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Role of Bacteria as A Causative Agent of Cause Acute Appendicitis and Its Resistance to Antibiotic in Karbala

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Abstract

Background: Acute appendicitis is an inflammation of the appendix and is a common acute surgical emergency; however, the pathogenesis of appendicitis remains poorly understood. The bacteria is increasingly thought to play a key role in appendicitis.

Objective: The objective of this study was to determine the bacterial infection and antibiotics sensitivity pattern and study the distribution of appendicitis with gender and age groups in addition to clinical signs in patients with acute appendicitis in Karbala city.

Methods: Patients with acute appendicitis presenting between January 2024- June 2024 were studied. At surgery, 1cm rim of appendix was cut from the base and transferred into the Stuart's transport medium. The specimen was cultured on different type of culture media to identification bacteria. Antibiotic sensitivity test was performed.

Results: Samples collected from patients between (8-57) years old, the majority rate of appendicitis were between (16-30) ages with a percentage 44%, (1-15) age with a percentage 40%, (31-45) age with 14% and the minority rate was 2 % which belong to age (46-60). All specimens were positive to bacterial culture, gram positive bacteria were isolated at a lower rate (6%) than gram-negative bacteria (94%). The rate of infection was 54% in males and 46% in females. All patients have abdominal pain. Results found that *Escherichia coli* was the predominant aerobes, all species of gram-positive bacteria were resistance to the Benzylpenicillin and Oxacillin (100%), and sensitive to Rifampicin, Ticarcillin, Vancomycin and Penicillin (100%), all species of gram-negative bacteria isolated were sensitive to Amikacin and Imipenem (100%).

Conclusion: From this study, we can conclude that there was a relation between bacterial infections and *Escherichia coli which* was predominant and it was recorded that the infection in males were more than females in patients with acute appendicitis. gram negative bacteria showed to be more resistance to antibiotics than gram positive bacteria.

دور البكتيريا كعامل مسبب لالتهاب الزائدة الدودية الحاد ومقاومتها للمضادات الحيوية في كربلاء

ندى جاسم الكروي ,علاء عبد الحسين الدعمي , علي رحيم حنظل

الخلاصة

المقدمة

التهاب الزائدة الدودية الحاد هو التهاب حاد في الزائدة الدودية وهو حالة جراحية شائعة , ومع ذلك لا يزال المسبب في التهاب الزائدة الدودية غير مفهوم جيدا. يعتقد بشكل متزايد أن البكتيريا تلعب دورا رئيسيا في التهاب الزائدة الدودية الحاد .

الهدف

الهدف من هذه الدراسة هو تحديد العدوى البكتيرية ومدى حساسيتها للمضادات الحيوية ودراسة توزيع التهاب الزائدة الدودية مع الفئات الجنسية والعمرية بالإضافة إلى العلامات السريرية في مرضى التهاب الزائدة الدودية الحاد في مدينة كربلاء.

طرائق العمل:- تمت دراسة المرضى الذين يعانون من التهاب الزائدة الدودية الحاد واجريت الدراسة في الفترة من كانون الثاني 2024 الى حزيران 2024 في الجراحة ، تم قطع حافة 1 سم من الزائدة الدودية من القاعدة ونقلها إلى المختبر بواسطة وسط نقل **Stuart ,** تم زرع العينة على أنواع مختلفة من الوسائط لتحديد البكتيريا**,** ثم تم إجراء اختبار الحساسية للمضادات الحيوية.

