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Factors Influencing the Quality of Life and Nutritional Status of 0-2 Years Old Children

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ABSTRACT

Objective: To investigate the effects of children factors, family factors, and access to healthcare services on children's quality of life as perceived by caregivers and nutritional status of 0 to 2 years old children.

Materials and Methods: This study employed predictive design. The sample group consisted of 106 caregivers with children aged 0 to 2 years old from five subdistricts in one province in Central region in Thailand. The research instruments included the Demographic Data of Parents and Children Questionnaire; the Access to Healthcare Services Questionnaire; the Child-Rearing Practices Questionnaire; the Quality of Life of 0-2-year-old Children Questionnaire. The data were analyzed by using the Chi-square, Fisher's exact test, and multivariate logistic regression.

Results: Logistic regression model accounted for 34 % of variance in children's quality of life (Nagelkerke R^2= 0.34) and 35.3% of variance in their nutritional status (Nagelkerke R^2=.35). Factors predicting the QoL of children were the maternal age (OR=4.75; 95%CI = 1.16, 19.45, p < .05), and the child-rearing practices (OR=5.68; 95%CI = 1.97, 16.40, p < .05). Factors predicting nutritional status were maternal age (OR=0.088; 95%CI = 0.01, 0.79; OR=0.225; 95%CI=0.02, 2.34, p < .05), and child-rearing practices (OR=7.84; 95%CI = 1.93, 31.84, p < .05). Finally, access to healthcare services had a significant association with QoL of children (χ^2 = 9.632, p < .05).

Conclusion: Healthcare personnel should improve children's quality of life and nutritional status by organizing programs to promote child-rearing practices and facilitating parents for accessibility to healthcare services.

Keywords: Children aged 0-2; quality of life; nutritional status; child-rearing practice; access to healthcare (Siriraj Med J 2022; 74: 142-151)

INTRODUCTION

The first 0 to 2 years of a child's life are critical for future health and development. One of the primary causes is a rapid change in one's physical, mental, and emotional development, which is fundamental for growth and development. According to a national survey conducted in 2014, 9.8 percent of Thai children aged 1 to 2 years had severely short stature (height for age < -3 SD.). The data regarding children in the central region of Thailand demonstrated the highest prevalence of short stature and obesity (9.2% and 7.3%, respectively).[1] According to a 2019 UNICEF survey, 4.3 percent of Thai children under the age of five had severely short stature. The highest prevalence of short stature was found in Bangkok and Central region (6% and 4.8%, respectively).[2] These data demonstrate that Thai children in Central region are malnourished. Malnutrition leads to child morbidity, which is the underlying cause of about 45 percent of

child fatalities worldwide.[3] Young children are more vulnerable to malnutrition because they require more protein and energy to grow and are more susceptible to infections than adults.[3-4]

Quality of life has become an essential component of pediatric outcome evaluation. It is a multi-dimensional concept with physical, psychological, social, and environmental dimensions.[5] The concerns about the QoL require capturing children's subjective sense of well-being.[6] Additionally, children are a vulnerable group because they are not empowered, or are unable to identify and address their own needs. When it comes to children, QoL involves their health status, capacity to participate in daily activities such as play, and other kinds of interactions and being reared in a healthy environment.[7] However, there are a variety of QoL dimensions in children, such as, physical, emotion, behavior, somatic, pain, discomfort, and basic needs of infants.[8-9] Those definitions are inconsistent with the definition by the WHO. The PedsQL™ Infant Scales for 1 to 12 months old[6] and TAPQOL for infants[10] (0-1-year-old) are two tools for assessing young children's QoL (0–1-year-old). In the meantime, Thailand utilizes the WHOQOL-BREF-THAI[11] scale to assess Thai QoL. This tool, on the other hand, was developed for adults and inappropriately for children. As a result, the researchers developed a quality-of-life assessment tool for children aged 0 to 2, based on the WHO's conceptual framework. A child's nutritional status and QoL are both essential indicators of a child's quality. Determining the relationship between individual variables and health-related factors in the child population is necessary to identify the priorities of the quality of children in the central region in Thailand. However, nutritional status refers to the health outcomes derived by measuring children's height and weight, whereas the QoL refers to caregivers' perceptions of physical, emotional, psychological, and social dimensions. As a result, these two aspects represent the quality of children from two perspectives.

To confirm the relationship of factors related to nutritional status and QoL in children aged 0 to 2 years in the central region of Thailand. The scoping literature review presented in this article addresses based on ecological framework which includes five levels of individual, interpersonal, organizational, community, and policy levels. However, three levels were selected based on the scope of problems. Factors influencing nutritional status and children's QoL were individual, interpersonal, and organizational levels. The individual level includes breastfeeding period and severity of illness; interpersonal level includes maternal age, maternal education and family income, child-rearing practices, and organizational level includes access to healthcare services. The rationale for selecting these factors was as follows 1) the incidence rate of breastfeeding in Thailand is decreasing[2] while breast milk can promote child's growth and significantly lower odds of wasting.[12,13,14] 2) A healthy child can encounter an illness such as diarrhea, cold, or pneumonia. The illness may have an impact on children's nutritional status or QoL.[12,14] However, the majority of the research discuss only the relationship between child with chronic illness and nutritional status or QoL.[15,16] 3-4) According to the 2019 MICS survey[2], underweight Thai children were detected in mothers aged 35 to 49 years old and mothers with less than a primary school education. Lower maternal education was associated with less healthy food choices, which could be detrimental to child health.[17] 5) Low-income families were associated with underweight children compared to families with adequate income owing to a lack of money to purchase adequate meals.[18,19] 6) Inappropriate child-rearing practices, such as nutritional support, child development stimulation, and hygiene care, impacted children's growth.[14,18,19] 7) Healthcare system in Thailand has been transformed since the adoption of universal healthcare coverage in 2002.[20] Improving access to healthcare services may have an impact on children health. However, some child health issues, such as child development, have persisted, and there is no literature on the impact of healthcare access on healthy young children.

The preceding research investigated the relationships of the studied variables on nutritional status and QoL of children as perceived by caregivers. However, there were few literatures that were specific to children aged 0 to 2 years, and even fewer that were investigated in terms of predictive study. As a result, the aim of this study is to investigate the effects of children factors (breastfeeding period and severity of illness), family factors (maternal age, maternal education, family income, and child-rearing practices), and access to healthcare services on children's quality of life as perceived by caregivers and nutritional status of children aged 0 to 2 years. The findings of this research will provide vital information to improve childcare practices and the system of care for children aged 0 to 2 years in Thailand.

MATERIALS AND METHODS
Ethical considerations

This research was approved by the Institutional Review Board, Faculty of Nursing, Mahidol University (COA No. IRB-NS2017/15-0506). The participants were informed about the purpose of the study, data collection

strategies, rights of research participants, including the right to withdraw at any time without repercussions, anonymity, and confidentiality issues. Those who consented to participate were asked to complete an informed consent form.

Methodology

This study is predictive design research. The sample group consisted of caregivers of children aged 0 to 2 years from five sub-districts: Ratchakram, Changyai, Potang, Chaingraknoi, and Bangsai in Bangsai district, Pranakorn Sri Ayutthaya, who participated in the project entitled "The academic advocacy for the well-being of children through community-based programs in the Central and Western regions." The inclusion criteria were that parents or caregivers be close relatives with children, ages between 18 and 59 years old, be able to communicate in Thai, live in the same house with children, and have cared for the children for at least three months. The sample size was calculated using G*Power, with the effect size computed from the proportion of nutritional status in low income (p1 = 0.234) and high income (p2 = 0.0322)[15], .9 power of test, and .05 errors. A total of 98 caregivers was included in the estimated sample group. For unanticipated missing questionnaires, the number of participants increased by 20% (118 samples). A total of 106 questionnaires were completed. The attrition rate was 10.17%.

Instruments

Data were collected using questionnaires and a child health handbook. The questionnaires consisted of five parts as follows:

1) The Parental Demographic Questionnaire was composed of seven items: parents' age, parents' academic level, family type, marital status, family income, and income sufficiency.

2) The Children's Demographics and Medical History Questionnaire was composed of gender, age, breastfeeding period, number of siblings, and medical history. The medical-history was classified into two categories, ranging from (0) no illness or mild symptoms (1) moderate or severe symptoms. The total possible score ranged from 0 to 1.

3) The Access to Healthcare Services Questionnaire was developed from literature review.[21-22] It consisted of 12 questions divided into two parts. There were six questions about access to healthcare services, including patients' waiting time, expenses, convenience, and availability of care. There were six questions on receiving healthcare services, including receiving information, the rights to

inquiries, and parental participation in childcare. The scale was a three-level rating scale ranging from (1) sometimes to (3) regularly. The total possible scores ranged from 12 to 36. The scores were cut by comparing the mean score to the midpoint score. Scores lower than the median (< 29 scores) indicated less access to healthcare services. Good access to healthcare service was defined as scores equal to or higher than the median (≥ 29 scores).

4) The Child-Rearing Practices Questionnaire, which included 30 items, was developed based on the child-rearing practice standard[23] and literature review.[24] There were five questions on nutritional status, eight on hygiene and fundamental care, and seventeen on growth and development. The scale was a four-level rating scale, ranging from (0) none to (3) regularly. The possible scores ranged from 0 to 90. The scores were cut by comparing the mean score to the median (the midpoint score). The scores less than the median (< 70 scores) denoted poor child-rearing practices, whereas scores equal to or more than the median (≥ 70 scores) indicated good child-rearing practices.

5) The Quality of Life of 0-2-Year-Old Children Questionnaire consisted of 20 items adapted by the researchers from the World Health Organization's short-form quality-of-life questionnaire in the Thai version (WHOQOL-BREF-THAI).[11] There were 20 questions: 17 positive and three negative related to four dimensions of health: physical, mental, social, and environmental dimensions. One item was asked on general quality of life. The scale was a five-level rating scale, ranging from (1) extremely dissatisfied to (5) extremely satisfied. The scores 20-73 indicated a poor quality of life, while the scores higher than 73 indicated a good quality of life.

6) The Children's Health Record includes the child's gestational age, birth weight, history of illness, and latest weight and height. Data were collected from child health handbook. According to the Thai standard growth chart for children 0 to 5 years old, children's growth was divided into three categories: (1) normal, which implies having an average weight and height, (2) overweight and obese, and (3), thin and relatively thin.

Instrument quality testing

The questionnaires were all developed by the researchers. Three specialists evaluated the validity. The CVI of the questionnaires are as follows: CVI = 1 for The Access to Healthcare Services Questionnaire; CVI = 0.92 for The Child-Rearing Practices Questionnaire, and CVI = 1 for The Quality of Life of Children aged 0-2 Years Old Questionnaire. The questionnaires' reliability was evaluated with 30 subjects who were all comparable to the

research participants. The Cronbach's alpha coefficients of the instruments were 0.821, 0.90, and 0.760, respectively.

Data collection methods

Data were collected from November 2017 to February 2018. The researchers requested permission to collect data from the 5 provincial administrators, as well as cooperation from administrators of the health promotion hospitals to introduce the projects to the village volunteers and survey the names of parents and children aged 0 to 2 years old who met inclusion criteria. The researchers trained data collection strategies to project staff and village volunteers who served as research assistants. Village volunteers visited participants' homes and requested permission to present the initiative introduce the project. The research assistants introduced themselves, explained the research objectives, data collection processes, rights protection, and requested permission to utilize data from child health book. The questionnaire could be completed by the participants individually or through a 30-minute interview.

Statistical analysis

Data were analyzed using the SPSS version 18. Statistical significance was configured at the level of 0.05. Descriptive statistics were used to examine demographic data and variables. The Chi-square and Fisher's Exact tests were used to analyze the relationships between parents and children's factors, child-rearing practices, and access to healthcare services, as well as their effects on QoL and nutritional status. The fundamental assumptions for binary logistic regression were satisfied. A multiple logistic regression analysis was performed to examine the predicting power of maternal age, child-rearing practices, and access to healthcare services on children's nutritional status and overall QoL.

RESULTS

Descriptive statistics

The majority of mothers with children aged 0 to 2 years were between the ages of 26 and 35 years old (48 percent), had completed high school (55.9 percent); had an extended family (53.8 percent), and were married (82.7 percent). The majority of caregivers who raised the children were parents, followed by grandparents (43.4 and 31.3 percent, respectively). They had a monthly salary of 10,000-30,000 baht (56.6 percent) and adequate income (74.2 percent). The majority had only one child (87.7 percent), with a breastfeeding period of 3 to 11 months (53.0 percent). The prevalence of low birth weight and/or preterm delivery was 11.3 and 15.1, respectively. Severity

of illness, such as fever and diarrhea, from birth to 2 years old, was 19.8 percent, while those with a normal weight and height was accounted for 77.4 percent; those with obesity was accounted for 15.1 percent; and those with thin weight was accounted for 7.5 percent. Access to HCS, child-rearing practices, and QoL all received high scores (Table 1).

Correlational analysis

The maternal age, access to HCS, and child-rearing practices were associated with the children's quality of life. ($p < 0.05$) (Table 2). The maternal age and child-rearing practices were also related to children's nutritional status. ($p < 0.05$) (Table 3).

Logistic regression analysis

A multivariate logistic regression analysis was employed to assess the predictive power of variables on the QoL as perceived by parents and the nutritional status of their children. According to the findings, this model accounts for 34 percent of the variance in these children's QoL (Nagelkerke R^2= .34) and 35.3 percent of the variance in the nutritional status of their children (Nagelkerke R^2= .35). The maternal age could predict the children's QoL (OR=4.75; 95%CI = 1.16, 19.45, $p < 0.05$). Maternal age of more than 36 years old and less than 25 years old increased the probability of children having a high QoL by 4.747 times that of a maternal age of less than 25 years old. Child-rearing practices could also predict children's QoL (OR=5.68; 95%CI = 1.97, 16.40, $p < 0.05$), indicating that each unit increment in child-rearing practices will increase a child QoL by 5.677 times.

In addition, the maternal age could predict the children's nutritional status (OR=0.088; 95%CI = .01, 0.79, $p < 0.05$). Maternal age of 26-35 years old reduced the probability of having a healthy nutritional status by 0.088 times that of maternal age of less than 25 years old. Child-rearing practices could predict the child nutritional status (OR=7.84; 95%CI = 1.93, 31.84, $p < 0.05$), indicating that each unit increment in child-rearing practice increases their nutritional status by 7.84 times. (Table 4)

DISCUSSION

Regarding nutritional status, 14.7 percent of the children in this study were obese, which was higher than the national average (10 percent).[25] This finding, however, was consistent with a 2016 survey of children's nutritional status at a child development center in the central region, which revealed that 13.9 percent of children

TABLE 1. The range, mean, standard deviation, and interpretation of each studied variables.

Variables	N (%)	Possible score	Range	Mean (S.D)	Median (IQR)	Interpretation by mean
Accessing and receiving HCS	101	12-36	16-36	28.93 (3.94)	29 (4.0)	High
Receiving HCS		6-18	8-18	16.06 (2.32)	17 (3.0)	
Accessing HCS		6-18	4-18	13.03 (2.47)	12 (2.0)	
Child-rearing practices	106	0-90	15-90	67.04 (15.73)	70.5 (19.0)	High
Nutrition,		0-15	0-15	10.38 (3.10)	11 (3.0)	
Hygiene and basic care		0-24	9-24	20.55 (3.82)	22 (6.0)	
Growth and development		0-51	0-51	37.92 (9.12)	40 (11.0)	
Quality of life	106	20-100	31-93	72.51 (9.09)	73 (10.0)	High
Physical health		1-25	11-22	19.73 (2.17)		
Mental health		1-25	12-25	18.24 (2.48)		
Social health		1-25	10-25	18.01 (3.23)		
Environmental health		1-25	10-25	19.00 (2.90)		
Overall quality of life		1-5	1-5	3.52		
Low QoL	54	20-100	31-73	66.04 (7.60)	68 (7.0)	
High QoL	52	20-100	74-93	79.23 (4.40)	78 (6.0)	
Nutritional status	106					
Appropriate	82 (77.4)					
Obese/	16 (15.1)					
Thin	8 (7.5)					

were obese.[26] Since 2000, the prevalence of overweight children under the age of five has grown by approximately 24 percent globally, with the highest incidence in low- and middle-income countries such as Thailand.[27] This situation may be owing to a more convenient lifestyle and easy availability of high-energy food. Because the data gathering locations were suburban, there are numerous factories and marketplaces where families could get a variety of meals for their children. In addition, parents and relatives believed that overweight children were healthy and that youngsters would lose weight as they grew older.[26]

Maternal age and child-rearing practices were potent predictors of children's nutritional status. Mothers under the age of 25 had more children with an adequate nutritional status than mothers in other age groups. The majority of mothers under the age of 25 worked in factories and had a high school diploma. This group of mothers had easy Internet access to search for childcare information. Not surprisingly, according to the findings of a survey conducted in Thailand, persons aged 19-38 years old were the most likely to utilize the Internet.[28] Income sufficiency was not shown to be associated with children's nutritional status. The explanation may be the majority of the participants in this study were middle-income individuals who could afford the infant food. This finding contradicts a childhood obesity study, which reported a positive association between high socioeconomic status (SES) of families and 2-19 years old childhood obesity in developing countries. Since high-SES households have more access to high-energy meals.[29] At the same time, a study in China reported that high-SES had a positive effect on the height of 10-15 years old city youngsters. Because a high-SES family was associated with higher education, the family had more knowledge to choose appropriate meals for their children.[30] The discrepancy may be because the children in this study were between the ages of 0 to 2. They consumed breast milk, milk, and supplementary diet, and children relied on caregivers for their meals.

TABLE 2. Factors associated with quality of life of 0–2-year-old children as perceived by caregivers.

Variables	N (%)	Quality of life of children		χ² Test	P Value
		High	Low		
Age of mother					
Younger than 25 years	31 (31.0)	15 (48.4)	16 (51.6)	6.740	0.034 *
26-35 years	48 (48.0)	18 (37.5)	30 (62.5)		
Older than 36	21 (21.0)	15 (71.4)	6 (28.6)		
Education of mothers					
Primary school	10 (9.8)	6 (60.0)	4 (40.0)	2.537	0.469
High school	57 (55.9)	29 (50.9)	28 (49.1)		
Vocational	12 (11.8)	5 (41.7)	7 (58.3)		
Bachelor's degree	23 (22.5)	8 (34.8)	15 (52.9)		
Income sufficiency					
Sufficient income	61 (62.9)	29 (47.5)	32 (52.5)	0.588	0.745
Sufficient income with saving	11 (11.3)	6 (54.5)	5 (45.5)		
Insufficient income	25 (25.8)	14 (56.0)	11 (44.0)		
Breastfeeding period					
Less than 2 months	29 (34.9)	17 (58.6)	12 (41.4)	1.214	0.545
3-11 months	44 (53.0)	20 (45.5)	24 (54.5)		
More than 12 months	10 (12.0)	5 (50.0)	5 (50.0)		
Severity of illness					
No	85 (80.2)	44 (51.8)	41 (48.2)	1.259	0.262
Yes	21 (19.8)	8 (38.1)	13 (61.9)		
Access to HCS					
Low	55 (51.9)	19 (34.5)	36 (65.5)	9.632	0.002*
High	51 (48.1)	33 (64.7)	18 (35.3)		
Child-rearing practices					
Low	51 (48.1)	15 (29.4)	36 (70.6)	15.178	< 0.001*
High	55 (51.9)	37 (67.3)	28 (32.7)		

[f] Fisher's Exact Test, * P Value < .05

Child-rearing practices also predicted children's nutritional status. The scores on child-rearing practices were high in all dimensions, including nutrition, hygiene care, and growth and development. When considering the item score, the parents provided the proper quantity of meals for their children had a high item score. On the other hand, the item score of being a parental role model for dietary behaviors was medium. These findings are consistent with Australian and New Zealand research of parental feeding practices at 20 months of age. The highest score was dietary restriction for health. Limiting unhealthy food consumption in children up to 20 months old predicted a lower risk of becoming overweight when they were five years old.[31] For the growth and development dimension of child-rearing practices, parents demonstrated high scores on providing child play and activities as well as routinely taking children for health check-ups and vaccinations. These practices were considered adequate

TABLE 3. Factors associate with nutritional status of 0–2-year-old children.

	N (%)	Nutritional status		χ^2 Test	P Value
		Normal (%)	Obese/ thin (%)		
Age of mother					
Younger than 25	28 (27.5)	27 (96.4)	1 (3.6)	8.798	0.012 *
25-36	52 (51.0)	35 (67.3)	17 (32.7)		
Older than 36	22 (21.5)	16 (72.7)	6 (27.3)		
Education of mothers					
Primary school	9 (8.7)	8 (88.9)	1 (11.1)	-	0.781^F
High school	55 (52.9)	43 (78.2)	12 (21.8)		
Vocational	15 (14.4)	11 (73.3)	4 (26.7)		
Bachelor's degree	25 (24.0)	18 (72.0)	7 (28.0)		
Income sufficiency					
Sufficient income	59 (61.5)	42 (71.2)	17 (28.8)	4.430	0.109
Sufficient income with saving	10 (10.4)	10 (100.0)	0 (0.0)		
Insufficient income	27 (28.1)	22 (81.5)	5 (18.5)		
Breastfeeding period					
Less than 3 months	31 (35.6)	20 (64.5)	11 (35.5)	4.477	0.107
3-12 months	47 (54.0)	40 (85.1)	7 (14.9)		
More than 12 months	9 (10.4)	7 (77.8)	2 (22.2)		
Severity of illness					
No	85 (80.2)	69 (65.2)	21 (19.8)	-	0.777
Yes	21 (19.8)	16 (75.0)	5 (25.0)		
Access to HCS					
Low	53 (52.0)	40 (78.5)	13 (24.5)	0.571	0.450
High	49 (48.0)	40 (81.6)	9 (18.4)		
Child-rearing practices					
Low	52 (50.0)	32 (61.5)	20 (38.5)	13.867	< 0.001 *
High	52 (50.0)	48 (92.3)	4 (7.7)		

^{f} Fisher's Exact Test, * P Value < .05

childcare under the 2003 Act's minimal requirements for child-raising. Children's play and activities will help them metabolize carbohydrates and energy as well as reduce fat deposits. Another explanation is that child-rearing practices are associated with healthcare accessibility. Caregivers who had a high score for their child-rearing practices pursued more information about childcare from healthcare personals, resulting in an appropriate nutritional status for their children.

The children in this study had a good QoL, with the highest score for environmental health, followed by physical health, and the lowest score for social relationships. This might be because the environmental and physical health elements included health promotion for children, such as safety, child health, and developmental care. Additionally, healthcare personnel encouraged caregivers to provide health promotion activities upon their visits to well-baby clinics. These findings are consistent with

TABLE 4. Factors predicting the quality of life and nutritional status of children 0-2 years old.

	QOL			Nutritional status		
	OR	95% CI	P Value	OR	95% CI	P Value
Constant	0.205	-	0.004	37.00	-	0.007
Age of mother						
Younger than 25	Ref.	Ref.	-	Ref.	Ref.	-
26-35	0.698	0.24, 2.03	0.509	0.088	0.01, 0.79	0.030 *
Older than 36	4.747	1.16, 19.45	0.030 *	0.225	0.02, 2.43	0.219
Access to HCS						
Low	Ref.	Ref.	-	-	-	-
High	2.017	0.74, 5.53	0.172	-	-	-
Child-rearing practices						
Low	Ref.	Ref.	-	Ref.	Ref.	-
High	5.677	1.97, 16.40	0.001 *	7.840	1.93, 31.84	0.004 *
Nagelkerke R²		0.340			0.353	
Hosmer and Lemeshow Test		0.720			0.968	

those of the QoL of healthy children aged 0 to 1 year measured by PedsQL™ in the United States6, and the QoL of healthy children aged 0 to 1 year measured by TAPQOL in the Netherlands[10], which caregivers reported that their children had high scores in both physical and psychosocial health. Similarly, parents in Europe place a high value on providing a safe physical environment for their children.[32] In comparison, parents in the United States place a high value on social functioning, while Thai parents had a lower score in this dimension. The discrepancy of QoL domains scores may be attributed to differences in caregiving and parenting styles. Thai caregivers become accustomed to responding to children's fundamental needs rather than allowing the children to do it independently. More study is needed to investigate the factors that differentiate QoL between Western and Eastern perceptions.

