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Antimicrobial Susceptibility of *Gram-negative* Bacteria Isolated from Clinical Isolates in Patients in El Jalaa Hospital for Surgery and Accidents in Benghazi City – Libya

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Abstract— ***Background: Gram-negative bacteria are most often resistant to antibiotics because of the acquisition of resistant genes or gene mutation. Studies have shown that newly developed antibiotics will shortly fail to be active against the bacteria because of the emergence of resistance. Aim: The aim of study was to evaluate the influence on the development of antibiotic resistance in these bacteria. Materials and Methods: 95 anatomical isolations from different clinical samples of negative gram bacteria were sent to the Medical Laboratories Department of Al-jalaa Hospital for Surgery and Accidents in the city of Benghazi-Libya between March 2022 and April 2022 and the antibiotics commonly used during the study period were used for all samples and antibiotics also showed activity in the laboratory regularly against all cultured organisms. Results: In this study, among 24(25.3%) samples from males and 71(74.7%) samples from women suspected of having gram-negative bacteria in Al-Galaa Hospital (Benghazi). Out of this ,7 (7.7%) were Proteus bacilla spp and 5 (5.3 %) were Alcaligenes faecalis. E. coli 41 (43.2 %) was the most frequently isolated gram-negative bacteria followed by Pseudomonas spp .15 (15.8 %) klebsiella spp 14 (14.7 %) Moraxella catarrhalis 11 (11.6%) and the least frequent was Neisseria meningitidis 1 (1.1%) and salmonella 1 (1.1 %). Conclusions: Our study shows that in our environment, gram-negative bacteria may be resistant to Antibiotics. The consumption of antibiotics in our society is one of the main drivers of the emergence and the spread of antibiotic resistance to bacteria, which poses a serious global threat to public health and clinical medicine.***

Keywords- ***Gram-negative Bacteria, hospital, patients***

I. INTRODUCTION

A Alcaligenes faecalis

Alcaligenes is a genus of Gram-negative, aerobic, rod-shaped bacteria. The species are motile with amphitrichous flagella and rarely nonmotile. It is a genus of non-fermenting bacteria (in the family *Alcaligenaceae*). Additionally, some strains of *Alcaligenes* are capable of anaerobic respiration, but they must be in the presence of nitrate or nitrite; otherwise, their metabolism is respiratory and never fermentative; The genus does not use carbohydrates. Strains of *Alcaligenes*(such as *A.faecalis*) are found mostly in the intestinal tracts of vertebrates, decaying materials, dairy products, water, and soil; they can be isolated from human respiratory and gastrointestinal tracts and wounds in hospitalized patients with compromised immune systems. They are occasionally the cause of opportunistic infections, including nosocomial sepsis[1].

B. Moraxella catarrhalis:

Moraxella catarrhalis is a gram-negative *diplococcus*, formerly known as Neisseria catarrhalis or Branhamella catarrhalis, that is found in the human upper respiratory tract as normal flora and was considered to occasionally cause infections.[2]

C. Klebsiella:

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Klebsiella is a genus of Gram-negative, oxidase-negative rod shaped bacteria with a prominent polysaccharide-based capsule.[3] *Klebsiella* species are found everywhere in nature. This is thought to be due to distinct sublineages developing specific niche adaptations, with associated biochemical adaptations which make them better suited to a particular environment. They can be found in water, soil, plants, insects and other animals including humans.[4][5] *Klebsiella* is named after German-Swiss microbiologist Edwin Klebs (1834–1913).

Carl Friedlander described *Klebsiella* bacillus which is why it was termed Friedlander bacillus for many years. The members of the genus *Klebsiella* are a part of the human and animal's normal flora in the nose, mouth, and intestines. The species of *Klebsiella* are all gram-negative and usually non-motile. They tend to be shorter and thicker when compared to others in the family Enterobacteriaceae. The cells are rods in shape and generally measures 0.3 to 1.5 µm wide by 0.5 to 5.0 µm long. They can be found singly, in pairs, in chains or linked end to end. *Klebsiella* can grow on ordinary lab medium and do not have special growth requirements , like the other members of Enterobacteriaceae.

The species are aerobic but facultatively anaerobic. Their ideal growth temperature is 35° to 37 °C, while their ideal pH level is about 7.2.[6] *Klebsiella pneumoniae*, or *Klebsiella spp*, is a type of gram-negative rod-shaped bacteria that can cause different types of infections ranging from pneumonia (lung), blood infections (septicaemia), wound or surgical infections, urinary tract infections, small intestinal bowel overgrowth (SIBO), ankylosing spondylitis, Crohn's disease, ulcerative colitis, and meningitis (brain) [7]

D. Neisseria meningitidis:

Neisseria meningitidis, often referred to as *meningococcus*, is a Gram-negative bacterium that can cause meningitis and other forms of meningococcal disease such as meningococcemia, a life-threatening sepsis. The bacterium is referred to as a coccus because it is round, and more specifically a diplococcus because of its tendency to form pairs. [8]

E. . Proteus bacilli

Proteus is a genus of Gram-negative bacteria. *Proteus bacilli* are widely distributed in nature as saprophytes, being found in decomposing animal matter, sewage, manure soil, the mammalian intestine, and human and animal feces. They are opportunistic pathogens, commonly responsible for urinary and septic infections, often nosocomial.[9]

F. . Pseudomonas:

Pseudomonas is a genus of Gram-negative, Gamma proteobacteria, belonging to the family Pseudomonadaceae and containing 191 described species.[10]The members of the genus demonstrate a great deal of metabolic diversity and onsequently are able to colonize a wide range of niches [11]. Their ease of culture in vitro and availability of an increasing number of *Pseudomonas* strain genome sequences has made the genus an excellent focus for scientific research; the best studied species include P. aeruginosa in its role as an opportunistic human pathogen, the plant pathogen P. syringae, the soil bacterium P. putida, and the plant growth-promoting P. fluorescens, P. lini, P. migulae, and P. graminis. [12][7] Because of their widespread occurrence in water and plant seeds such as dicots, the pseudomonads were observed early in the history of microbiology. The generic name Pseudomonas created for these organisms was defined in rather vague terms by Walter Migula in 1894 and 1900 as a genus of Gram-negative, rod-shaped, and polar-flagellated bacteria with some sporulating species.[13][14] The latter statement was later proved incorrect and was due to refractive granules of reserve materials.[15] Despite the vague description, the type species, Pseudomonas pyocyanea (basonym of Pseudomonas aeruginosa), proved the best descriptor.[15]

G. Salmonella:

Salmonella is a genus of rod-shaped (bacillus) Gram-negative bacteria of the family Enterobacteriaceae. The two species of *Salmonella* are *Salmonella enterica* and *Salmonella bongori*. *S. enterica* is the type species and is further divided into six subspecies[16][17] that include over 2,600 serotypes.[18] *Salmonella* was named after Daniel Elmer Salmon (1850–1914), an American veterinary surgeon.
Salmonella species are non-spore-forming, predominantly motile enterobacteria with cell diameters between about 0.7 and 1.5 µm, lengths from 2 to 5 µm, and peritrichous flagella (all around the cell body, allowing them to move)[19]. They are chemotrophs, obtaining their energy from oxidation and reduction reactions , using organic sources . They are also facultative anaerobes, capable of generating ATP with oxygen ("aerobically") when it is available, or using other electron acceptors or fermentation ("anaerobically") when oxygen is not available. [19] *Salmonella* species are intracellular

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pathogens[20]; of which certain serotypes cause illness. Most infections are due to ingestion of food contaminated by animal feces, or by human feces, such as by a food-service worker at a commercial eatery. *Salmonella* serotypes can be divided into two main groups—typhoidal and nontyphoidal. Nontyphoidal serotypes are zoonotic and can be transferred from animal-to-human and from human-to-human. They usually invade only the gastrointestinal tract and cause salmonellosis, the symptoms of which can be resolved without antibiotics. However, in sub-Saharan Africa, nontyphoidal *Salmonella* can be invasive and cause paratyphoid fever, which requires immediate treatment with antibiotics. Typhoidal serotypes can only be transferred from human-to-human, and can cause food-borne infection, typhoid fever, and paratyphoid fever[3]. Typhoid fever is caused by *Salmonella* invading the bloodstream (the typhoidal form), or in addition spreading throughout the body, invading organs, and secreting endotoxins (the septic form). This can lead to life-threatening hypovolemic shock and septic shock, and requires intensive care including antibiotics.

H. Escherichia coli

"*E. coli*" redirects here. For the protozoan commensal, see Entamoeba coli. For the grey whale, see Eschrichtius robustus. This article is about *Escherichia coli* as a species. For *E. coli* in medicine, see Pathogenic Escherichia coli. For E. coli in molecular biology, see Escherichia coli (molecular biology).[21][22] Also known as *E.coli*[22] is a Gram-negative , facultative anaerobic , rod shaped, coliform bacterium of the genus Escherichia that is commonly found in the lower intestine of warm-blooded organisms[23]. Most E. coli strains are harmless, but some serotypes (EPEC, ETEC etc.) can cause serious food poisoning in their hosts, and are occasionally responsible for food contamination incidents that prompt product recalls[24][25]. The harmless strains are part of the normal microbiota of the gut, and can benefit their hosts by producing vitamin K_2[26], and preventing colonisation of the intestine with pathogenic bacteria, having a mutualistic relationship[27][28]. E. coli is expelled into the environment within fecal matter. The bacterium grows massively in fresh fecal matter under aerobic conditions for three days, but its numbers decline slowly afterwards [29].
E.coli and other facultative anaerobes constitute about 0.1% of gut microbiota[30] and fecal–oral transmission is the major route through which pathogenic strains of the bacterium cause disease. Cells are able to survive outside the body for a limited amount of time, which makes them potential indicator organisms to test environmental samples for fecal contamination [30][31]. A growing body of research, though, has examined environmentally persistent E. coli which can survive for many days and grow outside a host [32].
The bacterium can be grown and cultured easily and inexpensively in a laboratory setting and has been intensively investigated for over 60 years. E. coli is a chemoheterotroph whose chemically defined medium must include a source of carbon and energy[33]. *E. coli* is the most widely studied prokaryotic model organism, and an important species in the fields of biotechnology and microbiology, where it has served as the host organism for the majority of work with recombinant DNA. Under favorable conditions, it takes as little as 20 minutes to reproduce.[34]

Diseases.

Alcaligenes faecalis: Alcaligenes spp. are opportunistic human pathogens causing sporadic cases of pneumonia, septicemia, peritonitis, urinary tract, and other infections. Achromobacter xylosoxidans and *Alcaligenes faecalis* are the most common isolates and agents of human disease in these genera, but little is known about factors promoting virulence. BSI, meningitis, and pneumonia are among the most common forms of infection, although these organisms have been recovered from many other sites including peritoneal fluid in CAPD, joint fluid, bone, and urine.[35]

Moraxella catarrhalis: M. catarrhalis is a recognized pathogen of upper and lower respiratory tract infections.[8] It has been found as the causative agent in infections, such as empyema, endocarditis, otitis media, and pneumonia, both in children and adults.[36] The beta-lactamase-producing *M. catarrhalis* not reported before 1976 is the significant cause of varying patterns of resistance.[37] The increase in occurrence of beta-lactamase strains can be regarded as the fastest dissemination of beta-lactamases within a bacterial species.[9]M. catarrhalis has particularly become an important pathogen in patients with immunocompromised status and in patients with chronic pulmonary diseases.[3]

Klebsiella:
• urinary tract infections, pneumonia., bloodstream infections (also called sepsis), wound or surgical site infections; and meningitis. To get a *Klebsiella* infection, a person must be exposed to the bacteria. For example, *Klebsiella* must enter the respiratory (breathing) tract to cause pneumoniae, or the blood to cause a bloodstream infection.

