RESEARCH ARTICLE

Prevalence of extended-spectrum beta-lactamase producing bacteria from animal origin: A systematic review and meta-analysis report from India

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Abstract

Antimicrobial resistance (AMR) due to the emergence and spread of extended-spectrum beta-lactamase (ESBL) producing bacteria are becoming a serious global public health concern. This article aims to assess the overall prevalence of ESBLs among animals in India, with year-wise, zone-wise and species-wise stratification. Systematic search from PubMed, Google Scholar and J-Gate Plus was carried out and 24 eligible articles from 2013–2019 in India were retrieved. The R Open source Scripting software was used to perform statistical analysis. The overall prevalence of ESBLs among animals in India was 9%. The pooled prevalence of ESBLs in animals were 26, 11, 6 and 8% for north, east, south and central zones, respectively. The reported prevalence of ESBLs in animals were 12, 5, 8, 8, 12, 13 and 33% were reported for the years 2013, 2014, 2015, 2016, 2017, 2018, 2019 respectively. The species-wise stratified results showed a predominance of ESBL producing Klebsiella pneumoniae strains (11%) when compared to Escherichia coli and Pseudomonas spp. which were 7% and 5%, respectively. The prevalence data generated could be utilized in infection control and in antibiotic use management decisions for developing appropriate intervention strategies.

Introduction

Antimicrobial resistance (AMR) has been universally recognized as an emerging global problem to public health. Although the prevalence of AMR is sporadic, it is widespread in the Asian region. India, located in the southern part of Asia, marks a high, immeasurable burden of AMR among livestock due to poor documentation, sub-standard regulations with a shortfall in forbidding protocol enforcement [1]. This study aims to estimate the pooled prevalence of Extended-spectrum β-lactamases (ESBLs) in India by conducting systematic review and meta-analysis with 23 available research articles under epidemiological study design. Beta-Lactam
antimicrobial agents are the most favored class of antimicrobials for the treatment of bacterial infections, hence becoming the main cause of resistance to \(\beta\)-lactam antibiotics, globally [2]. Prevalence of ESBLs producing *Klebsiella* is becoming a major concern in China, Korea, Japan and India [3]. ESBLs enzymes are produced by the gram-negative bacteria to incur resistance against the \(\beta\)-lactams. *Klebsiella pneumoniae* and *Escherichia coli* are the main gram-negative bacteria producing ESBLs [4]. However *Proteus mirabilis*, *Enterobacter* spp., *Salmonella*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* also produce ESBLs to acquire resistance [5]. The incessant liability of gram-negative strains to a myriad \(\beta\)-lactams has begotten rapid and vigorous production and mutation of \(\beta\)-lactamases in these bacteria, hence, incurring resistance against the newly developed \(\beta\)-lactam antibiotics [2]. Treatment for these disease causing multi-drug-resistant (MDR) organisms is a therapeutic challenge. The risk factors for developing infection with ESBL-producing organisms include indiscriminate and off-label use of antibiotics [6]. At present, animals without any recognized risk factor for multidrug-resistant organisms are found to have ESBL-producing organisms. Hence, diagnosis of ESBL-producing organisms has become vital [7]. MDRs are posing a treatment challenge, and a major cause of morbidity and mortality worldwide [1]. Unfortunately, India, being a developing country, does not have an adequate surveillance system that could track indiscriminate use or consumption of antibiotics in livestock populations. This meta-analysis will improve our understanding of the distribution of ESBLs in India. A set of similar events for which a study is conducted is called a population, in our study it refers to poultry, bovine and birds. The outcome of our study would indicate the prevalence of ESBLs by zone, year and species in India. It is a quantitative, epidemiological study designed to systematically assess the previous research studies to derive the conclusions of this research [8]. This study highlighted the prevalence of ESBL from the time period 2013–2019, with zone-wise and species-wise prevalence of ESBLs in India. A priori protocol was followed for this study with reference to a work done by Bulabula and co-workers [9].

