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Research article

Prevalence and distribution of methicillin-resistant *Staphylococcus aureus* among animals in Malaysia for the past 15 years: A systematic review

**Sharifo Ali Elmi[1,2], Mohammed Sani Gaddafi[3,*], Mohammed Dauda Goni[1], Erkihun Aklilu[1],
Ismail A. Odetokun[4] and Siew Shean Choong[1,*]**

[1]*Faculty of Veterinary Medicine, University Malaysia Kelantan, Kelantan 16100, Malaysia*
[2]*Ministry of Livestock Forestry and Range, Mogadishu 03010, Somalia*
[3]*Ministry of Animal Health, Husbandry and Fisheries, Kebbi 860101, Nigeria.*
[4]*Department of Veterinary Public Health and Preventive Medicine, Faculty of Veterinary Medicine, University of Ilorin, Kwara State 240003 Nigeria*

Abstract

This systematic review aimed to investigate the prevalence and molecular epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) in animals, human-animal interfaces, their antibiotic resistance profiles, and genotypic characteristics of MRSA isolates reported in Malaysia over the last 15 years. A comprehensive search of PubMed, Scopus, and Web of Science databases was conducted to identify relevant studies published between 2008 and 2023. Sixteen eligible articles were included in the review, and the systematic review protocol was published in Prospero (registration number: CRD42023432959). The prevalence of *S. aureus*, including MRSA, ranged from 0.95% to 100% among all the studies reviewed (poultry: 0.95% to 100%, cattle: 10% to 25%, pigs: 0.8% to 18.3%, sheep/goats: 18.3% to 46%). The MRSA isolates from Malaysian livestock production systems displayed pathogenic potential with diverse spa and sequence types. These isolates carried genes associated with virulence factors such as enterotoxins sea, seb, and exfoliative toxins eta, etb. One study reported the presence of the typical livestock-associated MRSA mecC gene. The review highlights the presence of potentially highly virulent strains of multi-drug-resistant MRSA in livestock, livestock products, and pets, which can be transmitted to high-risk individuals with frequent animal contact. Further studies are required to identify the impact of livestock on MRSA transmission and to understand the role of animals in the prevalence and occurrence of MRSA in Malaysia

Keywords: Livestock, Methicillin-Resistant *Staphylococcus aureus*, Malaysia.

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[*]**Corresponding author**:
Siew Shean Choong, Faculty of Veterinary Medicine, University Malaysia Kelantan, Kelantan 16100, Malaysia. E-mail: shean.cs@umk.edu.my.
Mohammed Sani Gaddafi, Ministry of Animal Health, Husbandry and Fisheries, Kebbi State 860101, Nigeria. E-mail: gaddafimohammedsani@yahoo.com.

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INTRODUCTION

Recently, the emergence of antimicrobial-resistant bacteria has become a concern worldwide, and one of the bacteria that has been known to develop resistance to antibiotics is methicillin-resistant *Staphylococcus aureus* (MRSA) (Alghamdi et al., 2023). MRSA also causes several infections in economically important animals (Chuang and Huang, 2015). Treatment of MRSA infection can be complex due to the ability of the bacteria to inhibit the response to antibiotics, thus limiting the effectiveness of antibiotic treatment. MRSA produces a penicillin-binding protein (PBP2a) encoded by the *mec*A gene (Cuny et al., 2015). PBP2a prevents beta-lactam antibiotics from binding to cell wall proteins, thus mediating the inhibitory effect of these antibiotics (Cuny et al., 2015).

MRSA was first identified in 1961 after the introduction of methicillin (Harkins et al., 2017). In the late 1990s, new MRSA clones emerged in the community (CA-MRSA), and in a healthy individuals outside the health care facilities which highlighted the change of the epidemiology of MRSA (Brennan et al., 2012). In the early 21st century, a livestock-associated MRSA (LA-MRSA) strain with sequence type 398 (ST398) was first found in pigs, suggesting the emergence of LA-MRSA (Smith, 2015). Recent studies have shown that LA-MRSA is frequently found in various livestock and food products worldwide (Lozano et al., 2016; Tegegne et al., 2017). In early studies, the antimicrobial resistance and genetic background of MRSA were thought to differ according to their specific hosts (Larsen et al., 2022). However, this perspective changed when MRSA from different sources was found to have low host specificity and a similar genomic sequence (Cuny et al., 2015). This suggests that MRSA can be transmitted across species, from animals to humans, and vice versa. This raises health and food hygiene concerns, as LA-MRSAs that are present in live animals and their products, such as raw milk, eggs, and meat, can transmit, colonize, and infect humans.

