



Review article

Epidemiology and antimicrobial resistance of *Campylobacter* spp. in animals in Sub-Saharan Africa: A systematic reviewDelfina Fernandes Hlashway^{a,b,*}, Betuel Sigaúque^c, Custódio Gabriel Bila^b^a Department of Biological Sciences, Faculty of Sciences, Eduardo Mondlane University, Maputo, Mozambique^b Faculty of Veterinary Science, Eduardo Mondlane University, Maputo, Mozambique^c Centro de Investigação em Saúde de Manhiça, Maputo, Mozambique

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ABSTRACT

Introduction: Low sanitary conditions characterize the rural and urban households in Sub-Saharan African region. Those environmental conditions propitiate the transmission of bacterial infections between animals and humans. *Campylobacter* spp. is a zoonotic bacterium and cause of human gastroenteritis worldwide, whose main symptom is diarrhea. It is normally found in the digestive tract of many farm animals as a commensal but some species cause diseases in animals. It is important to understand the occurrence of these bacteria in animals, as they may also play a role in transmission to humans. The main objective of this review was to describe the prevalence of *Campylobacter* in animals in Sub-Saharan Africa. We also report findings on antibiotic resistance.

Methods: We followed PRISMA guidelines to find studies about occurrence of *Campylobacter* spp. in animals in all countries from Sub-Saharan Africa. PubMed, Cochrane Library, CINAHL, African Index Medicus, African Journals Online, Google Scholar and Science Direct were searched for studies published between 2000 and 2019.

Results: We found 70 studies that described occurrence of *Campylobacter* spp. in animals in 18 out of 53 countries of Sub-Saharan Africa. *Campylobacter jejuni* and *C. coli* were the predominant species isolated. The majority of studies were found in Western Africa. Middle Africa had the lowest amount of data. Most records presented data from Nigeria (n = 25), South Africa (n = 14) and Tanzania (n = 11). Cattle and chickens appear to be important hosts and may be playing an important role in transmitting to humans. Most *Campylobacter* isolates were resistant to erythromycin (44%), ampicillin (39%), tetracycline (33%), nalidixic acid (31%) and ciprofloxacin (30%).

Conclusion: Several studies about *Campylobacter* spp. in animals have been published in the last 19 years but information on the epidemiology of campylobacteriosis is scarce in most Sub-Saharan African countries. Antibiotic resistance is an increasing concern in many countries. Measures should be taken to prevent infection by this pathogen in the region and to control antibiotic resistance.

1. Introduction

The genus *Campylobacter* is a group of zoonotic bacteria that cause diseases in animals and humans, although some are commensal in the intestinal tract of birds and ruminants (Sahin et al., 2017).

The genus has currently 39 species and 16 subspecies (<http://www.bacterio.net/campylobacter.html>, accessed 21.10.2019).

Campylobacter was described first in 1886 from stools of children who suffered diarrhea. At that time, it was reported in other studies and was associated with causes of enteric diseases. From 1913, the pathogen was isolated from aborted bovine fetuses, cows and calves with intestinal disorders and from swine with dysentery. From the 1970s *Campylobacter*

species were also recognized as human pathogens (García-Sánchez, Melero, and Rovira, 2018).

The most common *Campylobacter* species are *C. jejuni* and *C. coli*, which are associated with diarrheal disease in humans (García-Sánchez et al., 2018). This bacterium is also reported to cause enteritis, mainly characterized by diarrhea in many animals such as chicken (Humphrey et al., 2014), sheep (Pintar et al., 2015; Sahin et al., 2017), dogs, cats, goats, equids and pigs (Kaakoush et al., 2015; Pintar et al., 2015).

C. fetus subsp. *fetus* is a cause of reproductive failures in ruminants. In cattle, *C. fetus* subsp. *venerealis* causes bovine genital campylobacteriosis, a sexually transmitted infection that is characterized by early embryonic deaths and abortion (Sahin et al., 2017).

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Most human infections are due to consumption of poultry meat and poultry meat derived products, but also direct contact with animals (Berthenet et al., 2019; Cheng and Fischer, 2018; Kaakoush et al., 2015; Nichols et al., 2012; Sheppard et al., 2009; Sheppard, et al., 2014b; Thépault et al., 2017, 2018). Most countries from Sub-Saharan Africa are characterized by poor hygiene and sanitation (Osbyer et al., 2016). Moreover, the contact with animals or derived products contributes to the spread of this pathogen among animals and to human exposure.

It is important to know in which other animals besides poultry and cattle there are reports of the occurrence of *Campylobacter* in Sub-Saharan Africa, as well as the outcomes. It is equally important to know if exposure to these carrier animals constitutes a risk to humans.

Understanding the distribution of *Campylobacter* in animals in Sub-Saharan Africa is important in order to reduce morbidity and mortality associated with diarrheal disease. This is of particular interest in low and middle income countries where the epidemiology of this bacteria is poorly understood.

Incidence and prevalence of *Campylobacter* are thought to be increasing globally (Connerton and Connerton, 2017; Kaakoush et al., 2015), but an extensive overview of its distribution and epidemiology in animals in Sub-Saharan Africa is not available. The available animal systematic reviews are restricted to one country (Komba et al., 2013), to a single *Campylobacter* species (Pike et al., 2013; Wilkinson et al., 2018), or to household pets (Pintar et al., 2015). Moreover, it is known that different *C. jejuni* strains are found in multiple animal species (Sheppard et al., 2010, 2011; Sheppard, et al., 2014a).

This review provides an extensive and systematic overview of the epidemiology of *Campylobacter* spp. in animals in Sub-Saharan Africa from 2000 to 2019. To our knowledge, this is the first study of this magnitude that addresses such topic in Sub-Saharan Africa in the last 19 years. We report on the study site, *Campylobacter* prevalence, identified species, infected animals, diagnostic method and samples analyzed. We also discuss about antibiotic resistance findings due to the increasing reports of such occurrence (Sproston et al., 2018).

