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Review

Campylobacteriosis in North Africa

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Abstract: Foodborne bacterial infections, particularly those caused by contaminated food sources, pose significant public health challenges and result in substantial economic losses. This review aims to provide insights into recent literature on the prevalence of *Campylobacter* spp. in North African food supply chains and their pathogenicity. Additionally, it seeks to summarize the available information on health-related issues and the current state of antibiotic resistance. The reviewed evidence highlights a gap in our understanding of the prevalence of *Campylobacter* spp. in North African food supplies. Molecular characterization efforts to identify the sources of *Campylobacter* spp. are limited, and there are few surveys that have specifically targeted this bacterium in the food supply. While qualitative data indicates either the presence or absence of *Campylobacter* spp., quantitative data on the actual amounts of these bacteria in chicken meat supplies across North African countries are notably lacking. Despite frequent reports of *Campylobacter* spp. in animal-derived foods, the literature reviewed emphasizes the ongoing challenge that *Campylobacter* spp. pose to food safety and public health in North Africa.

Keywords: *Campylobacter*; virulence factors; antimicrobial resistance; North African countries; one health

1. Introduction

Globally, the presence of foodborne pathogens continues to pose significant challenges to both food safety and international trade. In Europe and various other regions, foodborne infections remain

a major public health concern [1]. Data compiled by the European Centre for Disease Prevention and Control (ECDC) and the Zoonoses Reports of the European Food Safety Authority (EFSA) suggest that instances of human campylobacteriosis, primarily associated with *Campylobacter jejuni*, have remained below the radar in the past, leading to intermittent periods over the past decade where reported cases surpassed those of salmonellosis [2,3]. In the United States of America (USA), *C. jejuni* has been identified as the primary pathogen that caused foodborne illnesses, closely followed by *Salmonella*. According to the Foodborne Diseases Active Surveillance Network (FoodNet) operated by the Centers for Disease Control and Prevention (CDC), documented hospitalizations due to foodborne campylobacteriosis and salmonellosis have increased over recent years [4].

In a 2015 World Health Organization (WHO) report, the Middle East and North Africa were ranked third regarding the global burden per population of foodborne diseases, just behind Africa and the South-East Asian regions [5]. Moreover, the study indicated that around 70% of the total foodborne illness in this region was caused by *Campylobacter*, *E. coli*, intestinal non-typhoidal *Salmonella*, and Norwalk Virus, underlining these pathogenic agents' crucial role in the foodborne infections in the area. However, determining the actual rate of food-borne infections in the region can be a bit challenging due to low systematic investigations. These efforts can help in the early identification of sporadic cases, the containment of outbreaks, and having isolates for source attribution and risk assessment nationally and regionally. Additionally, there is incomplete knowledge regarding antimicrobial resistance in bacteria that cause foodborne infections based on the Middle Eastern region [6,7]. Nevertheless, an understanding of this problem remains elusive.

This review presents the current and updated knowledge of the epidemiology of *Campylobacter* spp., which is often associated with global cases of foodborne infections around the world. Using the systematic review approach, where each included study is the basic unit of analysis, helps create the database. Authors extracted key characteristics from these studies, including the publication year, the methodologies employed, the data collection techniques, and the research outcomes. Subsequently, a frequency analysis was utilized to derive quantitative findings [8,9]. To identify pertinent research articles on foodborne infections across various food types in North African countries over the past two decades, searches were conducted on platforms such as PubMed, Science Direct, Scopus, Web of Science, and Google Scholar. Moreover, both electronic postgraduate theses and national reports were used to gather information on foodborne pathogens in the North African region. This region, which includes Algeria, Egypt, Libya, Morocco, and Tunisia, has difficult environments with limited water resources. This region covers approximately 4,758,160 square kilometers, where 90% of the region is characterized by arid or semi-arid climate, therefore posing difficulties in the control and management of foodborne infections.

In this research, our objective is to elucidate (i) the historical understanding and recent advancements, drawn from published research over the past twenty years, on the prevalence of *Campylobacter* spp. in the food chain and (ii) its pathogenicity in North African countries.

2. The organism

Campylobacter spp. were initially identified in 1913 as *Vibrio fetus* in veterinary specimens. Subsequently, *Vibrio jejuni* was coined in 1927, followed by *Vibrio coli* in 1944, and *Vibrio bubulus* in bovine reproductive tracts. In 1963, Sebald and Veron reclassified *Vibrio fetus* and *V. bubulus* as the *Campylobacter* species. Veron and Chatelain identified four primary species: *C. jejuni*, *Campylobacter coli*, *Campylobacter sputorum*, and *Campylobacter fetus* [10]. In 1980,

Campylobacter lari was discovered by Skirrow and Benjamin. The term "*Campylobacter*" was derived from the Greek words for "curved" and "rod," encompassing 31 species and 13 subspecies. *C. jejuni* has two subspecies: *jejuni* (common in human cases) and *doylei* (lacking an animal host). This distinction is vital when specifically referring to *C. jejuni*, typically indicating *C. jejuni* subsp. *jejuni* [11–13].

Campylobacter spp., microaerophilic bacteria, flourish in oxygen concentrations ranging from 5% to 10%, in conjunction with 10% carbon dioxide [14]. These microorganisms are Gram-negative and exhibit either a spiral-shaped, coccal, or curved morphology, presenting as motile rods with flagella. They commonly reside in the intestines of mammals and birds as commensals [15]. Given their slow growth, they require specialized growth media containing charcoal and antibiotics such as cephalothin to suppress the competing microorganisms in fecal samples. Notably, *C. jejuni* and *C. coli*, recognized for their thermotolerance, optimally thrive at 42 °C [16]. However, not all *Campylobacter* spp. demonstrate the same degree of thermotolerance; for instance, *C. fetus* lacks this trait [17]. Stool cultures for cases of human diarrhea typically follow standard practices at 42 °C, utilizing media containing cephalothin to isolate *C. jejuni* and *C. coli*; however, this method may not be suitable for other species such as *C. fetus* or *C. upsaliensis*, which cause illness less frequently [4,18,19].

3. Current status of human campylobacteriosis in North Africa

Campylobacteriosis is primarily caused by *Campylobacter* spp., and continues to pose a threat to public health in North African countries [20]. Although detailed statistics specific to the studied area could not be identified, the existing research suggests that the incidence of campylobacteriosis in the general population appears to be high. Campylobacteriosis is a zoonotic disease prevalent among humans in North Africa and is related to various factors, including the standard of living and habits, sanitation practices, and the availability of contaminated food and water [21]. The warm climate prevalent in many North African countries may also contribute to the survival and spread of *Campylobacter*. Strategies used in the diagnosis and monitoring of campylobacteriosis and the surveillance systems in each of the North African countries differ, impacting the accuracy of the reported cases. Moreover, low awareness, oversight, and misidentification may also contribute to the further ambiguity regarding the true burden of the disease in the region.