النتائج

تم جمع العينات من المرضى الذين تتراوح أعمارهم بين (8 -57) سنة , وكانت نسبة الإصابة بالتهاب الزائدة الدودية في الغالب بين (16 - 30) سنة بنسبة 44% من إجمالي الحالات ، (1- 15) سنة بنسبة 40% ، (31-45) سنة بنسبة 14% والنسبة الأقل 2% والتي تنتمي إلى الفئة العمرية (46 - 60) ، كما أظهرت هذه الدراسة أن التهاب الزائدة الدودية الحاد يؤثر على كلا الجنسين مع عدم وجود فروق ذات دلالة إحصائية بين المجموعتين ولكنه يؤثر على الذكور (54%) أكثر من الإناث (46%) , حيث أظهرت جميع العينات نموا إيجابيا, تم عزل البكتيريا الموجبة لصبغة جرام بمعدل أقل (6٪) من البكتيريا السالبة لصبغة جرام (94٪) .وجدت النتائج ان اكثر الانواع البكتيرية شيوعا في مرضى التهاب الزائدة الدودية الحاد هي الإشريشيا القولونية ، وكانت جميع أنواع البكتيريا المعزولة الموجبة لصبغة جرام مقاومة **Benzyl penicillin** و **Oxacillin** بنسبة (100٪) ، وحساسة **Rifampicin , Ticarcillin , Vancomycin** و **Pencillin** بنسبة (100٪) ، وكانت جميع أنواع البكتريا المعزولة السالبة لصبغة جرام حساسة **Amikacin** و **Imipenem** بنسبة (100٪).

الاستنتاج

من هذه الدراسة يمكننا أن نستنتج أن هناك علاقة بين الاصابات البكتيرية والإشريشيا القولونية التي كانت سائدة وتم تسجيل أن الاصابة عند الذكور كانت أكثر من الإناث كما أظهرت العزلات السالبة لصبغة جرام أنها أكثر مقاومة للمضادات الحيوية من العزلات الموجبة لصبغة جرام لدى مرضى التهاب الزائدة الدودية الحاد.

1. Introduction

Acute Appendicitis (AA) is one of the common causes in the emergency unit due to abdominal pain and that appendectomy is one of the most surgical procedures performed in the world, diagnosis of Acute appendicitis is still challenging and some controversies on its management are still present among different settings and practice patterns worldwide (Moris, Paulson and Pappas, 2021).Diagnosis of appendicitis is clinical and combined with laboratory investigations, supplemented with selectively focused imaging, delayed diagnosis lead to problems such us punctured of appendix and sepsis. Obstruction and microorganisms are the important reasons in the most patients with acute appendicitis (Horattas, Haller and Ricchiutti, 2003; Alelyani *et al.*, 2021). Bacterial infection is believed to be crucial for inflammation of the appendix (Takahashi *et al.*,2021). Some bacteria can pass through appendix wall before perforation, whereas progressive infection and tissue damage with the necrosis allow the bacteria to enter the abdominal cavity. Studies on appendicitis are few, as studies related to identifying bacterial isolates associated with appendicitis and their role in increasing the complications of inflammation are limited, so the aim of this study was to investigate the bacterial infections in patients with acute appendicitis and study the distribution of appendicitis according to the sex, age groups, and clinical signs (Toumi *et al.*, 2010; Fabi *et al.*, 2022).

2. Patients & Methods

2.1. Study Design

Between January 2024 and June 2024, a total of 50 specimens (27 males and 23 females) and the age of patients ranged from (8 to 57) were collected from patients who attended in the operating room at Imam Hussein medical city in Karbala and diagnosed by physicians as acute appendicitis.

2.2. Clinical Samples

Usually, all patients were under the follow up after the operation. The specimens were placed in 1 mL of the normal saline 0.9% in a sterilized screw-capped container (Bio-Rad, 2014). Specimens directly has been transferred to the laboratory. In the hood, 1 gram of specimen was taken and crushed and placed in screw capped (glass tube), the tubes containing specimens of appendices were mixed by Vortex following inoculation on culture media, macckonkey agar, blood agar and mannitol salt agar by using streaking method, the samples were cultured aerobically at 37°C for duration of 24 hrs. for Storage of Bacteria the remain of specimen placed in screw capped (glass tube) contain brain heart infusion broth (BHI) and stored at -20°C (MacFaddin, 2000). and after incubation period, the growth was examined. If no growth were detected, then the plates were re-incubated for a further 24 hrs before discarding as negative result.

