



Research article

Antimicrobial resistance burden in India and Germany in 2022: A systematic analysis along with One Health perspective

Gunjan^{a,b,1}, Ramendra Pati Pandey^{d,*,1}, Himanshu^{a,b}, Kirtanjot Kaur^e, Saheem Ahmad^f, Riya Mukherjee^{a,b}, Chung-Ming Chang^{b,c,**}^a Graduate Institute of Biomedical Sciences, Chang Gung University, No. 259, Wenhua 1st Road, Guishan District, Taoyuan City, 33302, Taiwan^b Biotechnology Industry, Chang Gung University, No. 259, Wenhua 1st Road, Guishan District, Taoyuan City, 33302, Taiwan^c Department of Medical Biotechnology and Laboratory Science, Chang Gung University, No. 259, Wenhua 1st Road, Guishan District, Taoyuan City, 33302, Taiwan^d Department of Biotechnology, SRM University, Delhi-NCR, Sonapat, Haryana, 131029, India^e University Centre for Research and Development, Chandigarh University, Mohali, Punjab, India^f Department of Medical Laboratory Sciences, College of Applied Medical Sciences, University of Hail, Hail City, Saudi Arabia

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ABSTRACT

Globally increasing antibiotic resistance has been linked to the extensive use of antibiotics in medical, veterinary, and agricultural Practices. This study aims to investigate the correlations of antimicrobial-resistant of various pathogens in three compartments: humans, animals and the environment in India and Germany. A systematic search was carried out in Medline via PubMed, Google Scholar, and science direct, including studies published in 2022. Out of 532 papers, 24 were considered for meta-analysis. Our findings reveals that in India, β -lactam is highly resistant in animals. Quinolone, on the other hand, was highly resistant in humans. In the environmental sectors, aminoglycosides and β -lactams is resistant. While in Germany, β -lactam resistance is high across all three sectors. However, *E. coli* was the most frequent and resistant pathogen in both countries, with significant resistance to β -lactams and cephalosporins across all compartments. These results underscore the critical need for monitoring antibiotic resistance patterns and developing targeted antibiotic regimens. A One Health-based intervention strategy is essential to mitigate the spread of AMR and improve health outcomes globally.

1. Introduction

Antibiotic-resistant (ABR) bacterial infections increase mortality, morbidity, social and impose significant social and economic burdens [1]. Besides from the discovery of novel antimicrobial medications, as misuse accelerates the development of resistance strains through positive selection pressure [2]. This issue is not confined to humans but extends to animals and the environment, making antimicrobial resistance (AMR) a global rather than a local concern. AMR can easily spread across borders, driven by factors such as misuse of antibiotics, inadequate hygiene, and ineffective infection control in healthcare settings [3].

* Corresponding author. School of Health Sciences and Technology (SoHST) UPES, Bidholi, Dehradun, 248007, Uttarakhand, India.

** Corresponding author. Biotechnology Industry, Chang Gung University, No. 259, Wenhua 1st Rd., Guishan Dist., Taoyuan City, 33302, Taiwan.
E-mail addresses: ramendra.pandey@gmail.com (R.P. Pandey), cmchang@mail.cgu.edu.tw (C.-M. Chang).

¹ Contributed equally as first authorship.

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Growing evidence suggests that the widespread use of antibiotics in agriculture and aquaculture may be a factor in the emergence of resistance to antibiotics frequently used in human treatment [4]; this is primarily a major issue considering the overlap between the antibiotics used for these many uses [1]. For instance, ABR bacteria in animals, treated with antibiotics, can carry resistance genes that may be transmitted to humans through food, direct contact, or shared environmental sources like sewage water. This interspecies transmission underscores the complexity of AMR and highlights the need for a One Health approach, which emphasizes the interconnectedness of human health, animal health, food safety, and the environment [5].

The One Health concept emphasizes the connections between human health, animal health, food safety, and the environment and encourages cooperation between the health agencies responsible for these areas [6]. In response to the growing AMR threat, the WHO plays an important role in monitoring antibiotic use and providing the necessary data to combat AMR. The WHO, the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE) have formed a tripartite partnership to coordinate global and national action plans (NAPs) to combat AMR. All the countries, including India and Germany, are now implementing AMR NAPs through multisectoral collaboration to enable comprehensive surveillance, monitoring, and policy implementation across human, animal, and environmental domains [7].

The global impact of AMR is stark, with projections suggesting it could cause 10 million deaths annually by 2050, with a total monetary cost of US\$100 trillion [8]. Although others have criticized these assumptions [9]. AMR bacteria caused more than 670,000 illnesses in European Union (EU) and European Economic Area (EEA) nations in 2015, resulting in an estimated 33,000 mortality [10]. World health organization (WHO) and numerous other organizations and researchers concur that the development of AMR is an important issue that requires a global, coordinated action plan to address [11–13]. A lack of knowledge and inadequately trained professionals may all be linked to the prevalent resistance in these areas. Despite this knowledge gap, many nations, especially those in the EU, have made significant efforts to reduce the overall use of antibiotics in animals raised for food.

In this systematic meta-analysis, we represented the AMR burden in India and Germany in 2022 in three compartments: human, animal and environment. India and Germany were selected for this study due to their significant influence on public health policies and their key roles in the global fight against AMR. India, with its major pharmaceutical industry and challenges in antibiotic use, contrasts with Germany's strict AMR policies and robust surveillance system. By incorporating up-to-date research findings, this study provides an accurate and relevant assessment of current AMR trends. The use of recent data is crucial, as it allows us to identify emerging patterns in resistance, which are essential for developing timely and effective interventions. Furthermore, the insights gained from this analysis are poised to have an immediate impact on public health policy and clinical practice, addressing the ongoing challenges of AMR with the most current evidence.

2. Materials and methods

2.1. Study methodology

A systematic review was carried out in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [14]. All 24 checklist literature were addressed in the study, is depicted in Fig. 1.

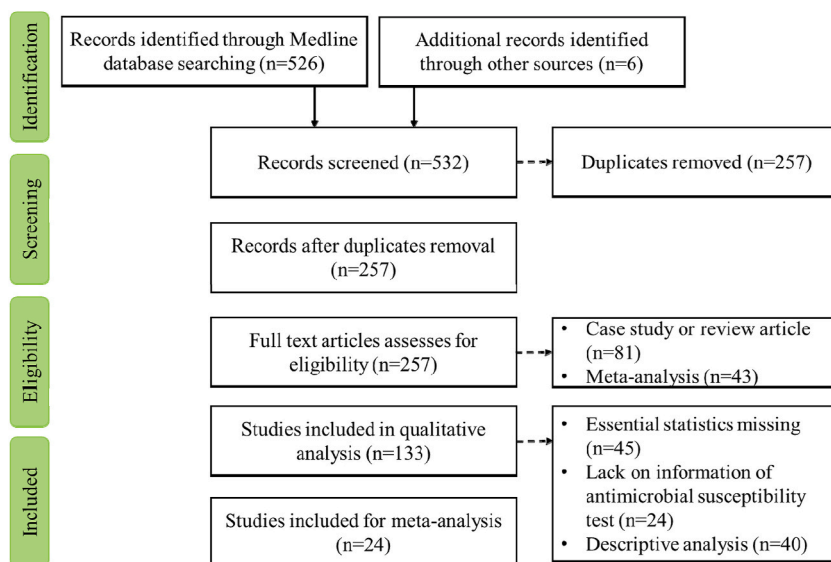


Fig. 1. Diagram illustrating the study selection process using PRISMA.