In healthcare settings, *Klebsiella* bacteria can be spread through person-to-person contact (for example, from patient to

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patient via the contaminated hands of healthcare personnel, or other persons) or, less commonly, by contamination of the environment. The bacteria are not spread through the air.
Patients in healthcare settings also may be exposed to *Klebsiella* when they are on ventilators (breathing machines) or have intravenous (vein) catheters or wounds (caused by injury or surgery). Unfortunately, these medical tools and conditions may allow *Klebsiella* to enter the body and cause infection.[38]

Neisseria meningitidis: Meningococcal disease is an infection caused by the bacterium *Neisseria meningitidis*. This bacterium can cause serious and sometimes fatal diseases including meningitis (infection of the brain lining) and meningococcal septicemia (infection of the blood).
There are many different subtypes of the bacteria, but five of the subtypes (A, B, C, Y and W135) are responsible for most meningococcal cases. The risk is low for most travellers. Travellers at higher risk include:
Anyone living or working with the local population (e.g. health care workers) in areas where meningitis is present or outbreaks are occurring (Such as the sub-Saharan African meningitis belt).
Anyone travelling to crowded areas or taking part in large gatherings, such as the Hajj.[39] [40]

Proteus bacilli:

Although they behave like commensal microorganisms in the human intestinal tract, bacilli of the genus Proteus can cause harm when they spread to other sites. In fact, once in the urinary tract, the bacillus can cause local infection: a subject appears more sensitive to these infections when his defenses are no longer sufficient to protect the body from bacterial insults.[9] Bacteria of the genus Proteus can be transmitted through contaminated catheters, or by accidental parenteral inoculation. Although the precise method of transmission has not yet been identified with certainty, the possibility of direct transmission is excluded.
Cystitis, pyelonephritis, and urolithiasis (stone formation in the bladder or kidneys) are the most common Proteus-mediated infections. However, following a Proteus insult, some particularly sensitive patients may also develop bacteremia and septicemia.

The most common symptoms associated with Proteus infections are: alkalization of urine, stone formation, persistence of infection, renal failure (advanced stage)

The involvement of other organs is less frequent, although possible: in these circumstances, complications can also be documented

- abdominal abscesses
- cholangitis
- surgical wound infections
- purulent meningitis: diagnosed only in the newborn
- pneumonia
- septicemia (in case of severity)
- sinusitis

The close relationship between the onset of Proteus infections and the presence of diabetic bedsores and ulcers has been observed: the pathogens, which entered the body through these lesions, can also infect the bone.[3][41]

Pseudomonas:

The infection occurs:

Blood
A bacterial infection of the blood is called bacteremia. A blood infection is one of the most severe infections caused by pseudomonas. Symptoms may include:

- fever
- chills
- fatigue
- muscle and joint pain

Bacteremia with pseudomonas can also cause very low blood pressure, known as hemodynamic shock, which can lead to failure of other organs including the heart, kidneys, and liver.

Lungs
Infection of the lungs is called pneumonia. Symptoms include:

- chills
- fever
- cough with or without sputum production
- difficulty breathing

Skin
When this bacterium infects the skin, it most often affects the hair follicles. This
is called folliculitis**.** Symptoms may include:

- redness of the skin
- abscess formation in the skin
- draining wounds

Ear
An external ear canal infection may sometimes be caused by pseudomonas and result in “swimmer’s ear.” Symptoms may include:

- swelling

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- ear pain
- itching inside the ear
- discharge from the ear.

- difficulty hearing

Eye

Symptoms of an eye infection may include:

- inflammation
- pus
- pain
- swelling
- redness
- impaired vision

Pseudomonas infections can be very aggressive, particularly infections in the lungs or skin.[42]

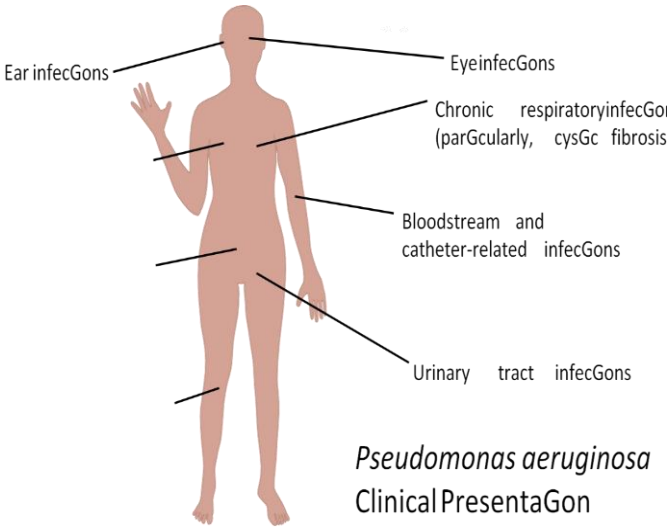

FIGURE **(I):** *Pseudomonas aeruginosa clinical presentagon.*

Salmonella:

Possible signs and symptoms of salmonella infection include:

- Diarrhea
- Stomach (abdominal) cramps
- Fever
- Nausea
- Vomiting
- Chills
- Headache
- Blood in the stool

Signs and symptoms of salmonella infection generally last a few days to a week. Diarrhea may last up to 10 days, but it may take several months before bowels return to usual stool habits.A few varieties of salmonella bacteria result in typhoid fever, a sometimes-deadly disease that is more common in developing countries.[43]

Escherichia coli:

- Urinary tract infection (UTI; most common)
- Enteric infection (certain strains)
- Invasive infection (rare, except in neonates)
- Infection at other sites

Most commonly, *E. coli* cause UTIs, which usually represent ascending infection (i.e., from the perineum via the urethra). *E. coli* may also cause prostatitis and pelvic inflammatory disease (PID). [44]

*Effect of antibiotics***.**

Alcaligenes faecalis:

Antibiotic resistance among pathogenic bacteria especially strains causing nosocomial infections, is particularly important. Also, due to acquisition of antibiotic resistance genes by bacteria over time in different geographical areas and changes in the pattern of bacterial susceptibility to different antibiotics, choosing the right antibiotic for treatment has become a challenge.[45] Based on the mentioned statements and due to few published data about the accurate diagnosis of clinical strains of *Alcaligenes* in Iran, in this study as the first time in Iran, we investigated the biochemically and genetically confirmation of the presence of *A. faecalis* and *A. xylosoxidans* in clinical samples and their antimicrobial susceptibility patterns. We performed the antimicrobial susceptibility tests for each isolate by the disc diffusion method (Kirby-Bauer). The results were interpreted as either sensitive, intermediate, or resistant according to the Clinical Laboratory Standards Institute (CLSI-2018) susceptibility breakpoints for non-fermenting gram-negative bacteria [46]. Antibiotic discs (*Mast* (*UK*)), used for the tests included: ampicillin (AP10 ug), trimethoprim/sulfamethoxazole (TS25 ug), ciprofloxacin (CIP5 ug) , imipenem (IMI0 ug) , Gentamicin (GM10 ug) , Meropenem (MEM10 ug), Ceftazidime-(CAZ30 ug), ceftriaxone (CRO30 ug), piperacillin-/tazobactam (PTZ110 ug), ampicillin/sulbactam (SAM20 ug), cefepime (CPM30 ug).

Antimicrobial Susceptibility

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The in vitro susceptibility of 36 *Alcaligenes* isolates to 11 antimicrobial agents is summarized in (TABLEI). The most susceptibility (80.55%) among *Alcaligenes* species was to Cefepime, followed by imipenem, piperacillin-tazobactam, and ceftazidime with a 75% rate. Also, the most resistance (92.3 %) was seen against Cefepime antibiotic in 13 *A. xylosoxidans* isolates followed by ciprofloxacin (76.92%) and meropenem (38.46%) (TABLE II).

TABLE (I): *In vitro susceptibility profile of 36 Alcaligenes species isolated from hospitalized patients to 11 Antimicrobial agent*

Antibiotic	**No. of isolates (%)**		
	Susceptible	Intermediate	Resistant
Gentamicin	12 (33.33)	3 (8.33)	21 (58.33)
Ceftazidime	27 (75.00)	1 (2.77)	8 (22.22)
Ceftriaxone	11 (30.55)	14 (38.88)	11 (30.55)
Piperacillin/Tazobactam	27 (75.00)	5 (13.88)	4 (11.11)
Ampicillin	9 (25.00)	6 (16.66)	21 (58.33)
Trimethoprim/sulfamethoxazole	21 (58.33)	3 (8.33)	12 (33.33)
Meropenem	21 (58.33)	1 (2.77)	14 (38.88)
Ampicillin/Sulbactam	17 (47.22)	3 (8.33)	16 (44.44)
Imipenem	27 (75.00)	7 (19.44)	2 (5.55)
Ciprofloxacin	8 (22.22)	2 (5.55)	26 (72.22)
Cefepime	29 (80.55)	1 (2.77)	6 (16.66)

TABLE (II): *In vitro susceptibility profile of 13 A. xylosoxidans and 3 A. faecalis strains isolated from hospitalized patients to 11 Antimicrobial agent***.**

	No. of isolates (%)					
Antibiotics	**Susceptible**		**Intermediate Susceptibility**		**Resistant**	
	A. xylosoxidans	*A. faecalis*	*A. xylosoxidans*	*A. faecalis*	*A. xylosoxidans*	*A. faecalis*
Gentamicin	4 (30.76)	1 (33.33)	8 (61.53)	0	1 (7.70)	2 (66.66)
Ceftazidime	11 (84.61)	3 (100)	0	0	2 (15.38)	0
Ceftriaxone	5 (38.46)	1 (33.33)	5 (38.46)	0	3 (23.07)	2 (66.66)
Piperacillin/Tazobactam	10 (76.92)	3 (100)	2 (15.38)	0	1 (7.70)	0
Ampicillin	7 (53.84)	0	3 (23.07)	2 (66.66)	3 (23.07)	1 (33.33)
Trimethoprim/sulfamethoxazole	11 (84.61)	2 (66.66)	1 (7.70)	0	1 (7.70)	1 (33.33)
Meropenem	8 (61.53)	3 (100)	0	0	5 (38.46)	0
Ampicillin/Sulbactam	9 (69.23)	2 (66.66)	1 (7.70)	0	3 (23.07)	1 (33.33)
Imipenem	11 (84.61)	3 (100)	0	0	2 (15.38)	0
Ciprofloxacin	2 (15.38)	1 (33.33)	1 (7.70)	1 (33.33)	10 (76.92)	1 (33.33)
Cefepime	12 (92.30)	3 (100)	0	0	1 (7.70)	0

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In three samples that were identified as *A. faecalis* isolates, the complete susceptibility (100%) to ceftazidime, piperacillin/tazobactam, imipenem, and cefepime were observed, and 66.66% of isolates were resistant to Gentamicin and Ceftriaxone.

Moraxella catarrhalis:

All the fourteen isolates (100%) were identified to be beta-lactamase producers
and showed susceptibility to amoxicillin/clavulanic acid combination (Figure II). Although all the isolates were sensitive to second- and third generation cephalosporins, the isolates displayed resistance to other groups of drugs. While 25% of the isolates were resistant to levofloxacin, 50% were resistant to ciprofloxacin among drugs belonging to the fluoroquinolone group. 75% of the isolates were resistant to azithromycin, and 66% showed intermediate results with clarithromycin in the macrolide group and all these are determined by the minimum inhibitory concentration (MIC) values using the CLSI guidelines.[47]

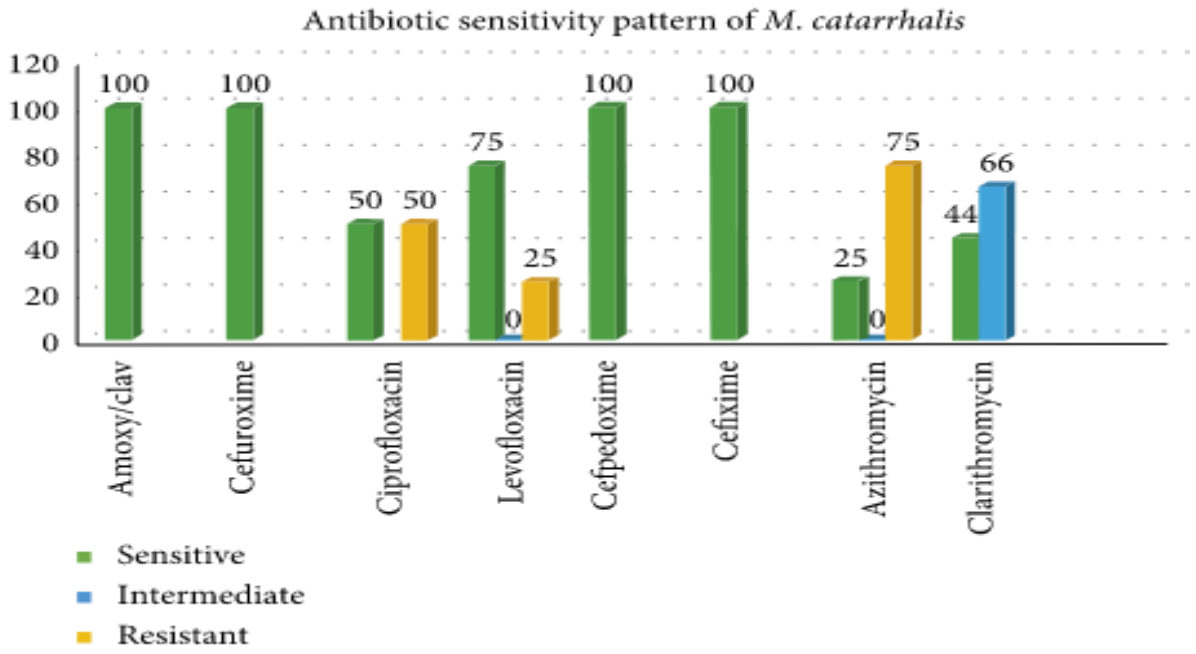

FIGURE (2): Antibiotic sensitivity pattern of M. catarrhalis.