2. Materials and methods

2.1. Identifying research evidence

We followed Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines to find data about animal *Campylobacter* infection available from all countries of Sub-Saharan Africa. We used the UN macro-geographical definition of Africa to define the geographical boundaries of this review (<https://unstats.un.org/unsd/methodology/m49/>). According to this UN definition, the Sub-Saharan Africa is divided into Eastern Africa, Middle Africa, Southern Africa and West Africa, as described below:

- **Eastern Africa:** British Indian Ocean Territory, Burundi, Comoros, Djibouti, Eritrea, Ethiopia, French Southern Territories, Kenya, Madagascar, Malawi, Mauritius, Mayotte, Mozambique, Réunion, Rwanda, Seychelles, Somalia, South Sudan, Uganda, United Republic of Tanzania, Zambia and Zimbabwe.
- **Middle Africa:** Angola, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon and Sao Tome and Principe.
- **Southern Africa:** Botswana, Eswatini (former Swaziland), Lesotho, Namibia and South Africa.
- **Western Africa:** Benin, Burkina Faso, Cabo Verde, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Saint Helena, Senegal, Sierra Leone and Togo.

PubMed, Cochrane Library, CINAHL, African Index Medicus, African Journals Online, Google Scholar and Science Direct were searched for studies published up to October 8, 2019 without language restrictions.

The systematic review protocol is in **Supplementary material 1** and the search strategy in **Supplementary material 2**. **Supplementary material 3** presents the PRISMA checklist.

Selection criteria for inclusion of studies were:

- The study population consisted of any group of animals in Sub-Saharan Africa, which had been tested for *Campylobacter* spp.,
- Descriptive, cross-sectional studies, prospective, or retrospective studies and case reports and series in which the prevalence rate of *Campylobacter* in any country in Sub-Saharan Africa was reported;
- Conference abstracts; and
- Only studies published from 2000 onwards.

The primary outcome was estimation of the prevalence of *Campylobacter* in animals from countries in Sub-Saharan Africa. The secondary outcome was to identify the antibiotics to which the different *Campylobacter* isolates were resistant.

2.2. Data extraction (selection and coding)

Titles and abstracts were screened for location, study population and general correlation with the research objectives. Full versions of potentially relevant articles were obtained to assess eligibility. These were then independently evaluated for inclusion. Cross-references of the full text retrieved articles were also searched. Data were collected independently from each publication and captured using a standardised Word document form. We extracted data from text, tables and figures.

2.3. Data analysis

In reports where the numerator and denominator of the study sample were available, prevalence data were calculated, if not already provided. When not presented in the manuscript, the 95% exact confidence intervals (CI) were calculated, using the "binom.test" function ("stats" package) in R 3.5.1.

3. Results and discussion

3.1. Search results

A total of 980 records were obtained from the database search (see Figure 1). One article was obtained through a previous search on <https://www.google.com/>. After removal of duplicate records (n = 229), 752 records were screened based on title and, thereafter, abstract. Thus, 100 records fulfilled the eligibility criteria for evaluation and 30 were excluded. All records were published in English.

From the 70 animal studies (Aboaba and Smith, 2005; Abubakar et al., 2019; Achá et al., 2004; Akwuobu et al., 2010; Bartkowiak-Higgo et al., 2006; Basardien, 2012; Bernadette et al., 2012; Bester and Essack, 2008, 2012; Cardinale et al., 2003, 2004; 2002; Chuma et al., 2016; Conan et al., 2017; Ewnetu and Muhret, 2010; Garin et al., 2012; Gwimi et al., 2015; Henry et al., 2011; Jonker and Picard, 2012; Julien et al., 2013; Kagambèga et al., 2018; Kalema-Zikusoka and Rothman, 2005; Kambuyi, 2018; Karama et al., 2019; Karikari et al., 2017b; Karshima et al., 2016; Karshima and Bobbo, 2016; Kashoma et al., 2015a, b; Kassa et al., 2007; Kaur et al., 2011; Komba et al., 2014; Kusiluka et al., 2005; Madoroba et al., 2011; Mai et al., 2013b, 2013a; Mai et al., 2015; Mdegela et al., 2006, 2011; Mokantla et al., 2004; Mpalang et al., 2014; Mshelia et al., 2010, 2012; Ngotho et al., 2006; Ngulukun et al., 2010, 2011; Nizeyi et al., 2001; Njiro et al., 2012; Nonga and Muhairwa, 2009; Nonga et al., 2009; Nwankwo et al., 2016; Ofukwu et al., 2008; Ogbor et al., 2019; Okunlade et al., 2015; Olabode et al., 2017; Raji et al., 2000; Salihu et al., 2008, 2010; 2012; Salihu, et al., 2009a, b, c; Swai et al., 2005; Uaboi-Egbenni et al., 2008, 2010; 2011a, 2011b; 2012; Villers et al., 2008; Woldemariam et al., 2009), 67 were articles, 1 conference abstract and 2 Master of