2.3. Questionnaire Sheets

The questionnaire sheet was filled out by the patients participating in our study and included knowledge of their age, gender, symptoms, medical and genetic history**.**

2.4. Identification of the Isolates

The isolated from pure colonies was phenotypically identified based on morphological, cultural, and biochemical properties. by using GN cards (ID) and GN cards (ID) of the VITEK 2 system (Biomérieux, France), As the protocol for institution, the ID results obtained using this traditional workflow were used as the standard for comparison. (Ha *et al.*, 2018).

2.5. Antimicrobial Sensitivity Test

Antimicrobial susceptibility testing determines a bacterial isolates susceptibility to a set of antibiotics. The cards were loaded into the VITEK 2 system automatic reader-incubator after being inoculated. Colony counts were used to make sure the number and density of microorganisms inoculated into the VITEK 2 cards were right (Bazzi *et al*., 2017).

2.6. Exclusion Criteria

We excluded only persons with abdominal pain at any location and with no particular suspicion of appendicitis, other patients excluded were those that had peritonitis from ruptured appendix and those that had incidental appendectomy whereby appendix was removed during laparotomy for indication other than acute appendicitis.

2.7. Statistical Analyses

The results were analyzed statistically in SPSS version 22 to find out Chi-square, ANOVA (One away). Probability levels were less than 0.05 is significant ($p < 0.05$).

3. Results and Discussion

3.1. Sex-Based Distribution of Acute Appendicitis and Comparison with Previous Studies

The results of our study showed that the prevalence of acute appendicitis in males were 27 (54%) whereas in females it was 23 (46%) in Fig.1., there were no significant differences ($P \geq 0.05$) between both genders. The results indicate that the majority of cases were be in males then females, this result agree with study reported by (Abdulla *et al*.,2023). It has been demonstrated a statistically significant difference that males by 77.2% outnumbered females with 27.8% which is in accordance with these studies. (Daldal and Dagmura, 2020)showed different results, which found (59.7%) of females and (40.3%) of male patient. Distribution differences of appendicitis between both sexes might be due to the different in specimens' size that involved in each research or due to exclusion of certain patients' cases, or may be due to the misdiagnosis with other diseases in females such as gynecological diseases (Zhong *et al.*, 2014).

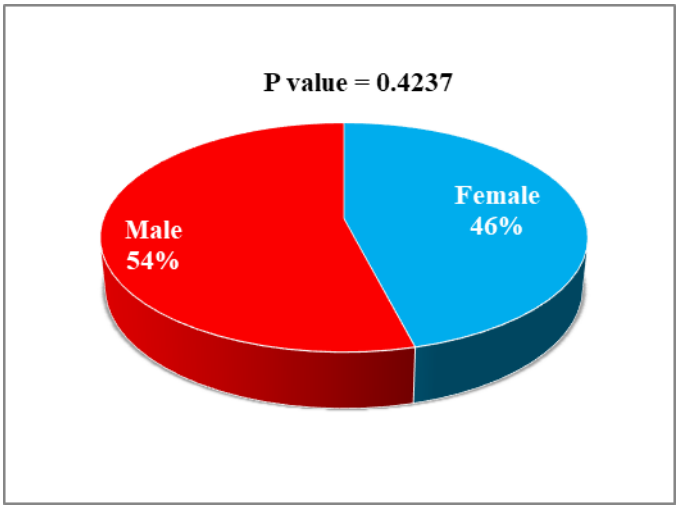

Figure1: Shows the Distribution of Appendectomy Specimens According to Gender

Ages of people who took part in this study varied from (7 to 52) years old in the healthy control and (8-57) in the patients. The age means of the patients (21.12±10.86 years), while the age means of the healthy control (21.76±11.79 years). Furthermore, there was no significant difference between the two groups according to age (p-value =0.7783). As shown in the Table1. Second research also discovered no statistically significant differences in age between the control and patients (Dinc *et al.*, 2015).In contrast, other research conducted in the same method comprised a total of 200 participants; however, the results of this investigation showed that there was strong significant difference in age between the two groups (Boshnak, Boshnaq and Elgohary, 2018; Haghi, Pourmohammad and Rabiee, 2019).