Klebsiella:

The *Klebsiella bacterial* infection can be fatal if left so you need to start antibiotics straight away. Most common that are used for this reason are cefotaxime, carbapenems and cephalosporins.[48] A worrying new strain There are many superbugs that are already around and appear in hospitals but unfortunately there is a new strain of pneumonia that has erupted In China. The worst part is it seems to be drug-resistant and deadly not to mention the fact it is spread easily. The bacterium killed five people in 2016 in the critical care unit in Hangzhou and the superbug resisted 26 antibiotics. The outbreak happened in a hospital that was recently built and has very high standards for hygiene says Sheng Chen a microbiologist. There is worry as the drug-resistant strain should not have erupted this quickly Sheng Chen has

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commented. All the drugs that are available in China were tried and all were resisted there is nothing available in China to stop it. There are rumors a drug in the U.S may be effective in stopping it, but this is yet to be confirmed. The five patients who died from the outbreak were older than 50 and were recovering on ventilators after major surgeries. The causes of death were lung failure, multiorgan failure and septic shock was what the research had found. Chen and the team were shocked to see that when they put the bacteria under the scope, they found two dangerous forms that are fused together this is unlike the other drug-resistant pneumonia reported before. There have been two types of the Klebsiella bacteria that have appeared in a broad of hospitals and they were CRE which is a drug-resistant form that has killed many. The next type of a very severe type of the disease known as hypervirulent this progresses fast starting in the lungs then furthering out infecting the rest of the organs. The hypervirulent form causes so much more damage than the other forms and will happily spread through towns sickening even the young and healthy.

Neisseria meningitidis:

Results from a study that assessed isolates of *Neisseria meningitidis* collected from patients with invasive meningococcal disease (IMD) found that more than 25% of isolates had intermediate susceptibility to penicillin and ampicillin. These findings were published in *The Journal of Infectious Diseases*.

Researchers conducted an antimicrobial resistance (AMR) survey using data captured by the Centers for Disease Control and Prevention (CDC) that assessed N meningitidis isolates collected from patients with IMD between 2012 and 2016. All N meningitidis isolates were detected via culture and polymerase chain reaction testing. A total of 508 isolates were included in the survey. Broth microdilution was used to determine whether isolates were susceptible to clinically relevant antibiotics, and whole-genome sequencing was used to characterize resistance mechanisms. In addition, strains of Streptococcus pneumonia and Escherichia coli were used as quality control. Among the *N meningitidis* isolates assessed, all were found to be susceptible to cefotaxime, ceftriaxone, meropenem, rifampin, minocycline, and azithromycin. Decreased antimicrobial susceptibility was observed for 5 antibiotics, including ampicillin, penicillin G, ciprofloxacin, levofloxacin, and trimethoprim-sulfamethoxazole. Further analysis of these antibiotics showed that 483 isolates were resistant to trimethoprim-sulfamethoxazole, and fewer than 6 were resistant to ampicillin, penicillin, ciprofloxacin, and levofloxacin. In addition, intermediate susceptibility to penicillin G and ampicillin was found among 208 and 229 *N meningitidis* isolates, respectively. After stratification by year of collection, no significant variation was found among the isolates that were resistant to penicillin G ($P > .70$), with similar variation found among isolates that were resistant to ampicillin. Of the 208 isolates that conferred resistance to penicillin G, 164 (78.8%) were associated with mutations commonly found in *penA* alleles, including F504L, A510V, I515V, H541N, and I566V. On analysis of 4 *N meningitidis* isolates with intermediate resistance to ciprofloxacin and 2 with resistance to levofloxacin, only 1 conferred intermediate resistance to both antibiotics and showed decreased susceptibility to fluoroquinolones.

This study was limited by the inability to determine whether findings that showed some isolates conferred resistance to penicillin were clinically significant. In addition, none of the patients involved in this survey exclusively received treatment with penicillin.

According to the researchers, "… [these findings] highlight the continued importance of N meningitidis AMR surveillance in the United States to monitor trends, paired with genotypic investigations to understand the underlying mechanisms of resistance." [49]

Proteus bacilli:

Urinary tract infection is the most common clinical manifestation of *Proteus* infections. Empiric treatment for community-acquired urinary tract infection will depend more on susceptibilities of *E. coli* than of *P. mirabilis* since *E. coli* is by far the more common pathogen. For hospitalized patients or those with urinary catheters, the first decision is whether the isolate is clinically significant. Isolates which are not accompanied by pyuria or symptoms do not warrant treatment. Based on the compiled antibiotic resistance data provided in Table 1, trimethoprim or cotrimoxazole may no longer be viable treatment options for *P. mirabilis* infections. Quinolone resistance is also increasing, and *P. mirabilis* is almost uniformly resistant to nitrofurantoin, tetracycline, and polymyxins. The most appropriate treatment for *P. mirabilis* may be aminoglycosides, carbapenems (except imipenem), and 3rd generation cephalosporins. Recent *P. mirabilis* isolates were also mostly susceptible to augmentin, ampicillin-sulbactam, and piperacillin/tazobactam. In general, treatment should be with intravenous agents (or oral therapy for quinolones) until fever has resolved. Correction of the underlying anatomical abnormality or removal of a urinary catheter is also frequently necessary.

The treatment of choice of *P. mirabilis* bacteremia depends on whether or not the organism is an ESBL producer. Carbapenems are the treatment of choice for ESBL producing isolates causing bacteremia. The basis for this statement is not

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just the almost uniform *in vitro* susceptibility but also increasingly extensive clinical experience. However, it must be pointed out that this experience is in organisms such as *K. pneumoniae* rather than *P. mirabilis*. Meropenem is preferred over imipenem for ESBL producing *P. mirabilis* in view of the superior *in vitro* susceptibility of meropenem against *P. mirabilis*. Piperacillin/tazobactam has been successfully used to treat ESBL producing *P. mirabilis* infections in Italy. Quinolones are probably a reasonable option if the isolate is susceptible. Cephalosporins are not recommended for the treatment of ESBL producing *P. mirabilis* isolates; failures have been observed.

In view of the presence of an inducible beta-lactamase in *P. vulgaris*, we would not recommend penicillin's, cefuroxime, ceftriaxone or cefotaxime as first line therapy for serious infections due to this organism. However, the MICs of ceftazidime and aztreonam are almost always less than 1 µg/mL, these antibiotics do not induce production of the beta-lactamase of *P. vulgaris* and the enzyme does not hydrolyze these antibiotics. Therefore , aztreonam , beta-lactam/ beta-lactamase inhibitor combinations, or carbapenems would be reasonable since these drugs are resistant to the hydrolytic activity of class A beta-lactamase.

The development of resistance to ceftriaxone, occurring during treatment, has been seen with *P. penneri* . Treatment recommendations are the same for this organism as for *P. vulgaris*. [50]

Pseudomonas:

Most *Pseudomonas* spp. are naturally resistant to penicillin and the majority of related beta-lactam antibiotics, but a number are sensitive to piperacillin, imipenem, ticarcillin, or ciprofloxacin.[3] Aminoglycosides such as tobramycin, gentamicin, and amikacin are other choices for therapy. This ability to thrive in harsh conditions is a result of their hardy cell walls that contain porins. Their resistance to most antibiotics is attributed to efflux pumps, which pump out some antibiotics before they are able to act.

Pseudomonas aeruginosa is increasingly recognized as an emerging opportunistic pathogen of clinical relevance. One of its most worrying characteristics is its low antibiotic susceptibility.[51] This low susceptibility is attributable to a concerted action of multidrug efflux pumps with chromosomally encoded antibiotic resistance genes (e.g., *mexAB-oprM*, *mexXY*, etc.,)[52] and the low £permeability of the bacterial cellular envelopes. Besides intrinsic resistance, *P. aeruginosa* easily develops acquired resistance either by mutation in chromosomally encoded genes or by the horizontal gene transfer of antibiotic resistance determinants. Development of multidrug resistance by *P. aeruginosa* isolates requires several different genetic events that include acquisition of different mutations and/or horizontal transfer of antibiotic resistance genes. Hypermutation favours the selection of mutation-driven antibiotic resistance in *P. aeruginosa* strains producing chronic infections, whereas the clustering of several different antibiotic resistance genes in integrons favours the concerted acquisition of antibiotic resistance determinants. Some recent studies have shown phenotypic resistance associated to biofilm formation or to the emergence of small-colony-variants, which may be important in the response of *P. aeruginosa* populations to antibiotic treatment.[53] Figure(III) - uploaded by Rashed Noor.

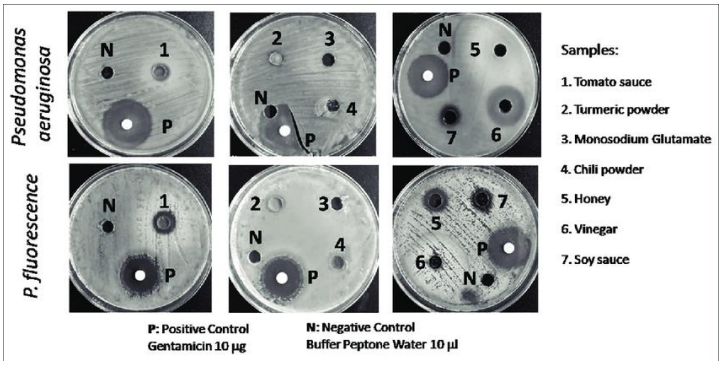

FIGURE (III): *Antibacterial activities of Pseudomonas spp.*

As described, lawns of Pseudomonas aeruginosa and Pseudomonas fluorescens were prepared on the MHA; around 10 mg/mL of the crude samples were introduced into the wells made on the corresponding plates, followed by incubation at 37°C for 15 h. Zones of inhibitions were observed and the results were recorded as S, R, or I as described in Materials and Methods. Experiments were performed five times and the results were found to be reproducible.

Salmonella:

Antibiotic-resistant *Salmonella* is a significant concern in poultry production.

After the approval of fluoroquinolones (enrofloxacin and sarafloxacin) in poultry husbandry in 1995, an extensive use of antibiotics started to augment poultry production. However, the reports from the National Antimicrobial Resistance Monitoring System (NARMS) presented incidences of the isolation of antibiotic-resistant *Salmonella*, eventually

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culminating in the withdrawal of major antibiotics such as fluoroquinolones from poultry production Interestingly, even after the withdrawal of some of these antibiotics from production, a high prevalence of *Salmonella* resistant to fluoroquinolones has been reported, posing a significant threat to poultry food safety and human health.

Often, farm environments are the reservoirs of pathogens, including antibiotic-resistant bacteria. Recently, *Salmonella* isolated resistant to multiple antibiotics, including streptomycin (30.9%), gentamicin (12.6%), sulfadimethoxine (20.9%), tetracycline (13.9%), and trimethoprim-sulfamethoxazole combination (8.6%) were recovered from broiler farms. Among these isolates, 20% were resistant to three or more antibiotics; 67% of *S.* Heidelberg and 54% of *S.* Kentucky isolates showed resistance to five or more antibiotics. In addition to a high prevalence of *S.* Enteritidis noticed in hatching eggs, litter, feed, drinkers, bird rinse, and ceca, 88% of *S.* Enteritidis were reported to be resistant to multiple drugs including ampicillin, nalidixic acid, and tetracycline.

