Prevalence of methicillin-resistant *Staphylococcus aureus* in India: A systematic review and meta-analysis

Sharanagouda S. Patil[1], Kuralayanapalya Puttahonnappa Suresh[1], Rajamani Shinduja[1], Raghavendra G. Amachawadi[2], Srikantiah Chandrashekar[3], Sushma P[4], Shiva Prasad Kollur[5], Asad Syed[6], Richa Sood[7], Parimal Roy[1] and Chandan Shivamallu[4,*]

[1]ICAR-National Institute of Veterinary Epidemiology and Disease Informatics (NIVEDI), Yelahanka, Bengaluru-560064, India.
[2]Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506, USA.
[3]Professor and Managing Director, ChanRe Rheumatology and Immunology Center and Research
No. 65 (414), 20th Main, West of Chord road, 1st Block, Rajajinagar, Bengaluru-560010, India.
[4]Department of Biotechnology and Bioinformatics, School of Life Sciences, JSS Academy of Higher Education & Research, Mysuru, Karnataka-570015, India.
[5]Department of Sciences, Amrita School of Arts and Sciences, Mysuru, Amrita Vishwa Vidyapeetham, Karnataka – 570 026, India.
[6]Department of Botany and Microbiology, College of Science, King Saud University, P.O. Box 2455, Riyadh 11451, Saudi Arabia. assyed@ksu.edu.sa
[7]ICAR-National Institute of High Security Animal Disease (NIHSAD), Anand Nagar, Bhopal-462021, M.P., India

Received: 19 December 2020
Accepted: 17 March 2021

***Corresponding author**: chandans@jssuni.edu.in*

DOI 10.5001/omj.2022.22

ABSTRACT

The emergence of Methicillin resistant *Staphylococcus aureus* (MRSA) has increased and becoming a serious concern world-wide including India. Additionally, MRSA isolates are showing resistance to other chemotherapeutic agents. Isolated and valuable reports on prevalence of MRSA are available in India and there is no systematic review on prevalence of MRSA at one place, hence this study was planned. The overall prevalence of MRSA in human population of India was evaluated by state-wise, zone-wise and year-wise. Systematic search from PubMed, Indian journals, Google scholar and J-Gate Plus was carried out and retrieved 98 eligible articles published from 2015 to 2019 in India. The statistical analysis of data was conducted using R software. The overall prevalence of MRSA was found to be 37% (95% CI: 32-41%) during 2015–

2019. The pooled prevalence of MRSA zone-wise was found to be 41% (95%CI: 33-50%), 43% (95% CI: 20-68%), 33% (95% CI: 24-43%), 34% (95% CI: 26-42%), 36 % (95% CI: 25-47%) and 40% (95% CI: 23-58%) for north, east, west, south, central and north east region-zones, respectively. The state-wise stratified results showed a predominance of MRSA in Jammu & Kashmir with 55% (95% CI: 42-67%) prevalence and that of lowest was 21% (95% CI: 11-34%) in Maharashtra. The study indicated that the prevalence data will be of help in formulating and strict implementation of control measures in hospital areas to prevent outbreak of MRSA infection and management of antibiotic usage.

***Keywords*:** Antimicrobial resistance, Humans, India, Meta-analysis, MRSA, prevalence, *Staphylococcus aureus.*

INTRODUCTION

Staphylococcus aureus (S. aureus) is an important pathogen responsible to cause a wide range of human infections such as minor skin infections, pimples, impetigo, boils, cellulitis, folliculitis, carbuncles, scalded skin syndrome, and abscesses including life threatening diseases.[1,2] *S. aureus* is an important pathogen of many nosocomial and community related infections leading to high morbidity and mortality.[3] *S. aureus* possesses various antibiotic resistance mechanisms including to resistance to methicillin (are called MRSA), which consequently becomes difficult in the management of infections. Over the last 50 years, antibiotics have reduced the rate of mortality nevertheless bacteria have known to develop maximum resistance to most of the available antimicrobial agents.[4]

The methicillin resistance expressed by *S. aureus* is contributed by the *mecA* gene that is harboured by the mobile segments of the MRSA strains, which encodes the penicillin-binding protein 2a (PBP2a) that has low-affinity for β-lactam and allows MRSA strains to survive in different concentrations of these antimicrobial agents.[5] It is known that MRSA is now endemic in

India with variation in the antimicrobial susceptibility patterns based on geographical region.[6] Early detection of MRSA and its susceptibility pattern becomes vital for the treatment of the condition as very few antimicrobial agents can be used in the management of the ailment. Hence, it is imperative to study the overall prevalence of MRSA in India so that improved and efficient treatment methods can be developed for the management of MRSA.

The present study concentrates on systematic review and meta-analysis to estimate the pooled prevalence of MRSA in India and state-wise, zone-wise and year-wise analysis was conducted using statistical tool, viz., meta-analysis.

MATERIALS AND METHODS

LITERATURE SEARCH

A systematic search was performed on the articles published from 2015 using the following keywords in various combinations: "*Staphylococcus aureus*", "*S. aureus"*, "MRSA", "prevalence", "India" and "Humans". The literature was screened systematically in various search engines such as J-Gate plus, PubMed and Google Scholar and Indian Journals. The search was limited to the publication dates from 2015 to 2020. In addition, manual searches on citations retrieved from original studies and review articles were also performed. The articles were chosen by screening through the titles and abstracts for relevance based on the inclusion and exclusion criteria.

1.1. *Study selection criteria*

The results after searching were tabulated into excel format, duplicate ones were removed and relevant studies were examined. Our preliminary inclusion criteria was to include all articles having title key word "prevalence of MRSA in India" during 2015 to 2020 only. Articles thus selected were subjected to abstract screening for titles. Studies were read in full for which they

had report on (a) the prevalence of MRSA (b) sample size data (c) events (positive) (d) year of study (e) geographical location of the study (f) diagnostic tests used as confirmatory tool for identification of MRSA. Those articles which did not satisfy the above screening criteria were excluded from the study. Articles containing large number of samples/events were also not included in the study. The studies that did not report the MRSA prevalence, that included review, reports, editorial articles and outbreak reports and studies that were duplicates of included studies, were excluded. The articles that are selected included humans of all age groups. The searches, scrutiny, and methodology were in accordance to the PRISMA protocol (http:// www.prisma-statement.org) (Table S1).

DATA EXTRACTION

The data was extracted from qualified studies that included first author, year of publication study setting/sampling location, number of investigated cases, number of MRSA isolates, sources of isolates, diagnostic methods employed for confirmation, antibiogram results and considered for meta-analysis. Also, we were interested in the year of publication and the location of study setting to stratify the studies based on the year of publication, zone-wise and state-wise. Studies were independently extracted by two investigators and discussed to arrive at a consensus.

RISK OF BIAS AND QUALITY ASSESSMENT

The quality assessment of different studies was done on a fixed rating scale.[7] The scoring was on a scale of 0 to 5, which included evaluation of author and year of study, representativeness of the sample used in the study, ascertainment of the exposure, comparability, and outcome.

META-ANALYSIS

Meta-analysis was carried out using the R Open Source Scripting Software (version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/). Metafor, Metaprop, and Meta of this software were statistical packages used. Tau square, I^2 (Higgin's I^2),

and *p* value were computed to determine the percentage of variation due to heterogeneity among various reports included in this study. Both the random effect and fixed effect model were used to calculate the pooled prevalence of individual diseases. This analysis facilitates generating a weighted average proportion of prevalence of various studies that provides a way forward for proper planning. Graphical representation of the data was depicted as Forest Plots. The restricted maximum-likelihood estimator was used to determine between-study variance (τ^2). The prevalence estimates for MRSA was expressed as a percentage with 95% Confidence Interval (CI). Subgroup analysis was performed as a means of investigating the significance of heterogeneity among the studies. The studies were stratified based on zones of country, year of publication and state-wise in this present study. Subgroup meta-regression analysis was performed to identify the stratified prevalence of MRSA in different regions, study period, sample size and diagnostic tests.