2.2. Search strategy

We conducted a comprehensive, systematic search of web databases for relevant literature, including PubMed (<https://pubmed.ncbi.nlm.nih.gov/>), Google Scholar (<https://scholar.google.com/>), and Science Direct (<https://www.sciencedirect.com/>), published in the year of 2022. To search the articles, MeSH terms and Boolean Logic tools with the connectors 'AND' and 'OR' were used, including (antimicrobial resistance OR antibiotic resistance) AND (human OR animal OR environment), AND (*E. coli* OR *Escherichia coli* OR *Salmonella* OR *Mycobacterium avium* subsp. *Paratuberculosis* OR *Citrobacter* OR *Klebsiella* OR *Clostridium difficile* OR *Proteus* OR *Staphylococcus* OR *Bacilli* OR *Morganella* OR *Chlamydia* spp. OR *Trichinella* spp. OR *Listeria* spp. OR *Vibrio* spp. OR *Aeromonas* spp.) AND (dairy OR meat OR beef OR pig OR pork OR chicken OR fish OR shrimp OR octopus OR lobster OR marine mammals OR vulture OR ostrich OR camel) AND (environment OR soil OR wastewater OR water OR drainage) AND (India OR Germany). For the study to be considered in our analysis, the available abstract must be written in English.

2.3. Selection criteria

Title, abstract, and full text were the three criteria for evaluating the articles. The prevalence of AMR in various microorganisms and sample collection must be discussed in the articles was from (1) humans (healthy/diseased people in hospitals); (2) animals (both terrestrial and aquatic); animal food items (meat, seafood and dairy products); and (3) the environment (water, drainage, soil). Furthermore, all investigations must follow the Clinical and Laboratory Standards Institute (CLSI) criteria for antimicrobial susceptibility testing (AST).

The following criteria were used to exclude articles: (1) conference papers, abstracts, perspectives, review articles, and meta-analysis; (2) study protocols and articles without full text or not published in English; (3) studies that did not provide the necessary data.

2.4. Data extraction and quality assessment

To create a baseline, complete versions of reported relevant articles were obtained. A pre-test was carried out before the complete extraction. The following information was extracted and recorded in a spreadsheet (Microsoft Excel® 2013) after reviewing the data from each retrieved publication: (a) locality of India and Germany (East/West/North/South/Central) (b) year of publication (2022) (c) host (humans/animals/environment/integrated studies between animals, humans and environment); (d) sample type (fecal sludge/water/retail/veterinary clinics/ice/nasopharyngeal swab/stool/faeces/rectal swab/urine/vaginal swab/other: abscess, appendix, small intestines/colon/stomach, gall bladder/liver, peritoneal fluid/placenta/tissue) (e) microbial species (*E. coli*, *Escherichia coli*, *Salmonella*, *Mycobacterium avium* subsp. *Paratuberculosis*, *Citrobacter*, *Klebsiella*, *Clostridium difficile*, *Proteus*, *Staphylococcus*, *Bacilli*, *Morganella*, *Chlamydia* spp., *Trichinella* spp., *Listeria* spp., *Vibrio* spp., *Aeromonas* spp.) (f) the number of isolates (g) animal species (dairy, meat, beef, pig, pork, chicken, fish, shrimp, octopus, lobster, marine mammals, vulture, ostrich and camel) (h) laboratory methods for AST (MIC or disk diffusion); (i) WHO categorized the prevalence of ABR bacteria, antimicrobial drugs, and antimicrobial classes (highest priority critically important/high priority critically important/highly important/important) [14]. (j) The proportion of multi-drug resistance (MDR) isolates resistant to at least one antimicrobial agent from more than three antimicrobial classes.

For a detailed analysis, the antimicrobial resistance patterns of various pathogens were evaluated using a spreadsheet (Microsoft Excel® 2013) and pre-tested before data extraction. The quantified data were then represented in pie charts for clarity. Additionally, Mendeley software (version 1.19.8) was used for citing the articles.

The assessment of included publications was conducted by two independent and unbiased reviewers to ensure objectivity and reduce potential bias in the data extraction and analysis process. Each reviewer independently evaluated the eligibility and quality of the studies based on predefined criteria, ensuring that the selection of studies was consistent and impartial. In cases where the reviewers disagreed on the inclusion of a study or its quality assessment, discrepancies were resolved through discussion or by consulting a third reviewer.

2.5. Risk of bias assessment

Assessing publication bias is crucial to ensure the robustness and reliability of our meta-analysis examining antimicrobial resistance effects in both India and Germany. The robvis tool for systematic reviews of prevalence studies was used to assess the study risk of bias [15].

To examine potential bias in publication, we employed three established methodologies commonly recommended in this field. One vital approach involved visually analyzing a bias risk graph for any asymmetry, which could indicate publication bias presence. Our aim in employing these comprehensive methodologies was to thoroughly address any potential bias and ensure our meta-analysis offered an unbiased synthesis of current evidence on antimicrobial resistance. Additionally, we utilized a bias checklist encompassing categories such as selection of articles (selection bias), selective reporting (reporting bias), deviation from intended intervention (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and other potential biases.

Table 1
The total number of studies in each category.