Efforts to combat campylobacteriosis in the North African region include adopting structural and educational strategies in food hygiene, augmenting sanitation facilities, and sensitizing the medical practitioners and general public [22,23]. A disjointed effort between health authorities, research institutions, and international organizations is necessary for the development of prevention and control strategies due to the peculiarities of the North African region. Campylobacteriosis is a major cause of gastrointestinal disease, and more studies and surveillance are needed to elucidate the disease profile in North Africa, to assess the risk factors, to develop specific points of control measures, and to reduce the impact of this disease in the area.

4. Source and modes of transmission to humans in North Africa countries

Campylobacter spp. mostly manifests the risks of passing from infected animals or animal products to humans or animals and other environments [21,24]. Despite the difficulties in pinpointing specific exposure routes of *Campylobacter* infections, current and emerging studies indicate poultry meat and products as the primary vehicles [25–27]. Another UK study compared wild and domestic

ducks and discovered differences in the genotypes of *C. jejuni* regarding domestic ducks as a source of campylobacteriosis [28]. In the same way, poultry products are considered the main reason for *C. jejuni* contaminations in Brazil. Wild birds in Malaysia brought *C. jejuni* into different environments, and cats or dogs with *C. jejuni* gastrointestinal issues also spread the bacteria [24,29,30]. In Italy, the risk of campylobacteriosis from pets, notably dogs, is increasing, as supported by molecular evidence linking human and pet strains [31]. *Campylobacter* spp. can be transmitted to humans through both direct and indirect means, with direct transmission commonly occurring among professionals with close animal contact, such as veterinarians and butchers [32] (Figure 1). The primary sources of infection are believed to be meat, milk, and water [24,29]. Despite being labor-intensive and costly, whole-genome sequencing (WGS) remains the most effective approach for genotyping *C. jejuni* isolates and understanding the epidemiological connections between them.

In North Africa, there is a rising apprehension regarding *Campylobacter* spp. infections in humans, predominantly attributable to *C. jejuni* and *C. coli* [20]. Given the impact of urbanization, dietary shifts, and population growth on exposure, grasping the origins of transmission is essential to implement efficient public health interventions. Tackling these origins is imperative for averting and controlling *Campylobacter* spp. infections in the North African region, underscoring campylobacteriosis as a notable public health issue [1].

Research in Algeria has primarily focused on chicken meat as a reservoir of *Campylobacter* spp. Baali et al. [17] found high levels of *C. jejuni* in East Algerian chicken meat, while Benamar et al. [33] and Messad et al. [34] detected *Campylobacter* spp. in poultry across Algiers. In Egypt, chicken products have been linked to human campylobacteriosis, with El-Naenaeey et al., [35] Barakat et al., and Abd El-Tawab et al. [36] identifying *Campylobacter* spp. in poultry. Sayed et al. found *C. jejuni* and *C. coli* in pigeon and turkey meats. Studies by Zeinhom et al., [37] Barakat et al., [38] and El-Zamkan and Abdel Hameed [39] confirmed these pathogens in dairy products. In Morocco, *Campylobacter* spp. were found in chicken, raw milk, and beef by El Baaboua et al. [40] and Jouahri et al. [41]. In Tunisia, *Campylobacter* spp. were detected in chicken, turkey, and eggs by Béjaoui et al. [42], Gharbi et al. [43], and Jribi et al [44]. Libyan research on *Campylobacter* spp. is limited (Table 1).

These findings underscore the need for the necessary steps to improve and ensure proper storage and handling practices in the poultry market to address *Campylobacter* spp. connection to poultry products, with a major emphasis on the enforcement of food safety. Based on the findings, the research highlights the need to analyze the *Campylobacter* pathogen in food safety protocols to improve safety standards in North African countries.

Table 1. Occurrence of *Campylobacter* spp. in foods in North Africa.

Country	Tested Food Samples (Total Number)	*Campylobacter* spp. %*	*C. jejuni* %	*C. coli* %	Other Species	References
Algeria	Chicken meats (*n* = 204)	86.2	ND**	ND	ND	[33]
	Kebab (*n* = 96)	38	ND	ND	ND	
	Chicken meats (*n* = 240)	55	56.8	2.3	40.9	[17]
	Chicken meats (*n* = 100)	80	ND	ND	ND	[34]
Egypt	Pigeon meat (*n* = 100)	16	9	7	ND	[45]
	Pigeon liver (*n* = 100)	17	4	13	ND	
	Turkey meat (*n* = 100)	12	4	8	ND	
	Turkey liver (*n* = 100)	19	8	11	ND	

