REVIEW ARTICLE

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Prevalence of Methicillin-resistant *Staphylococcus Aureus* in India: A Systematic Review and Meta-analysis

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ABSTRACT

The emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) has increased and become a serious concern worldwide, including India. Additionally, MRSA isolates are showing resistance to other chemotherapeutic agents. Isolated and valuable reports on the prevalence of MRSA are available in India. There is no systematic review on the prevalence of MRSA in one place; hence, this study was planned. The overall prevalence of MRSA in humans in India was evaluated state-wise, zone-wise, and year-wise. A systematic search from PubMed, Indian journals, Google Scholar, and J-Gate Plus was carried out and retrieved 98 eligible articles published from 2015 to 2020 in India. The statistical analysis of data was conducted using R software. The overall prevalence of MRSA was 37% (95% CI: 32–41) from 2015 to 2019. The pooled prevalence of MRSA zone-wise was 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 northeast region-zones, respectively. The state-wise stratified results showed a predominance of MRSA in Jammu and Kashmir with 55% (95% CI: 42–67) prevalence, and the lowest was 21% (95% CI: 11–34) in Maharashtra. The study indicated that the prevalence data would help in formulating and strict implementation of control measures in hospital areas to prevent the outbreak of MRSA infection and management of antibiotic usage.

Staphylococcus aureus (S. aureus) is an important pathogen responsible for a wide range of human infections, including 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 resistance to methicillin known as methicillin-resistant *S. aureus* (MRSA), which consequently becomes difficult in managing infections. Over the last 50 years, antibiotics have reduced the rate of mortality; nevertheless, bacteria have been 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 harbored by the mobile segments of the MRSA strains, which encodes the penicillin-binding protein 2a that has a 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 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 to manage the ailment. Hence, it is imperative

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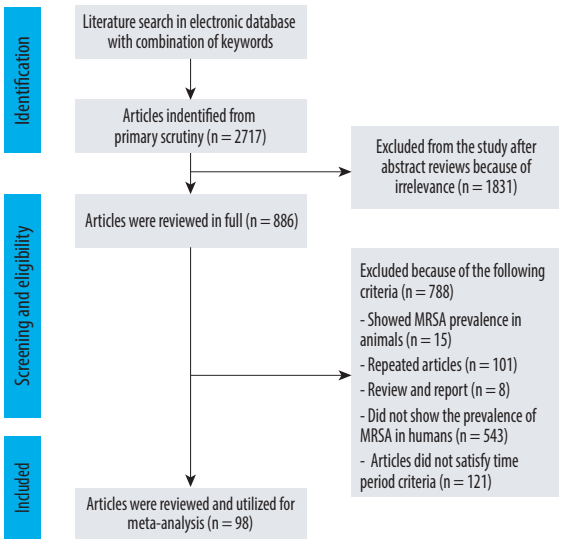

MRSA: methicillin-resistant Staphylococcus aureus.

Figure 1: Systematic review and meta-analysis.

to study the overall prevalence of MRSA in India to develop improved and efficient treatment methods for its management.

Our 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 tools, viz., meta-analysis.

METHODS

Literature search

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

Study selection criteria

The results after searching were tabulated into Excel, duplicates were removed, and relevant studies were examined. Our preliminary inclusion criteria were to include all articles having the title keyword "prevalence of MRSA in India" from 2015 to 2020 only. Selected papers were subjected to abstract screening for titles. Studies were read in full for which they had reported on: (a) the prevalence of MRSA, (b) sample size data, (c) events (positive), (d) year of study, (e) geographical location of the study, and (f) diagnostic tests used as confirmatory tool for identification of MRSA. Those articles that did not satisfy the above screening criteria were excluded from the study. Articles containing a large number of samples/events were also not included in the study. Studies that did not report the MRSA prevalence included reviews, reports, editorial articles and outbreak reports, and studies that were duplicates of included studies were excluded. The articles that were selected included humans of all age groups. The searches, scrutiny, and methodology were in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol (http:// www.prisma-statement.org).

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. We were also interested in the year of publication and the location of the 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 performed 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 (Higgins' I^2), and

Table 1: Overall prevalence of methicillin-resistant *Staphylococcus aureus*.