Description of selected studies	India					Germany			
	Human studies (n = 2) (14.29 %)	Animal studies (n = 9) (64.29 %)	Environment studies (n = 2) (14.29 %)	Integrated study (animal, environment) (n = 1) (7.14 %)	Total (n = 14) (%)	Human studies (n = 1) (10 %)	Animal studies (n = 6) (60 %)	Environment studies (n = 3) (30 %)	Total (n = 10) (%)
Bacterial species									
<i>E. coli</i>	–	3 (33.33)	1 (50)	1 (100)	5 (35.71)	1 (100)	1 (16.67)	1 (33.33)	3 (30)
<i>Salmonella</i> spp.	–	–	–	–	–	–	1 (16.67)	–	1 (10)
<i>Enterococcus</i> spp.	–	1 (11.11)	–	–	1 (7.14)	–	–	–	–
<i>Klebsiella</i> spp.	–	–	–	–	–	–	–	1 (33.33)	1 (10)
<i>Proteus</i> spp.	–	1 (11.11)	–	–	1 (7.14)	–	–	–	–
<i>Staphylococcus</i>	–	–	–	–	–	–	1 (16.67)	–	1 (10)
<i>Bacilli</i>	1 (50)	3 (33.33)	–	–	4 (28.57)	–	–	–	–
<i>Trichinella</i> spp.	–	–	–	–	–	–	1 (16.67)	–	1 (10)
<i>Listeria</i> spp.	–	–	–	–	–	–	1 (16.67)	–	1 (10)
<i>Vibrio</i>	–	–	–	–	–	–	–	1 (33.33)	1 (10)
<i>Enterococcus</i> , <i>Staphylococcus</i>	1 (50)	–	–	–	1 (7.14)	–	–	–	–
<i>E.coli</i> , <i>Enterococcus</i> , <i>Klebsiella</i> , <i>Staphylococcus</i> , <i>Aeromonas</i> spp.	–	–	1 (50)	–	1 (7.14)	–	–	–	–
<i>E.coli</i> , <i>Salmonella</i> , <i>Citrobacter</i> , <i>Klebsiella</i> spp., <i>Proteus</i> spp., <i>Staphylococcus</i> , <i>Bacilli</i> , <i>Morganella</i>	–	1 (11.11)	–	–	1 (7.14)	–	–	–	–
<i>E.coli</i> , <i>Salmonella</i> spp., <i>Mycobacterium avium</i> subsp. <i>Paratuberculosis</i> , <i>Clostridium difficile</i> , <i>Chlamydia</i> spp.	–	–	–	–	–	–	1 (16.67)	–	1 (10)
Study area									
East	–	–	–	–	–	–	1 (16.67)	–	1 (10)
West	–	2 (22.22)	–	–	2 (14.29)	–	–	1 (33.33)	1 (10)
North	1 (50)	5 (55.56)	1 (50)	–	7 (77.78)	–	2 (33.33)	2 (66.66)	4 (40)
South	–	2 (22.22)	1 (50)	–	3 (33.33)	–	2 (33.33)	–	2 (20)
Central	1 (50)	1 (11.11)	–	–	2 (14.29)	1 (100)	1 (16.67)	–	2 (20)
Sample type									
Fecal sludge/water	1 (50)	–	2 (100)	–	3 (21.43)	–	1 (16.67)	3 (100)	4 (40)
Retail/veterinary clinics/ice	–	7 (77.77)	–	–	7 (50)	–	–	–	–
Nasopharyngeal swab/ stool/feaces/rectal swab/urine/vaginal swab	1 (50)	1 (11.11)	–	1 (100)	3 (21.43)	1 (100)	2 (33.33)	–	3 (30)
Mixed sample	–	1 (11.11)	–	–	1 (7.14)	–	3 (50)	–	3 (30)
Antimicrobial susceptibility testing method									
Disc diffusion (DD)	2 (100)	9 (100)	2 (100)	–	13 (92.86)	–	2 (33.33)	3 (100)	5 (50)
Minimum Inhibitory Concentration (MIC)	–	–	–	1 (100)	1 (7.14)	1 (100)	4 (66.67)	–	5 (50)

3. Result

3.1. Study selection

We categorized 526 papers published in 2022 using three internet databases. After a preliminary evaluation of the title and abstract, 275 articles from these were excluded due to their relevancy and redundancy; however, the complete texts of the remaining 257 articles were examined. The following factors led to the exclusion of 124 of the 257 articles: 51 due to case study or review articles and 43 due to meta-analysis articles. 109 of these 133 full-text items were again excluded. 45 due to the absence of essential statistics, 24 due to lack of information on AST and 40 due to descriptive analysis. Finally, 24 studies total were incorporated into this meta-analysis and systematic review (Supplementary Data 1). The method of study selection follows the PRISMA flow diagram and is illustrated in Fig. 1.

3.2. Characteristics of included studies

24 articles were chosen for quantitative study published in the year of 2022. Out of this 14 [16–28] studies were from India and 10 [2,29–36] studies were from Germany.

3.2.1. AMR studies in different region of countries

A summary of the studies chosen for qualitative synthesis is provided in Table 1. All 24 selected studies were published in 2022. Fig. 3 depicts the study sites, and the number of papers published in three regions. In India, most of the studies were published in Northern (7/14, 77.78 %), followed by Southern (3/14, 33.33), Western (2, 14.29 %) and Central (2, 14.29 %) part. However, in Germany, most of the studies were published in Northern (4/10, 40%), followed by Southern (2/10, 20%), Central (2/10, 20%), Eastern



Fig. 2. Risk of bias graph.

(1/10, 10 %) and Western (1/10, 10 %) region.

3.2.2. Microbial prevalence in India and Germany

In the selected research, In India, *E. coli* was the most prevalent species (5/14, 35.71 %), followed by *Bacilli* (4/14, 28.57 %), *Enterococcus* spp. (1/14, 7.14 %), *Proteus* spp. (1/14, 7.14 %). Moreover, there was one study covering more than one pathogen together, i.e. *Enterococcus*, *Staphylococcus* (1/14, 7.14 %), and one covering *E. coli*, *Enterococcus*, *Klebsiella*, *Staphylococcus*, *Aeromonas* spp. (1/14, 7.14 %) and one study that covers *E. coli*, *Salmonella*, *Citrobacter*, *Klebsiella* spp., *Proteus* spp., *Staphylococcus*, *Bacilli*, and *Morganella* (1/14, 7.14 %). Retail/veterinary clinics/ice (7, 50 %) were the most selected studies, followed by faecal sludge/water (3, 21.43 %), nasopharyngeal swab/stool/faeces/rectal swab/urine/vaginal swab (3, 21.43 %) and mixed sample (1, 7.14 %). The agar disc diffusion (DD) method was employed by most of the selected research (13/14, 92.86 %) for AST, whereas other studies (1/14, 7.14 %) used agar/broth methods to assess the MIC of antimicrobial compounds.

E. coli (3/10) is also the most common species in Germany, followed by *Salmonella* spp. (1/10, 10 %), *Klebsiella* spp. (1/10, 10 %), *Staphylococcus* (1/10, 10 %), *Trichinella* spp. (1/10, 10 %), *Listeria* spp. (1/10, 10 %), *Vibrio* (1/10, 10 %). Furthermore, there was one study that covered more than one pathogen together, i.e. *E. coli*, *Salmonella* spp., *Mycobacterium avium* subsp. *Paratuberculosis*, *Clostridium difficile*, *Chlamydia* spp. (1/10, 10 %). Faecal sludge/water were the most selected studies (4, 40 %) along with nasopharyngeal swab/stool/faeces/rectal swab/urine/vaginal swab (3, 30 %) and mixed sample (3, 30 %). For AST, the agar DD method and MIC of antimicrobial agents (5/10, 50 %) were used (Table 1).

3.3. Risk of bias of included studies

Fig. 2 presents a comprehensive examination of both the overall risk and specific biases identified in each of the analyzed studies. Bias likelihood was assessed through researcher evaluations, revealing a notable level of consistency across all studies. The data showcased in Fig. 2 accentuates an increased bias risk in articles authored by P. Ronanki et al. [16] and Savin et al. [17], demonstrating a high risk of bias in deviation from intended intervention (Performance bias). Moreover, research conducted by Debbarma et al. [18], Amreen et al. [19], Basant et al. [20], Patel et al. [21], R Singh et al. [22], S. Nayakvadi et al. [23], Fleischmann et al. [24], Gross et al. [2], González-Santamarina et al. [25], Soundararajan et al. [26], Kresken et al. [27], and Klose et al. [28] exhibited a risk of bias in the binding of outcome assessment (Detection bias). This consistently applied rigorous methodology enhances confidence in the research paper's findings, underscoring the reliability of the identified biases and their impact on the study's outcomes.