Several studies have reported high MRSA colonization rates in livestock and livestock products (Aklilu and Chia, 2020; Gaddafi et al., 2021; Gaddafi et al., 2022; Gaddafi et al., 2023) and in humans, including animal owners, farm workers, slaughterhouse workers (Odetokun et al., 2018; Odetokun et al., 2022), and veterinarians (Aklilu et al., 2013; Gaddafi et al., 2020; Gaddafi et al., 2021). A study conducted in the Netherlands reported that pig and cattle farmers are often carriers of MRSA-ST398 (van Loo et al., 2007). According to a study conducted by Gaddafi et al. (2020), 14% of practicing veterinarians working in veterinary clinics in Nigeria were infected with MRSA. These studies show that transmission of MRSA can occur among humans (human-human), humans and animals, and vice versa, and direct exposure to MRSA-positive animals may lead to transmission to humans. In most European countries, CC398 remains the most commonly identified LA-MRSA (Mascaro et al., 2019). While CC398 strains that have been found in livestock worldwide, the epidemiology of livestock-associated *S. aureus* differs in other geographic areas. Several studies in Asian countries, such as China and Thailand, have shown that different strains of MRSA, ST9, appear to be a prominent type of LA-MRSA (Tanomsridachchai et al., 2021).

MRSA has been successfully isolated from both healthy and mastitis milk in dairy animals worldwide (Holmes and Zadoks, 2011; Tegegne et al., 2017; Gaddafi et al., 2023). This systematic review aimed to investigate the prevalence and molecular epidemiology of MRSA in animals, human-animal-interface, their antibiotic resistance profile and genotypic characteristics of MRSA isolates reported in Malaysia over the last 15 years. The occurrence of MRSA from livestock has been reported in Malaysia, ranging from pigs to dairy cattle. has Neela et al. (2009) Recently, Aklilu and Chia (2020) the first occurrence of *mec*C in dairy cattle was reported in Kelantan, Malaysia.

There is a paucity of data on the comprehensive prevalence of *S. aureus* and MRSA in animals, and their antibiotic resistance profiles in Malaysia are still limited. MRSA has been successfully isolated from milk samples, including those from healthy and mastitic dairy animals, highlighting its presence at the human-animal interface and its potential role in zoonotic transmission worldwide. The prevalence and molecular epidemiology data in this study will provide information on the spread and geographical distribution of the MRSA, thus helping to prevent further understand the transmission of MRSA to other animal farms and the human community, as well as raising awareness of good farm biosecurity practices. This systematic review will also identify the knowledge gap with regard regards research on this important public health pathogen. Therefore, his review compiles results from *S. aureus*/MRSA prevalence and molecular studies carried out in Peninsular Malaysia over the past fifteen (15) years to provide a better understanding of the dissemination of *S. aureus* MRSA strains in this region, together with their antibiotic resistance profiles, antibiotic resistance gene determinants, virulence factors, sequence types (ST), clonal complex (CC), and *spa* types (t). In addition, the comprehensive antibiotic resistance profile reported in this review will help Malaysian farmers and veterinary officers gain a better understanding of the current antimicrobial resistance (AMR) status in livestock and provide insight into drugs that can be used to treat *S. aureus* infection, particularly mastitis in livestock.

Methods

Information sources and search strategies

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2015). However, a search protocol was designed and registered on the International Prospective Register of Systematic Reviews (registration number: CRD42023432959). This registration guaranteed that no other systematic review on the same topic in Malaysia is registered.

Systematic searches of PubMed, Scopus, and Web of Science databases were conducted to find relevant papers published between January 1, 2008, and May 13, 2023. Boolean operators (AND, OR) were used to find studies using the keywords: SCOPUS = TITLE-ABS-KEY =("methicillin-resistant *Staphylococcus aureus* " OR MRSA) AND (animal OR livestock OR poultry OR companion animal OR wildlife) AND (Malaysia) AND (prevalence OR distribution) AND (PUBYEAR > 2008), WEB OF SCIENCE = TS=("methicillin-resistant *Staphylococcus aureus* " OR MRSA) AND (animal OR livestock OR poultry OR companion animal OR wildlife) AND (Malaysia) AND (prevalence OR distribution) AND (2008-2023) and Pubmed =(("methicillin-resistant *Staphylococcus aureus* "[MeSH Terms] OR MRSA[All fields]) AND (animal [MeSH Terms] OR livestock[MeSH Terms] OR poultry[MeSH Terms] OR companion animal[MeSH Terms] OR wildlife [All fields]) AND (Malaysia[MeSH Terms]) AND (prevalence[All fields] OR distribution[All fields]). Filters were applied for language, document type, and year range of publications. The final search was conducted on May 13, 2023. A total of 139 articles were identified. Additional studies were looked for in the identified studies' reference lists for possible inclusion in the review. The systematic review employed a comprehensive search strategy, including a blind search in addition to the primary database. This approach led to the inclusion of three additional articles, enhancing the review's scope and ensuring a thorough exploration of the relevant literature

Eligibility criteria and screening of articles

To determine the eligibility of the identified studies, the following inclusion criteria were employed to screen and evaluate the titles and abstracts: studies of any design, excluding experimental studies review articles, commentaries, opinion, and letters to editors, written in English, full-text journal articles published between 2008 and 2023, and conducted in Malaysia. Studies were excluded if they did not specify the animal source of the isolates, if *S. aureus* was not identified among the isolates, or if the results only indicated *Staphylococcus* spp. Two independent reviewers (S.A.E and M.S.G) did this, and discrepancies were resolved through discussion.