To our knowledge, this is the first meta-analysis report from India on animals, which would aid in updating the national treatment guidelines for ESBL infections among animals.

**Materials and methods**

**Literature search**

A Systematic search was conducted in “Pub Med”, “Google Scholar” and “J-Gate-Plus” databases from Jan 2013 to May 2019 using the search terms "ESBL", "prevalence", "India", "Animals", "Poultry", "Cattle" and “Bovine” in combinations. Bibliographies of eligible studies were also manually searched to identify additional significant articles. A comprehensive search was conducted to ensure none of the research were missed out. The search was restricted to articles published in English.

**Study selection criteria**

All the articles that described the frequency of ESBL producing pathogens among the total isolates from animal samples (clinical/healthy) were considered eligible and included in the study. The qualified articles described the specific laboratory methods used to identify the ESBL producing pathogen along with species of the ESBL producing organism (Table 1). All the enrolled studies were restricted to India. Review articles, case reports and outbreaks were excluded.

**Data extraction**

For consistency, data was extracted independently by two people from selected articles. The data extracted from qualified studies included year of publication, first author, location where
Table 1. Characteristics of studies included in the review.

| Author and year of publication | State        | Country  | Sample type                                                                 | Number of ESBL positive samples/Total number of samples (% prevalence) | Methodology                                                                 | ESBL producing species                                      |
|--------------------------------|--------------|----------|------------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------------|---------------------------------------------------------------|
| Bandyopadhyay et al., 2018 [25]| West Bengal | India    | Bovine milk samples                                                          | 12/424 (9.41%)                                                         | PCR-based detection of major ESBL blaCTX-M-15 gene                     | ESBL producing K. pneumoniae                                 |
| Bhattacharya et al., 2015 [21] | West Bengal | India    | Meat and meat products                                                       | 2/80 (2.5%)                                                            | Combined Disc Diffusion Test                                          | ESBL producing E. coli                                      |
| Bhave et al., 2019 [28]        | Maharashtra | India    | Cloacal swabs of broilers                                                   | 23/146 (15.75%)                                                        | PCR-based detection of major ESBL genes (blaTEM, blaSHV, blaCTX-M)       | ESBL producing E. coli                                      |
| Bhoomika et al., 2016 [10]     | Chhattisgarh | India    | Chicken meat                                                                | 2/65 (3.08%)                                                          | Multiplex-polymerase chain reaction for detection of blaTEM, blaCTX-M    | ESBL genes in E. coli                                       |
| Bhoomika et al., 2016 [10]     | Chhattisgarh | India    | Chevon meat                                                                 | 1/38 (2.63%)                                                          | Multiplex-polymerase chain reaction for detection of blaTEM, blaCTX-M    | ESBL genes in E. coli                                       |
| Bhoomika et al., 2016 [10]     | Chhattisgarh | India    | Raw milk                                                                     | 6/73 (8.22%)                                                          | Multiplex-polymerase chain reaction for detection of blaTEM, blaCTX-M    | ESBL genes in E. coli                                       |
| Brower et al., 2017 [12]       | Punjab       | India    | Cloacal swabs from birds                                                    | 305/1556 (19.60%)                                                     | Combination disk method and VITEK 2                                    | ESBL producing E. coli                                      |
| Chauhan et al., 2013 [13]      | Himachal Pradesh | India | Raw milk samples from Doon valley                                           | 27/100 (27%)                                                          | Double disc diffusion method                                           | ESBL producing K. pneumoniae                              |
| Das et al., 2017 [15]          | West Bengal | India    | Milk samples of subclinical mastitis infected cattle                        | 24/50 (48%)                                                           | PCR-based detection of major ESBL genes (blaTEM, blaSHV, blaCTX-M)       | ESBL producing gram negative isolates                       |
| Dewangan et al., 2017 [16]     | Chhattisgarh | India    | Chevon meat                                                                 | 8/126 (6.35%)                                                         | Phenotypic detection of ESBL                                           | ESBL producing E. coli                                      |