Maternal age and child-rearing practices were factors that predicted the QoL of 0–2-year-old children. Maternal age of more than 36 years old generally resulted in better parenting since such parents tend to have a higher SES and can afford better childcare. These findings are congruent with a study on Brazilian parenting practices, which discovered that mothers with higher education and economic status organized more activities to promote their children's motor development, such as playing, toy, lap time, and free movement space.[33]

Child-rearing practice predicted the QoL of children aged 0 to 2 years. According to the study, parents over the age of 36 offered adequate nutrition, hygiene, and developmental care than younger parents. Parents arranged play activities, a safe home environment, disease prevention, health check-ups, and vaccines for their children. These health-promoting behaviors can help children avoid illness and improve their QoL. In Malaysia, parents from various SES backgrounds provide various types of child-rearing to stimulate cognition and emotions, as well as to interact with children, leading to diverse cognitive and social functioning.[34]

Access to healthcare services was associated with QoL of children, but it did not predict the QoL and nutritional status in children aged 0 to 2 years. Parents reported that their children's access to and receiving healthcare services was excellent. The explanation might be universal healthcare coverage for children, under which children have rights to access care. Moreover, data were collected in five sub-districts of a single district. Two secondary hospitals and one tertiary level hospital are located near the sub-urban regions. Scores for accessing healthcare services, such as cost, convenience, time and

availability, were in moderate level. Whereas scores for receiving healthcare services, such as information on child growth and development screening, childcare suggestion, and listening and responding to concerns were high. The good relationship between caregivers and healthcare personnel might be attributed to parents' ability to obtain health services and childcare information, resulting in improving their child-rearing practices as well as the children's QoL. The findings of this study are consistent with those of a previous study conducted in the United States[21], which discovered that continued access to essential care was associated with improved health and QoL scores.[21] Another study in Brazil and Columbia reported that inequities in access to care between lower SES and higher SES groups resulting in disparities in accessing to primary care, outpatient secondary care, and having health issues in preventable and controlled diseases, such as caries, and glycemic control.[35] Access to health services was not associated with nutritional status of children. It is possible that these children had good health and development and did not require intensive healthcare. Similarly in Thailand, a study revealed no statistically significant relationship between access to care and nutritional status of preterm migrant children. As a result of Thailand's low-cost healthcare insurance for migrant workers and their families to have access to healthcare services.[13] Therefore, no variation in access to healthcare scores, resulting in non-significant relationship between healthcare access and nutritional status.

Regarding children's factors, breastfeeding period and severity of illness were not associated with children's QoL as perceived by caregivers or nutritional status. These children were healthy and their caregivers provided quality care for them. In contrast, a study in Thailand reported that exclusive breastfeeding from birth to six months of age, as well as a history of cold in infants predicted growth in preterm migrant children. The explanation may be that preterm infants are more susceptible to infections, resulting in a poorer child growth rate, and unemployed migrant mothers employed exclusive breastfeeding for their child.[13]

Recommendations and implications
1. Healthcare personnel should assess caregivers' child-rearing practices, recognize variations in those practices depending on maternal age, and design interventions accordingly.
2. The child-rearing practice program should focus on social functioning activities to help youngsters develop social skills.

Limitations
The use of the instrument based on WHO definitions to assess children's QoL is a strength of this study. The limitation is that the samples were randomly recruited from five suburban sub-districts. The samples might not be representative of Thai children and families. Missing data from the survey questionnaire were discovered in both dependent and independent variables.

CONCLUSION
When children are 0 to 2 years old, parental factors significantly influence their nutritional status and quality of life. Two of these factors are maternal age and child-rearing practices. Healthcare personnel should encourage caregivers to use age-appropriate child-rearing practices, such as using social media with younger parents. Access to and utilization of healthcare services was solely associated with children's quality of life. Caregivers should be assisted in increasing their access to and receipt of healthcare in order to improve the quality of life for children aged 0 to two.

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Increasing Dialysate Flow Rate over 500 ml/min for Reused High-Flux Dialyzers do not Increase Delivered Dialysis Dose: A Prospective Randomized Cross Over Study

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ABSTRACT

Objective: The primary objectives were: 1) to study the impact of Qd (500 vs 800 ml/min) on the delivered dose by reused dialyzers, and 2) to determine dialysis efficiency of a dialyzer reused 15 times.

Materials and Methods: A prospective randomized-controlled crossover study was conducted in 42 thrice-weekly hemodialysis (HD) patients (630 HD sessions in each Qd). Delivered doses at both Qds were assessed by single-pool Kt/V (spKt/V), equilibrated Kt/V (eKt/V) and online clearance monitoring Kt/V (Kt/V$_{OCM}$), measured at mid-week HD session using a new dialyzer and then again at every mid-week HD session.

Results: Although the spKt/V in HD sessions using new dialyzers at Qd of 500 ml/min was slightly lower than spKt/V at Qd of 800 ml/min (2.19±0.08 vs. 2.34±0.08, respectively, P=0.04), when accounting for urea rebound as assessed by eKt/V and Kt/V$_{OCM}$, there was no significant difference. The average delivered doses in dialyzers reused 15 times, with the mean average of spKt/V, eKt/V and Kt/V$_{OCM}$ at Qd 500 ml/min, were not significantly inferior to the delivered doses at Qd 800 ml/min. Reusing a dialyzer 15 times did not decrease dialysis efficiency and delivered doses in all HD sessions reached spKt/V >1.4.

Conclusion: Increasing Qd over 500 ml/min for modern dialyzers does not significantly increase delivered dose of dialysis. Dialyzer reuse does not affect dialysis efficiency and provides adequate dialysis therapy.

Keywords: Dialysate flow rate; hemodialysis adequacy; reused dialyzer; delivered Kt/V; online Kt/V; equilibrated Kt/V (Siriraj Med J 2022; 74: 152-160)

INTRODUCTION

An adequate hemodialysis dose delivery is an important and independent predictor of morbidity and all-cause mortality in maintenance hemodialysis (HD) patients.[1] Current clinical practice guidelines for hemodialysis adequacy recommend a delivered single-pool Kt/V (spKt/V) of at least 1.2 per HD session (for 3-time-weekly HD patients without significant residual renal function), and higher doses of up to 1.4 in females and patients with high comorbidities.[1,2] The delivered

dose of HD depends on dialyzer mass transfer-area coefficient (KoA), HD treatment time, and operating parameters, especially blood flow rate (Qb) and dialysate flow rate (Qd).[3] High-efficiency dialysis requires dialyzer with high KoA, Qb > 300 ml/min and Qd ≥ 500 ml/min. Increasing Qd from 500 ml/min to 800 ml/min has been recommended to maximize dialysis efficiency in high-efficiency HD. Previous studies[4-6] in early generation dialyzers showed that increasing Qd from 500 ml/min to 800 ml/min alter the dialyzer KoA and results in a larger increase in urea clearance than the predicted assuming a constant KoA, which was explained by a better flow distribution through the dialysate compartment and a decrease in dialysate-side boundary layer resistance. Recent studies[7-10] of newer dialyzers with improved dialysate flow distribution designs (such as hollow fiber undulations, spacer yarns, and changes in fiber packing density) have been accompanied by an increase in urea clearance of the dialyzer, and revealed that dialysate flow rate beyond 500 - 600 ml/min does not significantly increase delivered Kt/V. However, these studies were performed in single-use dialyzers.

In chronic hemodialysis, reuse of dialyzers has been widely practiced in developing countries, including Thailand. In our hemodialysis unit, patients who were treated with high-efficiency high-flux dialysis usually increasing Qd to 800 ml/min in order to maximize the dialysis dose and the dialyzer was reused 15 times. There is limited data on the effect of Qd in high-flux high-efficiency dialysis with a reused dialyzer related to delivered dose and hemodialysis adequacy. Increasing the dialysate flow rates results in a higher dialysis cost, require more water treatment, and leads to a higher risk of exposure to dialysis water impurities. The objectives of this study were to: 1) evaluate the effect of Qd of 800 ml/min and 500 ml/min on delivered dialysis dose in high-efficiency high-flux dialysis patients who used a reused dialyzer; 2) to determine dialysis efficiency and HD adequacy of a reused dialyzer.

MATERIALS AND METHODS
Study design

We performed a single-center prospective randomized-controlled crossover study in maintenance HD patients conducted at Siriraj Hospital, Mahidol University, Thailand between June 2018 - April 2020. Inclusion criteria for the study were age above 18, 4-hour three time weekly high-flux dialysis with a stable spKt/V (±5%) for at least two months, and the reuse of a dialyzer. The exclusion criteria were pregnancy, hepatitis B virus infection and being seropositive for HIV.

Before the intervention in each patient, bolus dose and maintenance dose of heparin were adjusted according to activated partial thromboplastin time (aPTT) level (at baseline, 3, 60, 180 and 240 minutes) to maintain a ratio of 1.8-2.5 for the duration of HD and at least 1.4 at the end of dialysis to prevent dialyzer clots and achieve reuse. Automatic dialyzer reprocessing machine (Meditop KIDNY- KLEEN®) was used to reprocess dialyzers and disinfected with peracetic acid, and measure blood compartment volume or total cell volume (TCV) of reused dialyzers. Percentage of TCV (%TCV) of a reused dialyzer was defined as the percentage of blood compartment volume measured by automatic dialyzer reprocessing machine divided by the priming volume value of the new dialyzer that provided by the manufacturer (Supplement Table 1). Reused dialyzers were discarded if its TCV less than 80% of baseline value or if it failed a leak test.

Patients were randomly assigned (using online software www.randomization.com) to be dialyzed according to an AB or BA schedule, where A represents 15 consecutive dialysis treatments with a Qd of 800 ml/min, and B represents 15 consecutive dialysis treatments with a Qd of 500 ml/min. The blood flow rate and dialyzer were kept constant for a given patient. The intervention of A and B began during a mid-week dialysis session with a new dialyzer followed by sessions with a reused dialyzer for a total of 15 times. The delivered dialysis dose was measured (during both A and B) at mid-week HD sessions with a new dialyzer and again at every mid-week HD session corresponding to the reused dialyzer no. 4, 7, 10, 13, and 15 (total of six measurements in each dialyzer). The delivered doses of dialysis were assessed by spKt/V (the Daugirdas second generation equation), equilibrated Kt/V (eKt/V) estimated by the rate equation[11], and online clearance monitoring Kt/V (Kt/V$_{OCM}$).[12] Kt/V$_{OCM}$ was calculated by serial measurements of ionic dialysance of sodium (as a surrogate for effective urea clearance) made throughout HD treatment by using HD machines equipped with an online conductivity monitor and software dose-calculation tool DCTool (Fresenius Medical Care, Germany). Volume distribution of urea (V) will be calculated by the system from the weight, height, age and sex using the formula developed by Watson.

Data collection

Baseline data included patient's age, sex, height, body weight, dialysis vintage, comorbidities, medical history, vascular access, and HD treatment parameters, which consist of dialysis dose, Qb, Qd, post-HD body weight (W), ultrafiltration (UF), total processed blood

Supplement TABLE 1. Summary of dialyzer specifications[#]

	Hdf 100s	Hf 80s	EL210HR	EL190HR	FB190U
Surface area (m²)	2.3	1.8	2.1	1.9	1.9
Priming volume (ml)	138	110	130	115	115
Ultrafiltration coefficient (Kuf) (ml/h/mmHg)	60	55	82	76	37.70
Dialyzer KoA$_{urea}$ (ml/min)	1,167	805	1,976	1,171	1,367
Inulin clearance (ml/min)*	145	120	145	132	N/A
Myoglobin clearance (ml/min)*	N/A	N/A	104	101	47
Membrane component	Polysulfone	Polysulfone	Polynephron	Polynephron	Cellulose triacetate
Number of patients n, (%)	15 (35.70%)	3 (7.10%)	22 (52.40%)	1 (2.40%)	1 (2.40%)

* Blood flow rate 300 ml/min, Dialysate flow rate 500 ml/min
# Data from the manufacturer's dialyzer specification sheets

Calculations

Single-pool delivered Kt/V (spKt/V) was calculated using the Daugirdas second generation equation** as follows: spKt/V = -Ln(R-0.008×t) + (4-3.5×R) × UF/W, where Ln is the natural logarithm, R is the post-dialysis/pre-dialysis blood urea nitrogen ratio, t is dialysis time (in hours), UF is ultrafiltration volume (in liters), and W is the patient's post-dialysis body weight (Kg).

Equilibrated Kt/V (eKt/V) was calculated by adjusting the spKt/V for postdialysis urea rebound using the rate equation described by Daugirdas and Schneditz as follows: eKt/V = spKt/V – [0.6 x(spKt/V)/t] + 0.03 (for arteriovenous access) and eKt/V = spKt/V – [0.47×(spKt/V)/t] + 0.02 (for venous catheters), where t represents the duration of dialysis in hours.
** Daugirda JT. Second generation logarithmic estimates of single-pool variable volume Kt/V: An analysis of error. J Am Soc Nephrol 1993; 4:1205-13.

volume (TBV), effective dialysis time, heparin dosage, type of dialyzer and number of dialyzer reuse with %TCV. Patients gave written informed consent to participate in this study as approved by the Human Research Protection Unit, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand.

Exposures and outcomes

The primary outcome was differences between delivered spKt/V, eKt/V and Kt/V$_{OCM}$ at two different dialysate flow rates. Secondary outcomes were differences between eKt/V and Kt/V$_{OCM}$, and how the number of times a dialyzer was related to dialyzer urea clearance efficacy and HD adequacy. In this study, the hemodialysis adequacy threshold was set to delivered spKt/V > 1.4, considering high proportion of comorbidities and females (43%) in the patient population.

Statistics

The data are reported as mean ± standard deviation (SD) or median (minimum-maximum), depending on the distribution analysis. A two-sided p value of <0.05

was considered as significant. The primary outcome was non-inferiority of delivered dialysis dose at two Qds in first use and reused dialyzer, which were assessed by ANOVA using NCSS program with significance, α = 0.05 and non-inferiority margin of spKt/V = 0.25.

RESULTS

Forty-two HD patients were studied and a total of 1,260 HD sessions (630 HD sessions in each Qd) were performed. The dialyzers used in this study were HdF100s 35.7%, HF80s 7.1%, EL210HR 52.4%, EL190HR 2.4%, FB210U 2.4% and FB190U 2.4%. The characteristics of the dialyzers were summarized in the Supplement Table 1. Eighty-one percent of patients needed heparin dose adjustments to achieve an appropriate aPTT level throughout the HD sessions for prevent dialyzer clots before the intervention. All dialyzers used in this study were reused 15 times. The average %TCV in reused dialyzers at both Qds were not significantly different (Qd 800 ml/min, %TCV 97.80±1.20% vs Qd 500 ml/min, %TCV, 97.99±0.96%).

Baseline patient characteristics

The patient's baseline characteristics are summarized in Table 1. The mean age of 42 patients was 66.3±15.3 years (range 29.2 - 84.4 years) and 57.1% were men.

The effect of dialysate flow rate on delivered spKt/V in reused dialyzers

The mean spKt/V in the HD sessions using new dialyzers at Qd of 500 ml/min was slightly less than the mean spKt/V at Qd of 800 ml/min (2.19± 0.08 vs. 2.34± 0.08, respectively, p=0.04) (Table 2). In the HD sessions of reused dialyzers no. 4, 7, 10 and 13, the mean spKt/V at Qd 500 ml/min were significantly inferior to spKt/V at Qd 800 ml/min, whereas, the mean spKt/V in reused dialyzers no. 15 at both Qds was not different.

However, the magnitude of differences in spKt/V was not clinically meaningful. The mean average spKt/V of dialyzers reused 15 times was calculated from the average of spKt/V of the new dialyzers and reused dialyzers (total of six measurements of spKt/V in each dialyzer). The mean average spKt/V of the reused dialyzers after 15 times at Qd 500 ml/min was not significantly inferior to spKt/V at Qd 800 ml/min (2.21±0.07 vs 2.31±0.07, respectively, p<0.01). All measurements of the delivered dose achieved hemodialysis adequacy thresholds of spKt/V > 1.4 at both dialysate flow rates.

The effect of dialysate flow rate on eKt/V

The mean eKt/V in the HD sessions of new dialyzers, and reused dialyzers no. 4, 7, and 13 at Qd of 500 ml/min

TABLE 1. Baseline characteristics of study population (n = 42 patients).

Parameters	
Age, years	66.3±15.3
Male sex, n (%)	24 (57.10)
Mean post-HD body weight, Kg	58.85±11.82
Comorbid diseases, n (%)	
Hypertension	39 (92.9)
Diabetes	16 (38.1)
Atherosclerotic heart disease	16 (38.1)
Polycystic kidney disease	2 (4.8)
Miscellaneous (hyperlipidemia (3)/chronic glomerulonephritis (1)/gout (1) /benign prostate hypertrophy (1)/ malignancy (1)	7 (16.7)
Dialysis vintage, months	106.2±68.4
Vascular access, n (%)	
Arteriovenous fistula	17 (40.48)
Arteriovenous graft	6 (14.29)
Permanent dual lumen catheter	19 (45.23)
Blood flow rate, n (%)	
300/350/400 ml/min	1 (2.4) / 11 (26.2) / 30 (71.4)
Heparin dose, units/session	
Total	4,431±3,712
Loading dose	1,681±1,761
Maintenance dose	2,750±1,944

TABLE 2. Mean delivered spKt/V at dialysate flow rate of 800 and 500 ml/min.

Dialyzer Reuse No.	Mean spKt/V		Mean difference	95%CI		P value Non-Inferiority
	Qd 800 ml/min	Qd 500 ml/min		Lower	Upper	
New	2.34±0.08	2.19±0.08	0.15	-0.07	0.37	0.04
4	2.35±0.07	2.22±0.07	0.13	-0.07	0.33	0.22
7	2.35±0.07	2.21±0.07	0.14	-0.07	0.35	0.29
10	2.30±0.08	2.24±0.08	0.07	-0.17	0.30	0.13
13	2.29±0.07	2.19±0.07	0.10	-0.10	0.30	0.14
15	2.23±0.07	2.23±0.07	0.00	-0.21	0.21	0.02
Average	2.31±0.07	2.21±0.07	0.10	0.05	0.14	<0.01

were not significantly inferior to the mean eKt/V at Qd of 800 ml/min (Table 3). In reused dialyzers no.10 and 15, the mean eKt/V at Qd 500 ml/min were significantly inferior to eKt/V at Qd 800 ml/min. However, the magnitude of difference of eKt/V may not be clinically significant. The mean average eKt/V of dialyzers reused 15 times at Qd 500 ml/min was not significantly inferior to eKt/V at Qd 800 ml/min (1.93±0.27 vs 2.03±0.29, respectively, p<0.01).

The effect of dialysate flow rate on Kt/V$_{OCM}$

The mean Kt/V$_{OCM}$ at Qd of 500 ml/min in HD sessions using new dialyzers and reused dialyzers were not significantly inferior to Kt/V$_{OCM}$ at Qd of 800 ml/min (Table 4). The mean average Kt/V$_{OCM}$ of dialyzers reused

15 times at Qd 500 ml/min was also not significantly inferior to Kt/V$_{OCM}$ at Qd 800 ml/min (1.85±0.04 vs 1.98±0.05, respectively, p<0.01).

Comparison between eKt/V and Kt/V$_{OCM}$

The mean average of Kt/V$_{OCM}$ at both Qds were significantly lower than the mean average eKt/V (Table 5). However, the magnitude of difference between Kt/V$_{OCM}$ and eKt/V may not be clinically significant. The Kt/V$_{OCM}$ was highly correlated with eKt/V at the both Qds, with r = 0.91 at Qd 800 ml/min (p<0.01), and r = 0.87 at Qd 500 ml/min (p<0.01).

The total processed blood volume and effective time in HD sessions of new dialyzers and reused dialyzers were not significantly different (Table 6). The average effective

TABLE 3. Mean eKt/V at dialysate flow rate of 800 and 500 ml/min.

Dialyzer reuse No.	Mean eKt/V		Mean of difference	95%CI		P value Non-Inferiority
	Qd 800 ml/min	Qd 500 ml/min		Lower	Upper	
New	2.03±0.35	1.92±0.30	0.10	0.04	0.17	<0.01
4	2.04±0.30	1.95±0.29	0.09	0.03	0.16	<0.01
7	2.00±0.34	1.97±0.31	0.03	-0.06	0.11	<0.01
10	2.08±0.54	1.94±0.31	0.14	0.01	0.27	0.11
13	1.98±0.29	1.93±0.30	0.06	-0.01	0.12	<0.01
15	2.04±0.36	1.90±0.43	0.15	0.02	0.26	0.09
Average	2.03±0.29	1.93±0.27	0.10	-0.12	-0.03	<0.01

TABLE 4. Online clearance Kt/V at dialysate flow rate of 800 and 500 ml/min.

Dialyzer Reuse No.	Mean Kt/V$_{OCM}$		Mean of difference	95%CI		P value Non-Inferiority
	Qd 800 ml/min	Qd 500 ml/min		Lower	Upper	
New	1.99±0.32	1.87±0.29	0.11	0.06	0.17	<0.01
4	1.99±0.32	1.85±0.28	0.14	0.08	0.19	<0.01
7	1.99±0.34	1.87±0.29	0.12	0.05	0.18	<0.01
10	1.93±0.34	1.87±0.29	0.06	0.00	0.12	0.05
13	1.96±0.32	1.82±0.30	0.14	0.07	0.20	<0.01
15	2.00±0.40	1.83±0.29	0.17	0.07	0.27	<0.01
Average	1.98±0.05	1.85±0.04	0.13	0.06	0.17	<0.01

TABLE 5. Comparison of Kt/V$_{OCM}$ and eKt/V at dialysate flow rate of 800 and 500 ml/min.

Dialyzer reuse No.	Kt/V$_{OCM}$	eKt/V	Mean difference	95% CI		P value Inferiority
				Lower	Upper	
Qd 800 ml/min						
New	1.99±0.32	2.03±0.35	-0.04	-0.11	0.03	<0.01
4	1.99±0.32	2.04±0.30	-0.05	-0.12	0.03	<0.01
7	1.99±0.34	2.00±0.34	-0.02	-0.08	0.04	0.61
10	1.93±0.34	2.08±0.54	-0.15	-0.28	-0.02	0.03
13	1.96±0.32	1.98±0.29	-0.03	-0.10	0.05	0.48
15	2.00±0.40	2.04±0.36	-0.04	-0.16	0.08	0.49
Average	1.98±0.30	2.03±0.05	-0.05	-0.00	0.11	<0.01
Qd 500 ml/min						
New	1.87±0.29	1.92±0.30	-0.05	-0.12	-0.02	<0.01
4	1.85±0.28	1.95±0.29	-0.09	-0.17	-0.02	<0.01
7	1.87±0.29	1.97±0.31	-0.10	-0.18	-0.02	<0.01
10	1.87±0.29	1.94±0.31	-0.07	-0.13	-0.00	0.04
13	1.82±0.30	1.93±0.30	-0.11	-0.19	-0.03	<0.01
15	1.83±0.29	1.90±0.43	-0.07	0.18	0.05	<0.01
Average	1.85±0.30	1.93±0.04	-0.08	0.02	0.14	<0.01

TABLE 6. Total processed blood volume (TBV), effective dialysis time, % total cell volume (TCV) related to Kt/V$_{OCM}$ and eKt/V at Qd 800 and 500 ml/min.

Qd 800 ml/min	New Dialyzer	Reused Dialyzer					P value
		no. 4	no. 7	no. 10	no. 13	no. 15	
TBV (L)	90.21±6.57	89.95±6.21	89.98±6.91	89.63±6.23	89.53±6.65	89.90±5.96	0.89
Time*	3.52±0.08	3.52±0.03	3.51±0.04	3.53±0.08	3.51±0.03	3.52±0.09	0.76
%TCV	100±0	98.63±2.59	98.46±2.54	97.42±3.61	96.62±4.36	96.49±5.04	0.00
Kt/V$_{OCM}$	1.99±0.32	1.99±0.32	1.99±0.34	1.93±0.34	1.96±0.32	2.00±0.40	0.53
eKt/V	2.03±0.35	2.04±0.30	2.00±0.34	2.08±0.54	1.98±0.29	2.04±0.36	0.23
Qd 500 ml/min	New Dialyzer	Reused Dialyzer					P value
		no. 4	no. 7	no. 10	no. 13	no. 15	
TBV (L)	90.66±6.44	89.67±6.50	89.97±7.24	90.59±6.60	90.08±6.00	89.51±7.12	0.33
Time*	3.54±0.11	3.51±0.05	3.53±0.08	3.51±0.08	3.54±0.11	3.51±0.04	0.07
%TCV	100±0	99.39±1.56	98.29±3.25	98.15±2.87	97.62±4.09	96.42±5.23	0.00
Kt/V$_{OCM}$	1.87±0.29	1.85±0.28	1.87±0.29	1.87±0.29	1.82±0.30	1.83±0.29	0.19
eKt/V	1.92±0.30	1.95±0.29	1.98±0.31	1.94±0.31	1.93±0.30	1.90±0.43	0.72

% TCV defined as % of blood compartment volume of a reused dialyzer divided by the priming volume value of new dialyzer provided by the manufacturer.
*Effective time (hr.min)

treatment time was 3 hours 52 minutes. The TCV remained above 80% of the baseline value for dialyzers reused up to 15 times, and the average decrease in %TCV was only 1.4-3.5%. The reused dialyzers did not alter efficacy of hemodialysis. The eKt/V and Kt/V$_{OCM}$ measured in HD sessions using new dialyzers and reused dialyzers were not significantly different at both Qds (Table 6).

