Original Research

Systematic Review and Meta-Analysis of Livestock Associated-Methicillin Resistant *Staphylococcus aureus* (LA-MRSA) Prevalence in Animals in India

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Abstract

Livestock Associated-Methicillin Resistant Staphylococcus aureus (LA-MRSA) is a antimicrobial resistant bacteria, which has the potential to be pathogenic in humans and animals. The present study aims at employing systematic review and meta-analysis to estimate LA-MRSA prevalence in data extracted from Indian studies. The prevalence of the LA-MRSA isolates was stratified based on type/source of samples (Clinical/healthy animal samples) and meta-analysis was done. Database searches yielded 21 articles published during the period 2014-17. The pooled prevalence estimate of LA-MRSA was 10.0% (95% CI: 7.0-13.0%, τ^2=0.6654; P<0.01). Further, samples were stratified as clinical samples and healthy animal samples and LA-MRSA prevalence were 12.0% (95% CI: 8.0-19.0%, τ^2=0.7476; P<0.01) and 7.0% (95% CI: 5.0-10.0%, τ^2=0.3583; P<0.01) for clinical samples and healthy animal samples, respectively. By using meta-analysis, an overall prevalence of LA-MRSA in animals in India was estimated, which will be useful for researchers, veterinarians and policy makers in planning appropriate intervention strategies.

Key words: Livestock Associated, Meta-analysis, Methicillin Resistant *Staphylococcus aureus*, Prevalence

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Introduction

Staphylococcus aureus is a gram-positive commensals organism that is known to inhabit the skin, in sebaceous glands and the mucosa of humans and various animals. In certain circumstances, when the skin surface is damaged or the animal is immunosuppressed or immunocompromised, *S. aureus* can turn into an opportunistic pathogen and cause various diseases. *S. aureus* causes mastitis in dairy-producing animals (including cattle and goats), bumble-foot in chickens and infects farmed rabbits and other animals (Smith,

2015). The prevalence of *Staphylococcus spp.* in mastitis in dairy animals was 45% (95% CI: 39-50%) based on previous meta-analysis in India as reported by Krishnamoorthy *et al.* (2017). During recent years, this bacteria has developed resistance to many antibacterial agents. One such example being methicillin resistant *Staphylococcus aureus* (MRSA) has mecA gene, which confers resistance and also encodes a penicillin-binding protein (PBP) with decreased affinity for β-lactam antibiotics. Additionally, MRSA continues to be resistant to all macrolides, aminoglycosides and tetracyclines (Khara *et al.*, 2016). Presence of Livestock associated-methicillin resistant *S. aureus* (LA-MRSA) in animals was first reported in 1972, in Belgium, from bovine mastitis samples, where MRSA was found to originate from humans (Devriese *et al.*, 1972). Widespread use of antibiotics in human, veterinary medicine and agricultural settings has played a significant role in the emergence of resistant MRSA clones due to selection pressure (Mehndiratta and Bhalla, 2014). Colonization of infection with this organism can be difficult to treat both in animals and humans.

Systematic review is done to solve the research question by reviewing the existing primary data available in databases, journals, etc. and without much cost in the study. Meta-analysis is a quantitative, formal, epidemiological study design used to systematically assess the results of previous research to derive conclusions about that body of research (Haidich, 2010). The main objective of performing meta-analysis is to summarize and integrate results from a number of individual studies, analyze differences in the results among studies, overcome small sample sizes of individual studies to detect effects of interest and analyze end points that require larger sample sizes, increase precision in estimating effects, determine if new studies are needed to further investigate an issue and generate new hypotheses for future studies. The critical steps to be addressed in a meta-analysis studies are, identification and selection of studies, heterogeneity of results, availability of information and analysis of the data (Walker *et al.*, 2008). Number of studies reported the prevalence of LA-MRSA in animals in India, but it varied widely in different regions. There is need for systematic review and meta-analysis of studies on LA-MRSA prevalence in India. Hence, a systematic review and meta-analysis was carried to provide an estimate of LA-MRSA prevalence in livestock of India.

Materials and Methods

Study Strategy

Literature was collected for the period January 2010 to December 2017 using various search engines such as PubMed, J-GATE Plus, Consortium of e-Resources in Agriculture (CeRA), Indian Journals and Google scholar to retrieve the studies related to India, using the key words "MRSA", "prevalence", "India", "Animals" and "Milk". We also performed manual searches on citations retrieved from original studies and review articles. Studies that presented frequency count or prevalence or proportion of LA-MRSA isolates

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were included. The search was restricted only to studies published in English language in peer-reviewed as well as grey literature.

Study Selection

All the search results were limited to observational, non-randomized, case control studies conducted on healthy and clinically sick animals and its products. The studies were chosen based on the following inclusion criteria- 1) They have to report the proportion of LA-MRSA prevalence, 2) Total number of animals tested, 3) Year of surveillance or year of study conducted and 4) Studies with standard confirmatory test such as antibiotic susceptibility testing by phenotypic and molecular methods. Studies such as case reports, review articles and outbreaks investigations were also excluded.