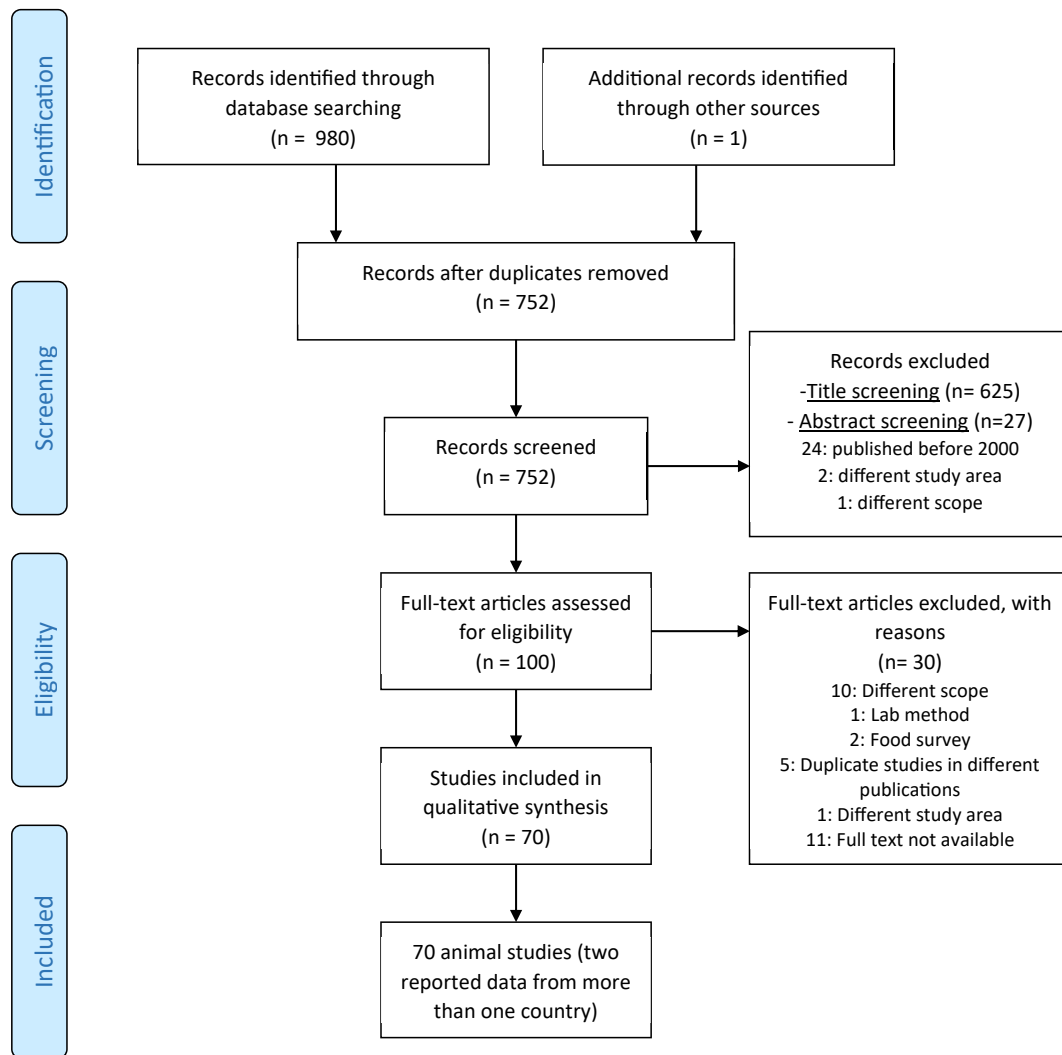


Figure 1. PRISMA flow diagram of study selection.

Science theses. In 2 of the 70 included animal studies, prevalence of *Campylobacter* was reported in more than one country. One of these reported data from Senegal, Cameroon and Madagascar (Garin et al., 2012). The other reported data from South Africa, Namibia, Zambia and Eswatini (Madoroba et al., 2011). That is why in Table 1 data are reported from 75 studies.

The studies included in this review were originated from 18 of 53 Sub Saharan African countries (Figure 2): Burkina Faso, Cameroon, Côte d'Ivoire, Democratic Republic of Congo, Eswatini, Ethiopia, Ghana, Kenya, Madagascar, Mozambique, Namibia, Nigeria, Réunion, Senegal, South Africa, Tanzania, Uganda and Zambia.

The majority of records were from Nigeria (n = 25), South Africa (n = 14) and Tanzania (n = 11).

Table 2 summarizes the information about the *Campylobacter* species, prevalence in different regions, studied animals, samples, locations and resistance to antibiotics. Additionally, Supplementary material 4 provides detailed information about surveys of *Campylobacter* in animals from this region.

3.2. General characteristics of studies (setting and methodology)

The included studies presented data that were collected from 1994 to 2017. Sixteen studies were recorded in the past 10 years. Twenty-one studies did not report about data collection time frame. Thirty studies were conducted in farms, nineteen in slaughterhouses or abattoirs, and the remaining ones in retail shops, markets, households, veterinary

Table 1. Overview of the studies included in the review.

Countries	Sub-Saharan Africa region	Number of studies	Percentage (%)
Tanzania (11), Ethiopia (3), Madagascar (2), Kenya (3), Uganda (2), Mozambique (1), Réunion (1) and Zambia (1)	Eastern Africa	24	32.0
Cameroon (1) and Democratic Republic of the Congo (1)	Middle Africa	2	2.7
South Africa (14), Namibia (1) and Eswatini (1)	Southern Africa	16	21.3
Nigeria (25), Senegal (4), Burkina Faso (1), Côte d'Ivoire (2) and Ghana (1)	Western Africa	33	44.0
	Total	75	100.0

