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Multi-drug resistance of micro-organisms isolated from cat skin and saliva of Quetta city

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Abstract

This study makes an assessment on the role of cats as potential carriers of pathogenic microorganisms. Totally, 360 samples from cats were collected and the pathogenic bacteria *E. coli spp., Klebsiella spp., Enterobacter spp., Pseudomonas aeruginosa* and *Staphylococcus aureus* were isolated from the different parts of cat's body. All the isolated bacteria were confirmed through different biochemical and sugar fermentation tests. A total of 8 antibiotics were used against each isolated bacteria to check the resistivity pattern. *E. coli spp.* were found highly resistant against Amoxicillin, Erythromycin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. *Enterobacter spp.* showed resistance against Amoxicillin, Colistin sulphate, Vancomycin and Rifampicin. The antibiotic resistivity pattern was observed in *Klebsiella spp.* against Amoxicillin, Erythromycin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. *Pseudomonas aeruginosa* were found highly resistant against most of the antibiotics, which includes Amoxicillin, Erythromycin, Vancomycin, Meropenem, Ceftazidime, Colistin sulphate and Rifampicin antibiotics. *Staphylococcus aureus* species were observed as highly resistant to almost all antibiotics such as Oxytetracycline, Amoxicillin, Ceftazidime, Erythromycin, Meropenem, Colistin sulphate and Rifampicin. The Oxytetracycline antibiotic was recorded as most effective drugs against all isolates except *Staphylococcus aureus* which was observed susceptible to only one antibiotics that is Vancomycin. Whereas Meropenem and Ceftazidime antibiotics were found effective against *Klebsiella spp.* and *Enterobacter spp.* The current finding of this study suggests that cats can act as potential vector and reservoir of some important bacterial pathogens.

Keywords: cats, vector, pathogen, potential carrier, susceptibility

1. Introduction

Microbial flora has spatial and temporal complexity that usually differs by individual, body niche, age, geographic location, health status, diet and type of host [1]. There is variation in the normal flora found in the oral cavity which depends on the area sampled (tooth enamel, tongue, gingivital surface, saliva) and the state of periodontal health [2]. Colony counts of aerobic bacteria from moist areas such as the axilla or toe web spaces can reach 10^7 bacteria per cm^2, whereas dry areas such as the forearm or trunk may harbor 10^2 or fewer bacteria per cm^2 [3]. Anaerobic bacteria are also present on skin, with colony counts to 10^6 bacteria per cm^2. Nutrients like lipids and protein (keratin) are provided by skin for selected colonizing bacteria. This dry and slightly acidic environment may limit the types of microbes that can survive on normal skin. The organisms compete for nutrients and space [4]. Many external factors can alter the ecosystem of the skin, with resulting changes in microbial populations [5]. Numerous bacteria have been cultivated from normal skin [3, 5]. These include *Staphylococci, Micrococci, Corynebacteria, Brevibacteria, Propionibacteria,* and *Acinetobacter* species [4].

There is growing antibiotic resistance found among many strains of pathogens in animals. Some have become resistant to many antibiotics and chemotherapeutic agents [6]. Ever since the discovery and subsequent clinical use of antibiotics, resistance to these agents has been observed [7]. There is use of large quantity of antibiotics for human therapy, as well as for farm animals and fish in aquaculture. The bacteria may accumulate multiple genes, each coding for resistance to a single drug, within a single cell. This accumulation occurs typically on resistance plasmids. There is increased expression of genes that code for multidrug efflux pumps, extruding a wide range of drugs [6]. There are three general mechanisms studied to confer antibiotic resistance namely: prevention of interaction of the drug with target, efflux of the antibiotic from the cell, and direct destruction or modification of the compound [8].

To be effective, antibiotics must accumulate in the bacterial cytoplasm. Poor permeability of outer membrane in Gram negative organisms hinders the accumulation of the drug and it pumps out the antibiotics. Gram-positive bacteria rely only to the later mechanism of protection [9]. The spread of resistant bacteria within the community increases problems for infection control [10].