Data Extraction and Quality Assessment

Initially the abstract screening of articles on LA-MRSA was carried out from various literature sources. Thereafter full length articles were collected and examined; two independent reviewers extracted the attributes or characteristics of each included study in a pre-defined data extraction format. These included year of publication, first author, geographical or study area, total number of samples, number of LA-MRSA positive samples and method used for confirmation of LA-MRSA. Any discrepancy in data extraction was resolved through discussion and consensus. The study quality was assessed by scoring defined parameters by simple scale system (Bian *et al.*, 2015). The parameters included were-

i) Was the research objective clearly described in the study? (Not clear=0, clear=1)
ii) Was the population defined? (not defined=0, defined=1)
iii) Was the sample size adequate? (sample size below 50=0, 50-100=1, above 100=2)
iv) Was confirmation test used for identification of MRSA? (No confirmation test used=0, Confirmation test used=1)
v) Was the sample collected from healthy animal or clinical case? (Clinical cases=0, healthy animals/environment=1).

Each study has the chance of maximum score of seven and studies that has score of four and above were considered for the analysis purpose.

Analytical Approach

The meta-analysis of prevalence of MRSA in animal in India was conducted using the R Open source Scripting software version 3.4.3. The R packages used for meta-analysis was meta. The Tau square test was conducted to assess the heterogeneity between the studies, evaluated by using Tau square (τ^2) value and its level of significance (Borenstein *et al.*, 2009; Krishnamoorthy *et al.*, 2017). Results of meta-analysis for random effect model were used if the heterogeneity between the studies was significant with higher τ^2 (Lean *et al.*, 2009; Krishnamoorthy *et al.*, 2017). I^2 value, describing the percentage variation between studies was

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used to indicate the degree of heterogeneity between studies. If the I^2 value indicated considerable heterogeneity, the summary measures were combined across the studies using random effect model, assuming that the included study represents a sample from a larger population.

Strategy Adopted for Addressing Heterogeneity

Numbers of options were used in the present study to address the heterogeneity.

i) **Checking the Correctness of Extracted Data**: Errors in unit of analysis, proportion or prevalence of present study, may lead to severe heterogeneity because of incorrect extraction.
ii) **Exploring Heterogeneity**: The cause of heterogeneity if present among the different studies have to be considered. The presence of heterogeneity, were validated by conducting analysis stratified by samples, region and year.
iii) **Performing Random-Effect Model:** Fixed-effect meta-analysis ignores heterogeneity. Pooled effect estimate from a fixed effect meta-analysis is normally interpreted as being best estimate or prevalence. However, presence of heterogeneity suggests that, there may not be a single population estimate but a distribution of number of population effect. Thus using fixed-effect model may be erroneous and random effect model is used to incorporate heterogeneity among the studies.
iv) **Refining Studies:** The presence of outlier studies with large τ^2 were excluded from study, in order to eradicate bias and unreliability.

Forest Plot

Forest plot, a method utilized to present the results of meta-analysis, displaying effect estimate and their confidence intervals for each study. Each study was represented by a square as a point estimate of the effect and a horizontal line extending either side of the block depicting a 95% confidence interval. The area of the block was proportional to the weight assigned to that study in the meta-analysis. Forest plots normally include the results of the overall effect from meta-analysis, normally at the bottom of the plot, in the form of a diamond to distinguish from the individual studies. The Q statistics were calculated as reported earlier (Krishnamoorthy *et al.,* 2017) to assess the level of significance between the studies and to select either fixed effect model or random effect model.

Sensitivity Analysis

Sensitivity analysis was used to examine the effect of studies identified as being highly influential in the analysis. This sensitivity analysis was used to explore sources of heterogeneity in the body of the research. The sensitivity analysis has been employed to detect the influential study, by omitting one study at each time.

Stratified Analysis

Stratified analysis has been frequently used to reduce the level of heterogeneity in the studies. The data was stratified based on the type of samples: clinical samples and samples from healthy animals. The studies

were stratified per year from 2010 to 2017 and geographical five zones, namely North zone (Jammu and Kashmir, Punjab, Uttar Pradesh, Haryana), East zone (Bihar, West Bengal, Sikkim, Assam), West zone (Rajasthan, Gujarat), South zone (Telangana, Andhra Pradesh, Tamil Nadu, Puducherry) and Central zones (Madhya Pradesh).

Results

Article Description and characteristics

A total of 46 studies were identified from the database search performed using the key words. The schematic diagram of article review process is presented in Fig.1.