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Country	Tested Food Samples (Total Number)	*Campylobacter* spp. %*	*C. jejuni* %	*C. coli* %	Other Species	References
	Chickens (*n* = 195)	86.2	59.5	26.7	ND	[35]
	Breast meat (*n* = 40)	75	55	20	ND	
	Raw milk (*n* = 47)	83	70.2	12.8	ND	
	Raw milk (*n* = 50)	18	18	0	0	[37]
	Talaga cheese (*n* = 50)	6	6	0	0	
	Feta cheese (*n* = 50)	0	0	0	0	
	Kareish cheese (*n* = 50)	14	14	0	0	
	Turkey meats (*n* = 30)	20	13.3	6.7	ND	[46]
	Liver (*n* = 30)	27	20	10	ND	
	Chicken meats (*n* = 547)	37.8	ND	ND	ND	[38]
	Liver (*n* = 127)	37	ND	ND	ND	
	Raw milk (*n* = 274)	5.1	ND	ND	ND	
	Cheese (*n* = 180)	7.8	ND	ND	ND	
	Yoghurt (*n* = 193)	13.9	ND	ND	ND	
	Chicken Liver (*n* = 70)	27	68.4	31.6	*C. lari* (0)	[47]
	Chicken breast (*n* = 70)	7.1	100	0	*C. lari* (0)	
	Chicken thigh (*n* = 70)	14	50	40	*C. lari* (10)	
	Raw milk (*n* = 52)	11	33.3	66.7	*C. lari* (0)	
	Kariesh cheese (*n* = 40)	8	66.7	33.3	*C. lari* (0)	
	Yoghurt (*n* = 30)	0	0	0	*C. lari* (0)	
	Broiler (*n* = 101)	16.8	ND	4	ND	[48]
	Slaughterhouses (*n* = 104)	24	ND	3.9	ND	
	Fresh chicken meat products (*n* = 30)	53	46.7	46.7	ND	[49]
	Frozen chicken meat products (*n* = 30)	53	46.7	40	ND	
	Chicken burger (*n* = 15)	ND	ND	ND	ND	
	Chicken nuggets (*n* = 15)	13	13.3	13.3	ND	
	Raw milk (*n* = 50)	22	20	20	ND	[39]
	Kareish cheese (*n* = 50)	34	14	14	ND	
	Yoghurt (*n* = 50)	18	8	8	ND	
	Skin (*n* = 39)	31	12.8	17.9	*C. lari* (17.9), *C. hyointestinal* (0)	[36]
	Thigh meat (*n* = 39)	39	17.9	20.5	*C. lari* (20.5), *C. hyointestinal* (1)	
	Breast meat (*n* = 39)	41	33.3	5.1	*C. lari* (5.1), *C. hyointestinal* (2.7)	
	Raw milk (*n* = 50)	ND	4	ND	ND	[50]
	Laban Rayeb (*n* = 25)	ND	ND	ND	ND	
	Stored Domiati cheese (*n* = 39)	ND	ND	ND	ND	
	Fresh Domiati cheese (*n* = 38)	ND	11	ND	ND	
	Zabady (*n* = 25)	ND	ND	ND	ND	
	Ras cheese (*n* = 25)	ND	ND	ND	ND	
	Kariesh cheese (*n* = 25)	ND	ND	ND	ND	

Continued on the next page

Country	Tested Food Samples (Total Number)	*Campylobacter* spp. %*	*C. jejuni* %	*C. coli* %	Other Species	References
Morocco	Raw milk (*n* = 61)	ND	1.6	0	ND	[40]
	Beef (*n* = 16)	ND	0	6.3	ND	
	Minced meat (*n* = 38)	ND	5.6	7.9	ND	
	Eggs (*n* = 44)	ND	0	0	ND	
	Breast and minced meat (*n* = 60)	ND	6.7	50	ND	
	Chicken thigh (*n* = 48)	ND	6.6	50	ND	
	Chicken wings (*n* = 23)	ND	4.3	60.9	ND	
	Chicken meats (*n* = 39)	ND	5.1	38.5	ND	
	Poultry (*n* = 140)	73	ND	ND	ND	[51]
	Broiler (*n* = 105)	71.4	ND	40	ND	[52]
	Raw poultry meat (*n* = 50)	62	ND	ND	ND	[41]
Tunisia	Chicken meats (n = 257)	18.7	68.7	31.2	ND	[42]
	Eggs (*n* = 86)	26	81.8	18.2	ND	[43]
	Broiler chickens (*n* = 590)	22.4	ND	ND	ND	[53]
	Chicken meat (*n* = 149)	26.8	16.1	3.4	ND	[44]
	Turkey meat (*n* = 101)	23.7	13.8	1.9	ND	

* The percentage (%) of *Campylobacter* species is calculated from the positive samples (isolated target bacteria).

** ND: Not determined.

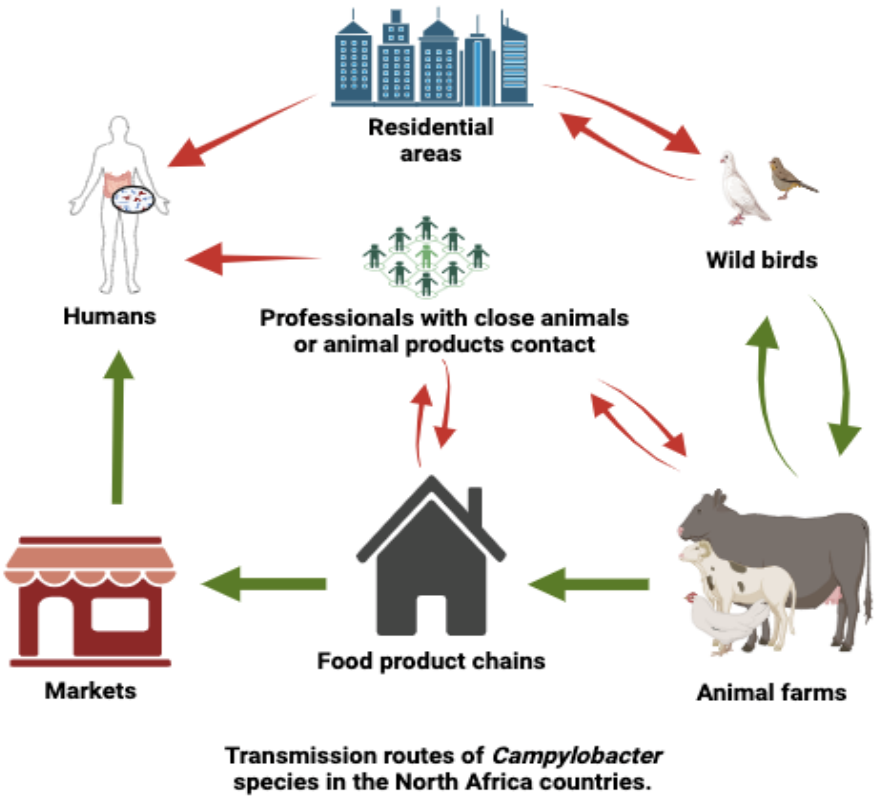

Figure 1. Displays both the direct and indirect routes of *Campylobacter* spp. transmission to humans in North Africa. Red arrows: direct routes; Green arrows: indirect routes. Created using Biorender.com (accessed on January 20, 2024).

5. Occurrence in humans

These curved-rod-shape bacteria include *Arcobacter butzleri*, *A. cryaerophilus*, *Helicobacter bilis*, and *H. canis,* and have been known to cause gastroenteritis in humans in recent studies [54,55]. Nevertheless, *C. jejuni* is still the leading causative agent for gastroenteritis in the developed world [56]. The disease caused by *Campylobacter* is a serious public health concern, especially during the summer, in many European countries [32]. People who handle animals or animal products, such as veterinarians, farmers, poultry workers, and individuals who work in abattoirs or butcheries, also have a higher risk of getting infected due to occupational exposure [21].