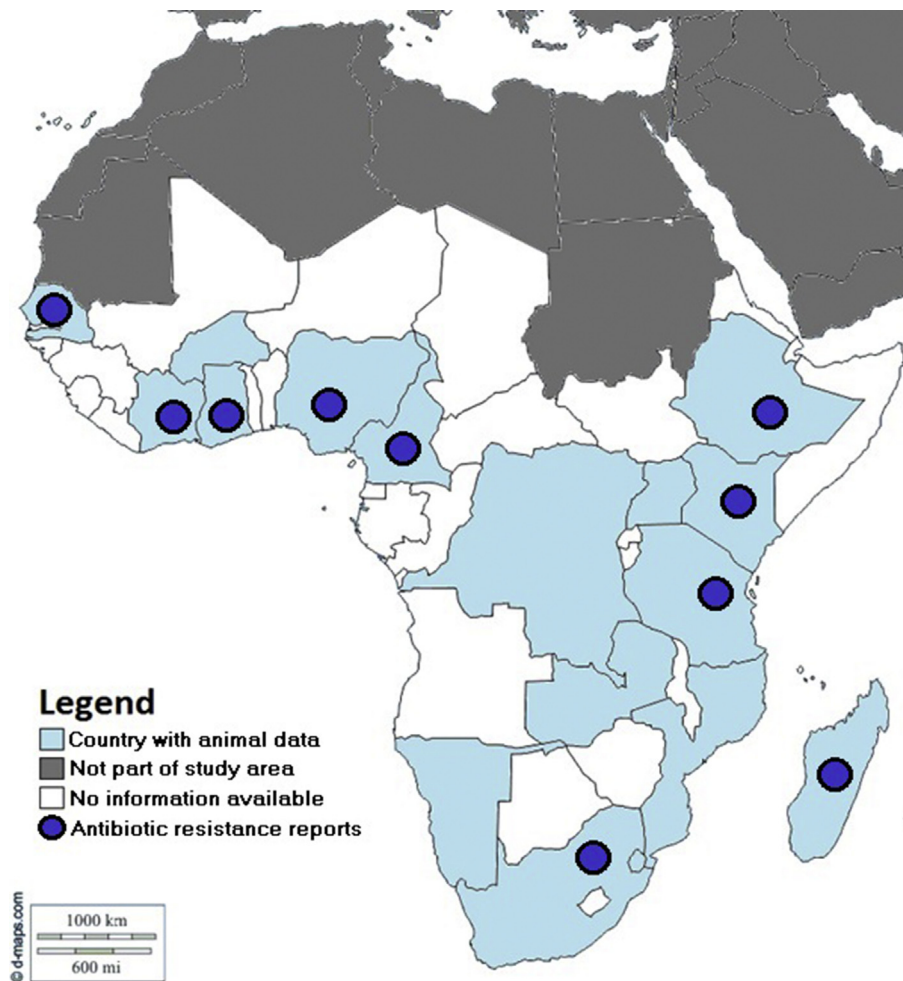


Figure 2. Map with distribution of animal *Campylobacter* spp. studies published from Sub-Saharan Africa from 2000 to 2019.

clinics, wild, national parks, reserves, urban or rural areas and some included records from laboratory. Seventy studies were cross-sectional, four retrospective and one longitudinal.

Cattle and chickens were the most studied animals. Other animals were camels, cats, goats, quails, horses, guinea fowls, guinea pigs, dogs, pigs, mountain gorillas, ring-tailed lemurs, sheep, rabbits, rats, mice, grass-cutter, wild chimpanzees, monkeys, crows, donkeys, pigeons, turkeys and ducks.

Sixty-six studies used culture along with other methods to identify *Campylobacter* spp. in the samples. Other methods to identify the bacterium were biochemical tests, microscopy, haemagglutination tests, hemolysis, commercial identification tests [API CAMPY] and phenotypic tests. Twenty-three studies used PCR along with other methods to identify the bacteria, of which four used only PCR. One study used only ELISA test, whereas one other study did not report how *Campylobacter* was detected.

Collected samples were feces (droppings, cloacal swabs, rectal swabs and fecal sample), carcasses, sheath washings, preputial scrapings, intestinal contents, liver tissue, caeca, vaginal swab and cervico-vaginal mucus. The number of samples ranged from 2 to 1912.

The prevalence rates ranged from 0% to 100%. Identified species were: *C. jejuni*, *C. coli*, *C. lari*, *C. upsaliensis*, *C. fetus*, *C. fetus* subsp. *fetus*, *C. f. venerealis* biovar *intermedius*, *C. fetus* subsp. *venerealis*, *C. hyointestinalis*, *C. troglodytis* sp. nov., *C. sputorum* subsp. *sputorum* and other unidentified species. The most prevalent species in the studies were *C. jejuni* and *C. coli*; while the least prevalent were *C. sputorum*, *C. hyointestinalis* and *C. troglodytis*.

3.3. Epidemiology of *Campylobacter* spp. in animals in Sub-Saharan Africa

The information on the prevalence of *Campylobacter* in animals in Sub-Saharan Africa varies considerably because different methods were used to detect the bacterium, different animals were tested within each study and different isolates were found as well. However, we have found that Western Africa had majority of the data from Sub-Saharan Africa (44.0%, $n = 33$), mainly for Nigeria ($n = 25$), while Middle Africa had the least amount of data (2.7%, $n = 2$) from Cameroon and Democratic Republic of the Congo.

Comparing regions, Western Africa reported higher prevalence of different *Campylobacter* species such as *C. jejuni*, *C. coli*, *C. lari*, *C. upsaliensis*, *C. fetus*, *C. hyointestinalis* and *C. sputorum*. In this region a wide variety of animals were tested, mainly cattle and chickens. Other animals included: sheep, goats, pigs, camels, dogs, japanese quails, cats and grasscutters. This region was the most represented because of Nigeria that had 25 studies. This country had many published studies probably because the bacteria is a well-established cause of diarrhea, sometimes equal or exceeding *Salmonella* and *Shigella* rates (Aboaba and Smith, 2005; Aboderin et al., 2002). Still in this country, *Campylobacter fetus* subsp. *venerealis* was identified as a cause of bovine genital campylobacteriosis, that is characterized by reproductive failure and infertility in cattle (Mai et al., 2015; Mshelia et al., 2010). These reproductive problems are common occurrences amongst livestock in the country (Mshelia et al., 2010). Studies from Western Africa also reported about the

Table 2. Summary of *Campylobacter* prevalence in different Sub-Saharan Africa regions; occurrence of the species in different animals, locations, samples and resistance to antibiotics. In brackets are the number of studies reporting such occurrence.