DISCUSSION

We found little improvement in delivered dialysis dose as assessed by spKt/V, eKt/V and Kt/V$_{OCM}$ while increasing Qd from 500 ml/min to 800 ml/min. Although the mean spKt/V in HD sessions using new dialyzers at Qd of 500 ml/min was slightly lower than spKt/V at Qd of 800 ml/min (2.19±0.08 vs. 2.34±0.08, P =0.04), when accounting for urea rebound by assessing eKt/V and Kt/V$_{OCM}$, there was no significant difference at both Qds (eKt/V 1.93±0.27 vs. 2.03±0.29; Kt/V$_{OCM}$ 1.85±0.04 vs.1.98±0.05 at Qd 500 and Qd 800 ml/min, respectively). When comparing the average delivered dialysis dose of dialyzers reused 15 times between Qd of 500 ml/min and 800 ml/min, the mean average spKt/V was not significantly

different (2.21±0.07 vs 2.31±0.07), as well as the mean average eKt/V and Kt/V$_{OCM}$. A study by Bhiman JP, et al[10] showed that the urea KoA was independent of Qd in the range 500 ml/min to 800 ml/min for dialyzers with enhanced dialysate flow distribution features, suggesting that increasing the dialysate flow rate in this range would not significantly increase delivered Kt/V in modern dialyzers. Consistent with our results, a study by Ward RA, et al[8] in 42 patients comparing delivered Kt/V at Qd of 600 and 800 ml/min with a median Qb of 450 ml/min showed that an increase in Qd beyond 600 ml/min for dialyzer with enhanced Qd distribution does not offer extra benefit in delivered spKt/V and Kt/V$_{OCM}$. A recent randomized crossover study[13] reported that reducing the Qd from 500 ml/min to 400 ml/min in small patients (body weight < 65 kg) had no impact on Kt/V, interdialytic weight gain, blood pressure or electrolyte disturbance.

The equilibrated Kt/V, which accounts for the postdialysis urea rebound, can be determined by eKt/V estimated from rate equation or Kt/V$_{OCM}$ by ionic dialysance method.[14] Although Kt/V$_{OCM}$ was slightly lower than

eKt/V, but the magnitude of difference did not appear to be clinically meaningful, and it is highly correlated with eKt/V. Our results showed that Kt/V_{OCM} is a practical instrument and the easiest method to use to monitor delivered dialysis doses in each HD treatment, and help maintain recommended HD adequacy, especially in patients using reused dialyzers.

We found that reused dialyzers did not alter efficacy of hemodialysis and the delivered dose in all HD sessions at both Qds reached the HD adequacy thresholds of spKt/V > 1.4. Our results are consistent with Cheung AK's study[15] which showed that urea clearance decreased only slightly in reused dialyzers (approximately 1 to 2% per 10 reuses). A study by Ousseph et al[16] showed that both high-flux cellulosic and high-flux polysulfone dialyzers maintained their Kt/V at the 12th and 15th use, respectively, when dialyzers were reprocessed with Renalin and %TCV above 80% of the original value. In our study, 81% of patients needed heparin dose adjustment to achieve adequate aPTT level throughout HD session, and this resulted in a high residual TCV (mean %TCV > 96%) in dialyzers reused up to 15 times. The delivered dialysis doses of dialyzers reused for 15 times were not significantly different from those of new dialyzers (Table 6). This may result from a high residual TCV as well as the optimized effective HD time and adequate total processed blood volume (Table 6).

In our study, 78% of high-efficiency high-flux dialysis patients were prescribed with large dialyzers (dialyzer KoA > 1,160 ml/min with dialyzer surface area ≥ 2.1 m^2 and Kuf ≥ 60 ml/h/mmHg), which resulted in high delivered Kt/V in the range of 2, especially in patients with small body size (mean body weight 58.8 kg). High Kuf of the dialyzer has the benefit of a higher convective clearance from back filtration, resulting in increased middle molecule clearance. However, in the subgroup of small body size patients with this high range of Kt/V, dialysis prescription (especially Qd and Qb) should be adjusted to a more appropriate Kt/V range to save resources and preserve vascular access.

Our findings have some practical applications. First, the effect of reducing the Qd from 800 ml/min to 500 ml/min on delivered dialysis doses of high-efficiency dialysis using modern dialyzers is minimal. The delivered dialysis dose at Qd of 500 ml/min is preferred and this would result in dialysate cost savings of around 72 liters per dialysis session, less raw water consumption, and less the wear and tear on water treatment systems.[17] Reducing in water consumption will also decrease waste water production and electrical consumption, and these have a positive effect on the environment and carbon emissions, which has been recently concerned in dialysis practice as green nephrology and eco-dialysis.[17,18] However, increasing the Qd beyond 500 ml/min should be considered in selected patients who have not achieved HD adequacy despite using an appropriate dialyzer KoA and optimized Qb, especially in patients with high body weight. Second, reusing a dialyzer up to 15 times does not affect dialysis efficiency and provides adequate dialysis therapy as long as adequate anticoagulation throughout HD session and high residual TCV are maintained. Dialyzer reuse has some advantages, including less environmental impact from limiting waste disposal from dialyzers and packaging, and cost saving favoring in some developing countries. However, reprocessing of dialyzers requires additional personnel, disinfectants, room maintenance for safety and sterilization, and oversight mechanism of the dialyzer reuse standard. In developed countries, single-use practice is now preferable to reuse of dialyzers because the price of a high-flux dialyzer has recently gone down, and the operational cost of dialyzer reprocessing is rising, along with safety regulatory burden.[19,20]

Our study had some limitations. It was a single-center study. The Qbs used in this study were Qb of 400 ml/min in 71.4% of patients, and Qb of 350 ml/min in 26% of patients. Therefore, our results cannot be extrapolated to different dialysis treatment conditions that maximize Qb to >400 -450 ml/min. We did not evaluate the effect of Qd on other solutes removal such as protein-bound solutes or middle molecules, and the effect of reused dialyzer on sieving coefficient of middle molecule. However, increasing Qd in the range from 500 ml/min to 800 ml/min would not have any significant effect on clearance of these solutes.

CONCLUSION

Our data suggest that increasing dialysate flow rate beyond 500 ml/min for modern high-flux dialyzers does not significantly increase delivered dialysis dose. The delivered dose at Qd of 500 ml/min is more cost-effectiveness. Reuse of a dialyzer up to15 times does not affect dialysis efficiency and provides adequate dialysis therapy.

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Survival of Non-Small Cell Lung Cancer Patients with Unexpected N2 after Complete Resection: Role of Aggressive Invasive Mediastinal Staging should be Considered

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ABSTRACT

Objective: Mediastinal lymph node (N2) metastasis is one of the poor prognostic factors in non-small cell lung cancer patients (NSCLC). However, the accuracy of mediastinal lymph node staging in real practice is uncertain and inadequate. Consequently, the aim of this study was to determine the survival of NSCLC patients with clinically non-suspicious mediastinal lymph node metastases who underwent complete resection but were pathologically confirmed as having N2 metastases (unexpected N2).

Materials and Methods: A retrospective review was performed of all pathology-proven N2 metastases NSCLC patients who underwent curative surgical resection from January 2007 to December 2016. A total of 158 patients were initially included in the study. After the exclusions (known N2, small cell carcinomas, neuroendocrine tumor), 125 unexpected N2 patients who underwent complete resection were analyzed. Survival analysis was determined using the Kaplan–Meier method and multivariate analysis was determined using the Cox regression method.

Results: The overall 2-year, 3-year, and 5-year survival rates were 40%, 24%, and 20% respectively. Complete resection was achieved in all patients. Invasive mediastinal staging (IMS) was performed in 47 patients (37.6%), by endobronchial ultrasonography (EBUS) in 46 (36.8%) patients (82.6% negative and 17.4% inadequate tissue) while only 1 patient underwent mediastinoscopy. The factors affecting the survival rate upon comparison were the histology type (p=0.019), differentiate characteristics (p=0.004), adjuvant therapy (p=0.011), and presence of distant metastasis by postoperative re-staging (p=0.003). The independent predictive factors for survival were chemo-radiation therapy (odds ratio 0.367, 95% confidence interval 0.176–0.766) and distant metastasis (odds ratio 2.280, 95% confidence interval 1.334–3.897). However, a small size, periphery lesion, T staging, and number of N2 lesions were not significant factors.

Conclusion: The survival rate of unexpected N2 patients was low despite complete resection being achieved in these patients. Adjuvant therapy seemed to improve survival for those with unexpected N2 metastasis as it is a systemic disease. However, not all patients received IMS, which was mostly done by EBUS and which had a high false negative, leading to underestimating the staging. Other modalities, such as cervical mediastinoscopy, video-assisted mediastinoscopic lymphadenectomy (VAMLA) or open biopsy should be considered for the adequate e valuation of N2 metastasis, nonetheless further study is still needed.

Keywords: N2 disease, Unexpected N2, Non-small lung cancer (NSCLC), Invasive mediastinal staging (IMS), Stage 3A NSCLC (Siriraj Med J 2022; 74: 161-168)

INTRODUCTION

The prognosis of non-small cell lung cancer (NSCLC) patients with mediastinal lymph node metastases (N2 disease) is usually poor.[1-3] N2 involvement is one of the important factors that determine the prognosis and treatment. Because N2 disease seems to indicate systemic spreading, systemic therapy, such as chemotherapy, radiation therapy, or combined chemo-radiation therapy, has better 5-year survival than surgery alone (38% vs 30%).[4] Despite the recommendation for mediastinal lymph node tissue confirmation when there is a high suspicion of N2 by imaging, such as enlarged lymph nodes seen by computed tomography (CT) or an increased uptake in the mediastinum by positron-emission tomography (PET)[5], the accuracy of the clinical staging still has a high false negative rate ranging from 25% to 40%[6]; therefore, some patients undergo surgery as the first course of treatment. Previous reports showed that unexpected N2 disease patients had a poor prognosis and a survival rate ranging from only 10%-35%.[7-10]

Consequently, the objective of this study is to determine survival rate in Thai population of the clinical N0 NSCLC patients who underwent complete pulmonary resection with systematic mediastinal lymph nodes dissection and who had unexpected N2 as a final pathological result.

MATERIALS AND METHODS

Patients and staging

This study is a retrospective review of all the pathology-proven N2 metastases NSCLC patients included in the data registry of the Division of Cardio-Thoracic Surgery and in reports from the Department of Pathology, Siriraj Hospital, Bangkok, Thailand, between January 2007 and December 2016. Among all the patients aged 18 years old and older who received complete pulmonary resection with systematic mediastinal lymphadenectomy (n = 158), we excluded patients (n = 33) who had a diagnosis of N2 disease as either highly suspicious (14 patients whose CT shows enlarged N2 lymph node more than 1 cm in short axis) or confirmed from preoperative imaging (2 patients whose N2 uptake in PET-CT), small cell carcinoma (10 patients), and neuroendocrine tumor (7 patients). Following the exclusions, the remaining patients (n = 125) were proven to be NSCLC preoperatively or at the time of surgery, and had been clinically staged as N0 or N1 from an imaging study (CT or FDG-PET scan) and from invasive mediastinal staging if done. All of the included patients had not received neoadjuvant systemic chemotherapy nor radiation therapy before surgical resection. The Siriraj Ethic and Clinical Research Institutional Review Board approved this study as well

as the electronic database used. The need for individual patient consent was waived due to the nature of the retrospective study design.

Staging was primarily performed by chest computed tomography (CT). Only a small number of patients received positron-emission tomography (PET-CT scan) due to the cost and availability. Invasive mediastinal staging, such as endobronchial ultrasound fine needle aspiration (EUS-FNA) or cervical mediastinoscopy, were performed in cases with a mediastinal lymph node larger than 1 cm in short axis as determined by the imaging and when all the results were negative for N2 disease. Nevertheless, there is no specific criteria in the institution for selecting patients to receive particular preoperative invasive mediastinal staging, the decision depends on experienced pulmonologists or surgeons.

Surgery was performed by both standard thoracotomy and video-assisted thoracoscopic surgery (VATS). Anatomical complete resection (R0 resection) was achieved by lobectomy, bi-lobectomy, or pneumonectomy. Systematic lymphadenectomy was performed in all patients and included lymph node stations 2R, 4R,[7-9] for the right-sided lesions, and stations[5-9] for the left-sided lesions. The pathological review was done using the standard technique for both the primary lung lesions and mediastinal lymph nodes.

All the patients received routine follow-up examination in the thoracic out-patient unit and were referred to an oncologist and radiotherapist for appropriate adjuvant chemotherapy or radiation therapy.

Statistical analysis

Data analysis was performed using SPSS statistical software (SPSS version 25, 2017, IBM Corporation). Categorial data are presented as the percentage and continuous variables are expressed as the mean. Continuous variables between groups were compared using the t test and discrete variables using Pearson's chi square test. Survival rates were calculated using the Kaplan–Meier method and log-rank test for adjusting for the differences between subgroups. Univariate analysis for the prognostic factors was performed using the log-rank test and multivariate analysis using multiple logistic regression analysis method. A p-value of less than 0.05 was defined as statistically significant.

RESULTS

In total, 125 patients were included in this study. Complete surgical lung resection and systematic mediastinal lymphadenectomy were achieved in every patient. As shown in Table 1, male and female in age group of 60 is

TABLE 1. Patients' characteristics (n = 125).

Gender	
Male	60 (48%)
Female	65 (52%)
Median age (years, range)	62 (31-82)
Clinical presentation	
Abnormal chest radiograph	66 (52.8%)
Chest discomfort	4 (3.2%)
Prolong cough	34 (27.2%)
Hemoptysis	16 (12.8%)
Dyspnea	3 (2.4%)
Weight loss	1 (0.8%)
Pneumonia	1 (0.8%)
Site of primary tumor	
Right upper lobe	32 (25.6%)
Right middle lobe	14 (11.2%)
Right lower lobe	30 (24%)
Left upper lobe	33 (26.4%)
Left lower lobe	16 (12.8%)
Invasive mediastinal staging (IMS)	47 (37.6%)
EBUS*(negative result)	38 (30.4%)
EBUS (inadequate tissue)	8 (6.4%)
Mediastinoscopic biopsy (negative result)	1 (0.8%)
Mean time to surgery (months)	1.29 (±0.875)
Extent of surgery	
Segmental resection	2 (1.6%)
Lobectomy	104 (83.2%)
Bilobectomy	11 (8.8%)
Pneumonectomy	8 (6.4%)
Adjuvant therapy	102 (81.6%)
Chemotherapy	45 (36%)
Radiation therapy	4 (3.2%)
Chemo-radiation therapy	53 (42.4%)
Distant metastases (restaging)	71 (56.8%)

*EBUS endobronchial ultrasonography.

not different for the lung cancer characteristics. The most common presentation was an abnormal chest radiography on annual check-up followings with prolong cough and hemoptysis. One-third of the patients received an invasive mediastinal staging procedure by endobronchial ultrasonography (EBUS), for which the results were all negative or there was inadequate tissue for evaluation, and only 1 patient received mediastinoscopy with lymph node biopsy. The mean time from diagnosis to surgery was less than 60 days. Lobectomy was performed most often, which was equally performed in the right upper lobe, right lower lobe, and left upper lobe. Among the study, almost patients received adjuvant therapy, comprising chemotherapy alone, radiation therapy alone, or combined chemo-radiation therapy.

For the tumor characteristics (Table 2), the most common T staging was still early (T2a). Adenocarcinoma was the predominant histologic subtype along with moderate differentiation. There was a rather high incidence of visceral pleural invasion and lymphovascular invasion. The most common site of mediastinal nodal metastasis for unexpected N2 disease was station 7 followed by stations 4R and 4L, while three quarters of patients had multiple N2 station metastases.

The overall 2-year, 3-year, and 5-year Kaplan–Meier survival rates were 40%, 24%, and 20%, respectively (Fig 1). For the pathological characteristics, the histologic subtype and differentiation had significant differences in their effect on the survival rates (Fig 2). The adenocarcinoma group had a better 5-year survival rate compared to the squamous cell carcinoma group (24% vs. 14%, p = 0.019), whereas good differentiation had a better 5-year survival rate than moderate and poor differentiation (45%, 24%, and 13%, p = 0.004). There was no significant difference among the T staging classes (p = 0.282, Fig 2). The presence of visceral pleural invasion of the tumor had a 5-year survival rate of 16% compared to the absence group, but this was not significantly different (p = 0.199, Fig 3). Lymphovascular invasion also showed no significant difference (p = 0.097, Fig 3), and the 5-year survival rate was 15% in the presence of lymphovascular invasion.

For unexpected N2 metastasis, the numbers of nodal stations were analyzed. Fig 4 shows the Kaplan–Meier 5-year survival for 39 patients with single nodal station metastasis compared to 86 patients with multiple nodal stations metastases (25% vs. 18% respectively), but the difference was not statistically significant (p = 0.103). In terms of the patient follow-ups, 23 patients declined the adjuvant therapy. Here, all the patients with or without adjuvant therapy were compared, and the best prognosis was found in the adjuvant chemo-radiation therapy

TABLE 2. Tumors' characteristics (n = 125).

Size of primary tumor (cm)	4.31 ± 1.921
Histology	
Adenocarcinoma	104 (83.2%)
Squamous cell carcinoma	16 (12.8%)
Other	5 (4%)
Differentiation	
Well	6 (4.8%)
Moderate	84 (67.2%)
Poor	27 (21.6%)
Not evaluated	8 (6.4%)
Visceral pleural invasion	87 (69.6%)
Lymphovascular invasion	94 (75.2%)
Adjacent structure invasion	16 (12.8%)
T staging (from pathology)	
T1a	5 (4%)
T1b	10 (8%)
T2a	69 (55.2%)
T2b	20 (16%)
T3	16 (12.8%)
T4	5 (4%)
N1 station involvement	
10R, 10L	45 (36%)
11R, 11L	71 (56.8%)
N2 station	
3	6 (4.8%)
4R,4L	55 (44%)
5	33 (26.4%)
6	3 (2.4%)
7	62 (49.6%)
8R,8L	2 (1.6%)
9R,9L	10 (8%)
Number of N2	
Single	39 (31.2%)
Multiple	86 (68.8%)

For the tumor characteristics (Table 2), the most common T staging was T2a (55.2%) with the median size of 4.31 cm. Adenocarcinoma was the predominant histologic subtype (83.2%) along with moderate differentiation (67.2%). There was a rather high incidence of visceral pleural invasion (69.6%) and lymphovascular invasion (75.2%). The most common site of mediastinal nodal metastasis for unexpected N2 disease was station 7 (49.6%) followed by stations 4R and 4L (44%), while 68.8% of patients had multiple N2 station metastases.
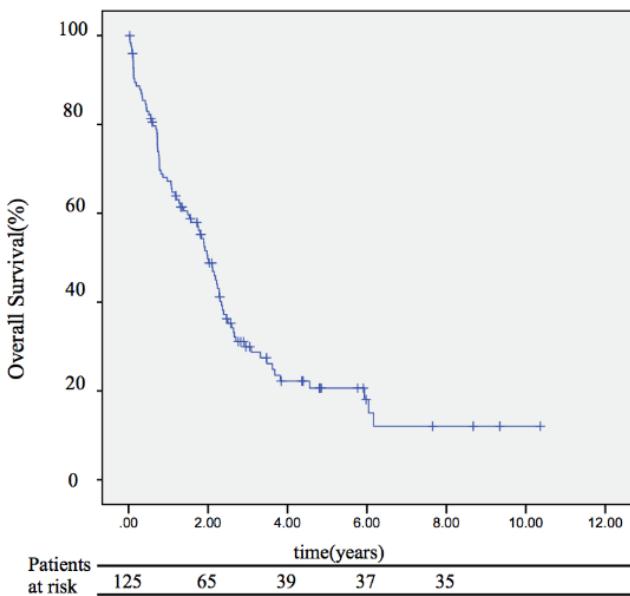
Fig 1. Overall 2-, 3-, and 5-year survival rates, which were 40%, 24%, and 20%, respectively.

group, which had a 5-year survival rate of 30%, while the 5-year survival rates of the radiation therapy alone group, chemotherapy alone group, and did not receive adjuvant therapy group were 25%, 15%, and 10%, and the difference was statistically significant (p = 0.011, Fig 4).

Post-treatment re-staging data were also collected and analyzed. The survival graph demonstrated the 5-year survival rate of patients with a presentation of distant metastasis in any organ was 10%; while for the group with no distant metastasis, it was 40%, and there was a highly significant difference in statistical terms as the *p*-value was 0.003 (Fig 4). The univariate analysis was insignificant. The multivariate analysis results in Table 3 depict that the independent predictive factors for survival were receiving adjuvant chemo-radiation therapy and a distant metastasis on re-staging.

DISCUSSION

Recently, Krantz and colleagues[11] did a study based on The Society of Thoracic Surgeons General Thoracic Surgery Database (STS-GTSD) participants in the United States (US) and reported that 34% of lung cancer patients staged by computed tomography and positron-emission tomography and first treated with anatomical resection underwent invasive mediastinal staging (IMS). Compatible with our study, which found that in all 125 "unexpected N2" disease patients, only 47 patients (37.6%) received IMS, which included 46 EBUS and only 1 who underwent

Fig 2. Survival rates according to histologic subtype (left upper) with significant difference between the subgroups (p = 0.019), where it can be seen the five-year survival rate in the adenocarcinoma group was 24% and 14% in the squamous cell carcinoma group. Right upperpicture shows the survival rates according to cell differentiation; where the five-year survival rates of well, moderate and poor differentiation were 45%, 24%, and 13%, respectively. Difference between the subgroup was significant (p = 0.004). Survival rates according to T-staging of the tumor characteristic (right lower). There was no significant difference between T1, T2, T3, and T4 (p = 0.282).

Fig 3. Survival rate according to visceral plural invasion (left) and lymphovascular invasion (right). The 5-year survival rate of patients with pleural invasion was 16%, while it was 26% in the absence group, with no significant difference (p = 0.199). For the lymphovascular invasion, the presence group had a 5-year survival of 15%, while the absence group it was 38%; however, there was no significant difference (p = 0.097).
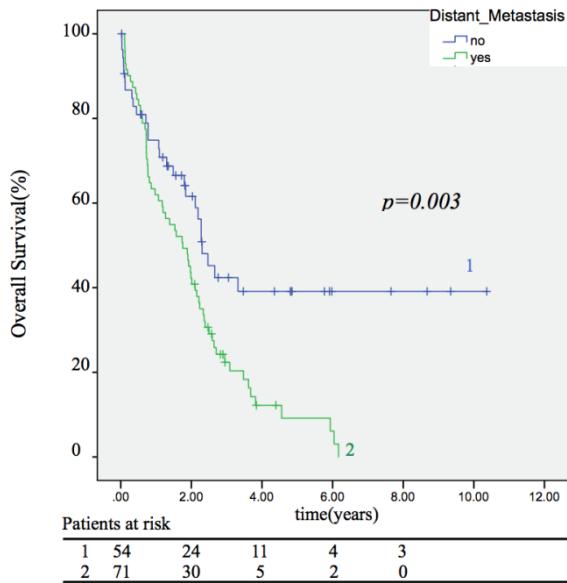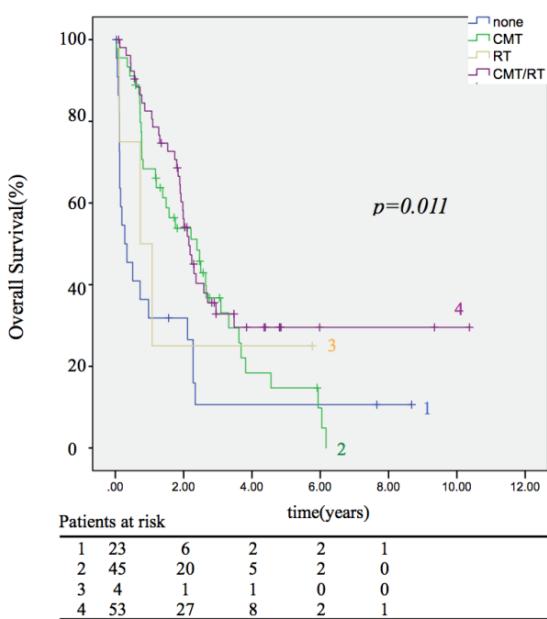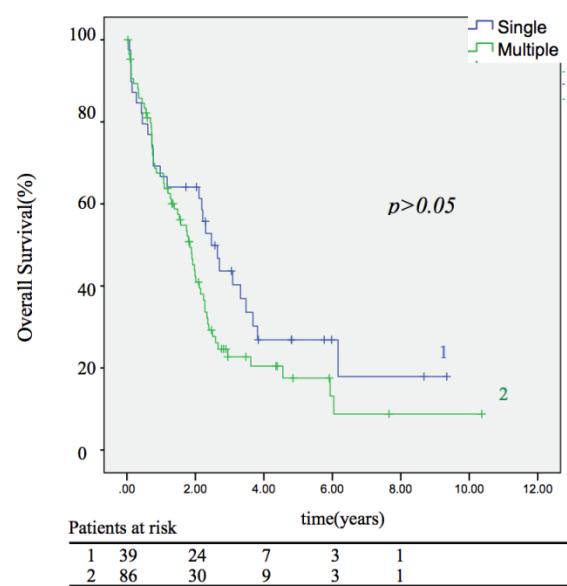
Fig 4. Survival rate according to number of N2 station metastasis (left upper); the 5-year survival rate of single station metastasis was 25% while the multiple station metastasis was 18%. However, there was no statistically significant difference (p = 0.103). Survival rate according to receiving adjuvant therapy (Right upper); the 5-year survival rate of patients who had received CMT/RT was 30%, while for radiation therapy alone, chemotherapy alone or had not received adjuvant therapy, the rates were 25%, 15%, and 10%, and the difference was statistically significant. The left lower figure showed survival rate according to post-treatment re-staging; the 5-year survival of patients with the presentation of distant metastasis in any organ was 10% while the group with no distant metastasis was 40%. The significant difference was high, p = 0.003.