In Egypt, as documented by Zeinhom et al. [37], a study was conducted on 53 individuals with gastrointestinal symptoms who visited an outpatient clinic between January and June 2019. The research revealed that among the analyzed human stool samples, 21 (39.6%) tested positive for *C. jejuni*. Of these, 12 (48%) patients experienced diarrhea, while 9 (32.1%) did not show any diarrheal symptoms. Additionally, the isolates from human stool samples demonstrated notable resistances to nalidixic acid, ciprofloxacin, and tetracycline, with resistance rates of 70%, 60%, and 70%, respectively. In another study by Lobna et al. [47], samples were collected from 128 human stool swabs obtained from patients with gastroenteritis symptoms from Toukh Central Hospital in Toukh city, Kalyoubia, Egypt. *Campylobacter* spp. were isolated from 26 human stool samples (20.3%). Among these isolates, 22 (84.6%) were identified as *C. jejuni* and 4 (15.3%) as *C. coli*. In a separate outbreak investigation in Cairo, Egypt, by Ghoneim et al. [57], 75 stool samples were collected from individuals with diarrhea, leading to the identification of thirteen *C. jejuni* isolates (17.33%).

El-Naenaeey et al. [35] collected 44 human stool samples from gastroenteritis patients in Zagazig City, Egypt, from March 2017 to September 2019, isolating *Campylobacter* spp. from 91% of the samples. The highest isolation rates were for *C. jejuni* (73%) and *C. coli* (18%), with all isolates resistant to ampicillin, amoxicillin, and erythromycin. Abushahba et al. [48] found *Campylobacter* spp. in 22 of 80 samples (28%) from Assiut University Hospital, with *C. coli* in 5% of the samples and an absence of *C. jejuni*. Abdelhady et al. [58] found a 34.8% (15/43) prevalence rate for the *Campylobacter* genus in 43 stool swabs from children at Assuit University Children's Hospital, identifying *C. coli* at 33.3% (5/15), *C. jejuni* at 6.7% (1/15), and mixed infections at 6.7% (1/15). El-Tawab et al. [36] found a 5.3% prevalence rate for *Campylobacter* spp. in 246 stool swabs from Al-Ahrar public hospital, with 10 cases of *C. jejuni* and 3 cases of *C. coli*.

In Morocco, as reported by Baaboua et al. [40], a study conducted between July 2015 and June 2018 involved six stool samples from patients with diarrhea in Northern Morocco, where only one sample tested positive for *C. jejuni*. No studies on patients with diarrhea have been conducted in Algeria, Libya, and Tunisia.

Surveys conducted in Egypt depicted elevated rates of *Campylobacter*, particularly *C. jejuni* infection, among individuals with diarrheal symptoms. Zeinhom et al. [37] found out that 40% of stool samples were positive for *C. jejuni*, where a notable portion of patients experienced diarrhea. These isolates exhibited a high resistance to common antibiotics, reflecting a concerning trend. Similarly, other studies corroborate widespread *Campylobacter* infections in Egypt. Conversely, Baaboua et al. [40] observed a lower prevalence of *C. jejuni* in patients with diarrhea in Northern Morocco, suggesting the possibility of other pathogens causing diarrheal illnesses in Morocco. Limited research of the Algerian, Libyan, or Tunisian populations highlighted the knowledge deficit concerning *Campylobacter* distribution in North African countries; therefore, there is a necessity for future related exploration for a healthy population consequence (Table 2).

Table 2. Prevalence of *Campylobacter* spp. on patients with diarrhea in North Africa.

Location	Sample Size	*Campylobacter* spp. %*	*C. jejuni* %**	*C. coli* %**	Confirmation Methods	References
Egypt (Beni-Suef)	53	40	ND***	ND	PCR technique	[37]
Egypt (Kalyoubia)	128	20.3	85	15	Biochemical tests	[47]
Egypt (Cairo)	75	17	ND	ND	PCR technique	[57]
Egypt (Sharkia Governorate)	100	ND	30	ND	PCR technique	[14]
Egypt (Zagazig City)	44	91	73	18	PCR technique	[35]
Egypt (Giza)	40	ND	92.5	7.5	PCR technique	[38]
Egypt (Assiut)	80	28	0	5	PCR technique	[48]
Egypt (Assuit)	43	11	7	33	PCR technique	[58]
Egypt (Zagazig City)	246	5.3	77	23	PCR technique	[36]
Morocco (Northern)	6	17	100	0	PCR technique	[40]

* The isolation rate was calculated from the total number of the examined samples

** The isolation rate of each species was calculated from the total number of the isolated *Campylobacters* spp.

*** ND: Not determined.

6. Virulence factors

The term "virulence genes" typically refers to genes within microorganisms, such as bacteria, that impact their ability to cause disease and adapt to challenging environmental conditions. These genes are closely associated with the microorganism's pathogenicity and its capacity to thrive and cause infections within a host organism [6]. In the case of bacteria like *Campylobacter* spp., which are known to cause foodborne illnesses in humans, virulence stress genes may include those involved in processes such as bacterial adhesion to host cells, tissue invasion, and an evasion of the host's immune defenses. Additionally, these genes may contribute to the microorganism's ability to withstand adverse conditions, such as temperature fluctuations or acidic environments, encountered during infection or in external settings [59]. Researching virulence stress genes is crucial for understanding the mechanisms underlying bacterial pathogenesis and survival across different environments. Identifying and characterizing these genes can provide insights into microbial pathogenicity and potentially inform the development of treatments or preventive strategies against infections.

Virulence genes such as *cadF* and *flpA* code for fibronectin-binding proteins, which help the bacterium firmly adhere to the cells of the small intestinal epithelia. Adherence is very important because it marks the initial point in the process of colonization and infection [60]. These easily identifiable proteins allow the bacteria to adhere to the inner lining of the host's cells and effectively avoid being washed out of the gastrointestinal tract [61]. *ciaB* is a member of the *Campylobacter* invasion antigen (Cia) protein subfamily and plays a role in the invasion of epithelial cells. The bacteria require invasion into the epithelial cells totranslocate across the intestinal barrier and cause further disease and subsequent systemic spread[62]. Cytolethal distending toxin (CDT) genes *cdtA*, *cdtB*, and *cdtC* form the subunits of CDT that induce host cell cycle arrest and apoptosis. This leads to cell death and tissue damage which, in a way, are responsible for the symptoms associated with gastroenteritis such as diarrhea and inflammation [63]. The *flaA* and *flaB* genes are responsible for the motor flagellin

proteins that enable motion. Motility is crucial for the movement of *Campylobacter* in the mucous layers of the gastrointestinal tract to facilitate colonization and diffusiveness [64].