Study	Events	Total	Proportion	95% CI	Weight, (fixed) %	Weight, (random) %
Abbas et al,[5] 2015	201	500	0.4	0.36–0.45	240.0	1.1
Agarwal et al,[6] 2015	28	96	0.29	0.20–0.39	0.5	1
Agarwala et al,[8] 2016	7	1550	0	0.00–0.01	7.6	1.1
Akhtar et al,[9] 2016	87	250	0.35	0.29–0.41	1.2	1.1
Ambika et al,[10] 2017	15	39	0.38	0.23–0.55	0.2	1
Arunkumar et al,[11] 2017	5	100	0.05	0.02–0.11	0.5	1
De Backer et al,[12] 2019	5	9	0.56	0.21–0.86	0	0.7
Banerjee et al,[13] 2018	12	26	0.46	0.27–0.67	0.1	0.9
Baruah et al,[14] 2019	13	190	0.07	0.04–0.11	0.9	1
Bhat et al,[15] 2016	54	89	0.61	0.50–0.71	0.4	1
Bhatt et al,[16] 2015	103	510	0.20	0.17–0.24	2.5	1.1
Bhattacharya et al,[17] 2015	47	100	0.47	0.37–0.57	0.5	1
Bhattacharyya et al,[18] 2017	20	122	0.16	0.10–0.24	0.6	1
Bhavana et al,[19] 2017	89	200	0.44	0.37–0.52	1	1.1
Bhavana et al,[20] 2019	70	187	0.37	0.30–0.45	0.9	1
Bhavsar et al,[21] 2015	65	150	0.43	0.35–0.52	0.7	1
Bhowmik et al,[22] 2019	71	127	0.56	0.47–0.65	0.6	1
Bhutia et al,[23] 2015	53	150	0.35	0.28–0.44	0.7	1
Bouchiat et al,[24] 2015	48	92	0.52	0.42–0.63	0.4	1
Chaudhary et al,[25] 2015	77	178	0.43	0.36–0.51	0.9	1
Choudhury et al,[26] 2016	311	724	0.43	0.39–0.47	3.5	1.1
Cugati et al,[27] 2017	92	161	0.57	0.49–0.65	0.8	1
Dass et al,[28] 2016	64	100	0.64	0.54–0.73	0.5	1
Datta et al,[29] 2019	5	26	0.19	0.07–0.39	0.1	0.9
Deepika et al,[30] 2015	25	29	0.86	0.68–0.96	0.1	0.9
Dhiman et al,[31] 2017	24	150	0.16	0.11–0.23	0.7	1
Dixit,[32] 2018	21	42	0.5	0.34–0.66	0.2	1
Farooq et al,[33] 2016	210	343	0.61	0.56–0.66	1.7	1.1
Geetha et al,[34] 2015	44	166	0.27	0.20–0.34	0.8	1
Ghosh et al,[35] 2016	11	46	0.24	0.13–0.39	0.2	1
Govindan et al,[36] 2015	17	441	0.04	0.02–0.06	2.2	1.1
Gupta and Sinha,[37] 2017	344	450	0.76	0.72–0.80	2.2	1.1
Gupta et al,[38] 2015a	19	60	0.32	0.20–0.45	0.3	1
Gupta et al,[39] 2015b	12	30	0.4	0.23–0.59	0.1	0.9
Gupta et al,[40] 2016	69	174	0.4	0.32–0.47	0.8	1
Gupta et al,[41] 2017	408	505	0.81	0.77–0.84	2.5	1.1
Hemamalini et al,[42] 2015	14	40	0.35	0.21–0.52	0.2	1
Hussain et al,[43] 2015	53	80	0.66	0.55–0.76	0.4	1
Jana et al,[44] 2015	23	122	0.19	0.12–0.27	0.6	1
Jindal et al,[45] 2016	161	248	0.65	0.59–0.71	1.2	1.1
John et al,[46] 2019	18	100	0.18	0.11–0.27	0.5	1
Joshi et al,[47] 2017	34	231	0.15	0.10–0.20	1.1	1.1
Kaur et al,[48] 2019	83	162	0.51	0.43–0.59	0.8	1
Kavitha et al,[49] 2017	22	207	0.11	0.07–0.16	1	1.1
Kogekar et al,[50] 2015	16	30	0.53	0.34–0.72	0.1	0.9
Kulshrestha et al,[51] 2017	82	161	0.51	0.43–0.59	0.8	1
Kulshrestha et al,[52] 2019	73	214	0.34	0.28–0.41	1	1.1
Kumar et al,[53] 2016	79	147	0.54	0.45–0.62	0.7	1
Kumari et al,[54] 2016	88	291	0.3	0.25–0.36	1.4	1.1

continued.