RESULTS

STUDY DETAILS

Articles reporting the prevalence of MRSA were thoroughly screened and irrelevant ones were excluded. A total of 1,831 of 2,717 articles were identified were excluded following the exclusion criteria described above. 886 potential articles were selected using a combination of key words. A total of 98 articles were selected suitable for systematic review and meta-analysis (Figure 1). All the articles described the prevalence of MRSA in India and were for the period of 2015–2020. The prevalence data for this study was extracted and tabulated as per the requirement of the statistical software. 22 states of India had the reports of prevalence of MRSA. Six zones of the country viz., north (Uttara Pradesh, Haryana, Jammu and Kashmir, Himachal Pradesh, Punjab, New Delhi and Uttarakhand), east (West Bengal and Odisha), west (Rajasthan, Maharashtra and Gujarat), south (Tamil Nadu, Telangana, Karnataka Andhra Pradesh, Kerala

and Puducherry), central (Madhya Pradesh) and north east region (Assam, Tripura and Sikkim) zones had varied pooled prevalence of MRSA.

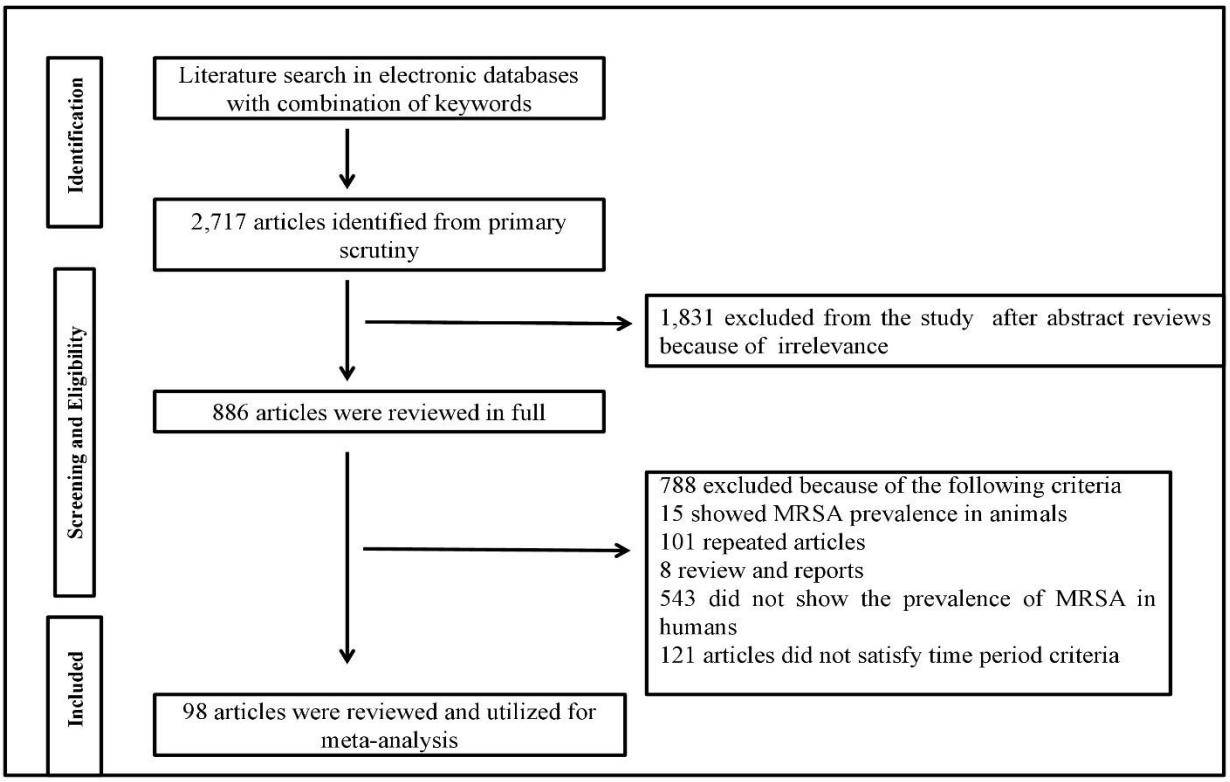

Figure 1: Systematic review and meta-analysis.

RISK OF BIAS AND QUALITY ASSESSMENT

Each section of risk of bias and quality assessment were awarded maximum number of two stars and the score given was on a scale of 0 to 5. Hence, the overall quality assessment has a maximum score of 5 and a minimum score of 3 (Table S2).

META-ANALYSIS OF THE PREVALENCE OF MRSA

The percentage prevalence of MSA in India was estimated statistically using R Open Source Scripting Software. The overall prevalence of MRSA using 17,525 samples in 98 studies was found to be 37% (95% CI: 32-41%) in India during 2015–2019 (I^2 -99%, τ^2 - 0.0571, p=0) (Figure 2). The pooled data was stratified into state-wise and zone-wise.

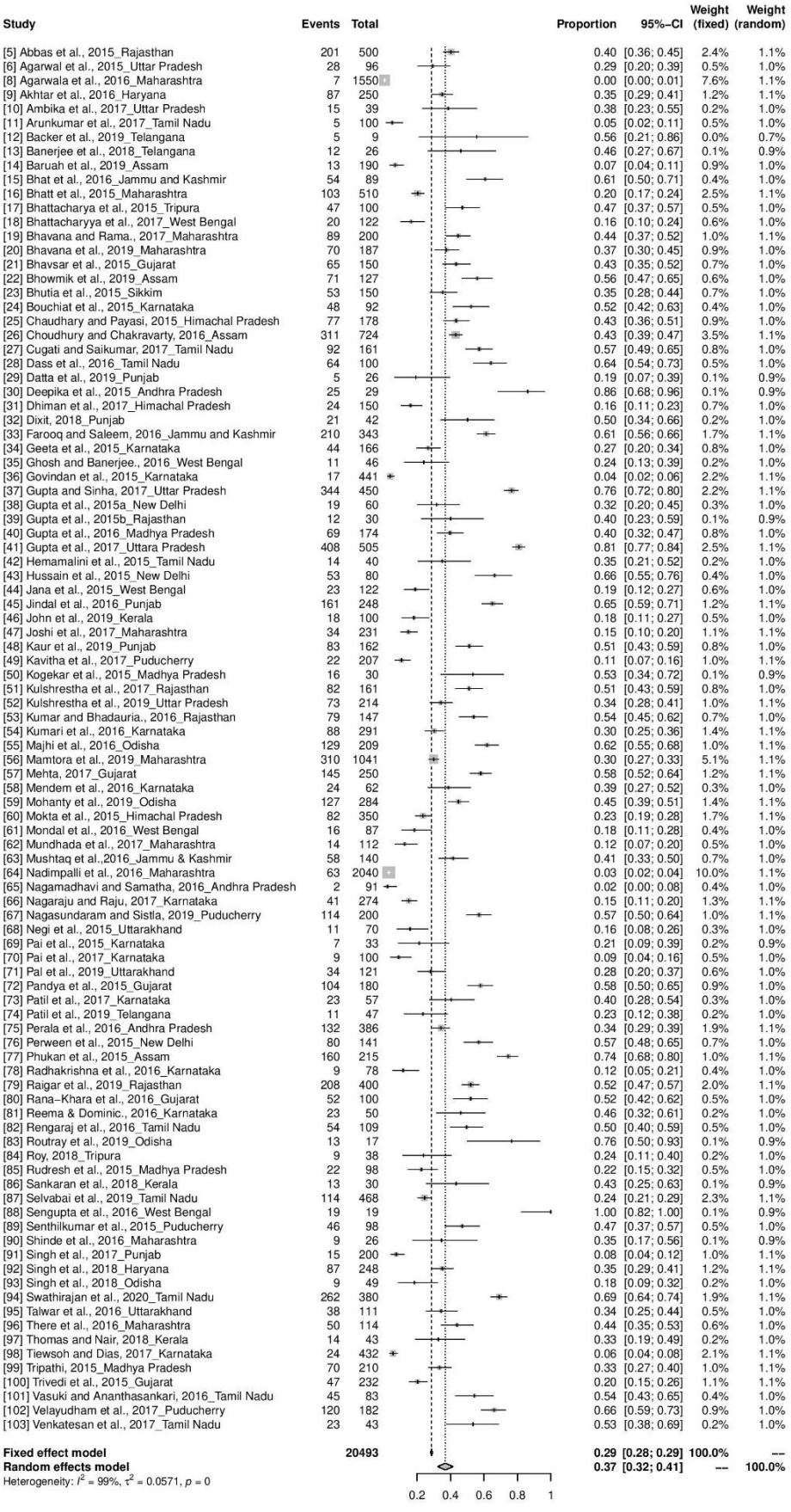

Figure 2: Overall prevalence of MRSA.