Genes involved in overcoming stress *htrA* encode a serine protease that is useful in the degradation of misfolded proteins and is useful in protein refolding under stress. This aids the bacterium to live under heat shock and oxidative stress, which are realities in the host organism [65]. *clpB* encodes a molecular chaperone that disaggregates and refolds proteins damaged by stress. This gene helps in surviving heat and osmotic stress, and hence helps in carrying out various functions within a cell during an infection [66]. *sodB* encodes superoxide dismutase, which is an enzyme that neutralizes reactive oxygen species. This helps the bacteria avoid oxidative stress, which is inflicted by the host immune system, and thus retains a foothold in the host. Other adaptations include *katA,* which encodes catalase that decomposes hydrogen peroxide into water and oxygen, which subsequently helps the bacterium to resist the host's immune system [67].

Even though there are differences in the primary roles of virulence and stress response genes in *Campylobacter*, there are instances where both are connected. For example, the ability to adhere to host cells and transgress their membranes (regulated by genes such as *cadF* and *ciaB*) not only helps bacteria cause disease, but also puts them in an environment that triggers a powerful immune response [63]. In such conditions, stress response genes such as *htrA* and *sodB* are found to play an important role in helping the bacteria to survive. Furthermore, it was established that some stress response mechanisms could promote survival in a way that is beneficial to pathogens [67]. For instance, while *sodB* and *katA* help the detoxification of reactive oxygen species to save the bacteria, they may also decrease local inflammatory reactions, which may otherwise hinder colonization and persistence. *Campylobacter* possesses an impressive inventory of virulence factors and stress response genes to facilitate infection, subvert/intrude the host defenses, and survive in harsh conditions within the host. These genes are genetically controlled, may exist analogously, and are linked; this makes the bacterial pathogenicity and survival strategies intricate [60].

In Egypt, as reported by Abdelhady et al. [58], they investigated the presence and expression levels of *flaA*, *cadF*, and *cdtB* genes. Among the 8 *C. coli* isolates, *flaA*, *cadF*, and *cdtB* genes were detected in 25%, 12.5%, and 75% of cases, respectively. Conversely, the single *C. jejuni* isolate expressed only *cadF* and *cdtB* genes, while the *flaA* gene remained undetectable. According to the research conducted by Ammar et al. [14], 25 isolates of *C. jejuni* were analyzed to detect three vital virulence genes pivotal for *C. jejuni*'s pathogenicity: *flaA*, *virB11*, and *wlaN*. Out of the 25 isolates examined, 13 (52%) were positive for the *virB11* gene, 9 (36%) for the *wlaN* gene, and all 25 (100%) for the *flaA* gene. In a separate investigation conducted in Egypt by Barakat et al. [38], the virulence profile of 302 *Campylobacter* isolates was examined. The findings revealed that all strains carried the *cadF* gene (100%), while the *cdtB* gene was detected in 284 out of the 302 isolates (94%). Specifically, 282 out of 285 (98.94%) of the *C. jejuni* isolates and 2 out of 17 (11.76%) of the *C. coli* isolates tested positive for the *cdtB* gene. Saif et al. [68] conducted an analysis of 90 *C. jejuni* isolates obtained from retail chicken using WGSF technology to identify the Multilocus Sequence Typing (MLST) of the isolates. This revealed 36 sequence types distributed across 15 clonal complexes (CCs). At the sequence type (ST) level, five types (ST-48, ST-21, ST-50, ST-464, and ST-122) were predominant, collectively representing 41.1% (37/90) of the isolates. Additionally, one novel ST (ST-10073) was identified. These findings highlight the significant role of retail chicken in transmitting campylobacteriosis to humans in Egypt, thus offering valuable insights to guide national control measures. Zeinhom et al. [37] detected the virulent *cadF* and *cdtA* genes in all the 40 *C. jejuni* isolates,

where 21 isolates were obtained from human stool and 19 were obtained from raw milk. As milk and dairy products are important sources of contamination, reducing the level of *C. jejuni* in them will lower the risk to consumers.

In Tunisia, Béjaoui et al. [42] found a high prevalence of virulence genes in *Campylobacter* strains, with an average of six genes per strain. The most commonly detected genes were *cadF*, *flaA*, *cdtA*, *cdtB*, and *cdtC*, with all strains (100%) testing positive for *flaA* and *cadF*. Genes related to cytotoxin production were notably prevalent, especially in *C. coli*, where all the isolates tested positive for the three *cdt* genes. In the *C. jejuni* isolates, *cdtA*, *cdtB*, and *cdtC* genes were also widespread, with proportions of 88% (n = 29/33), 73% (n = 24/33), and 76% (n = 25/33), respectively. The *ceuE* gene, which is responsible for encoding the enterochelin uptake substrate-binding protein involved in iron acquisition, was carried by 93.9% (n = 31/33) of *C. jejuni* isolates and 33.3% (n = 5/15) of *C. coli*. *virB11*, primarily involved in cell invasion, was detected in 36.4% of *C. jejuni* (n = 12/33) and 40% of *C. coli* (n = 6/15) isolates. The *cgtB* and *wlaN* genes, which encode a β-1, 3-galactosyltransferase enzyme associated with triggering Guillain-Barré syndrome, were also investigated, with the *cgtB* gene found in 21.2% (n = 7/33) of the *C. jejuni* isolates, while none of the strains carried the *wlaN* gene. Regarding the virulence patterns, 10 different virulotypes were identified, with the most prevalent combination being "*flaA*, *cadF*, *cdtA*, *cdtB*, *cdtC*, *ceuE*" detected in 13 isolates, followed by combinations such as "*flaA*, *cadF*, *cdtA*, *cdtB*, *cdtC*" and "*flaA*, *cadF*, *cdtA*, *cdtB*, *cdtC*, *ceuE*, *virB11*." Additionally, it was noted that the *C. jejuni* strains exhibited a statistically higher percentage of virulence genes (63.7% carried six or more genes; $p < 0.05$) compared to *C. coli* (only 46.7% carried six genes).

