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ORIGINAL ARTICLE

Genotypic diversity of *Streptococcus suis* strains isolated from humans in Thailand

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Abstract

The purpose of this study is to characterize *Streptococcus suis* isolates recovered from human infections regarding serotype distribution, genotypic profile, clinical manifestations, and epidemiology. A total of 668 *S. suis* isolates recovered from human infections in Thailand were characterized based on serotyping by multiplex PCR and co-agglutination, genotypic profiles by multilocus sequence typing, and PCR for virulence-associated genes, as well as review of medical records. Serotype 2 (94.6%) was predominant, followed by serotype 14 (4.5%), 24 (0.45%), 5 (0.3%), and 4 (0.15%). Multilocus sequence typing analyses revealed seven clonal complexes (CC): CC1 (56.43%), CC104 (31.74%), CC233/379 (5.4%), CC25 (4.5%), CC28 (0.9%), CC221/234 (0.6%), CC94 (0.15%), and two singletons. The CC1 group contained serotype 2 and 14 isolates, while CC25, 28, 104, and 233/379 consisted of serotype 2 isolates only. CC221/234 contained serotype 5 and 24 isolates, whereas the single serotype 4 isolate belonged to CC94. Two singletons contained serotype 5 (ST235) and 2 (ST236) isolates. Our data showed that ST1 isolates were more associated with meningitis than those of other STs ($p < 0.001$). The major route of infection was shown to be close contact with infected pigs or contaminated raw pork-derived products, including occupational exposure and recent consumption of raw pork products. This study revealed a relatively large number of CCs of *S. suis* causing human infection in Thailand. Among them, CC1 followed by CC104, with serotype 2 isolates, are predominant. Food safety campaigns and public health interventions would be important for controlling the *S. suis* infection in humans.

Introduction

Streptococcus suis, an important zoonotic pathogen, causes invasive infections in humans in close contact with infected pigs or contaminated pork-derived products [1]. The number of reported human cases, especially in Southeast Asian countries, has dramatically increased in the past few years [1, 2]. Currently, 29 serotypes of *Streptococcus suis* have been recognized [3]. Of these serotypes, serotype 2 is the most prevalent in *S. suis* human infections, although cases caused by serotypes 4, 5, 9, 14, 16, 21, 24, and 31 have also been reported [1, 2, 4–8]. In a retrospective study that included human field strains recovered from 2006 to 2008 in Thailand, clonal complexes (CC) 1, 25, 28, and 104 were shown to be responsible for human infections, with sequence type (ST) 1 (within CC1) being the most frequently found, followed by ST104 (CC104) [8].

In the present study, an additional 668 *S. suis* isolates recovered from human infections in Thailand between 2009 and 2012 were further characterized regarding serotype distribution, genotypic profile, and clinical manifestations.

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Materials and methods

Bacterial isolates and identification A total of 668 isolates of *S. suis* recovered from blood, cerebrospinal fluid (CSF), synovial fluid, or other body fluids were collected from 41 hospitals in 39 provinces distributed in 5 regions (north, northeast, central, east, and south) of Thailand between January of 2009 and December of 2012 [Supplemental file 1]. Presumptive identification and antimicrobial susceptibility of *S. suis* were carried out in the hospitals where the pathogen was originally isolated and sent us to confirmation. A multiplex PCR assay and the co-agglutination test were used to identify and serotype these *S. suis* isolates [9, 10].

Genotypic profiles Multilocus sequence typing (MLST) was performed as described elsewhere [11, 12]. MLST alleles, resulting STs, and the CC were assigned and analyzed using the *S. suis* MLST database, which can be accessed at https://pubmlst.org/ssuis/. The presence of virulence-associated genes (VAG), including the extracellular protein factor (*epf*), the muramidase-released protein (*mrp*), and the suilysin (*sly*), was determined by PCR as described by Silva et al. [13].