3.4. Meta-analysis for antibiotic resistance in each sector

3.4.1. AMR in India

A total of 14 studies on AMR phenotypic susceptibility to 69 distinct antimicrobial agents (16 antimicrobial classes) among 10 Pathogens were considered. For ease of understanding, we categorized the studies into 4 groups: animals, humans, the environment, and integrated studies (animal and environment). In Animals, there are 7 bacteria which are found to be highly prevalent. The highest resistance shown by antibiotics in pathogens is as follows: in *E. coli*, β -lactam found highly prevalent (38 %), followed by

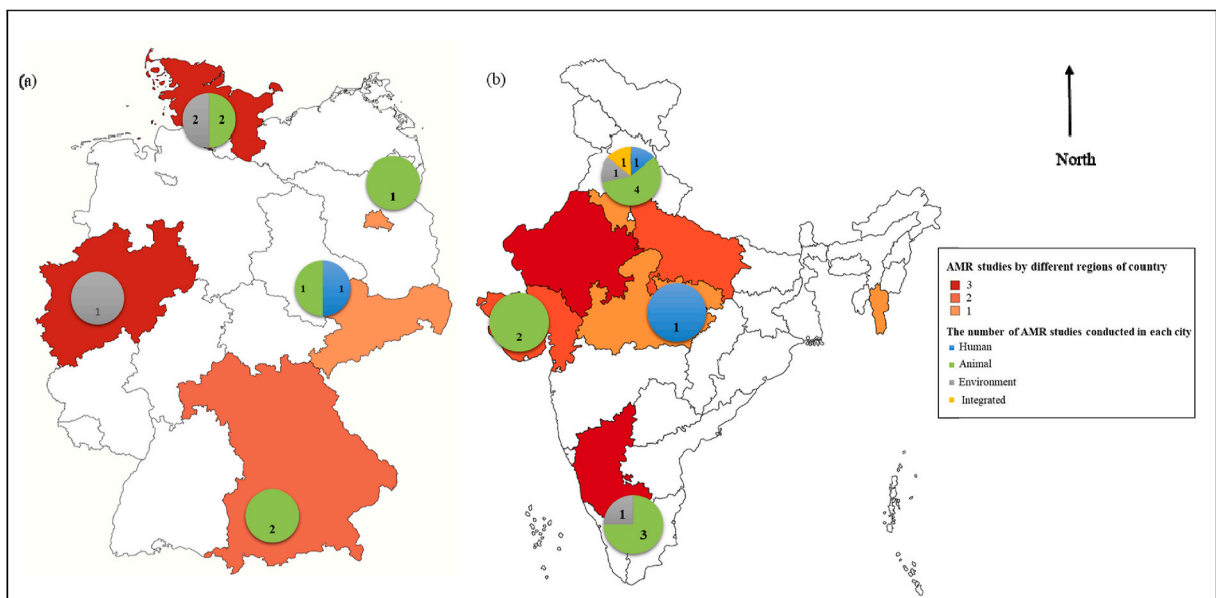


Fig. 3. The number of articles and study sites in each compartment i.e. Human, Animal and Environment. (a) Germany (b) India.

cephalosporins (26 %); in *Enterococcus*, cephalosporins (77 %); in *Staphylococcus*, quinolones (21 %) followed by other (18 %); in *Salmonella*, quinolones (20 %); in *Klebsiella*, lincosamide (16 %) followed by macrolides (16 %) and sulfonamides (16 %); *Morganella morganana*, lincosamide (18 %) followed by sulfonamide (18 %) and macrolides (18 %); *Bacilli*, β -lactam (16 %), macrolides (16 %), lincosamide (16 %), sulfonamide (16 %), other (16 %). However, in humans 3 bacteria found high resistance to antibiotics, including *Bacilli*, a quinolone (40 %) followed by Cephalosporin (38 %); in *Staphylococcus*, β -lactam (29 %) followed by tetracycline (21 %); in *Enterococcus*, tetracycline (40 %). Moreover, in the environment, only *E. coli* was highly resistant to antibiotics such as Quinolone (31 %), followed by Aminoglycosides (27 %). In addition, in integrated studies (animal and environment), only *E. coli* was found to be highly resistant to antibiotics such as β -lactam (52 %), followed by cephalosporin (25 %) (Fig. 4).

3.4.2. AMR in Germany

We analyzed 10 research on the AMR phenotypic susceptibility to 69 different antimicrobial drugs (16 antimicrobial classes) across 11 Pathogens. For clarity, we divided the studies into four categories: animals, humans, the environment, and integrated studies (animal and environment). In Animal, there are 5 bacteria found to be highly prevalent. The highest resistance showed by antibiotics in pathogens as follows: in *E. coli*, Cephalosporin (25 %) followed by β -lactam (23 %); *Listeria*, lincosamide (100 %); *Staphylococcus*, MDR (38 %) followed by β -lactam (29 %); *Enterococcus*, Cephalosporin (44 %) followed by macrolides (19 %) and other (19 %); *Salmonella*, tetracyclines (100 %). However, in humans, only *E. coli* found high resistance to antibiotics such as β -lactam (43 %) followed by Cephalosporin (23 %). Moreover, in environment 3, bacteria found high resistance to antibiotics such as including *Vibrio*, β -lactam (79 %) followed by Cephalosporin (14 %); *Klebsiella*, Cephalosporin (57 %) followed by carbapenem (16 %); *E. coli*, Aminoglycosides (25 %) followed by β -lactam (20 %) (Fig. 5).

4. Discussion

This study comprehensively reviews the prevalence of pathogens in various sectors, including humans, animals and the environment along with One Health perspective; the burden of AMR and the existence of AMR genes in India and Germany are also described. Data from 2022 were studied to establish a link between the occurrence of AMR and specific bacteria. In different sectors. Out of 532 papers, 24 met the criteria for inclusion in the meta-analysis. Our findings underscore the widespread presence of AMR in these two countries, with notable differences and similarities observed across the sectors. For example, β -lactam is the antibiotic that is most frequent in the bacteria studied. Quinolone and cephalosporin's, on the other hand, were highly resistant to the pathogens tested in humans. Furthermore, in the environment and integrated studies (which include animals and the environment), resistance to aminoglycosides and β -lactams is significant in India. While in Germany, a high rate of AMR resistance in animals, humans, and the environment was reported in β -lactam. Surprisingly, this data shows how different antibiotics interact with the food chain, and it is a serious concern if it is unchecked.

Several studies and reports have documented resistance to the β -lactam group of antibiotics, cephalosporins, and fluoroquinolones, consistent with our findings. In Germany, a 2022 surveillance report from the European Centre for Disease Prevention and Control (ECDC) [37] discusses trends in antibiotic consumption and resistance patterns, particularly focusing on beta-lactams. The report highlights a high prevalence of resistance to these antibiotics, especially among Gram-negative bacteria. Additionally, a study by Sup Lee et al. [38] identified significant resistance to third-generation cephalosporins, while L. Stelmaszyk et al. [39] reported that