Study	Events	Total	Proportion	95% CI	Weight, (fixed) %	Weight, (random) %
Majhi et al,[55] 2016	129	209	0.62	0.55–0.68	1	1.1
Mamtora et al,[56] 2019	310	1041	0.3	0.27–0.33	5.1	1.1
Mehta,[57] 2017	145	250	0.58	0.52–0.64	1.2	1.1
Mendem et al,[58] 2016	24	62	0.39	0.27–0.52	0.3	1
Mohanty et al,[59] 2019	127	284	0.45	0.39–0.51	1.4	1.1
Mokta et al,[60] 2015	82	350	0.23	0.19–0.28	1.7	1.1
Mondal et al,[61] 2016	16	87	0.18	0.11–0.28	0.4	1
Mundhada et al,[62] 2017	14	112	0.12	0.07–0.20	0.5	1
Mushtaq et al,[63]2016	58	140	0.41	0.33–0.50	0.7	1
Nadimpalli et al,[64] 2016	63	2040	0.03	0.02–0.04	10	1.1
Nagamadhavi et al,[65] 2016	2	91	0.02	0.00–0.08	0.4	1
Nagaraju et al,[66] 2017	41	274	0.15	0.11–0.20	1.3	1.1
Nagasundaram et al,[67] 2019	114	200	0.57	0.50–0.64	1	1.1
Negi et al,[68] 2015	11	70	0.16	0.08–0.26	0.3	1
Pai et al,[69] 2015	7	33	0.21	0.09–0.39	0.2	0.9
Pai et al,[70] 2017	9	100	0.09	0.04–0.16	0.5	1
Pal et al,[71] 2019	34	121	0.28	0.20–0.37	0.6	1
Pandya et al,[72] 2015	104	180	0.58	0.50–0.65	0.9	1
Patil et al,[73] 2017	23	57	0.4	0.28–0.54	0.3	1
Patil et al,[74] 2019	11	47	0.23	0.12–0.38	0.2	1
Perala et al,[75] 2016	132	386	0.34	0.29–0.39	1.9	1.1
Perween et al,[76] 2015	80	141	0.57	0.48–0.65	0.7	1
Phukan et al,[77] 2015	160	215	0.74	0.68–0.80	1	1.1
Radhakrishna et al,[78] 2016	9	78	0.12	0.05–0.21	0.4	1
Raigar et al,[79] 2019	208	400	0.52	0.47–0.57	2	1.1
Rana-Khara et al,[80] 2016	52	100	0.52	0.42–0.62	0.5	1
Reema et al,[81] 2016	23	50	0.46	0.32–0.61	0.2	1
Rengaraj et al,[82] 2016	54	109	0.5	0.40–0.59	0.5	1
Routray et al,[83] 2019	13	17	0.76	0.50–0.93	0.1	0.9
Roy,[84] 2018	9	38	0.24	0.11–0.40	0.2	1
Rudresh et al,[85] 2015	22	98	0.22	0.15–0.32	0.5	1
Sankaran et al,[86] 2018	13	30	0.43	0.25–0.63	0.1	0.9
Selvabai et al,[87] 2019	114	468	0.24	0.21–0.29	2.3	1.1
Sengupta et al,[88] 2016	19	19	1	0.82–1.00	0.1	0.9
Senthilkumar et al,[89] 2015	46	98	0.47	0.37–0.57	0.5	1
Shinde et al,[90] 2016	9	26	0.35	0.17–0.56	0.1	0.9
Singh et al,[91] 2017	15	200	0.08	0.04–0.12	1	1.1
Singh et al,[92] 2018	87	248	0.35	0.29–0.41	1.2	1.1
Singh et al,[93] 2018	9	49	0.18	0.09–0.32	0.2	1
Swathirajan et al,[94] 2020	262	380	0.69	0.64–0.74	1.9	1.1
Talwar et al,[95] 2016	38	111	0.34	0.25–0.44	0.5	1
There et al,[96] 2016	50	114	0.44	0.35–0.53	0.6	1
Thomas et al,[97] 2018	14	43	0.33	0.19–0.49	0.2	1
Tiewsoh et al,[98] 2017	24	432	0.06	0.04–0.08	2.1	1.1
Tripathi,[99] 2015	70	210	0.33	0.27–0.40	1	1.1
Trivedi et al,[100] 2015	47	232	0.2	0.15–0.26	1.1	1.1
Vasuki et al,[101] 2016	45	83	0.54	0.43–0.65	0.4	1
Velayudham et al,[102] 2017	120	182	0.66	0.59–0.73	0.9	1
Venkatesan et al,[103]2017	23	43	0.53	0.38–0.69	0.2	1
Fixed effect model		20493	0.29	0.28–0.29	100%	
Random effect model			0.37	0.32–0.41		100%

Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0571$, $p < 0.001$.