TABLE 3. Multivariate analysis of the risk factors of mortality.

Variables	Number of patients	Adjusted OR (95%CI)	*p*-value
Adenocarcinoma	103	1.378 (0.655–2.902)	0.398
Poor differentiation	27	2.345 (0.734–7.489)	0.150
Visceral pleural invasion	81	0.838 (0.477–1.474)	0.541
Lymphovascular invasion	88	0.725 (0.421–1.247)	0.245
Multiple N2	82	1.429 (0.819–2.494)	0.209
Adjuvant therapy (CMT/RT)	52	0.367 (0.176–0.766)	0.008
Distant metastasis	66	2.280 (1.334–3.897)	0.003

Adjusted OR, adjusted odds ratio; CI, confidence interval.

mediastinoscopy; all the invasive study results were either negative for malignancy or had inadequate tissue for evaluation. Although our population was based on a clinical non-N2 group with pathological N2 disease confirmed by the final pathological report, the rate of patients who received IMS was not different. Whereas numerous population-based studies have shown low rates of lung cancer patients who have underwent IMS, ranging from 21%-27%,[12-18] our result showed higher rates of IMS.

The information suggests that preoperative non-invasive image staging only revealing a low suspicion of N2 metastasis is not adequate. For patients who had a preoperative PET/CT done, the information provided was also inadequate. Further prospective randomized trials on the role of PET/CT are needed. All the patients who received IMS staging, such as by EBUS, had many false negatives, leading to a dispute over inadequate tissue. This was similar to a previous study by Sawhney,[19] which showed a very low incidence of unexpected N2 disease by EBUS (3%) when only a CT scan was performed for preoperative staging, which, when compared to other modalities, such as mediastinoscopy, video-assisted mediastinoscopic lymphadenectomy (VAMLA), or open biopsy of mediastinal lymph node, might play an important role in the preoperative staging consensus with previous studies. Further, Bendzsak et al,[20] showed 85% of patients used IMS, which concorded with the guidelines,[6,21-23] Call et al,[24] concluded that VAMLA is a feasible and highly accurate technique, with a rate of unexpected N2−3 of 18%.

Compared to previous reports[3,4,25], we considered the different results about which adenocarcinoma cell type and cell differentiation were factors impacting the survival rate in the comparisons; however, not T staging (T2), visceral pleural invasion, and lymphovascular invasion, which had insignificant differences in the survival rates in comparison, even though we found this coincident with the N2 metastasis (71.2%, 69.6%, and 75.2%). The number of N2 stations and associated N1 did not show a statistical relation with unexpected N2, although the coincidence of multiple N2 stations was rather high (68.8%). Mediastinal lymph node station 7 was the most common position for finding unexpected N2 (49.6%), which was compatible with Eckardt and colleagues[26], who reported subcarinal lymph node metastases were common in NSCLC regardless of the primary location and should be considered an IMS modality or routinely dissected during operation.

The present study reported an overall 5-year survival of only 20% for patients with unexpected N2 disease despite complete pulmonary resection and systematic mediastinal lymphadenectomy being achieved, which correlated with previous studies that reported 5-year survival rates varying from 10%–38%.[7-10] Surgery is beneficial in early stage NSCLC[27] but still controversial in stage IIIA-N2, reflecting the general trend away from surgery.[28,29] Pneumonectomy for lung cancer also results in poor prognosis and followed by several post operative complication[30], since then this operation is less performed. Comparison of the survival rate showed that in our series, patients who had received adjuvant chemo-radiation therapy had a better survival rate than the others (p = 0.011). Pathological N2 disease indicates a systemic spreading, and like in a previous study, it was found that systemic therapy tends to play a more important role and improve survival more than surgery alone[31-33], whereby we found a correlation to distant metastases in 71 patients (56.8%), with a significant difference in the survival comparison (p = 0.003). The multivariate analysis results also supported that CMT/RT and distant metastases are independent factors for survival.

There are several limitations of this study to note. First, the study population only involved a single group of clinical N0/N1 patients with unexpected N2 disease, and we did not compare the overall survival rates of early stage (stage I–II) patients. Second, as a result of the limited population, IMS results showing false negatives were analyzed with the unexpected N2 base patients, and so the overall IMS information was inadequate. Other than that, in general, adjuvant chemotherapy is considered in all patients with N2 disease, despite complete resection previously being performed. However, in our study, it depended on the patient preference. In particular, some patients who were diagnosed distant metastases after complete re-staging declined receiving adjuvant therapy, which might have resulted in a different survival rate.

CONCLUSION

The overall 5-year survival rate of unexpected N2 patients was low despite complete pulmonary resection and mediastinal lymphadenectomy being achieved. Adjuvant chemo-radiation therapy seems to improve survival for those with unexpected N2 metastasis as it is a systemic disease. However, not all patients received IMS, and those who did it was mostly by EBUS and which had a high false negative, leading to underestimating the staging. Other modalities, such as cervical mediastinoscopy, video-assisted mediastinoscopic lymphadenectomy (VAMLA) or open biopsy should be considered for the adequate evaluation of N2 metastasis, nonetheless further study is still needed to compare each methods.

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Incidence and Risk Factors of Neonatal Sepsis in Preterm Premature Rupture of Membranes before 34 Weeks of Gestation

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ABSTRACT

Objective: Early-onset neonatal sepsis (EONS) is a leading cause of newborn morbidity and mortality, particularly in preterm premature rupture of membranes (PPROM) before 34 weeks of gestation, in which expectant management was performed until reaching 34 weeks of gestation, evidence of maternal chorioamnionitis, or unfavorable fetal conditions. The interval between membrane rupture and delivery has a positive correlation with neonatal sepsis. The purpose of this study was to investigate the incidence and risk factors of EONS in PPROM.

Materials and Methods: This was a retrospective cross-sectional study. The medical records of pregnant women who gave birth between 2005 and 2018 and their newborns were reviewed. The inclusion criterion was singleton pregnancies complicated by PPROM between 24 and 33^{+6} weeks of gestation. Multifetal pregnancies, fetal malformation, stillbirths, and records with incomplete data were excluded. PPROM was diagnosed by obstetricians while EONS was diagnosed by neonatologist.

Results: The incidence of EONS in with PPROM was 24%. Risk factors included excessive maternal weight gain based on IOM (OR = 2.40, 95% CI = 1.16-4.94), extremely preterm at admission (before 28 weeks of gestation) (OR = 3.38, 95% CI 1.12-10.21) and very low birth weight (≤ 1,500 g) (OR 3.68, 95% CI = 1.86-7.30). Maternal hematologic laboratory results were not associated with neonatal sepsis.

Conclusion: The incidence of EONS in PPROM was similar to data provided by other studies. Obstetricians and pediatricians should be cautious about neonatal sepsis, especially in cases of excessive maternal weight gain, extremely preterm admissions, and very low birth weight.

Keywords: Early-onset neonatal sepsis; incidence; PPROM; risk factors (Siriraj Med J 2022; 74: 169-177)

INTRODUCTION

Preterm birth is defined as babies born prior to completion of 37 weeks of gestation. At Siriraj Hospital, the incidence of preterm birth between 28 and 37 weeks of gestation is 9-13%.[1,2] Due to the immature development of several organs, these babies tend to have short-term or long-term morbidities in the respiratory system (respiratory distress syndrome, bronchopulmonary dysplasia, apnea of prematurity), gastrointestinal system (feeding intolerance, necrotizing enterocolitis, growth failure), immunological system (infection) and central nervous system (intraventricular hemorrhage, cerebral palsy, neurodevelopmental delay, hearing loss, retinopathy of prematurity).[3]

One of the causes of preterm birth is preterm premature rupture of membranes (PPROM) in which the fetal

membranes spontaneously rupture before completion of 37 weeks of gestation and onset of labor. At Siriraj Hospital, the incidence of PPROM between 24 and 37 weeks of gestation is 2.93%.[4] After the rupture of fetal membranes, microorganisms from the maternal lower genital tract ascend the uterine cavity, resulting in infectious morbidities such as chorioamnionitis, fetal inflammation and neonatal sepsis. Besides PPROM, risk factors of neonatal sepsis include preterm labor, low birth weight, maternal colonization of group B *streptococcus*, chorioamnionitis and intrapartum infection.[5,6] The interval between the rupture of membranes and delivery has a positive correlation with neonatal sepsis.[7] Early-onset neonatal sepsis (EONS) is an important cause of morbidity and mortality of newborns. Short-term outcomes are hypotension requiring vasopressor support; respiratory distress or suppression requiring intubation or noninvasive ventilation; and hyper- and hypoglycemia, thrombocytopenia, and disseminated intravascular coagulation (DIC). Long-term outcomes are bronchopulmonary dysplasia (BPD), brain injury, including periventricular leukomalacia (PVL), neurodevelopmental delays, and cerebral palsy.[8]

Management of PPROM remains challenging as it is difficult to balance the risk of terminating a pregnancy as long as expectant management exists. While expectant management poses a risk of maternal and fetal infection, placental abruption, and umbilical cord accidents, termination of pregnancy, especially at an early gestational age, presents a danger of prematurity.[9] Over the last few decades, the decision to terminate a pregnancy with PPROM complications have been based on evidence of maternal chorioamnionitis or unfavorable fetal conditions. Chorioamnionitis is defined by maternal fever and uterine tenderness, which results in severe infection in newborn babies. Indications of early stage chorioamnionitis have been proposed, however, they remain controversial and unreliable. Our aim was to study the incidence of EONS and parameters associated with this condition.

MATERIALS AND METHODS
Study design
This was a retrospective cross-sectional study approved by the institutional ethical committee.

Participants
Based on previous report from Arora and colleagues[10], the sample size of 274 samples would yield a power of 80% and type I error of 5%, 2-sided. The medical records of pregnant women who gave birth between 2005 and 2018 were reviewed. The inclusion criterion was singleton pregnancies affected by PPROM between 24 and 33^{+6} weeks of gestation. Multifetal pregnancies, fetal malformation, stillbirths, indicated preterm birth conditions such as maternal diseases, preeclampsia and placenta previa, and records with incomplete data were excluded. Gestational age was defined by menstrual history or ultrasonography performed before 20 weeks of gestation.

Outcomes
The clinical parameters included maternal demographic data, parity, history of previous preterm birth, body mass index (BMI), weight gain during pregnancy according to the Institute of Medicine (IOM) pregnant women, diabetes mellitus status, gestational age at PPROM and at delivery, interval between rupture of membranes and delivery, dexamethasone dosage, delivery mode, birth weight of newborns, APGAR score, diagnosis of EONS, length of neonatal hospital stay, and neonatal discharge status. The maternal hematological parameters included complete blood count (CBC), neutrophils to lymphocytes (N/L) ratio, and erythrocyte sedimentation rate (ESR). The IOM recommended that pregnant women should have a total weight gain of 12.5 to 18 kg, 11.5 to 16 kg, 7 to 11.5 kg, and 5 to 9 kg for those whose pre-pregnancy BMI were categorized as underweight (<18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), overweight (25.0-29.9 kg/m^2), and obesity (≥30 kg/m^2), respectively.[11,12]

All newborns were assessed by neonatologist at Siriraj Hospital. The EONS was defined by a positive culture of pathogenic bacteria in the blood or cerebrospinal fluid (CSF) within 72 hours after birth. Blood culture remains the diagnostic standard for EONS. CSF culture should ideally be performed along with blood culture for newborns who are at the highest risk for EOS. However, lumbar puncture should not be performed if the newborn's clinical condition was compromised, or antibiotic initiation would be delayed by the procedure.[13]

In our institute, all PPROM cases of less than 34 weeks of gestation were managed by a combined administration of antibiotics (ampicillin/amoxicillin plus erythromycin)[14], corticosteroids, and short-term tocolytics to complete course of corticosteroids. After completing the course of antibiotics and corticosteroids, expectant management was performed until 34 weeks of gestation when delivery was induced. Termination of each pregnancy was individually encouraged before 34 weeks using evidence of maternal chorioamnionitis or unfavorable fetal conditions. Complete blood count and ESR were checked every other day from admission until delivery.

Statistical analysis

The continuous variables are presented as mean ± SD, median, and range. The categorical variables are presented as frequencies and percentage. A T-test was used to compare two groups of continuous data which were normally distributed while the Mann-Whitney U test was used to compare differences between two independent groups when the dependent variables were either ordinal or continuous, but not normally distributed. The Chi-square test was used to compare a group with a value or to compare two or more groups, always using categorical data. Risk factors of EONS were shown as an odds ratio by binary logistic regression analysis. IBM SPSS Statistics version 21 (Copyright International Business Machines Corporation and other(s) 1989, 2012) was used for statistical analysis. A P-value of less than 0.05 was considered statistically significant.

RESULTS

A total number of 407 medical records were initially included into this study. One hundred and thirty-three records were excluded. Data from the remaining 274 records were used for further analysis (Fig 1).

The overall incidence of EONS in PPROM before 34 weeks of gestation was 24%. The trend of incidence has decreased over the past 14 years (Fig 2). The maternal characteristics and pregnancy outcomes were shown in Table 1. Maternal age was not significantly different between those with and without EONS, which was similar to parity and history of previous preterm birth. The PPROM interval prior to delivery, clinical chorioamnionitis and unfavorable fetal conditions did not relate to neonatal sepsis. Most pregnant women received four doses of dexamethasone before delivery. There was only one case of prolapsed cord among those without EONS. Placental abruption was not found in both groups.

Included 407 cases

- Pregnant women with PPROM during 24 0/7 and 33 6/7 gestational weeks.
- delivered at Siriraj Hospital

Excluded 133 cases

- Maternal disease 10
- Fetal anomaly 20
- Preeclampsia 15
- No newborn data 1
- Multifetal gestation 59
- Placenta previa 10
- Incomplete maternal data 18

Remaining 274 cases
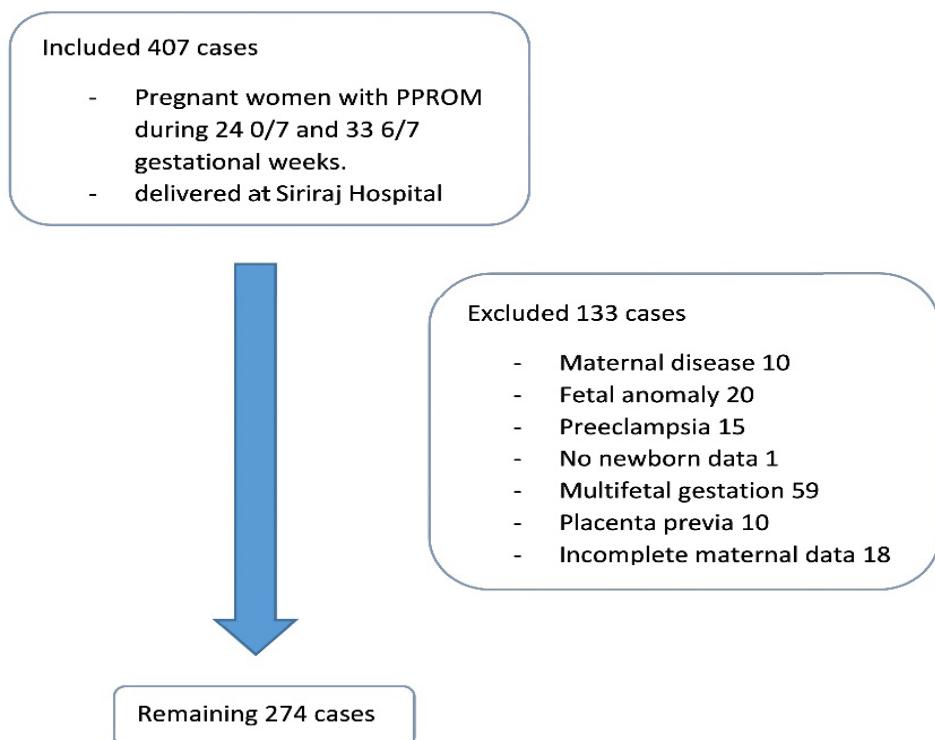
Fig 1. Flow of PPROM cases in Siriraj Hospital from 2005 to 2018
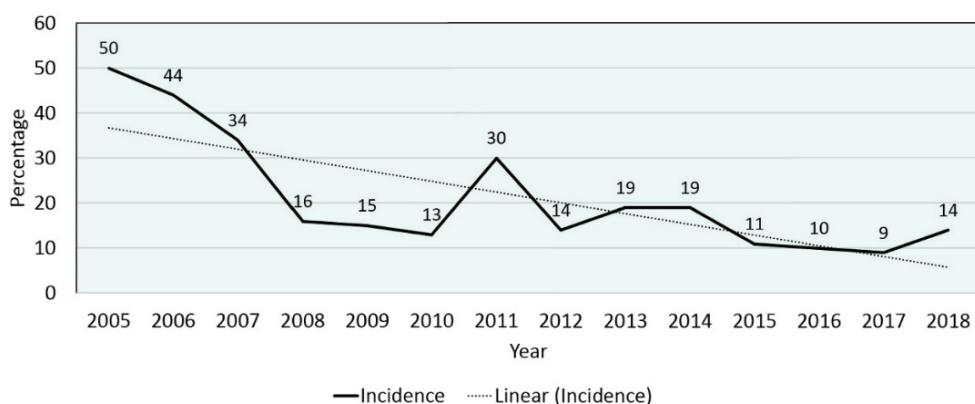
Fig 2. Incidence of EONS in PPROM pregnancies before 34 weeks of gestation at Siriraj Hospital from 2005 to 2018.

TABLE 1. Maternal characteristics and pregnancy outcomes of 274 women enrolled in the study in the PPROM without EONS or PPROM with EONS group.

Variables	PPROM without EONS (n=221)	PPROM with EONS (n=53)	*P*
Maternal age (years)	27.9 ± 7.2	28.8 ± 6.5	0.386*
<20	37 (16.7%)	5 (9.4%)	0.381#
20-34	139 (62.9%)	38 (71.7%)	
≥35	45 (20.4%)	10 (18.9%)	
Parity			
Nulliparous	125 (56.6%)	37 (69.8%)	0.088#
Multiparous	96 (43.4%)	16 (30.2%)	
Previous PTB history	23 (10.4%)	1 (1.9%)	0.056##
Weight gain (kg)	9.8 ± 4.7	11.7 ± 5.0	0.021*
Non-excessive	161 (81.7%)	28 (65.1%)	0.016#
Excessive	36 (18.3%)	15 (34.9%)	
GA at admission (weeks)	32 (25 - 34)	31 (25 - 34)	0.007†
24-27+6	8 (3.6%)	6 (11.3%)	0.027#
28-31+6	60 (27.1%)	18 (34.0%)	
32-33+6	153 (69.2%)	29 (54.7%)	
GA at delivery (weeks)	33 (25 - 34)	32 (26 - 34)	0.003†
24-27+6	8 (3.6%)	6 (11.3%)	0.150
28-31+6	50 (22.6%)	13 (24.5%)	
32-33+6	163 (73.8%)	34 (64.2%)	
PPROM interval prior to delivery (hr)	26 (0 - 523)	25 (0 - 241)	0.279†
<18	99 (44.8%)	25 (47.2%)	0.353#
18-48	35 (15.8%)	12 (22.6%)	
>48	87 (39.4%)	16 (30.2%)	
Dexamethasone (dose)			
0	14 (6.3%)	6 (11.3%)	0.164#
1	80 (36.2%)	15 (28.3%)	
2	17 (7.7%)	9 (17.0%)	
3	11 (5.0%)	2 (3.8%)	
4	99 (44.8%)	21 (39.6%)	
Delivery mode			
Vaginal delivery	163 (73.8%)	40 (75.5%)	0.863#
Cesarean section	58 (26.2%)	13 (24.5%)	
Clinical chorioamnionitis	8 (3.6%)	2 (3.8%)	1.000##

TABLE 1. Maternal characteristics and pregnancy outcomes of 274 women enrolled in the study in the PPROM without EONS or PPROM with EONS group. (Continue)

Variables	PPROM without EONS (n=221)	PPROM with EONS (n=53)	P
Unfavorable fetal conditions	16 (7.2%)	6 (11.3%)	0.396##
Birth weight (g)	1891 ± 389	1626 ± 350	<0.001*
<1,500	29 (13.1%)	19 (35.8%)	<0.001#
1,500-2,499	179 (81.0%)	34 (64.2%)	
2,500-3,999	13 (5.9%)	0	
APGAR score at 1 min	8 (0 - 10)	8 (1-10)	0.149†
APGAR score at 5 mins	10 (0 - 10)	9 (5 - 10)	0.016†
Length of neonatal hospital stay (days)	10 (0 - 158)	30 (2 - 218)	<0.001†
<7	61 (27.6%)	1 (1.9%)	<0.001#
7-30	111 (50.2%)	26 (49.1%)	
>30	49 (22.2%)	26 (49.1%)	
Neonatal discharge status			
Alive	217 (98.2%)	52 (98.1%)	1.000#
Deceased	4 (1.8%)	1 (1.9%)	

Abbreviations: PPROM=preterm premature ruptured of membranes, EONS=Early-onset neonatal sepsis, PTB=preterm birth, GA= gestational age

* Mean ±SD, p-value (T-test)

Count, p-value (Chi-square)

Count, p-value (Fisher's exact test)

† Median, p-value (Mann-Whitney U test)

The parameters significantly associated with EONS included excessive maternal weight gain, gestational age at admission, gestational age at delivery and birth weight. An earlier gestational age at admission meant higher incidence of EONS as well as gestational age at delivery. Again, a lower birth weight meant higher chance for neonatal sepsis.

Newborns with EONS stayed in the hospital longer. The overall mortality rate of newborns from PPROM mothers is 2%. There is no statistical difference in mortality rate between the two groups.

Laboratory results were obtained from 241 women and data comparing cases with and without EONS at admission, before delivery and difference from admission to delivery are shown in Table 2. All maternal laboratory results were similar between the EONS and no EONS group.

Pregnant women in the EONS group gained more weight than the other group. According to IOM guidelines for weight gain during pregnancy, the odds ratio (OR) of EONS among pregnant women with excessive weight gain was 2.40 (95% CI 1.16-4.94). Furthermore, risk factors of EONS at admission before 28 weeks of gestation was preterm (OR = 3.38, 95%CI 1.12-10.21) and low birth weight ≤ 1,500g (OR 3.68, 95%CI = 1.86-7.30), as shown in Table 3.