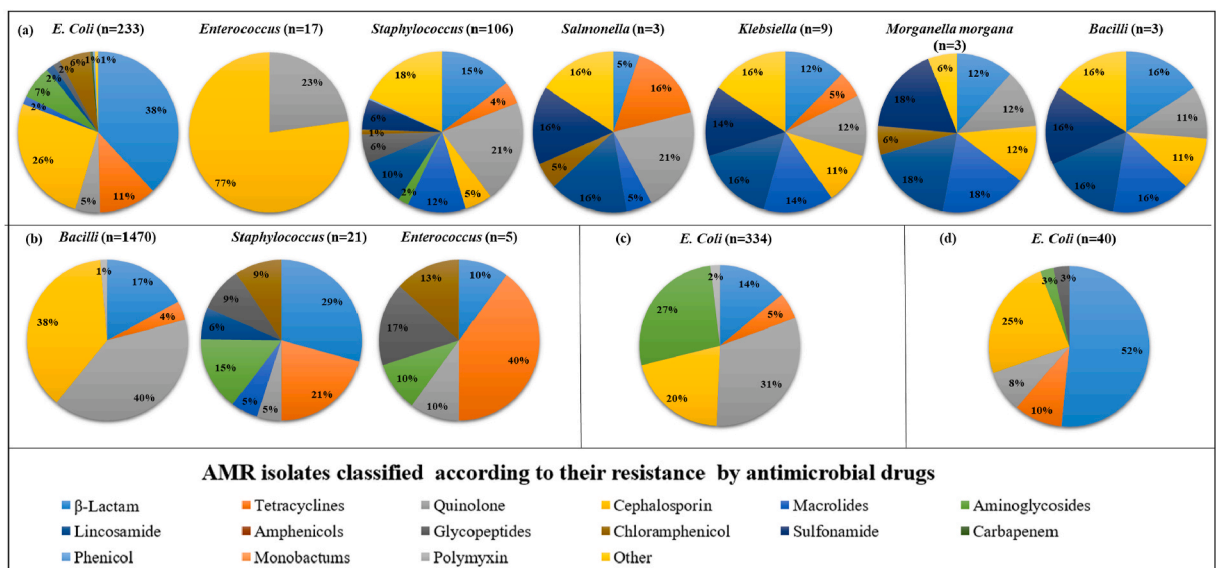


Fig. 4. AMR positive isolates in different sectors (a) Animal (b) Human (c) Environment (d) Integrated (Animal and Environment).

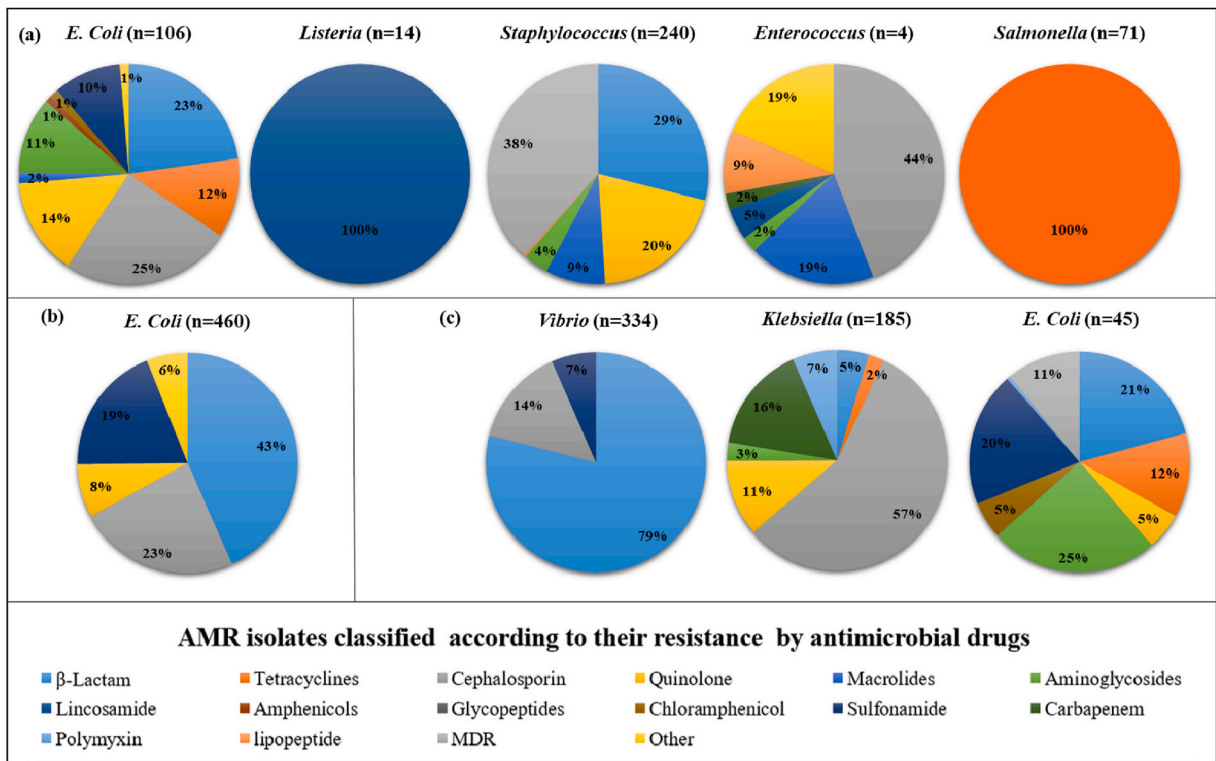


Fig. 5. AMR positive isolates in different sectors (a) Animal (b) Human (c) Environment.

oligotrophic bacteria in German surface waters exhibit a high prevalence of β-lactam resistance. Further, research by Dehbashi et al. [40] revealed that nearly half of the *P. aeruginosa* strains in Germany were Extended-Spectrum Beta-Lactamase (ESBL) producers, specifically Class A β-lactamases. Another study by Wu G. et al. [41] found that the blaCTX-M-group-1 gene, a prevalent ESBL gene, was detected in 93 % of human isolates, conferring resistance to a wide range of beta-lactam antibiotics. In India, the situation is similarly concerning. A meta-analysis by Kuralayanapalya SP et al. [42] highlights the significant public health risk posed by ESBL-producing bacteria in animals, with a pooled prevalence rate of 9 %. This prevalence varies by region, year, and animal species, indicating a considerable risk of transmission to humans through direct contact or the food chain. Charles H. Brower et al. [43] also reported a high prevalence of *Escherichia coli* resistant to nalidixic acid, ampicillin, and tetracycline, with ESBL-producing Enterobacteriaceae found in a significant percentage of broilers and layers in poultry farms. Bhargava et al. [44] similarly found widespread resistance to cephalosporins, quinolones, aminoglycosides, and beta-lactams among various isolates. Furthermore, another study highlighted that many colistin-resistant strains in India carried beta-lactamase genes, such as blaNDM-1, blaOXA-48, and blaCTX-M, which confer resistance to a broad range of beta-lactam antibiotics, including cephalosporins and carbapenems. In the study done by La Via et al. [45] showed sepsis and septic shock a major concern of AMR. Infections caused by AMR pathogens often lead to delays in effective treatment, as standard antibiotic therapies become ineffective, increasing the risk of mortality.