Table 2: Details of pooled prevalence of methicillin-resistant *Staphylococcus aureus* in 22 districts during 2015–2020.

Sl No	Name of the state	Pooled prevalence, % (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.*

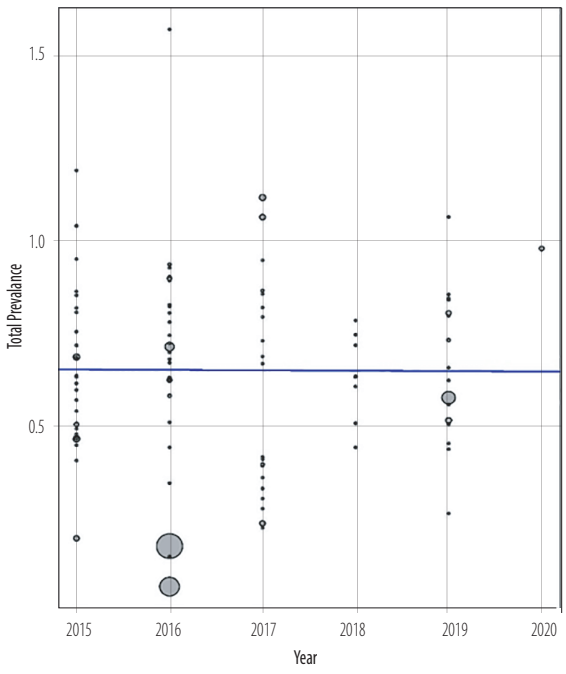

Figure 2: Heterogeneity assessment.

p-values were computed to determine the percentage of variation due to heterogeneity among various reports included in this study. The random-effect and fixed-effect models were used to calculate the pooled prevalence of individual diseases. This analysis facilitates generating a weighted average proportion of prevalence of various studies, providing 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 were expressed as a percentage with 95% CI. Subgroup analysis was performed to investigate the significance of heterogeneity among the studies. The studies were stratified based on zones of the country, year of publication, and state-wise. Subgroup meta-regression analysis was performed to identify the stratified prevalence of MRSA in different regions, study periods, sample size, and diagnostic tests.

Table 3: Year-wise prevalence of methicillin-resistant *Staphylococcus aureus* in India during 2015–2020.

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*

Table 4: Zone-wise prevalence of methicillin-resistant *Staphylococcus aureus* in India during 2015–2020.

Sl No	Region	Pooled Prevalence, % (95% CI)	I^2, %	τ^2	Heterogeneity test		Egger test (predictor = ninv*)		Chi-square test
					Q	*p*-value	*t*	*p*-value	
1	**North** (Uttar 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	0.0514	2551.24	< 0.001	2.3	0.030	2559.54
4	**East** (West Bengal and Odisha)	43 (20–68)	96	0.01401	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

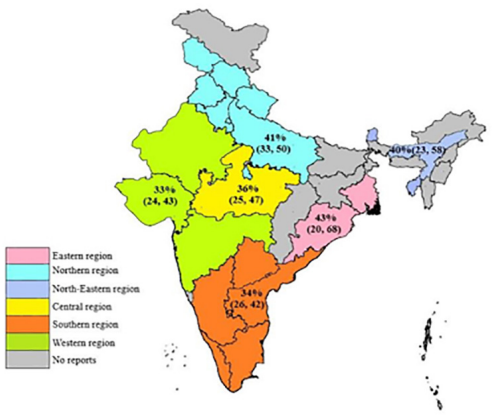

Figure 3: Zone analysis.

RESULTS

Study details

Articles reporting the prevalence of MRSA were thoroughly screened, and irrelevant ones were excluded. A total of 1831 of 2717 articles identified were excluded following the exclusion criteria described above; 886 potential articles were selected using a combination of keywords. 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 published between 2015 and 2020. The

Table 5: Test for residual heterogeneity.

Sl no	Predictor	R^2, %	τ^2	I^2,%	H^2, %	QM value	*p*-value
1	Year	0.00	0.0577	97.91	47.78	0.0039	0.950
2	Sample size	7.03	0.0531	97.61	41.79	7.8623	0.005
3	Region	0.00	0.0588	97.89	47.29	2.3638	0.796
4	Confirmatory test	3.78	0.0549	97.75	44.38	6.4073	0.093

Table 6: Meta-regression parameter estimate.