Table1: Distribution of Study Groups According Age

Groups	No.	mean ± SE	Median	Range
Healthy	50	21.76±11.79	19	7 – 52
Patients	50	21.12±10.86	19	8 – 57
P value	0.7783			

The majority rate of appendicitis was between (16-30) ages with a percentage 44%, (1-15) with a percentage 40%, (31-45) with a percentage 14 % and the minority rate was 2 %which belong to age (46-60), as in Fig.2. Our results agree with (Abdulla *et al.*, 2023). Also, study was done on 90 cases and the majority ratio were (46.09%) (35.65%) in age group with mean (15 & 25.5) respectively (Zhong *et al.*, 2014). Another study recorded that the age group ranging from 10 to 25 years was the most group affected by appendicitis (63%) (Karim, Shah and Durrani, 2019). (Almaramhy, 2017)concluded that increasing in the incidence of appendicitis in the age (15-25) might be because the occurrence of appendicitis due to the obstruction of appendix as a result of lymphoid hyperplasia because appendix contains extreme amount of lymphoid tissue in sub mucosa increasing in the number and size with increasing age, reaching extreme number and size through teenager with a higher probability of developing Appendicitis, or may be because an increased number of people in this group are exposed to the pathogens, which is transmitted through the digestive tract as a result of various foods**,** children are four times as likely than adults to get appendicitis Because of their physiological and metabolic traits and their comparably immature immune system, children are exposed to ambient climatic factors more than the adults .Appendicitis is most common between 10-20 years, yet, can occur at any age (Hancerliogulları *et al.*, 2017). Therefore, it is feasible to refer to the fact that appendicitis is more common in younger than in elder people, also elucidated that lower ratio was in age above 35 years that might be due to the regression in a mount of lymphatic tissue in the appendix. Differences in prevalence of appendicitis between age groups may be related to family history and genetics, as a family member is more likely to become infected (if previously infected) than in families that have not had infectious diseases before (Ross and Pawlina, 2011; Kleif, Vilandt and Gögenur, 2016; Goel, 2022).

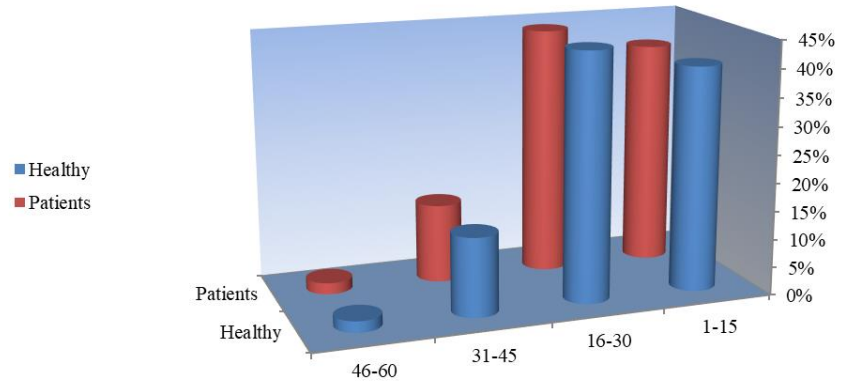

Figure2: Represents the Age Groups of the Study Sample

The clinical features correlated with acute appendicitis are showed in the Table2. 50 (100%) showed abdominal pain, vomiting was seen in 38(76%) patients, while 37(74%) patients were with nausea, Other features were fever 13(26%) and diarrhea 5(10%), the differences were significant between the symptoms and patients. From the results described above one can concluded that the abdominal pain is the commonest symptoms which may draw attention to the case as suspected appendicitis, these results were in accordance with related study who notice that abdominal pain was the most common feature of acute appendicitis (Goudie, 2023).