In a separate study conducted in the northern region of Tunisia by Gharbi et al. [69], a total of 177 *Campylobacter* isolates obtained from layer hens and eggs (124 *C. jejuni* and 53 *C. coli*) underwent examination to determine their virulotype. All 177 isolates (100%) were found to carry the *flaA*, *cadF*, *ciaB*, and *cdt* genes, with the *racR* gene closely following at 161 (90.9%). Similar findings were observed in the analysis of the 124 *C. jejuni* isolates, where all the isolates (100%) possessed the *flaA*, *cadF*, *ciaB*, and *cdt* genes, followed by *dnaJ* at 119 (95.9%) and *ceuE* at 115 (92.74%). No notable differences in the prevalence of the most common virulence genes were observed among *C. coli* isolates, as all of them contained the *flaA*, *cadF*, *racR*, *ciaB*, and *cdt* genes, with the *pldA* gene detected in 51 (96.22%) isolates. However, a significant difference was noted regarding the *ceuE* gene, which was absent in all *C. coli* isolates, though highly prevalent in the *C. jejuni* isolates (92.74%).

Another study conducted in Tunisia by Jribi et al. [70] provided additional insights into the pathogenic mechanisms of *Campylobacter* disease, focusing on 37 *C. jejuni* and 8 *C. coli* isolates. It studied the prevalence of essential virulence-associated genes such as *flaA*, *cadF*, *iamA*, and virB11 and the genes for CDT (*cdtA*, *cdtB*, and *cdtC*) among the strains isolated from poultry. The research provided an understanding of the various virulence markers of the *Campylobacter* strains that have been tested in this research study. At first, the research focused on genes that are linked to CDT, which is a toxin responsible for inducing cell cycle arrest and the eventual of cell death in sensitive eukaryotic cells. Activation of CDT synthesis required the expression of three toxin genes (*cdtA*, *cdtB*, and *cdtC*). Evaluations using PCR demonstrated that 86%, 42%, and 51% of the isolates harbored the *cdtA*, *cdtB*, and *cdtC* genes, respectively, with 31% of *Campylobacter* isolates containing all three toxin subunit genes simultaneously (Table 3).

Table 3. Presents the prevalence of virulence genes in *C. jejuni* and *C. coli* found in both food samples and humans across North Africa.

Country	Source	Isolates	Gene or ST	*C. coli* (%)	*C. jejuni* (%)	References
Egypt	Poultry	*C. jejuni* (*n* = 1)	*flaA*	25	(0)	[58]
		C. coli (*n* = 8)	*cadF*	12.5	100	
			cdtB	75	100	
	Human (100) and broiler chicken	*C. jejuni* (*n* = 25)	*flaA*	ND*	100	[14]
			virB11	ND	52	
			wlaN	ND	36	
	Humans and foods of animal	*C. jejuni* (*n* = 285)	*cadF*	100	0	[38]
		C. coli (*n* = 17)	*cdtB*	11.76	98.94	
	Human	*C. jejuni* (*n* = 90)	ST-48	ND	100	[68]
			ST-21	ND	100	
			ST-50	ND	100	
			ST-464	ND	100	
			ST-122	ND	100	
			ST-10073	ND	100	
	Raw milk, cheese, and human stool samples	*C. jejuni* (*n* = 40)	*cadF*	ND	100	[37]
			cdtA	ND	100	
Tunisia	Chicken meats	*C. jejuni* (*n* = 33)	*flaA*	100	100	[42]
		C. coli (*n* = 15)	*cadF*	100	100	
			cdtA	0	88	
			cdtB	0	72.7	
			cdtC	0	75.7	
			ceuE	33.3	93.9	
			virB11	40	36.4	
			cgtB	0	21.2	
			wlaN	0	0	
	Layer hens and eggs	*C. jejuni* (*n* = 124)	*flaA*	100	100	[69]
		C. coli (*n* = 53)	*cadF*	100	100	
			ciaB	100	100	
			cdt	100	100	
			racR	0	90.9	
			dnaJ	0	95.9	
			ceuE	0	92.74	
			pldA	96.22	0	
	Poultry and poultry products	*C. jejuni* (*n* = 37)	*flaA*	0	100	[70]
		C. coli (*n* = 8)	*cadF*	0	100	
			iamA	0	0	
			virB11	0	0	
			cdtA	0	86.66	
			cdtB	0	42.22	
			cdtC	0	51.11	

* ND: Not determined.

Studies performed in Egypt and Tunisia help in understanding the distribution of virulence genes and the transmission dynamics of *Campylobacter*. Studies conducted in Egypt by Abdelhady et al. [58], Ammar et al. [14], Barakat et al. [38], and Saif et al. [68] revealed different gene expression profiles and sequence types of the *Campylobacter* isolates obtained from poultry and retail chicken. Hence, these studies support the view that poultry is the main source of *Campylobacter* and emphasize the urgent need for rigorous control measures. Similarly, research carried out in Tunisia by Béjaoui et al. [42] and Gharbi et al. [69] examined the virulence factors and genetic characterization of *Campylobacter* strains obtained from poultry. The high incidence of virulence genes in *C. jejuni* and *C. coli* is an indication of the potential risk posed by contaminated poultry products to public health. Surprisingly, there were no studies identified from Algeria, Libya, or Morocco that revealed a gap in understanding the epidemiology of *Campylobacter* in North African countries. Further studies in these areas are crucial to compare the current knowledge about the prevalence, pathogenicity, and transmission patterns of *Campylobacter* and to establish effective measures to reduce the effect of this pathogen on public health.

7. Antibiotic resistance

The most investigated and pathogenically known species is *C. jejuni* within this genus; the identified antibiotic sensitivities include macrolides such as erythromycin, which are commonly used for its treatment, and quinolones such as ciprofloxacin [71]. Although *Campylobacter* enteritis commonly resolves without intervention, erythromycin or ciprofloxacin are preferred when antibiotic therapy is necessary. Nevertheless, *Campylobacter* resistance to antibiotics was recently observed and is increasing; in addition, different resistance patterns are detected worldwide [71,72]. There is a growing apprehension that the extended use of antibiotics in the context of veterinary practices and poultry production may augment the prevalence of antibiotic-resistant *Campylobacter* spp. Some of these strains could further be passed on to humans through the food chain [71,73].

Baali et al. [17] in Eastern Algeria studied 612 isolates obtained from chickens to analyze antimicrobial resistance. They reported that each strain showed resistance to ampicillin and amoxicillin/ clavulanic acid, and all the strains were sensitive to gentamicin resistance. Notably, the resistance patterns were high, with erythromycin at 83. 3% and tetracycline at 66. 2%. Furthermore, the resistance patterns showed moderate resistance to two antibiotics: ciprofloxacin (46. 7%) and chloramphenicol (52. 6%). In a different study that took place in Algiers, Messad et al. [34] evaluated the antimicrobial resistance patterns of 263 *Campylobacter* isolates obtained from numerous poultry farms and abattoirs. The authors reported that all the isolated strains were resistant to nalidixic acid, but sensitive to gentamicin and chloramphenicol. Additionally, 83.7% (n = 220) of the strains showed resistance to both tetracycline and ciprofloxacin, 75.3% (n = 198) to ampicillin, 46.8% (n = 123) to amoxicillin/clavulanic acid, and 21.7% (n = 57) to erythromycin.

