.01; *p < 0.05
HRQOL, health-related quality of life; SPKD, symptoms/problems of kidney disease; EKD, effect of kidney disease; BKD, burden of kidney disease; PCS, physical component summary; MCS mental component summary

to the demographic data of the participants. Decreased interest in sex and/or difficulty becoming sexually aroused may also be related to the relatively older age of patients undergoing HD (26). In a study by Chang and colleagues, patients undergoing HD with a mean age of 61.3 (SD=12.4) had a greater reduction in interest in sex and more difficulty becoming sexually aroused than patients with a mean age of 58.4 (SD=11.0) (26). However, in this study, the mean age was 49.49 (SD = 12.52), nearly half of the patients (47.9%) were between 40 and 60 years old, and 31.0% were less than 40 years old. In addition, although some researchers found that the incidence of decreased interest in sex or difficulty becoming sexually aroused in male patients undergoing HD was higher than that in females in China (27), the proportion of males and females was almost equal in this study. These factors may have lead to lower scores for the symptom burden items of decreased interest in sex and difficulty becoming sexually aroused.

Secondly, in contrast to the study in Guangdong Province, China (28), dry skin was not one of the top three symptom burden items in this study. A possible explanation is related to demographics. Studies have shown that women are more sensitive to the severity and are more bothered by dry skin than men (28). In this study, 40.8% of patients undergoing HD were women, while in the study in Guangdong Province, women accounted for 55.7%.

The mean scores of PCS, SPKD, and EKD were 30.15 (SD=5.98), 77.27 (SD=10.37), and 59.62 (SD=11.18), respectively, are similar to the studies by Chen et al. (22) and Cohen et al. (28).

The mean score of MCS was 40.29±7.91, which is lower than the previous studies of Chen et al. (22) in Hong Kong (mean=50.99, SD = 10.287), Goh et al. (29) in Malaysia (mean = 53.1), and Cohen et al. (28) in the United States (mean = 49.0, SD = 13.4). A plausible explanation of the lower score in this study is related to the patients' demographics. Previous studies have shown that patients undergoing HD who have low income, low education, and are unemployed have a low MCS score (30,31). In this study, 71.8% of patients undergoing HD had an education level of middle school or below,

and 90.1% were unemployed. In addition, only 9.9% of patients undergoing HD had a monthly income of more than 4,000 ¥. These may have contributed to the low MCS scores.

The mean score of BKD in this study was 15.67 ± 15.29, which is inconsistent with previous studies. The mean scores of BKD in Hong Kong, the United States, Colombia, and Malaysia were 33.08, 51.3, 35.0, and 37.5, respectively (22,28,29,32). One possible explanation for the difference may be the demographics related to the disease. Kidney damage is irreversible; it causes a lot of inconvenience for patients and interferes with daily life (6). In this study, more than half of the patients with HD hemodialysis (63.5%) had a blood urea nitrogen value greater than 20 mmol/L, and 72.0% of patients had a creatinine value greater than 1,000 μmol/L. Patients with end-stage renal disease need long-term HD treatment to prolong their life. In this study, 52.1% of the patients had received HD for more than three years, which means they had spent a lot of time dealing with kidney disease which can increase their symptom burden and make them feel frustrated. Another explanation is that being unemployed makes patients perceive themselves as being a financial burden on their families. In this study, the majority of the patients undergoing HD (90.1%) were unemployed.

Feeling tired was found to be significantly associated with the subscales of HRQOL (SPKD, EHD, BKD, PCS, and MCS) (rs = –0.41, rs = –0.38, rs = –0.32, rs = –0.50, and rs = –0.37, $p < 0.01$, respectively). This finding indicates that the higher the burden of fatigue perceived by patients undergoing HD, the lower the HRQOL. The main explanation for this result is that fatigue can limit a patient's daily and social activities (10). Firstly, most patients undergoing HD are unable to work because of fatigue, and unemployed patients accounted for 90.1% of this study. This deprives them of the opportunity to provide financial resources for the family or to contribute to society and makes the patients feel that they have no goals; they sit at home and do nothing and feel that they are useless people (1). Secondly, fatigue and regular HD treatment prevent patients from doing things they like to do, such as traveling (10).

Thirdly, fatigue reduces the participation rate of patients in social activities (10); for example, fatigue limits the time patients undergoing HD can play with their children. They do not have the energy to accompany their children while camping, playing ball, or doing other strenuous activities, which can make them feel sad and guilty. In addition, fatigue inhibits sexual relations, making the patient feel guilty for their partner and affecting family harmony (1).