Sl No	Predictor	Estimate	95% CI	*p*-value
1	Year	-0.0011	-0.0354–0.0332	0.935
2	Sample size	-0.0002	-0.0004–-0.0001	0.005
	Group I (more than median)		0.5810–0.7210	3.744778e-75
	Group II (less than median)		0.5840–0.7200	1.910528e-78
3	Region			
	Central	Reference		
	East	0.0592	-0.2354–0.3537	0.693
	North	0.0482	-0.2151–0.3116	0.719
	Northeast	0.0339	-0.2711–0.3389	0.827
	South	-0.0349	-0.2927–0.2228	0.790
	West	-0.0221	-0.2901–0.2459	0.871
4	Confirmatory test			
	MeReSa agar screening	Reference		
	Double disk diffusion erythromycin and clindamycin	0.54	0.0499–1.0302	0.060
	Kirby Bauer disk diffusion method Cefoxitin	0.1621	-0.0036–0.3278	0.055
	mecA PCR	0.1528	-0.1180–0.4236	0.268

prevalence data for this study were extracted and tabulated as per the requirement of the statistical software. Twenty-two states of India had reports of the prevalence of MRSA. Six zones of the country, namely; North (Uttar 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 Northeast (Assam, Tripura, and Sikkim) zones had a varied pooled prevalence of MRSA.

Risk of bias and quality assessment

Risk of bias and quality assessment were awarded a maximum 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 minimumscore of 3.

Meta-analysis of the prevalence of MRSA

The percentage prevalence of MRSA in India was estimated statistically using R Open source Scripting software. The overall prevalence of MRSA using 17 525 samples in 98 studies was 37% (95% CI: 32–41) in India during 2015–2020 (I^2 = -99%, τ^2 = 0.0571, $p < 0.001$) [Table 1]. The pooled data were stratified into state-wise and zone-wise.

Twenty-two states of India have reported the prevalence of MRSA. Jammu and Kashmir showed the highest pooled prevalence of MRSA at 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 at 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 2].

Year-wise prevalence of MRSA

Heterogeneity assessment was performed year-wise [Figure 2]. It was found that the studies published in 2015, 2016, 2017, 2018, and 2019 have independent significant heterogeneity; hence subgroup analysis is

Table 7: Pooled prevalence of methicillin-resistant *Staphylococcus aureus* in community settings.