Study quality

The quality of reporting and bias selection in the eligible studies were assessed using the McMaster critical evaluation methods for both quantitative and qualitative studies. The evaluation considered the year of the study, study purpose, study design, study location, animal type, sample type, and the method of detection (Ducat and Kumar, 2015). This was done by two independent reviewers (S.A.E and M.S.G) and discrepancies were resolved through discussion.

Data Extraction Process

A standardized data extraction form was developed to extract the following details were feasible: author names, study design, study state, proportion of MRSA isolates, sample type, host type, detection method used, animal prevalence, human livestock contact prevalence, antimicrobial resistance profiles, and molecular types/genotypes of MRSA isolates. These factors were considered important for data extraction. Two independent reviewers (S.A.E and M.S.G) were employed for this stage and discrepancies were settled through discussion.

RESULTS

Characteristics of reviewed studies

For this review, sixteen articles (Figure 1) from all states in Peninsular Malaysia were found worthy. Most articles reported studies from more than one (1) state, with the majority being conducted in Selangor, Malaysia. Most of the studies used more than one (1) detection method to report *S. aureus*/MRSA, while some did not report prevalence/occurrence rate as one of their findings.

Prevalence of *S. aureus*/MRSA among livestock, livestock products, Livestock farm workers and pets in Malaysia

Among the sixteen (16) studies reviewed, three were on pigs, four were on cattle, three on poultry, two on horses, dogs and cats, sheep, and goats, and five on humans with animal contact. The prevalence of *S. aureus*/MRSA among the animals in this review varied across different animal species. The overall prevalence of *S. aureus*/MRSA ranged from 0.95% to 100% among all the studies reviewed, with poultry ranging from 0.95% to 100%, cattle ranging between 10% and 25%, pigs ranging between 0.8% and 18.3%, and sheep and goats ranging between 18.3% and 46% and cats ranging between 2% to 6% and 6.7% to 10% of dogs (Table 1). Most studies included in the review reported prevalence rates of MRSA ranging from 3.7% to 25%, indicating relatively low to moderately high rates (Table 1). Some studies did not provide the specific prevalence or occurrence rates of MRSA in their findings. Most of the studies focused on Selangor state. Only six (6) out of thirteen (13) states in Malaysia reported the prevalence/occurrence or detection of MRSA (Figure 2). There was a noticeable variation in the prevalence of MRSA among different sources of animal samples in the reviewed studies. Different anatomical sites may yield varying detection rates of MRSA due to differences in bacterial colonization pattern. It is worth noting that most studies have utilized multiple methods to identify and detect methicillin resistance among the isolates (Table 1). The detection and diagnosis of MRSA in animals greatly depends on the type of sample collected and the method used for identification, as these factors influence the sensitivity, specificity, and overall reliability of the results.

In five studies, both animals and humans (veterinarians, veterinary students, and livestock farm workers) were sampled (Table 1). The prevalence of MRSA among human-livestock contacts ranged from 3.6% to 16%.