| Dewangan et al., 2017 [16]     | Chhattisgarh | India    | Raw milk samples                                                             | 8/104 (7.69%)                                                         | Phenotypic detection of ESBL                                           | ESBL producing E. coli                                      |
| Kar et al., 2015 [22]          | West Bengal | India    | Fecal samples from poultry                                                  | 16/170 (9.41%)                                                        | Combination disc method and ESBL E-test                                | ESBL producing E. coli                                      |
| Kar et al., 2015 [22]          | West Bengal | India    | Milk samples from cattle                                                     | 2/135 (1.48%)                                                         | Combination disc method and ESBL E-test                                | ESBL producing E. coli                                      |
| Karuppasamy et al., 2015 [23]  | Mizoram      | India    | Raw milk                                                                     | 7/35 (20%)                                                            | Kirby-Bauer disc diffusion method                                     | ESBL producing E. coli                                      |
| Koovapra et al., 2016 [40]     | West Bengal | India    | Bovine milk samples                                                          | 7/159 (4.40%)                                                         | Combination disc diffusion test and ESBL Etest                         | ESBL producing K. pneumoniae                              |
| Koovapra et al., 2016 [40]     | Jharkhand    | India    | Bovine milk samples                                                          | 10/78 (12.82%)                                                        | Combination disc diffusion test and ESBL Etest                         | ESBL producing K. pneumoniae                              |
| Koovapra et al., 2016 [40]     | Mizoram      | India    | Bovine milk samples                                                          | 6/103 (5.82%)                                                         | Combination disc diffusion test and ESBL Etest                         | ESBL producing K. pneumoniae                              |
| Lalzampaia et al., 2013 [16]   | Mizoram      | India    | Fecal samples of pigs                                                       | 7/138 (5.07%)                                                         | PCR based detection of ESBLs genes                                     | ESBL genes in E. coli                                      |
| Lalzampaia et al., 2013 [17]   | Mizoram      | India    | Fecal samples of poultry birds                                              | 4/102 (3.92%)                                                         | PCR based detection of ESBLs genes                                     | ESBL genes in E. coli                                      |
| Lalzampaia et al., 2014 [18]   | Mizoram      | India    | Fecal samples of poultry birds                                              | 1/11 (9.09%)                                                          | PCR-based detection of ESBLs genes                                     | ESBL genes in K. pneumoniae                                |
| Mahanti et al., 2017 [14]      | West Bengal | India    | Cloacal swabs from healthy broiler, indigenous, and kuroiler birds          | 33/307 (10.75%)                                                       | PCR-based detection of major ESBL genes (blaTEM, blaCTX-M)              | ESBL producing K. pneumoniae                              |
| Mandakini et al., 2015 [24]    | Mizoram      | India    | Fecal samples of piglets suffering from diarrhea                            | 43/170 (25.29%)                                                       | Double disc synergy test                                               | ESBL producing E. coli                                      |
| Nirumapa et al., 2018 [26]     | Uttar        | India    | Fecal samples of pigs                                                       | 243/741 (32.79%)                                                      | Double disc diffusion method and Hi-comb MIC test strip                | ESBL producing E. coli                                      |

(Continued)
study was conducted, total sample size, strains detected ESBL positive, and method used for confirmation of ESBL producing pathogen. Any inconsistency in data collection was rectified by re-checking the articles for accuracy.

Quality assessment

Since it is a prevalence study, use of Newcastle-Ottawa scale is not recommend. However, quality assessment of the study was done on fixed rating scale. This scale includes evaluation of study selection, comparability and outcome, with each section having maximum number of stars as 5, 3 and 2 respectively. Hence, the overall quality assessment has a maximum score of 10 and minimum score for inclusion is 3 stars. Table 2 shows the risk of bias assessment for the studies included in quantitative synthesis.