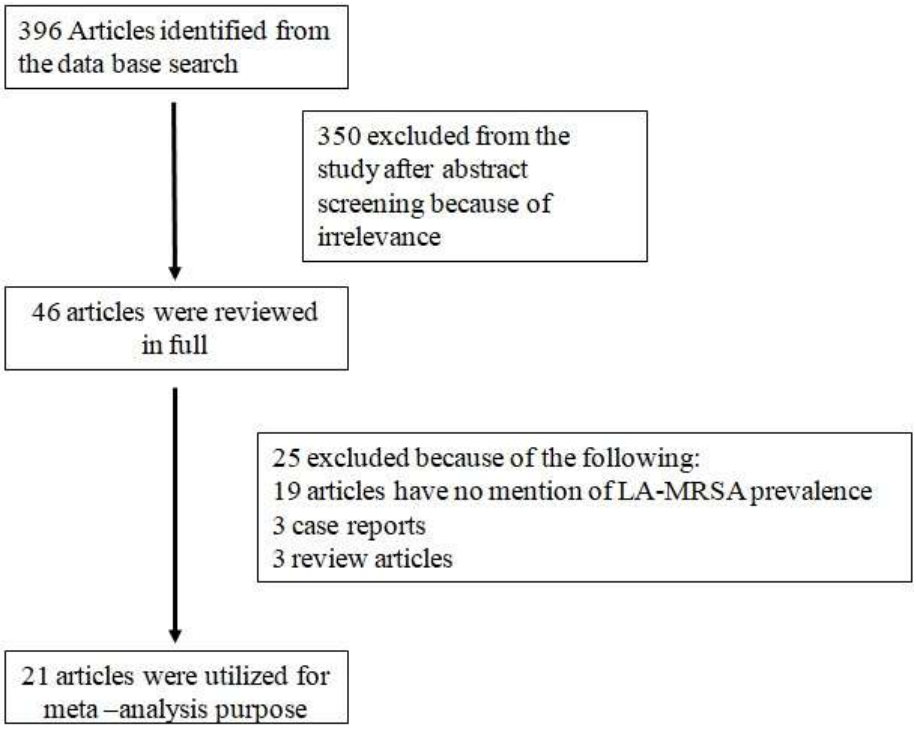

Fig. 1: Schematic diagram showing the review process of studies on MRSA prevalence.

These articles were reviewed completely and 21 articles were included for meta-analysis. A total of 25 articles were excluded because the prevalence of MRSA was not discussed, it included case reports or review articles. The sensitivity analysis of the studies were carried and their details are given in Table 1. The studies with total score of 4 and above were included for the meta-analysis. The total studies included were from North (n=10), East (n=4), West (n=2), South (n=4) and Central (n=1) zones of India. The animal samples (n=5,026) were considered, which includes, clinically sick animal samples (n=1,894) and healthy animal samples (n=3,132) from 14 and 8 studies, respectively. In the animal clinical samples studied were

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mainly from mastitis milk, samples from clinical settings and wound samples. In healthy animals, the study samples included were nasal swab, skin swab, fecal, milk and dairy farm environment samples.

Table 1: Quality assessment of studies included for meta-analysis for LA-MRSA prevalence

S. No.	Author/Year	Research Question/objective	Population defined	Sample size adequacy	Test used for confirmation	Sample type	Score
1.	Chandrasekaran *et al.*, 2014	Clear	Defined	Adequate	Yes	Clinical	5
2.	Chaturvedi and Kumar 2017	Clear	Defined	Adequate	No	Healthy	5
3.	Ganai *et al.*, 2015	Clear	Defined	Partially adequate	Yes	Healthy	5
4.	Ganai *et al.*, 2015	Clear	Defined	Partially adequate	Yes	Clinical	4
5.	Ganai *et al.*, 2016	Clear	Defined Cattle	Partially adequate	Yes	Clinical	4
6.	Ganai *et al.*, 2016	Clear	Defined Buffalo	Partially adequate	Yes	Clinical	4
7.	Ganai *et al.*, 2016	Clear	Defined Goat	Partially adequate	Yes	Clinical	4
8.	Hamid *et al.*, 2017	Clear	Defined	Adequate	Yes	Clinical	5
9.	Kumar *et al.*, 2010	Clear	Defined	Adequate	No	Clinical	4
10.	Kumar *et al.*, 2011	Clear	Defined	Adequate	Yes	Clinical	5
11.	Kumar *et al.*, 2017	Clear	Defined	Adequate	Yes	Healthy	6
12.	Kutar *et al.*, 2015	Clear	Defined	Adequate	Yes	Clinical	5
13.	Mistry *et al.*, 2016	Clear	Defined	Adequate	Yes	Clinical	5
14.	Patel *et al.*, 2017	Clear	Defined	Adequate	Yes	Healthy	6
15.	Paul *et al.*, 2015	Clear	Defined	Adequate	Yes	Clinical	5
16.	Rai and Tiwari 2016	Clear	Defined	Adequate	No	Healthy	5
17.	Rajkhowa *et al.*, 2016	Clear	Defined Nasal swab	Adequate	Yes	Healthy	6
18.	Rajkhowa *et al.*, 2016	Clear	Defined Skin swab	Adequate	Yes	Healthy	6
19.	Rajkhowa *et al.*, 2016	Clear	Defined Faecal swab	Adequate	Yes	Healthy	6
20.	Sharma *et al.*, 2017	Clear	Defined	Adequate	Yes	Healthy	6
21.	Sharma *et al.*, 2015	Clear	Defined	Adequate	No	Clinical	4
22.	Shrivastava *et al.*, 2017	Clear	Defined	Adequate	Yes	Clinical	5
23.	Swetha *et al.*, 2017	Clear	Defined	Adequate	No	Healthy	5
24.	Tiwari *et al.*, 2016	Clear	Defined	Adequate	No	Clinical	4
25.	Vishnupriya *et al.*, 2014	Clear	Defined	Adequate	Yes	Clinical	4
26.	Yadav *et al.*, 2016	Clear	Defined	Partially adequate	Yes	Clinical	4

Pooled LA-MRSA Prevalence in Different Samples

Using the random effect model, obtained from screening 5,026 animal samples, the pooled prevalence of LA-MRSA was 10% (95% CI: 7-13%; τ^2=0.6654; I^2=90%; p<0.01). The details of the studies including author, year, sample details, positive samples, total samples studied, statistical analysis values along with forest plot is depicted in Fig. 2.