TABLE 2. Maternal laboratory results in PPROM without EONS and PPROM with EONS groups

Variables	At admission			Before delivery			Difference from admission to delivery		
	No EONS (n=193)	EONS (n=48)	*P*	No EONS (n=193)	EONS (n=48)	*P*	No EONS (n=92)	EONS (n=20)	*P*
Hb (g/dl)	11.5 ± 1.3	11.3 ± 1.2	0.21*	11.2 ± 1.5	11.2 ± 1.2	0.89*	-0.6 ± 1.2	-0.1 ± 0.9	0.08*
Hct (%)	35.2 ± 3.8	34.2 ± 3.6	0.10*	34.3 ± 4.4	34.1 ± 3.6	0.73*	-1.8 ± 3.3	-0.2 ± 2.8	0.06*
WBC (10³ cells/ul)	13.5 ± 7.3	13.3 ± 4.2	0.86*	14.5 ± 7.5	15.1 ± 4.6	0.60*	2.1 ± 5.0	4.3 ± 4.2	0.74*
N (%)	78.2 ± 7.3	76.9 ± 8.7	0.32*	80.0 ± 8.2	80.0 ± 8.7	0.99*	3.9 ± 9.8	7.4 ± 11.4	0.16*
L (%)	15.4 ± 6.0	16.3 ± 6.9	0.40*	14.1 ± 6.6	14.0 ± 6.9	0.93*	-2.7 ± 7.0	-5.4 ± 8.2	0.14*
N/L ratio	5.2 (1.1–27.4)	4.3 (1.7–21.5)	0.32†	5.6 (1.1–46.4)	6.4 (1.7–36.8)	0.99†	1.6 (-2.3–40.1)	3.0 (-8.1–34.2)	0.74†
Plt (10³ cells/ul)	271.4 ± 62.9	272.7 ± 78.7	0.90*	268.7 ± 61.6	269.6 ± 73.3	0.93*	-5.6 ± 38.2	-7.4 ± 38.5	0.84*
ESR (mm/hr)	64.2 ± 19.5	62.2 ± 18.0	0.56*	64.2 ± 21.2	62.7 ± 18.2	0.69*	0.1 ± 18.8	7.6 ± 14.4	0.15*

Abbreviations: Hb = Hemoglobin, Hct = Hematocrit, WBC = White Blood Cells Count, N = Neutrophils, L = Lymphocytes, Plt = Platelets, ESR = Erythrocyte Sedimentation Rate
* Mean ±SD, p-value (T-test)
† Median, p-value (Mann-Whitney U test)

TABLE 3. Maternal laboratory results in PPROM without EONS and PPROM with EONS groups

Risk factors	OR	95% CI	P
Excessive weight gain	2.40	1.16 – 4.94	0.016
BMI at admission	1.04	0.96 – 1.12	0.324
Gestational age at admission			
24-27[+6] weeks	3.38	1.12 – 10.21	0.023
28-31[+6] weeks	1.57	0.81 – 3.04	0.177
32-33[+6] weeks	1.00	-	-
VLBW (≤ 1,500 g)	3.68	1.86 – 7.30	<0.001

Abbreviations: BMI = body mass index, VLBW = very low birth weight

DISCUSSION

The overall incidence of EONS in pregnant women with PPROM before 34 weeks of pregnancy was found to be 24% in this study. We chose to study gestational age less than 34 weeks because PPROM that arises beyond 34 weeks of gestation is not treated expectantly, newborn sepsis is infrequent. Our incidence was in agreement with certain research[10] but not with others.[15,16] We hypothesize that the difference in incidence between hospitals is due to the varying diagnostic criteria used to identify EONS. During the 14-year period, the incidence of EONS in PPROM pregnancies before 34 weeks of gestation seems to have decreased. This could either be the result of better guideline management for premature rupture of membranes[14] or more advanced neonatal management. However, EONS incidence in preterm was higher than term deliveries. In Siriraj Hospital, the perinatal mortality rate has continuously declined and was less than 10%. The survival rate of premature babies has been increased due to the improvement of obstetric and newborn care. The well-trained neonatologists and excellent equipment result in the best care for newborns.[1]

Our study found that a maternal risk factor for EONS was excessive weight gain during pregnancy, according to IOM recommendations (OR = 2.40, 95%CI = 1.16-4.94; p=0.016). According to Stotland NE, et al., who conducted a retrospective cohort study in singleton births, the rate of neonatal infection was higher when maternal weight gain was above IOM guidelines, when compared to the appropriate or low weight gain group (5.86%, 4.44% and 3.38% respectively).[17] It was reported earlier that the incidence of sepsis among newborns of obese women was higher than those of normal-weight women.[18,19] Maternal overweight and obesity increased the risk of EOS by group B Streptococcus, Staphylococcus aureus, and Escherichia coli. Half of the association was mediated through preeclampsia, cesarean section, and preterm delivery.[19] Furthermore, obesity is a low-grade inflammatory state mediated primarily by leptin[20], which is associated with an increase in circulating inflammatory markers that are well characterized in the context of preeclampsia and maternal intrauterine infections. Since incremental weight gain has been associated with higher leptin levels[21], systemic inflammation may play a role in the higher incidence and trends of neonatal morbidities.[18]

Neonatal conditions at birth affect a baby's life in many aspects. According to previous studies[22-26], unanimous agreement states that gestational age, birth weight and APGAR scores play a vital role in neonatal well-being and complications. A study by Belachew A, et al. found that prematurity increased the risk of neonatal sepsis 3.36 times compared with term newborns (95% CI 2.50-4.54), and low birth weight (birth weight <2,500 grams) increased the risk of neonatal sepsis 1.42 times compared to the normal birth weight group (95% CI 1.07-1.88).[22] Meanwhile, Thavarajah H, et al. claimed that there was a statistically significant difference in the incidence of neonatal sepsis among different APGAR groups (low = 0-3, intermediate 4-6, normal = 7 or more).[23] Prematurity impairs adequate tissue oxygenation due to an immature respiratory function. An underdeveloped immune system along with hypoxic conditions put these babies at higher risk of infection. Our study found that a very low birth weight ≤ 1,500 g was associated with increased risk of EONS (OR 3.68, 95%CI 1.86-7.30).

Maternal hematological parameters such as white blood cell count (WBC) and erythrocyte sedimentation rate (ESR) have been proposed as predictors of chorioamnionitis and fetal infection but with some degree of controversy.[27-31] Panwar C, et al. mentioned that maternal WBC >12,000/mm³ could predict EONS with a sensitivity of 67.2% and a specificity of 77.5% but without achieving statistical significance.[32] However, Mayuka WAB, et al. concluded that maternal WBC >12,000 /mm³ was significantly associated with neonatal sepsis.[33] Our goal was to find parameters associated with EONS, but we did not notice any significant relationship between maternal hematological parameters and EONS. One possible explanation is that leukocytosis in PPROM mothers was the result of corticosteroids injections and not infection.[34] Many studies have advocated the usefulness of an elevated Neutrophils/Lymphocytes (N/L) ratio to predict adverse outcomes in PPROM and is associated with chorioamnionitis and EONS in preterm babies.[30,35,36] Contradicting this suggestion, the N/L ratio in our study was not significantly associated with EONS in PPROM. Future studies that can control the effect of corticosteroids might show the true relationship between leukocytosis, chorioamnionitis, and neonatal sepsis.

The strength of this study was that it found more information about maternal hematological parameters and EONS, about which there is relatively little knowledge. However, it was limited by its retrospective nature, low power in subgroup analysis and incomplete data of some parameters. More prospective studies should be carried out to eliminate these limitations.

CONCLUSION

In conclusion, the incidence of EONS in pregnant women with PPROM before 34 weeks of gestation was 24%, indicating a decrease over time. Excessive maternal weight gain, extremely preterm at admission and low birth

weight are associated with increased incidence of EONS, which affects the well-being of babies born prematurely. From this study, some maternal hematologic parameters may not reveal any risk factors of EONS. A regular check of some parameters to guide the management of PPROM cases should be considered.

ACKNOWLEDGEMENTS

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Incidence of Adverse Perioperative Airway Complications in Obese Non-Pregnant and Pregnant Patients Undergoing General Anesthesia

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ABSTRACT

Objective: Airway complications in obese patients are a major concern during surgical operation. This study aimed to determine the incidence of airway- and respiratory-related anesthetic complications for obese (including maternal) patients undergoing general anesthesia.

Materials and Methods: This multicenter, retrospective, observational study evaluated obese female patients (BMI ≥ 30 kg/m^2), both non-pregnant and pregnant, undergoing general anesthesia in 5 hospitals across Thailand during May 2013 - August 2016. The primary observation was anesthesia-related airway complications (difficult and failed intubations, aspiration, desaturation, and airway injuries) detected during anesthesia. An analysis was performed to compare the incidents of the adverse events and to determine the risk factors for airway-related adverse events in both groups.

Results: There were 1,347 obese patients enrolled (777 non-pregnant and 570 pregnant). The overall incidence of airway and respiratory complications was observed in 129 patients (9.6%), with a higher rate in pregnant patients (12.5% vs. 7.5%; p<0.05). The most common complications were desaturation (5.6%) followed by airway injuries (3.6%) and difficult intubation (1.5%). The factors significantly associated with adverse airway-related events were obesity class II (OR=1.63 [1.05–2.54]), obesity class III (OR=2.25 [1.19–4.25]), pregnancy (OR=1.73 [1.18–2.54]), Mallampati classifications III–IV (OR=1.69 [1.16–2.48]), and neck circumference <43 cm (OR=3.33 [1.02-10.81]), p<0.05.

Conclusion: The incidence of the anesthesia-related airway and respiratory complications was 9.6%, with a higher rate in pregnant patients. The most common adverse airway event was desaturation. However, the frequency of serious airway events was low.

Keywords: Airway; obesity; perioperative; complication (Siriraj Med J 2022; 74: 178-184)

INTRODUCTION

Obesity is a major risk factor of various diseases and associated with an increase in all-cause mortality.[1] According to the World Health Organization, obesity rates have almost tripled worldwide since 1975. In 2016, 39.8% of adults in the USA were overweight,[2] and during 2013-2014, 7.7% of adults in the USA were extremely obese.[3]

Performing general anesthesia in obese patients is challenging, beginning from induction to immediate post operation. The airway and respiratory system are the most common area in which complications occur in obese patients, accounting for more than 80% of all events.[4] The incidence of difficult intubation in obesity varies from 4% to 15%[5], depending on the population and the definition of difficult intubation utilized by studies. The incidence of difficult airway in obese patients was 3 times that of non-obese patients.[6] Moreover, it is a risk factor for aspiration, which is one of the main causes of airway-related mortality in anesthesia.[7]

Anesthesia is one of the leading cause of maternal mortality. Of all the causes of maternal complication from anesthesia, difficult intubation and aspiration is the second only to high spinal block in frequency.[8] The pregnancy-related anatomical and physiological changes heighten the risk of airway and respiratory problems occurring during general anesthesia. Thus, it is important to be aware of the risks of complications associated with general anesthesia in obese patients. Furthermore, it is very likely that the risk would be even higher in obese patients with pregnancy.

The main aims of the present study were to determine the incidences of airway- and respiratory-related anesthetic complications in female obese patients, and to ascertain the resulting airway management outcomes. The secondary objectives were to compare the airway-complication incidences between obese non-pregnant patients and obese pregnant patients, and to assess the characteristics of the patients in order to identify factors associated with the occurrence of such complications.

MATERIALS AND METHODS

This retrospective analysis evaluated on obese non-pregnant and pregnant female patients undergoing general anesthesia during May 2013 to August 2016 from a university hospital (Siriraj Hospital, Bangkok) and 4 tertiary hospitals across Thailand (Taksin hospital, Bangkok; Surat Thani Hospitals, Surat Thani Province; Phaholpolpayuhasena Hospital, Kanchanaburi Province; and Maharat Nakhon Ratchasima Hospital, Nakhon Ratchasima Province).

The inclusion criteria were female patients, aged ≥18 years old, having undergone surgery under general anesthesia with conventional endotracheal tube intubation, a BMI of ≥30 kg/m², and gestational age of 34-42 weeks for obese pregnant patients. Exclusion criteria included patients who had a significant orofacial pathology likely to disturb intubation; having a history of difficult intubation; having a condition leading to an abnormally increased BMI (such as a huge intra-abdominal tumor, massive ascites, or a patient with a full stomach).

Data collected were extracted by an anesthesiologist from each hospital. The details were compiled on a standardized data collection form and comprised each patient's demographic profile (sex, age, body weight, and height), ASA physical status, diagnosis, type of operation, and airway assessment parameters. In this study, the airway and respiratory adverse events during anesthesia were (1) difficult intubation, (2) desaturation, (3) aspiration, (4) failed intubation and (5) airway injury. Difficult intubation was defined and classified according to the Intubation Difficulty Scale,[9] a score of > 5 indicates difficult intubation. Desaturation was defined as having at least one episode of oxygen saturation (SpO_2) below 90% for more than 10 seconds intra-operatively.[10] Aspiration was defined as the entry of liquid or solid material into the trachea and/or lungs.[11] An airway injury included various levels of injury, ranging from a sore throat; lip, gum, or tongue trauma; palate and tonsil abrasion; to tooth mobility or tooth extraction. The postponement of the operation; remaining on endotracheal intubation to the post anesthesia care unit as a result of an airway or respiratory event; an unplanned, intensive-care-unit admission; brain damage; and an in-hospital, anesthesia-related death were also recorded.

Statistical analysis

Using the estimated prevalence of 3% and a 1% error, a minimum sample size of 1,118 cases was obtained. To compensate for a 20% dropout for unforeseen reason, the size was adjusted to 1,342 cases. Demographic variables were presented as median and interquartile range for continuous data, and frequency and percentage for categorical data. Comparison of the categorical data were performed using Chi-square or Fisher's exact test. Comparison of the continuous data were performed using T-test or Mann-Whitney U test. The characters associated with the adverse airway events were identified using logistic regression. Risk factors with a univariable p–value of < 0.2 were entered into a multiple logistic regression model. Crude odds ratio (OR) and adjusted odds ratios, with their respective 95% confidence intervals, were

reported. The data were analyzed using SPSS Statistics for Windows, version 18 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study included a total of 1,347 obese patients (777 not pregnant, and 570 pregnant) who had undergone surgery under general anesthesia using conventional endotracheal intubation. The median age of the patients was 37 years old. Their average BMI was 33.1 kg/m^2; the majority were in obesity class I under World Health Organization criteria (66.5%), with about 8.3% being morbidly obese. As to ASA status, 69.0% were class II due to obesity or pregnancy (Table 1). The most frequently performed surgical procedure types were general surgery; gynecological; head, neck, and breast surgery; and cesarean sections. Mallampati classification III or IV was recorded in 30.5% of the patients. The median mentosternal distance and neck circumference were 16.0 and 37.0 cm, respectively. Almost all patients were successfully intubated on the first attempt by the first operator, with the initial technique being applied without the need for a high lifting effort or external laryngeal pressure. Most patients had a laryngoscopic-view grade of I or II (66.1% and 28.5%, respectively).

The incidence of anesthesia-related airway and respiratory complications was observed in 129 patients (9.6%), with a higher incidence occurring among pregnant than non-pregnant patients (12.5% vs. 7.5%; p=0.002) (Table 2). Among them, there were over all 147 airway-related complications. The most common was a briefly sustained, oxygen desaturation below 90% (5.6%), with a significantly greater incidence for the pregnancy group than the non-pregnancy group (11.6% vs. 1.3%; p<0.001). The second most common event was airway injury (3.6%), followed by difficult intubation (1.5%). There was no patients experiencing aspiration or a failed intubation.

The characteristics of the patients with airway and respiratory complications are listed in Table 3. Compared with patients without any complications, those with complications had a higher frequency of Mallampati classifications III and IV (39.5.% vs. 28.2%). Patients with obesity class III had a higher incidence of complications (15.2%) than those with obesity class I (7.9%), and II (12.1%). In the multivariate analysis, the independent risk factors for adverse airway-related events were determined to be obesity class II (OR=1.63 [1.05–2.54]; p=0.031), obesity class III (OR=2.25 [1.19–4.25]; p=0.012); pregnancy (OR=1.73 [1.18–2.54]; p=0.005); and Mallampati classifications III–IV (OR= 1.69 [1.16–2.48]; p=0.007). Neck circumference > 42 cm had adjusted odds ratio of 0.30 [0.09–0.98]; p=0.046).

Only 1 patient remained on endotracheal intubation upon transferred to the post anesthesia care unit. No operation postponement, unplanned intensive care unit admission, brain death, or in hospital mortality occurred.

DISCUSSION

Obesity can have a profound impact on anesthesia-related morbidity and mortality, particularly the airway and respiratory system. In the current research, the incidence of airway and respiratory complications was 9.6% (7.5% for the non-pregnancy group, and 12.5% for the pregnancy group; p=0.002), which was higher than the overall incidence of airway-related events in the Thai general population previously reported (0.61%).[12]

Difficult intubation and airway injuries occur in the presence of the excess fatty tissue.[13] Physiological changes that arise during pregnancy can cause difficult intubation through both capillary engorgement and enlarged breasts.[14] Additionally, obesity causes reduced functional residual capacity; atelectasis; greater work of breathing; and worsened ventilation-perfusion mismatch. All of these resultant conditions cause rapid desaturation in obese patients relative to non-obese patients, and they are aggravated during pregnancy.[15]

In the current research, desaturation was found to be the most common adverse event among obese patients (5.6%), and its incidence was significantly higher among the obese pregnant patients than the non-pregnant patients (11.6% vs. 1.3%; p<0.001). A total of 66 out of 78 events (84.6%) in the pregnancy group involved oxygen desaturation. In 2 studies reporting anesthesia-related events in Thailand[16,17], the most common adverse event during cesarean delivery was desaturation (13.8%–17.39% of all adverse events).

More than half of the patients in our study were easily intubated (60.3%). The incidence of difficult intubation was 1.5%, which was higher than the figure of 0.08% reported for general patients by the Perioperative Anesthetic Adverse Events in Thailand Study.[4] A meta-analysis has found the incidences of difficult intubation for obese patients to be 4.2%-4.3%.[5] As for the current research, the low incidence of difficult intubation relative to other studies could result from 3 factors. Firstly, the majority of the patients were of class I obesity status (which carries a lower risk for difficult intubation than the higher obesity classes). Secondly, the population in the current study were female patients; fat in females tends to be localized to the hips and buttocks, where it has a negligible effect on intubation difficulty. Thirdly, the present study was undertaken at tertiary hospitals, where the anesthesiologists are likely to have had considerable

TABLE 1. Demographic and airway management data.

Characteristic	Total (n = 1347)	Obesity without pregnancy (n=777)	Obesity with pregnancy (n=570)	p-value
Age (years)	37.0 (29.0, 51.0)	49.0 (38.0, 59.0)	29.0 (25.0, 34.0)	<0.001
Body mass index (kg/m²)	33.1 (31.2, 36.1)	33.0 (31.2, 36.1)	33.2 (31.2, 36.0)	0.405
Obesity (kg/m²)				0.977
Obesity class I (30–34.9)	896 (66.5)	515 (66.3)	381 (66.8)	
Obesity class II (35–39.9)	339 (25.2)	197 (25.4)	142 (24.9)	
Obesity class III (≥ 40)	112 (8.3)	65 (8.4)	47 (8.2)	
ASA classification				<0.001
II	929 (69.0)	599 (77.1)	330 (57.9)	
III	414 (30.7)	178 (22.9)	236 (41.4)	
IV	4 (0.3)	0	4 (0.7)	
Operation				<0.001
Cesarean section	570 (42.3)	0	570 (100)	
General surgery	237 (17.6)	237 (30.5)	0	
Gynecology	175 (13)	175 (22.5)	0	
Head-neck and breast	131 (9.7)	131 (16.9)	0	
Orthopedic	83 (6.2)	83 (10.7)	0	
Ear, nose, and throat	52 (3.9)	52 (6.7)	0	
Other	99 (7.3)	99 (12.7)	0	
Mallampati classification				<0.001
I	315 (24.3)	250 (32.2)	65 (12.5)	
II	585 (45.2)	296 (38.1)	289 (55.8)	
III	305 (23.6)	150 (19.3)	155 (29.9)	
IV	90 (6.9)	81 (10.4)	9 (1.7)	
Sternomental distance (cm)	16 (15.0, 17.2)	16.0 (15.0, 17.5)	16.0 (15.0, 17.0)	0.038
Neck circumference (cm)	37.0 (36.0, 39.0)	37.5 (36.0, 39.5)	37.0 (35.0, 38.0)	<0.001
Intubation data				
First attempt successful	1325 (98.4)	756 (97.3)	569 (99.8)	<0.001
First operator successful	1334 (99.0)	769 (99.0)	565 (99.1)	0.415
First technique successful	1335 (99.1)	772 (99.4)	563 (98.8)	0.099
Lifting force				0.002
Little effort	891 (66.1)	523 (67.3)	368 (64.6)	
Increase lift force	384 (28.5)	201 (25.9)	183 (32.1)	
Maximal lift force	72 (5.3)	53 (6.8)	19 (3.3)	
No external pressure	1171 (86.9)	688 (88.5)	483 (84.7)	0.040
Cord position: Abduction	1164 (86.4)	660 (84.9)	504 (88.4)	0.066
Laryngoscopic view				0.006
I	891 (66.1)	523 (67.3)	368 (64.6)	
II	384 (28.5)	201 (25.9)	183 (32.1)	
III	67 (5)	49 (6.3)	18 (3.2)	
IV	5 (0.4)	4 (0.5)	1 (0.2)	

Data presented as n (%) or median (IQR)

TABLE 2. Airway and respiratory system adverse events.

Adverse events	Total (n = 1,347)	without pregnancy (n = 777)	with pregnancy (n = 570)	p-value
Patients experiencing ≥1 adverse event	129 (9.6)	58 (7.5)	71 (12.5)	0.002
Overall adverse events (n)	147 (100)	69 (46.9)	78 (53.1)	0.002
Difficult intubation				0.107
Easy (IDS score = 0)	812 (60.3)	478 (61.5)	334 (58.6)	
Slight difficulty (IDS score = 1-5)	515 (38.2)	291 (37.5)	224 (39.3)	
Major difficulty (IDS score >5)	20 (1.5)	8 (1.0)	12 (2.1)	
Desaturation	76 (5.6)	10 (1.3)	66 (11.6)	< 0.001
Airway injury: Patients with injury	48 (3.6)	48 (6.2)	0	< 0.001
Lip, gum, tongue injury	17 (1.2)	17 (2.2)	0	
Sore throat	30 (2.2)	30 (3.9)	0	
Tooth injury	3 (0.2)	3 (0.4)	0	
Soft palate injury	1 (0.1)	1 (0.1)	0	

Data presented as n (%), IDS = Intubation Difficulty Scale

TABLE 3. Characteristic of patients with airway and respiratory events.

Factor	Without event (n = 1,218; 90.4%)	With event (n = 129; 9.6%)	Crude OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age (years)	37 (29, 52)	35 (29, 49)	1.00 (0.98-1.01)	0.423		
Obesity (kg/m^2)						
Obesity class I	825 (67.7)	71 (55.0)	1		1	
Obesity class II	298 (24.5)	41 (31.8)	1.60 (1.07-2.40)	0.024	1.63 (1.05-2.54)	0.031
Obesity class III	95 (7.8)	17 (13.2)	2.08 (1.18-3.68)	0.012	2.25 (1.19-4.25)	0.012
ASA classification						
II	850 (69.8)	79 (61.2)	1			
III–IV	368 (30.2)	50 (38.8)	1.46 (1.01-2.13)	0.047	1.04 (0.67-1.63)	0.853
Pregnancy	499 (41.0)	71 (55.0)	1.76 (1.22-2.54)	0.002	1.73 (1.18-2.54)	0.005
Mallampati Classification						
I–II	874 (71.8)	78 (60.5)	1		1	
III–IV	344 (28.2)	51 (39.5)	1.66 (1.14-2.42)	0.008	1.69 (1.16–2.48)	0.007
SMD < 12 cm	62 (5.1)	6 (4.7)	0.91 (0.39-2.15)	0.829		
NC < 43 cm	78 (6.4)	3 (2.3)	2.87 (0.89-9.24)	0.076	3.33 (1.02-10.81)	0.046

Data presented as n (%) or median (IQR), OR: Odds ratio; 95% CI: 95% confidence interval, SMD = sternomental distance, NC = Neck circumference

experience in the intubation of obese patients. This is supported by the absence of failed intubations despite 30.5% of the patients having Mallampati classifications III-IV. The neck circumference < 43 cm was a sensitive predictor for uneventful airway intubation.[18] In contrast, the current research found neck circumference < 43 cm to be risk factor for airway complication, which could be explained by the complication recorded in the study were not only difficult airway but the most common adverse event was desaturation.

Airway injuries were recorded in 3.6% of the cases, and all were in the non-pregnancy group. Of the injuries, the most common was a sore throat (2.0%). The absence of airway injuries in the pregnancy group might have resulted from the use of smaller-sized endotracheal tubes in the pregnancy group than in the non-pregnancy group.

The major consequences of events was very low (0.1%). The endotracheal tube remained intubated in only 1 patient, who had undergone a tonsillectomy with a difficult intubation. However, the sample size in this study does not mirror the population since the incidence of fatal complications in the general population during anesthesia is low (0.004%-0.006%).

The risk factors associated with adverse airway-related events have previously been identified to be Mallampati classification III or IV, obstructive sleep apnea syndrome, reduced mobility of the cervical spine, limited mouth opening, severe hypoxemia (< 80%), and coma.[19] Some of those factors were observed in the current research. From the multivariate analysis conducted for this study, it was found that a higher obesity class and that Mallampati classifications III–IV were associated with a higher frequency of adverse airway events. Pregnancy was also determined to be associated with elevated risks of adverse airway events, compared with that for obesity without pregnancy.

This research compared obese female patient and showed that difference pathophysiology associated with obesity might contribute to difference adverse events. Pregnant obese patients were more susceptible to desaturation. Therefore, ensuring optimum pre-oxygenation are crucial. While non pregnant patient associated with higher incidence of airway injury, appropriate intubation plans and prophylaxis technique should be considered.

This study had limitation primarily due to its retrospective design. Another limitation was that no records of pre-pregnancy weights were available, not possible to ascertain whether the pregnant patients were obese before - or only during - their pregnancy. The durations might have influenced the pathophysiology and consequences of the obesity. Because the present study did not compare obese and non-obese patients, a comparison of the incidence of adverse events with those might prove difficult.[12] Differences in the intubation management of the pregnancy and non-pregnancy groups might have provided relatively easier access for the endotracheal tube in the pregnancy group. As well, the rapid sequence induction employed for the pregnant patients might have increased their susceptibility to rapid desaturation. On the other hand, as the respective anesthesia techniques used for the non-pregnant and pregnant patients were standard, the incidence of adverse events would still reflect what is found in normal anesthesiological practice. It would be beneficial if a future study compared obese non-pregnant patients and obese pregnant patients in a controlled design. Further study is also recommended to improve the anesthesiological procedures for patients with different levels of obesity.