	<i>C. jejuni</i>	<i>C. coli</i>	<i>C. lari</i>	<i>C. upsaliensis</i>	<i>C. fetus</i>	<i>C. hyointestinalis</i>	<i>C. sputorum</i>	<i>C. troglodytis</i>
Prevalence range per region								
EA	0%–100% (19)	0%–50% (17)	0%–2.4% (2)	4% (1)	2.4%–5.1% (2)	-	-	0%–87.5% (1)
MA	13.6%–28.7% (2)	24.8%–77.3% (2)	0% (1)	0% (1)	-	-	-	-
SA	0.4%–73.3% (10)	2%–48.2% (9)	-	3%–13.1% (2)	0%–2.1% (4)	-	-	-
WA	0%–64.2% (23)	0%–73% (25)	0%–12.5% (11)	0%–20.6% (6)	0.1%–31.2% (6)	0.4%–1.7% (3)	0.7%–2.8% (2)	-
Animals								
	Poultry (2) [chickens (25), ducks (3), guinea fowls (2), turkeys (1), pigeons (1)], cattle (11), camels (1), cats (2), crows (1), dogs (5), goats (5), guinea pigs (1), horses (1), quails (1), monkeys (1), pigs (8), rats (1), sheep (9)	Poultry (2) [chickens (26), ducks (2), guinea fowls (3)], cattle (11), camels (1), cats (1), crows (1), dogs (4), goats (7), grasscutters (1), guinea pigs (1), horses (1), pigs (9), quails (1), rats (1), sheep (9)	Camels (1), cattle (3), chickens (6), ducks (1), goats (1), guinea fowls (1), pigeons (1), pigs (1), sheep (3)	Camels (1), cats (1), cattle (1), chickens (2), dogs (2), pigs (1), sheep (1)	Cattle (12)	Cattle (2), pigs (1)	Camels (1), cattle (1)	Wild chimpanzees (1)
Locations								
	Abattoirs (16), farms (23), laboratory (1), rural or urban households (4), live bird markets (1), urban or peri-urban area (2), research institute (1), retail market/shop (1), rural area (2), state (4), town/metropolis (2), urban or rural veterinary clinics/premises (3), warehouses (1), wild (1)	Abattoirs (16), community (1), farms (24), households (3), laboratory (1), live bird markets (1), research institute (1), retail market/shop (2), rural area (2), state/town (7), veterinary clinics (2), warehouse (1)	Abattoirs (3), farms (3), live bird market (1), state (4)	Abattoirs (1), farms (2), households (2), state (3), veterinary clinics (2)	Farms (7), laboratory records (4), state (1)	State (1), farms (2), households (1)	State (1), farms (1)	National parks (1)
Samples tested for <i>Campylobacter</i>								
	Caeca (5), carcass (11), cloaca (7), colon (1), feces (37), vaginal swab (1)	Caeca (4), carcass (14), cloaca (9), colon (1), feces (33)	Carcass (3), cloaca (3), feces (7)	Carcass (1), feces (7)	Cervico-vaginal mucus (1), rectal (1), preputial (10), vaginal mucus (1)	Feces (2), preputial washings and cervico-vaginal mucus (1)	Feces (1), preputial washings and cervico-vaginal mucus (1)	Feces (1)
Resistance to antibiotics (above 10% of the isolates)								
	Erythromycin (48.7%), Ampicillin (42.5%), Tetracycline (35.8%), Nalidixic Acid (32.0%), Ciprofloxacin (30.7%), Streptomycin (12.1%), Trimethoprim/Sulfamethoxazole (10.6%), Gentamicin (10.5%)	Erythromycin (59.1%), Ampicillin (45.3%), Ciprofloxacin (40.2%), Nalidixic Acid (37.4%), Tetracycline (36.8%), Streptomycin (16.7%), Trimethoprim/Sulfamethoxazole (14.7%), Chloramphenicol (12.9%), Gentamicin (12.9%)	Erythromycin (89.1%), Ampicillin (78.2%), Ciprofloxacin (51.2%), Nalidixic Acid (43.8%), Trimethoprim/Sulfamethoxazole (19.4%), Tetracycline (17.9%), Cephalixin (16.7%), Chloramphenicol (16.5%), Cefotaxime (14.9%)	Erythromycin (90.4%), Ampicillin (73.9%), Ciprofloxacin (49.2%), Nalidixic Acid (46.7%)	NR	NR	NR	NR

EA: Eastern Africa; MA: Middle Africa; SA: Southern Africa; WA: Western Africa; NR: Not reported.

transport of bacteria in different countries such as from Niger to Nigeria because of the large live bird market whereby poultry are transported unchecked (Nwankwo et al., 2016). This consequently leads to high prevalence rates in poultry and humans.

A high prevalence of different *Campylobacter* species was found in pigs (92.7%) (Gwimi et al., 2015). Authors stated that it might have been due to extensive system farming with indiscriminate defecation along with unhygienic disposal of human wastes in the environment and poor personal hygiene. One study from Senegal found an association between poor hygienic practices and *Campylobacter* occurrence (Cardinale et al., 2004).

The isolation of *Campylobacter* in poultry, camels, dogs, cats and quails was an indication that the presence of these animals was reservoir for human infection (Akwuobu et al., 2010; Karikari et al., 2017b; Karshima et al., 2016; Karshima and Bobbo, 2016; Ngulukun et al., 2010; Ogbor et al., 2019; Salihu et al., 2010; Salihu, et al., 2009b).

Probably in Nigeria there are many research projects focused in *Campylobacter* and other enteric bacteria. This contributes to the large number of publications. However, the other countries in the region with data on *Campylobacter* reported such occurrence mainly in poultry. This demonstrates that these food-animals constitutes an important reservoir of the bacterium.

Eastern Africa was the second region with the highest percentage of *Campylobacter* studies, where Tanzania stood out with 11 studies in total. In this region, as well as in Western Africa, a large diversity of animals were tested for the presence of *Campylobacter* with emphasis in cattle and poultry (including ducks and chicken), and other animals such as: pigs, guinea pigs, mice, rabbits, rats, goats, sheep, horses, camels, crows, mountain gorillas, ring-tailed lemurs, donkeys, dogs, cats and monkeys. Isolates were *C. jejuni*, *C. coli*, *C. lari*, *C. upsaliensis*, *C. fetus* and *C. troglodytis* that was a new species discovered in Tanzanian wild chimpanzees. This region was the only one that found 100% prevalence of *C. jejuni* in fecal samples from wild monkeys.

Studies from Eastern Africa reported possible cross-contamination between animals in farms, such as from pigs and chickens to horses and sheep, due to their proximity (Komba et al., 2014). There are probably many studies of the bacterium in Tanzania because it is one important cause of disease in children (Kashoma, et al., 2015a). Some studies addressing *Campylobacter* prevalence in pigs suggested a potential risk of infection to people through consumption of contaminated pork or contact with infected pigs (Mdegela et al., 2011). Some factors affecting

prevalence are reported to be farming and slaughtering practices, geographical locations, and other risk factors, including the concentration of the farms in each location and their proximity to other livestock such as poultry (Kashoma, et al., 2015a).