In Egypt, Ammar et al. [14] conducted a study on 113 *C. jejuni* isolates gathered from both human (30) and chicken (83) sources to assess antimicrobial resistance. They found that all the examined isolates displayed complete resistance to both erythromycin and ampicillin (100% each). Additionally, the majority of *C. jejuni* isolates showed resistance to tetracycline (90.3%), trimethoprim/sulfamethoxazole (82.3%), and nalidixic acid (80.5%). Conversely, high rates of susceptibility were observed to gentamicin (69.9%), followed by kanamycin (67.3%) and norfloxacin (59.3%). Additionally, the authors observed no statistically significant differences in the resistance profiles among *C. jejuni* isolates obtained from the combined chicken and human samples, nor between different chicken samples, regarding the tested

antimicrobials ($p > 0.05$). However, a statistically significant difference was noted in the resistance profile to nalidixic acid between the *C. jejuni* isolates from chicken cloacal swabs and the human stool samples ($p = 0.016$). Regarding the antimicrobial resistance patterns among *C. jejuni* isolates from various sources, it was found that the resistance rates to tetracycline, nalidixic acid, and trimethoprim/sulfamethoxazole were more prevalent among the isolates from both chicken (91.6%, 83.1%, and 79.5%, respectively) and human (86.7%, 73.3%, and 90%, respectively) origins. Notably, all examined *C. jejuni* isolates were multidrug resistant (MDR), with 96.5% of the analyzed isolates showing resistance to five or more antimicrobial agents, and 25 *C. jejuni* isolates being resistant to 8 or 9 antimicrobials (22.1%).

According to another investigation in Egypt by El-Naenaeey et al. [35], an evaluation of the antimicrobial resistance among 247 *Campylobacter* isolates against 22 different antimicrobial agents revealed complete resistance in all isolates (100%) to ampicillin, amoxicillin, and erythromycin. Furthermore, the analysis indicated notably high resistance rates against trimethoprim-sulfamethoxazole (99%), clindamycin (97%), cephalothin (97%), azithromycin (91%), and nalidixic acid (90%). Additionally, a majority of *Campylobacter* isolates exhibited resistance to aztreonam (82%), doxycycline (81%), amoxicillin-clavulanic acid (81%), cefepime (81%), chloramphenicol (80%), colistin (76%), and linezolid (73%). Conversely, the findings indicated lower resistance rates for amikacin, imipenem, and cefoxitin against the tested isolates (29%, 32%, and 48%, respectively). (Top of Form)

In a study conducted in Kalyoubia, Egypt, on 19 *C. jejuni* isolates obtained from various sources to assess antimicrobial resistance, the researchers investigated the susceptibility of the isolated *C. jejuni* strains. The results revealed that *C. jejuni* showed resistance to ampicillin (21%), cephalothin (95%), oxytetracycline (63%), erythromycin (53%), nalidixic acid (64%), and gentamicin (5%) [47].

In Morocco, according to a study by Asmai et al. [52], an assessment of antimicrobial resistance was conducted among 42 *C. coli* isolates obtained from broilers in the Marrakesh Safi region. All strains exhibited resistance to one or more antimicrobial agents. The percentage of strains resistant to various antimicrobials, in descending order, was as follows: ampicillin (95%), erythromycin and tetracycline (93%), and ciprofloxacin (86%). The lowest resistance was observed for gentamicin (7%). MDR, which is defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories, was evident among the resistant isolates. Specifically, 42 (100%) were resistant to more than 2 classes of antibiotics, and 40 isolates (95%) displayed resistance to ≥3 drugs.

Baaboua et al. [40] carried out a separate study to assess antimicrobial resistance among 108 *C. jejuni* isolates and 22 *C. coli* isolates gathered from various food samples in Northern Morocco. The findings indicated that all isolates were nearly entirely susceptible to colistin and florfenicol across the four categories of specimens. Furthermore, there was a notably high level of susceptibility to gentamicin, streptomycin, and erythromycin, with *C. jejuni* exhibiting a higher proportion compared to *C. coli*. The resistance analysis revealed a complete resistance among the *C. jejuni* and *C. coli* strains to cephalothin, followed by a high percentage of resistance to aztreonam, enrofloxacin, trimethoprim-sulfamethoxazole, oxolinic acid, nalidixic acid, flumequine, and tetracycline across cattle, turkey, and various samples, particularly in broiler specimens for both species. Moreover, the study noted a widespread presence of multidrug-resistant *Campylobacter*, especially in *C. jejuni* (over 72%), predominantly in broiler chicken samples, across antibiotic categories including cephalosporin, penicillin, monobactam, quinolone, fluoroquinolone, sulfamide, and tetracycline. Es-soucratti et al. [51] observed the occurrence of antimicrobial resistance among *C. jejuni* isolates from poultry in Casablanca-Settat, Morocco. All isolates (41) exhibited resistance to tetracycline, with a notably high resistance observed

against erythromycin (97%), ampicillin (85%), and fluoroquinolone (ciprofloxacin) (77%). Resistance to gentamicin was observed to a lesser extent, at 12.0%. Similar resistance rates were also noted for amoxicillin/clavulanic acid (61.4%).

In Tunisia, according to findings by Béjaoui et al. [42], an examination of antimicrobial resistance was conducted on 48 *Campylobacter* isolates obtained from chicken meats. All isolates displayed resistance to tetracycline, with only one strain showing susceptibility to erythromycin. Resistance to ampicillin was observed in 83% of the isolates, whereas a higher susceptibility was seen towards amoxicillin/clavulanic acid, with 77% of isolates being susceptible. The resistance rates to ciprofloxacin, nalidixic acid, and chloramphenicol were recorded at 73%, 85.4%, and 75%, respectively. Additionally, thirteen strains (27%) exhibited resistance to gentamicin.