CONCLUSION

The incidence of anesthesia-related airway and respiratory events was 9.6%, with a significant higher incidence in the pregnant than the non-pregnant patients. Based on the findings, patients with obesity should be closely monitored during general anesthesia. Anesthesiologists should be aware on the most common complication as identified in this study so as to be well prepared to minimize undesirable outcomes.

ACKNOWLEDGEMENTS

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Burnout among Mental Health Professionals in a Tertiary University Hospital

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ABSTRACT

Objective: To examine the level of burnout syndrome, and to investigate the relationship between burnout, personality traits, coping strategies, and other related personal factors among mental health professionals working in a tertiary hospital.

Materials and Methods: Online questionnaires were sent to 160 mental health professionals at Siriraj Hospital. The questionnaire comprised questions collecting demographic data, the Copenhagen Burnout Inventory (Thai version), the Big Five Inventory, and the Coping Scale. The data were analyzed through descriptive statistics, analysis of variance, Pearson correlation, and stepwise multiple regression.

Results: A total of 121 (75.6%) responses were collected. Of the 121 participants, 41.3% reported high total burnout levels. However, no difference in total burnout was found between the different mental health professions. The group aged between 20-29 years demonstrated higher burnout than the others. Individuals with bachelor's and master's degrees showed greater burnout than those with lower than undergraduate degrees. Moreover, individuals who worked for less than five years had higher burnout than those in other groups. Furthermore, neuroticism and avoidance significantly predicted the burnout syndrome.

Conclusion: In contrast to previous studies in Thailand, the results highlighted the risk factors for burnout syndrome in terms of personal, work-related, and client-related burnout. These results can strengthen awareness surrounding mental health conditions, for the effective provision of psychoeducation and psychological interventions.

Keywords: Burnout; coping strategies; health care professionals; personality traits (Siriraj Med J 2022; 74: 185-192)

INTRODUCTION

Burnout syndrome is a mental health condition commonly found in present-day society among working populations, with an annually ascending number. Rising concern about the adverse impacts of burnout syndrome has led the World Health Organization (WHO) to include burnout syndrome in ICD-11, which will be in effect 2022 onwards. Burnout is not defined as a medical disorder, but rather as an abnormality caused by occupational phenomena, specifically in the workplace environment.[1]

Burnout syndrome may arise from chronic stress that affects an individual's daily functioning, thus contributing to mental and physical health problems among those who fail to cope with stress and consequently seek treatment. Burnout is a state when work-related chronic stress has not been handled appropriately, thus, causing physical, emotional, and mental consequences.[2] Physical symptoms of burnout are fatigue, lethargy, headache, and insomnia while mental symptoms include apathy, despair, and frustration. Some consequences of burnout in healthcare

workers included an impaired work ability and high turnover intention.[3,4] Borritz, Rugulies, Bjorner, Villadsen, Mikkelsen, and Kristensen described burnout with an emphasis on exhaustion with both physical and mental effects, in which burnout consists of three components: personal, work-related, and client-related burnout.[5]

Burnout can occur due to external factors such as workplace environment, stressful job, high workload, and jobs related to interpersonal interactions.[6] However, researchers have noticed that not everyone in the same workplace environment would experience similar burnout; thus, there may be personal factors besides job specific factors that affect how individuals perceive, respond, and cope with stress. Past research revealed that the number of patients a physician attends to per day directly contributes to their burnout.[7] Further, individuals who employ harm avoidant strategies to cope with stress experience the most burnout. Moreover, self-control plays an important role in burnout prevention, where stress, neuroticism, negative affectivity, and disengagement coping has a positive relationship with burnout.[8] Furthermore, in the same study, negative relationships have been found between burnout and certain personality traits, including extraversion, agreeableness, conscientiousness, positive affectivity, and engagement coping. Additionally, young married females with a bachelor's degree tend to have higher stress.[9] Neuroticism is considered a risk factor that increases stress levels, while extraversion and active coping styles are the best at stress prevention. Previous studies in Thailand demonstrated many significant factors that were associated with burnout such as work hours per week, perception of sleeping/rest quality, perception of having stress from work and family relationships.[10] In addition, the prevalence of burnout syndrome among residents in medical school training was 95.4%, with the highest score revealed to be emotional exhaustion.[11] The associated factors of sleep quality were environmental problems in the bedroom while being on duty and emotional exhaustion.

Burnout syndrome can occur to anyone in any profession, but it is common in the medical field.[3,4,12] As medical professionals engage with activities related to safety, specialistic skills must be properly delivered so that clients recover effectively, particularly in mental health services. Previous studies on burnout syndrome showed that 67% (2 out of 3) mental health professionals experienced burnout as their profession is a health-related service that entails dealing with clients' emotional problems, mood swings, and expectations of illness improvement.[13] Despite the increasing number of patients with mental health problems, the number of mental health professionals is still limited, making them prone to experience negative emotions, thus causing chronic work stress and, eventually, burnout. Overall, burnout syndrome may affect people at all levels, including service providers, clients, and organizations as a whole.[14]

Therefore, this study aimed to examine the influence of personal factors on burnout syndrome among mental health professionals in Siriraj Hospital. The findings may aid in the assistance and prevention of burnout syndrome in both, mental health professionals and patients.

MATERIALS AND METHODS
Participants
In June 2020, the online questionnaires were sent to all 160 mental health professionals who were working as a multidisciplinary team to deliver integrated care for patients with mental health problems and were employed in three departments at that time, including the Department of Psychiatry, Division of Child and Adolescent Psychiatry of the Department of Pediatrics, and Medical Nursing Department, at Siriraj Hospital, a tertiary referral university hospital in Thailand. The sample included psychiatrists, psychiatric residents, registered nurses providing psychiatric nursing, practical nurses providing psychiatric nursing, psychologists, social workers, occupational therapists, special educators (evaluate children's educational needs and make those specific needs more accessible to each person with learning disability), and speech therapists (help children who have difficulties in speaking and communication such as patients with delayed speech development, intellectual disability and autistic disorder).

The sample size was calculated by using G power program version 3.1.9.4. The appropriate sample size for this research was 109; however, the sample size was increased by 10% to compensate for incomplete questionnaires and random responses. Hence, the total sample size was 121.

MATERIALS AND METHODS
The demographic questionnaire contained six items recording gender, age, education, marital status, years of work experience, and number of work hours per week.

The Thai version of the Copenhagen Burnout Inventory (T-CBT) consists of 19 items separated into three components: personal burnout, work-related burnout, and client-related burnout. The overall internal coefficient was .96.[15] T-CBT was measured on a 5 point Likert scale from 1 (Never/Almost Never) to 5 (Always).

The Big Five Inventory (BFI) consists of 12

items categorized into five components: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness. The overall internal consistency was .80 for 60 items.[16-17]

The Coping Scale comprises 39 items that measure coping strategies in three aspects: problem-focused coping, social support coping, and avoidance coping, with scores ranging from 1 (not at all) to 5 (always).[18] The score tabulation is represented by each coping strategy according to the scale.

Data collection

This study was approved by the Siriraj Institutional Review Board (SIRB) of the Faculty of Medicine Siriraj Hospital (Si 433/2020). Participants who matched the inclusion criteria were invited to participate using an online survey (Google form) which could be accessed through an online link or QR code. Participants were informed via an online platform with a description of the study and types of questions that they would be asked. They were also allowed to withdraw from the study if they found it distressful. We ensured them that the questionnaires did not ask about the information that could identify their identity.

Statistical analysis

Data were analyzed using SPSS version 18. Descriptive statistics were used to analyze demographic data and the main variables (frequency, percentage, mean, and standard deviation). Independent t-tests and analysis of variance (ANOVA) were conducted to compare the means between personal characteristics and burnout syndrome. Pearson's correlation coefficient was used to determine the relationship between burnout syndrome, personality traits, and coping strategies. The predictive value of personality traits and coping strategies regarding burnout syndrome of mental health professionals in Siriraj Hospital were examines using stepwise multiple regression analysis.

RESULTS

Demographic data of participants

There were totally 160 mental health professionals, and the response rate was 75.6% (n=121). The most participants were nurses (54.5%) followed by psychiatrists (25.6%) and others (29.8%). Their personal characteristics are summarized in Table 1. The majority of participants were female (86%) and the mean age was 34.36 ± 10.6. Working hours per week ranged between 0 and 72 hours, with an average of 40.2 hours ± 14.1.

TABLE 1. Demographic data of the sample in this study (n=121).

Demographics		N	%
Gender	Male	17	14
	Female	104	86
Age	20 – 29	56	46.3
	30 – 39	36	29.7
	40 – 49	11	9.1
	50 – 59	18	14.9
	Mean ± SD	34.36	± 10.6
Education	Undergraduate Degree	25	20.7
	Bachelor's Degree	55	45.5
	Master's Degree	31	25.6
	Doctoral Degree	10	8.3
Marital Status	Single	86	71.1
	Married	32	26.4
	Widow/Divorced	3	2.5
Occupational Psychiatrists	Psychiatrist	11	9.1
	Psychiatry Resident	20	16.5
Nurses	Registered Nurse	39	32.2
	Practical Nurse	27	22.3

Demographics	n	%	
Others	Psychologist	13	10.7
	Social Worker	5	4.1
	Occupational Therapist	2	1.7
	Special Educator	3	2.5
	Speech Therapist	1	0.8
Year in present working	< 5 years	50	42.1
	5 – 10 years	28	23.5
	11 – 15 years	11	9.2
	16 – 20 years	5	4.2
	> 20 years	25	21
	Mean ± SD	10.34	± 10.3
Working hours per week	Less than 40 hours	23	20.2
	40 – 50 hours	73	64
	More than 50 hours	18	15.8
	Mean ± SD	40.2	± 14.1

Burnout syndrome among mental professionals

The study found that 41.3% of the participants scored a high level of total burnout; specifically, in subscales, personal burnout was 46.3%, work-related burnout was 43.8%, and client-related burnout was 27.3%. When considered by occupation, 51.6% of psychiatrists had a high mean burnout score (Table 2).

Personal characteristics and burnout syndrome

The 20-29 years-old group showed higher average and work-related burnout scores than the 40-49 years-old group and 50-59 years-old group. Additionally, the average personal burnout score was lower in the 40-49 year-old group than in the 20-29 and 30-39 year-old groups. The average burnout score, personal-related burnout, and work-related burnout were greater in participants with master's and bachelor's degrees as opposed to undergraduate degree holders. Moreover,

participants with less than five years of work experience had significantly higher average scores, work-related burnout, and client-related burnout than those with 5-10 years and more than 20 years of work experience. However, no significant difference was detected between total burnout and demographic factors, including gender, marital status, occupation, and weekly work hours.

Relationship between burnout syndrome, personality traits and coping strategies

A moderate positive correlation between burnout syndrome, avoidance, and neuroticism was detected, while low negative correlations were found between burnout syndrome and conscientiousness, agreeableness, and extraversion. Additionally, burnout was negatively correlated with openness and problem-focused coping at a negligible level (Table 3).

TABLE 2. Burnout syndrome among mental professionals (n=121).

Occupational		Level		M	SD
		low	high		
Psychiatrists	Total Burnout	15 (48.4%)	16 (51.6%)	2.52	0.63
(n=31)	Personal Burnout	15 (48.4%)	16 (51.6%)	2.52	0.55
	Work-related Burnout	15 (48.4%)	16 (51.6%)	2.58	0.77
	Client-related Burnout	20 (64.5%)	11 (35.5%)	2.46	0.67
Nurses	Total Burnout	41 (62.1%)	25 (37.9%)	2.40	0.69
(n=66)	Personal Burnout	37 (56.1%)	29 (43.9%)	2.50	0.68
	Work-related Burnout	37 (56.1%)	29 (43.9%)	2.49	0.87
	Client-related Burnout	49 (74.2%)	17 (25.8%)	2.21	0.70
Others	Total Burnout	15 (62.5%)	9 (37.5%)	2.27	0.71
(n=24)	Personal Burnout	13 (54.2%)	11 (45.8%)	2.56	0.85
	Work-related Burnout	16 (66.7%)	8 (33.3%)	2.26	0.79
	Client-related Burnout	19 (79.2%)	5 (20.8%)	2.01	0.68
Total	Total Burnout	71 (58.7%)	50 (41.3%)	2.41	0.68
	Personal Burnout	65 (53.7%)	56 (46.3%)	2.52	0.68
	Work-related Burnout	68 (56.2%)	53 (43.8%)	2.47	0.83
	Client-related Burnout	88 (72.7%)	33 (27.3%)	2.24	0.70

Note: Psychiatrists = psychiatrists and psychiatric residents; nurses = registered nurses and practical nurses; Others = psychologists, social workers, occupational therapists, special educational needs, and speech therapists. The level of burnout syndrome was classified using a cut-off point equal to 2.5.

TABLE 3. Pearson's correlation coefficients between burnout syndrome, personality traits, and coping strategies.

	N	E	O	A	C	PFC	SSS	AVO
Total Burnout	.648**	-.422**	-.194*	-.428**	-.451**	-.190*	.019	.680**
Personal	.562**	-.331**	-.152	-.351**	-.357**	.143	.053	.640**
Work-related	.631**	-.417**	-.223*	-.409**	-.455**	-.188*	-.001	650**
Client-related	.573**	-.401**	-.141	-.408**	-.411**	-.184*	.008	572**

Abbreviations: N = neuroticism, E = extraversion, O = openness to experience, A = agreeableness, and C = conscientiousness. PFC = problem-focused coping; SSS = Seek social support; AVO = avoidance
*p < .05; **p < .01

The personal burnout subscale was positively correlated with avoidance and neuroticism at a moderate level, but negatively associated with conscientiousness, agreeableness, and extraversion at a low level.

For the work-related burnout subscale, positive correlations were found for avoidance and neuroticism, while low negative correlations were detected for conscientiousness, extraversion, and agreeableness. Moreover, work-related burnout was negatively correlated with openness and problem-focused coping at a negligible level.

Client-related burnout was positively correlated with neuroticism and avoidance at a moderate level, but negatively correlated with conscientiousness, agreeableness, and extraversion at a low level. The relationship with

problem-focused coping was correlated at a negligible level.

The effect of personality traits and coping strategies on burnout

Multiple regression analysis was conducted using the stepwise method. Avoidance and neuroticism (predictive variables) could explain burnout (dependent variable) at a significant level (F=63.82, P <.001). After adjusting the value, avoidance and neuroticism could predict burnout by 51.1% (adjusted R^2 =.511). When considering multiple regression at a standardized value, the highest value fell to avoidance (β= .444), followed by neuroticism (β =.336) (Table 4).

TABLE 4. Stepwise multiple regression analysis for the predictive variable of burnout syndrome.

Model	Predictors	R	R^2	R^2 change	Coefficients			t	p
					b	SE	β		
1	AVO	.680	.462	.462	.783	.077	.680	10.113	<0.001
2	AVO	.721	.520	.057	.512	.103	.444	4.959	<0.001
	N				.373	.099	.336	.3756	<0.001
		Adjusted R^2 =.511			F = 63.820			P <0.001	
		Constant = .145			SE = .207				

Abbreviations: N = neuroticism, AVO = avoidance

DISCUSSION

This research illustrated that the overall burnout syndrome among mental health professionals in Siriraj Hospital was low. However, 41.3% of mental health professionals in Siriraj Hospital reported having high burnout, which corresponds with past research.[9,19,20] In line with Ogresta and Rusac, no significant associations between professions in the mental health field were detected. Close investigation of a group with a high burnout rate showed that 51.6% were psychiatrists, 37.9% were nurses, and 37.5% belonged to other professions.[20] This is consistent with previous research suggesting that high burnout was detected among psychiatrists in Thailand, with greater emotional exhaustion (49.3%).[21]

When examining burnout components, the results showed that personal burnout was the highest among mental health professionals in Siriraj Hospital. This is congruent with a previous study examining burnout patterns in Australian midwives.[22] However, our results contradict research on physicians where work-related burnout (46.7%) was highest, followed by personal burnout (44.8%) and client-related burnout (35.1%); while all sub-scale scores indicated high burnout.[23] Consistently, although no significant difference in burnout level was detected between different mental health professions, psychiatrists still had the highest risk of burnout compared to other professions.[24,25] One possible explanation is that psychiatrists are more involved with work associated with complex emotional problems alongside high patient expectations; thus, they are more likely to experience stress, pressure, and burnout.

Consistent with previous studies, our results showed no significant difference between genders and burnout.[7,26,27] This may be due to the low number of male samples (14%) in this study. Therefore, samples may not be representative of gender and burnout score differences among mental health professionals. Moreover, there is a very limited number of studies that have examined gender and burnout among mental health professionals using the Copenhagen Burnout Inventory (CBI). The current findings are supported by Erik Erikson's theory on psychosocial development, where the age between 21 and 40 years is a period when individuals hold greater responsibilities, and thus are more prone to stress and burnout. Additionally, previous research reported similar results where older staff had lower scores for all burnout components than younger staffs.[24] Older ages seemed to signify lower burnout, particularly in personal and work-related burnout.[23,28] Similarly, younger age was found to be correlated with high emotional exhaustion.[19]

Moreover, there were differences in the burnout average scores and burnout component scores across different education levels. Samples with education of lower than undergraduate degrees had lower personal and work-related burnout than those with bachelor's and master's degrees. This is in line with a Taiwanese research demonstrating that a graduate school group had higher average burnout than college group.[24] Furthermore, a research also showed that master's-level education corresponded with greater burnout scores.[6] Taking the above research into consideration, this suggested that bachelor's and master's degrees require a more specified level of training, expertise, and work experiences in mental health services, and thus, are more prone to experiencing burnout. Strikingly, the differences in burnout scores were not significant in those with a doctorate level of education. This may be due to the collected experiences related to work that had already been adjusted and managed.

Concerning marital status, no significant difference between being single, married, or divorced and experiencing burnout was detected, which is consistent with other studies.[7,28] The uneven number of single samples (71.1%) and married samples (26.4%) might explain the above finding. Therefore, future research conducted with mental health professionals should further investigate whether there are differences in burnout scores based on marital status.

Moreover, our study showed that individuals who had worked for less than five years had significantly higher average scores. Although research on years of employment using CBI is very limited, one study found an association between longer working hours and lower personal and work-related burnout.[23] Furthermore, a study revealed that greater emotional exhaustion correlated with fewer years of work experience among mental health providers.[29]

Furthermore, we found that only neuroticism and avoidance could predict higher burnout, similar to past research showing that neuroticism was a risk factor for workplace stress.[9] Similarly, openness, extraversion, agreeableness, conscientiousness, and active coping styles could be protective factors against stress.[9] Correspondingly, neuroticism was one of the main factors that could predict burnout, whereas social support and self-blame affected personal and work-related burnout.[30] Additionally, behavioral disengagement influenced work-related and client-related burnout.[30] Furthermore, factors such as gender, job stress, weekly work hours, positive affectivity, negative affectivity, extraversion, conscientiousness, and problem-focused disengagement could predict burnout.[8]

Study limitations and suggestions for future research

This research was a cross-sectional design which explained factors related to work exhaustion in mental health professionals in a certain period. Therefore, future research may include a continual burnout monitoring and evaluating with interventions such as a group therapy, workplace health promotion programs or stress management training to assess whether there are changes in burnout scores after participating in the interventions or not. Moreover, our research employed a self-report in the data collection method, a sort of an online questionnaire, in which straightforward responses from participants might not be provided, and the evaluation was merely based on their point of views; subsequently, the result accuracy was diverse. In addition, The online survey may not be able to reach participants who do not use the social network platforms or those who find this type of survey bothersome. There might also be a potential confounding factor like the COVID-19 pandemic situation which could have emotional impacts on health care workers; however, this issue was not included in our questionnaires since we would like to investigate participants' overall perceptions on themselves, work and clients in the first place so further studies to explore the COVID-19-related burnout should be done. Furthermore, for the reason that burnout is merely a syndrome without specific diagnosis criteria while an assessment tool is simply a questionnaire, further research may include responses from participant's associate people, for example, superiors, colleagues and intimate friends or, on the contrary, an additional interview with the participant. Lastly, it is feasible to establish more precise diagnosis criteria for burnout as the syndrome threatens mental health of working age people. Another limitation is that our samples only comprised mental health professionals, and thus the findings cannot be generalized to other populations. Therefore, it might be useful for future studies to examine the effect of other positive factors and different workplace settings (such as general and psychiatric hospitals) on burnout among mental health professionals. In addition, future studies should examine other positive factors (such as sleep factors, exercise, and job description) that may be useful in preventing or reducing work-related exhaustion among mental health professionals.

CONCLUSION

The present research is one of the first studies in Thailand that examined factors related to burnout in mental health professionals. Our results highlighted personal, work-related and client-related factors that could predict a high level of burnout. These results could be used to inform future research and aid prevention schemes for more specific work-related exhaustion among the Thai population.

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Attitudes Toward Long-Acting Injectable Antipsychotics among Schizophrenia Patients in Southern Thailand: A Multihospital-Based Cross-Sectional Survey

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ABSTRACT

Objective: To identify the attitudes toward long-acting injectable antipsychotics (LAIs) among schizophrenia at three psychiatric outpatient clinics in Southern Thailand from February to April 2021.

Materials and Methods: A study was conducted at three psychiatric outpatient clinics. All patients, who met the criteria of having schizophrenia based on ICD-10 criteria, aged 20-60 years were included. The questionnaires utilized were:1) Demographic information, 2) Profile of schizophrenia disorder, and 3) Attitude, knowledge, and satisfaction towards LAIs. All data were analyzed using descriptive statistics.

Results: There were 259 participants who completed the questionnaires. From the participants, 39% had a history of being treated with LAIs. A quarter of them felt LAIs made them feel stigmatized (26.3%), that they lost autonomy (24.7%), and embarrassed (16.6%). The reasons for refusing to receive LAIs were not fear of needles or pain at the injection site (49%), but rather that LAIs had more adverse effects than oral medications (47.9%). Half of them (51.8%) knew that they must continue to use LAIs, even though their symptoms had improved as LAIs played an important role by improving their symptoms (68.8%), and preventing relapse (51.8%). They were satisfied about having been involved in the decision making of using LAIs for their treatment (63.6%), having information on the risk-benefits from LAIs provided to them (72.3%), and the cost of LAIs (75.2%).

Conclusion: Before deciding to prescribe LAIs, we should ensure that all patients receive information about the risks, and benefits of LAIs, boosting acceptance for this formulation and mitigating concerns about patient autonomy reduction and stigmatization.

Keywords: Antipsychotics; attitude; knowledge; long-acting injectable; schizophrenia (Siriraj Med J 2022; 74: 193-201)

INTRODUCTION

Schizophrenia is a mental illness affecting about 0.7% of adults globally.[1] It is a long-term chronic disease, has residual symptoms and functional impairment. Therefore, using integrated treatment strategies; in terms of medication, psychosocial interventions,[2] including psychiatric rehabilitation, and decreasing stigmatization for schizophrenia are essential to both lessen the burden for family members and improve patients' quality of life.[3-5]

In the past, the core concept of schizophrenia management was a combination of ensuring patients gain insight, medical treatment, and the teaching of

essential community-living skills, so as to integrate patients back into society.[6] Moreover, occupations and employment can reduce stigma and promote quality of life.[4-6] Although, some schizophrenia patients gain insight well, the truth of this illness makes them suffer from stigmatization. Because of this, patients usually deny or refuse medication, which in turn makes them relapse.[4] In addition, the relapse rate after the first episode of schizophrenia (FES) is high, often due to non-adherence with medication.[7]

Presently, antipsychotic medications play an effective role in schizophrenia symptom control and relapse prevention;[1,7] however, non-adherence to medication is still a major problem in the treatment of schizophrenia,[8] and is one of the most important predictors for relapse rates of more than 80% within 5 years.[9] Although, treatment response is better in FES than in multi-episode patients,[10] and within one-year response rates of about 87%, relapse rates are still high;[9] therefore, long-acting injectable antipsychotics (LAIs) have a role for promoting adherence to medication[1,7] in schizophrenia patients who having poor drug compliance.[11,12] However, in many countries, fewer than 20% of schizophrenia patients receive LAIs. The rate of LAIs usage among schizophrenia at the psychiatry department of the Faculty of Medicine, Prince of Songkla University, in 2018, was 12.7%.[13] The reason for this low prescribing rate of LAIs may be the patient attitudes and reluctance to accept depot treatment.[10] Despite good clinical evidence, depot treatment rates are still low across countries,[7] and depot antipsychotics are only seldom prescribed for patients with FES.[12]

Currently, some systematic review studies have reported that patients have generally positive attitudes toward LAIs compared with oral medication.[14-17] Additionally, it is generally considered that providing adequate information to patients and having a therapeutic relationship with the psychiatrist, which includes a shared decision-making processes, can promote a positive image to depot injections.[7] Although, some previously reviewed literature found that LAIs are associated with a better outcome, as a reduction of re-hospitalization and better adherence, schizophrenia patients are particularly fearful of being stripped of their autonomy when treated with LAIs, and that the injections may be painful. Moreover, the lack of adequate information given to patients may be a reflection of their negative attitudes towards LAIs. Providing adequate information on LAIs can help promote positive attitudes, especially as LAIs don't particularly increase the risk of side-effects such movement disorder.[11] Therefore, to enhance the use of LAIs, psychiatrists could improve their practice, by providing patients with more information regarding the different forms of available treatment during the early stages of this illness.[12] In addition, the availability of the deltoid route of administration would offer increased choices in LAIs administration, and may be perceived as more respectful and less socially embarrassing.[16] The aim of this study was to identify the prevalence of LAIs usage, attitudes, and satisfaction toward LAIs among schizophrenia outpatients, as this may provide useful, basic knowledge for enhancing the use of LAIs.