Human cases and statistical analyses The medical records of 659 cases were reviewed by attending physicians at local hospitals in Thailand using the clinical case record form approved by the Ethics Committee of the Department of Medical Sciences, Ministry of Public Health, Thailand. The medical records of the remaining nine patients were not available. The clinical manifestations of *S. suis* infections were classified into meningitis, sepsis, septic arthritis, infective endocarditis, and spontaneous peritonitis according to a criteria described elsewhere [8, 14–17]. Clinical isolates were categorized according to ST and VAG profiles. The association between these categories and two clinical manifestations (meningitis and non-meningitis) was analyzed by Fisher's exact test with the Stata version 10.0 software (StataCorp, College Station, TX, USA). Data were considered significant at $p < 0.01$.

Results

Serotype distribution of *S. suis* isolates Of the 668 isolates, multiplex PCR and the co-agglutination test with specific antisera revealed 632 isolates of serotype 2 (94.6%), 30 of serotype 14 (4.5%), three of serotype 24 (0.45%), two of serotype 5 (0.3%), and one of serotype 4 (0.15%) (Table 1).

Genotypic profiles of *S. suis* isolates MLST classified 668 isolates into seven CCs and two singleton (Table 1 and Fig. 1). The CCs were identified as follows: CC1 (56.43%), CC104 (31.74%), CC233/379 (5.4%), CC25 (4.5%), CC28 (0.9%), CC221/234 (0.6%), and CC94 (0.15%). The CC1 contained more than 50% of all serotype 2 isolates, with ST1 being the predominant sequence type. Interestingly, CC1 also contained all 30 serotype 14 isolates, with 29 being ST105 and only one belonging to ST11. CC104 was the second most important group with 212 isolates, all serotype 2, with seven different STs. CC25 was composed by 30 isolates, also all serotype 2, with 7 different STs, whereas CC233/379, a newly herein described CC responsible for human infections, included ST233 and ST379, with all isolates also belonging to serotype 2 (Table 1 and Fig. 1). Interestingly, CC233/379 was closely related to CC104, with two locus variants (*gki* and *thrA*). Indeed, the allelic profile of CC233/379 is 8-30-5-(72/97)-44-21-75, whereas that of ST104 is 8-30-5-1-44-21-4. CC28 was also composed of serotype 2 isolates belonging to either ST28 or ST382. Isolates belonging to serotypes other than 2 and 14 were distributed in CC94 (serotype 4) and CC221/234 (serotypes 5 and 24). Two isolates could not be attributed to any known CC, belonging to ST235 (serotype 5) and ST236 (serotype 2) (Table 1).

As shown in Table 1, eight VAG profiles were obtained by PCR: $epf^{+}/sly^{+}/mrp^{+}$ ($n = 377$, 56.4%), $epf^{-}/sly^{+}/mrp^{+}$ ($n = 2$, 0.3%), $epf^{-}/sly^{+}/mrp^{s}$ ($n = 2$, 0.3%), $epf^{-}/sly^{-}/mrp^{+}$ ($n = 20$, 3%), $epf^{-}/sly^{-}/mrp^{*}$ ($n = 12$, 1.8%), $epf^{-}/sly^{-}/mrp^{**}$ ($n = 4$, 0.6%), $epf^{-}/sly^{+}/mrp^{-}$ ($n = 248$, 37.2%), and $epf^{-}/sly^{-}/mrp^{-}$ ($n = 3$, 0.4%). Serotype 2 showed six VAG profiles: $epf^{+}/sly^{+}/mrp^{+}$ or $epf^{-}/sly^{+}/mrp^{s}$ profiles, mainly found in CC1; $epf^{-}/sly^{-}/mrp^{+}$ or $epf^{-}/sly^{-}/mrp^{*}$ or $epf^{-}/sly^{-}/mrp^{**}$ profile associated with CC25; $epf^{-}/sly^{-}/mrp^{+}$ profile found in CC28; and $epf^{-}/sly^{+}/mrp^{-}$ profile associated with CC104 and CC233/379. Serotype 14 (CC1) isolates presented $epf^{+}/sly^{+}/mrp^{+}$ or $epf^{-}/sly^{+}/mrp^{s}$ profiles, while serotype 4 (CC94) showed $epf^{-}/sly^{+}/mrp^{+}$. Finally, two serotype 5 isolates (ST221 and ST235) revealed a $epf^{+}/sly^{+}/mrp^{+}$, while the VAG profile of isolates of serotype 24 (CC221/234) was $epf^{-}/sly^{-}/mrp^{-}$.