In Northern Tunisia, Gharbi et al. [53] investigated the prevalence of antibiotic resistance patterns among 91 *C. jejuni* and 41 *C. coli* isolates obtained from broiler chickens. They found that all isolates were resistant to tetracycline and erythromycin, with very high resistance observed against ciprofloxacin (98.9% and 100%) and chloramphenicol (84% and 100%) for *C. jejuni* and *C. coli*, respectively. Additionally, resistance rates were observed for ampicillin (74% and 34%), amoxicillin/clavulanic acid (53% and 34%), nalidixic acid (57% and 22%), and gentamicin (14% and 10%) for *C. jejuni* and *C. coli*, respectively. The distribution of antibiotic resistance genes in *C. jejuni* and *C. coli* isolated from broiler chickens in Tunisia was investigated. Among resistant isolates of *C. jejuni* and *C. coli*, the rates of antimicrobial resistance genes were as follows: *tet*(O), which encodes a ribosomal protection protein that confers tetracycline resistance, was present in 100% (91/91) and 80% (33/41) of the isolates, respectively; *cmeB*, which encodes an efflux pump that contributes to multidrug resistance, was found in 80% (73/91) and 100% (41/41) of the isolates, respectively; and $bla_{OXA\text{-}61}$, which encodes a beta-lactamase that provides resistance to beta-lactam antibiotics, was detected in 81% (54/67) and 93% (13/14) of the isolates, respectively. Notably, the *aphA*-3 gene, which encodes an aminoglycoside-modifying enzyme that provides resistance to aminoglycosides, was not detected in any isolate [62].

Gharbi et al. [43] observed a significantly high resistance among 106 *C. jejuni* and 49 *C. coli* isolates collected from eggs and laying hens in the North-East region of Tunisia. All isolates exhibited resistance to tetracycline, erythromycin, nalidixic acid, ciprofloxacin, and chloramphenicol. Notably, there was a high resistance rate (85.8%) among strains against ampicillin, with 98% of *C. coli* and 80% of *C. jejuni* being resistant. The percentage of isolates resistant to amoxicillin/clavulanic acid was 43% in *C. coli* compared to 18% in *C. jejuni*. The lowest rate of resistance was observed for gentamicin, with 1.9% among the *C. jejuni* isolates and 0% among the *C. coli* isolates.

8. Discussion

Campylobacter spp. presents a significant risk for transmission from infected animals or animal-derived products to humans, animals, and the environment. Recent research highlighted poultry products as a primary reservoir, with domestic poultry implicated in various regions worldwide. In North Africa, there is a growing concern regarding *Campylobacter* spp. infections in humans, primarily associated with *C. jejuni* and *C. coli*. Poultry, including chicken meat and eggs, emerges as a major source of these infections, as evidenced by studies conducted across Algeria, Egypt, Morocco, and Tunisia. Poultry is the leading animal reservoir for *C. jejuni* infections that are associated with gastroenteritis illness globally. Poultry and poultry products, especially chickens, are the primary source of *C. jejuni*. Previous research has established that well over half the retail poultry products are

likely to harbor *Campylobacter* [20]. The main ways through which the disease spreads to man are via ingestion of poultry products that are not well cooked or through direct contact between poultry products and humans via food handlers contaminated poultry products. *Campylobacter* is among the primary causative agents of bacterial diarrhea worldwide. *C. jejuni* is the most frequent isolate from patients affected by campylobacteriosis among all the *Campylobacter* species [32]. *C. jejuni* is especially well adapted to colonizing poultry; this is why this pathogen is found more commonly in poultry than other *Campylobacter* species. This adaptation helps it flourish in human infections, primarily due to the high rates of poultry meat consumption [27]. Moreover, studies showed the possibility that dairy products and other meats may also contribute to *Campylobacter* spp. transmission. Other ways the bacteria can spdread to humans include direct contact with infected animals, fecal matter, and contaminated food products or water, or coming across other environmental sources containing the bacteria. The dynamic and reciprocal relationship between population density, eating patterns, and food consumption in North Africa needs unique and specific public health approaches to prevent the effects of campylobacteriosis.

The threat of campylobacteriosis in North Africa is considerable due to its impact on public health and the fact that *C. jejuni* is the main cause of gastroenteritis. Several research studies performed in Egypt provided evidence of the high rates of *Campylobacter* spp. among individuals with gastrointestinal symptoms and that poultry could be a probable source of infection. Similarly, studies conducted in Tunisia enriched the knowledge of the common occurrence of *Campylobacter* spp. in human stool samples, and emphasized the need for comprehensive surveillance and control measures. Nonetheless, there were a few studies conducted in Algeria, Libya, and Morocco that underscored the gaps in understanding *Campylobacter* epidemiology in these regions, warranting further investigation to inform effective public health interventions.

The identification of virulence factors among *Campylobacter* spp. is important to understand the pathogenesis and capacity of bacteria to survive and persist. In Egypt and Tunisia, several scholars researched many virulence genes that were associated with *Campylobacter* pathogenicity, including adhesins, invasins, toxin production, and immune evasion. The determination of the virulence genes enhances the understanding of the risks associated with *Campylobacter* strains originating from poultry to human health. Moreover, the high genetic variation confirmed with the *Campylobacter* isolates reinforces the need for more surveillance and monitoring to identify virulence factors and create relevant control measures.

The spread of the antibiotic-resistant *Campylobacter* strains raises a potential concern in public health as it increases the difficulties in the effective treatments of *Campylobacter* infections. Investigations in various North African countries such as Algeria, Egypt, Morocco, and Tunisia have shown that *Campylobacter* isolates from chicken and human clinical specimens display strong resistances to antibiotics frequently employed in poultry production and human practices. This is further supported by the fact that resistance against several classes of antibiotics points towards the need for the appropriate use of antibiotics in vet practices and food animal production. It is necessary to enhance the tubules of surveillance and implement the principles of antimicrobial stewardship to tackle the emergence of *Campylobacter* antibiotic resistance and maintain the effectiveness of antimicrobial drugs for future generations.

In conclusion, this systematic review underlines the need to conduct further research and study of all the routes whereby *Campylobacter* transmits to humans in the North African nations. Frequent molecular studies from these countries have shown the factors of the pathogenicity of *Campylobacter*,

which point towards the importance of such findings for the application of prevention and control measures. Overall, these results portray the complexity of *Campylobacter* infections within the area. Furthermore, the review of antibiotics stresses the need for effective monitoring, the proper use of antibiotics, and combined approaches in the fight against the emergence of antimicrobial resistance in *Campylobacter*. Preventing approaches play a significant role in maintaining an individuals' health and ensuring the proper treatment strategy for *Campylobacter* infections. Collectively, dealing with these challenges aims to achieve the common goal of improving the overall condition of health and safety in North African countries.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Conflict of Interest

The author declare that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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