The results showed that there was a negative relationship between itching and SPKD as well as MCS (rs = –0.52, p < 0.01 and rs = –0.17, p < 0.05, respectively). Compared with fatigue, itching mainly affects the SPKD of HRQOL among patients undergoing HD. An explanation for this is that the effect of itching on patients undergoing HD is primarily manifests as a series of symptoms, e.g., trouble staying asleep, trouble falling asleep, irritability, and anxiety, which indirectly reduce the patient's HRQOL (16). Moreover, the effect of itching on daily and social activities of patients undergoing HD may not be as significant as fatigue (1). Furthermore, fatigue is troublesome and challenging to manage, unlike itching (33).

Trouble staying asleep was significantly associated with four subscales (SPKD, EKD, PCS, and MCS) of HRQOL (rs = –0.51, rs = –0.34, rs = –0.40, and rs=–0.26, p < 0.01, respectively). Some reasons for this include that trouble staying asleep can cause headaches, fatigue, dizziness, shortness of breath, and other symptoms in patients undergoing HD. If patients undergoing hemodialysis suffer from trouble staying asleep for a long time, they will feel emotionally upset or anxious (34). Additionally, in patients receiving HD these symptoms can be aggravated by having trouble staying asleep as well. Recurrent trouble sleeping will increase the symptom burden of patients undergoing HD, which will seriously affect their HRQOL. Trouble staying asleep causes patients undergoing HD to have difficulty paying attention, memory decline, and decreased work efficiency (35). In addition, the decline in concentration and memory can easily make patients misunderstand, despise, or ignore the true meaning of information conveyed by others and thus worsen their interpersonal relationships

(3,34). Trouble staying asleep can lead to a reversal of sleep patterns: night insomnia and daytime sleepiness. This phenomenon will reduce the patient's daytime and social activities (13). A study showed that patients undergoing HD who had trouble staying asleep had twice as many restricted-activity days and bed-ridden days as patients who did not have trouble staying asleep (13).

CONCLUSIONS

This study found the top three symptom burden items among patients undergoing HD were feeling tired, itching, and having trouble staying asleep. Moreover, there was a negative relationship between each symptom burden item and HRQOL. Based on the results of this study, nursing measures should be taken not only in response to common symptoms and symptoms with a high incidence, but the frequency, severity, and distress of the patient's symptoms should be comprehensively evaluated as well. Nurses should pay increased attention to patients' HRQOL. Additionally, clinical nurses should develop symptom monitoring and treatment plans for patients undergoing HD and should provide effective interventions to reduce the symptom burden as a means of improving patients' HRQOL.

The top three symptom burden items among patients undergoing HD are inconsistent in different countries and even among different provinces in China. It is necessary to systematically identify the symptom burden of patients undergoing HD in different locations. That will not only enrich our understanding of this phenomenon but will also help identify possible new targeted interventions. Intervention studies on how to reduce the burden of fatigue, itching, and trouble staying asleep should be conducted as well.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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Review Article

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Occupational Health and Safety of Sex Workers: A Review Article

Pitchaya Chevasutho and Wiroj Jiamjarasrangsri

Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Correspondence: Pitchaya Chevasutho, MD, Department of Preventive and Social Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10700, Thailand.
E-mail: che.pitchaya@gmail.com

ABSTRACT

The sex industry in Thailand is estimated to be one of the largest grey market businesses in the country, grossing approximately 0.2-billion baht per year. However, a thorough occupational hazards investigation has not been performed on this industry, and full healthcare services for workers in the industry are rarely provided, supposedly due to the illegality of their jobs and to the substantial stigmatization from society. This study reviewed the relevant literature, news and articles related to the occupational health and safety of commercial sex workers, then classified the findings into several related factors: legal viewpoint, violence, mental health problems, alcohol and drug abuse, sexually transmitted diseases, musculoskeletal disorders, and unwanted pregnancies. Increasing the occupational health and reducing the safety risk of sex workers is an area with promising growth potential, as these workers are a valuable workforce whose intrinsic needs are not being met.