Isolation sites and dates Of the 668 isolates, 391 (58.53%) were recovered from patients of the northern region, 140 (20.96%) from patients of the northeastern region, 102 (15.26%) from those of the central region, 30 (4.5%) from those of the east region, and 5 (0.75%) from those of the southern region (Supplemental file 1). The dates of *S. suis* isolation as well as their relationship with temperature or rainfall are shown in Fig. 2. In 2009, human cases occurred more frequently in September, whereas 1 year later, the peak was between April and June. Human cases in 2011 increased from April to August and in 2012, the peaks were increased from March to May. It is interesting that the peak of human cases in 2010–2012 are, in general, in agreement with rising rainfall (Fig. 2). In general, the mean

Table 1 *S. suis* clonal complexes and their serotype distribution among isolates recovered from human patients in Thailand

CC	ST	VAG	Serotype and no. of isolates					Total
			Serotype 2	Serotype 14	Serotype 4	Serotype 5	Serotype 24	
1	1	$epf^{+}_{+}/sly^{+}/mrp$	329					329
	11	$epf^{-}_{s}/sly^{+}/mrp$	1	1				2
	105	$epf^{+}_{+}/sly^{+}/mrp$	4	29				33
	144		7					7
	298		1					1
	337		5					5
25	25	$epf^{-}_{+}/sly^{-}/mrp$	3					3
		$epf^{-}_{*}/sly^{-}/mrp$	5					5
		$epf^{-}_{**}/sly^{-}/mrp$	2					2
	103	$epf^{-}_{+}/sly^{-}/mrp$	2					2
		$epf^{-}_{*}/sly^{-}/mrp$	2					2
	380	$epf^{-}_{+}/sly^{-}/mrp$	3					3
		$epf^{-}_{*}/sly^{-}/mrp$	4					4
		$epf^{-}_{**}/sly^{-}/mrp$	2					2
	381	$epf^{-}_{+}/sly^{-}/mrp$	3					3
		$epf^{-}_{*}/sly^{-}/mrp$	1					1
	395	$epf^{-}_{+}/sly^{-}/mrp$	1					1
	515		1					1
	516		1					1
28	28	$epf^{-}_{+}/sly^{-}/mrp$	4					4
	382		2					2
104	104	$epf^{-}_{-}/sly^{+}/mrp$	186					186
	391		9					9
	392		4					4
	393		1					1
	512		8					8
	513		1					1
	514		3					3
233/379	233	$epf^{-}_{-}/sly^{+}/mrp$	33					33
	379		3					3
94	94	$epf^{-}_{+}/sly^{+}/mrp$			1			1
221/234	221	$epf^{+}_{+}/sly^{+}/mrp$				1		1
		$epf^{-}_{-}/sly^{-}/mrp$					2	2
	234	$epf^{-}_{-}/sly^{-}/mrp$					1	1
None	235	$epf^{+}_{+}/sly^{+}/mrp$				1		1
	236	$epf^{-}_{+}/sly^{+}/mrp$	1					1
Total			*632*	*30*	*1*	*2*	*3*	*668*

mrp^{s} = the small variant of *mrp* (PCR product size ≈747 bp); *mrp** = the large variant of *mrp* (PCR product size ≈1556 bp); *mrp*** = the larger variant of *mrp* (PCR product size ≈1600 bp)

temperature in the whole of Thailand between 2009 and 2012 was about 27.2 °C (range 23.2–29.1), 27.9 °C (range 25.1–30.8), 26.8 °C (range 24.1–28.4), and 27.7 °C (range 25.4–29.4), respectively. Indeed, no significant changes of temperature during these years could be associated with the number of diagnosed cases (Fig. 2).