Zoonoses are infectious diseases that can be transmitted naturally between humans and wild or domestic animals. These diseases are important in the context of emerging infectious diseases of humans. Cleaveland *et al*. [11] identified 1,415 species of infectious organisms known to be pathogenic to humans, including 217 viruses and prions, 538 bacteria and rickettsia, 307 fungi, 66 protozoa and 287 helminths. Some pathogens are largely confined to animal reservoirs-human cases are infrequent or represent dead-end infections (e.g. anthrax, rabies, west nile and nipah/hendra viruses), whereas others are well-established in both animals and humans (e.g. bovine tuberculosis, salmonellosis). Zoonotic diseases have relatively little impact on human health when compared to major diseases such as influenza (flu), measles, smallpox, diphtheria, or HIV/acquired immune deficiency syndrome (AIDS). It is however, increasingly clear that most of these diseases started out as zoonotic and the aetiology of the pandemics that have occurred during the 20th Century tend to support the notion that emerging diseases in humans originated directly from animal reservoirs rather than gradually evolving from known and existing zoonotic agents [12].

Several million people are bitten by animals every year which result in about 300,000 visits to emergency departments, 10,000 hospitalizations, and 20 deaths, which include large number of the young children [13]. In which Ninety percent of these bites are cats, and 28 to 80 percent of cat bites become infected, which cause the occasional consequence of meningitis, endocarditis, septic arthritis, and septic shock [14]. Bacteriologic analyses of these wound infections have focused on certain zoonotic and potentially invasive pathogens such as *Pasteurella multocida*, Capnocytophaga canimorsus (DF-2), and Weeksella zoohelcum [15].

Hundreds of millions of cats are kept as a pet around the world. Cat have either mutualistic or commensal relationship with humans. Cat are the common pets in all continent of the world (excluding Antarctica), and their global population is difficult to a certain, with estimate ranging from anywhere between 200 million to 600 million. That’s why we chose the “cat” over other pet animals for this research. Cat’s saliva and different body parts contain number of micro- organisms, which may get resistant to the antibiotics, and other antimicrobial agents. There are chances that humans may get infected with those microorganisms, and if infection gets spread into human it will be very difficult to treat. The objective of this research was to isolate, identify and check antibiotic resistance in isolated bacterial pathogens from saliva and different body parts of cats.

2. Materials and methods

2.1. Sample collection

This study was conducted in “Centre for Advanced Studies in Vaccinology and Biotechnology (CASVAB)” University of Balochistan, Quetta, and an ethics approval was taken from the same research institute. The current study was conducted at the above premises during the period March to December 2019. During which different micro- organisms were isolated and identified from the cat’s body and saliva. A total of 360 samples were randomly collected from 4 different body sites such as skin, body fur, tail fur and saliva of cat. Sample collection was done by swabbing with sterile cotton ear buds from cat’s saliva and different body parts (body fur, tail fur and skin). Samples were collected in sterile tubes and brought to laboratory for further procedure.

2.2 Isolation and identification

All the bacterial isolates were identified using morphological, microscopy and biochemical tests following standard procedures.

2.3 Culture of the samples

All the samples were cultured primarily in brain heart infusion broth at 37°C for 24 hour, then sub cultured onto the eosin methyl blue agar, mannitol salt agar, Pseudomonas cetrimide agar plate to observe the colony morphology (shape, size, surface texture, edge, elevation, color and opacity etc.). The organisms showing characteristic colony morphology was repeatedly sub cultured onto their selective agar until the pure culture with homogenous colonies were obtained.

2.4 Gram’s staining method

Gram’s staining was performed as per procedures described by Merchant & Packer [16] to determine the size, shape and arrangement of bacteria.

2.5 Biochemical characterization

The biochemical test employed were IMVIC (Indole production, methyl red, voges proskauer, citrate tests) sugar fermentation tests (glucose, dextrose, sorbitol, mannitol, trehalose, inositol and mannose) catalase, oxidase and urease tests for the confirmation of isolates following standardized procedure [17].