Study	Events	Total	Proportion	95% CI	Weight, %
Community					
Abbas et al,[5] 2015	201	500	0.4	0.36–0.45	1.1
Agarwal et al,[6] 2015	28	96	0.29	0.20–0.39	1
Ambika et al,[10] 2017	15	39	0.38	0.23–0.55	1
Banerjee et al,[13] 2019	12	26	0.46	0.27–0.67	0.9
Bhavana et al,[19] 2017	89	200	0.44	0.37–0.52	1.1
Bhutia et al,[23] 2015	53	150	0.35	0.28–0.44	1
Bouchiat et al,[24] 2015	48	92	0.52	0.42–0.63	1
Deepika et al,[30] 2015	25	29	0.86	0.34–0.66	0.9
Dixit,[32] 2018	21	42	0.5	0.68–0.96	1
Govindan et al,[36] 2015	17	441	0.04	0.02–0.06	1.1
Jana et al,[44] 2015	23	122	0.19	0.12–0.27	1
John et al,[46] 2019	18	100	0.18	0.11–0.27	1
Kogekar et al,[50] 2015	16	30	0.53	0.34–0.72	0.9
Kulshrestha et al,[51] 2017	73	214	0.34	0.43–0.59	1.1
Mondal et al,[61] 2016	16	87	0.18	0.11–0.28	1
Mundhada et al,[62] 2017	14	112	0.12	0.07–0.20	1
Nagamadhavi et al,[65] 2016	2	91	0.02	0.00–0.08	1
Nagaraju et al,[66] 2017	41	274	0.15	0.11–0.20	1.1
Patil et al,[74] 2019	11	47	0.23	0.12–0.38	1
Radhakrishna et al,[78] 2016	9	78	0.12	0.05–0.21	1
Roy,[84] 2018	9	38	0.24	0.11–0.40	1
Shinde et al,[90] 2016	9	26	0.35	0.17–0.56	0.9
Singh et al,[91] 2017	15	200	0.08	0.04–0.12	1.1
Tiewsoh and Dias,[98] 2017	24	432	0.06	0.04–0.08	1.1
Random effects model			0.27	0.19–0.5	24.2
Heterogeneity : $I^2 = 99\%$, $\tau^2 = 0.0521$, $p = 0.01$					
Hospital					
Agarwala et al,[8] 2016	7	1550	0	0.00–0.01	1.1
Akhtar et al,[9] 2016	87	250	0.35	0.29–0.41	1.1
Arunkumar et al,[11] 2017	5	100	0.05	0.02–0.11	1
De Backer et al,[12] 2019	5	9	0.56	0.21–0.86	0.7
Baruah et al,[14] 2019	13	190	0.07	0.04–0.11	1
Bhat et al,[15] 2016	54	89	0.61	0.50–0.71	1
Bhatt et al,[16] 2015	103	510	0.2	0.17–0.24	1.1
Bhattacharya et al,[17] 2015	47	100	0.47	0.37–0.57	1
Bhattacharyya et al,[18] 2017	20	122	0.16	0.10–0.24	1
Bhavana et al,[20] 2019	70	187	0.37	0.30–0.45	1
Bhavsar et al,[21] 2015	65	150	0.43	0.35–0.52	1
Bhowmik et al,[22] 2019	71	127	0.56	0.47–0.65	1
Chaudhary et al,[25] 2015	77	178	0.43	0.36–0.51	1
Choudhury et al,[26] 2016	311	724	0.43	0.39–0.47	1.1
Cugati et al,[27] 2017	92	161	0.57	0.49–0.65	1
Dass et al,[28] 2016	64	100	0.64	0.54–0.73	1
Datta et al,[29] 2019	5	26	0.19	0.07–0.39	0.9
Dhiman et al,[31] 2017	24	150	0.16	0.11–0.23	1
Farooq et al,[33] 2016	210	343	0.61	0.56–0.66	1.1
Geetha et al,[34] 2015	44	166	0.27	0.20–0.34	1
Ghosh et al,[35] 2016	11	46	0.24	0.13–0.39	1
Gupta et al,[37] 2017	344	450	0.76	0.72–0.80	1.1
Gupta et al,[38] 2015	19	60	0.32	0.20–0.45	1
Gupta et al,[39] 2015	12	30	0.4	0.23–0.59	0.9

continued.