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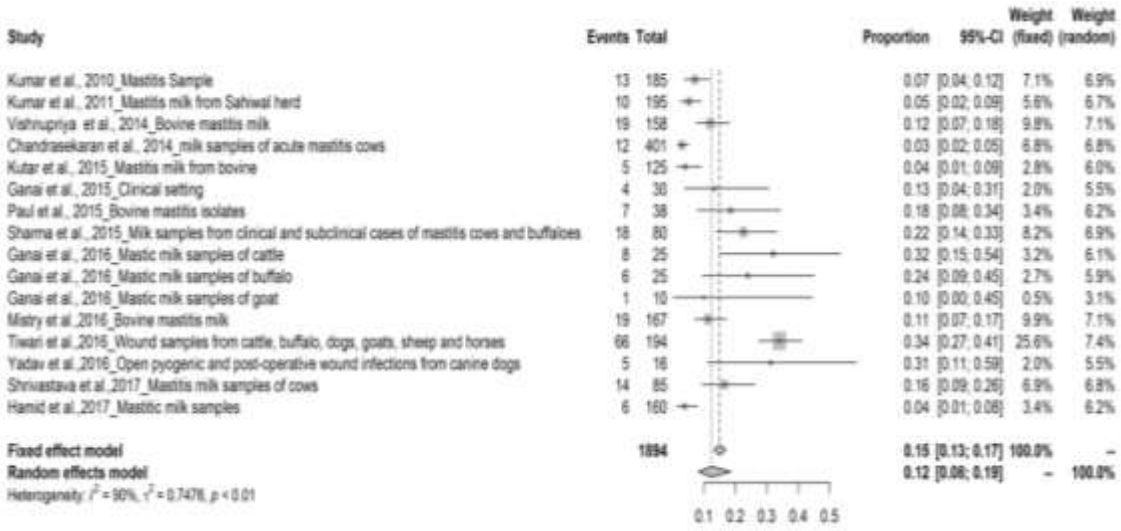

Fig. 2: Forest plot of studies on the prevalence of Livestock Associated-Methicillin-resistant *Staphylococcus aureus* (LA-MRSA) from various animals in India.

There was significant heterogeneity (p <0.01) among the 21 studies. Therefore, to reduce the heterogeneity, the studies were stratified based on sample type into clinically sick and healthy animal samples. The sample, geographical zones and year meta-analysis results were given in Table 2.

Table 2: Meta-analysis of LA-MRSA prevalence in animals in India

S. No.	Stratum	Period	Number of Studies	Total samples	Pooled Prevalence[%] (95% C I)	I^2 Value	τ^2 Value	Degrees of Freedom	Q Statistic Value
All 21 Studies Included									
1	LA-MRSA in Animals	2010-2017	21	5026	10 (7-13)	0.9	0.6654	20	200.00**
Stratified by Type of Samples									
1	Clinical Samples	2010-2017	14	1894	12 (8-19)	0.9	0.7476	13	130.00**
2	Healthy Animal Samples	2015-2017	8	3132	7 (5-10)	0.86	0.3583	7	50.00**
Stratified by Geographical Zones									
1	North Zone	2010-2017	10	1200	12 (7-19)	0.9	0.9397	9	90.00**
2	East Zone	2015-2017	4	2368	8 (5-15)	0.91	0.5945	3	33.33**
3	West Zone	2017	2	547	6 (3-12)	0.76	0.2227	1	4.17ns
4	South Zone	2014-2017	4	826	8 (4-15)	0.84	0.4139	3	18.75**
5	Central Zone	2017	1	85	16 (9-26)	-	-	0	0
Stratified per Year									
1	2010	2010	1	185	7 (4-12)	-	-	0	0
2	2011	2011	1	195	5 (2-9)	-	-	0	0
3	2014	2014	2	559	6 (2-22)	0.93	1.0352	1	14.29**
4	2015	2015	4	303	12 (6-22)	0.74	0.5098	3	11.54**
5	2016	2016	6	2631	13 (7-22)	0.95	0.9499	5	100.00**
6	2017	2017	7	1153	8 (5-13)	0.86	0.5167	6	42.86**

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The prevalence of LA-MRSA among 1,894 clinical samples was 12% (95% CI: 8-19%; τ^2=0.7476; I^2=90%; p<0.01). The details of the studies with forest plot is given in Fig. 3.