State-wise prevalence of MRSA

Twenty two states of India had reported the prevalence of MRSA. Jammu and Kashmir showed the highest pooled prevalence of MRSA as 55% (95% CI: 42-67%) with I^2-88, τ^2-0.0112, p=<0.01 and Maharashtra showed the lowest pooled prevalence of MRSA as 21% (95% CI: 11-34%) with I^2-99, τ^2-0.0517, p=<0.01. A single article from Sikkim had a prevalence of MRSA as 35% (95% CI: 28-44%) (Table 1).

TABLE 1: Details of pooled prevalence of MRSA in 22 districts during 2015-2020

Sl No	Name of the Stae	Pooled Prevalence (%) at 95% CI	I^2 (%)	τ^2	p value
1	Andhra Pradesh	37 (0-89)	98	0.2642	<0.01
2	Assam	43 (15-74)	99	0.1071	<0.01
3	Gujarat	46 (31-60)	96	0.0268	<0.01
4	Haryana	35 (31-39)	0	0	0.95
5	Himachal Pradesh	27 (13-44)	94	0.0229	<0.01
6	Jammu and Kashmir	55 (42-67)	88	0.0112	<0.01
7	Karnataka	23 (14-33)	96	0.0399	<0.01
8	Kerala	30 (16-45)	77	0.0156	0.01
9	Madhya Pradesh	36 (25-47)	78	0.0112	<0.01
10	Maharashtra	21 (11-34)	99	0.0517	<0.01
11	New Delhi	52 (32-71)	89	0.0288	<0.01
12	Odisha	49 (25-73)	93	0.0599	<0.01
13	Puducherry	44 (19-70)	98	0.0730	<0.01
14	Punjab	37 (16-61)	98	0.0738	<0.01
15	Rajasthan	48 (42-54)	77	0.0031	<0.01
16	Sikkim*	35 (28-44)	-	-	-
17	Tamil Nadu	44 (29-60)	97	0.0544	<0.01
18	Telangana	38 (20-58)	66	0.0202,	0.05
19	Tripura	36 (15-60)	85	0.0260	<0.01
20	Uttar Pradesh	53 (30-75)	98	0.0670	<0.01
21	Uttarakhand	26 (16-37)	76	0.0089	0.02
22	West Bengal	39 (6-79)	96	0.2330	<0.01

*, Single article

Year wise prevalence of MRSA

Heterogeneity assessment was performed year-wise (Figure 3). It was found that the studies published during 2015, 2016, 2017, 2018 and 2019 have independent significant heterogeneity, hence sub-group analysis is more appropriate using random effect model to deal with heterogeneity.

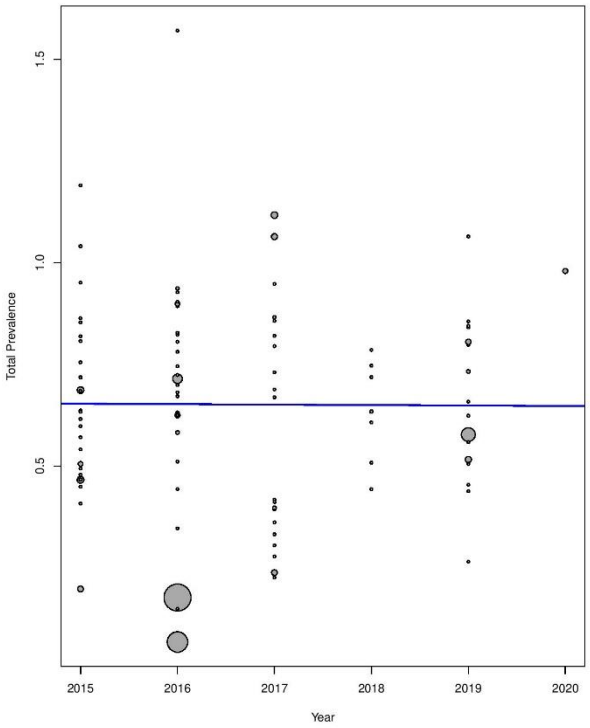

Figure 3: Heterogeneity assessment.

Year 2015: 27 articles in this year showed a prevalence of MRSA as 38% (95% CI: 30-45%) with I^2-97, τ^2-0.0414, p<0.01. Year 2016: 27 articles in this year showed a prevalence of MRSA as 39% (95% CI: 29-50) with I^2-99, τ^2-0.0797, p=<0.01. Year 2017: 20 articles in this year showed a prevalence of MRSA as 31% (95% CI: 20-44) with I^2-99, τ^2-0.0835, p=*0.* Year 2018: 7 articles in this year showed a prevalence of MRSA as 35% (95% CI: 26-43) with I^2-62, τ^2-0.0091, p=0.02. Year 2019: 16 articles in this year showed a prevalence of MSA as 37% (95% CI: 28-46) with I^2-95, τ^2-0.0343, p=<0.01. Year 2020: A single article showed prevalence of MRSA as 69% (64-74) (Table 2).

TABLE 2: Zone wise prevalence of MRSA in India during 2015-20.

Sl No	Region	Pooled Prevalence (%) (95% CI)	I^2 (%)	τ^2	Heterogeneity test		Egger test (predictor=ninv*)		Chi square test
					Q	*P*	t	*P*	
1	**North** (Uttara Pradesh, Haryana, Jammu and Kashmir, Himachal Pradesh, Punjab, New Delhi and Uttarakhand)	41 (33-50)	98	0.0446	991.31	<0.01	-1.55	0.14	1000.57
2	**South** (Tamil Nadu, Telangana, Karnataka Andhra Pradesh, Kerala and Puducherry)	34 (26-42)	98	0.0614	1351.91	<0.01	1.19	0.24	1369.91
3	**West** (Rajasthan, Maharashtra and Gujarat)	33 (24-43)	99	0.514	2551.24	<0.01	2.3	0.030	2559.54
4	**East** (West Bengal and Odisha)	43 (20-68)	96	0.1401	193.14	<0.01	0.57	0.58	209.95
5	**North East** (Assam, Tripura and Sikkim)	40 (23-58)	98	0.0601	260.52	<0.01	-0.27	0.8	264.06
6	**Central** (Madhya Pradesh)	36 (25-47)	78	0.0112	13.3	<0.01	0.58	0.62	13.54
7	**Overall**	37 (32-41)	99	0.0571	6901.21	<0.01	2.44	0.02	1031.2

Zone-wise prevalence of MRSA

In zone-wise analysis (Table 3 and Figure 4), east zone with nine articles (West Bengal and Odisha) showed highest pooled prevalence of 43% (95% CI: 20-68) with I^2-98, τ^2-0.01401, p=<0.01. The lowest prevalence of MRSA was recorded by west zone with 20 articles (Rajasthan, Maharashtra and Gujarat) as 33% (95% CI: 24-43%) with I^2-99, τ^2-0.0514, p=0 and these states are geographically large and densely populated. Twenty four articles in north zone comprising of Uttara Pradesh, Haryana, Jammu and Kashmir, Himachal Pradesh, Punjab, New Delhi and

Uttarakhand was having a pooled prevalence of 41% (95% CI: 33-50%) with I^2-98, τ^2-0.0446, p<0.01. Thirty four articles in south zone consisting of Tamil Nadu, Telangana, Karnataka Andhra Pradesh, Kerala and Puducherry revealed a pooled prevalence of MRSA as 34% (95% CI: 26-42%) with I^2-98, τ^2-0.0614, p<0.01. Four articles in central zone (Madhya Pradesh) showed a pooled prevalence of 36% (95% CI: 25-47%) with I^2-78, τ^2-0.0112, p<0.01. Assam, Tripura and Sikkim are part of north east zone (7 articles) which showed a pooled prevalence of MRSA as 40% (95% CI: 23-58%) with I^2-98, τ^2-0.0601, p<0.01.