Currently, intervention strategies are practiced at the farm level to control antibiotic-resistant *Salmonella* in poultry and its spread to carcasses during processing. However, antibiotic-resistant strains of *Salmonella* serovars such as *S.* Enteritidis, *S.* Infantis, *S.* Typhimurium, and *S.* Heidelberg have frequently been isolated from broiler carcasses. Augusto et al. reported high resistance of the isolates towards ceftriaxone (75%) and ceftiofur (44%). Recently, a Canadian study reported a significant correlation between the isolation of ceftiofur-resistant *S.* Heidelberg from retail chicken meat and the incidence of human clinical infections with *S.* Heidelberg during 2003–2008.

Escherichia coli:

Therapeutic options vary depending on the type of infection. For example, for urinary tract infections, trimethoprim/sulfamethoxazole and fluoroquinolones are treatments of choice,[60] whereas for Shiga toxin–producing *E. coli* infections, antimicrobial drug therapy is not recommended.[61] *E. coli* is sometimes used as a sentinel for monitoring antimicrobial drug resistance in fecal bacteria because it is found more frequently in a wide range of hosts, acquires resistance easily,[62] and is a reliable indicator of resistance in salmonellae.[63] Surveillance data show that resistance in *E. coli* is consistently highest for antimicrobial agents that have been in use the longest time in human and veterinary medicine.[64] The past 2 decades have witnessed major increases in emergence and spread of multidrug-resistant bacteria and increasing resistance to newer compounds, such as fluoroquinolones and certain cephalosporins.[57] For example, a study of the susceptibility of *E. coli* isolates recovered from hospitals during a 12-year period (1971–1982) showed no major change in resistance to any of the antimicrobial drugs tested.[65] In contrast, a retrospective analysis of *E. coli* from urine specimens collected from patients during 1997–2007 showed an increasing resistance trend for ciprofloxacin, trimethoprim/sulfamethoxazole, and amoxicillin/clavulanic acid.[66] Similarly, a 30-year (1979–2009) follow-up study on *E. coli* in Sweden showed an increasing resistance trend for ampicillin, sulfonamide, trimethoprim, and gentamicin.[67]

Aim of study.

The current study was performed to see the incidence of antibiotic resistance and virulence determinates in gram-negative bacterium sourced from clinical samples isolates against varied styles of normally used antibiotics in Aljalaa Hospital for surgery and accidents from March to April 2022.

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II. METHODS AND MATERIALS

A. Study Populations:

The study design was prospective, observational, and included 95 samples of patients in Al-jalaa Hospital–Benghazi in 2022. After microscopic examination, samples were cultured for bacterial identification and antibiotic susceptibility.

B. Laboratory analysis:

Cultures of samples were performed at the Al-jalaa Hospital Laboratories in Benghazi. When the samples were collected, they were transported in trans-isolate medium at room temperature to the Al-jalaa Hospital Laboratories. Sediment from a centrifuged specimen of blood was cultured on blood agar (BA), Mac Conkey agar (MA) and vitox-enriched chocolate agar (CA) plates. Plates were incubated for 24–48 h at 35 °C in an aerobic atmosphere (BA and MA), an anaerobic atmosphere (BA) or in an incubator at a gas concentration of 5% CO2 (CA). Isolates from cultures were identified by standard methods. All bacterial isolates were tested for in vitro antibiotic disc sensitivity.

C. Statistical analysis:

The data were analyzed by SPSS 22.

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D. Treatment:

Antibiotic treatment varied from patient to patient. In our study, both of The antibiotics we used belong to for all specimens is:

A. Cell Wall Synthesis:

Bata Lactam like:
Penicillin: Alexander Fleming discovered the first in 1928. derived from *Penicillium* fungi e.g.:
Natural (P- Penicillin G) Semi-synthesis (AMP- Ampiclox) & Artificial (AMC-amoxicillin)
B. Protein Synthesis:
This group of antibiotics divides in to
A. 30 S like:
Aminoglygcoside e.g: GN-Gentamycin., Tetracycline e.g: TE-Tetracycline.
3. DNA Topoisomerasis like:
Fuorquinolones e.g /CIP-Ciprofloxacin &, LEV-levofloxacin.
4.Antibiotics based on chemical structure: Macrocyclic lactone antibiotics: eg. E-Erythromycin.
5. Inhibitor of cytoplasmic membrane like: CL-Colistin
6.IMP-Imipenem is a semisynthetic carbapenem antibiotic, cilastatin is an inhibitor of the enzyme **dehydropeptidase** secreted by the kidneys and works to destroy imipenem.

FOX- Flucloxacillin, it is a narrow-spectrum beta-lactam antagonist used to treat infections with Gram-positive bacteria.

Cephalosporin:
First generation of cephalosporin like (CZ-cefazoline).
Third generation of cephalosporin like (CRO-Ceftriaxone & CXM-cefuroxime).

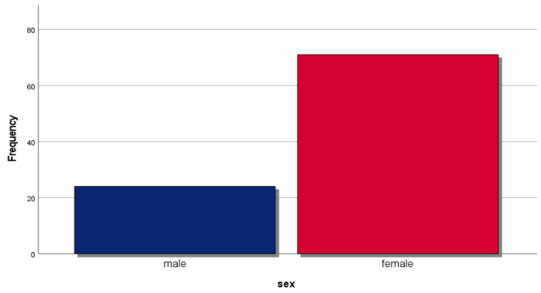

FIGURE (V): *Distribution of sex included in the study*

III. RESULTS AND DISCUSSION

This cross-sectional study was on a group of 95 of children and adults in the age group from 1 month to over 46 years in laboratory department of aljala hospital from 76 urine samples,11 stool samples and 7 swab samples and 1 semen sample as shown in the table (III) & figure (IV).

A. SEX:

Among 95 investigated, different world about 24 (25.3 %) were males and 71 (74.7 %) were females as shown in the table (III) & figure (V).

Table (III): Distribution of sex included in the study

Sex		
Samples	Frequency	Percent
Male	**24**	**25.3**
Female	**71**	**74.7**
Total	**95**	**100.0**

Age group:

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The study subjects was between 1 day and over 46 years divided into 4 age groups, the first group (0-14) 20%, the second group (15-30 years) 18.9% ,the third group (30-45 years) 35.8% and the fourth group (+46 years) 25.3% as shown in the table (4) & figure(V)

Table (IV): *Distribution of age included in the study.*

Age	Frequency	Percent
0-14	19	20.0
15-30	18	18.9
30-45	34	35.8
+46	24	25.3
Total	**95**	**100.0**

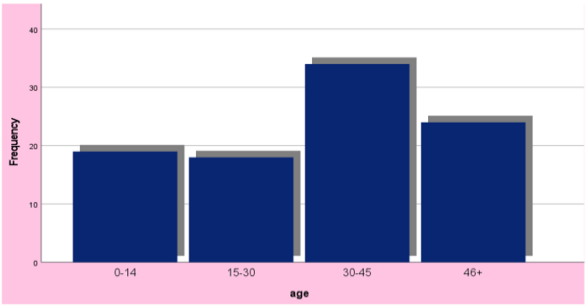

FIGURE (V): *Distribution of age included in the study.*

4.2. Culture results:

Microscopic examination for samples, gram staining and culture for bacteria for the 95 sample that was positive to culture test, found that of 95 causes positive infection urine 72(75.8%) stool 9(9.5%) swab 7(7.4%) urine RIE 3 (3.2%) urine CLS 1 (1.1%) stool RIE Stool CLS 1 (1.1%) semen 1 (1.1%) as shown in the table (5) & figure (6).

Table (V): *Microscopy and culture results.*

Samples	Frequency	Percent
Urine	72	75.8
Stool	9	9.5
Swab	7	7.4
Urine RIE	3	3.2
Urine CLS	1	1.1
Stool RIE	1	1.1
Stool CLS	1	1.1
Semen	1	1.1
Total	**95**	**100.0**

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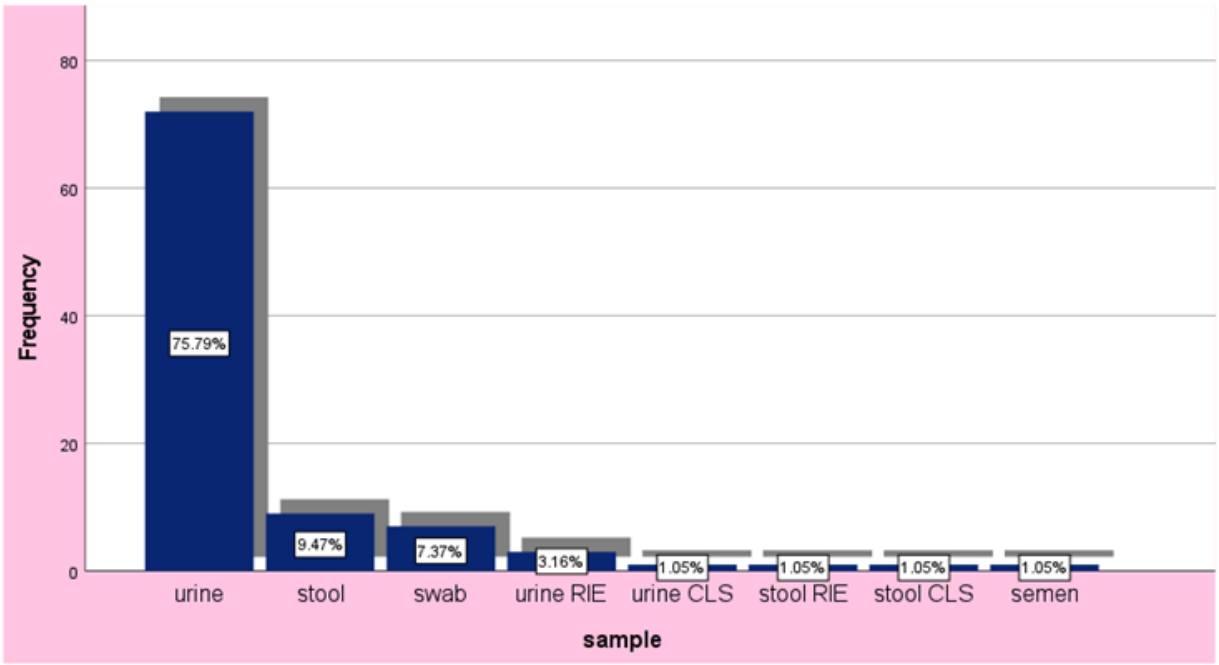

FIGURE (VI): *Microscopy and culture results***.**

Culture results of bacterial isolates:
As results and in the table investigated bacteria and samples isolated as shown in the table (VI) & figure (VII).

TABLE (VI): Culture results of bacterial isolates.

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	Urine	Stool	Swab	Urine RIE	Urine CLS	Stool RIE	Stool CLS	Sem -en	Tota l
E. coli	31	7	1	1	0	1	0	0	41
Alcaligenes	5	0	0	0	0	0	0	0	5
Moraxella catarrhalis	7	0	3	0	0	0	0	1	11
Klebsiella spp	12	0	0	2	0	0	0	0	14
Pseudomonas	11	1	2	0	1	0	0	0	15
Proetus spp	5	1	1	0	0	0	0	0	7
Neisseria meningitidis	1	0	0	0	0	0	0	0	1
Salmonella	0	0	0	0	0	0	1	0	1
Total	72	9	7	3	1	1	1	1	95

Chi-Square Tests			
Asymptotic Significance (2-sided)	**Df**	**Value**	
0.000	49	132.574[a]	Pearson Chi-Square
a. 59 cells (92.2%) have expected count less than 5. The minimum expected count is .01.			

Since the significant value of 0.000 = p value is less than 0.05, this means that there is a very high significant relationship between the sample and the type of bacteria, and the following figure is between the relationship between them.