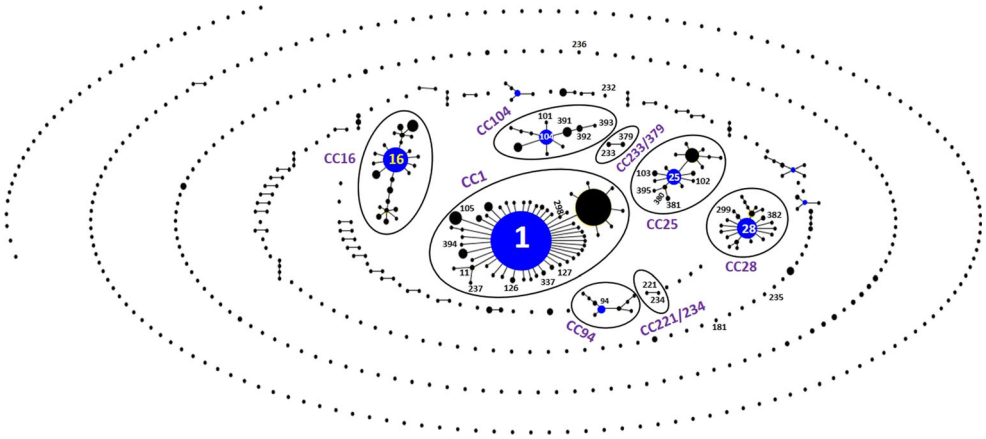

Fig. 1 An eBURST analysis of the entire *S. suis* MLST database (accessed on July 25, 2017). Clonal complexes relevant to human infection in Thailand are circled and labeled. Clonal complexes and the predicted founding STs are indicated by blue dots. The size of the dots is relative to the number of isolates with the respective ST present in the database (Color figure online)

Clinical features and relationship with the genotypic profiles of *S. suis* isolates The demographic data revealed that *S. suis* cases were recovered from 134 females (20.3%) and 525 males (79.7%). The mean age was 56.5 years old, and median age was 56 (range 23–92 years old). The clinical features of the 659 human cases of *S. suis* infection are summarized in Table 2. Meningitis cases ($n = 141$) were mainly caused by CC1 isolates ($n = 118$; 83.7%), especially ST1 ($n = 106$), followed by CC104 ($n = 21$; 14.9%). Sepsis ($n = 501$) could be associated with isolates belonging to all CCs and two singletons (ST235 and ST236). CC1 isolates ($n = 239$) also accounted for 47.7% of the sepsis cases, followed by those of CC104 ($n = 187$; 37.3%). Infective endocarditis ($n = 10$) was mainly caused by CC1 isolates ($n = 7$). Septic arthritis