Implementing and establishing policies, legislation, and research to connect diverse sectors that can collaborate is part of the One Health concept [46]. If proper methods are not implemented, the incidence of microbes developing resistant to various antimicrobial agents may continue to rise, posing a global danger [47]. As a result, there is an urgent need to reduce antibiotic use in order to lower the burden of antimicrobial resistance. This can be accomplished using the One Health method, which takes into account hazards to the animal-human environment in number of different circumstances. In order to do that along with Global Action Plan (GAP) on AMR, India and Germany have launched several one-health strategies besides NAP. In India National Centre for Disease Control (NCDC), New Delhi is the focal point for implementing and coordinating the AMR program. (1) In April 2017, the Indian Ministry of Health and Family Welfare released the NAP to Combat AMR [48]. The 12th Five-Year Plan (2012–17) is still in effect as the "National One Health Program for Zoonosis Prevention and Control" during the 15th Finance Commission (2021–26) term, Antimicrobial Resistance Surveillance & Research Network (AMRSN) established by the Indian Council of Medical Research (ICMR) [49] started with six reference labs located in four tertiary care medical institutions, Infection prevention and control (IPC) programs [50]. On the other hand in Germany, German Antimicrobial Resistance Strategy (DART) 2020 [51], Antibiotic Resistance Dynamics: the influence of geographic origin and management (ARDIG) [43–48], European Antimicrobial Resistance Surveillance Network (EARS-Net) and Global Antimicrobial Resistance Surveillance System (GLASS).

While this study provides valuable insights into AMR in India and Germany, several limitations are present. First, the potential for publication bias exists, as the meta-analysis included only published studies, which may overrepresent positive findings and

underreport negative or null results. This bias could affect the overall conclusions drawn from the analysis. Second, the reliance on data exclusively from 2022 limits the study's ability to capture long-term trends in AMR. The lack of recent data also means that emerging resistance patterns or the effectiveness of recent interventions may not be fully represented. Third, the study faced considerable heterogeneity due to the inclusion of studies from diverse geographic locations within India and Germany and across various sample types, including humans, animals, and environmental sources. This heterogeneity complicates the comparison of findings across studies and may reduce the generalizability of the results. Future research should aim to address these limitations by incorporating a broader range of data, including more recent studies, and by employing methods to reduce or account for heterogeneity in the analysis.

5. Conclusion

Our investigations have provided some data on the burden of AMR, which should be useful as a baseline for ongoing research into the development and transmission processes of AMR bacteria in all three compartments of humans, animals, and the environment in India and Germany in 2022. Given the significant frequency of resistance to the most vital antimicrobials, we suggest limiting their usage, particularly in Animals. A wide range of pathogens are involved, and resistance to important medicines, including beta-lactams and quinolones, is widespread. Finding strategies that can effectively lessen the burden of bacterial AMR is a top priority, whether they are applied in various settings or are precisely tailored to the resources available and the most effective pathogen-drug combinations in a given environment. The findings from this study underscore the importance of integrating the One Health approach in tackling AMR, as the interconnectedness of humans, animals, and the environment plays a crucial role in the spread and persistence of resistant bacteria. The data suggests that unchecked AMR could severely impact public health by limiting the effectiveness of essential antibiotics, leading to more difficult-to-treat infections, longer hospital stays, and increased mortality. It also emphasizes the need for robust public health strategies, including improved surveillance, stricter antibiotic stewardship, and enhanced infection control measures across all sectors. These efforts are vital to curbing the spread of AMR and safeguarding the effectiveness of antibiotics for future generations. Hence, in the future, broader adoption of One Health techniques will bring together various disciplines and data sources, resulting in considerably deeper insights. Multiple scales and levels under the One Health approach to tackle the AMR problem.

Availability of data and material

Data will be made available on request.

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CRediT authorship contribution statement

Gunjan K: Writing – review & editing, Writing – original draft, Visualization, Data curation. **Ramendra Pati Pandey:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision. **Himanshu:** Writing – review & editing, Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Kirtanjot Kaur:** Writing – review & editing, Visualization, Validation, Resources. **Saheem Ahmad:** Writing – review & editing, Visualization, Validation, Data curation, Conceptualization. **Riya Mukherjee:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Chung-Ming Chang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The author declares no conflict of interest, financial or otherwise.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e37910>.

References

- [1] K.L. Tang, N.P. Caffrey, D.B. Nóbrega, S.C. Cork, P.E. Ronksley, H.W. Barkema, A.J. Polachek, H. Ganshorn, N. Sharma, J.D. Kellner, W.A. Ghali, Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis, *Lancet Planet. Health* 1 (2017) e316–e327, [https://doi.org/10.1016/S2542-5196\(17\)30141-9](https://doi.org/10.1016/S2542-5196(17)30141-9).
- [2] S. Gross, A. Müller, D. Seinige, P. Wohlsein, M. Oliveira, D. Steinhagen, C. Kehrenberg, U. Siebert, Occurrence of antimicrobial-resistant *Escherichia coli* in marine mammals of the north and Baltic Seas: Sentinels for human health, *Antibiotics* 11 (2022) 1–23, <https://doi.org/10.3390/antibiotics11091248>.