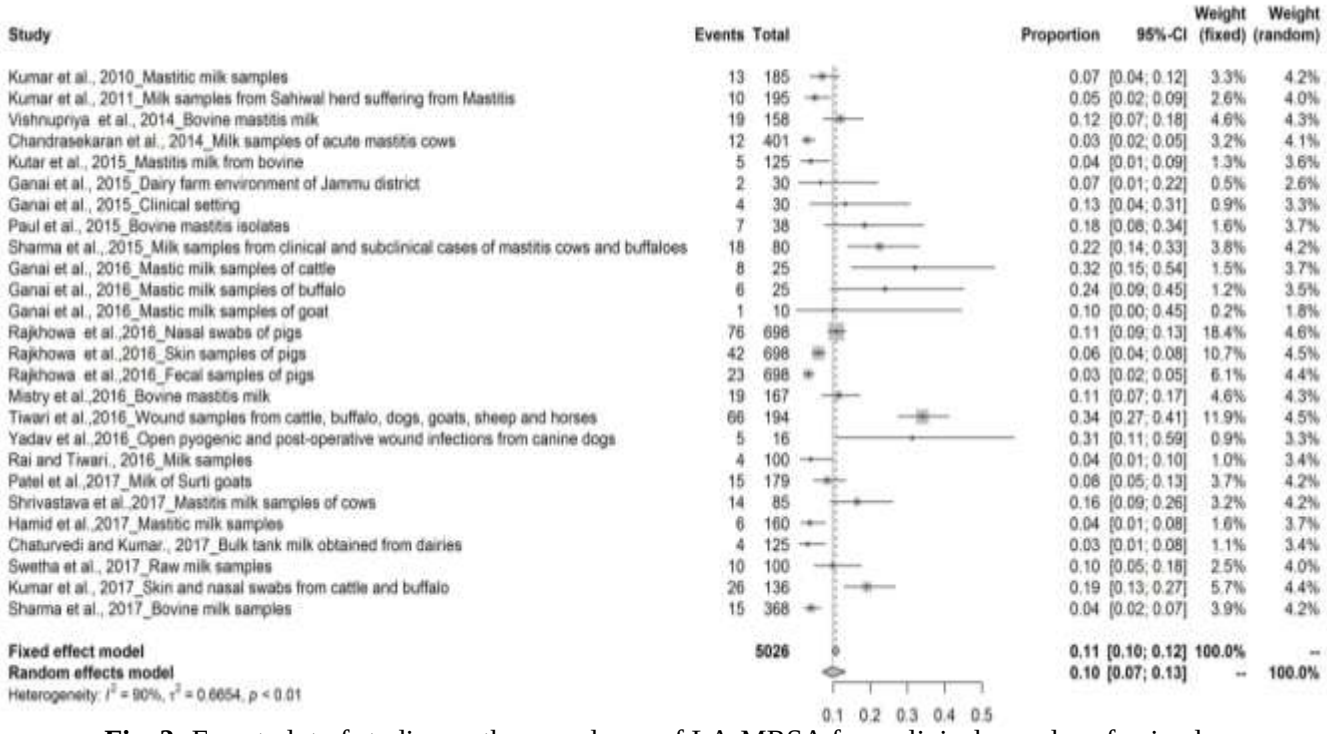

Fig. 3: Forest plot of studies on the prevalence of LA-MRSA from clinical samples of animals.

There was significant heterogeneity (p <0.01) among the 14 studies selected and random effect model was used to determinate an estimate of LA-MRSA prevalence among clinical samples. The prevalence of MRSA among 3,132 samples from healthy animals and from the environment was 7% (95% CI: 5-10%; τ^2=0.3583; I^2=86%; p<0.01). The details of the study and forest plot is detailed in Fig. 4.

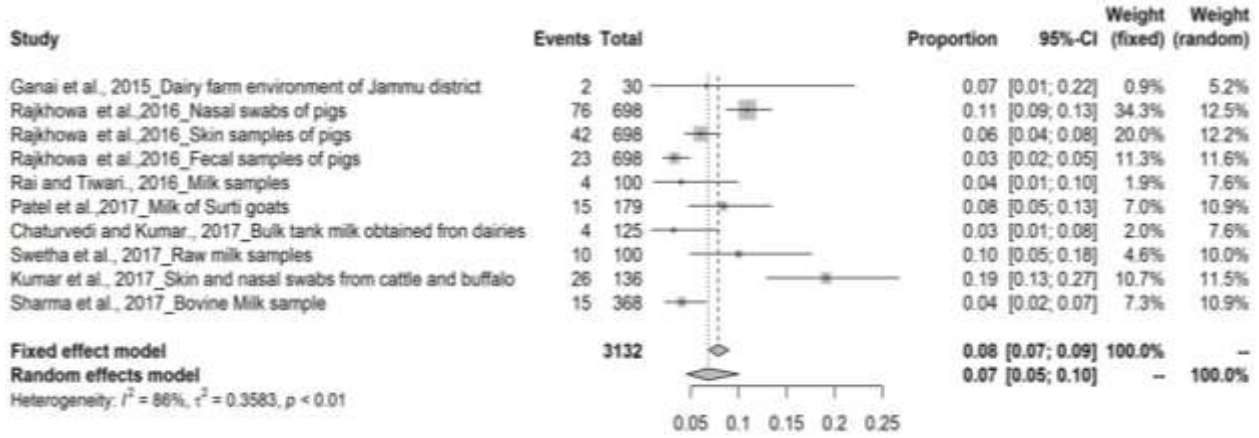

Fig. 4: Forest plot of studies on the prevalence of LA-MRSA from environmental and healthy animal samples.

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There was significant heterogeneity ($p < 0.01$) among the 8 studies selected. Stratified by zones analysis revealed LA-MRSA prevalence were 12%, 8%, 6%, 8% and 16% in North, East, West, South and Central zones, respectively ,whereas only one study was reported from Central zone. When the five different zones were compared for the MRSA prevalence in India, the North and Central zone revealed high prevalence of MRSA than other zones. It indicated the importance of LA-MRSA in these zones in animals. The per year analysis revealed LA-MRSA prevalence were 6%, 12%, 13% and 8% for the period 2014, 2015, 2016 and 2017, respectively. Based on the per year prevalence, it showed increasing trend in the prevalence up to 2016 and declined during the year 2017 and but the number of studies on LA-MRSA prevalence showed increasing trend over the years.