MATERIALS AND METHODS

After being approved by the Ethics Committee of the Faculty of Medicine, Prince of Songkla University (REC: 63-521-3-4) and Rajanagarindra Psychiatric Hospital (SKPH.IRB.COA 1/2021), this cross-sectional study was conducted at the three listed psychiatric outpatient clinics: Songklanagarind Hospital, which is an 800-bed university hospital serving as a tertiary referral center in Southern Thailand, Songkla Hospital, which is a 508-bed provincial hospital, and Songkhla Rajanagarindra Psychiatric Hospital, which is a 200-bed psychiatric hospital serving as a referral center in Southern Thailand. All schizophrenia outpatients, who had an appointment and were followed up at three psychiatric outpatient clinics; from February to April 2021, were invited to participate in the study. To be included, they had to meet the criteria of being adult schizophrenia outpatients by their psychiatrists and their case files were selected in the medical register, based on the following criteria: ICD-10 code F20.0-F20.9, aged 20-60 years, agreeing to participate in the study, able to understand and use the Thai language well and to complete all of the questionnaires. Patients who had more than one psychiatric diagnosis or comorbidity, did not wish to participate or decided to withdraw from the study and/or lacked mental capacity (judged by an outpatient psychiatric nurse) to complete all of the questionnaires, were excluded. We tried to calculate a sample size to determine the minimum number of subjects to enroll in our study. Following a literature review we could not find any information from studies about the prevalence of patient attitudes in regards to long-acting antipsychotic injections, in Thailand. Therefore, we simply identified all patients with an appointment and we followed them up during that period.

Data collection

All of the eligible schizophrenia outpatients were approached by the research assistant for recruitment, and were provided with an information sheet; which delineated the rationale for the study and the allotted time to complete the survey. All eligible participants had at

least 20-30 minutes to consider whether to participate in the study or not. Participants willing to collaborate were invited to a private location to complete the questionnaire, and were informed that they could stop at any time if they felt distressed, uneasy or were unwilling to perform any further. All participants were allowed to finish and return the questionnaires immediately, or at a later time. Participants could submit the questionnaires via two options: by dropping them in a secure box at the front of the clinic upon leaving, or by returning them later by placing them in a secure box located at the Psychiatry Department and/or Unit. Therefore, protecting respondent confidentiality.

Instruments

1) Personal and demographic information: inquiries around areas related to age, gender, marital status, religion, education, income, occupation, and history of physical illnesses.

2) Profile of schizophrenia disorder: the number of hospital admissions, duration of illness, and history of injection experience.

3) Self-rating questionnaires to evaluate attitude, knowledge, and satisfaction toward LAIs: 4 tools. The Drug Attitude Inventory (DAI-30) containing 30 questions concerning the aspects of the patient's perceptions and experiences of treatment.[18] The Satisfaction With Antipsychotic Medication scale (SWAM scale) containing 33 questions evaluating the patient's beliefs, patient's concerns, and other aspects of treatment; including social support and information regarding the patients.[19] A questionnaire from a study in Nigeria;[20] and a questionnaire from a study in Croatia.[21] Our tool consisted of 15 questions, in 3 domains: attitude, knowledge, and satisfaction. The response to each question ranged from disagree; neutral; agree, and strongly agree. This questionnaire's modification and content validity was reviewed by 5 psychiatrists; the content validity (CVI) score was 0.8. A pilot study was conducted with 20 volunteers; thus, Cronbach's alpha was 0.8.

Statistical analysis

Descriptive statistics; such as frequency, percentage, proportion, mean, and standard deviation (SD) were calculated. Chi-square tests were used in regards to the comparison of 'knowledge', 'attitude of schizophrenia patients who received LAIs' and 'no experience of receiving LAIs'. The analyses were conducted using R version 3.4.1 (R Foundation for Statistical Computing). Statistical significance was defined as a p-value of less than 0.05.

RESULTS

Demographic characteristics

From February to April 2021, 262 schizophrenia patients attended all three Psychiatric Clinics, and 259 of them agreed to collaborate and complete the questionnaires. The response rate was 98.9%. The majority of participants were male (62.5%), Buddhist (74.9%), and unmarried (82.2%). Overall, their mean age was 41.2 ± 10.9 years, and their median income (IQR) was 9,000 (4,000-15,000) baht, per month. Fifty-three participants (20.5%) reported having history of physical illness (Table 1). The most common physical illness were diabetes mellitus (32.7%), hypertension (25%), and dyslipidemia (21.2%). No statistically significant difference in demographic data was detected between the participants, according to the three hospitals.

Profile of schizophrenia disorder

For all the participants, their mean (S.D) duration of illness was 139.8 (104.5) months. The majority of participants (58.3%) reported having a history of inpatient admission; with the mean (S.D) number of admissions at 2.6 (2.4). No statistically significant difference in the profile of schizophrenia was observed between the participants, according to all three hospitals. 101 (39%) participants had a history of being treated with LAIs (Table 2), with the most common LAIs received being conventional LAIs; there were only 5 (4.9%) participants who had received novel LAIs.

However, a statistically significant difference in the history of psychiatric inpatient admission was detected between the participants who had received and those who had no experience of receiving LAIs. Of all participants who received LAIs, 75% of them had history of psychiatric inpatient admission; whereas, 52.6% of participants who had no experience of receiving LAIs had a history of psychiatric inpatient admission (Table 3).

Knowledge and attitude toward long-acting injectable antipsychotics

In regards to knowledge and attitude toward LAIs, the majority of participants knew that LAIs played an important role and improved their symptoms (68.8%), and that they must continue to use LAIs even though their mental health was improved (51.8%). They also knew that LAIs prevented symptom relapse (51.8%). However, 64 (24.7%) participants felt that LAIs made them feel a loss of autonomy, and 68 (26.3%) participants reported feeling stigmatized due to LAIs. Only 98 (37.8%) participants felt that LAIs were more convenient than oral

TABLE 1. Demographic characteristics (N = 259).

Demographic characteristics	Number (%)
Gender	
Male	162 (62.5)
Female	97 (37.5)
Religion	
Buddhism	194 (74.9)
Islam/Christianity/Other	62 (23.9)
No answer	3 (1.2)
Marital Status	
Single/Divorced	213 (82.2)
Married	39 (15.1)
No answer	7 (2.7)
Education level	
Secondary school/below	99 (38.2)
High school/diploma	92 (35.5)
Bachelor's degree or above	64 (24.7)
No answer	4 (1.5)
Occupation	
Employee/Agriculture	68 (26.3)
Government employees officer/state Enterprise officer/Private company employee	32 (12.4)
Merchant/Personal business	37 (14.3)
Unemployed/Student	118 (45.6)
No answer	4 (1.5)
Having income	
No	127 (49.0)
Yes	127 (49.0)
No answer	5 (1.9)
Having physical illness	
No	199 (76.8)
Yes	53 (20.5)
No answer	7 (2.7)

TABLE 2. Profile of schizophrenia disorder (N = 259).

Schizophrenia profile	Number (%)
Having history of inpatient admission	
No	97 (37.5)
Yes	151 (58.3)
Not answer	11 (4.2)
Having history of being treated with injectable antipsychotic agents	
No	89 (34.4)
Yes	170 (65.6)
Type of injectable antipsychotic agents	
Short-acting injectable antipsychotics	69 (26.6)
Long-acting injectable antipsychotics	53 (20.5)
Both	48 (18.5)

TABLE 3. The demographic characteristics comparison between a group of being treated with LAIs or not.

Demographic characteristics	Total (n=259)	History of being treated with LAIs		Chi2 P-value
		Yes (n=101)	No (n=158)	
Gender				0.054
Male	162 (62.5)	71 (70.3)	91 (57.6)	
Female	97 (37.5)	30 (29.7)	67 (42.4)	
Education level				0.006
Secondary school/below	99 (38.8)	49 (50.0)	50 (31.8)	
High school/diploma	92 (36.1)	33 (33.7)	59 (37.6)	
Bachelor's degree or above	64 (25.1)	16 (16.3)	48 (30.6)	
Occupation				0.78
Employee/Agriculture	68 (26.7)	29 (29.6)	39 (24.8)	
Government employees officer/ state Enterprise officer/ Private company employee	32 (12.5)	12 (12.2)	20 (12.7)	
Merchant/Personal business	37 (14.5)	12 (12.2)	25 (15.9)	
Unemployed/ Student	118 (46.3)	45 (45.9)	73 (46.5)	
Religion				0.024
Buddhism	194 (75.8)	67 (67.7)	127 (80.9)	
Islam/Christianity/Other	62 (24.2)	32 (32.3)	30 (19.1)	
Marital Status				0.095
Single/ Divorced	213 (84.5)	88 (89.8)	125 (81.2)	
Married	39 (15.5)	10 (10.2)	29 (18.8)	
Having income				0.302
No	127 (50.0)	53 (54.6)	74 (47.1)	
Yes	127 (50.0)	44 (45.4)	83 (52.9)	
Having physical illness				0.637
No	199 (79.0)	77 (81.1)	122 (77.7)	
Yes	53 (21.0)	18 (18.9)	35 (22.3)	
Having history of admission				< 0.001
No	97 (39.1)	23 (25.0)	74 (47.4)	
Yes	151 (60.9)	69 (75.0)	82 (52.6)	

medications. However, more than half of the participants (61.8%) felt that their families accepted LAIs treatments. The reasons for refusing to receive LAIs did not appear to be due to a fear of needles or pain at the injection site (49%), but due to a belief that LAIs had more adverse effects than oral medications (47.9%) (Fig 1).

From a comparison between 101 participants who had experienced receiving LAIs and 158 participants who had no experience in receiving LAIs, statistically significant differences in knowledge, and attitude were

identified between these two groups. In regards to the knowledge of LAIs, participants who had experience in receiving LAIs had higher percentages of knowledge in connection to LAIs improving their symptoms (79.6%) and that they must continuously use them even though their mental health had improved (65.3%) than the participants who had no experience of receiving LAIs who had percentages of knowledge at 63.5%, 40.8%, respectively. Regarding attitude toward LAIs, the participants who had an experience of receiving LAIs had less percentage
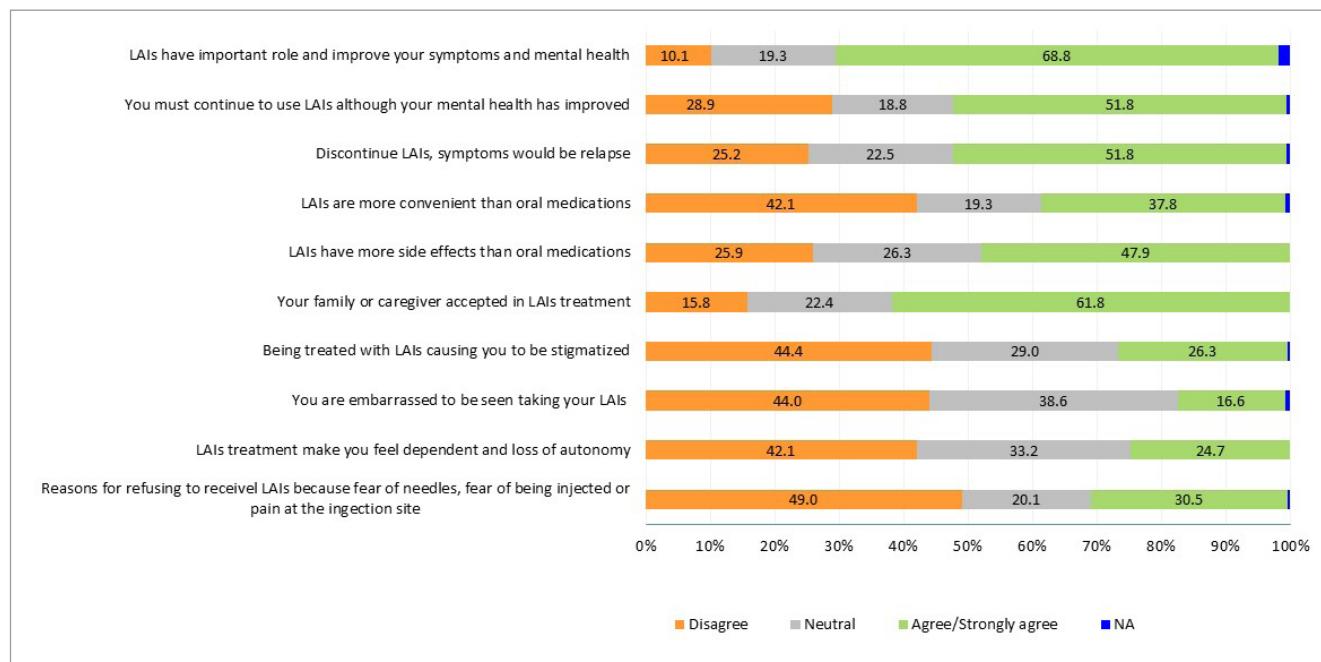
Fig 1. Knowledge and attitudes toward LAIs (N = 259).

of negative attitude and of feeling embarrassed and stigmatized than the participants who had no experience of receiving LAIs. Additionally, they were more likely to have families accepting LAIs treatment (78.2%) than the residual group who had no experience of receiving LAIs (51.3%) (Fig 2).

Satisfaction toward long-acting injectable antipsychotics
Of all 101 schizophrenia patients who had an

experience of receiving LAIs, the majority of them (63.6%) thought that they were involved in the decision or choice of LAIs treatments. Despite this, they were satisfied with the provided information of the risk-benefits from LAIs, type, and cost of LAIs that they received (72.3%, 64.3%, and 75.2% respectively). Regarding LAIs causing any adverse effects, 41 (40.6%) participants agreed that LAIs caused adverse effect, whereas, 40 (39.6%) participants disagreed with LAIs causing any adverse effects (Fig 3).
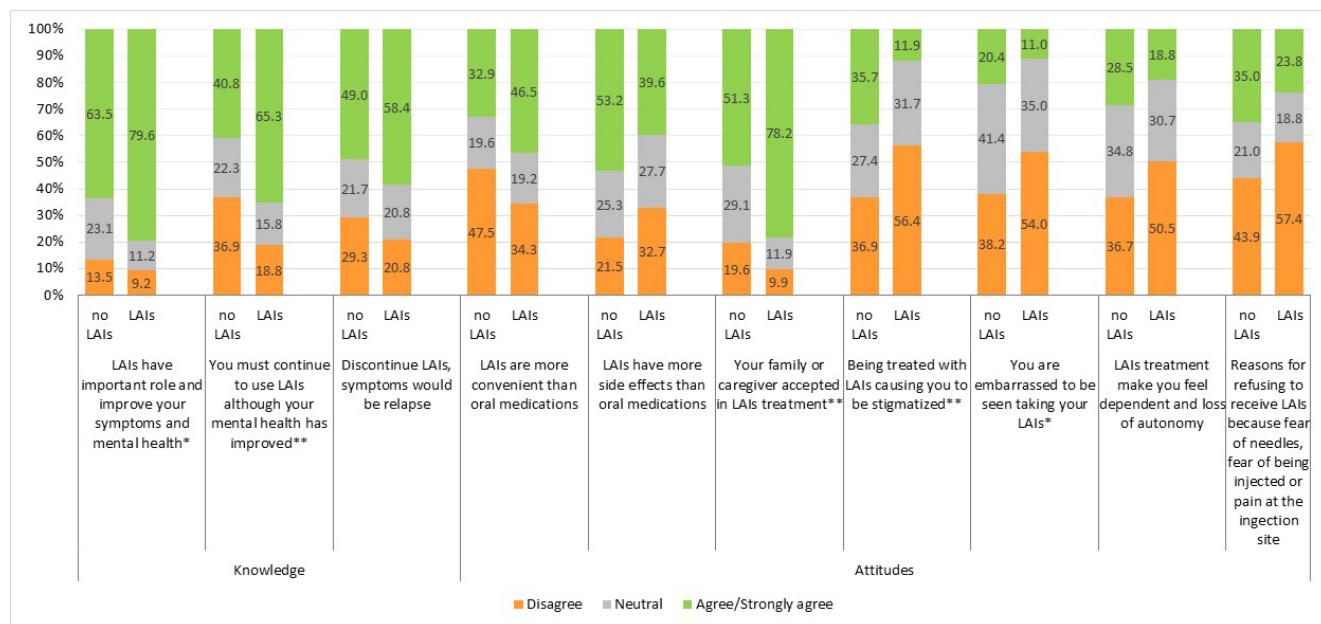
Fig 2. Comparison of knowledge, attitude of schizophrenia patients who received LAIs (N=101) or no experience of receiving LAIs (N = 158).

*p-value<0.05, **p-value<0.001
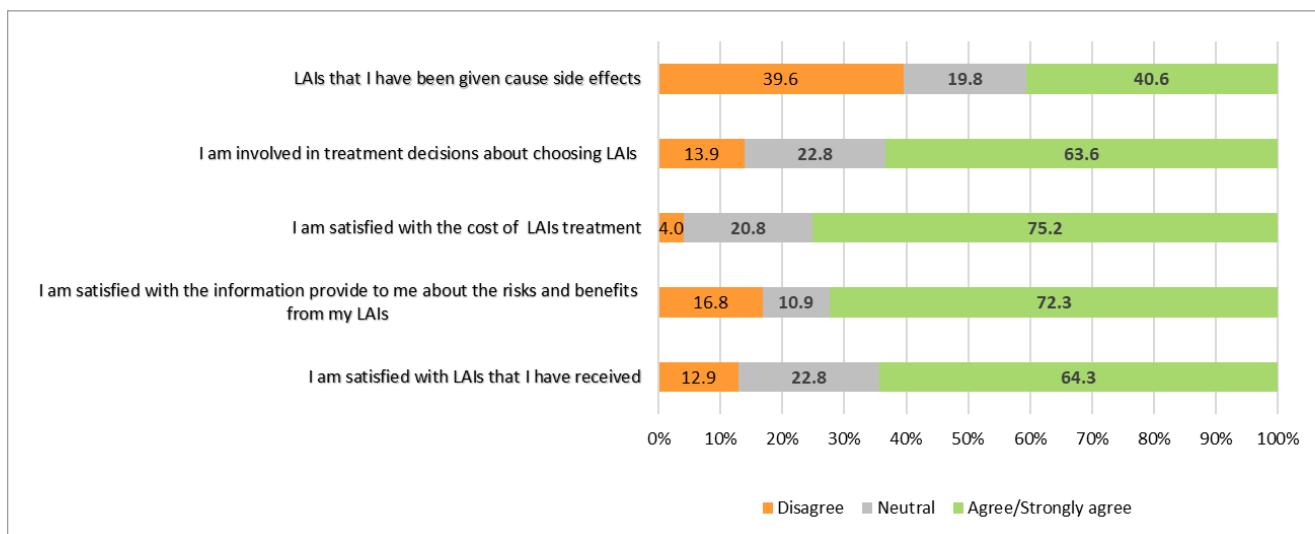
Fig 3. Satisfaction of schizophrenia patient toward LAIs (N = 101).

DISCUSSION

In clinical practice, the advantages and disadvantages of LAIs are still controversial. A better understanding of attitudes toward LAIs would likely enhance their acceptance and use in patients with schizophrenia. The objective of this study was to evaluate the attitudes of schizophrenia patients in regards to LAIs. In our study, there were 101 (39%) participants receiving LAIs. Furthermore, patients who received LAIs had favorable attitudes about LAIs in regards to: being involved in the decision or choice of treatment, family acceptance, efficacy, relapse prevention, type, and cost. However, participants who were receiving LAIs had a higher frequency of past psychiatric inpatient admission than the participants who had no experience of receiving LAIs.

According to the number of patients who received LAIs, this survey found a higher rate than the study in Japan[22] that found twenty-nine (18.2%) participants were on LAIs. However, another study from Australia showed that more than half of schizophrenia patients were receiving LAIs prescriptions.[23] The reason for the different rates of LAIs prescription might be the same as shown in previous studies; that LAIs prescriptions by psychiatrists and the patients' preference for LAIs depended on their preference of antipsychotic treatment in terms of their attitude and experience with the formulation.[10] Some psychiatrists frequently assume that patients with a FES would not recognize depot medication, and that depots were mostly suitable for chronic patients.[8] However, a recent study from several European countries found physicians willing to accept the usage of LAIs, and that having a positive attitude toward LAIs could influence the acceptance and usage of them to treat patients with schizophrenia.[24]

This study found that most patients had favorable attitudes towards LAIs, in regards to their cost. The reason might be that most prescriptions of LAIs in this study were of the conventional type, which incurred less economic burden to the patient and their family than a novel type.

Attitudes toward LAIs in this study identified that, the participants had favorable attitudes toward LAIs concerning efficacy because LAIs improved their symptoms (68.8%), and assisted them to prevent relapse (51.8%). They did not fear needles, being injected, or pain (49%). This finding was the same as a prior study that identified that the expectation of relapse prevention was significantly related with patients' acceptance of LAIs.[22] Moreover, some studies revealed that patients receiving LAIs prescribing rated their current medication useful and helpful, even among patients lacking insight.[23] Choosing the appropriateness of LAIs treatment, providing information of risks and benefits, and side effects from LAIs to patients might enhance the recognition and acceptance of this formulation, among schizophrenia patients. Besides, the discrepancy between the psychiatrists' and patients' opinions regarding the suitability of LAIs treatment was significantly associated with symptom severity, expectations about relapse prevention, beliefs that LAIs are painful, and LAIs providing a reduced range of antipsychotic choices.[22]

Moreover, mental health professionals are required to have a range of competencies to assist patients handle their medication effectively; and when clinicians and patients make a joint decision then they are both more likely to adhere to the treatment plan. Good practice in the administration of LAIs that points on where and when they should be given and administration techniques is

therefore very important. Clinician ability for talking with patients concerning their medication, including the exchange of data, monitoring the effects of medication, and planning choices in advance about treatment, in the event of a crisis should also be scrutinized.[25] This study revealed that the patients felt LAIs were not more convenient than oral antipsychotics (42.1%) and also had more adverse effects than oral antipsychotics (47.9%).

Concerning autonomy and stigmatization, our results indicated that even though more than half of the participants (63.6%) were involved in the choice of LAIs and had family acceptance for LAIs treatment (61.8%); a quarter of them (24.7%) regarded LAIs treatment as something that was limiting their autonomy, caused them to be stigmatized (26.3%), and made them feel embarrassed when seen by others to be taking LAIs (16.6%). A previous study showed that patients, more than psychiatrists, felt that LAIs restricted patient autonomy.[15] Therefore, psychiatrists and the patients' caretakers should be concerned about these ethical issues; especially regarding coercion. In addition, minimizing the patients' feelings of coercion by providing complete information to all patients in a therapeutic relationship, which includes a shared decision-making processes, could also reduce the negative image, being embarrassed by, and the stigmatization attached to depots.[8,17]

Finally, as the destinations of schizophrenia treatment are to manage symptoms, prevent relapse, and enhance both functioning and quality of life, the recommendations should include: 1) adopting a patient-centered approach; 2) selecting medications based on a balanced risk-benefit assessment, including a point on addressing symptoms related to the agents; 3) considering LAIs as an alternative to oral medications, as they offer benefits; such as, uncovering poor adherence, and reduced relapse risk; and 4) implementing psychosocial interventions that have been proven to be effective in enhancing adherence and overall outcomes.[26]

Strengths and limitations

This study had both strengths and limitations worth mentioning. To our knowledge, this is the only study on this topic conducted in Southern Thailand over the past decade. However, this study had some limitations as it was a cross-sectional survey and utilized self-administered questionnaires; therefore, some misunderstanding regarding the intended meaning of the questions may have taken place. Another drawback was that our data was quantitative, the sample size, and that participants were only schizophrenia outpatients in lower, Southern Thailand. Hence, its findings may not fairly represent

the situation of schizophrenia patients throughout the country. Henceforward, studies are recommended to enclose a larger number of schizophrenia patients, with age group and gender differences from other hospitals in Thailand. Therefore, a more comprehensive, multi-centered research study should be performed. Moreover, other studies should retain more qualitative or in-depth methods.