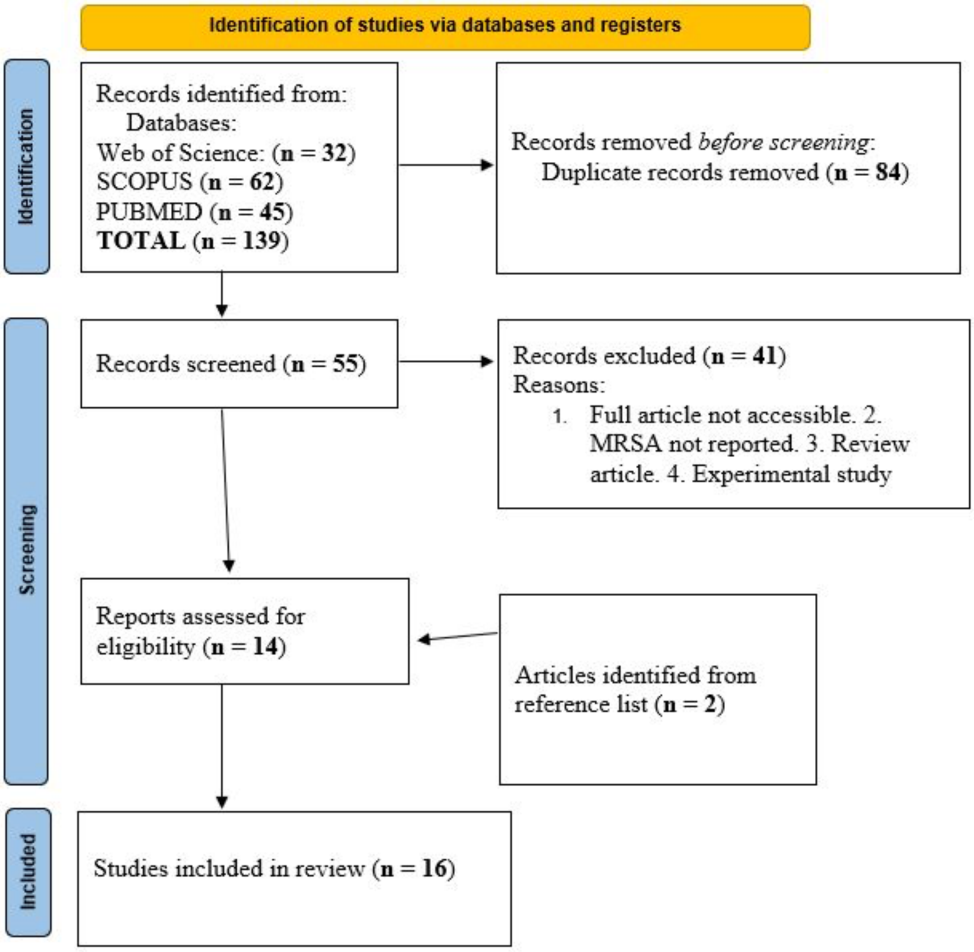

Figure 1 Flow diagram of the study selection process for inclusion in the review

Table 1 Prevalence of LA-MRSA in Malaysia

Author, year	Study State	Sample Type	Host Type	Method of Detection	Study Design	Animal Prevalence (%)	H-L-C Prevalence (%)	Remark
Sasidharan et al., (2011)	Kedah	Milk	Cattle	Phenotypic	Cross-sectional	10 (5/50)	NR	*S. aureus*
Aklilu and Hui Ying, (2020)	Kelantan	Milk and Nasal swab	Cattle	Phenotypic & Genotypic	Cross-sectional	25 (4/16)	NR	MRSA
Neela et al., (2013)	Selangor	Nasal Swab	Poultry & Human	Phenotypic & Genotypic	Cross-sectional	0.95 (4/420)	3.61 (3/83)	*S. aureus*
Hian et al., (2020)	Malaysian Peninsular	Oral and Nasal Swab	Human	Phenotypic & Genotypic	Cross-sectional	18.3 (73/241)	22.5 (45/200)	*S. aureus*
Geidam et al., (2012)	Selangor	Skin, Feather, Nostril, Trachea & Cloacal swab	Poultry	Phenotypic	Cross-sectional	100 (96/96)	NR	*S. aureus*
Khalid et al., (2009)	Selangor & Perak	Nasal Swab	Pigs	Phenotypic & Genotypic	Cross-sectional	0.8 (4/500)	NR	MRSA
Aklilu et al., (2013)	Selangor	Nasal & Oral swab	Human (Vets)	Phenotypic & Genotypic	Cross-sectional	NR	16 (21/131)	MRSA
Chai et al., (2022)	Malaysian Peninsular	Nasal & Oral swab	Human (Animal Handlers)	Phenotypic & Genotypic	Cross-sectional	NR	3.8 (6/155)	MRSA
A. Bitrus et al., (2018)	Selangor	Stock culture	Dogs, cats, chickens, environment & Human	Phenotypic & Genotypic	Archived	NR	NR	MRSA
Ariffin et al., (2019)	Terengganu	Milk	Sheep & Goat	Phenotypic & Genotypic	Cross-sectional	46 (18/39)	NR	*S. aureus*
Chai et al., (2020)	Terengganu	Milk	Goat	Phenotypic & Genotypic	Cross-sectional	2 (1/50)	NR	MRSA
Neela et al., (2009)	Selangor	Nasal Swab	Pigs & Human	Phenotypic & Genotypic	Cross-sectional	1.38 (5/360)	5.5 (5/90)	MRSA
Saeed et al., (2022)	Kelantan & Pahang	Milk	Cattle	Phenotypic	Cross-sectional	16.5 (39/235)	NR	*S. aureus*
Afshar et al., (2023)	Central Region of Peninsular Malaysia	Nasal & Oral swab	Dogs, cats, and human	Phenotypic & Genotypic	Cross-sectional study	10 (5/50),	2 (2/100)	MRSA
Chai et al., (2021)	Malaysia	Nasal & Oral swab	Dogs, cats, and human	Phenotypic & Genotypic	Cross-sectional study	6.7 (2/30)	1.4 (1/70)	MRSA
Kanagarajah et al., (2017)	Selangor	fecal samples	canines and felines	Phenotypic	Cross-sectional study	11.6 (33/283)	7.7 (131/169)	MRSA