TABLE 3: Year wise prevalence of MRSA in India during 2015-20.

Year	Pooled prevalence % (95% CI)	I^2 (%)	τ^2	p value
2015	38 (30-45)	97	0.0414	<0.01
2016	39 (29-50)	99	0.0797	<0.01
2017	31 (20-44)	99	0.0835	<0.01
2018	35 (26-43)	62	0.0091	0.02
2019	37 (28-46)	95	0.0343	<0.01
2020*	69 (64-74)	-	-	-

*, Single article

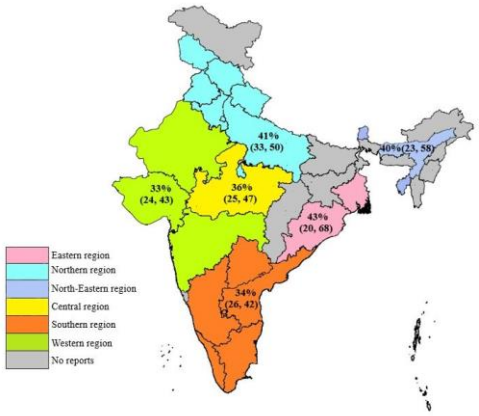

Figure 4: Zone analysis.

Meta-regression analysis

Meta regression is a tool used to examine the effect of moderators on MRSA prevalence rates. In this study, year of publications, samples size, geographical regions and confirmatory tests used for diagnosis of samples are the moderators. After conducting the meta regression, sample size

was found significant (R^2= 7.03; *p*=0.005). The heterogeneity contribution of the moderator variables ranged from 0 to 7.03%. Further investigation of subgroup analysis of sample size was performed, dividing the sample size moderator into two groups viz., less than median and more than median using mixed effect model which yielded I^2=99%, p=0.990. The results of the tests for residual heterogeneity and parameter estimation by meta regression is presented in Table 4 a&b.

TABLE 4a: Test for residual heterogeneity.

Sl no	Predictor	R2(%)	τ^2	I^2 (%)	H^2 (%)	QM value	*p* value
1	Year	0.00	0.0577	97.91	47.78	0.0039	0.9502
2	Sample Size	7.03	0.0531	97.61	41.79	7.8623	0.0050
3	Region	0.00	0.0588	97.89	47.29	2.3638	0.7969
4	Confirmatory test	3.78	0.0549	97.75	44.38	6.4073	0.0934

TABLE 4b: Meta regression parameter estimate

Sl No	**Predictor**	**Estimate**	**95 % CI**	**p value**
1	Year	-0.0011	-0.0354 to 0.0332	0.9356
2	Sample Size	-0.0002	-0.0004 to -0.0001	0.0050
	Group I (More than Median)		0.581 to 0.721	3.744778e-75
	Group II (Less than Median)		0.584 to 0.720	1.910528e-78
3	Region			
	Central	Reference		
	East	0.0592	-0.2354 to 0.3537	0.6938
	North	0.0482	-0.2151 to 0.3116	0.7196
	Northeast	0.0339	-0.2711 to 0.3389	0.8275
	South	-0.0349	-0.2927 to 0.2228	0.7904
	West	-0.0221	-0.2901 to 0.2459	0.8715
4	Confirmatory test			
	MeReSa Agar Screening	Reference		
	Double disk diffusion erythromycin and clindamycin	0.54	0.0499 to 1.0302	0.0608
	Kirby Bauer disk diffusion method Cefoxitin	0.1621	-0.0036 to 0.3278	0.0552
	mecA PCR	0.1528	-0.118 to 0.4236	0.2687

The study included 74 hospital and 24 community settings (total 98 articles). Further investigation of subgroup analysis of hospital and community settings was conducted. The pooled prevalence of MRSA for community settings was 27% (95% CI: 19-35%) (I^2-96, τ^2-0.0521, p<0.01) and that for hospital setting was 49% (95% CI: 35-45%) (I^2-99, τ^2-0.0542, p=0) (Figure 5).

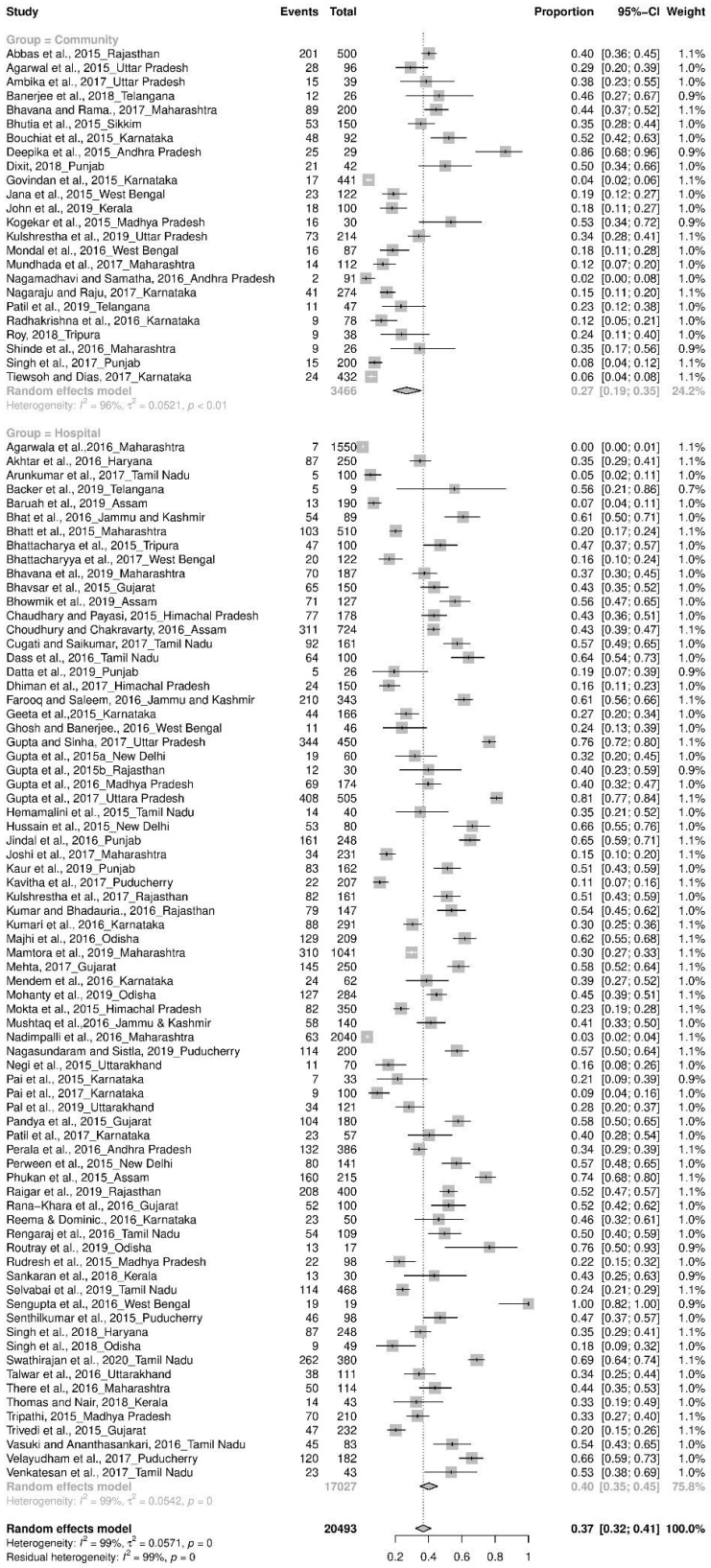

Figure 5: Pooled prevalence of MRSA for community settings.