Statistical analysis

Meta-analysis for the prevalence of ESBL producing pathogens among animal samples were conducted using the R Open source scripting software (version 3.4.3, R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/) [10]. The inbuilt packages used for analysis were Metafor and Meta R packages.

In the analysis, both random effect and fixed effect model were used to calculate the pooled prevalence of ESBL and $I^2$ statistic (to measure inconsistency). The $r^2$ statistic was also calculated to measure the heterogeneity. Further, sub-group analysis was performed to reduce heterogeneity. In the present study, the data was stratified based on: year-wise (2013–2019) zone-wise (North, East, West, South and Central zones) and species-wise (E. coli, Pseudomonas spp., and K. pneumoniae).

![Table 1. (Continued)](https://doi.org/10.1371/journal.pone.0221771.t001)
Results

Distribution and characteristics of articles describing ESBLs in India

The electronic database searches returned 32 potential articles based on the keyword search. Review articles studying the ESBL prevalence in humans were excluded. A total of 23 articles were selected suitable for the study. The flowchart of systematic article selection is shown in Fig 1. All the articles included in the study described the prevalence of ESBL producing pathogens isolated from animals/animal samples from India. The maximum number of studies on this subject were found in the eastern zone followed by central, south and north zone. No studies were found from western zone of India. In total, 20 studies were on ESBLs produced by *Escherichia coli*, 6 on ESBLs produced by *K. pneumoniae* and 2 on ESBLs produced from *Pseudomonas* spp. The animal samples studied in the articles mainly included meat samples, milk samples, rectal swabs, cecal swabs and cloacal swabs from poultry birds, sheep, pig and cattle.

Pooled prevalence of ESBLs in animal samples

The meta-analysis revealed the overall pooled prevalence of ESBL in animals to be 9% (95% CI: 6–13%; $\tau^2 = 0.6654$; $P < 0.01^{**}$). The prevalence estimates of ESBL producing pathogens in India is depicted in the forest plot in Fig 2, which also displays the author, year, samples, events and total samples [11–20]. In order to reduce the heterogeneity, the studies on ESBL producing isolates were categorized by Year, Zone and Species-wise (Table 3). The pooled prevalence...
of ESBL producing pathogens in animals were 12, 5, 8, 8, 12, 13 and 33% for the years 2013, 2014, 2015, 2016, 2017, 2018 and 2019 respectively, as depicted in the forest plot [20–30] in (Fig 3A–3G). The zone-wise prevalence percentage of ESBLs were 26, 11, 6 and 8% for the north, east, south and central zones are shown in (Fig 4A–4D). The species-wise prevalence of ESBLs were found to be 9, 10 and 5% for E.coli, K. pneumoniae and Pseudomonas spp. respectively. Figs 5–7 explains the forest plot of species-wise Meta-analysis.

Discussion

Our study revealed that, the ESBL producing clinical isolates in India may not be very high, nonetheless it is significant. These drug-resistant pathogens are a serious concern worldwide...
Table 3. Risk of bias assessment for studies included in the quantitative synthesis.