Also in this region *C. fetus* subsp. *veneralis* was reported as the agent of enzootic infertility in smallholder herds (Swai et al., 2005).

After all, in one of the studies from Kenya the authors did not find any association between the presence of *Campylobacter* and other pathogens in household animals, and moderate to severe diarrhea in children (Conan et al., 2017). Nevertheless, it is known that these animals contribute to the transmission to humans.

Middle Africa region had the lowest amount of data from Sub-Saharan Africa, with only 2 studies in total (2.7%) from Cameroon and Democratic Republic of the Congo. Species found were *C. jejuni* and *C. coli*, although the presence of *C. lari* and *C. upsaliensis* was tested and had negative results. Slaughtered chicken and goats were the only tested animals and chicken had the higher prevalence of 92.7% (Garin et al., 2012). This emphasizes again the role of this food animal in *Campylobacter* epidemiology. In Lubumbashi city in Democratic Republic of the Congo, live goat and goat meat were the major sources of human and environmental contamination by *Campylobacter* spp., also because they are the major source of the meat supply in the city (Mpalang et al., 2014). In this region it was also found that slaughtering process is performed under poor hygienic conditions and this also contributes to bacterial proliferation (Mpalang et al., 2014). In general, Middle Africa is the second sub-region with the least countries, and probably for this reason it had fewer reports. On the other hand, the poor diagnostic capacity in Middle Africa may have limited the development of research on *Campylobacter*, since the published studies were supported by international collaborators.

Southern Africa had 21.3% of the total studies found in Sub-Saharan Africa, with more emphasis in South Africa that had 14 studies. South Africa was probably best represented because it has specialized research teams for zoonotic bacteria and appropriate diagnostic labs. Poultry and cattle were more studied in this region, although pigs, sheep, goats and dogs were also studied. Isolates of this region were *C. jejuni*, *C. coli*, *C. upsaliensis* and *C. fetus*. *C. jejuni* and *C. coli* had higher prevalence in diarrheic chicken and goats (Uaboi-Egbenni et al., 2010, 2012), indicating that they are potentially causes of diarrhea in these animals, although they are often known as commensals. The only study in non-food animals was in healthy dogs attending rural veterinary clinics,

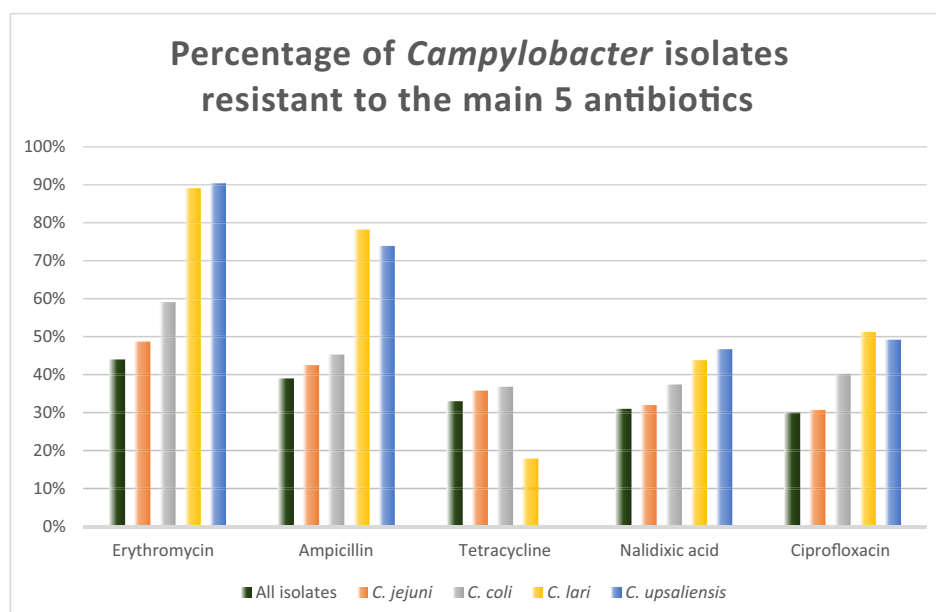


Figure 3. Percentage of *Campylobacter* isolates resistant to the main 5 antibiotics.

where almost half (41.6%) were positive for *Campylobacter* spp. In addition to *C. jejuni* and *C. coli*, *C. upsaliensis* was also found in these dogs. Living conditions influenced the occurrence of bacteria in these animals (Karama et al., 2019). Moreover, *C. fetus* was not identified as major problems of reproductive disorders in cattle from Southern Africa. However, this information should be carefully analyzed due to the low number of studies and representativeness (Madoroba et al., 2011; Njiro et al., 2012).

This systematic review confirmed that *Campylobacter* occurs in animals in Sub-Saharan Africa. Poor hygiene seems to be one of the major contributors to the spread of these bacteria in the region. The bacterium is commensal but also reported as potential cause of diarrhea in poultry and cattle and reproductive failure in cattle. Understudied animals such as quails, pigeons, camels, horses, grasscutters, guinea pigs, rats and especially crows deserve attention in future studies to know about the occurrence of different strains of this bacteria. The animals whose presence of *Campylobacter* was tested but was not found (0%) were donkeys (Conan et al., 2017), ring-tailed lemurs (Villers et al., 2008), mice and rabbits (Komba et al., 2014). All of these animals were tested only once and in Eastern Africa. Further research is needed to identify whether the bacteria occurs in these animals in different regions of Sub-Saharan Africa.

Countries such as Nigeria, Tanzania and South Africa are better represented in animal campylobacteriosis studies probably due to the economic development of the countries that have funds for research into *Campylobacter*. South Africa is best positioned in the human development index ranking, while Nigeria and Tanzania are ranked below (<http://hdr.undp.org/en/content/2019-human-development-index-ranking>). Many other Sub-Saharan African countries are in very low ranks. Less developed countries tend to invest less in research compared to most developed ones. In some studies, international partners were present as co-authors and probably supported the funding of the projects. In many Sub-Saharan African studies, local funding is insufficient to cover all areas of research. Most likely for this reason, many countries have few or no studies on *Campylobacter*.