LA-MRSA is probably not a major zoonotic and public health concern, we obtained an estimate of prevalence of 10% (7-13%) in animals which was lesser when compared to humans, where the prevalence was 25-50% as reported earlier (Patel *et al.,* 2010; Gopalakrishnan and Sureshkumar, 2010). However, a study from organized dairy farms in Andhra Pradesh recorded 23.1% of mec A gene presence by PCR from samples collected from cattle, buffalo and animal handlers (Reshma *et al.,* 2017), which was high when compared to the present study. The use of antibiotics in animals is not strictly regulated by law in India. In livestock sector, the antibiotics are used for the treatment purpose by Veterinarians and Para-veterinarians without any control in India. However, certain restrictions are there on the use of antibiotics in livestock products, poultry products and seafood for export purposes are available (Srivastava *et al.,* 2011). In recent times, methicillin-resistant bacteria have been reported in wastewater treatment plants and environmental water samples. Since a large part of the antibiotics consumed by humans and animals end up in wastewater, the antibiotics may exert selective pressure resulting in the emergence and transmission of the resistance conferring genes in antibiotic susceptible organisms as reported (Goldstein *et al.,* 2012). Hence, it is imperative to improve sanitation systems to eliminate resistant bacteria in wastewater as stated previously (Economou and Gousia, 2015). The pooled prevalence of MRSA from clinical samples was higher than healthy animal samples. This could be due to imprudent use of antibiotics used to treat the clinical condition as described earlier (Kumar *et al.,* 2011). Therefore, it is very important to implement a systematic application of an *in vitro* antibiotic susceptibility test prior to the use of antibiotics in both treatment and prevention of infections (Unakal and Kaliwal, 2010). MRSA strains have been observed to be multidrug resistant, such as aminoglycosides, macrolides, lincosamides, streptogramins and tetracyclines in animals which are often used in the treatment of mastitis (Chandrasekaran *et al.,* 2014). The prevalence of LA-MRSA among clinical samples indicated that these animals can act as reservoir for the LA-MRSA transmission to other animals and humans. The mode of transmission of MRSA to healthy animals and humans can be through direct contact with the infected animals or through environmental contamination or contaminated meat, consumption of raw milk (WHO 1997, Khachatourians 1998). However,

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microbiological and clinical evidences have shown that non therapeutic use of antibiotics in animals has led to the selection of resistant forms of bacteria particularly in favorable ecosystems (WHO 1997, Khachatourians, 1998).

The prevalence of MRSA increased over the time, from 2014 to 2016 and may be due to the drug selection pressure as a result of abuse of antibiotics for treatment of the clinical condition (Mehndiratta and Bhalla, 2014). However in 2017, there was a decrease in the prevalence of LA-MRSA, which could be due to awareness of antibiotics use in India and also globally. Hence, in order to tackle the antibiotic resistant microorganisms, routine mass medication should be avoided by reducing the antimicrobial selective pressure in animals, transmission of MRSA between and within the farms should be prevented by taking proper sanitary measures. The colonized animals should be identified and isolated to minimize the risk for zoonotic infection, contact precautions such as protective clothing, overalls, aprons or coats and boots or overshoes should be used when handling and treating MRSA positive animals (Mohammed and Nigatu, 2015). Efforts are being made to meet the challenges of antibiotic resistance in India by monitoring and promoting rational drug use by imparting education and training, conducting surveillances, setting up international partnership programs and making national antibiotic policies with the Government to regulate the use of antibiotics in humans as well as in veterinary medicine (GARP India Working Group 2011, Srivastava *et al.*, 2011).

There are several limitations to this study, first, some information was discarded, because only articles containing information on total number of samples, total LA-MRSA positive samples and method used for confirmation of MRSA were considered for the meta-analysis. Second, another limitation is that most studies (14 out of 21) were based in clinical samples, which may not be representative of the population. Third, among the 21 included studies, the sample size, sample type, species from which the sample was drawn and sampling method varied. Hence, due to difference in sensitivity of test used and sample type the prevalence rates may vary between the studies.

Conclusion

To the best of our knowledge, the current study is the first systematic review and meta-analysis of the prevalence of LA-MRSA among animal samples from India. The pooled prevalence of MRSA in animals in India was found to be 10% which is lower than that of MRSA prevalence in humans. However, cautious use of antibiotics in veterinary medicine, awareness campaigns and maintenance of fundamental hygiene is necessary to control MRSA prevalence in India. The higher prevalence rate of MRSA in clinical samples, in comparison with healthy samples clearly depicts the rise of MRSA due to overuse and abuse of antibiotics to treat the clinical conditions in animals. Geographical Zones indicated higher prevalence in north and central zones which requires necessary action to tackle the situation. Further studies, on relationship

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between use of antibiotics and LA-MRSA prevalence can be performed in different geographical areas in India. Moreover, a collaborative approach of both human and animal health on antibiotics can be performed to establish a better comparison between the prevalence rate in human and animals respectively.