Study	Events	Total	Proportion	95% CI	Weight, %
Gupta et al,[40] 2016	69	174	0.4	0.32–0.47	1
Gupta et al,[41] 2017	408	505	0.81	0.77–0.84	1.1
Hemamalini et al,[42] 2015	14	40	0.35	0.21–0.52	1
Hussain et al,[43] 2015	53	80	0.66	0.55–0.76	1
Jindal et al,[45] 2016	161	248	0.65	0.59–0.71	1.1
Joshi et al,[47] 2017	34	231	0.15	0.10–0.20	1.1
Kaur et al,[48] 2019	83	162	0.51	0.43–0.59	1
Kavitha et al,[49] 2017	22	207	0.11	0.07–0.16	1.1
Kulshrestha et al,[52] 2019	82	161	0.51	0.28–0.41	1
Kumar et al,[53] 2016	79	147	0.54	0.45–0.62	1
Kumari et al,[54] 2016	88	291	0.3	0.25–0.36	1.1
Majhi et al,[55] 2016	129	209	0.62	0.55–0.68	1.1
Mamtora et al,[56] 2019	310	1041	0.3	0.27–0.33	1.1
Mehta,[57] 2017	145	250	0.58	0.52–0.64	1.1
Mendem et al,[58] 2016	24	62	0.39	0.27–0.52	1
Mohanty et al,[59] 2019	127	284	0.45	0.39–0.51	1.1
Mokta et al,[60] 2015	82	350	0.23	0.19–0.28	1.1
Mushtaq et al,[63] 2016	58	140	0.41	0.33–0.50	1
Nadimpalli et al,[64] 2016	63	2040	0.03	0.02–0.04	1.1
Nagasundaram et al,[67] 2019	114	200	0.57	0.50–0.64	1.1
Negi et al,[68] 2015	11	70	0.16	0.08–0.26	1
Pai et al,[69] 2015	7	33	0.21	0.09–0.39	0.9
Pai et al,[70] 2017	9	100	0.09	0.04–0.16	1
Pal et al,[71] 2019	34	121	0.28	0.20–0.37	1
Pandya et al,[72] 2015	104	180	0.58	0.50–0.65	1
Patil et al,[73] 2017	23	57	0.4	0.28–0.54	1
Perala et al,[75] 2016	132	386	0.34	0.29–0.39	1.1
Perween et al,[76] 2015	80	141	0.57	0.48–0.65	1
Phukan et al,[77] 2015	160	215	0.74	0.68–0.80	1.1
Raigar et al,[79] 2019	208	400	0.52	0.47–0.57	1.1
Rana-Khara et al,[80] 2016	52	100	0.52	0.42–0.62	1
Reema et al,[81] 2016	23	50	0.46	0.32–0.61	1
Rengaraj et al,[82] 2016	54	109	0.5	0.40–0.59	1
Routray et al,[83] 2019	13	17	0.76	0.50–0.93	0.9
Rudresh et al,[85] 2015	22	98	0.22	0.15–0.32	1
Sankaran et al,[86] 2018	13	30	0.43	0.25–0.63	0.9
Selvabai et al,[87] 2019	114	468	0.24	0.21–0.29	1.1
Sengupta et al,[88] 2016	19	19	1	0.82–1.00	0.9
Senthilkumar et al,[89] 2015	46	98	0.47	0.37–0.57	1
Singh et al,[92] 2018	87	248	0.35	0.29–0.41	1.1
Singh et al,[93] 2018	9	49	0.18	0.09–0.32	1
Swathirajan et al,[94] 2020	262	380	0.69	0.64–0.74	1.1
Talwar et al,[95] 2016	38	111	0.34	0.25–0.44	1
There et al,[96] 2016	50	114	0.44	0.35–0.53	1
Thomas et al,[97] 2018	14	43	0.33	0.19–0.49	1
Tripathi,[99] 2015	70	210	0.33	0.27–0.40	1.1
Trivedi et al,[100] 2015	47	232	0.2	0.15–0.26	1.1
Vasuki et al,[101] 2016	45	83	0.54	0.43–0.65	1
Velayudham et al,[102] 2017	120	182	0.66	0.59–0.73	1
Venkatesan et al,[103] 2017	23	43	0.53	0.38–0.69	1
Random effects model		17027	0.4	0.35–0.45	75.8
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0542$, $p < 0.001$					
Random effects model		20493	0.37	0.32–0.41	100
Heterogeneity: $I^2 = 99\%$, $\tau^2 = 0.0571$, $p < 0.001$					
Residual heterogeneity: $I^2 = 99\%$, $p < 0.001$					

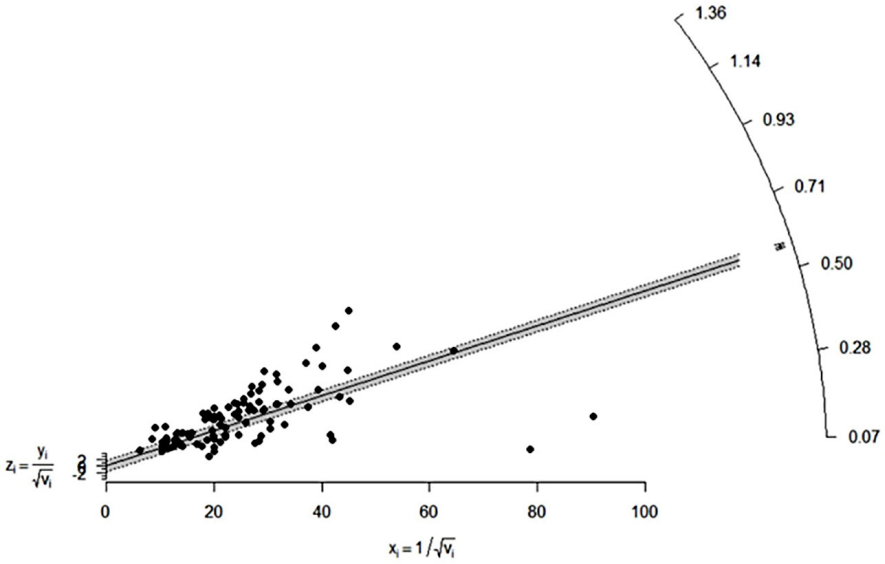

Figure 4: Galbraith plot assessment between study reports.

more appropriate using the random effect model to deal with heterogeneity.