To assess the heterogeneity between-study reports, a Galbraith plot was generated (Figure 6). The standardized effect estimates against inverse standard error were shown as scattered points in the plot. The points representing the study reports outside confidence bounds may be contributing to the heterogeneity. In the absence of heterogeneity, all points (reports) are expected to lie within the confidence limits centring around the line.

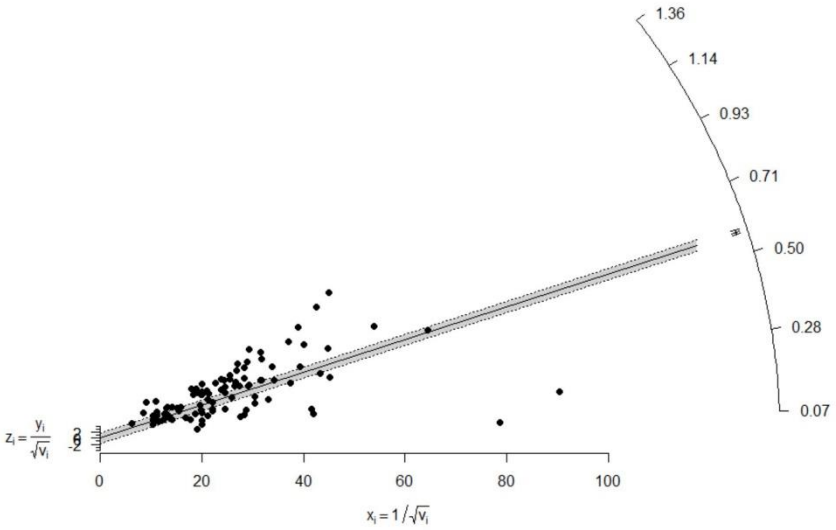

Figure 6: Galbraith plot assessment between study reports.

DISCUSSION

Antibiotic resistance is one of the foremost health concerns of India. There is an alarming increase in the prevalence of *S. aureus* that is resistant to methicillin (MRSA) in India in recent years especially community associated MRSA. MRSA is now endemic in India and incidence is varied. The current policy shows a growing political commitment at the highest levels to take strong action on AMR and, provide adequate support for a nationwide surveillance and stewardship to mitigate the resistance problem.[80]

In the present study, meta-analysis study reveals the pooled prevalence of MRSA in human from India at 37% (95% CI: 32-41%) during 2015–2019. The epidemiology of MRSA in humans is changing gradually in India and the prevalence has increased over the years due to lack of

awareness, overuse of antimicrobial medicines in human health, increase in the infections caused due to lack of sanitation and hygiene, and the paucity of stringent rules and regulations for use of antibiotics. Although the cost of antibiotics is high, the consumption rate has increased due to inappropriate prescribing, indiscriminate use of antibiotics, and sales of antibiotics without prescription. Self-medication with antibiotics that are bought without prescription is also a serious concern in India.

A pooled prevalence of MRSA varied between 31-39% during the 2015-19 (69% in 2020) against total prevalence of 37% at all India level. Jammu and Kashmir showed the highest prevalence of MRSA (55%) which shares a border with Pakistan, though illegal movement may not be ruled out alongside borders. Maharashtra has lowest prevalence of MRSA (21%) and has more number of sophisticated hospitals.

In zone wise analysis, east zone has showed highest prevalence of MRSA (43%) which has West Bengal and Odisha. It is to be mentioned that West Bengal shares a porous border with Bangladesh and there is no restriction of movement of men and material between them. North east zone which comprises of Assam, Tripura and Sikkim has shown the second highest prevalence of MRSA (40%). Assam has porous border with Bhutan and Bangladesh; Tripura shares a porous border with Bangladesh whereas Sikkim sharing with Bhutan, Tibet and Nepal wherein there is no restriction in movement of men and material. In a similar study[104], 46% and 54% of prevalence of MRSA among female and male respectively was recorded in west zone of Iran. 84 isolates from intensive care unit of a hospital of Iran was quite alarming of antimicrobial resistance issue[105].

In year wise analysis, pooled prevalence of MRSA was more during 2016 (39%), followed by that of 38% prevalence during 2015. The reports on prevalence of MRSA (35%) were more homogenous (I^2=62%). It appears that there was a consistency in reporting of prevalence rate of MRSA in all zones India.

The moderate heterogeneity may be due to the total variability effect among the sizes which might not have been caused by sampling error. Further, the heterogeneity between studies can be attributed to the different study settings and study populations since the studies on the prevalence of MRSA from different regions are limited. Heterogeneity between studies could also be due to different population settings under investigation, type of samples used, geographical locations, and hospital/community practices. However, upon scrutinising the forest plots, weight (fixed) assigned to 24 studies under community settings do not exhibit outlier feature. Therefore, the effect of two settings (hospital and community) of pooled prevalence of MRSA is not found to have large difference, the subgroup analysis of studies revealed that the pooled prevalence of MRSA in hospital setting was 40% and that for community was 27%.

Further to meta-analysis, barring selection bias, systematic reviews helps the revision of all the scientific evidence on a given topic. Based on the output, the summarized information can be used to propose hypotheses that explain the behaviour of the data and to identify areas of gaps where further research is needed.[106] However, it is a controversial tool because several conditions are critical and even small violations of these can lead to misleading conclusions. While designing and performing a meta-analysis, several decisions concerning personal judgment and expertise need to be made that may eventually create bias or expectations that influence the result.[107]

CONCLUSION

In this study, the overall pooled prevalence of MRSA in humans in India was found to be very high (37%). Studies comprising of large population in different locations with rapid tests would be of much help in computing prevalence of MRSA. This increase in the prevalence of MRSA builds more emphasis on the need to develop more stringent policies and regulations for the use of antibiotics in the human health-care system. Strict adherence of hand hygiene and judicious use of any antibiotics will greatly reduce the incidence of MRSA. Awareness of the indiscriminate

use of antibiotics and the preventive strategies should be introduced to combat the epidemic spread of the drug resistance bacteria in India.

Declaring of Competing Interest

The authors declare that they do not have any conflict of interests

Acknowledgements

Authors are thankful to the Director of the institute, DG, ICAR and DDG (AS), ICAR for their support and guidance throughout the study. Special thanks are due to Ms K N Mandara in typesetting.

REFERENCES

1. Ki V, Rotstein C. Bacterial skin and soft tissue infections in adults: A review of their epidemiology, pathogenesis, diagnosis, treatment and site of care. Can J Infect Dis Med Microbiol 2008;19(2):173-184.
2. Tong SYC, Davis JS, Eichenberger E, et al. Staphylococcus aureus Infections: Epidemiology, Pathophysiology, Clinical Manifestations, and Management. Clin Microbiol Rev 2015;28(3).
3. Sasirekha B, Usha MS, Amruta AJ, Ankit S, et al. Evaluation and Comparison of Different Phenotypic Tests to Detect Methicillin Resistant Staphylococcus aureus and their Biofilm Production. Int J Pharm Tech Res 2012;4(2):532-4.
4. Ventola CL, The Antibiotic Resistance Crisis Part 1: Causes and Threats. P.T 2015;40(4): 277-283.
5. Abbas A, Nirwan PS, Srivastava P, et al. Prevalence and antibiogram of hospital acquired-methicillin resistant *Staphylococcus aureus* and community acquired-methicillin resistant *Staphylococcus aureus* at a tertiary care hospital National Institute of Medical Sciences. Communit Acquir Infect 2015;2(1):13.