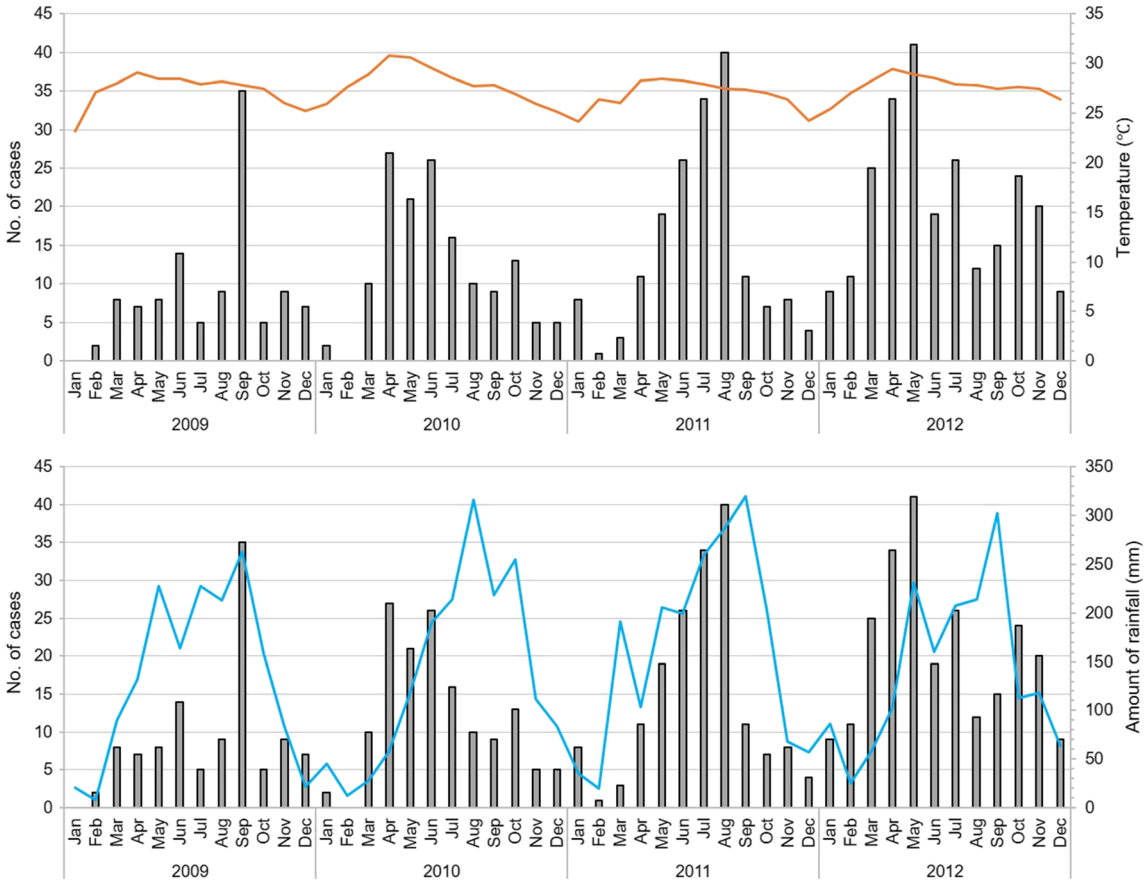

Fig. 2 Seasonal distribution of the cases, temperature, and rainfall from 2009 to 2012 in Thailand

Table 2 Clinical manifestations and clonal complexes of *S. suis* isolates recovered from human patients in Thailand

CC	ST	VAG	Clinical manifestation					Total
			Sepsis	Meningitis	Infective endocarditis	Septic arthritis	Spontaneous peritonitis	
1	1	*epf*$^{+}$/*sly*$^{+}$/*mrp*$^{+}$	204	106	7	4		321
	11	*epf*$^{-}$/*sly*$^{+}$/*mrp*^{s}	2					2
	105	*epf*$^{+}$/*sly*$^{+}$/*mrp*$^{+}$	22	11				33
	144		6			1		7
	298		1					1
	337		4	1				5
25	25	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				2		1
				3				
		epf^{-}/*sly*$^{-}$/*mrp**				5		
			5					
	epf	*epf*$^{-}$/*sly*$^{-}$/*mrp***				2		
			2					
	103	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				2		
				2				
	epf	*epf*$^{-}$/*sly*$^{-}$/*mrp**				2		
			2					
	380	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				3		
				3				
		epf^{-}/*sly*$^{-}$/*mrp**				4		
		4						
epf		*epf*$^{-}$/*sly*$^{-}$/*mrp***				2		
		2						
	epf	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				3		
381								
			3					
epf		*epf*$^{-}$/*sly*$^{-}$/*mrp**				1		
		1						
	epf	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				1		
395								
			1					
							1	
515		1						
	1					1		
516								
28	28	*epf*$^{-}$/*sly*$^{-}$/*mrp*$^{+}$				4		
				4				
	2					2		
382								
104	104	*epf*$^{-}$/*sly*$^{+}$/*mrp*$^{-}$	165	19			1	185
	391		6	1	2			9
	392		4					4
	393		1					1
	512		7	1				8
	513		1					1
	514		3					3
233/379	233	*epf*$^{-}$/*sly*$^{+}$/*mrp*$^{-}$	31	2				33
	379		2				1	3