KEYWORDS sex workers, occupational health

INTRODUCTION

Presently, health checkups for commercial sex workers are believed to be solely for the benefit of customers rather than for the benefit of the sex workers themselves, and there currently exists no legal framework specifically addressing the health and safety of commercial sex workers in Thailand. This situation is due to several factors, including the country's religious beliefs, moral dilemmas, and other social limitations. Additionally, as most commercial sex workers are women, including both genetic and transgender women, their experiences tend to be devalued, and they face sexual discrimination stemming from Thailand's deep-rooted patriarchal system. As a result, some commercial sex workers conceive of themselves as being inferior in terms of the country's social hierarchy, so seeking proper health care and safety seems to be out of the question for them.

This review aims to illustrate sex workers occupational hazards, as understanding those hazards is essential to improving their occupational health and safety.

METHODS

The authors explored associated aspects using several keywords including 'occupational health' and 'safety' together with 'sex workers' via online research database platforms, i.e., PubMed and Scopus. Related news and articles were collected through online search engines both in Thai and English and then screened.

After researching the occupational hazards faced by commercial sex workers, the findings were classified into several categories followed by a discussion on the nature of the occupation's legality along with possible future solutions.

RESULTS

Characteristics of sex workers in Thailand

Until BE 2503, sex work was a lawful occupation in Thailand. That year the first Prostitution Suppression Act was enacted. That act, which criminalized sex work, was later replaced by the BE 2539 Prostitution Suppression Act, which is still currently in place. As a result of these acts, voluntary sex work became illegal under Thai law, and sex workers were generally criminalized, a situation that has resulted in several concerns (1).

It is speculated that there are approximately 250,000 commercial sex workers in Thailand. Sex work is also considered to constitute the largest portion of the 'grey business market' based on the yearly gross income it generates, which is believed to be around 0.2-billion baht (2,3).

According to the sex workers support charity Service Workers in Group (SWING) president and Thammasat University political science professor Dr. Chalidaporn Songsamphan, there are approximately 50,000 commercial sex workers in Pattaya, contributing about 268 billion baht a year to Thailand's economy (4).

Since the initial enactment of the Prostitution Suppression Act in BE 2503, several types of entertainment businesses have either been permanently closed or have been operated clandestinely, e.g., as massage parlors, traditional Thai massage parlors, bathhouses, karaoke bars, beer bars, go-go bars, snack bars and barber shops (5). Some of these service places were established ostensibly for other purposes under a facade. Some might even provide sex workers a fixed revenue share while others provide only proffer rental opportunities for self-employed sex workers. Since the emergence of the internet era, more and more sex workers have preferred to work as freelancers and to garner customers across several internet platforms, for example, 'pretty or PR', sideliners, and even street wanderers.

Overall, sex workers in Thailand are categorized into a slipshod hierarchy, distinguished either by their physical appearance, workplace, or monthly revenues. A study by Plumridge (6) found that this social hierarchy is one of the factors determining the level of occupa-tional risk sex workers encounter. That study also stated that sex workers seldom, if ever, moved from a lower to a superior status level. This is because sex workers from different hierarchies rarely interact or exchange information regarding their work problems or possible solutions, nor are they able to engage in network-building as workers in labor unions do in other occupations.

This existing social hierarchy can potentially have a drastic, and even potentially fatal, effect on sex workers. A study (7) of sex workers in Glasgow, Scotland showed that female sex workers with lower socioeconomic status are at much greater risk when dealing with customers. Sex workers who work on the street face the highest risk, while those who work at a service establishment face a medium level of risk, and escorts are at a lower risk compared to the others (8). Even in countries with legalized sex work, sex workers who work as freelancers and those who come from marginalized communities are at greater risk than those who work in a registered establishment because they are likely to face greater health and safety hazards, lack legal protection, and lack appropriate access to health services.

According to the International Labor Organization of the United Nations (ILO), occupational safety and health (OSH) is defined as, "the science of the anticipation, recognition, evaluation and control of hazards arising in or from the workplace that could impair the health and well-being of workers, taking into account the possible impact on the surrounding communities and the general environment" (9). The authors classify sex workers' occupational health hazards as mental health problems, alcohol and drug abuse, sexually transmitted diseases, musculoskeletal disorders, and unwanted pregnancies, whereas occupational safety includes violence, e.g., bodily assaults. Finally, the legal aspects are important, as they undeniably hinder sex workers from moving towards healthy, safe, and decent working conditions.

Violence against sex workers

One study (10) researching violence against sex workers found that it could be divided into two main categories: physical abuse and de-

liberate avoidance of payment, i.e., theft. Most violence originates from clients, but is not limited to them. Perpetrators of these two forms of violence might include members of the police, the neighborhood, or the community, or they may even be the partners or spouses of the sex workers themselves.