3.4. Antibiotic resistance of *Campylobacter* spp. isolated from animals

From the 75 studies included in this review, a total of 26 studies from 10 countries have reports on antibiotic resistance, as described below:

- Eastern Africa: Ethiopia (2 studies), Kenya (1), Madagascar (1) and Tanzania (4);
- Middle Africa: Cameroon (1);
- Southern Africa: South Africa (8)
- Western Africa: Côte d'Ivoire (1), Ghana (1), Nigeria (5) and Senegal (2).

Supplementary material 5 summarizes the information of the antibiotic resistance studies. *Campylobacter* isolates for antibiotic resistance testing were found in ten different animals, namely: poultry (n = 2 studies; including chickens [16], ducks [1], guinea fowls [1]), cattle (8), pigs (5), sheep (4), goats (2), guinea pigs (1), horses (1) and rats (1).

C. jejuni and *C. coli* were the most studied species, followed by *C. lari* and *C. upsaliensis*. A total of 49 different antibiotics were analyzed for 2481 isolates. Antibiotics with resistance in more than 10% of the isolates were: **macrolides**: erythromycin (44%); **penicillins**: ampicillin (39%); **tetracycline** (33%); **fluoroquinolones**: nalidixic acid (31%) and ciprofloxacin (30%); **trimethoprim/sulfonamides**: trimethoprim/sulfamethoxazole (14%); **aminoglycosides**: streptomycin (13%) and gentamicin (12%) and **cephalosporins**: cephalothin (10%). Figure 3 shows the percentage of *Campylobacter* isolates resistant to erythromycin, ampicillin, tetracycline, nalidixic acid and ciprofloxacin.

Fifteen antibiotics had no isolates with resistance, namely: **aminoglycosides**: neomycin; **rifamycins**: rifampicin; **fluoroquinolones**:

levofloxacin, enrofloxacin and danofloxacin; **lincosamides**: lincomycin; **tetracyclines**: doxycycline; **pleuromutilins**: tiamulin; **macrolides**: telithromycin, tylosin, tulathromycin and tilmicosin; **amphenicol**: florfenicol and **others**: fosfomycin and spectinomycin.

The high percentage of isolates resistant to antibiotics, particularly for erythromycin (44%) is of particular concern as it is one of the drugs of choice for the clinical treatment of campylobacteriosis in complicated human cases (Igwaran and Ifeanyi, 2019; Zhou et al., 2016). The same is observed for ciprofloxacin that is used as therapeutic agent in countries from Sub-Saharan Africa (Abubakar et al., 2019; Bernadette et al., 2012; Ewnetu and Muhret, 2010; Kashoma, et al., 2015a, b; Komba et al., 2014; Uaboi-Egbenni et al., 2012). Resistance to ciprofloxacin is thought to have been caused by antibiotic use in humans, that is reported to be frequent in the region (Kashoma, et al., 2015a).

These resistances may be due to misuse in animal husbandry and also in human treatment (Kashoma, et al., 2015a). Poultry and cattle were the most tested animals for antibiotic resistance, followed by pigs and sheep. These are food animals commonly raised by both small breeders and large companies. The farmers commonly administer antibiotics to these animals as growth promoters and for prophylaxis purposes (Basardien, 2012; Karikari et al., 2017b; Uaboi-Egbenni et al., 2011a). In certain cases the farmers do not respect the withdrawal period and proper dosages (Ewnetu and Muhret, 2010; Olabode et al., 2017; Salihu et al., 2012) and this leads to antibiotic resistance. Moreover, many studies reported high levels of resistance to antibiotics commonly used in the poultry, cattle and swine industry (erythromycin, ciprofloxacin and tetracycline) (Akwuobu et al., 2010; Bester and Essack, 2012; Ewnetu and Muhret, 2010; Garin et al., 2012; Jonker and Picard, 2012; Kassa et al., 2007; Uaboi-Egbenni et al., 2011a, 2012).

Another fact that shows that large-scale food animals production contributes to antibiotic resistance is the significantly less resistance of the isolates from rurally raised chickens against ciprofloxacin (7.9%), erythromycin (0%) and tetracycline (21.6%) than those from commercially produced chickens in Kwazulu-Natal (Bester and Essack, 2012).

Prolonged exposure of animals to antibiotics may also contribute to increased resistance, such as observed in ducks in Tanzania (Nonga and Muhairwa, 2009).

Beta lactamase production by *Campylobacter* may be responsible for the high frequency of beta-lactam resistant strains (Jonker and Picard, 2012) such as to ampicillin (Kashoma, et al., 2015b; Nonga and Muhairwa, 2009). Additionally, treatment of *Campylobacter* using beta lactamases is not recommended as it is believed that *C. jejuni* wall is impenetrable for these antibiotics (Jonker and Picard, 2012).

High tetracycline resistance may be because it is the most widely used drug in veterinary medicine in some countries in the region, such as Tanzania and Ghana (Karikari et al., 2017a; Nonga and Muhairwa, 2009). It may also be due to overuse, which has led to the development of new resistance genes that have been transmitted between the bacteria (Nonga and Muhairwa, 2009). Resistance to many antibiotics may also be due to efflux pumps that remove antibiotics from the bacteria's cytosol (Jonker and Picard, 2012).

Antibiotic resistance was also found in isolates from animals not used for human consumption such as horses, guinea pigs and rats. Studies from other Sub-Saharan African countries, animals and other *Campylobacter* species (such as *C. fetus*, *C. hyointestinalis*, *C. sputorum* and *C. troglodytis*) did not test for antibiotic resistance. However, this does not indicate that there are no resistant circulating species in these cases. This should be the subject of future studies.