2.6 Antimicrobial susceptibility testing

Antimicrobial susceptibility was performed on Mueller-Hinton agar following the standard disk diffusion method recommended by Clinical and Laboratory Standards Institute. The isolates were streaked on nutrient agar and incubated for 24 hour at 37°C. The opacity was adjusted to 0.5 McFarland opacity standards and inoculums were well spread over the agar surface with the help of sterilized swab. Then, following commercially available antibiotics and disc potencies were used: OT: Oxytetracycline (30µg), AML: Amoxicillin (25µg), CAZ: Ceftazidime (30µg), E: Erythromycin (15µg), MEM: Meropenem (10µg), CT: Colistin sulphate (25µg), VA: Vancomycin (30µg), RD: Rifampicin (05µg). The antimicrobial discs were placed at equi-distance and the antibiotic discs were gently and firmly placed with forceps on the agar plates. The plates were then incubated at 37°C for 24 hours. The diameter of the inhibition zones was measured in millimeter at 24 hours using a scale. An organism was interpreted as highly susceptible if the diameter of inhibition zone was more than 10 mm and resistant if the diameter was less than 10 mm. [18].

3. Results

The cats were belonged to family Felidae and genus *Felis*. Out of 360 samples, 88.8% were found positive for bacterial pathogens, while 11.1% were found negative as shown in Figure-1.

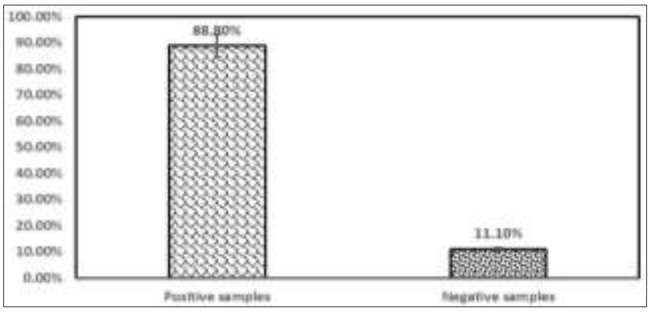

Fig 1: Percentage of positive and negative samples for bacterial pathogens isolated from various body sites of cats

The study results revealed the higher percentage of contamination in body fur (97.50%) followed by skin (94.40%), tail fur (93.50%) and least in saliva (92%) as shown in Figure-2.

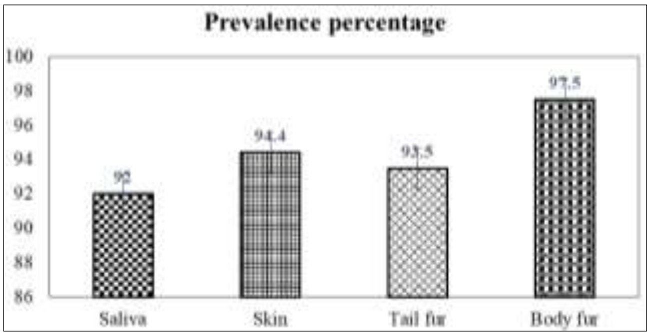

Fig 2: Prevalence % age of bacterial pathogens from different sites of cat body

The *E. coli spp*. isolated from body fur were (40%), from saliva (35%), from tail fur (30%) and from skin (30%). The *E. coli* was found higher in saliva and body fur as compared to other parts of body as shown in Figure-3.

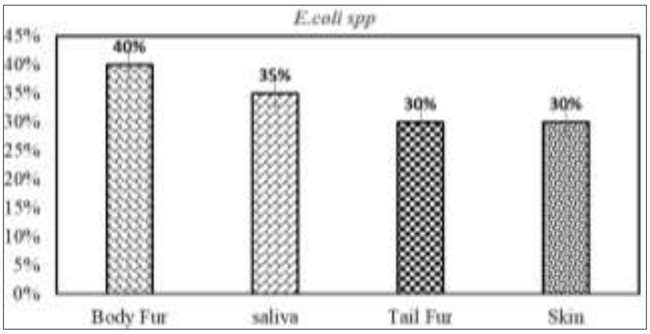

Fig 3: The overall prevalence of *E. coli spp.* in cat's body

The *Klebsiella spp.* isolated from tail fur were (45%), from skin (35%), from body fur (35%) and from saliva (30%). The tail fur of cats was observed more contaminated with *Klebsiella spp.* as compared to other parts of body as shown in Figure-4.