Table2: Distribution of the Acute Appendicitis According to Symptoms (N=50)

Clinical feature	No. (%)
Abdominal pain	50 (100%)
Vomiting	38 (76%)
Nausea	37 (74%)
Fever	13 (26%)
Diarrhea	5 (10%)

In this study all specimens yielded positive results for bacterial growth , a total of nine genera bacterial appendicitis, seven genera were gram- negative and two genera were gram- positive as shown in the Table3, gram negative bacteria was the common causes of acute appendicitis compared with that of gram positive, they were 47(94%) isolates and 3(6%) isolates respectively and there where highly significant difference between gram positive bacteria and gram negative bacteria (p-value= 0.00001**) show in Fig.3. The most common microorganism was *E. coli* which accounted for 29(58%) isolates, followed by *Klebsiella pneumoniae* isolates 8 (16 %), 5(10%) isolates of *Psedomonas aeruginosa*, 2(4%) isolates of *Enterococcus faecalis*, 1(2%) isolates of *Enterobacter aerogenes*, 1(2%) isolates of *Salmonella typhi* and 1(2%) of *Proteus mirabilis*. *Staphylococcus aureus* was the most frequent microorganism among gram-positive bacteria which accounted as 2(4%). While *Staphylococcus epidermmidis* was accounted as 1(2%). Our results being found were in agreement with other results recorded by (Rasmussen *et al.*, 2024). Those results were accepted and suspected since *E. coli* is the most common organism multiplying and quickly adheres on the surfaces of tissue. *E. coli* has other virulence factors such as host cell surface modifying factors, toxins, hemolysin and cytotoxic necrotizing factor type I (CNFI) (Garcia *et al.*, 2013).

Klebsiella pneumonia isolates were 8 (16 %) , this organism has a capsule that plays an essential role through the initial steps of the pathogenicity by interact with the mucus producing cells, mucus membranes colonization by bacteria is enjoyed to an adhesion process involved specific adhesions on the surface of bacterial. In addition to several pili involved in adhesion to the epithelial cells of intestine (Riwu, Effendi and Rantam, 2020; Abbas *et al.*, 2024). *Klebsiella pneumoniae* strains are an emerging threat in medical center and should be targeted for early identification and stringent control of infections brought on by *Klebsiella pneumoniae*. The explanation for the detection of *Pseudomonas aeruginosa* in appendix as causative agent of appendicitis due to the ability of this organism to attach and colonize epithelial tissue probably by pili and by a gene layer surrounding bacterial cells, also *Pseudomonas aeruginosa* possesses other virulence factors (enzymes and toxins), enable it to cause infection (Riwu *et al.*, 2022). Other gram- negative *Enterococcus faecalis*, *Salmonella typhi*, *Proteus mirabilis* and *Enterobacter aerogenes* were also detected in acute appendicitis but in low frequencies in compared with the other gram-negative bacteria. The implication of these bacteria in acute appendicitis are suspected, as they belong to the enteric group and all these bacteria have virulence factors permitting them to cause disease (Wang *et al.*, 2023). In our study several gram-positive bacteria characterized by *Staphylococcus aureus*, *Staphylococcus epidermmidis* also isolated and identified from patients with acute appendicitis but in low frequencies in comparative with gram negative bacteria. Gram positive bacteria are rarely reported due to adhesive and colonizer factor being less in gram positive in compared with gram negative furthermore most of gram-positive bacteria are fastidious require for special growth factors (vitamin, amino acids, etc) and growth condition (O_2, $CO_{2\ \ldots etc}$). However qualitatively, gram positive infections are more serious such as infection with bacteria *Clostridium spp*. The correlation between bacterial infection and appendicitis is characterized by an increase in bacterial presence leading to a higher incidence of appendicitis, studies have shown that specific bacteria, such as *Escherichia coli* and *Streptococcus spp.* are commonly found in patients with appendicitis, particularly in complicated cases (Zachos *et al.*, 2023).