| Author and year of publication | Representativeness of the sample | Ascertainment of exposure | Comparability | Outcome Assessment of outcome | Overall Quality Assessment score |
|--------------------------------|---------------------------------|---------------------------|---------------|-------------------------------|---------------------------------|
| Bandyopadhay et al. 2018 [25]  | Truly representative bovine milk samples | ESBL production confirmed by PCR | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Bhattacharyya et al., 2015 [20] | Truly representative Meat and meat products with antibiotic resistance | ESBL production diagnosed by Combined Disc Diffusion Test | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Bhave et al., 2019 [26]       | Truly representative Cloacal swabs from broiler | ESBL production diagnosed by Combined Disc Diffusion Test | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Bhoomika et al., 2016 [10]    | Truly representative of chicken meat samples with antibiotic resistance | Chicken meat samples diagnosed with clinical isolates producing ESBL confirmed by Multiplex PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Bhoomika et al., 2016 [10]    | Truly representative of chevon meat samples with antibiotic resistance | Chevon meat samples diagnosed with clinical isolates producing ESBL confirmed by Multiplex PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Bhoomika et al., 2016 [10]    | Truly representative of raw milk samples with antibiotic resistance | Raw milk samples diagnosed with clinical isolates producing ESBL confirmed by Multiplex PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Bower et al., 2017 [11]       | Truly representative Cloacal swabs from birds with antibiotic resistance | ESBL production diagnosed by Combination disk method and VITEK 2 | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Chauhan et al., 2013 [12]     | Truly representative Raw milk samples from Doon valley with antibiotic resistance | ESBL production diagnosed by Double disc diffusion method | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Das et al., 2017 [14]         | Truly representative of sub-clinical mastic milk samples with antibiotic resistance | Sub-clinical mastic milk samples diagnosed with clinical isolates producing ESBL confirmed by PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Dewangan et al., 2017 [15]    | Truly representative Chevon meat with antibiotic resistance | ESBL production diagnosed by Phenotypic detection of ESBL | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Dewangan et al., 2017 [15]    | Truly representative Raw milk samples with antibiotic resistance | ESBL production diagnosed by Phenotypic detection of ESBL | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Kar et al., 2015 [21]         | Truly representative Fecal samples from poultry with antibiotic resistance | ESBL production diagnosed by Combination disc method and ESBL E-test | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Kar et al., 2015 [21]         | Truly representative Milk samples from cattle with antibiotic resistance | ESBL production diagnosed by Combination disc method and ESBL E-test | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Karuppasamy et al., 2015 [22]| Truly representative Raw milk samples with antibiotic resistance | ESBL production diagnosed by Kirby Bauer disc diffusion test | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Koovapra et al., 2016 [33]    | Truly representative Bovine milk samples with antibiotic resistance | ESBL production diagnosed by Combination disc diffusion test and ESBL Etest | Study did not control for other factors | 4-Independent blind assessment | 3 |
| Lalmampia et al., 2013 [16]   | Truly representative Fecal samples of pigs with antibiotic resistance | Pigs with history of diarrhea diagnosed with clinical isolates producing ESBL confirmed by PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Lalmampia et al., 2014 [17]   | Truly representative Fecal samples of poultry birds with antibiotic resistance | Poultry birds with history of diarrhea diagnosed with clinical isolates producing ESBL confirmed by PCR | Study did not control for other factors | 4-Independent blind assessment | 4 |
| Author and year of publication | Selection | Ascertainment of exposure | Comparability | Outcome Assessment of outcome | Overall Quality Assessment score |
|-------------------------------|-----------|---------------------------|--------------|-------------------------------|---------------------------------|
| Lalzampuia et al., 2014 [17]  | "Truly representative Fecal samples of poultry birds with antibiotic resistance" | "Poultry birds with history of diarrhea diagnosed with clinical isolates producing ESBL confirmed by PCR" | Study did not control for other factors | *Independent blind assessment | 4 |
| Mahanti et al., 2017 [13]    | "Truly representative Cloacal swabs from healthy broiler, indigenous, and kuroiler birds with antibiotic resistance" | "ESBL production confirmed by PCR" | Study did not control for other factors | *Independent blind assessment | 4 |
| Mandakini et al., 2015 [23]  | "Truly representative Fecal samples of piglets suffering from diarrhea with antibiotic resistance" | "ESBL production diagnosed by Double disc synergy test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Nirumapa et al., 2018 [26]   | "Truly representative Fecal samples of pigs" | "ESBL production diagnosed by Double disc diffusion method and Hi-comb MIC test strip" | Study did not control for other factors | *Independent blind assessment | 3 |
| Raj et al., 2019 [29]        | "Truly representative Food-animal environment" | "ESBL production diagnosed by PCR" | Study did not control for other factors | *Independent blind assessment | 3 |
| Rasheed et al., 2014 [18]    | "Truly representative Unpasteurized milk of buffalo with antibiotic resistance" | "ESBL production diagnosed by Phenotypic Confirmatory Disc Diffusion Test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Rasheed et al., 2014 [18]    | "Truly representative Raw chicken with antibiotic resistance" | "ESBL production diagnosed by Phenotypic Confirmatory Disc Diffusion Test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Rasheed et al., 2014 [18]    | "Truly representative Fresh raw meat of sheep with antibiotic resistance" | "ESBL production diagnosed by Phenotypic Confirmatory Disc Diffusion Test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Samanta et al., 2015 [24]    | "Truly representative Samples from backyard and farmed poultry with antibiotic resistance" | "ESBL production confirmed by PCR" | Study did not control for other factors | *Independent blind assessment | 4 |
| Sharif et al., 2017 [19]     | "Truly representative Rectal swab samples from healthy dogs with antibiotic resistance" | "ESBL production diagnosed by Combined Disc Diffusion Test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Sharif et al., 2017 [19]     | "Truly representative Rectal swab samples from diarrheic dogs with antibiotic resistance" | "ESBL production diagnosed by Combined Disc Diffusion Test" | Study did not control for other factors | *Independent blind assessment | 3 |
| Shrivastav et al., 2016 [35] | "Truly representative Cecal swab samples in healthy broilers with antibiotic resistance" | "ESBL production diagnosed by CDDT, DDST and Enz MIC strip in Healthy broilers" | Study did not control for other factors | *Independent blind assessment | 3 |
| Tewari et al., 2018 [27]     | "Truly representative Fecal samples of livestock" | "ESBL production confirmed by PCR" | Study did not control for other factors | *Independent blind assessment | 3 |
| Tewari et al., 2019 [30]     | "Truly representative Fecal samples of livestock" | "ESBL production confirmed by PCR" | Study did not control for other factors | *Independent blind assessment | 3 |