- [3] A. Pormohammad, M.J. Nasiri, T. Azimi, Prevalence of antibiotic resistance in escherichia coli strains simultaneously isolated from humans, animals, food, and the environment: a systematic review and meta-analysis, *Infect. Drug Resist.* 12 (2019) 1181–1197, <https://doi.org/10.2147/IDR.S201324>.
- [4] M. Huemer, S. Mairpady Shambhat, S.D. Brugger, A.S. Zinkernagel, Antibiotic resistance and persistence—implications for human health and treatment perspectives, *EMBO Rep.* 21 (2020), <https://doi.org/10.15252/EMBR.202051034/ASSET/SCCE3AEC-A048-400B-BBEC-5D160A68172A/ASSETS/GRAPHIC/EMBR202051034-FIG-0005-M.PNG>.
- [5] T.F. Landers, B. Cohen, T.E. Wittum, E.L. Larson, A review of antibiotic use in food animals: perspective, policy, and potential, *Publ. Health Rep.* 127 (2012) 4, <https://doi.org/10.1177/003335491212700103>.
- [6] R. Dahal, A. Upadhyay, B. Ewald, One Health in South Asia and its challenges in implementation from stakeholder perspective, *Vet. Rec.* 181 (2017) 626, <https://doi.org/10.1136/VR.104189>, 626.
- [7] T. Jinks, N. Lee, M. Sharland, J. Rex, N. Gertler, M. Diver, I. Jones, K. Jones, S. Mathewson, F. Chiara, J. Farrar, A time for action: antimicrobial resistance needs global response, *Bull. World Health Organ.* 94 (2016) 558, <https://doi.org/10.2471/BLT.16.181743>.
- [8] The review on antimicrobial resistance, Tackling drug-resistant infections globally: final report and recommendations, UK, https://amr-review.org/sites/default/files/160518_Finalpaper_withcover.pdf, 2016.
- [9] M.E.A. de Kraker, A.J. Stewardson, S. Harbarth, Will 10 million people die a year due to antimicrobial resistance by 2050? *PLoS Med.* 13 (2016) e1002184 <https://doi.org/10.1371/JOURNAL.PMED.1002184>.
- [10] A. Cassini, L.D. Högberg, D. Plachouras, A. Quattrocchi, A. Hoxha, G.S. Simonsen, M. Colomb-Cotinat, M.E. Kretzschmar, B. Devleeschauwer, M. Cecchini, D. A. Ouakrim, T.C. Oliveira, M.J. Struelens, C. Suetens, D.L. Monnet, R. Strauss, K. Mertens, T. Struyf, B. Catry, K. Latour, I.N. Ivanov, E.G. Dobreva, A. Tambic Andrašević, S. Soprek, A. Budimir, N. Paphitou, H. Zemlicková, S. Schytte Olsen, U. Wolff Sönksen, P. Märtin, M. Ivanova, O. Lyytikäinen, J. Jalava, B. Coignard, T. Eckmanns, M. Abu Sin, S. Haller, G.L. Daikos, A. Gikas, S. Tsiodras, F. Kontopidou, A. Tóth, A. Hajdu, O. Guólaugsson, K.G. Kristinsson, S. Murchan, K. Burns, P. Pezzotti, C. Gagliotti, U. Dumpis, A. Liiumiemi, M. Perrin, M.A. Borg, S.C. de Greeff, J.C. Monen, M.B. Koek, P. Elström, D. Zabička, A. Deptula, W. Hryniewicz, M. Caniça, P.J. Nogueira, P.A. Fernandes, V. Manageiro, G.A. Popescu, R.I. Serban, E. Schréterová, S. Litvová, M. Štefkovicová, J. Kolman, I. Klavs, A. Korosec, B. Aracil, A. Asensio, M. Pérez-Vázquez, H. Billström, S. Larsson, J.S. Reilly, A. Johnson, S. Hopkins, Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis, *Lancet Infect. Dis.* 19 (2019) 56–66, [https://doi.org/10.1016/S1473-3099\(18\)30605-4](https://doi.org/10.1016/S1473-3099(18)30605-4).
- [11] F. Prestinaci, P. Pezzotti, A. Pantosti, Antimicrobial resistance: a global multifaceted phenomenon, *Pathog. Glob. Health* 109 (2015) 309–318, <https://doi.org/10.1179/2047773215Y.0000000030>.
- [12] Antimicrobial Resistance Threats Report, CDC, 2019. <https://www.cdc.gov/drugresistance/biggest-threats.html>.
- [13] Antimicrobial resistance, <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.
- [14] J.D. Harris, C.E. Quatman, M.M. Manning, R.A. Siston, D.C. Flanigan, How to write a systematic review, *Am. J. Sports Med.* 42 (2014) 2761–2768, <https://doi.org/10.1177/0363546513497567>.
- [15] Risk of bias tools - robvis (visualization tool), <https://www.riskofbias.info/welcome/robvis-visualization-tool>.
- [16] S.P. Ronanki, P. Ramya, A.J. Babu, B. Sreedevi, Multidrug resistant- *Proteus mirabilis* and *Proteus vulgaris* isolated from milk and meat samples in Tirupati, Andhra Pradesh : An emerging public health threat 11 (2022) 1427–1434.
- [17] Microbiological Contamination of Retail Meat from Mizoram (India) with Special Reference to Molecular Detection and Multi-Drug Resistance of *Escherichia coli*, 2022, pp. 16–19.
- [18] F. Amreen, Quarantine and Antibiotic Susceptibility of Enterobacteriaceae Strains and Other Gram Negative Bacteria in Dairy Sweetmeat Milk (Doodh) Peda, vols. 1–17, 2022.
- [19] I. Charles, A. Boniface, ANTI-MICROBIAL RESISTANCE PROFILE OF *Escherichia coli* ISOLATES, vol. 2, 2005, pp. 322–328.
- [20] N.M. Patel, R. Kumar, C.V. Savalia, I.H. Kalyani, J.B. Solanki, Public Health risk of antibiotic resistant phenotypes and molecular confirmation of *Staphylococcus aureus* isolated from bovine raw milk of South Gujarat, India 11 (2022) 327–334.
- [21] B.R. Singh, R. Karthikeyan, D. K Sinha, V. Or, V. Jaykumar, A. Yadav, H. Agri, Potentially pathogenic bacteria in water bodies and drinking water supplies in and around Bareilly, India, *Acta Sci. Microbiol* 113–126 (2022), <https://doi.org/10.31080/asmi.2022.05.1139>.
- [22] D. Desai, S. Rajkumar, Isolation and characterization of ESBL producing *Escherichia coli* from healthy goats and from their environment in west coastal. <https://doi.org/10.5958/0973-9718.2023.00010.7>, 2023.
- [23] J.B. Moktan, R. Venkataraman, Y. Shrestha, The prevalence of multidrug-resistant bacteria detected in poultry products in Mandya, India, *Arch. Pharm. Pract.* 14 (2023) 35–39, <https://doi.org/10.51847/uwgyw11wyg>.
- [24] J. Ahamad Khan, R.S. Rathore, I. Ahmad, R. Gill, F.M. Husain, J. Akhtar, High prevalence of multidrug resistant *Staphylococcus aureus* from Buffalo beef sold at retail butcheries in Northern India, *Acta Sci. Microbiol* (2022) 12–21, <https://doi.org/10.31080/asmi.2022.05.1146>.
- [25] K. Panwar, T. Bhati, S. Ritod, B.N. Shringi, Detection of antibiotic resistance in *Escherichia coli* isolates from Egyptian vultures from arid regions of India, *Environ. Conserv.* J. 23 (2022) 65–71, <https://doi.org/10.36953/ecj.021800-2115>.
- [26] K. Grakh, D. Mittal, A. Prakash, N. Jindal, Characterization and antimicrobial susceptibility of biofilm-producing Avian Pathogenic *Escherichia coli* from broiler chickens and their environment in India, *Vet. Res. Commun.* 46 (2022) 537–548, <https://doi.org/10.1007/s11259-021-09881-5>.
- [27] M. Sharma, M.R. Qurashi, S. Sharma, Phenotypic and genotypic characterizations of antimicrobial resistance among gram-negative bacilli of clinical isolates, *Microb. Biosyst.* 7 (2022) 1–8, <https://doi.org/10.21608/mb.2022.153994.1062>.
- [28] G.K. Sivaraman, A. Vijayan, S. Visnuvinayagam, T. Muthulakshmi, M.M. Prasad, C.N. Ravishankar, Incidence of multi drug resistant coagulase-negative *Staphylococci* from seafood samples, Veraval, Gujarat, Indian J. Anim. Health (2022), <https://doi.org/10.36062/ijah.2022.14621>.
- [29] M. Savin, G. Bierbaum, N.T. Mutters, R.M. Schmithausen, J. Kreyenschmidt, I. García-Meniño, S. Schmogger, A. Käsbohrer, J.A. Hammerl, Genetic characterization of carbapenem-resistant *Klebsiella* spp. from municipal and slaughterhouse wastewater, *Antibiotics* 11 (2022) 1–14, <https://doi.org/10.3390/antibiotics11040435>.
- [30] S. Fleischmann, I. Herrig, J. Wesp, J. Stiedl, G. Reifferscheid, E. Strauch, T. Alter, N. Brennholt, Prevalence and distribution of potentially human pathogenic *Vibrio* spp. on German north and Baltic Sea Coasts, *Front. Cell. Infect. Microbiol.* 12 (2022) 1–15, <https://doi.org/10.3389/fcimb.2022.846819>.
- [31] B. González-Santamarina, C. Schnee, H. Köhler, M. Weber, U. Methner, C. Seyboldt, C. Berens, C. Menge, Survey on shedding of selected pathogenic, zoonotic or antimicrobial resistant bacteria by South American camels in Central Germany, *Berl. Münchener Tierärztliche Wochenschr.* 135 (2022), <https://doi.org/10.2376/1439-0299-2021-21>.
- [32] M. Soundararajan, G. Marincola, O. Liang, T. Marciniak, F.D.R. Wencker, F. Hofmann, H. Schollenbruch, I. Kobusch, S. Linnemann, S.A. Wolf, M. Helal, T. Semmler, B. Walther, C. Schoen, G. Nyasinga, G. Revathi, M. Boelhaue, W. Ziebuhr, Farming practice influences antimicrobial resistance burden of non-aureus staphylococci in pig husbandries, *Microorganisms* 11 (2022) 31, <https://doi.org/10.3390/microorganisms11010031>.
- [33] M. Kresken, Y. Pfeifer, F. Wagenlehner, G. Werner, E. Wohlfarth, Resistance to Mecillinam and nine other antibiotics for oral use in *Escherichia coli* isolated from urine specimens of primary care patients in Germany, 2019/20, *Antibiotics* 11 (2022), <https://doi.org/10.3390/antibiotics11060751>.
- [34] C. Klose, N. Scuda, T. Ziegler, D. Eisenberger, M. Hanczaruk, J.M. Riehm, Whole-genome investigation of *Salmonella* Dublin considering mountain pastures as reservoirs in Southern Bavaria, Germany, *Microorganisms* 10 (2022), <https://doi.org/10.3390/microorganisms10050885>.
- [35] V. Oswaldi, S. Lüth, J. Dzierzon, D. Meemken, S. Schwarz, A.T. Feßler, B. Félix, S. Langforth, Distribution and characteristics of *Listeria* spp. in pigs and pork production chains in Germany, *Microorganisms* 10 (2022), <https://doi.org/10.3390/microorganisms10030512>.
- [36] G.M. Quality, P. Beindorf, O. Kovalenko, S. Ulrich, H. Geißler, R. Korbel, K. Schwaiger, S. Dorn-in, I. Esteban-cuesta, Resistance, 2022.
- [37] Ecde: Antimicrobial Consumption in the EU/EEA (ESAC-NET) - AER for 2022.
- [38] D.S. Lee, S.J. Lee, H.S. Choe, D.R. Giacobbe, Community-acquired urinary tract infection by *Escherichia coli* in the era of antibiotic resistance, *BioMed Res. Int.* 2018 (2018) 7656752, <https://doi.org/10.1155/2018/7656752>.
- [39] L. Stelmazyk, C. Stange, M. Hügl, J.P.S. Sidhu, H. Horn, A. Tiehm, Quantification of β -lactamase producing bacteria in German surface waters with subsequent MALDI-TOF MS-based identification and β -lactamase activity assay, *Heliyon* 10 (2024) e27384, <https://doi.org/10.1016/J.HELIYON.2024.E27384>.