Table 2 (continued)

CC	ST	VAG	Clinical manifestation					Total
			Sepsis	Meningitis	Infective endocarditis	Septic arthritis	Spontaneous peritonitis	
94	94	$epf^{-}/sly^{+}/mrp^{+}$	1					1
221/234	221	$epf^{+}/sly^{+}/mrp^{+}$	1					1
		$epf^{-}/sly^{-}/mrp^{-}$	2					2
	234	$epf^{-}/sly^{-}/mrp^{-}$	1					1
None	235	$epf^{+}/sly^{+}/mrp^{+}$	1					1
	236	$epf^{-}/sly^{+}/mrp^{+}$	1					1
Total			*501*	*141*	*10*	*5*	*2*	*659*

cases ($n = 5$) were caused by CC1 isolates, whereas CC104 and CC233/379 isolates were associated with spontaneous peritonitis ($n = 2$) (Table 2).

A total of 423 out of 659 cases had a history of raw pork product consumption (64.2%), 74 cases (11.2%) had an occupation related to pig/pork products (slaughterer/farmer/butcher), and 162 cases (24.6%) did not have any information regarding pig contact or pork consumption. Eighty-four out of the 659 cases were fatal (12.7%), of which 21 cases were assigned to meningitis, 62 cases to sepsis, and one case was associated to infective endocarditis. Regarding antibiotic treatment, 598 patients (90.7%) received third-generation cephalosporin, such as ceftriaxone, 42 patients (6.4%) received penicillin, and 19 patients (2.9%) received both third-generation cephalosporin and penicillin. Susceptibility test by either disk diffusion or E-test (only penicillin) revealed all *S. suis* isolates including fatal 84 isolates were susceptible to antibiotics used for treatment (penicillin, ceftriaxone, cefotaxime). The characteristic symptom of hearing loss was found in 20.5% (135 cases), mostly associated with meningitis and/or sepsis. Associations of genotypic profiles with the clinical presentation showed that ST1 isolates were associated with meningitis ($p < 0.001$), whereas the ST104 isolates could be associated with non-meningitis cases ($p < 0.001$) (Table 3). In addition, VAG profile of $epf^{+}/sly^{+}/mrp^{+}$ was also associated with meningitis whereas $epf^{-}/sly^{+}/mrp^{-}$ and $epf^{-}/sly^{-}/mrp^{+}$ were associated with non-meningitis (Table 3).

Discussion

Our present data indicate that Thai patients are uniquely infected with a large variety of serotypes, differently from what has been described in other countries/regions [4, 5, 8]. Serotype 2 remained the main serotype causing human infections in Thailand during the period 2009–2012. This study confirms that serotype 14 is also more prevalent in Thailand than in other countries/regions [2, 6]. We also report here a second case of human infection due to a serotype 4 (Tables 1 and 2), this serotype having been described 30 years ago in a case of meningitis in the Netherlands [18]. The serotype 4 isolate in this study was recovered from a sepsis case and belongs to ST94 of CC94, while no information is available for the previous Dutch isolate [18].