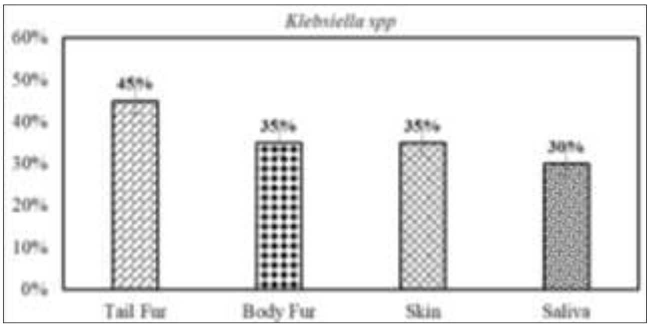

Fig 4: The overall prevalence of *Klebsiella spp.* in cat's body

The *Enterobacter spp.* isolated from saliva were (75%), from tail fur (55%), from skin (40%) and from body fur (40%). The saliva and tail fur of the cats was observed more contaminated with *Enterobacter spp.* as compared to the other part of body as shown in Figure-5.

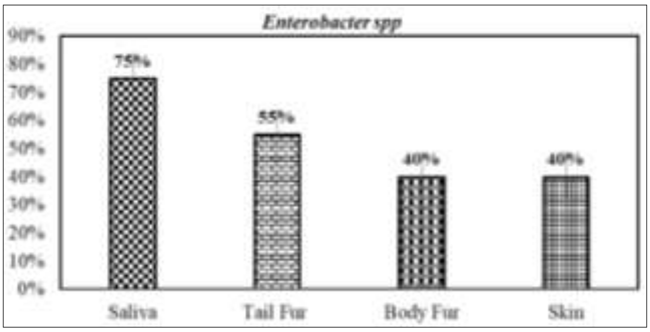

Fig 5: The overall prevalence of *Enterobacter spp.* in cat's body

The rate of isolation of *Pseudomonas aeruginosa* was found higher in saliva (65%) followed by body fur (40%), tail fur (40%) and skin (25%). The saliva was more contaminated with *Pseudomonas aeruginosa* as compared other part of body of cat as shown in Figure-6.

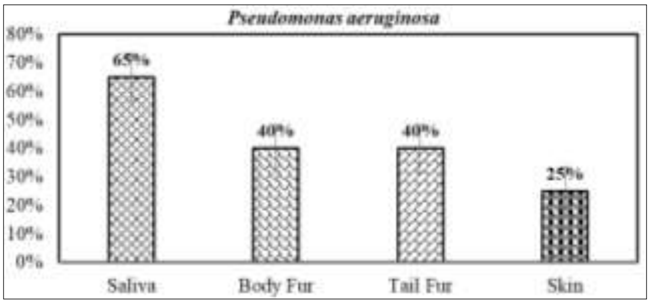

Fig 6: The overall prevalence of *Pseudomonas aeruginosa* in cat's body

The *Staphylococcus aureus* isolated from skin were (65%), from tail fur (65%), from body fur (55%) and from saliva (45%). The skin and tail fur of the cats was more contaminated with *Staphylococcus aureus* as compared to the other part of body as shown in Figure-7.

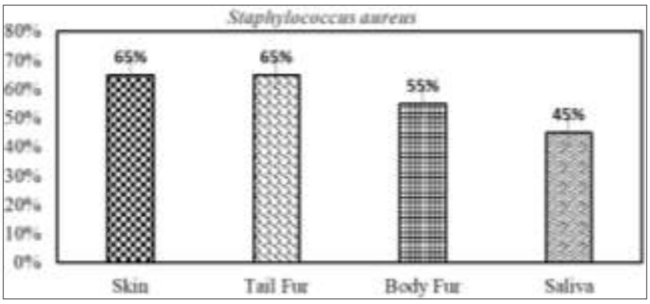

Fig 7: The overall prevalence of *Staphylococcus aureus* in cat's body

Biochemical tests

Gram negative isolates, *Pseudomonas aeruginosa*, *Enterobacter spp.*, *Klebsiella spp.* and *E.coli spp.* were observed as pink straight and clustered rods while gram positive isolates, *Staphylococcus aureus* appeared as round purple color in clustered cocci under the microscope after gram staining.