In Thailand, legal reports of violence and bodily assault against sex workers are rarely recorded, mostly because the sex workers prefer not to report them out of fear of the police officers and the risk of being criminally charged with sex work (11). In a study conducted in England (12) among 240 female sex workers, 63.8% had encountered violence from clients in the past, and 37.5% claimed to have been assaulted recently or within the past 6 months. Of those incidents, only 34% were reported to the police.

In terms of physical violence, Farley (13) studied the incidence of traumatic brain injury among 66 female and transgender sex workers. Sixty-one percent of them had experienced either being hit with an object or having had their heads slammed into objects while engaging in sex work. These women sustained several types of injuries with symptoms including dizziness, headaches, difficulty sleeping, depression, memory problems, fatigue, and weight change. Symptoms varied in duration, ranging from acute to long-term health effects.

A study in India (14) showed that 43.9% of the 222 burn patients in hospitals were injured as a result of deliberate action; hundreds of these victims were commercial sex workers. These burn victims endured scalding water, fire, cigarette burns, or chemical burns such as acid burns, mostly used to humiliate and dehumanize them. The more severe cases suffered permanent disfiguration and contracture scars, permanently limiting their range of motion.

During times of economic duress, authorities and pimps alike tend to exploit people working at the economic fringes. Presently, some sex workers have chosen to resort to recruiting customers online, resulting in potentially risking their lives by being assaulted or entrapped (15). Previous research reports have stated that repealing the criminalization of sex workers would reduce the risk of violent acts against them (16). Furthermore, as violence against sex workers seems to be under-reported, anti-violence campaigns should be promoted and reporting of violent crimes should be encouraged among sex workers, so that proper and timely management can be ensured.

Mental health issues

Farley (17) studied female sex workers in 9 countries, including Thailand, and reported that 2 out of 3 met the diagnostic criteria for PTSD (post-traumatic stress disorder). This number was roughly comparable in every country studied. The researcher then concluded that working in the sex industry had a negative impact on mental health that did not vary based on geographical location. On the other hand, a study by Vanwesenbeeck (18) came to different conclusions. That study found the associated victim-blaming, homelessness, and instances of drug abuse might also contribute to the prevalence of PTSD among sex workers.

Vanwesenbeeck also reviewed the level of burnout experienced by 96 female sex workers. The only characteristic clearly distinguishing sex workers from a control group was their level of depersonalization. Forty-two percent of the variance in the sex workers' symptoms of depersonalization was explained by their lack of choice, negative social reactions, experiences of violence, and lack of control when interacting with clients. As such, depersonalization might be a coping strategy for the negative conditions and experiences associated with sex work. Depersonalization is also one of the indicators of stress and emotional exhaustion, of which the latter could be the result of a lack of managerial support, negative social reactions, lack of choice, and negative work motivation. All things considered, mental health awareness programs might be beneficial for sex workers, along with accessible mental counselling and proactive mental health programs although there have been very few studies in this field in Thailand.

Alcohol and drug abuse

In some situations, sex workers might not be in a position to negotiate or to decide whether to drink alcoholic beverages or not. For instance,

cantineras, or Latina women who make a living as drinking partners in working class Latino bars, reported consuming an average of 11 beers per night, equal to 110 grams of alcohol based on the 8 oz (approximately 240 mL) size of a typical beer (19). The maximum amount consumed per night could be as high as 21 beers. This is not unlike beer bar girls or other entertainment workers in Thailand who, enticed by sales commissions, have been found to be exhorted to consume around 4-10 standard drinks per night, equal to 80 grams of alcohol. One notorious case of extreme alcohol intoxication causing mortality occurred in the case of a 'pretty' or party entertainer girl whose blood alcohol level was found to be 418 grams per 100 mL (20). Sexual propositioning was found to be frequent in these circumstances even though sex work is not mentioned in the workers' job description. Once under the influence of alcohol, workers are prone to being more vulnerable to sexual advances and to more easily misjudge clients as the acute effects of alcohol include delayed speech, loss of decision-making ability and coordination, and attention impairment. Workers in these situations receive unsolicited sexual favors and could potentially be raped, robbed, or coerced into using recreational drugs.