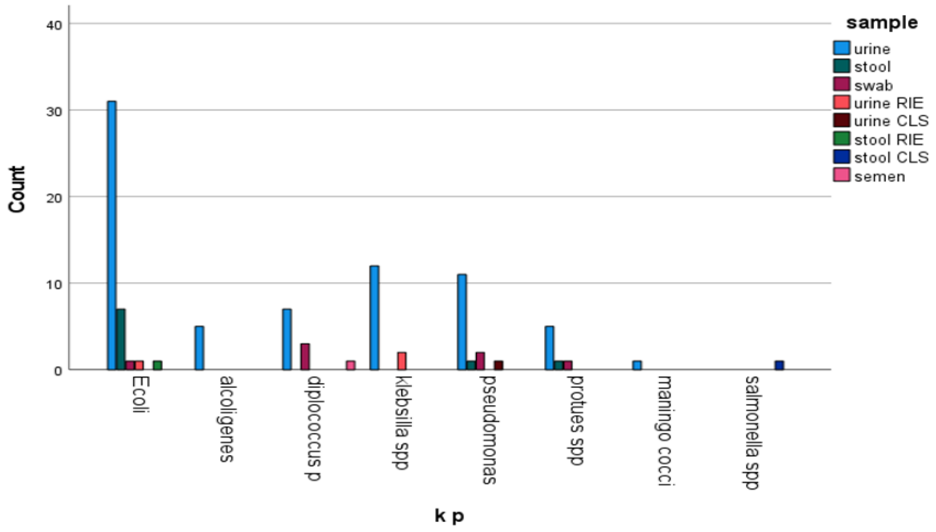

FIGURE (VII): *Culture results of bacterial isolates.*

*Bacterial Etiologies***:**

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A total of 95 %-gram negative bacteria were isolated. Out of this ,7 (7.7%) were proteus spp and 5 (5.3%) were alcaligenes. E. coli 41 (43.2%) was the most frequently isolated gram-negative bacteria followed by Pseudomonas spp .15 (15.8%) klebsiella spp 14 (14.7%) Moraxella catarrhalis 11 (11.6%) and the least frequent was Neisseria meningitidis 1 (1.1%) and salmonella 1 (1.1%) as shown in the table (VII) & figure (VIII).

TABLE (VII): *Distribution of gram-negative bacteria*

	Kp	
	Frequency	**Percent**
E. coli	41	43.2
Alcaligenes	5	5.3
Moraxella catarrhalis	11	11.6
Klebsiella spp	14	14.7
Pseudomonas	15	15.8
Proetus spp	7	7.4
Neisseria meningitidis	1	1.1
Salmonella	1	1.1
Total	**95**	**100.0**

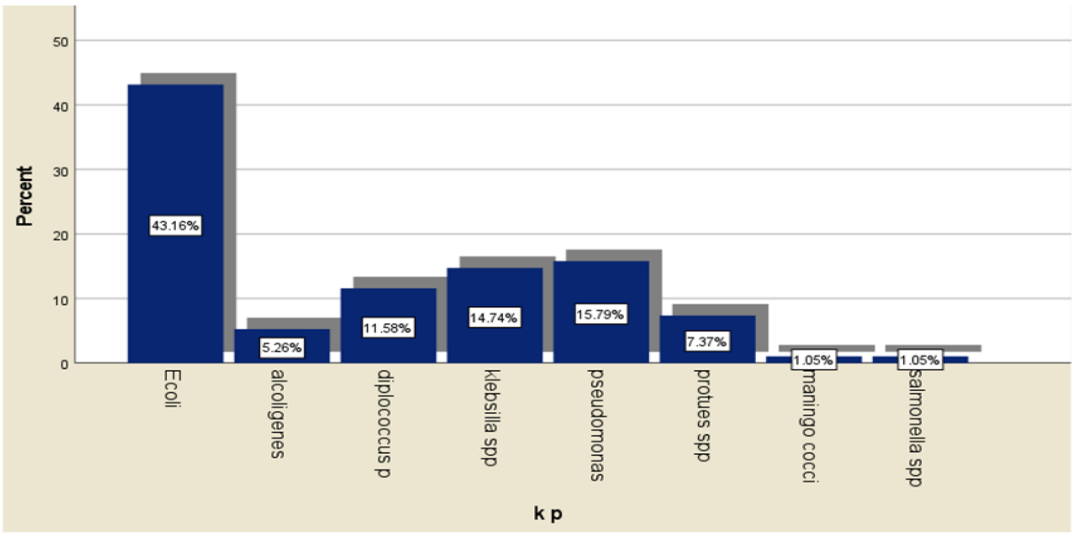

FIGURE (IX): Distribution of gram-negative bacteria.

*Alcaligenes faecalis***:**

As show in the figure (IX) these from we shown that the alcaligenes faecalis is gram negative, In the figure (X) this

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hemolysis gamma in Macconkey agar show the bacteria is alcaligenes faecalis gram negative, From the table (8) & the figure (11) we show that the more sensitive antibiotics for the alcaligenes faecalis is LEV-levofloxacin and CIP-ciprofloxacin and more resistant antibiotics is CXM-cefuroxime.

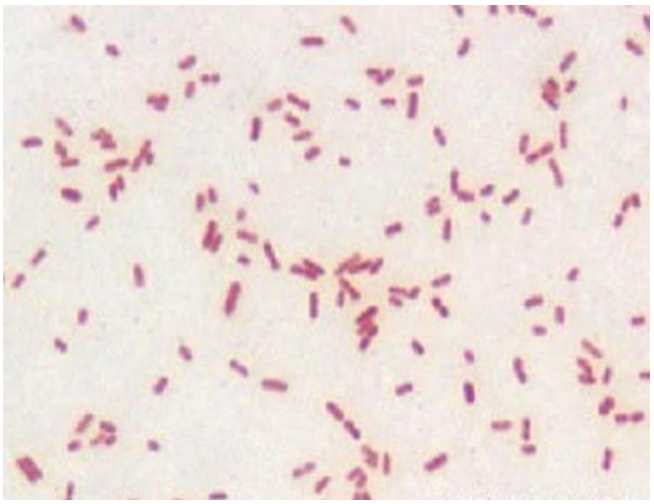

Figure (IX): *Alcaligenes faecalis in gram stain*

FIGURE (X): *Alcaligenes faecalis on macconkey agar*

TABLE (IX): *Antibiotics sensitive test for alcaligenes faecalis.*

	None	Sensitive	Intermediate	Resistant
AMC	1	1	0	3
IPM	5	0	0	0
TGC	5	0	0	0
CXM	1	0	0	4
CL	5	0	0	0
FEP	4	0	0	1
ETP	4	1	0	0
C	3	0	0	2
CIP	0	5	0	0
TE	1	3	0	1
LEV	0	5	0	0
CIV	5	0	0	0
SXT	0	2	1	2
CTX	5	0	0	0
CRO	5	0	0	0
AZM	0	3	0	2

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FA	0	3	0	2
AX	4	1	0	0
NA	1	2	1	1
GN	1	2	1	1
AM	2	3	0	0
CFM	3	0	0	2
CZ	5	0	0	0
FOX	5	0	0	0
NV	5	0	0	0
OX	4	0	0	1
TOB	5	0	0	0
PRL	5	0	0	0
ATM	5	0	0	0
AK	5	0	0	0
LNZ	5	0	0	0
DO	3	2	0	0
CAZ	5	0	0	0
TPZ	5	0	0	0

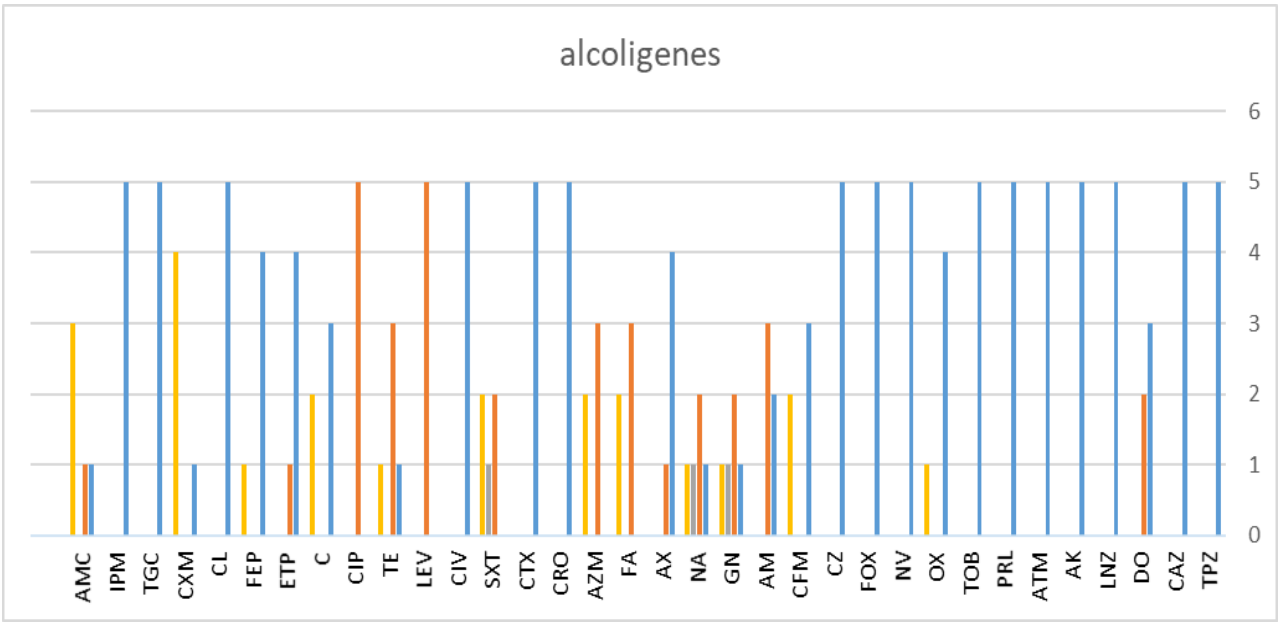

FIGURE (XI): *Antibiotics sensitive test for alcaligenes faecalis.*

Moraxella catarrhalis:

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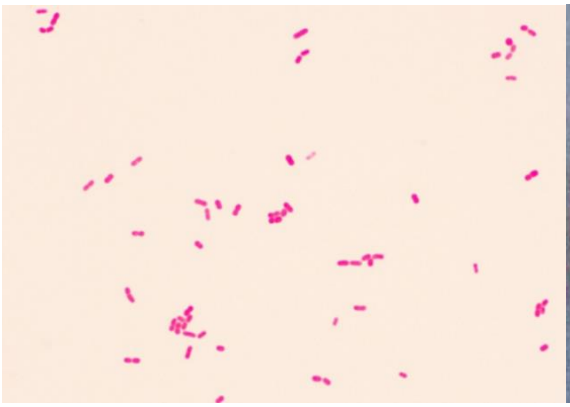
As show in the figure (12) these from we shown that the Moraxella catarrhalis is gram negative, In the figure (13) this hemolysis gamma in Macconkey agar show the bacteria is Moraxella catarrhalis gram negative, From the table (9) & the figure (14) we show that the more sensitive antibiotics for the Moraxella catarrhalis is LEV-levofloxacin and more resistant antibiotics is AMC-amoxicillin.



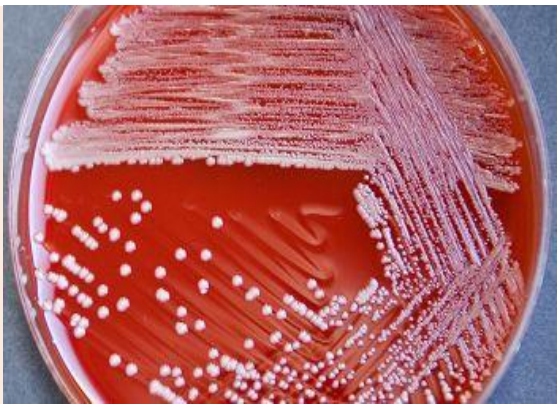


FIGURE (12): *Moraxella catarrhalis in gram stain*. **FIGURE (13):** *Moraxella catarrhalis on macconkey agar*.