6. Agarwal L, Singh AK, Sengupta C, et al. Nasal carriage of methicillin-and mupirocin-resistant *S. aureus* among health care workers in a tertiary care hospital. J Res Pharm Pract 2015:4:182.
7. Suresh KP, Patil SS, Hamsapriya S, et al. Amachwadi, Prevalence of extended-spectrum beta-lactamase producing bacteria from animal origin: A systematic review and meta-analysis report from India. PLOS One 2015;14(9):1-15.
8. Agarwala S, Lad D, Agashe V, Sobti A, et al. Prevalence of MRSA colonization in an adult urban Indian population undergoing orthopaedic surgery. J Clin Orthop Trauma 2016;7:12-
9. Akhtar S, Chattopadhyay D, Sharma M, et al. Detection of Methicillin-Resistant Staphylococcus Aureus in a Rural Hospital of Haryana by Phenotypic and Genotypic Methods. Ind J of Health Sci and Care 2016;3(3):110-115.
10. Ambika B, Sony Y, Nidhi P, et al. Prevalence of carriage of methicillin resistance *Staphylococcus aureus* among health care workers in a tertiary care center, Kanpur (U.P*).* Int J Curr Microbiol App Sci 2017;6(5):739-746.
11. Arunkumar KV, Prabagaravarthanan R, Bhaskar M, et al. Prevalence of Methicillin-resistant *Staphylococcus aureus* (MRSA) infections among patients admitted in critical care units in a tertiary care hospital. Int J Res Med Sci 2017;5(6):2362-2366.
12. Backer S, Xavier BB, Vanjari LJ, et al. Remarkable geographical variations between India and Europe in carriage of the staphylococcal surface protein-encoding sasX/sesI and in the population structure of methicillin-resistant Staphylococcus aureus belonging to clonal complex 8. Clin Micro Infect 2019;25:1-7.
13. Banerjee J, Madhavi K, Kiranmai S, et al. Screening for nasal carriage of methicillin resistant *Staphylococcus aureus* among healthcare workers at a Rural Teaching Hospital in Medchal District, Telangan. IJMM 2019;7(2):1-7.

14. Baruah K, Borthakur AK, Shamsuddin. Acteriological (aerobic) profile of chronic suppurative otitis media with antibiotic sensitivity testing in a tertiary care hospital of north east India. GJRA 2019;8(3):3.
15. Bhat YJ, Hassan I, Bashir S, et al. Clinico-bacteriological profile of primary pyodermas in Kashmir: a hospital-based study. J R Coll Physicians Edinb 2016;46:8–13.
16. Bhatt MP, Bhalla GS, Tandel K, et al. Antimicrobial susceptibility profile of methicillin-resistant *Staphylococcus aureus* at a tertiary care centre. Arch Clin Microbiol 2015;6(3):6.
17. Bhattacharya S, Bir R, Majumdar T. Evaluation of multidrug resistant *Staphylococcus aureus* and their association with biofilm production in a Tertiary Care Hospital, Tripura, Northeast India. JCDR 2015;9(9):DC01.
18. Bhattacharyya C, Dey R, Roy T, Ghosh A, Jana H. Methicillin-resistant *S. aureus* in Eastern India: Some molecular epidemiological perspectives. Int J Sci Study 2017;4(11): 66-69.
19. Bhavana J, Rama NK. Study of HA-MRSA and CA-MRSA isolated from clinical cases in a tertiary care hospital. Indian J Public Health Res Dev 2017;8(2):106-111.
20. Bhavana MV, Joshi S, Adhikary R, et al. Mupirocin Resistance in *Staphylococcus Aureus* in A Tertiary Care Hospital of South India – A Prospective Study. Asian J Pharm Clin Res 2019;12(1):98-100.
21. Bhavsar R, Garala NJ, Garala RN, et al. Antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus* isolated from various clinical samples at SSG hospital, Baroda. J Res Med Dent Sci 2015;3(1):43-46.
22. Bhowmik D, Chetri S, Paul D, Chanda DD, et al. Detection and molecular typing of methicillin resistant *Staphylococcus* aureus from northeastern part of India. med J armed forces india 2015;75:86-89.

23. Bhutia KO, Singh TSK, Adhikari L. Molecular characterization of community-hospital-acquired methicillin-resistant methicillin-sensitive *Staphylococcus aureus* isolates in Sikkim. Indian J Med Res 2015;142:330.
24. Bouchiat C, El-Zeenni N, Chakrakodi B. Epidemiology of *Staphylococcus aureus* in Bangalore, India: emergence of the ST217 clone and high rate of resistance to erythromycin and ciprofloxacin in the community. New Microbe and New Infect 2015;7:15–20.
25. Chaudhary M, Payasi A. Surveillance study for MRSA prevalence and susceptibility trends against mecA and vanA positive clinical isolates. IJAPBC 2015,4(2):469-477.
26. Choudhury D, Chakravarty P. Prevalence and antimicrobial susceptibility pattern of methicillin resistant *Staphylococcus aureus* in Silchar Medical College and Hospital, Assam, India. Int J Basic Clin Pharmacol 2016;5(5):2174-2177.
27. Cugati S, Saikumar. Prevalence and antibiotic susceptibility pattern of *Staphylococcus aureus* isolated from blood culture in a teritiary care centre. J Med Sci Clin Res 2017;5(4):20842-20847.
28. Dass BS, Udayakumar P, Malaiyan J, et al. Prevalence of virulence determinants among HA-MRSA and CA-MRSA isolates and pathogenicity testing using *Caenorhabdidtis elegans* model. Int J Infect Dis 2016;45:76-77.
29. Datta P, Chander J, Gupta V, et al. Evaluation of various risk factors associated with multidrug-resistant organisms isolated from diabetic foot ulcer patients. Lab Physicians 2019;11(1):58-62.
30. Deepika G, Anaparthy U. P.B.M. Krishna et al. Prevalence of nasal carriage of MRSA among patients undergoing haemodialysis and in health care workers working in the haemodialysis units. J Pharm Sci Innov 2015;4(1):40-43.
31. Dhiman M, Bhatt N, Chau-Han V, et al. Emergence of methicillin resistant *Staphylococcus aureus* (MRSA) isolates from north India harboring a novel sasX gene: further analyzing its role in biofilm formation. Annals of Med and Biomed Sci 2017; 3(1):46-50.

32. Dixit R. Carriage of Methicillin Resistant *Staphylococcus aureus (*MRSA) among Health Care Workers in Cardiac Unit of a Tertiary Care Hospital. Int.J.Curr.Microbiol.ASci 2018;7(3):2674-2679.
33. Farooq S, Saleem M. Prevalence of constitutive and inducible clindamycin resistance among clinical isolates of staph aureus in Kashmir valley: A hospital-based study. J Evol Med Dent Sci 2017;5(17):828-831.
34. Geetha SH, Kalghatgi AT, Rama NK, et al. Characterization of methicillin resistant *Staphylococcus aureus* strains from clinical isolates in a tertiary care hospital of south India. Int J Med Res Rev 2015;3(9):1077-1083.
35. Ghosh S, Banerjee M. Methicillin resistance inducible clindamycin resistance in Staphylococcus aureus. Indian J Med Res 2016;143:362-364.
36. Govindan S, Maroli AS, Ciraj AM, et al. Molecular epidemiology of methicillin resistant *Staphylococcus aureus* colonizing the anterior Nares of school children of Udupi Taluk. Indian J Med Microbiol 2015;33(1):129-133.
37. Gupta BP, Sinha S. Prevalence of methicillin resistant *staphylococcus aureus* in clinical samples of Teerthankar Mahaveer Medical College Hospital and Research Centre (TMMCH RC): Moradabad (UP): India. Int J Med Res Health Sci 2017;6(6):17-20.
38. Gupta L, Agarwal M, Bala K. Nasal carriage of methicillin resistant *Staphylococcus aureus* (MRSA) in health care workers and healthy individuals in a tertiary care hospital. Int J Pharm Biol Sci 2015;5(4):7-17.
39. Gupta S, Dongre A, Pandey AC, et al. Antibiogram of methicillin resistant *Staphylococcus aureus* (MRSA) in healthcare settings. J Chem Pharma Res 2015;7(8): 61-66.
40. Gupta M, Kaore N, Gupta A. Comparative evaluation of MIC by E-test and Cefoxitin disc diffusion for detection of Methicillin Resistant *Staphylococcus aureus* (MRSA). Indian J Microbiol Res 2016;3(4):407-410.