Biochemical tests including IMVIC, sugar fermentation tests, catalase test, oxidase test and urease tests were successfully applied, and results were summarized in Table 1.

Table 1: Biochemical tests applied for classical bacterial species identification isolated from cat's different parts of body.

Gram staining	IMVIC test				Other biochemical tests test			Sugar fermentation tests						
Biochemical tests	**Indole Production Test**	**Methyl Red Test**	**Voges Proskauer Test**	**Simmon Citrate Test**	**Catalase Test**	**Oxidase Test**	**Urease Test**	**Glucose Fermentation Test Test**	**Dextrose Fermentation Test**	**Sorbitol Fermentation Test**	**Mannitol Fermentation Test**	**Trehalose Fermentation Test**	**Inositol Fermentation Test**	**Mannose Fermentation Test**
E.coli spp. Gram negative bacteria Rod shaped Facultative anaerobe	+	+	-	-	+	-	-	+	+	+	+	+	-	-
Enterobacter spp. Gram negative bacteria Rod shaped Facultative anaerobe	-	-	+	+	+	-	-	+	+	+	+	+	+	+
Klebsiella spp. Gram negative bacteria Rod shaped Facultative anaerobe	-	-	+	+	+	-	+	+	+	+	+	+	+	+
Pseudomonas aeruginosa Gram negative bacteria Rod shaped Facultative anaerobe	-	-	-	+	+	+	-	+	-	-	+	-	-	-
Staphylococcus aureus Gram positive bacteria Round shaped Facultative anaerobe	-	+	+	+	+	-	+	+	+	-	+	+	-	+

Table 2: Antimicrobial resistance and sensitivity evaluated for gram positive and negative bacterial species isolated from cats of Quetta Balochistan

Bacterial isolates						
	Antibiotic name	***Pseudomonas aeruginosa***	***Klebsiella Spp.***	***E.coli Spp.***	***Staphylococcus aureus***	***Enterobacter Spp.***
	Gram	G-Negative	G-Negative	G-Negative	G-Positive	G-Negative
1	Oxytetracycline	16mm	17mm	19mm	Resistance	24mm
2	Amoxicillin	Resistance	Resistance	Resistance	Resistance	Resistance
3	Ceftazidime	Resistance	26mm	22mm	Resistance	28mm
4	Erythromycin	Resistance	Resistance	Resistance	Resistance	18mm
5	Meropenem	Resistance	28mm	35mm	Resistance	28mm
6	Colistin sulphate	Resistance	Resistance	Resistance	Resistance	Resistance
7	Vancomycin	Resistance	Resistance	Resistance	18mm	Resistance
8	Rifampicin	Resistance	Resistance	Resistance	Resistance	Resistance

Antibiotic susceptibility test

A total of 8 antibiotics from 8 different classes were used against each isolated bacteria to check the patterns of sensitivity and resistivity of isolates. Results revealed that most of the bacterial pathogens were highly sensitive to Oxytetracycline (Tetracycline), Ceftazidime (Cephalosporin) and Meropenem (Carbapenem) as shown in Table-2.