In 2015, 27 articles showed the prevalence of MRSA as 38% (95% CI: 30–45) with I^2 = -97, τ^2 = -0.0414, p < 0.01. In 2016, 27 articles showed the prevalence of MRSA as 39% (95% CI: 29–50) with I^2 = -99, τ^2 = -0.0797, p < 0.01. In 2017, 20 articles showed the prevalence of MRSA as 31% (95% CI: 20–44) with I^2 = -99, τ^2 = -0.0835, p < 0.001. In 2018, 7 articles showed the prevalence of MRSA as 35% (95% CI: 26–43) with I^2 = -62, τ^2 = -0.0091, p = 0.02. In 2019, 16 articles showed the prevalence of MRSA as 37% (95% CI: 28–46) with I^2 = -95, τ^2 = -0.0343, p < 0.01. In 2020, a single article showed prevalence of MRSA as 69% (95% CI: 64–74) [Table 3].

Zone-wise prevalence of MRSA

In zone-wise analysis [Table 4 and Figure 3], the east zone with nine articles (West Bengal and Odisha) showed the highest pooled prevalence of 43% (95% CI: 20–68) with I^2 = -96, τ^2 = 0.01401, p < 0.01. The lowest prevalence of MRSA was recorded in the west zone with 20 articles (Rajasthan, Maharashtra, and Gujarat) as 33% (95% CI: 24–43) with I^2 = -99, τ^2 = -0.0514, p < 0.001, and these states are geographically large and densely populated. Twenty-four articles in the north zone comprising Uttara Pradesh, Haryana, Jammu and Kashmir, Himachal Pradesh, Punjab, New Delhi, and Uttarakhand had a pooled prevalence of 41% (95% CI: 33–50) with I^2 = -98, τ^2 = -0.0446, p < 0.01. Thirty-four articles in the 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 the northeast zone (seven 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.

Meta-regression analysis

Meta-regression is a tool used to examine the effect of moderators on MRSA prevalence rates. In this study, the year of publications, sample size, geographical regions, and confirmatory tests used for the 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 a 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 are presented in Tables 5 and 6.

The study included 74 hospitals and 24 community settings (total of 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 < 0.001) [Table 7].

To assess the heterogeneity between study reports, we generated a Galbraith plot [Figure 4]. 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 centering around the line.

DISCUSSION

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

Our meta-analysis study reveals the pooled prevalence of MRSA in India at 37% (95% CI: 32–41) during 2015–2020. 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 bought without prescription is also a serious concern in India.

A pooled prevalence of MRSA varied between 31%–39% from 2015 to 2019 (69% in 2020) against a total prevalence of 37% across India. 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. On the other hand, Maharashtra has the lowest prevalence of MRSA (21%) and has more sophisticated hospitals.

In zone-wise analysis, the east zone has shown the highest prevalence of MRSA (43%), including West Bengal and Odisha. West Bengal shares a porous border with Bangladesh, and there is no restriction on the movement of men and material between them. The north zone, which included Uttar Pradesh, Haryana, Jammu and Kashmir, Himachal Pradesh, Punjab, New Delhi, and Uttarakhand states, had the second-highest (41%) MRSA prevalence. The northeast zone, which comprises Assam, Tripura, and Sikkim, has shown the third-highest prevalence of MRSA (40%). Assam has a porous border with Bhutan and Bangladesh; Tripura shares a porous border with Bangladesh whereas Sikkim shares with Bhutan, Tibet, and Nepal. There is no restriction on the movement of men and materials. In a similar study,[104] 46% and 54% of prevalence of MRSA among females and males, respectively, was recorded in the west zone of Iran. Eighty-four isolates from the intensive care unit of a hospital in Iran were antimicrobial-resistant, which is quite alarming.[105]

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

The moderate heterogeneity may be due to the size's total variability effect, 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 MRSA prevalence 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, the weight (fixed) assigned to 24 studies under community settings did not exhibit outlier features upon scrutinizing the forest plots. Therefore, the effect of two settings (hospital and community) on pooled prevalence of MRSA was not found to have a large difference. The subgroup analysis of studies revealed that the pooled prevalence of MRSA in the hospital setting was 49% and 27% in the community setting.

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 data's behavior and 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

The overall pooled prevalence of MRSA in India was very high (37%). Studies comprising large populations in different locations with rapid tests would be of much help in computing the 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 healthcare system. Strict adherence to hand hygiene and judicious use of any antibiotics will greatly reduce the incidence of MRSA. Awareness of the indiscriminate use of antibiotics and preventive strategies should be introduced to combat the epidemic spread of drug-resistant bacteria in India.

Disclosure
The authors declared no conflicts of interest.

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