41. Gupta V, Pachori R, Goyal RK. Antibiotic susceptibility pattern of *Staphylococcus aureus* in tertiary care hospital, SRMSIMS, Bareilly, UP. Int J Com Med Pub Health 2017;4(8):2803-9.
42. Hemamalini V, Kavitha V, Ramachandran S. In *vitro* antibiogram pattern of *Staphylococcus aureus* isolated from wound infection and molecular analysis of mecA gene and restriction sites in methicillin resistant *Staphylococcus aureus*. J Adv Pharmal Technol Res 2015;6(4):170-5.
43. Hussain JH, Thakur A, Mishra B, et al. Antimicrobial susceptibility pattern of methicillin-resistant strains of *Staphylococcus aureus* in a super specialty hospital. Int J Health Allied Sci 2015;4(2):69-72.
44. Jana H, Roy T, Dey R, et al. Mondal, Prevalence and antimicrobial susceptibility pattern of different clinical isolates of HA-MRSA and CA-MRSA in a tertiary care rural hospital, Bankura, West Bengal, India. Sch J App Med Sci 2015;3(2F):944-948.
45. Jindal N, Malhotra R, Grover P, Singh S, et al. Methicillin resistant *Staphylococcus aureus* (MRSA) in Malwa region of Punjab (North-West India). Indian J Med Res 2016; 143:371.
46. John SJ, Prakasan G, Sandeep PM, Sunil AE, Mukunda A, Sadiya RV. Nasal screening of dental students as MRSA carriers – An Institutional study. Indian J Appl Res 2019;9(6):30-32.
47. Joshi SA, Barua S, et al. Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary care hospital in Navi Mumbai, India. Indian J Microbiol Res 2017;4(2):187-189.
48. Kaur K, Gill AK, Kaur M. Methicillin resistance, vancomycin intermediate and vancomycin resistance *Staphylococcus aureus* prevalence in a Tertiary Care Hospital of Punjab, India. National J Lab Med 2019;8(3),MO01-MO03.
49. Kavitha Y, Mohan S, Moinuddin SK. Bacteriological profile of diabetic foot infection with special reference to ESBL and MRSA in a coastal tertiary care teaching hospital. Indian J Microbiol Res 2017;4(1):68-73.

50. Kogekar SP, Jain K, Kumari P, et al. High level of MRSA colonization in health care worker: Alarm to implement health care policy. World J Clin Pharmacol Microbiol Toxicol 2015;1(2):21-25.
51. Kulshrestha A, Anamika V, Mrithunjay K, et al. A prospective study on the prevalence and antibiotic sensitivity pattern of methicillin resistant *Staphylococcus aureus* isolated from various clinical specimen at a tertiary care post graduate teaching institute. Int J Curr Microbiol Ap Sci 2017;6(3):1859-1869.
52. Kulshrestha M, Ghatak T, Gupta P, et al. Surveillance of health-care workers for nasal carriage to detect multidrug-resistant Staphylococcus s in a tertiary care center: An observational study. Med J DY Patil Vidyapeeth 2019;12(11):39-43.
53. Kumar S, Bhadauria S. Increasing trend of methicillin-resistant *Staphylococcus aureus* in Jaipur, Rajasthan, India. AJMR 2016;10(34):1417-1421.
54. Kumari J, Shenoy SM, Baliga S, et al. Clinical characteristics and antibiotic resistance profile with emphasis on macrolide-lincosamide-streptogramin B resistance. Sultan Qaboos Univ Med J 2016;16(2):175–181.
55. Majhi S, Dash M, Mohapatra D, et al. Detection of inducible and constitutive clindamycin resistance among *Staphylococcus aureus* isolates in a tertiary care hospital, Eastern India. Avicenna J Med 2016;6(3):75-80.
56. Mamtora D, Saseedharan S, Bhalekar P, et al. Microbiological profile and antibiotic susceptibility pattern of Gram-positive isolates at a tertiary care hospital. J Lab Physicians 2019;11(2):144-8.
57. Mehta S. Incidence of methicillin resistant *Staphylococcus aureus* and its antibiotic susceptibility pattern in a tertiary care hospital. Indian J Microbiol Res 2017;4(1):40-3.
58. Mendem SK, Triveni AG, Shivannavar CT, et al. Prevalence of MRSA and VRSA in Kalaburagi region. Int J Pharm Biol Sci 2016;6(3):81-85.

59. Mohanty S, Behera B, Sahu S, et al. Recent pattern of antibiotic resistance in *Staphylococcus aureus* clinical isolates in Eastern India and the emergence of reduced susceptibility to vancomycin. J Lab Physicians 2019;11(4):340-345.
60. Mokta KK, Verma S, Chauhan D, et al. Inducible clindamycin resistance among clinical isolates of *Staphylococcus aureus* from Sub Himalayan Region of India. JCDR 2015;9(8):20-23.
61. Mondal H, Gupta I, Nandi P, et al. Nasal screening of healthcare workers for nasal carriage of methicillin resistance *Staphylococcus aureus*, vancomycin vancomycin resistance *Staphylococcus aureus* and prevalence of nasal colonization with Staphylococcus aureus in Burdwan Medical College and Hospital. Med Coll Hosp 2016; 3(11):3342-3346.
62. Mundhada SG, Shaikh NK, Gudlani VR, et al. Screening for Methicillin-Resistant *Staphylococcus aureus* (MRSA) carriage among the health care workers in a tertiary care center. Indian J Microbiol Res 2017;4(2):150-153.
63. Mushtaq A, Imran S, Bhat MY, et al. Prevalence and antimicrobial susceptibility of methicillin resistant *staphylococcus* in a tertiary Care hospital in Kashmir. Int J Adv Res 2016;4(4):267-271.
64. Nadimpalli G, Bhamare S, Rao NP, et al. Incidence of methicillin-resistant *Staphylococcus aureus* (MRSA) infection among patients and hospital staff and impact of preventive measures in reduction of MRSA infection rate: a prospective observational stud. Int J Basic Clin Pharmacol 2016;5(6):2336-2340.
65. Nagamadhavi V, Samatha P. Assessing the prevalence of *Staphylococcus Aureus*, Particularly MRSA, from anterior nares of medical students. Indian J Microbiol Res 2016;3(1):22-23.
66. Nagaraju U, Raju BP. Methicillin-resistant *Staphylococcus aureus* in community-acquired pyoderma in children in South India. Indian J Pediatr Dermatol 2017;18(1):14-17.

67. Nagasundaram N, Sistla S. Existence of multiple SCCmec elements in clinical isolates of methicillin-resistant *Staphylococcus aureus*. J Med Microbiol 2017;68:720-727.

68. Negi V, Pal S, Juyal D, et al. Bacteriological Profile of Surgical Site Infections and Their Antibiogram: A Study From Resource Constrained Rural Setting of Uttarakhand State, India. J Clinic and Diagnostic Res 2015;9(10):DC17-DC20.

69. Pai AKB, Kamath MR, Karnaker VK, et al. Nasal colonisation with MRSA in patients undergoing cardiac surgery. Int J Biol Med Res 2015;6(3):5131-5134.

70. Pai AKB, Kamath MR, Karnaker VK, et al. Mupirocin and vancomycin susceptibility in MRSA colonising anterior nares of patients scheduled for cardiac surgery. Indian J Microbiol Res 2017;4(1):83-86.

71. Pal S, Sayana A, Joshi A, et al. *Staphylococcus aureus*: A predominant cause of surgical site infections in a rural healthcare setup of Uttarakhand. J Family Med Prim Care 2019;8(11):3600-6.

72. Pandya N, Chaudhary A, Mehta S, et al. Characterization of methicillin resistant *Staphylococcus aureus* from various clinical samples at tertiary care hospital of rural Gujarat. Int J Health Sci Res 2015;5(9):202-206.