TABLE (9): *Antibiotics sensitive test for Moraxella catarrhalis.*

	None	Sensitive	Intermediate	Resistant
AMC	4	1	0	6
IPM	7	1	0	3
TGC	9	2	0	0
CXM	5	2	0	4
CL	7	1	0	3
FEP	11	0	0	0
ETP	9	1	0	1
C	8	2	0	1
CIP	2	7	0	2
TE	3	4	0	4
LEV	2	8	1	0
CIV	10	1	0	0
SXT	2	6	0	3
CTX	9	0	0	2
CRO	6	1	0	4
AZM	1	5	0	5
FA	5	4	0	2
AX	8	1	0	2
NA	5	3	1	2
GN	2	5	0	4
AM	6	0	0	5
CFM	9	0	0	2
CZ	10	0	0	1
FOX	10	0	0	0

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NV	10	1	0	0
OX	9	0	0	2
TOB	11	0	0	0
PRL	11	0	0	0
ATM	11	0	0	0
AK	10	1	0	0
LNZ	10	1	0	0
DO	9	2	0	0
CAZ	9	0	0	2
TPZ	11	0	0	0

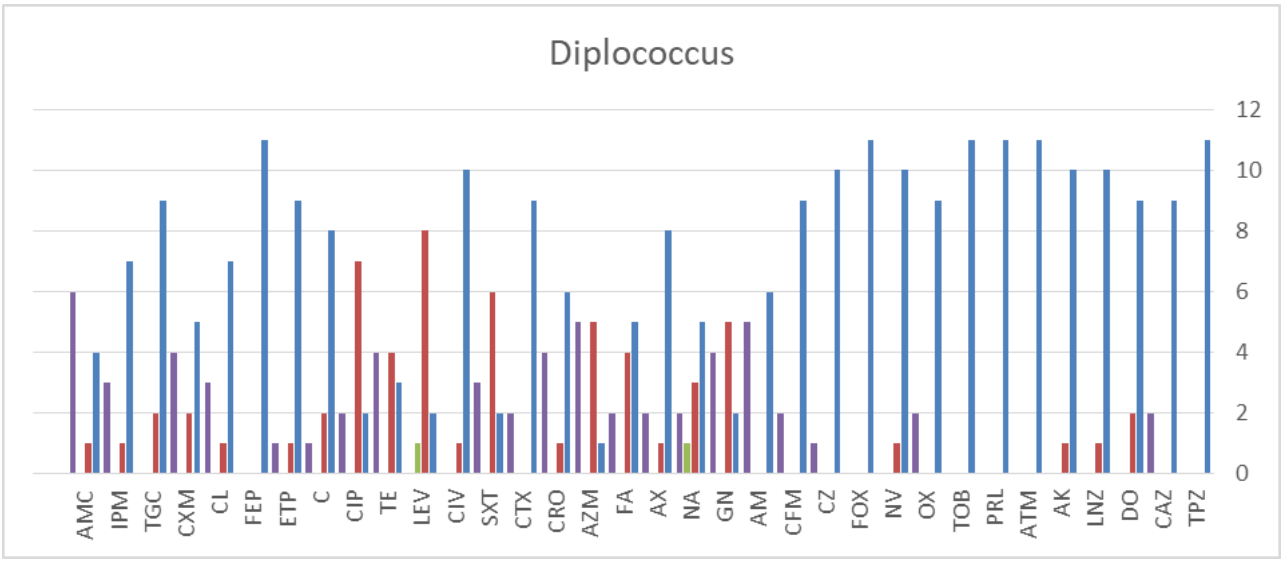

FIGURE (14): *Antibiotics sensitive test for Moraxella catarrhalis.*

*Klebsiella***:**

As show in the figure (15) these from we shown that the Klebsiella is gram negative, In the figure (16) this hemolysis gamma in Macconkey agar show the bacteria is Klebsiella gram negative, From the table (10) & the figure (17) we show that the more sensitive antibiotics for the Klebsiella is TE-tetracycline and GN-gentamicin, and more resistant antibiotics is IPM-imipenem and CL-colistin.

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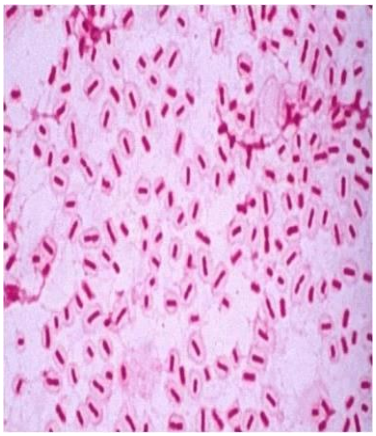

Figure (15): *Klebsiella in gram stain***.**

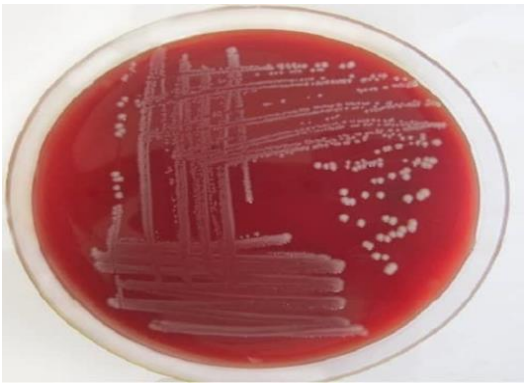

FIGURE (16): ***Klebsiella on macconkey agar*.**

TABLE (10): ***Antibiotics sensitive test for Klebsiella*.**

	None	Sensitive	Intermediate	Resistant
AMC	2	6	0	6
IPM	5	1	0	8
TGC	10	3	1	0
CXM	6	3	1	4
CL	6	0	0	8
FEP	13	1	0	0
ETP	13	1	0	0
C	12	1	0	1
CIP	4	6	0	4
TE	1	9	1	3
LEV	3	7	0	4
CIV	7	5	0	2
SXT	5	4	0	5
CTX	7	2	0	5
CRO	11	0	0	3
AZM	5	2	0	7
FA	6	5	1	2
AX	7	2	1	4
NA	5	4	1	4
GN	2	9	1	2
AM	9	2	0	3
CFM	14	0	0	0
CZ	14	0	0	0
FOX	14	0	0	0

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NV	14	0	0	0
OX	13	0	0	1
TOB	14	0	0	0
PRL	14	0	0	0
ATM	14	0	0	0
AK	14	0	0	0
LNZ	13	0	1	0
DO	10	4	0	0
CAZ	11	0	0	3
TPZ	14	0	0	0

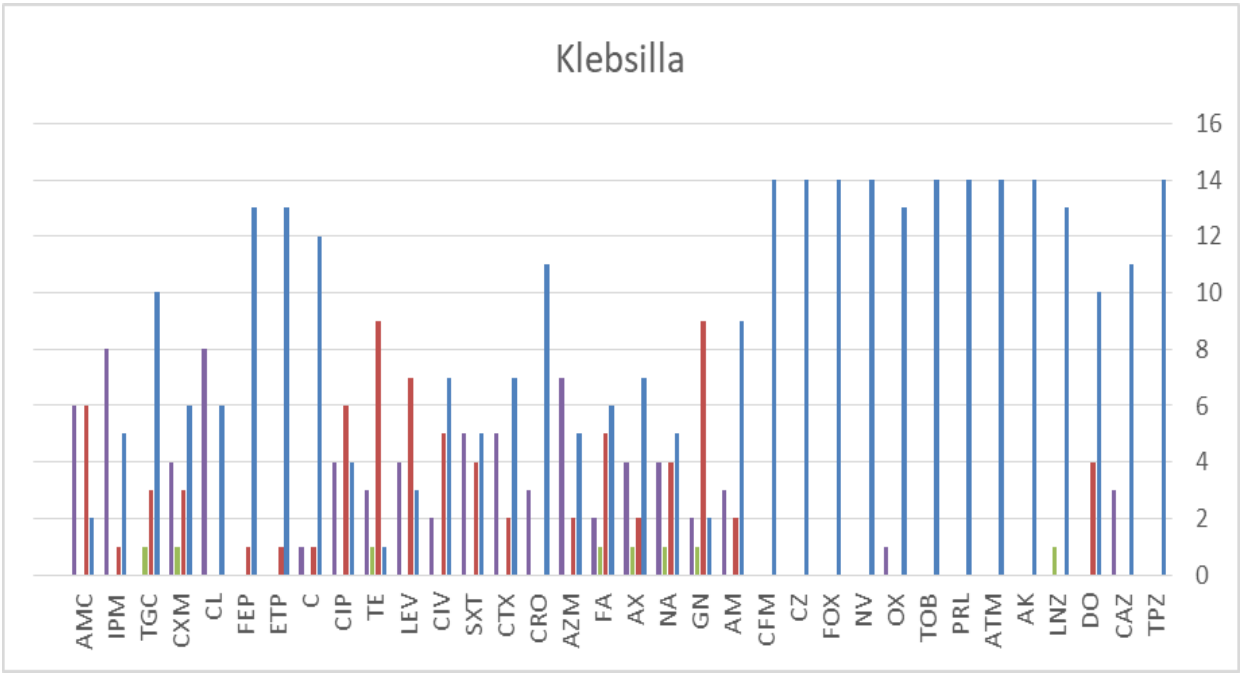

FIGURE (17): Antibiotics sensitive test for Klebsiella.

Neisseria meningitidis:

As show in the figure (18) these from we shown that the Neisseria meningitidis is gram negative, In the figure (19) this hemolysis gamma in Macconkey agar show the bacteria is Neisseria meningitidis gram negative, From the table (11) & the figure (20) we show that the more sensitive antibiotic for the Neisseria meningitidis is AMC-amoxicillin and CIP-ciprofloxacin, and CXM-cefuroxime and more resistant antibiotics is AM-ampicillin.

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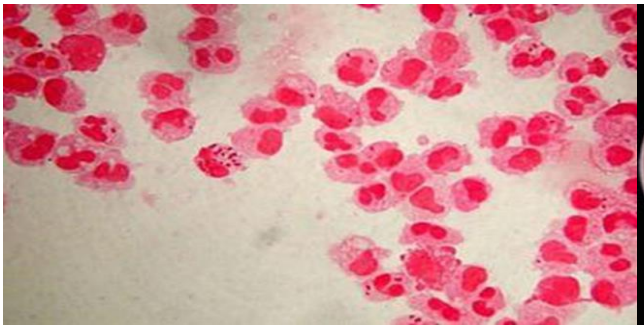

FIGURE (18): *Neisseria meningitidis in gram stain.*

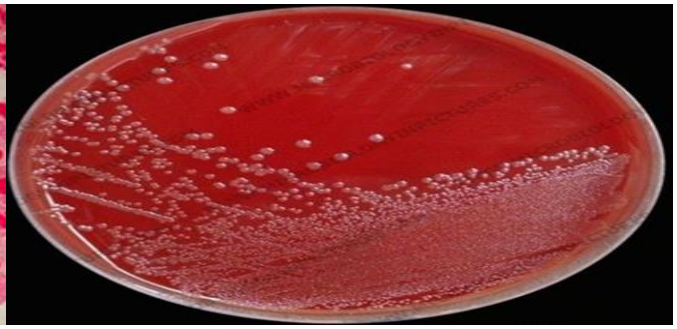

FIGURE (19): *Neisseria meningitidis on macconkey agar***.**

TABLE (11): ***Antibiotics sensitive test for Neisseria meningitidis*.**

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	None	Sensitive	Intermediate	Resistant
AMC	0	1	0	0
IPM	1	0	0	0
TGC	1	0	0	0
CXM	0	1	0	0
CL	1	0	0	0
FEP	1	0	0	0
ETP	1	0	0	0
C	1	0	0	0
CIP	0	1	0	0
TE	0	1	0	0
LEV	1	0	0	0
CIV	1	0	0	0
SXT	1	0	0	0
CTX	1	0	0	0
CRO	1	0	0	0
AZM	0	1	0	0
FA	0	1	0	0
AX	1	0	0	0
NA	0	1	0	0
GN	0	1	0	0
AM	0	0	0	1
CFM	1	0	0	0
CZ	1	0	0	0
FOX	1	0	0	0
NV	1	0	0	0
OX	1	0	0	0
TOB	1	0	0	0
PRL	1	0	0	0
ATM	1	0	0	0
AK	1	0	0	0
LNZ	1	0	0	0
DO	1	0	0	0
CAZ	1	0	0	0
TPZ	1	0	0	0