During antibiotic experimental trial the bacterial pathogen *E.coli spp.* was found highly sensitive against Meropenem (35mm), Ceftazidime (22mm), and Oxytetracycline (19mm) antibiotics. Resistance pattern were observed against Amoxicillin, Erythromycin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. *Enterobacter spp.* showed resistance against Amoxicillin, Colistin sulphate, Vancomycin and Rifampicin. *Enterobacter spp.* were observed more sensitive to Ceftazidime (28mm), Meropenem (28mm), Oxytetracycline (24mm) and Erythromycin (18mm) antibiotics. The antibiotic resistivity pattern was observed in *Klebsiella spp.* against Amoxicillin, Erythromycin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. *Klebsiella spp.* were found highly sensitive to Meropenem (28mm), Ceftazidime (26mm) and Oxytetracycline (17mm) antibiotics. *Pseudomonas aeruginosa* was found highly resistant against most of the antibiotics, which includes Amoxicillin, Erythromycin, Vancomycin, Meropenem, Ceftazidime, Colistin sulphate and Rifampicin antibiotics. *Pseudomonas aeruginosa* showed sensitivity to a lesser extend to Oxytetracycline (16mm). *Staphylococcus aureus* species were observed as highly resistant to almost all antibiotics including Oxytetracycline, Amoxicillin, Ceftazidime, Erythromycin, Meropenem, Colistin sulphate and Rifampicin except class Glycopeptide (Vancomycin) which was used during experimental trial of antibiotic sensitivity. Antibiotics sensitivity pattern of *Staphylococcus aureus* was only seen in Vancomycin (18mm) as shown in Table-2.

5. Discussion

Animal domestication has spread from long ago, the number of households keeping animals has increased, and the relationship between humans and animals has become closer under the life environment in contemporary society where technology has developed. The connection of humans and companion animals has been specifically defined as an attachment that is friendly and involves physical and psychological effects [19]. Recently, pets have been renamed companion animals [20], because changes have refined the relationship between humans and pets. However, companion animals are associated with a risk of transmission of pathogenic bacteria to humans (zoonoses). More than 200 infectious diseases of animals have been confirmed worldwide [21].

Humans may acquire antimicrobial-resistant bacteria or the corresponding resistance genes via contact with their companion animals. Several studies in the literature indicated or carried out for the isolation of different pathogenic micro-organisms from the various parts of cats around the globe. There is a potential risk of transmission of these bacteria to humans from infected or colonized companion animals. In addition, there is the possibility of transfer of resistance genes [22].

In the present study, 5 bacterial strains have been isolated from various parts of cat’s body such as body fur, tail fur, skin and saliva. Body fur (97.5%) exhibited the high rate of prevalence of isolates, followed by skin (94.4%) and tail fur (93.5%) while least prevalence was noticed (92%) from saliva.

Our findings show the frequency of contamination of bacterial species varies among type of sample, the tail fur and skin were found more contaminated in a similar rate with *Staphylococcus aureus. Pseudomonas aeruginosa* was isolated more frequently from saliva and body fur of the cats. The frequency of isolation of *E. coli spp.* was found higher in saliva and body fur. The *Klebsiella spp.* were observed dominantly in tail fur while the rate of isolation in body fur and skin of the cats were observed similar. The saliva and tail fur of the cats were detected more contaminated with *Enterobacter spp.* as compare to the other parts of body.

In our study overall, *Staphylococcus aureus* showed resistant against all classes of antibiotics except Vancomycin, our findings were similar to the findings of Lilenbaum *et al* [23], who reported that *Staphylococcus aureus* isolated from skin samples of clinically healthy cats showed resistance to Rifampicin and Amoxicillin antibiotics. Our study showed resistance to macrolides (Erythromycin) like previous study [24, 25]. While Vancomycin was the only antibiotic that was susceptible against *Staphylococcus aureus* in this study. In our report *Staphylococcus aureus* isolates showed resistance to Ceftazidime and Meropenem antibiotics, our findings were similar to observations by Ibadin *et al* [26].

Pseudomonas aeruginosa was also observed resistant to all antibiotics except Oxytetracycline. Similar kind of results were described by Ahmadi *et al* [27]. An Iranian investigation [28] showed that *P. aeruginosa* strains of clinical infections exhibited resistance to Erythromycin. Another study which was conducted on the *Pseudomonas aeruginosa* veterinary strains recovered from dogs, cats and bovine from the French network Resapath [29] confirm the occurrence of Carbapenem (Meropenem) resistance in strains infecting animals. Our findings were similar to the previous study antibiogram of ESBL producing *P. aeruginosa* that showed high-level resistance to Ceftazidime and Rifampicin [30].