MRSA=Methicillin-Resistant *Staphylococcus aureus* ; MSSA= Methicillin-Susceptible *Staphylococcus aureus* , NR = Not reported, H-L-C = Human Livestock Contact

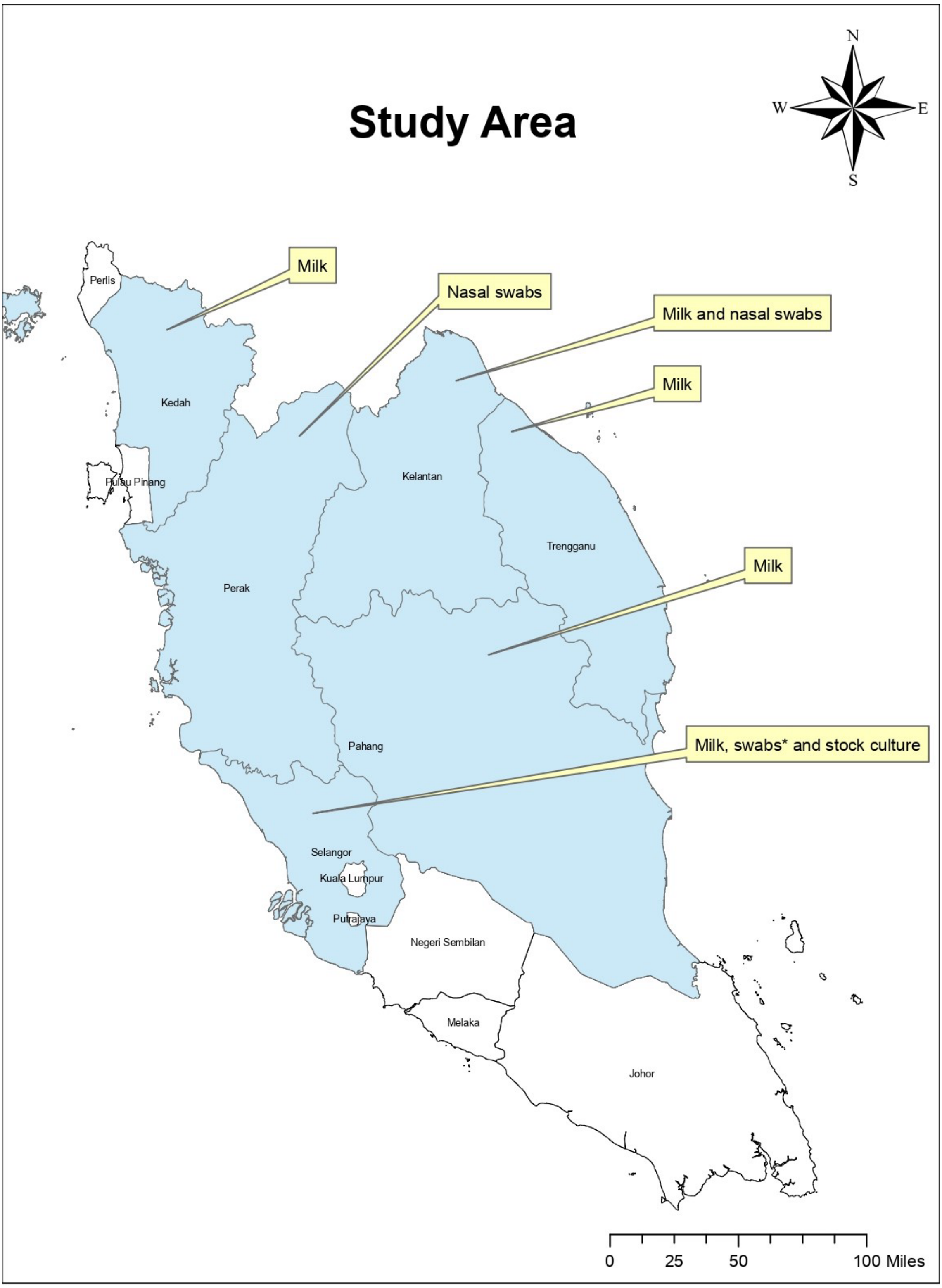

Figure 2 Geographic distribution of studies conducted in Malaysia showing the states where studies were conducted and sample types collected

Antimicrobial resistance profiles

Most studies that reported resistance profiles of *S. aureus*/MRSA against penicillin, oxacillin, and cefoxitin consistently stated high resistance rates ranging from approximately 40% to 100%. Only two (2) studies reported resistance rates of 0% and 7.69%, and 0% and 34% respectively (Table 2). Most studies indicated resistance of *S. aureus*/MRSA isolates to erythromycin, tetracycline, ciprofloxacin, and trimethoprim-sulfamethoxazole, with varying percentages reaching up to 100% (Table 2). Four (4) out of the sixteen (16) studies demonstrated some level of vancomycin resistance. For chloramphenicol, three (3) studies reported 100% susceptibility, whereas three other studies reported varying degrees of resistance (100 %) (Table 2).