CONCLUSION

Before deciding to prescribe LAIs formulations, the schizophrenia patient's attitude, and knowledge needs to be considered. This is particularly relevant as the care for schizophrenia is focused on symptom control, relapse prevention, and optimizing their quality of life. Clinicians should ensure that patients receive access to information such as the risks and benefits of treatment with LAIs, helping to improve the acceptance and use of such formulations and addressing any concerns that LAIs treatment is limiting their autonomy or causing stigmatization.

ACKNOWLEDGMENTS

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Kidney Health for all: Bridging the Gap in Kidney Health Education and Literacy

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ABSTRACT

The high burden of kidney disease, global disparities in kidney care, and poor outcomes of kidney failure bring a concomitant growing burden to persons affected, their families, and carers, and the community at large. Health literacy is the degree to which persons and organizations have or equitably enable individuals to have the ability to find, understand, and use information and services to make informed health-related decisions and actions for themselves and others. Rather than viewing health literacy as a patient deficit, improving health literacy largely rests with health care providers communicating and educating effectively in codesigned partnership with those with kidney disease. For kidney policy makers, health literacy provides the imperative to shift organizations to a culture that places the person at the center of health care. The growing capability of and access to technology provides new opportunities to enhance education and awareness of kidney disease for all stakeholders. Advances in telecommunication, including social media platforms, can be leveraged to enhance persons' and providers' education; The World Kidney Day declares 2022 as the year of "Kidney Health for All" to promote global teamwork in advancing strategies in bridging the gap in kidney health education and literacy. Kidney organizations should work toward shifting the patient-deficit health literacy narrative to that of being the responsibility of health care providers and health policy makers. By engaging in and supporting kidney health–centered policy making, community health planning, and health literacy approaches for all, the kidney communities strive to prevent kidney diseases and enable living well with kidney disease.

Keywords: Educational gap; empowerment; health literacy; health policy; information technology; kidney health; partnership; prevention; social media (Siriraj Med J 2022; 74: 202-210)

Given the high burden of kidney disease and global disparities related to kidney care, in carrying forward our mission of advocating *Kidney Health for All*, the challenging issue of bridging the well-identified gap in the global understanding of kidney disease and its health literacy is the theme for World Kidney Day (WKD) 2022. Health literacy is defined as the degree to which persons and organizations have-or equitably enable individuals to have-the ability to find, understand, and use information and services to inform health-related decisions and actions for themselves and others.[1] Not only is there is growing recognition of the role that health literacy has in determining outcomes for persons affected by kidney disease and the community in general, but there is an emergent imperative for policy makers worldwide to be informed and cognizant of opportunities and real measurable outcomes that can be achieved through kidney-specific preventative strategies.

The global community of people with kidney disease

Most people are not aware of what kidneys are for or even where their kidneys are. For those afflicted by disease and the subsequent effects on overall health, an effective health care provider communication is required to support individuals to be able to understand what to do, to make decisions, and to take action. Health literacy involves more than functional abilities of an individual; it is also the cognitive and social skills needed to gain access to, understand, and use information to manage health condition.[2] It is also contextual[3] in that as health needs change, so too does the level of understanding and ability to problem solve alter. Health literacy is, therefore, an interaction between individuals, health care providers, and health policy makers.[4] This why the imperatives around health literacy are now recognized as indicators for the quality of local and national health care systems and health care professionals within it.[5] For Chronic Kidney Disease (CKD), as the disease progresses alongside other health changes and increasing treatment complexities, it becomes more difficult for individuals to manage.[6] Promoted in health policy for around a decade involving care partnerships between health-centered policy, community health planning, and health literacy,[7] current approaches need to be shifted forward (Table 1).

Assessing health literacy necessitates the use of appropriate multidimensional patient-reported measures, such as the World Health Organization–recommended Health Literacy Questionnaire (available in over 30 languages) rather than tools measuring only functional health literacy (e.g., Rapid Estimate of Adult Literacy in Medicine or Short Test of Functional Health Literacy

in Adults).[8] It is therefore not surprising that studies of low health literacy (LHL) abilities in people with CKD have been demonstrated to be associated with poor CKD knowledge, self-management behaviors, and health-related quality of life and in those with greater comorbidity severity.[7] Unfortunately, most CKD studies have measured only functional health literacy, so the evidence that LHL results in poorer outcomes, particularly that it increases health care utilization and mortality,[9] and reduces access to transplantation,[10] is weak.

Recently, health literacy is now considered to be an important bridge between lower socioeconomic status and other social determinants of health.[4] Indeed, this is not a feature that can be measured by the gross domestic product of a country, as the effects of LHL on the extent of CKD in the community are experienced globally regardless of country income status. The lack of awareness of risk factors of kidney disease, even in those with high health literacy abilities, is testament to the difficulties in understanding this disease, and why the United States, for instance, recommends that a universal precautions approach toward health literacy is undertaken.[11]

So, what does the perfect health literacy program look like for people with CKD? In several high-income countries, there are national health literacy action plans with the emphasis shifted to policy directives, organizational culture, and health care providers. In Australia, for instance, a compulsory health literacy accreditation standard makes the health care organization responsible for ensuring providers are cognizant of individual health literacy abilities.[12] Although many high-income countries, health care organizations, nongovernmental organizations, and jurisdictions are providing an array of consumer-facing web-based programs that provide detailed information and self-care training opportunities, most are largely designed for individual/family use that are unlikely to mitigate LHL. There is, however, substantial evidence that interventions improving health care provider communication are more likely to improve understanding of health problems and abilities to adhere to complex treatment regimens.[13]

Access to information that is authentic and tailored specifically to the needs of the individual and the community is the aim. The challenge is recognized acutely in more remote and low- to middle-income countries of the world, specifically the importance of culturally appropriate knowledge provision. The principals of improving health literacy are the same, but understanding how to proceed, and putting consumers in charge, with a codesign approach, is critical and may result in a different outcome in more remote parts of the world. This principal especially applies to communities that are smaller, with less access to

TABLE 1. Summary characteristic of kidney health promotion, involving kidney health–centered policy, community kidney health planning, and kidney health literacy, and proposed future direction.

Kidney health promotion	Definition	Stakeholders	Current status	Limitations/ challenges	Suggested solutions /future research

Kidney health-centered policy	• Incorporate kidney health into policy decision making
	• Prioritize policies with primary prevention for CKD
		• Governance
		• Policy makers
		• Insurance agencies
			• Policy emphasizing treatment for CKD and kidney failure rather than kidney health prevention	• Economic-driven situation challenging CKD risk factor minimization (e.g., food policy)	• Promote implementation of public health program for primary CKD prevention
					• Promote sustainable treatment for CKD and dialysis
					  - Increase kidney transplant awareness
					  - Enhance visibility and encourage brother-sister nephrology and transplant program in LMIC
					• Support research funding from government
					  - Health care cost-effectiveness for caring for CKD
					  - Kidney failure, including maintenance dialysis and transplant
					  - Promote surveillance programs for kidney diseases and their risk factors

Community kidney health planning	• Building up preventive strategies to promote healthy communities and primary health care facilities	• Community leadership • Kidney patient advocacy	• Belief in community leaders in LMIC	• Education and understanding kidney health promotion of community leadership and people	• Improve role model of community • Enhance kidney support networks
Kidney health literacy	• Receive knowledge, skills, and information to be healthy	• People with CKD • Care partners • Health care providers	• Lack of awareness of CKD and risk factors • Care partner burden and burnout • Inadequate health care workers • High patients-to-health care workers ratio, especially in rural areas	• Inadequate policy direction • Ineffective health care providers' communication skills	• Organizational paradigm shift toward health literacy • Improving communication between health care providers with patients and care partners • Using teach-back methods for consumer education • Adapting technologies for appropriate health literacy and sociocultural environments • Family engagement in the patient care • Incentive for community health care providers in rural areas

Abbreviations: CKD = chronic kidney disease; LMIC = low- to middle-income country.

electronic communication and health care services, where the level of health literacy is shared across the community and where what affects the individual also affects all the community. Decision support systems are different, led by elders, and in turn educational resources are best aimed at improving knowledge of the whole community.

A systematic review of the evaluation of interventions and strategies shows this area of research is still at an early stage,[14] with no studies unravelling the link between LHL and poor CKD outcomes. The best evidence is in supporting targeted programs on improving communication capabilities of health care professionals as central. One prime example is Teach-back, a cyclical, simple, low-cost education intervention, shows promise for improving communication, knowledge, and self-management in the CKD populations in low- or high-income countries.[15] Furthermore, the *consumer*-led voice has articulated research priorities that align closely with principals felt to be important to success of education: building new education resources, devised in partnership with consumers, and focused on the needs of vulnerable groups. Indeed, programs that address the lack of culturally safe, person-centred and holistic care, along with improving the communication skills of health professionals, are crucial for those with CKD.[16]

The networked community of kidney health care workers

Nonphysician health care workers, including nurses and advanced practice providers (physician assistants and nurse practitioners) as well as dietitians, pharmacists, social workers, technicians, physical therapists, and other allied health professionals, often spend more time with persons with kidney disease, compared with nephrologists and other physician specialists. In an ambulatory care setting at an appointment, in the emergency department, or in the inpatient setting, these health care professionals often see and relate to the patient first, last, and in between, given that physician encounters are often short and focused. Hence, the nonphysician health care workers have many opportunities to discuss kidney disease-related topics with the individuals and their care partners and to empower them.[17,18] For instance, medical assistants can help identify those with or at risk of developing CKD and can initiate educating them and their family members about the role of diet and lifestyle modification for primary, secondary, and tertiary prevention of CKD while waiting to see the physician.[19] Some health care workers provide networking and support for kidney patient advocacy groups and kidney support networks, which have been initiated or expanded via social media platforms (Fig 1).[20,21] Studies examining the efficacy of social media in kidney care and advocacy are on the way.[22,23]

Like physicians, many activities of nonphysician health care workers have been increasingly affected by the rise of electronic health recording and growing access to internet-based resources, including social media, that offer educational materials related to kidney health, including kidney-preserving therapies with traditional and emerging interventions.[24] These resources can be used for both self-education and for networking and advocacy on kidney disease awareness and learning. Increasingly, more health care professionals are engaged in some types of social media-based activities, as shown in Table 2. At the time of this writing, the leading social media used
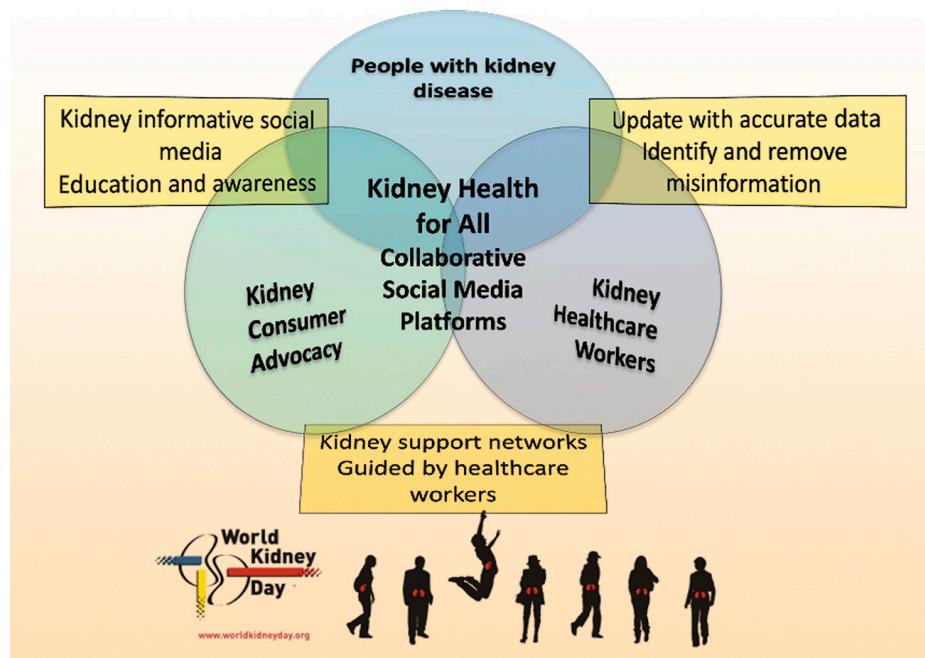

Fig 1. Schematic representation of consumer and health care professionals' collaborative advocacy using social media platforms with the goal of Kidney Health for All.

TABLE 2. Social media that are more frequently used for kidney education and advocacy.

Social media	Strength	Limitations	Additional comments
Facebook	► Frequently used social media platform by many kidney patients and patient groups	► Widely used for entertaining purposes, which can dilute its professional utility	► User-friendly platform for kidney advocacy, enabling wide ranges of outreach goals
Instagram	► Photo-predominating platform	► Not frequently used by health care professionals	► Picture friendly, potentially effective for illustrative educational purposes
Twitter	► Often used by physician specialists and scientists, including nephrologists	► Less frequently used by patients and care partners	► Increasing popularity among physician and specialty circles
LinkedIn	► More often used by professionals, including in industry	► Originally designed for employment and job-seeking networking	► Mostly effective to reach out to industry and managerial professionals
YouTube	► Video-predominating platform	► Less effective with non–video-based formats	► Wide ranges of outreach and educational targets
WeChat	► Widely used in mainland China	► Access is often limited to those living in China or its diaspora	► Effective platform to reach out to patients and health care professionals in China
Pinterest	► Picture-based, often used by dietitians	► Currently limited use by some health care workers	► Useful for dietary and lifestyle education

Other popular social media at the time of this publication include, but not limited to, Tik Tok, Snapchat, Reddit, Tumblr, Telegram, Quora, and many others that are currently only occasionally used in kidney advocacy activities. Mobile and social media messaging apps include, but not limited to, WhatsApp, Zoom, Facebook Messengers, Skype Teams, and Slack.
Note: That platforms that are more often used as internet-based messaging are not included.

by many-but not all-kidney health care workers include Facebook, Instagram, Twitter, LinkedIn, and YouTube. In some regions of the world, certain social media are more frequently used than others given unique cultural or access constellations (e.g., WeChat is a platform often used by health care workers and patient groups in China). Some health care professionals, such as managers and those in leadership and advocacy organization positions, may choose to embark on social media to engage those with CKD and their care partners or other health care professionals in alliance building and marketing. To that end, effective communication strategies and outreach skills specific to responsible use of social media can provide clear advantages given that these skills and strategies

are different and may need modification in those with LHL. It is imperative to ensure the needed knowledge and training for accountable approach to social media is provided to health care providers, so that these outreach strategies are utilized with the needed awareness of their unique strengths and pitfalls, as follows[25]:

(i) Consumers' and care partners' confidentiality may not be breached upon posting anything on social media, including indirect referencing to a specific individual or a particular description of a condition unique to a specific person (e.g., upon soliciting for transplant kidney donors on social media).[26,27]

(ii) Confidential information about clinics, hospitals, dialysis centers, or similar health care and advocacy

entities may not be disclosed on social media without ensuring that the needed processes, including collecting authorizations to disclose, are undertaken.

(iii) Health care workers' job security and careers should remain protected with thorough review of the content of the messages and illustrations/videos before online posting.

(iv) Careless and disrespectful language and emotional tones are often counterproductive and may not be justified under the context of freedom of speech.

The global kidney community of policy and advocacy

Policy and advocacy are well-recognized tools that, if properly deployed, can bring about change and paradigm shift at jurisdictional level. The essence of advocating for policy change to better address kidney disease is, in itself, an exercise in improving health literacy of the policy makers. Policy development, at its core, is a key stakeholder or stakeholder group (e.g., the kidney community, who believes that a problem exists that should be tackled through governmental action). There is an increasing recognition of the importance of formulating succinct, meaningful, and authentic information, akin to improving health literacy, to present to government for action.

Robust and efficacious policy is always underpinned by succinct and applicable information; however, the development and communication of this message, designed to bridge the gap in knowledge of relevant jurisdictions, is only part of the process of policy development. An awareness of the process is important to clinicians who are aiming to advocate for effective change in prevention or improvement of outcomes in the CKD community.

Public policies, the plans for future action accepted by governments, are articulated through a political process in response stakeholder observation, usually written as a directive, law, regulation, procedure, or circular. Policies are purpose fit and targeted to defined goals and specific societal problems and are usually a chain of actions effected to solve those societal problems.[28] Policies are an important output of political systems. Policy development can be formal, passing through rigorous lengthy processes before adoption (such as regulations), or it can be less formal and quickly adopted (such as circulars). As already mentioned, the governmental action envisaged by the key stakeholders as solution to a problem is at its core. The process enables stakeholders to air their views and bring their concerns to the fore. Authentic information that is meaningful to the government is critical. The policy development process can be stratified into 5 stages (i.e., the policy cycle), as depicted by Anderson (1994)[29] and adapted and modified by other authors[30] (Fig 2).
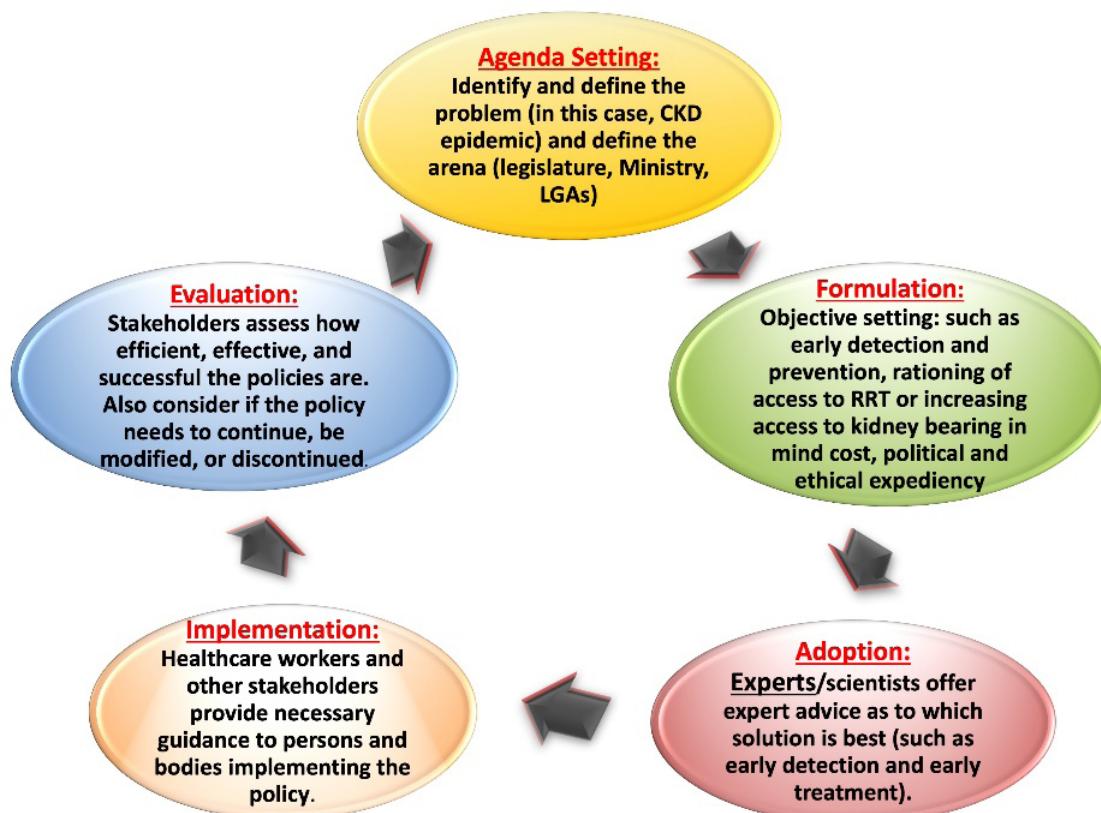

Fig 2. Policy cycle involving 5 stages of policy development.
Abbreviations: CKD=chronic kidney disease; KRT=kidney replacement therapy; LGA=local government area.

The policy cycle constitutes an expedient framework for evaluating the key components of the process.

Subsequently, the policy moves on to implementation phase. This phase may require subsidiary policy development and adoption of new regulations or budgets (implementation). Policy evaluation is integral to the policy processes and applies evaluation principles and methods to assess the content, implementation, or impact of a policy. Evaluation facilitates understanding and appreciation of the worth and merit of a policy as well as the need for its improvement. More important, of the 5 principles of advocacy that underline policy making,[31] the most important for clinicians engaged in this space is that of commitment, persistence, and patience. Advocacy takes time to yield the desired results.

The Advocacy Planning Framework, developed by Young and Quinn in 2002,[30] consists of overlapping circles representing 3 sets of concepts (way into the process, the messenger, and message and activities) that are key to planning any advocacy campaign:

(i) "Way into the process": discusses the best approaches to translate ideas into the target policy debate and identify the appropriate audience to target.

(ii) Messenger: talks about the image maker or face of the campaign and other support paraphernalia that are needed.

(iii) Message and activities: describe what can be said to the key target audiences that is engaging and convincing. And how best it can be communicated through appropriate communication tools.

Advocacy is defined as "an effort or campaign with a structured and sequenced plan of action which starts, directs, or prevents a specific policy change."[31] The goal being to influence decision makers through communicating directly with them or getting their commitment through secondary audiences (advisers, the media, or the public) to the end that the decision maker understands, is convinced, takes ownership of the ideas, and finally has the compulsion to act.[31] As with improving health literacy, it is the communication of ideas to policy makers for adoption and implementation as policy that is key. There is much to be done with bridging this gap in understanding of the magnitude of community burden that results from CKD. Without good communication, many good ideas and solutions do not reach communities and countries where they are needed. Again, aligned with the principles of developing resources for health literacy, the approach also needs to be nuanced according to the local need, aiming to have the many good ideas and solutions be communicated to communities and countries where they are needed.

Advocacy requires galvanizing momentum and support for the proposed policy or recommendation. The process is understandably slow as it involves discussions and negotiations for paradigms, attitudes, and positions to shift. In contemplating advocacy activities, multiple factors must be considered, interestingly not too dissimilar to that of building health literacy resources: What obstructions are disrupting the policy-making process from making progress? What resources are available to enable the process to succeed? Is the policy objective achievable considering all variables? Is the identified problem already being considered by the policy makers (government or multinational organizations)? Any interest or momentum generated around it? Understandably, if there is some level of interest and if government already has its spotlight on the issue, it is likely to succeed.

Approaches to choose from include the following[31,32]:

- Advising (researchers are commissioned to produce new evidence-based proposals to assist the organization in decision making).
- Activism: involves petitions, public demonstrations, posters, fliers, and leaflet dissemination, often used by organizations to promote a certain value set.
- Media campaign: having public pressure on decision makers helps in achieving results.
- Lobbying: entails face-to-face meetings with decision makers; often used by business organizations to achieve their purpose.

Here lies the importance of effective and successful advocacy to stakeholders, including policy makers, health care professionals, communities, and key change makers in society. The WKD, since inception, has aimed at playing this role. WKD has gained people's trust by delivering relevant and accurate messaging and supporting leaders in local engagement, and it is celebrated by kidney care professionals, celebrities, those with the disease, and their care givers all over the world. To achieve the goal, an implementation framework of success in a sustainable way includes creativity, collaboration, and communication.

The ongoing challenge for the International Society of Nephrology and International Federation of Kidney Foundations-World Kidney Alliance, through the Joint Steering Committee of WKD, is to operationalize how to collate key insights from research and analysis to effectively feed the policy-making process at the local, national, and international levels, to inform or guide decision making (i.e., increasing engagement of governments and organizations, like World Health Organization,

United Nations, and regional organizations, especially in low-resource settings). There is a clear need for ongoing renewal of strategies to increase efforts at closing gap in kidney health literacy, empowering those affected with kidney disease and their families, giving them a voice to be heard, and engaging with the civil society. This year, the Joint Steering Committee of WKD declares *"Kidney Health for All"* as the theme of the 2022 WKD to emphasize and extend collaborative efforts among people with kidney disease, their care partners, health care providers, and all involving stakeholders for elevating education and awareness on kidney health and saving lives with this disease.

CONCLUSION

In bridging the gap of knowledge to improve outcomes for those with kidney disease on a global basis, an in-depth understanding of the needs of the community is required. The same can be said for policy development, understanding the processes in place for engagement of governments worldwide, all underpinned by the important principal of codesign of resources and policy that meets the needs of the community for which it is intended.

For World Kidney Day 2022, kidney organizations, including the International Society of Nephrology and International Federation of Kidney Foundations-World Kidney Alliance, have a responsibility to immediately work toward shifting the patient-deficit health literacy narrative to that of being the responsibility of clinicians and health policy makers. LHL occurs in all countries regardless of income status; hence, simple, low-cost strategies are likely to be effective. Communication, universal precautions, and teach back can be implemented by all members of the kidney health care team. Through this vision, kidney organizations will lead the shift to improved patient-centered care, support for care partners, health outcomes, and the global societal burden of kidney health care.

Conflict of Interest disclosure

APPENDIX

The World Kidney Day Joint Steering Committee includes coauthors Robyn G. Langham, Kamyar Kalantar-Zadeh, Alessandro Balducci, Li-Li Hsiao, Latha A. Kumaraswami, Paul Laffin, Vassilios Li

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