- [40] S. Dehbashi, H. Tahmasebi, M.Y. Alikhani, F. Keramat, M.R. Arabestani, Distribution of class b and class β -lactamases in clinical strains of pseudomonas aeruginosa: comparison of phenotypic methods and high-resolution melting analysis (HRMA) assay, *Infect. Drug Resist.* 13 (2020) 2037–2052, <https://doi.org/10.2147/IDR.S255292>.
- [41] G. Wu, M.J. Day, M.T. Mafura, J. Nunez-Garcia, J.J. Fenner, M. Sharma, A. van Essen-Zandbergen, I. Rodríguez, C. Dierikx, K. Kadlec, A.K. Schink, J. Wain, R. Helmuth, B. Guerra, S. Schwarz, J. Threlfall, M.J. Woodward, N. Woodford, N. Coldham, D. Mevius, Comparative analysis of ESBL-positive Escherichia coli isolates from animals and humans from the UK, The Netherlands and Germany, *PLoS One* 8 (2013) e75392, <https://doi.org/10.1371/JOURNAL.PONE.0075392>.
- [42] S.P. Kuralayanapalya, S.S. Patil, S. Hamsapriya, R. Shinduja, P. Roy, R.G. Amachawadi Id, Prevalence of extended-spectrum beta-lactamase producing bacteria from animal origin: a systematic review and meta-analysis report from India. <https://doi.org/10.1371/journal.pone.0221771>, 2013.
- [43] Brower, C.H., Mandal, S., Hayer, S., Sran, M., Zehra, A., Patel, S.J., Kaur, R., Chatterjee, L., Mishra, S., Das, B.R., Singh, P., Singh, R., Gill, J.P.S., Laxminarayan, R.: The Prevalence of Extended-Spectrum Beta-Lactamase-Producing Multidrug-Resistant Escherichia Coli in Poultry Chickens and Variation According to Farming Practices in Punjab, India. <https://doi.org/10.1289/EHP292>.
- [44] O.L. Franco, G. Dhungana, A. Sultan, N. Jain, G. Nath, K. Bhargava, A. Bhargava, R. Kumari, G.K. Aseri, OPEN ACCESS EDITED BY Bacterial profile and antibiotic susceptibility pattern of uropathogens causing urinary tract infection in the eastern part of Northern India. <https://doi.org/10.3389/fmicb.2022.965053>, 2022.
- [45] L. La Via, G. Sangiorgio, S. Stefani, A. Marino, G. Nunnari, S. Cocuzza, I. La Mantia, B. Cacopardo, S. Stracquadanio, S. Spampinato, S. Lavalle, A. Maniaci, The global burden of sepsis and septic shock, *Epidemiology* 5 (2024) 456–478, <https://doi.org/10.3390/EPIDEMIOLOGIA5030032>, 2024, Vol. 5, Pages 456-478.
- [46] Gunjan, J. Vidic, M. Manzano, V.S. Raj, R.P. Pandey, C.M. Chang, Comparative meta-analysis of antimicrobial resistance from different food sources along with one health approach in Italy and Thailand, *One Heal* 16 (2023) 100477, <https://doi.org/10.1016/J.ONEHLT.2022.100477>.
- [47] C.J.H. Von Wintersdorff, J. Penders, J.M. Van Niekerk, N.D. Mills, S. Majumder, L.B. Van Alphen, P.H.M. Savelkoul, P.F.G. Wolfs, Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer, *Front. Microbiol.* 7 (2016) 173, <https://doi.org/10.3389/FMICB.2016.00173/BIBTEX>.
- [48] India: National action plan on antimicrobial resistance (NAP-AMR) 2017 – 2021, [https://www.who.int/publications/m/item/india-national-action-plan-on-antimicrobial-resistance-\(nap-amr\)-2017-2021](https://www.who.int/publications/m/item/india-national-action-plan-on-antimicrobial-resistance-(nap-amr)-2017-2021).
- [49] AMRSN, <https://iamrsn.icmr.org.in/index.php/amrsn/amrsn>.
- [50] National Guidelines for Infection Prevention and Control in Healthcare Facilities, MoHFW 2020 Training Modules: National Centre for Disease Control (NCDC), <https://ncdc.gov.in/index1.php?lang=1&level=2&sublinkid=1019&lid=794>.
- [51] BMEL - Animal health - "DART 2020" continues the German Antibiotic Resistance Strategy, <https://www.bmel.de/EN/topics/animals/animal-health/DART2020.html>.