In the present study *Klebsiella spp.* were found resistant againts Amoxicillin, Erythromycin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. A research study conducted earlier in South East Region of Bangladesh [31] reported *Klebsiella* isolates exhibited resistance to Amoxicillin isolated from urine, swab, pus and sputum samples. Suh *et al* [32] worked on *Klebsiella pneumoniae* in tertiary care South Korean hospitals and found Colistin sulphate resistance *Klebsiella spp.* isolates from blood samples. In our study *Klebsiella spp.* were found sensitive to Oxytetracycline which was in good agreement with Bhattacharya *et al* [33].

In present study the *E.coli spp.* showed high resistance to Erythromycin, Amoxicillin, Colistin sulphate, Vancomycin and Rifampicin. The results of this study are in line with the findings of other studies conducted in different parts of the world. In an Ethopian study *E.coli spp.* were isolated from different clinical samples showed high resistance rates to Erythromycin [25] and Amoxicillin [34]. Rao *et al.,* [35] reported *E. coli* isolates were highly sensitive to Meropenem. The antibiogram revealed that all *E. coli* isolates were found resistant against Vancomycin. Similar resistance patterns have been reported in other study from

Nigeria [36]. In present study isolate of *E. coli* were found resistant to Colistin sulphate, this finding is similar to Hassan *et al* [37].

Enterobacter spp. showed resistance against Amoxicillin, Colistin sulphate, Vancomycin and Rifampicin antibiotics. Sharma *et al* [38] reported isolates of *Enterobacter spp.* exhibited multidrug resistance pattern and were found resistant to Rifampicin, Ceftazidime, Vancomycin and sensitive to class Tetracycline from the samples of acute respiratory tract infected camels. The results of the present study confirm that all *Enterobacter spp.* were found sensitive to Ceftazidime antibiotic as observed in previous research [39]. *Enterobacter spp.* isolated from feline and canine urine samples showed sensitivity to erythromycin, similar resistance patterns have been reported in another study [40]. In this study, Meropenem were most sensitive against *Enterobacter spp.* which is supported by other reports [41]. In current study resistance to Amoxicillin was observed in *Enterobacter* species, similar findings regarding drug resistance patterns of *Enterobacter spp.* have been observed by another researcher [42]. In the current study, *Enterobacter spp*. were observed resistant to Colistin, Similar findings have been described by Jayol *et al.* [43]

6. Conclusion

Cats are considered one of the most innocent and favorite pet animal, in human society specially in children, that's why are allowed to go indoors or outdoors freely. In this study number of pathogenic bacteria were isolated from cat's saliva and different body parts. *E. coli spp.*, *Enterobacter spp. Klebsiella spp.* and *Pseudomonas aeruginosa* commonly cause infectious diseases. *Staphylococcus aureus* have caused medically important infectious diseases transmitted from pets. Humans are always exposed to pathogenic bacteria through contact indoor and outdoor via animal feces, saliva, animal bites, scratches, contact with infected animal products such as skin, hair, excreta and parasites (ticks and fleas) and aerosol transmission over long distances. Our results suggest that not only bites and scratches of cats but also direct contact with cats can play a role in transmitting infectious diseases. The close contact between cats and humans offers favorable conditions for the transmission of bacteria by direct contact (petting, licking, physical injuries, etc.) or through the domestic environment (contamination of food, furnishings, etc.). Children are at greater risk than adults because of their closer physical contact with cats as well as with household environments contaminated by pets (floors, carpets etc.). Owners of animals should have correct knowledge about infectious diseases for their prevention and should use proper methods to reduce the risk of contact with pathogenic bacteria**.** All the isolates were found multidrug resistance as they showed resistance against more than 4 antibiotics**.** The higher sensitivities were observed in Oxy-tetracycline, Meropenem and Ceftazidime antibiotics from almost all isolates except *Staphylococcus aureus* and *Pseudomonas aeruginosa* that were observed susceptible only to vancomycin and oxytetracycline respectively. The present outcome of this research study proposes that cats can play an important role as a reservoir and vector of some important pathogenic micro-organisms.

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