MLST genotyping of *S. suis* collected between 2009 and 2012 also revealed a higher diversity than that observed in our previous study [8]. That study had shown four CCs (CC1 CC25, CC28, and CC104) while this study revealed seven CCs as described previously. CC94 and CC233/379 are newly emerging human infectious clones that have not been reported elsewhere before [2]. To the best of our knowledge, CC104, CC221/234, and CC233/379 are CCs exclusively found in Thailand. The unusual high number of isolates included in this study allowed us to note that *S. suis* serotype 2 strains isolated from humans in Thailand are much more diverse than previously thought [1, 2]. However, the major *S. suis* CCs caused human infection in worldwide are restricted to well-recognized CCs, for example, CC1 and CC20 are found in the Netherlands [19]; CC1, CC25, CC28, CC104, and CC221/234 in certain Asian countries (China, Vietnam, Thailand, Japan, Hong Kong, and Cambodia) [2, 5–8, 20]; CC1 in South America (Argentina) [21]; CC25 in North America (Canada and USA); and CC28 in North America and Japan [2, 20].

Our previous study also revealed that peaks of *S. suis* human cases occurred during the rainy season between 2006 and 2008 [8], which had also been described in China [22] and Northern Vietnam [23]. The peak in this study changed between years with no clear pattern; however, human cases seem to increase in accordance with rising rainfall, although no

Table 3 The association between sequence type or virulence-associated gene profile (VAG) and clinical manifestations

Feature	Clinical category, no. (%)			*p* value
	All, *n* = 659	Meningitis (*n* = 141)	Non-meningitis (*n* = 518)	
Sequence type				
1	321	106 (33)	215 (67)	< 0.0001*
11	2	0 (0)	2 (100)	1.0000
25	10	0 (0)	10 (100)	0.1300
28	4	0 (0)	4 (100)	0.583
94	1	0 (0)	1 (100)	1.0000
103	4	0 (0)	4 (100)	0.583
104	185	19 (10.3)	166 (89.7)	< 0.0001**
105	33	11 (33.3)	22 (66.7)	0.1238
144	7	0 (0)	7 (100)	0.3556
221	3	0 (0)	3 (100)	1.0000
233	33	2 (6.1)	31 (93.9)	0.0278
234	1	0 (0)	1 (100)	1.0000
235	1	0 (0)	1 (100)	1.0000
236	1	0 (0)	1 (100)	1.0000
298	1	0 (0)	1 (100)	1.0000
337	5	1 (20)	4 (80)	1.0000
379	3	0 (0)	3 (100)	1.0000
380	9	0 (0)	9 (100)	0.2166
381	4	0 (0)	4 (100)	0.583
382	2	0 (0)	2 (100)	1.0000
391	9	1 (11.1)	8 (88.9)	0.6923
392	4	0 (0)	4 (100)	0.583
393	1	0 (0)	1 (100)	1.0000
395	1	0 (0)	1 (100)	1.0000
512	8	1 (12.5)	7 (87.5)	1.0000
513	1	0 (0)	1 (100)	1.0000
514	3	0 (0)	3 (100)	1.0000
515	1	0 (0)	1 (100)	1.0000
516	1	0 (0)	1 (100)	1.0000
VAG profile				
$epf^{+}/sly^{+}/mrp^{+}$	369	118 (32)	251 (68)	< 0.0001*
$epf^{-}/sly^{+}/mrp^{s}$	2	0 (0)	2 (100)	1.0000
$epf^{-}/sly^{+}/mrp^{-}$	247	23 (9.3)	224 (90.7)	< 0.0001**
$epf^{-}/sly^{-}/mrp^{+}$	20	0 (0)	20 (100)	0.0113**
$epf^{-}/sly^{-}/mrp^{*}$	12	0 (0)	12 (100)	0.0797
$epf^{-}/sly^{-}/mrp^{**}$	4	0 (0)	4 (100)	0.5830
$epf^{-}/sly^{+}/mrp^{+}$	2	0 (0)	2 (100)	1.0000
$epf^{-}/sly^{-}/mrp^{-}$	3	0 (0)	3 (100)	1.0000