Table 2 Antimicrobial susceptibility pattern of LA-MRSA isolates in Malaysia

Author, year	FOX	IPM	SXT	GEN	ERY	OXA	TET	CHL	VAN	CIP	ENR	P
Aklilu and Hui Ying, (2020)	96.3	0	NR	NR	NR	100	NR	NR	NR	NR	0	NR
Neela et al., (2013)	NR	NR	0	0	0	NR	NR	0	0	NR	NR	0
Hian et al., (2020)	NR	NR	63.6	47.1	NR	NR	47.9	NR	NR	NR	34	32.9
Geidam et al., (2012)	NR	NR	14	NR	98	28	85	53	NR	41	NR	53
Aklilu et al., (2013)	46.15	7.69	NR	NR	NR	57.69	NR	NR	3.85	NR	NR	NR
Bitrus et al., (2016)	20	NR	NR	NR	27	60	40	NR	40	NR	NR	NR
Chai et al., (2022)	100	NR	72	0	22	NR	82	50	NR	96.8	NR	100
Ariffin et al., (2019)	0	NR	NR	0	NR	0	11	0	NR	NR	NR	22
Chai et al., (2020)	26	NR	NR	NR	NR	10	6	26	26	NR	NR	26
Neela et al., (2009)	100	NR	100	100	100	NR	100	NR	NR	100	NR	NR
Saeed et al., (2022)	NR	NR	0	0	18	31	26	0	NR	0	NR	46

FOX = Cefoxitin (30 µg), IPM = Imipenem, SXT = Trimethoprim-sulfamethoxazole (25 µg), GEN = Gentamicin (10 µg), Ery = Erythromycin (15 µg), Oxa = Oxacillin (1 µg), Tet = Tetracycline (30 µg), Chl = Chloramphenicol (30 µg), Van = Vancomycin (30 µg), Cip = Ciprofloxacin (5 µg), Enr = Enrofloxacin (5 µg), P = Penicillin (2ug), NR= Not reported.

Genotypes of livestock-associated MRSA isolates

Nine (9) studies provided information on the genotypic characteristics of MRSA isolates (Table 3). *mec*A was detected in eight (8) out of the nine (9) studies, while *mec*C was only detected in one of the reviewed studies published recently. Among the reported studies, two (2) studies reported the presence of SCC*mec* III and SCC*mec* V (Table 3).

Spa types were identified in four (4) out of the nine (9) studies that conducted genotyping (Table 3). All the studies reported divergent *spa* types. MLST analysis was performed in four (4) studies, and two (2) of the studies reported a similar sequence type (ST1). None of the reviewed studies reported the presence of CC398 in isolates. Other reported sequence types include ST5, ST1241, ST149, ST15, and ST508 (Table 3).

Several virulence factors were examined, including the presence of the Panton-Valentine leukocidin (PVL) gene, enterotoxins, and exfoliative toxins. PVL was not reported in the nine (9) studies that reported the genotypic characteristics of *S. aureus*/MRSA. Five (5) studies reported various enterotoxin genes (*sea*, *seb*, *sem*, *seh*, *ser*, *sed*, *sec*, and *sep*) and exfoliative toxin genes (*eta* and *etb*) (Table 3).

Table 3 Genotypic characteristics of LA-MRSA isolates in Malaysia

S/No	Author, year	*mecA*	*mecC*	Resistant gene	SCC*mec* Typing	*spa* Type	MLST	PVL	Virulence genes
1	Aklilu and Hui Ying, (2020)	25 (4/16)	15.79 (15/95)	ND	ND	ND	ND	ND	ND
2	Neela et al., (2013)	Done	ND	ND	ND	t2247, t359, t189	ST692, ST97, ST188, ST1179	ND	*ica*A, *ica*D and *fnb*
3	Bitrus et al., (2018)	Done	ND	ND	III	ND	ND	ND	ND
4	Khalid et al., (2015)	0.8	ND	ND	ND	ND	ND	ND	ND
5	Aklilu et al., (2013)	16	ND	ND	ND	t2636, t5697, t346	ST5, ST1241, ST149, ST15, ST508	ND	ND
6	Bitrus et al., (2016)	Done	ND	ND	III	ND	ST1, ST177	ND	*etA, etB, geh, hla, hlβ, pvl, seu, set-1, sspA*
7	Chai et al., (2022)	3.8	ND	*tet*K, *tet*L, *tet*M, *erm*A, *erm*B, *erm*C & *msr*A	ND	t189, t3293, t3080	ND	ND	*scn, chp, sak, sea* & *sep*
8	Chai et al., (2020)	2	ND	ND	ND	ND	ND	ND	ND
9	Neela et al., (2009)	Done	ND	ND	V	t4358, t1784	ST9, ST1	ND	*seb, see, seg, can, fnb*