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References

1. Antoci E, Pinzone MR, Nunnari G, Stefani S and Cacopardo B. (2013). Prevalence and molecular characteristics of methicillin-resistant Staphylococcus aureus (MRSA) among subjects working on bovine dairy farms. *Le Infezioni in Medicina, 21,* 125-129.
2. Bian CR, Lu DB, Su J, Zhou X, Zhuge HX and Lamberton PH. (2015). Serological prevalence of Schistosoma japonicum in mobile populations in previously endemic but Now Non-endemic regions of china: a systematic review and meta-analysis. *PLoS One, 10,* 1-21.
3. Borenstein M, Hedges LV, Higgins J and Rothstein HR. (2009). Introduction to Meta-Analysis. New York, USA: John Wiley & Sons Ltd. 409-414.
4. Chandrasekaran D, Venkatesan P, Tirumurugaan KG, Nambi AP, Thirunavukkarasu PS, Kumanan K, Vairamuthu S and Ramesh S. (2014). Pattern of antibiotic resistant mastitis in dairy cows. *Veterinary World, 7,* 389-394.
5. Chaturvedi R and Kumar Y. (2017). Prevalence of Staphylococcus aureus in Bulk Tank Milk Collected from Dairies of District Allahabad India. *International Journal of Current Microbiology and Applied Science, 6,* 1297-1303.
6. Devriese LA, Damme LV and Fameree L. (1972). Methicillin (Cloxacillin) - Resistant *Staphylococcus aureus* strains isolated from Bovine Mastitis Cases. *Zoo Pub Health, 19,* 598-605.
7. Dixit NS, Kothari D and Chandrakar SS. (2017). Prevalence of Methicillin Resistant *Staphylococcus aureus* in Surgical Units of a Tertiary Care Hospital. *Intl J Innov Res Medical Science, 2,* 1075-1079.
8. Economou V and Gousia P. (2015). Agriculture and food animals as a source of antimicrobial resistant bacteria. *Infection Drug Resistance, 8,* 49-61.
9. Ganai AW, Kotwal S, Malik M, Sharma H, Wani N and Jeelani R. (2015). Prevalence of Staphylococcus aureus and Methicillin Resistant *Staphylococcus aureus* (MRSA) in Clinical Setting and Dairy Farm Environment of Jammu. *Journal of Animal Research, 5,* 539.
10. Ganai AW, Kotwal S, Wani N, Malik M, Jeelani R, Kour S and Zargar R. (2016). Detection of mecA gene of methicillin resistant Staphylococcus aureus by PCR assay from raw milk. *Indian Journal of Animal Science, 86,* 508-511.
11. Goldstein RER, Micallef SA, Gibbs SG, Davis JA, He X, George A and Joseph SW. (2012). Methicillin-resistant *Staphylococcus aureus* (MRSA) detected at four US wastewater treatment plants. *Environmental Health Perspectives, 120,* 1551.
12. Gopal S and Divya KC. (2017). Can methicillin-resistant *Staphylococcus aureus* prevalence from dairy cows in India act as potential risk for community-associated infections? A review. *Veterinary World, 10,* 311-318.
13. Gopalakrishnan R and Sureshkumar D. (2010). Changing trends in antimicrobial susceptibility and hospital acquired infections over an 8 year period in a tertiary care hospital in relation to introduction of an infection control programme. *Journal of Association of Physicians of India, 58,* 25-31.

14. GARP. (2011). Global Antibiotic Resistance Partnership India Working Group, Rationalizing antibiotic use to limit antibiotic resistance in India. *The Indian Journal of Medical Research, 134,* 281.
15. Haidich AB. (2010). Meta-analysis in medical research. *Hippokratia, 14,* 29-37.
16. Hamid S, Bhat MA, Mir IA, Taku A, Badroo GA, Nazki S and Malik A. (2017). Phenotypic and genotypic characterization of Methicillin-resistant *Staphylococcus aureus* from bovine mastitis. *Veterinary World, 10,* 363-367.
17. Khachatourians GG. (1998). Agricultural use of antibiotics and the evolution and transfer of antibiotic-resistant bacteria. *Canadian Medical Association Journal, 159,* 1129-1136.
18. Krishnamoorthy P, Suresh KP, Saha S, Govindaraj G, Shome BR and Roy P. (2017). Meta-analysis of prevalence of Subclinical and Clinical Mastitis, Major Mastitis Pathogens in Dairy Cattle in India. *International Journal of Current Microbiology and Applied Science, 6*(3), 1214-1234.
19. Kumar A, Kaushik P, Kumar PA and Kumar M. (2017). Prevalence of methicillin-resistant *Staphylococcus aureus* skin and nasal carriage isolates from bovines and its antibiogram. *Veterinary World, 10,* 593-597.
20. Kumar R, Yadav BR and Singh RS. (2011). Antibiotic resistance and pathogenicity factors in *Staphylococcus aureus* isolated from mastitic Sahiwal cattle. *Journal of Bioscience, 36,* 175-188.
21. Kumar R, Yadav BR and Singh RS. (2010). Genetic determinants of antibiotic resistance in *Staphylococcus aureus* isolates from milk of mastitic crossbred cattle. *Current Microbiology, 60,* 379-386.
22. Kutar K, Verma A, Sharma B, Kumar A and Yadav SK. (2015). Analysis of mec A Gene and Antibiotic Resistance in *Staphylococcus aureus* isolates from Bovine Mastitis. *Indian J Comp Microbiol Immunol Infectious Disease, 36,* 22.
23. Lean IJ, Rabiee AR, Duffield TF and Dohoo IR. (2009). Invited review: Use of meta-analysis in animal health and reproduction, methods and applications. *Journal of Dairy Science, 92,* 3545-3565.
24. Mehndiratta PL and Bhalla P. (2014). Use of antibiotics in animal agriculture and emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) clones: Need to assess the impact on public health. *Indian Journal of Medical Research, 140,* 339-344.
25. Mistry H, Sharma P, Mahato S, Saravanan R, Kumar PA and Bhandari V. (2016). Prevalence and characterization of Oxacillin susceptible mecA positive clinical isolates of *Staphylococcus aureus* causing bovine mastitis in India. *PLoS One, 11,* 1-10.
26. Mohammed S and Nigatu S. (2015). Review on Livestock associated Methicillin resistant *Staphylococcus aureus* and its zoonotic importance. *International Journal of Microbiological Research, 6,* 164-174.
27. Patel SA, Savalia CV, Kumar R, Gamit MA, Nair S, Patel RK and Patel NG. (2017). Incidence of Methicillin Resistant *Staphylococcus aureus* in the milk of Surti Goats. *International Journal of Agricultural Science, 9,* 3637-3639.
28. Patel AK, Patel KK, Patel KR, Shah S and Dileep P. (2010). Time trends in the epidemiology of microbial infections at a tertiary care center in west India over last 5 years. *Journal of Association of Physicians in India, 58,* 37-40.
29. Paul I, Isore D, Joardar S, Mukhopadhayay S, Jana C and Ganguly S. (2015). Investigation on Methicillin resistant gene of *Staphylococcus aureus* causing Bovine Mastitis. *Indian J Comp Microbiol Immunol Infectious Disease, 36,* 35.
30. Rai A and Tiwari HK. (2016). Prevalence and Antimicrobial Resistance of Methicillin Resistant *Staphylococcus aureus* (MRSA) in Cow Milk from Gangtok, East Sikkim. *Intl Interdisciplinary Research Journal, 6,* 91-102.
31. Rajkhowa S, Sarma DK and Pegu SR. (2016). SCC mec typing and antimicrobial resistance of methicillin-resistant *Staphylococcus aureus* (MRSA) from pigs of Northeast India. *Veterinary Research Communication, 40,* 117-122.