Multiple drug resistance is also commonly reported and a major concern (Abubakar et al., 2019; Akwuobu et al., 2010; Basardien, 2012; Cardinale et al., 2002; Jonker and Picard, 2012; Kambuyi, 2018; Karikari et al., 2017b; Kashoma, et al., 2015a, b; Kassa et al., 2007; Nonga and Muhairwa, 2009; Ogbor et al., 2019; Okunlade et al., 2015; Salihu et al., 2012; Uaboi-Egbenni et al., 2010, 2011a, 2012) as resistance genes can

be shared between the bacteria (Uaboi-Egbenni et al., 2012) which leads to increasing resistant species. Some recent studies also report on antibiotic resistance genes (Abubakar et al., 2019; Kambuyi, 2018).

This antibiotic resistance can be transmitted to humans through the close contact between animals and humans and consumption of the contaminated food-animals meat (Nonga and Muhairwa, 2009; Uaboi-Egbenni et al., 2012). It is a major concern for both human and animal health.

The resistance scenario may be even more worrying than reported in this study, as the type of test influences the results. For example, in Tanzania, some isolates that were susceptible or intermediate to different antibiotic through disk diffusion were resistant to same antibiotics using broth microdilution methods (Kashoma, et al., 2015a, b).

As mentioned before, food-animals were more prominent in studies of antibiotic resistance. This shows that animal husbandry practices are having a major impact in increasing antibiotic resistance. Meanwhile, guinea pigs, horses and rats were also found to have resistant *Campylobacter* isolates. This also deserves particular attention in future studies as potential transmitters of resistant isolates to other animals and to humans.

This review reiterates that *Campylobacter* is resistant to fluoroquinolones, which was already a WHO concern (WHO, 2017), and there is also the concern of high resistance to macrolides as erythromycin (44%), penicillins as ampicillin (39%) and to tetracyclines (33%).

The use of antibiotics must be monitored and antibiotic surveillance must be done in order to reduce the spread of resistant strains into the environment. The antimicrobial resistance in both humans and animals leads to treatment failure and difficulty in case management (Ogbor et al., 2019). It will also limit the therapeutic choice, increasing hospitalization rates and cost of therapy, and decreasing the survival rate of patients (Jonker and Picard, 2012).

Bearing in mind the devastating consequences of antibiotic resistance within the African continent, countries like Nigeria, South Africa, Tanzania and Mozambique already have in place national plans to promote the rational use of antimicrobials in the context of "One Health" approach (DAFF, 2018; Federal Ministries of Agriculture Environment and Health, 2017; GARP-Mozambique, 2015; Ministry of Agriculture Livestock and Fisheries; and MoHCDEC, 2017).

For animals, the common objectives of these national plans include antimicrobial resistance surveillance at all levels of the agriculture food chain. Greater emphasis is given to food-producing animals such as meat, milk and eggs producing animals. The plans propose to set the minimum residue limits for antimicrobials in animals and animal products; promote appropriate use of antimicrobials through antimicrobial stewardship practices and controlled access to antimicrobials; establish a functioning vaccination program to prevent new infections and orient animal health workers on hygiene and safety standards and waste management.

However, the efficient implementation of those plans is still challenging due to limited access of financial and technical resources in most of Sub-Saharan African countries (IACG, 2018; ReAct, 2017).

4. Conclusions

The information on the prevalence of *Campylobacter* spp. in animals in Sub-Saharan Africa varies considerably because different methods were used to detect and identify the bacteria. Thus, the prevalences can be higher than those reported here, taking into account the different precision and accuracy of each method. For example, depending on the time and form of storage of the sample, the culture may not identify all bacteria that were previously present, since *Campylobacter* is anaerobic and extremely fragile. On the other hand, PCR can reveal very high prevalences, which may not correspond to a current infection, but may result from previous infections in which fragments of DNA from the bacteria are being eliminated after treatment. ELISA is a test used less frequently to

detect *Campylobacter* and depending on the test, it may not discriminate between recent and old infections. Likewise, different sample matrices were used in the different studies. Some studies used fecal samples, sheath washings, preputial scrapings, intestinal contents, liver tissue, caeca, vaginal swabs and cervico-vaginal mucus, whereas others have used carcass samples at slaughterhouses. Therefore, the choice of matrix has significant impact on the outcome since each type of sample can hold different amounts of the bacteria and depending on the storage, the survival of the bacteria in the sample can be compromised, which influences its detection. Additionally different animals were tested using different sampling methods, in different geographic locations and conditions, which also influences the prevalence.

Overall, *Campylobacter* spp. infections are common in animals in Sub-Saharan Africa, mainly in cattle and chickens. Poor hygiene seems to be a major contributor to the spread of the bacteria in the region. However, food animals, household animals or animals that inhabit the forests harbor this bacteria in the region. These animals may be a source of contamination to humans. Frequently isolated species are *C. jejuni* and *C. coli*. New *Campylobacter* species were discovered and isolated from wild chimpanzees. The sub-region with the least studies was Middle Africa, where studies focused on food animals. It is necessary to know if household or other animals are also contaminated by *Campylobacter* in that region.

Understudied animals such as quails, pigeons, camels, horses, grass-cutters, rats, guinea pigs and crows deserve attention in future studies to understand about the occurrence of different strains of these bacteria. Animals that had 0% of prevalence also deserve attention in future studies, namely: donkeys, ring-tailed lemurs, mice and rabbits.

Antibiotic resistance is a worrisome concern mainly in food-animals probably due to misuse by humans with disease and farmers. Erythromycin, ampicillin, tetracycline, nalidixic acid and ciprofloxacin are the drugs with most resistant isolates and this is a major public health concern.

Meanwhile, guinea pigs, horses and rats were also found to have resistant *Campylobacter* isolates. These also deserve particular attention in future studies as potential transmitters of resistant isolates to other animals and to humans.

Campylobacter species are not only a risk of disease to humans but are also associated with disease in animals such as *C. fetus* that causes reproductive failure in cattle; and *C. jejuni* and *C. coli* that are potentially causes of diarrhea in poultry and cattle.

Updated data on *Campylobacter* spp. epidemiology and antibiotic resistance are lacking in most of Sub-Saharan African countries. Therefore, more research work is warranted to obtain an updated and detailed data on these subjects. These data would allow the development of control strategies to tackle campylobacteriosis in animals and humans in the region and to reinforce the implementation of antibiotic resistance control plans in each country.

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