PCR, Polymerase chain Reaction; CDDT, Combined disc diffusion test; DDST, Double disc synergy test, Enz MIC strip, Enz Minimum Inhibitory Concentration strip; E test, Epsilometer test.

(*)Stars represent the number of points awarded for the category;

* = 1,
** = 2.

https://doi.org/10.1371/journal.pone.0221771.t003

as they are associated with increase in morbidity and mortality rate due to infections they cause [31]. Extended-Spectrum Beta-Lactamases are produced by species of bacteria in order
to inactivate antibiotics, causing antibiotic resistance. Beta-lactamase seems to be the prime cause in multidrug resistant (MDR) *E. coli* strains. Early detection of *E. coli* that produce beta lactamase is necessary in order to prevent MDR *E. coli* from spreading [32]. Activity of ESBLs caused by different beta-lactamases resulted in resistant genes within the farm [33]. The strains that were isolated showed that a small portion of the resistant genes were present in one farm [4]. The steep rise in income and the growing population has driven an increase in demand for animal products in India. India is one of the top consumers of antibiotics worldwide, it accounts for about 3% of global consumption which is estimated to double by 2030. This could be due to the non-therapeutic use of antibiotics in cases of prophylaxis and growth promotion [34]. Currently, the usage of antibiotics is high in poultry, swine and cattle production as compared to that being used by the human population [35–36].

To address the concern of antimicrobial resistant bacteria, it is crucial to raise awareness of the problem by collecting data on antibiotic resistance from various countries and regions. The paucity of studies available from India affirms attention for future research. To our

![Fig 3. Forest plots of ESBL prevalence in (a) 2013; (b) 2014; (c) 2015; (d) 2016; (e) 2017; (f) 2018; and (g) 2019.](https://doi.org/10.1371/journal.pone.0221771.g003)

Meta-analyses of ESBL bacteria from animal origin

![Fig 4. Forest plots of ESBL prevalence in (a) north-zone; (b) east-zone; (c) south-zone; and (d) central-zone.](https://doi.org/10.1371/journal.pone.0221771.g004)
knowledge, this is the first meta-analysis regarding the magnitude of the ESBL problem in Indian animal population. From the 23 articles chosen in the study, the overall pooled prevalence of ESBL producing isolates from the animal samples was found to be 10%. In Asia, high rates of ESBL producing *Enterobacteriaceae* are seen with variation in the prevalence and the genotype of the ESBL producing isolates over the large geographical area [30].