Potential long-term health effects of alcohol ingestion include liver disease, cardiovascular disease, pancreatic disease, and several forms of cancer. Both men and women working in bars are said to have the highest risk of mortality from cirrhosis of the liver. Periodic health examination and regular screening for drug and alcohol addiction is a simple and effective preventive method that could be implemented among sex workers.

Sexually transmitted diseases

Venereal diseases are generally one of the first things that come to mind when discussing the health hazards faced by sex workers. In Australia (21), the prevalence of bacterial sexually transmitted diseases in illegal sex workers was 80 times higher than their legal counterparts, partially because of a lack of venereal disease screening over the previous three months. The lifetime prevalence of sexually-transmitted

infection (STI) among street workers was also remarkably higher (22).

Several false beliefs were found to be factors contributing to sexually transmitted diseases among sex workers. Male sex workers assumed that transrectal intercourse would not transmit human immunodeficiency virus, or HIV (23). Some extremists (24) might even extrapolate the Undetectable = Untransmittable ideation into having unprotected sex with their clients while on their antiviral regimens when their viral load was undetectable. Religious beliefs prohibiting condom use and superstitious beliefs regarding HIV not infecting dedicated devotees are also causes of STI spread.

Presently, most sex workers are aware of the benefits of condom use during transvaginal sexual intercourse. However, some might not use condoms during oral favors, leading to the spread of pharyngeal gonorrhea infection. An additional issue found was that for some female sex workers, condomless sex was the only way to distinguish their 'partners' from 'clients'. However, socioeconomic status tends to play the primary role in a sex worker's decision to use condoms or not (25).

Bladder infections can also arise from a lack of urinary voiding after a sexual act or from using a vaginal diaphragm as a contraceptive method. An acute infection could eventually turn into a chronic one if it occurs frequently (26).

Another misunderstanding among female sex workers is that vaginal douching reduces the risk of infection when condomless sexual intercourse is performed. In fact, studies show that vaginal douching increases the risk of PID (pelvic inflammatory disease), bacterial vaginosis, chlamydia, HIV, and cervical cancer (27,28).

In order to be able to work throughout the entire month, some female sex workers choose to use a menstrual sponge during sexual intercourse with their clients, which causes irritation and increases the risk of bacterial infection; some workers also mistakenly believe that it is an effective method of contraception. The U.S. Food and Drug Administration (FDA) has reported finding of vaginal sponges contaminated with grit, sand, mold, fungus, and bacteria such as *Staphylococcus aureus*, which can cause toxic shock syndrome (29).

From the 2017 annual report of the Bureau of AIDS TB and STIs, Department of Disease Control, Thai Ministry of Public Health, the median prevalence of HIV infection among male and female sex workers was 12 and 1 per cent, respectively (5). From a report of the Thai Division of Innovation and Research, gonorrhea infection prevalence in 2016 among nonvenue and venue female sex workers was 7.3 and 4.2 per cent, respectively. Syphilis in the general population has also tended to increase over the past few years (30).

Musculoskeletal disorders

Aside from injuries sustained from trauma or from customers violence, female sex workers also suffer from musculoskeletal illnesses such as chronic pain in the wrist, arm, shoulder, jaw, back, heel and foot from repeated hand jobs, fellatio, and prolonged standing or crouching on high heels. Most of these injuries qualify as RSIs (repetitive strain injuries) and therefore could be considered work-related disorders (31). Apart from that, sex workers also face problems seeking medical attention as they are usually hindered by fear of social stigmatization and the fact that doctors' opening hours may be noncongruent with their time off.

Unwanted pregnancy

In a meta-analysis by Ampt (32), the prevalence of unwanted pregnancy among female sex workers was reported to be 27.1 per 100 person-years. Unwanted pregnancies among female sex workers can potentially lead to several health problems, such as stress regarding preterm delivery or abortion and health issues caused by undergoing an illegal abortion. Faini's study (33) claimed that proper contraception was difficult for female sex workers as bargaining over condom use can be tricky due to the power imbalance between the sex workers and their clients. Access to other contraceptive methods such as injections was also arduous as sex workers were often deterred by nonsynchronous working hours and heavy social stigmatization.

In Brazil (34), a study of 310 female sex workers found that 52.6 % had undergone an abortion, and 16.5% had had three or more abortions. Misoprostol was the most common method, along with probing and curettage in unregulated clinics. Almost half of the cases needed to be hospitalized afterward. Some female sex workers reported being afraid of losing revenue if they carried on with their gestation.