DOI 10.5455/ijlr.20180918100103

32. Reshma, S., Rao, S. T., Rao, M. T., Subramanyam, K., & Sekhar, M. (2017). Occurrence of Bovine and Human Methicillin-Resistant Staphylococcus aureus in Organised Dairy Farms of Andhra Pradesh, India. *International Journal of Livestock Research, 7*(10), 154-160.
33. Sharma L, Verma AK, Kumar A, Rahat A, Neha, R and Nigam R. (2015). Incidence and Pattern of Antibiotic Resistance of *Staphylococcus aureus* isolated from Clinical and Subclinical Mastitis in Cattle and Buffaloes. *Asian Journal of Animal Science, 9*, 100-109.
34. Sharma V, Sharma S, Dahiya DK, Khan A, Mathur M and Sharma A. (2017). Coagulase gene polymorphism, enterotoxigenecity, biofilm production, and antibiotic resistance in Staphylococcus aureus isolated from bovine raw milk in North West India. *Annals of Clinical Microbiology and Antimicrobials, 16,* 1-14.
35. Shrivastava N, Sharma V, Nayak A, Shrivastava A, Sarkhel B, Shukla P and Shrivastava A. (2017). Prevalence and Characterization of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Mastitis in Dairy Cattle in Jabalpur, Madhya Pradesh. *Journal of Animal Research, 7,* 77-84.
36. Srivastava RK, Chaudhury RR, Bramhachari SK, Singh S, Guleria R, Sinha A and Kotwani A. (2011). National policy for containment of antimicrobial resistance India. DGHS, Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi.
37. Smith TC. (2015). Livestock-associated *Staphylococcus aureus*: the United States experience. *PLoS Pathogens, 11,* 1-8.
38. Swetha CS, Supriya RA, Goud SS, Babu AJ and Rao TM. (2017). A study on the prevalence of zoonotic important methicillin resistant and vancomycin resistant *Staphylococcus aureus* (MRSA & VRSA) and coagulase negative Staphylococci (MR-CNS & VR-CNS) in raw milk samples of Tirupati, Andhra Pradesh. *The Pharmacology International Journal, 6,* 17-24.
39. Tiwari R, Yadav SK and Singh S. (2016). Methicillin resistant *Staphylococcus aureus* Isolated from Wounds of Livestock and Companion Animals of Uttar Pradesh India, A Preliminary Study. *International Journal of Pharmacology, 12,* 821-829.
40. Unakal CG and Kaliwal BB. (2010). Prevalence and antibiotic susceptibility of *Staphylococcus aureus* from bovine mastitis. *Veterinary World, 3,* 65-67.
41. Vishnupriya S, Antony PX, Mukhopadhyay HK, Pillai RM, Thanislass J, Srinivas, VVM and Kumar RS. (2014). Methicillin resistant staphylococci associated with bovine mastitis and their zoonotic importance. *Veterinary World, 7,* 422-427.
42. Walker E, Hernandez AV and Kattan MW. (2008). Meta-analysis: Its strengths and limitations. *Cleveland Clinical Journal of Medicine, 75,* 431-439.
43. WHO. (1997). The Medical Impact of Antimicrobial Use in Food Animals, Report of a WHO Meeting. Berlin, Germany. WHO/EMC/ZOO/97.4.
44. Yadav R, Singh VK, Kumar A and Yadav SK. (2016). Characterization of Antibiogram and some virulence attributes in Methicillin Resistant *Staphylococcus aureus* (MRSA) of Canine Origin. *Indian J Comp Microbiol Immunol Infectious Disease, 37,* 92.

DOI 10.5455/ijlr.20180918100103