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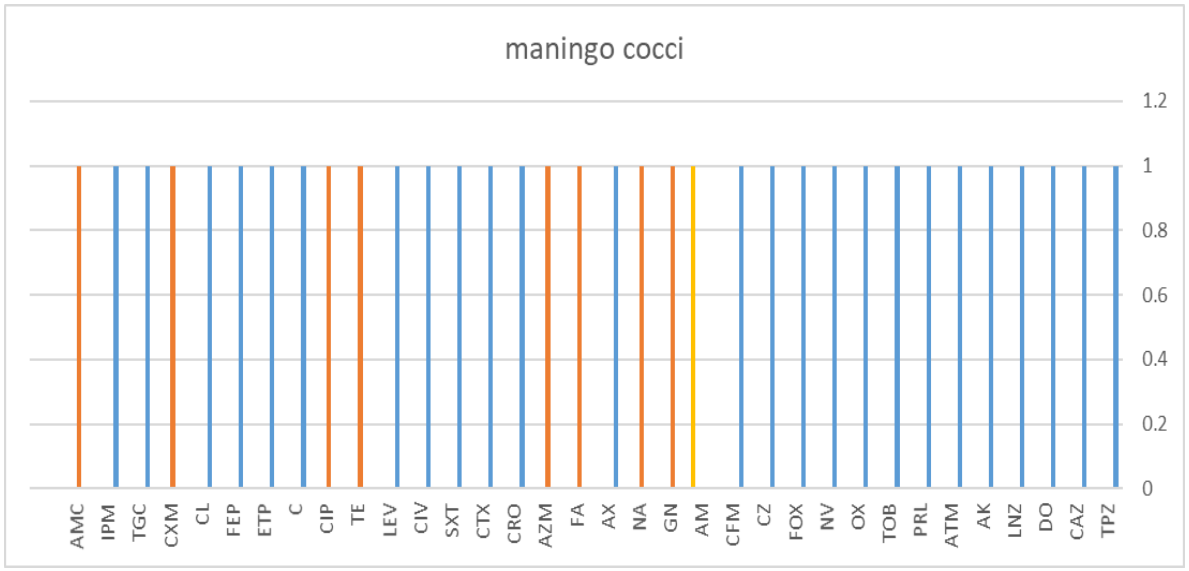

FIGURE (20): *Antibiotics sensitive test for Neisseria meningitidis***.**

Proteus bacilli:

As show in the figure (21) these from we shown that the Proteus bacilli is gram negative, In the figure (22) this hemolysis gamma in Macconkey agar show the bacteria is Proteus bacilli gram negative, From the table (12) & the figure (23) we show that the more sensitive antibiotics for the Proteus bacilli is CIP-ciprofloxacin and LEV-levofloxacin, and more resistant antibiotics is AMC-amoxicillin.

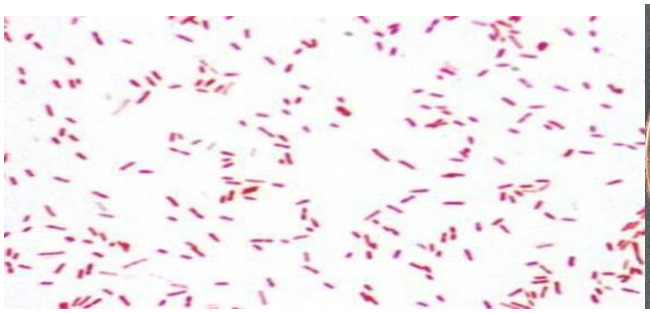

FIGURE (21): *Proteus bacilli in gram stain.*

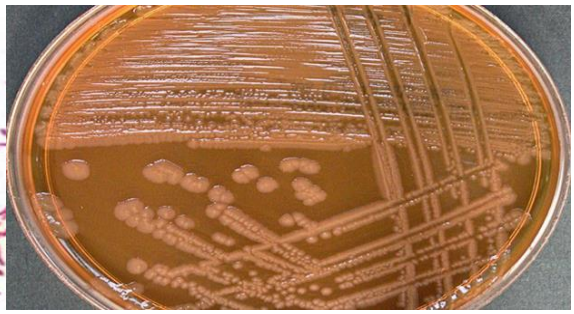

Figure (22): Proteus bacilli on macconkey agar.

TABLE (12): *Antibiotics sensitive test for Proteus bacilli*.

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	None	Sensitive	Intermediate	Resistant
AMC	0	0	0	7
IPM	6	1	0	0
TGC	4	3	0	0
CXM	3	1	0	3
CL	6	0	0	1
FEP	5	1	0	1
ETP	6	0	0	1
C	5	2	0	0
CIP	2	5	0	0
TE	4	0	1	2
LEV	2	5	0	0
CIV	7	0	0	0
SXT	3	0	0	4
CTX	6	0	0	1
CRO	6	0	0	1
AZM	2	2	1	2
FA	3	1	1	2
AX	2	1	0	4
NA	4	1	0	2
GN	2	3	0	2
AM	5	0	0	2
CFM	6	0	0	1
CZ	5	0	0	2
FOX	7	0	0	0
NV	7	0	0	0
OX	6	0	0	1
TOB	7	0	0	0
PRL	7	0	0	0
ATM	7	0	0	0
AK	7	0	0	0
LNZ	7	0	0	0
DO	6	0	0	1
CAZ	6	0	0	1
TPZ	6	1	0	0

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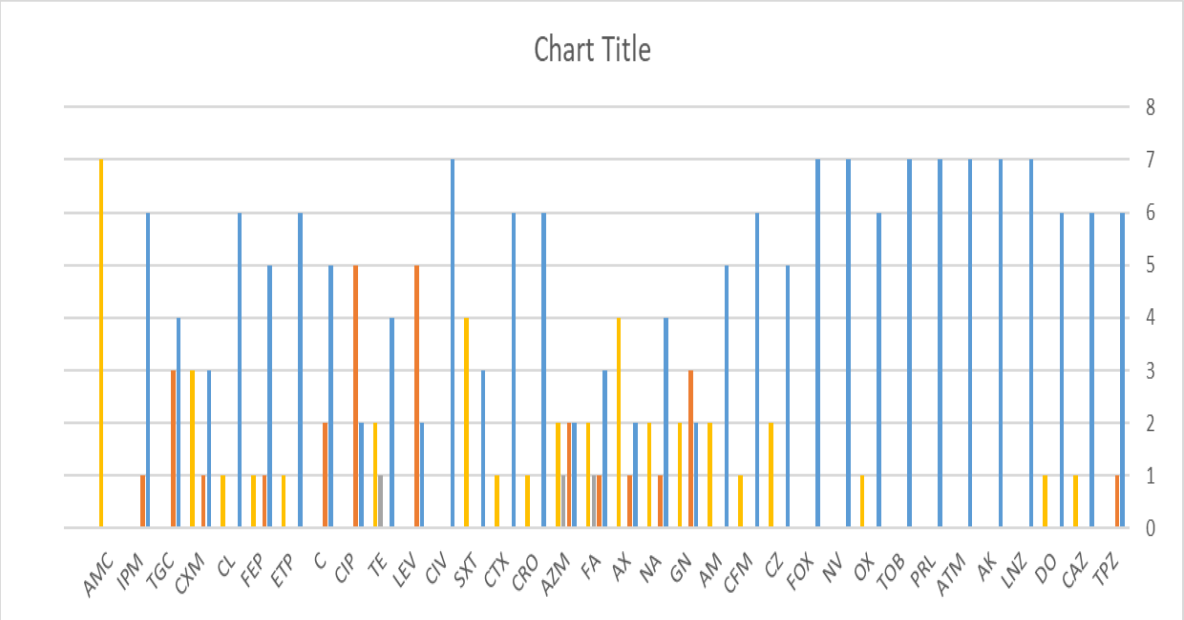

FIGURE (23): *Antibiotics sensitive test for Proteus bacilli.*

*Pseudomonas***:**

As show in the figure (24) these from we shown that the Pseudomonas is gram negative, In the figure (25) this hemolysis gamma in Macconkey agar show the bacteria is Pseudomonas gram negative, From the table (13) & the figure (26) we show that the more sensitive antibiotic for the Pseudomonas is LEV-levofloxacin and more resistant antibiotics is AMC-amoxicillin.

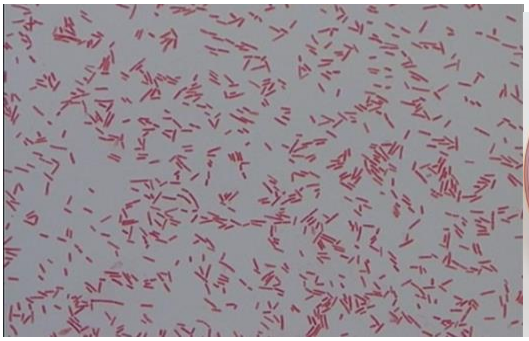

FIGURE (24): *Pseudomonas in gram stain*.

FIGURE (25): *Pseudomonas on macconkey agar*

TABLE (13): ***Antibiotics sensitive test for Pseudomonas.***

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	None	Sensitive	Intermediate	Resistant
AMC	2	3	0	10
IPM	13	0	0	2
TGC	13	2	0	0
CXM	3	4	0	8
CL	13	0	0	2
FEP	13	1	0	1
ETP	13	2	0	0
C	12	2	0	1
CIP	3	10	0	2
TE	2	7	1	5
LEV	2	12	0	1
CIV	15	0	0	0
SXT	2	10	0	3
CTX	13	0	0	2
CRO	13	0	0	2
AZM	2	4	0	9
FA	4	4	1	6
AX	9	2	0	4
NA	4	6	0	5
GN	3	6	0	6
AM	8	0	0	7
CFM	11	2	0	2
CZ	14	0	0	1
FOX	15	0	0	0
NV	15	0	0	0
OX	12	0	0	3
TOB	11	0	0	4
PRL	13	0	0	2
ATM	13	1	0	1
AK	15	0	0	0
LNZ	15	0	0	0
DO	12	3	0	0
CAZ	12	0	0	3
TPZ	15	0	0	0

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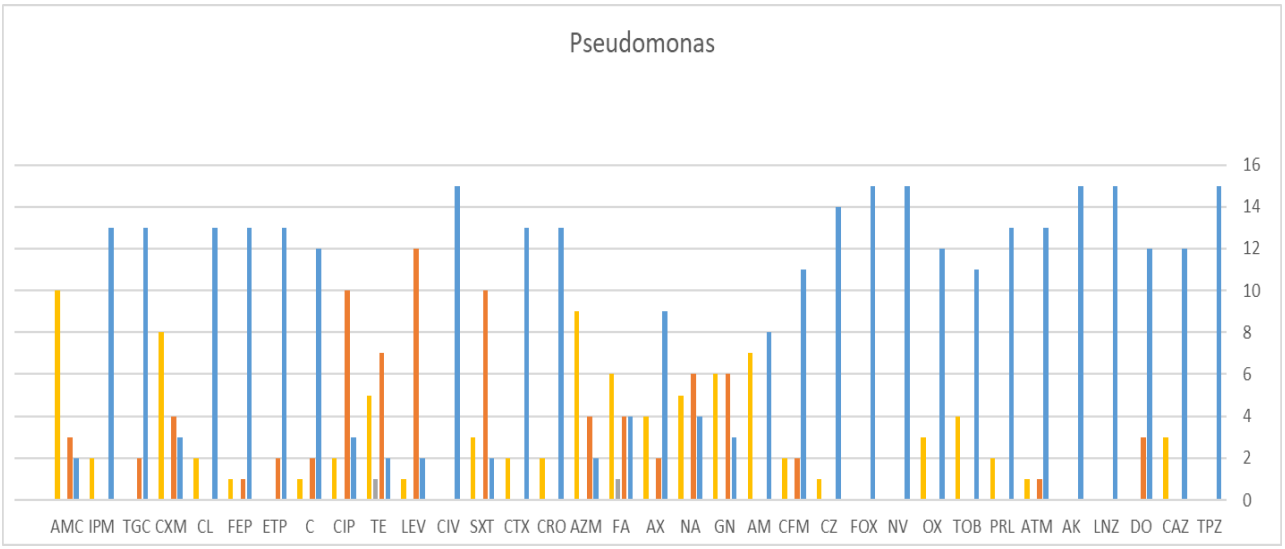
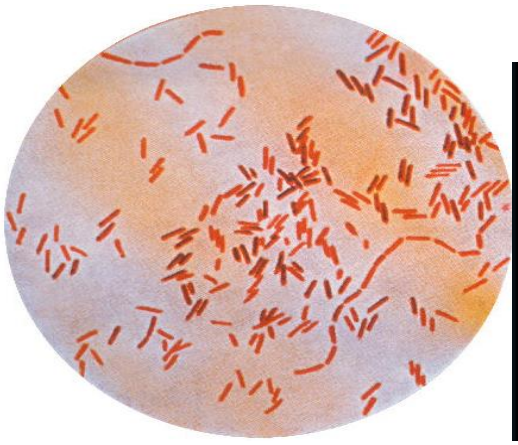


FIGURE (26): *Antibiotics sensitive test for Pseudomonas.*

Salmonella:

As show in the figure (27) these from we shown that the salmonella is gram negative, In the figure (28) this hemolysis gamma in Macconkey agar show the bacteria is salmonella gram negative, From the table (14) & the figure (29) we show that the more sensitive antibiotic for the salmonella is CRO-ceftriaxone and CZ-cefazoline and more resistant antibiotics is AMC-amoxicillin and CL-colistin and CIP-ciprofloxacin and CTX-cefotaxime and GN-gentamicin.