In Thailand, among 1,000 masseuses in massage parlors surveyed, 19% reported having had an unwanted pregnancy. Odzer interviewed female sex workers in Patpong in 1997 and discovered that some of the workers who had experienced an unwanted pregnancy decided not to terminate the pregnancy. The researcher suggested that the reluctance could be partially due to Buddhist beliefs combined with other superstitious and supernatural beliefs held by the subject (26). Data from the Thai Division of Reproductive Health, Department of Disease Control in 2019 reported 63,831 unwanted pregnancies per year in women 15-19 years old, and 2,180 in individuals younger than 15 years old. Data from the Thai AIDS Access Foundation hotline reported 2,490 calls per month from women with unwanted pregnancies, including some from teenage moms (35). However, there seems to have been no proper research regarding the number among female sex workers. A more up-to-date in-depth investigation in this field is urgently needed.

Legal aspects affecting the health and safety of commercial sex workers

Among the most influential factors affecting the health and safety of sex workers is legislation and the working circumstances of sex workers, i.e., whether they are legal or not (31).

In Australia (31), where sex work has been legalized, more than half of the illegal sex workers interviewed reported being abused or raped by their clients in the past year, compared to legal sex workers who reported an incidence of only 3-15%. Furthermore, 50% of the illegal sex workers were more likely to be propositioned for condomless sexual intercourse, compared to 8-18% among legal sex workers.

As mentioned above, even though Thai people generally feel sex work is abundantly common, sex workers and the proprietors that employ them at entertainment venues still face potential charges under the BE 2539 Prostitution

Suppression Act. However, strict law enforcement has not proven to be effective against this prosperous business; on the contrary, it has brought forth discrimination (36) against sex workers, marginalized them, and forced them to do their jobs in secret, resulting in bribery and 'protection fees' paid to local authorities or officials. Some of these sex workers also encounter entrapment by the police in order to charge them with a criminal offense.

There have been attempts to repeal the criminalization of sex work instituted by the BE 2539 Prostitution Suppression Act. To remove the stigmatization these workers face, a decriminalization or legalization approach needs to be pursued.

Legalization is defined as the regulation of sex work with laws regarding where, when, and how sex work can take place (37). Legalization alone, however, leaves room for law-enforcement officials to criminalize those sex workers who cannot or will not fulfill various related bureaucratic responsibilities. Some say this approach will further exclude sex workers who are already marginalized, such as undocumented workers or individuals with drug addiction, making the situation even more precarious (38).

Decriminalization, on the other hand, eliminates all relevant laws and prohibits state and other law-enforcement officials from intervening in any sex work-related activities or transactions unless other laws have been broken. In the case of sex work, other criminal charges which could still be brought against wrongdoers include those relating to human trafficking, child labor, deprivation of minors, and exploitation.

In Nevada, the only state in the U.S.A. where sex work is legal, female sex workers are asked to be tested for gonorrhea and chlamydia every week as well as syphilis and HIV testing every month. Rhode Island also allowed the decriminalization of sex work from 2003-2009. A study (39) found that during that 7-year period, the incidence of rapes in Rhode Island reported to the Federal Bureau of Investigation (FBI) dropped drastically, as did the incidences of gonorrhea infection according to the US Centers for Disease Control and Prevention (CDC).

Legislation is one of several potential methods used to modify the definition of sex work. In 1999, Sweden prohibited the purchase of sex, while the selling of sex was still considered legal. Additionally, sex work was officially redefined from being a crime that women were blamed for to a crime relating to gender inequality and the personal responsibility of the clients. This idea was quickly adopted in Norway and Iceland in 2009. However, there is still speculation about the efficacy of this legislation because these regulations left sex workers in an awkward situation: as the number of clients per sex worker rose and the overall quality of the clients declined, the remaining clients were only those not fearful of law enforcement.

Apprehension or criminal charges by government officials also results in multiple health problems, a lack of safety, and a general worsening of the working conditions faced by many sex workers (31). For example, sex workers might be forced to accept clients before proper negotiation or without using sound judgement for fear that the police might detain them. Some street workers have reported that they have refused to carry condoms or lubricants around because those items might be later used as evidence for sex work charges against them (15). Sex workers facing criminal charges under the BE 2540 Criminal Code Amendment Act, Section 282 could receive 1 to 10 years imprisonment and fines of 2,000 to 20,000 baht (40).