Statistical analyses were performed by using the Fisher's exact test

*Significant association with the meningitis category

**Significant association with the non-meningitis category

cause-effect explanation of such observations could be found. A study in Vietnam also showed a clear association between porcine reproductive and respiratory syndrome virus (PRRSv) outbreaks in pigs and *S. suis* infection in humans [24]. A highly virulent PRRSv strain was introduced in Thai swine herds in 2008 causing major outbreaks, and the virus was first

isolated in 2010 [25]. More studies are needed to evaluate if the introduction of such a virus may have influenced the pattern of *S. suis* isolation from humans in Thailand.

Oral consumption of raw pork products is the major transmission route of this disease in Thailand. The existence of deep-rooted habitual consumption of raw pork products mainly in the northern part of Thailand may explain the higher number of isolates from these areas. In fact, this is another factor that may influence the peak of infection during the years, since there is, in general, an increase in the frequency of raw pork products consumed by local people during traditional Thai festivals. A recent study confirmed the effectiveness of a food safety campaign for controlling *S. suis* infection in humans in the Phayao Province of Thailand between January 2011 and December 2011 [26]. The trends of incidence proportion before (2008–2010) and after (2011–2013) the campaign revealed a 3.94/100,000 persons decrease in the trend of incidence proportion after campaign ($p < 0.001$), with the cost to reduce to an incidence proportion of 1.0/100,000 persons around US$380 [26]. Therefore, a continuous campaign including introducing educational programs in childhood or improve the sanitation of pork processing or additional and alternative public health interventions are needed to decrease or eliminate the disease.

The findings reported herein confirm the association between ST1 strains and meningitis cases, whereas ST104 strains are associated with non-meningitis cases as previously reported [8]. This may indicate that ST1 strains might have an advantage in bacterial survival resisting host immunity, with rapid multiplication in the bloodstream, and high levels of bacteremia, which was already associated with the development of meningitis [27]. In addition, the suilysin, a *S. suis* hemolysin typically present in ST1 strains, was confirmed to contribute to the development of bacterial meningitis in a mouse model [28].

This study revealed a higher mortality (12.7%) of *S. suis* cases than in a retrospective study from 2006 to 2008 in Thailand (9.5%) [8]; indeed, a population-based study in Phayao Province in Thailand revealed 16.1% of the case fatality rate, which is even higher [29]. In other countries, the case fatality rates were 2.6% in Vietnam, 18.6% in China, 5% in Hong Kong, and 6.7% in the Netherlands [23, 30]. Globally, the fatality rate of *S. suis* infection is around 12% [31]. Regarding antibiotic treatment, no relationship between the treatment used and the fatality could be found. Since all *S. suis* isolates in this study revealed susceptible to antibiotics used for treatment, the cause of death in our patients remains uncertain; however, this may be due to delayed admission, underlying diseases, rapid disease progression, or infection with higher virulence strains of *S. suis*, although the latter cause remains to be confirmed.

In conclusion, this study revealed a relatively large number of CCs of *S. suis* causing human infection in Thailand. Among them, CC1 followed by CC104, with serotype 2 isolates, are predominant. Food safety campaigns and public health interventions would be important for controlling the *S. suis* infection in humans.

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Contributors All authors have read and approved the final article. AK, YA, DT, and KO participated in the conception and design of the study and analysis and interpretation of data. AK, MG, and KO drafted the manuscript. All authors have final approval of the version to be submitted.

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Compliance with ethical standards

Ethics This study was reviewed and approved by the Ethics Committees of the Department of Medical Sciences, Ministry of Public Health, Thailand. Medical record reviews were conducted by the medical doctors under the protocol approved by the Ethics Committees.

Conflict of interest The authors declare that they have no conflict of interest.

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