73. Patil AB, Chikkaraddi U, Sambrani PN, et al. Trends in antibiotic resistance among methicillin-resistant *Staphylococcus aureus* (MRSA) isolate. Indian J Microbiol Res 2017;4(4):454-458.

74. Patil AK, Namineni S, Cheruku SR, et al. Prevalence of community-associated methicillin-resistant *Staphylococcus aureus* in oral and nasal cavities of 4 to 13-year-old rural school children: A cross-sectional study. Contemp Clin Dent 2019; 10(1):99-104.

75. Perala BMK, Koripella RL, Vani TMS, et al. Prevalence of methicillin resistant *Staphylococcus aureus* in a tertiary care hospital. IOSR J Dent Med Sci 2016;15(5):29-31.

76. Perween N, Krishanprakash S, Bharara T. Bacteriological profile of burn wound infection in a tertiary care hospital in north India with special reference to methicillin resistant *Staphylococcus aureus.* IMJ Health 2015;8:6-11.
77. Phukan C, Ahmed GU, Sarma PP. Inducible clindamycin resistance among *staphylococcus aureus* isolates in a tertiary care hospital of Assam. Ind J Med Microbiol 2015;33(3):456-458.
78. Radhakrishna M, Taneja A, Rao P. Nasal carriage of *Staphylococcus aureus* with special emphasis on methicillin-resistant *Staphylococcus aureus* among students of a south Indian Medical College — Prevalence and antibiogram pattern. Asian J Pharm Clin Res 2016;9(2):129-132.
79. Raigar M, Vyas A, Sharma R, et al. Detection of vancomycin intermediate and vancomycin resistance in clinical isolates of *Staphylococcus aureus* in Tertiary Care Hospital. IJMHR 2019;5(6):01-04.
80. Rana-Khara R, Lakhani SJ, Vasava S, et al. Methicillin resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant *Staphylococcus aureus* (VRSA) from a rural based tertiary care and teaching hospital in Vadodara district, Gujarat. IAIM 2016;3(7): 187-195.
81. Reema HA, Dominic SRM. Prevalence and antimicrobial susceptibility pattern of clinical isolates of methicillin-resistant *Staphylococcus aureus* in a tertiary care hospital in Mangalore. J Int Med Dent 2016;3(3):134-139.
82. Rengaraj R, Mariappan S, Sekar U, et al. Detection of vancomycin resistance among *Enterococcus faecalis* and *Staphylococcus aureus*. JCDR 2016;10(2):DC04-06.
83. Routray S, Rath S, Mohanty N. Prevalence of methicillin resistant *Staphylococcus aureus* isolated from saliva samples of patients with oral squamous cell carcinoma. J Oral Res 2019;8(1):30-36.

84. Roy SS. Spectrum of Public Health Significant and Antibiotic Resistant Microorganisms Isolated from Mobile Phones of Meat and Fish Handlers of Tripura, India. Int. J. Curr. Microbiol. A Sci 2018;7(7):13-204.

85. Rudresh MS, Ravi GS, Motagi A, et al. Prevalence of Mupirocin resistance among *Staphylococci*, its clinical significance and relationship to clinical use. J Lab Physicians 2015;7(2):103-7.

86. Sankaran G, Zacharia B, Roy A, et al. Current clinical and bacteriological profile of septic arthritis in young infants: a prospective study from a tertiary referral centre. European Journal of Orthopaedic Surgery & Traumatology 2018;28:573–578.

87. Selvabai AP, Sattar SBA, Jayaraman P, et al. Detection and characterisation of heteroresistant vancomycin intermediate *Staphylococcus aureus* (hVISA) using phenotypic and genotypic methods**.** J Clin Diag Res 2019;13(5):DC01-DC05.

88. Sengupta M, Banerjee S, Banerjee P, et al. Outstanding prevalence of methicillin resistant *Staphylococcus aureus* in neonatal omphalitis. JCDR 2016;10(9):DM01-03.

89. Senthilkumar KK, Biswal N, Sistla S. Risk factors associated with methicillin-resistant *Staphylococcus aureus* infection in children. Indian Paediatr 2015;52:31-3.

90. Shinde RV, Pawar SK, Mohite RV, et al. Study of nasal carriage of *Staphylococcus aureus* with special reference to methicillin resistance among nursing staff. Arch Clin Microbiol 2017;7:1-6.

91. Singh S, Malhotra R, Grover P, et al. Antimicrobial resistance profile of Methicillin-resistant *Staphylococcus* aureus colonizing the anterior nares of health-care workers and outpatients attending the remotely located tertiary care hospital of North India. J Lab Physicians 2017;9(4):317-21.

92. Singh G, Broor S, Agarwal P. Molecular characterisation of *Staphylococcus aureus* using spa typing as a diagnostic tool in Haryana, India. Indian J Med Microbiol 2018;36(1):26-31.

93. Singh N, Mohanty S, Panda SS, et al. Methicillin resistant *Staphylococcus aureus* (MRSA) carriage among health care workers in a tertiary care hospital in Bhubaneswar. Int J Community Med Public Health 2018;5(8):3276-82.
94. Swathirajan CR, Rameshkumara MR, Solomona SS, et al. Changing antibiotic resistance profile of *Staphylococcus aureus* isolated from HIV patients (2012–2017) in Southern India. Journal of Infection and Public Health 2020;13:75–79.
95. Talwar A, Saxena S, Kumar A. Screening for detection of methicillin-resistant *Staphylococcus aureus* in Doon Valley Hospitals, Uttarakhand. J Environ Biol 2016;37:247-251.
96. There YW, Wadhai VS, Bhandari P. Prevalence of vancomycin resistance *Staphylococcus aureus* among MRSA isolates from district hospital Gadchiroli (m.s.) India. IJRBAT 2018;4(1):214-218.
97. Thomas MG, Nair SP. MRSA in Dermatology Inpatients with a Vesiculobullous Disorder. Cutis 2018;101(6):458-461.
98. Tiewsoh JB, Dias M. Screening of methicillin-resistant *Staphylococcus aureus* in healthcare workers and students and its susceptibility to mupirocin in a tertiary care teaching hospital in South India. J Lab Physicians 2017;9(4):239-42.
99. Tripathi A. Prevalence and antimicrobia pattern of methicillin resistant *Staphylococcus aureus* in central India. Med Pulse Int Med J 2015;2(1):45-48.
100. Trivedi MB, Vegad M, Soni S. Prevalence of methicillin-resistant *Staphylococcus aureus* in various clinical samples in a tertiary-care hospital. Int J Med Sci Public Health 2015;4(12):1735-1738.
101. Vasuki V, Ananthasankari S. Evaluation of antibiotic resistance among methicillin resistant *Staphylococcus aureus* isolates in a tertiary care teaching hospital, South India. IJCMAAS 2016;10(2):46-49.

102. Velayudham A, Jayavarthinni M, Sindhanai V, et al. Bacteriophage typing of methicillin resistant *Staphylococcus aureus* and changing trend in their antibiotic profile. Ann Int Med Den Res 2017;3(1):MB01- MB05.

103. Venkatesan P, Shanmugam P, Satter SBA. Bacteriological profile and resistance pattern of the microorganisms causing bacteraemia with special emphasis on unusual blood isolates. Indian J Microbiol Res 2017;4(2):171-176.

104. Arabestani MR , Rastiyani S, Alikhani MY, et al. The Relationship Between Prevalence of Antibiotics Resistance and Virulence Factors Genes of MRSA and MSSA Strains Isolated from Clinical Samples, West Iran. Oman Med J (2018); 33(2): 134-140.

105. Goudarzi M, Fazeli M, Eslami G, et al. Genetic Diversity Analysis of Methicillin resistant Staphylococcus aureus Strains Isolated from Intensive Care Unit in Iran. Oman Med J (2019); 34(2): 118-125.

106. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int. J.Surg 2010;8:336-341.

107. Greco T, Zangrillo A, Biondi-Zoccai G, et al. Meta-analysis: pitfalls and hints. Heart, Lung and Vessels 2013;5:219-225.