Stringent law enforcement has also been found to be associated with greater violence against sex workers from customers, drug dealers, community members, local gangsters, spouses, or, even more, law enforcement officials (31). Scrupulous police patrolling forces sex workers to not accept clients in public places or known establishments. Instead they are forced to do their business in private, risking potential violence or even death.

In Thailand, police may 'kindly ask' for the brothel owners to "sign off" some of their sex workers to a police station. Those sex workers would then be charged a specific amount of money and receive criminal records. This type of situation often occurs when senior police officials decide that cracking down on sex work is a pressing matter. There have also been a sig-

nificant number of incidents where violence by authorities has occurred to coerce sexual and other favors, such as 'protection fees', which harm the health and safety of sex workers (11).

Apart from the BE 2539 Prostitution Suppression Act, sex workers face even more obstacles through the enforcement of the BE 2551 Suppression of Human Trafficking Act, the Entertainment Places Act, and Labor Laws. The BE 2541 Labor Protection Act theoretically provides protection for sex workers, but in reality the aforementioned law has not been properly enforced in the sex industry. Lowe stated in a report to United Nations Development Programme (UNDP) that "the reasons for lack of compliance with labor laws relates to the weak regulatory environment in Thailand and the stigma faced by sex workers" (40).

As COVID-19 has significantly negatively affected Thailand's economy, the tourism industry has been no different from the rest. Having previously garnered more than 10 per cent of gross national income, the sex business now seems to be left behind. Sex workers are not properly compensated for pay loss as they are, in fact, illegal workers and hence cannot be compensated under section 33 of the Social Security Act (41).

DISCUSSION

From an outsider's perspective, deliberately making a career out of sex work in and of itself is an act of free will. While that may ring true for some, for other who are less fortunate there is more to this grey business than meets the eye. Ever-growing daily expenditures inconsistent with wages could be one of the factors compelling an individual to choose sex work as an occupation, as it generates 25 times more revenue than other jobs in the market (26). Other individuals are so determined to earn money that they decide to leave their hometown and move to a tourist destination to make a living as a sex worker, some with the additional burden of supporting their extended family.

Major obstacles blocking the path to successful health and safety promotion among sex workers are undeniably legislation and stigmatization (42). It is nearly impossible to provide full healthcare service for sex workers

under the current circumstances. Even in the absence of radical uprisings against the occupation or fatal punishment under religious law as in some countries, political movements by activists in Thailand have not been as successful as they should be. Nevertheless, advocates need to try their best to repeal the acts criminalizing sex work and to promote welfare and basic healthcare support for sex workers. They also need to advocate for sexual equality as a means of closing the economic gap as much as possible.

Legal change in Thailand could follow examples from several other countries and states where various regulations regarding sex work have been promulgated, each with distinctive degrees of success and failure. Currently, legal experts suggest that a criminalization approach alone might not create the desired outcomes and could further negatively impact sex workers. Rather, legalization, partial legalization, and decriminalization are among the approaches that the state could take as a means of improving the health and safety of sex workers.

Campaigning against sex work stigmatization is another way to help sex workers gain access to healthcare services. From a study in four countries in Africa (43), some sex workers were rejected for basic healthcare service related to sexually transmitted diseases or injuries from physical assaults and rape, primarily male and transgender sex workers. They were then compelled to seek healthcare from private hospitals or clinics at a higher price. Health promotion and protection from the government alone would not reach these groups of people.

Periodic screening for sexually transmitted diseases, brain injuries, mental health problems such as burnout syndrome, depression, and PTSD should be encouraged. Sexual health literacy, along with health education and promotion, could be beneficial for sex workers, clients, and others, e.g., government authorities and officials, police, community members, and the general public. Quantitative studies, including cost-benefit analyses, should be conducted to determine which policies should be implemented for maximum effectiveness. Operation of the sex business is based on having at least two consenting parties. For that reason,

trying to focus the entirety of resources on sex workers alone might not be the most effective. Sometimes it takes two (or more) to tango.

It is time that Thailand view this occupation in a new light, that of equal human beings who are pursuing a respectable occupation to feed their families and who are entitled to basic welfare, just like other members of the general population.

CONCLUSIONS

Occupational health and safety for sex workers in Thailand is an area which urgently needs to be explored. In order to ensure the well-being of sex workers be at the same level as individuals engaged in any other respectable occupation, a review of legal and medical aspects related to sex workers is a pressing matter requiring immediate attention.

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