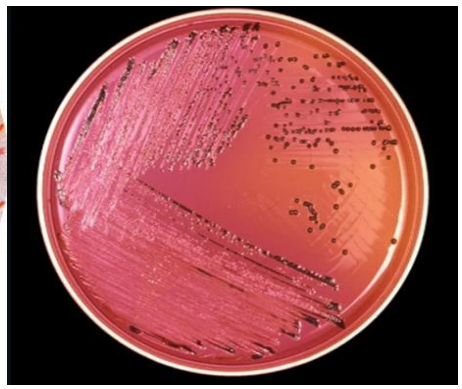


FIGURE (27): *Salmonella in gram stain*. **FIGURE (28):** *Salmonella on macconkey agar*

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TABLE (14): ***Antibiotics sensitive test for Salmonella.***

	None	Sensitive	Intermediate	Resistant
AMC	0	0	0	1
IPM	0	1	0	0
TGC	1	0	0	0
CXM	1	0	0	0
CL	0	0	0	1
FEP	1	0	0	0
ETP	1	0	0	0
C	1	0	0	0
CIP	0	0	0	1
TE	1	0	0	0
LEV	1	0	0	0
CIV	1	0	0	0
SXT	0	0	0	1
CTX	0	0	0	1
CRO	0	1	0	0
AZM	1	0	0	0
FA	1	0	0	0
AX	1	0	0	0
NA	1	0	0	0
GN	0	0	0	1
AM	1	0	0	0
CFM	1	0	0	0
CZ	0	1	0	0
FOX	1	0	0	0
NV	1	0	0	0
OX	1	0	0	0
TOB	1	0	0	0
PRL	1	0	0	0
ATM	1	0	0	0
AK	1	0	0	0
LNZ	1	0	0	0
DO	1	0	0	0
CAZ	0	0	0	1
TPZ	1	0	0	0

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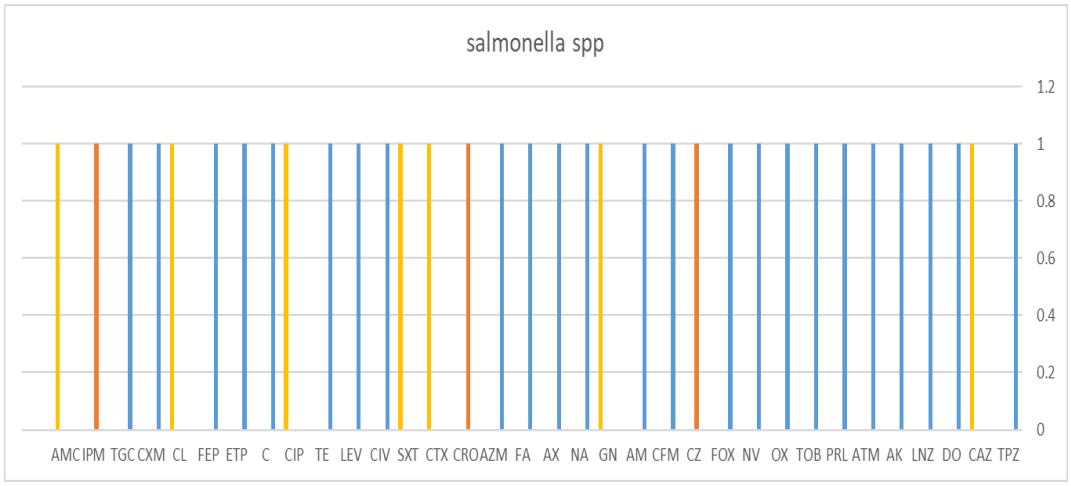

FIGURE (29): *Antibiotics sensitive test for Salmonella***.**

Escherichia coli:

As show in the figure (30) these from we shown that the Escherichia coli is gram negative, In the figure (31) this hemolysis gamma in Macconkey agar show the bacteria is Escherichia coli gram negative, From the table (15) & the figure (32) we show that the more sensitive antibiotics for the Escherichia coli is CIP-ciprofloxacin and more resistant antibiotics is AMC-amoxicillin.

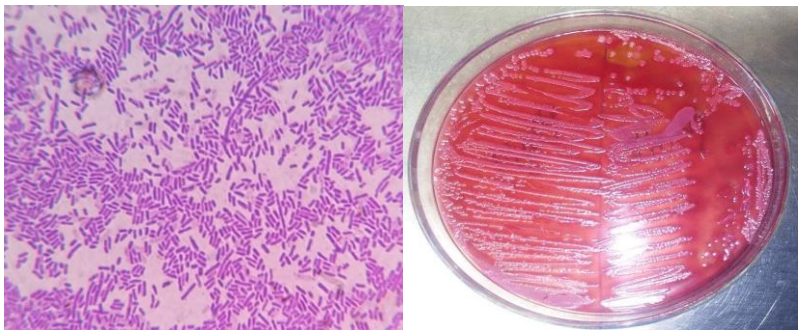

FIGURE (30): *E. coli in gram stain***. Figure (31): E. coli on macconkey agar.**

TABLE (15): *Antibiotics sensitive test for E. coli.*

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	None	Sensitive	Intermediate	Resistant
AMC	5	7	2	27
IPM	33	8	0	0
TGC	34	6	0	1
CXM	8	12	2	19
CL	34	4	1	2
FEP	31	5	0	5
ETP	39	2	0	0
C	33	7	0	1
CIP	2	32	0	7
TE	13	16	0	12
LEV	10	28	0	3
CIV	39	2	0	0
SXT	8	15	1	17
CTX	35	1	0	5
CRO	32	4	0	5
AZM	9	10	0	22
FA	16	22	1	2
AX	29	1	0	11
NA	15	15	0	11
GN	8	29	1	3
AM	24	1	1	15
CFM	31	4	0	6
CZ	33	3	0	5
FOX	40	0	0	1
NV	41	0	0	0
OX	40	0	0	1
TOB	40	0	0	1
PRL	41	0	0	0
ATM	41	0	0	0
AK	35	3	0	3
LNZ	41	0	0	0
DO	31	7	0	3
CAZ	41	0	0	0
TPZ	41	0	0	0

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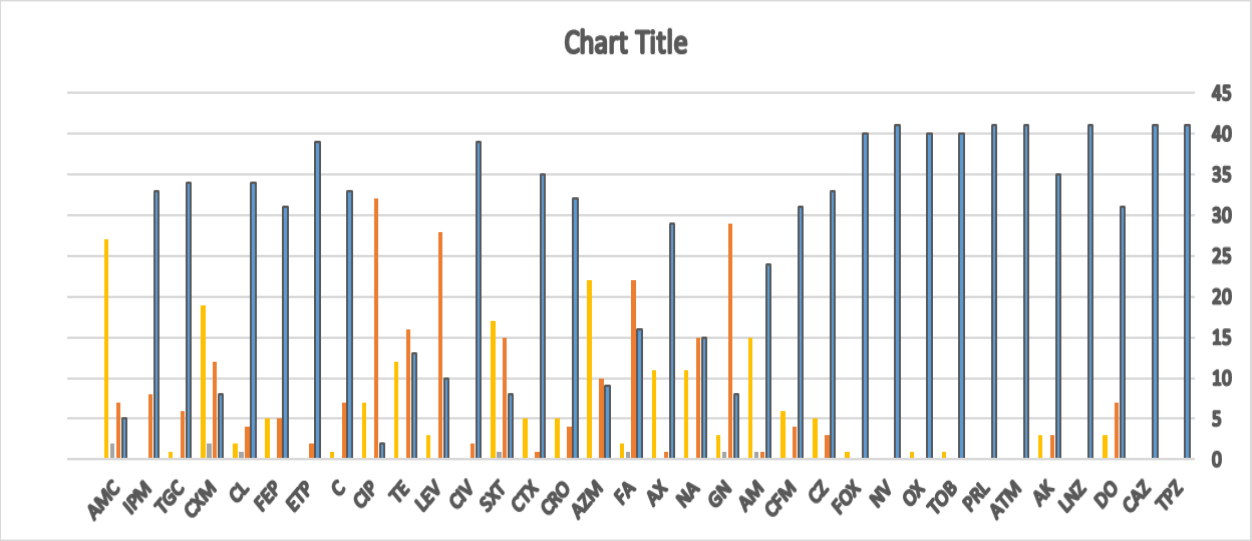

FIGURE (32): *Antibiotics sensitive test for E. coli.*

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In this study, among 24 samples from males and 71 samples from women suspected of having gram-negative bacteria in Al-Galaa Hospital (Benghazi), 25.3% of the male samples and 74.7% of the female samples were positive. In our study E. coli has showed a high resistance to AMC-amoxicillin which is similar to the study reported by Simona Claudia Cambrea 2014 [78]. And in our study K. pneumoniae has shown resistance high to IPM-imipenem and CL-colistin which is in unsimilarity with the study reported by Manjula N. G.1 , Girish C. Math. 2014 [72]. The Moraxella isolates showed maximum resistance to AMC-amoxicillin, followed by AZM-azithromycin and AMC-ampicillin which is in similarity with study reported by Ramana and Abhijit Chaudhury 2012 [79]. And also in our study of meningococcus bacteria, it has a lower resistance to antibiotics, which is similar to the study reported by L.Arreaza,L.de la Fuenta,and J.A.Vazquez 2000 [80]. And as our study showed that alcaligenes faecalis bacteria are resistant to is CXM-cefuroxime, which is not similar to the study of the report by Huang BMC 2020 [81]. And in salmonella, our study showed resistance to the antibiotics CRO-ceftriaxone , which is similar to the study reported by Abe Kebede,Jelalu Kemal, Haile Alemayehu, and Solomon Habte Mariam2016 [82].In our study, Pseudomonas bacteria showed us a high resistance to AMC-amoxicillin and AZM-azithromycin, which is similar to the study reported by Mahmudullah Bhuiya, Mohammad K.I.Sarkar 2018 [83]. Also in our study of Proteus bacilli bacteria showed resistance to AMC-amoxicillin, which is similar to the study reported by Orhue O. Philips 2014[84]. Carbapenems are the drugs of choice for many infections caused by Gram negative bacteria and were found to be the most effective antibiotics, and our study revealed 100% susceptible whereas, consistent rise was observed with other studies [85]. Multi-drug resistance (MDR) is a major problem in the management of Multiple pathogens [86]. The reason for this MDR resistance may be due to plasmids containing many resistance genes that are transferred from one bacterium to another [86] and this resistance pattern has been linked to the presence of integrons [87]. Multidrug Resistance (MDR) in all types of bacteria is increasing the worldwide [88].

IV. CONCLUSION

This study shows the increase in resistance to the antibiotics commonly used in the treatment of these gram-negative bacteria. The emerging resistance pattern emphasises the need for antibiotic surveillance and appropriate antibiotic stewardship program to salvage the currently available antibiotics and a new class of drugs to treat serious infections with these bacteria. Therefore, antibiotic therapies should consider the history of pre-exposed antibiotics to prevent the development of antibiotic resistance. Further studies are needed to assess the risk of antibiotic resistance in sequential and combination antibiotic therapies, which is essential to design an effective strategy for controlling multiple antibiotic resistance bacteria.

rational use of antibiotics could prevent the emergence and spread of resistant bacteria.

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