The prevalence of ESBL producing isolates were 12, 5, 8, 8, 12, 13 and 33% for the years 2013, 2014, 2015, 2016, 2017, 2018 and 2019 respectively, indicating an increase in the percent drug resistance since 2014 to 2019. The pooled prevalence of ESBL producing isolates was determined zone-wise and North zone showed a higher prevalence rate in comparison to other zones. Nonetheless, no studies on prevalence of ESBL producing isolates for animal samples from the Western zone of India are reported. Prevalence of species-wise classification was found to be 9, 10 and 5% for *E. coli*, *K. pneumoniae* and *Pseudomonas* spp. respectively, signifying that the ESBL producing *K. pneumoniae* is the most predominant ESBL producing isolate in India.

A study conducted in the intensive care units (ICUs) of an Indian hospital concluded that there is a need for constant surveillance to detect resistant bacterial strains, strict guidelines on antibiotic therapy, and effective infection control measures in order to reduce the spread of antibiotic resistant bacteria. The same study also revealed that there is a high number of ESBL producing *E. coli* in the ICUs of that hospital [31]. A study with pediatric and neonatal patients estimated the number of poor outcomes and indicated the association of blood stream infections (BSIs) with Extended-Spectrum Beta-Lactamase- producing *Enterobacteriaceae* (ESBL-PE). The results showed a high prevalence of BSIs due to ESBL-PE and increase in neonatal mortality [37–39]. A study from Germany demonstrated that direct transfer of ESBL- producing *E. coli* could occur between livestock and the farm workers who were in close contact with farm animals. The study also suggests an existence of epidemiological links between livestock and farm workers. A high prevalence of ESBL-producing *E. coli* in pig and cattle farms emphasizes the fact that livestock animals are a constant source for these potential human pathogens [33, 40–41].

![Fig 5. Forest plot of *E. coli* producing ESBL prevalence.](https://doi.org/10.1371/journal.pone.0221771.g005)

![Fig 6. Forest plot of *K. pneumoniae* producing ESBL prevalence.](https://doi.org/10.1371/journal.pone.0221771.g006)
Our research findings do have some minor limitations, which includes the lack of sufficient information on the prevalence of ESBL producers from different animal species. Upon advanced literature survey, we could find only a few articles that addressed the prevalence of ESBLs in animals.

**Conclusion**

India being a developing country, has the highest burden of bacterial infections. Hence, to combat this downfall, antibiotics are used widely and indiscriminately. The overuse, lack of awareness and non-therapeutic use of antibiotics is driving an increase in the antibiotic resistance among animals. This meta-analysis, indicated that the pooled prevalence of ESBLs for animals in India is not high, however, the overall prevalence remains significant at 10%. Additionally, only little information is currently available that addresses the prevalence of ESBLs in animals in India. The paucity of data on the clinical outcomes, magnitude and prevalence of the resistant ESBLs, calls for active surveillance which can help understand the epidemiology of ESBL burden in India. Furthermore, emphasis on awareness programs, personal and environmental hygiene should be implemented to stop and manage the spread of ESBLs to the animals and environment. Further studies are needed to better understand the complexity of the AMR problem in animal and human population.

**Supporting information**

S1 File. PRISMA checklist.  
(DOC)

S2 File. Listed references for underlying data.  
(DOCX)

**Acknowledgments**

We would like to thank Mal Hoover for her assistance with the images.

**Author Contributions**

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**Fig 7. Forest plot of *Pseudomonas* spp. producing ESBL prevalence.**

https://doi.org/10.1371/journal.pone.0221771.g007
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