SCCmec = Staphylococcal cassette chromosome mec, MLST = Multilocus sequence typing, PVL = Panton-Valentine leucocidin, *spa* = Staphylococcal protein A, ND = Not done

DISCUSSION

This systematic review aimed to examine MRSA prevalence and distribution in Malaysia over the last 15 years. While numerous articles were gathered, only 16 studies met the criteria for inclusion in this review. The limited research on LA-MRSA in Malaysia, despite its significance and potential risks, is concerning. Previous studies have highlighted colonization in both animals and individuals in close contact (Aklilu et al., 2013). All sixteen studies were conducted across different regions in Peninsular Malaysia, with the majority in Selangor. The higher concentration of studies in Selangor is likely linked to the presence of the oldest veterinary faculty in Malaysia. Gaddafi et al. (2025) opined that, animal related researches are more likely to be conducted in regions/states with veterinary faculties than regions/states without veterinary faculty. All reviewed studies employed multiple detection methods for MRSA, showcasing improved laboratory diagnostic capabilities in Malaysia. Employing different detection methods enhances accuracy in MRSA identification, addressing concerns about misidentification (Lee et al., 2018).

The median MRSA infection rate in Malaysian livestock is 3.7%, notably lower than rates in other regions like Belgium (37.8%), the Netherlands (39%), and Germany (70%), as reported in studies by De Neeling et al. (2007), Denis et al. (2009), and (Köck et al., 2013). The reviewed studies noted MRSA levels in Malaysia (<3.7%), significantly lower than other countries (>30%) like Belgium, the Netherlands, and Germany (De Neeling et al., 2007; Denis et al., 2009; Köck et al., 2013). This disparity could stem from the limited research on livestock-associated MRSA in Malaysia, despite the expanding livestock industry, particularly in poultry. Yet, a limited number of studies reported 100% MRSA rates. Among the reviewed studies, four focused on cattle, three on pigs and poultry each, and two each on horses, dogs and cats, and sheep and goats. Despite the expanding livestock and poultry industry, widespread pet ownership, and the elevated risk of MRSA colonization in animals with potential zoonotic transmission, research on its prevalence in animals remains sparse in Malaysia. Moreover, despite Malaysia's divergence terrain and a notable population of wild pigs (as per personal communication), only three studies among those reviewed sampled domestic pigs, and none included wild pigs. The limited research can be attributed to a lack of awareness of MRSA's zoonotic nature and the associated public health implications associated with its colonization. Recently, the LA-MRSA strain was identified in cattle farms in Malaysia for the first time (Aklilu and Chia, 2020; Aklilu and Hui Ying, 2020). This discovery implies that this MRSA strain is circulating within the country's livestock population. Of particular concern is its public health and zoonotic implications, as it has been documented to cause infections in humans (Gaddafi et al., 2023).

In Malaysian hospitals, MRSA prevalence among clinical isolates ranges from 17.2% to 28.1%, causing infections (Hamzah et al., 2019). Continuous surveillance of MRSA especially the LA-MRSA strains in Malaysia is crucial to prevent their emergence in hospital settings as reported from Germany (Köck et al., 2013) indicate high prevalence of LA-MRSA in the hospital setting. This is of particular importance for healthcare facilities already strained for resources, as it could complicate treatment options.

The analysis of antimicrobial susceptibility of the reviewed studies indicates that most did not report the profile against isolated MRSA. Among those that did, varying degrees of susceptibility and resistance to different antimicrobials were observed. Interestingly, articles reporting AMR against cefoxitin/methicillin showed a notably high resistance rate. Conversely, those reporting AMR against vancomycin indicated a high susceptibility rate among isolated MRSA. This finding aligns with the infrequent use of vancomycin in livestock production for infection treatment or prophylaxis (Gaddafi et al., 2021). The varying antimicrobial resistance rates observed may stem from the limited number of studies relative to the expanding livestock industry in Malaysia. Additionally, the relatively high susceptibility of some antimicrobials in the reviewed articles could be linked to small sample sizes. Research indicates that livestock density per farm contributes to antimicrobial resistance, including methicillin resistance (Fang et al., 2016). Therefore, conducting more studies on MRSA among animals in Malaysia is crucial, especially considering the reported presence of the LA-MRSA strain in cattle farms, the risk of zoonotic transmission of LA-MRSA, and the effect on public health and antibiotic resistance patterns.

Remarkably, only one study in the review, conducted by Aklilu and Hui Ying (2020), reported the existence of typical livestock-associated MRSA isolates on a cattle farm in Malaysia, particularly noting the presence of *mec*C. This finding offers evidence of the presence of such MRSA isolates in the Malaysian livestock production system. Hence, there is a need for coordinated efforts and measures to curb the spread of these strains. Moreover, comprehensive molecular epidemiological studies employing advanced techniques should be conducted on livestock, dogs, cats, and wild pigs to grasp their role in sustaining MRSA colonization in Malaysia. Among the recent studies reviewed, antimicrobial resistance determinants including *tetA, tetM, tetK, ermA, ermB, ermC*, and *msrA* were identified (Chai et al., 2022). The presence of these genes in MRSA isolates suggests that the strains exhibit multi-drug resistance. Further studies on genotypic resistant determinants among animals and human-animal contact will give an insight into the multidrug-resistance status of the isolates which in turn has a serious public health consequence.

Two studies conducted by Bitrus et al. (2018) and Neela et al. (2009), reported the presence of scc*mec* types III and V, respectively. The detection of scc*mec* type-III, a community-acquired MRSA strain, in livestock is concerning, suggesting a potential zoonotic transmission from humans to animals. Ongoing surveillance of scc*mec*-types is highly recommended, as it yields valuable insights into the epidemiological niche of MRSA isolates. Among the reviewed studies, four studies conducted *spa*-typing on MRSA isolates, revealing various *spa* types (Neela et al., 2009; Aklilu et al., 2013; Neela et al., 2013; Chai et al., 2022). *Spa*-typing, a crucial molecular technique, provides epidemiological insights into the geographical spread of MRSA isolates. The presence of different *spa* types noticed from the reviewed studies suggests that MRSA isolates in Malaysia may belong to different strains. For instance, *spa* type (t032) has been associated with the MRSA epidemic that occurred in the United Kingdom during the 1980s (Jones et al., 2021). Similarly, four studies in the review documented various STs of MRSA isolates using multi-locus sequence typing (MLST), with only two studies identifying ST1 among the recovered ST in Malaysia (Neela et al., 2009; Aklilu et al., 2013; Neela et al., 2013; Bitrus et al., 2016). Interestingly, the two studies reporting ST1 were both conducted in Selangor State (Neela et al., 2009; Bitrus et al., 2016). This suggests a potential circulation of ST1, a recognized LA-MRSA strain, in the study areas within the State. Therefore, additional studies are warranted to ascertain the prevailing ST and CC circulating in Malaysia as regards MRSA. Furthermore, four reviewed studies documented diverse virulent genes among MRSA isolates from animals in Malaysia (Neela et al., 2009; Neela et al., 2013; Bitrus et al., 2016; Chai et al., 2022). The identification of these genes indicates that some circulating isolates may be pathogenic and potentially zoonotic (Lawal et al., 2024). Notably, the *pvl*-gene, typically found in community-associated MRSA isolates and specific to humans Tam and Torres (2019), was among the reported virulent genes. Its presence suggests a higher likelihood of MRSA originating from humans rather than livestock. Further studies are imperative as MRSA significantly influences the evolution of various genetic lineages of *Staphylococcus aureus* . There is a significant dearth of data on the risk factors related to the transmission of livestock-associated MRSA from animals to humans in Malaysia. Previous study indicated that individuals with direct contact with livestock, particularly pigs, poultry and cattle, are at higher risk of MRSA colonization or infection (Gaddafi et al., 2021).

CONCLUSION

This systematic review analyzed sixteen studies on MRSA in animals across Peninsular Malaysia over the past 15 years. The findings confirm the presence of MRSA in a variety of animal hosts, including poultry, pigs, cattle, goats, sheep, horses, dogs, and cats, as well as among individuals in frequent contact with these animals. The prevalence rates varied widely across species and regions, with notably high resistance to commonly used antibiotics such as penicillin, oxacillin, and cefoxitin. Genotypic analysis revealed diverse sequence types (e.g., ST1, ST5, ST9), spa types, and resistance genes (e.g., tet, erm, msrA), indicating multiple MRSA lineages circulating in Malaysia's livestock ecosystem. The recent detection of the mecC gene and livestock-associated MRSA strains, including SCCmec types III and V, further emphasizes the zoonotic and public health implications.

Given the expanding livestock and pet population, and the limited geographical spread of available studies (with most centered in Selangor), there is a pressing need for broader, more geographically representative epidemiological investigations. Such efforts should focus on surveillance, molecular characterization, and antimicrobial resistance profiling of MRSA in both domestic and wild animal populations. These data are critical for informing public health policy and guiding veterinary antimicrobial stewardship in Malaysia.

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AUTHORS CONTRIBUTIONS

Sharifo Ali Elmi: Conceptualization (Lead), data extraction (Lead), Writing - original draft (Supporting). MSG: Conceptualization (Lead), Data extraction (Lead), analysis (Lead), manuscript writing (Lead). MDG: Conceptualization (Supporting), Supervision (Lead), Writing - review and editing (Equal). EA: Conceptualization (Supporting), Supervision (Lead), Writing - review and editing (Equal). IAO: Formal analysis (Equal), Writing - review and editing (Equal). SSC: Conceptualization (Lead), Supervision (Lead), Writing - review and editing (Equal).

CONFLICT OF INTEREST

None to be declared.

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