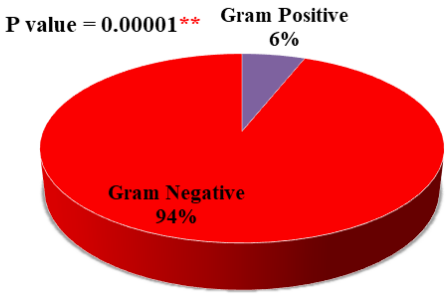

Figure3: Distribution of Bacteria Isolated from Appendicitis Patients

Table3: The Type of Bacteria Isolated from Appendicitis Patients

Bacteria	No.	Percentage (%)
Gram Positive		
Staphylococcus aureus	2	4 %
Staphylococcus epidermmidis	1	2 %
Total	**3**	**6 %**
Gram Negative		
Escherichia coli	29	58 %
Enterobacter aerogenes	1	2 %
Klebsiella pneumonia	8	16 %
Enterococcus faecalis	2	4 %
Proteus mirabilis	1	2 %
Psedomonas aeruginosa	5	10 %
Salamonella typhi	1	2 %
Total	**47**	**94 %**

3.2. Sensitivity Patterns to Antimicrobial Agents

This is an academic and practical study that determines the effect of different types of antimicrobial on microorganisms isolated from patients' specimens. Also taken into consideration is the extent to which bacteria respond to these antimicrobial, and to determine what alternatives are available for Iraqi surgeon to use in cases like these.

3.2.1. Antimicrobial Susceptibility for Gram Positive Bacteria

From observation the results of antimicrobial susceptibility profile for gram positive bacteria in patients with acute appendicitis were found all species isolated were resistance to the benzylpenicillin and oxacillin (100%), and all species isolated were sensitive to the rifampicin, ticarcillin, vancomycin and penicillin (100%). Isolates of gram-positive aerobic cocci were resistant to clindamycin, fusaric acid, erythromycin and tetracycline (66.6%) ,and resistant to gentamicin and ciprofloxacin 33.3% Fig.4.

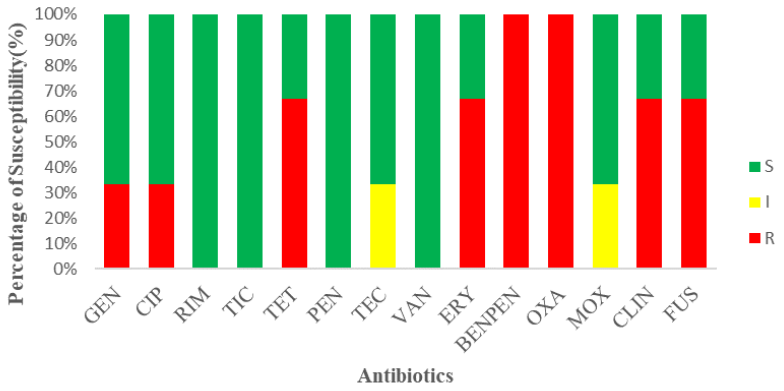

Figure4: Percentage of Bacterial Susceptibility to Various Antibiotics.
The bar chart illustrates the susceptibility profile of bacterial isolates against a range of antibiotics. Susceptibility (S) is shown in green, intermediate resistance (I) in yellow, and resistance (R) in red. Antibiotics such as ciprofloxacin (CIP), vancomycin (VAN), and teicoplanin (TEC) exhibited high effectiveness with 100% susceptibility, while penicillin (PEN), benzylpenicillin (BENPEN), erythromycin (ERY), oxacillin (OXA), and clindamycin (CLIN) showed high resistance rates. These results highlight the variability in antibiotic efficacy and emphasize the importance of antimicrobial susceptibility testing in guiding appropriate therapy.

3.2.2. Antimicrobial Susceptibility for Gram Negative Bacteria:

From the observed of the results of the antimicrobial susceptibility of gram-negative bacteria showed that all species had be isolated were sensitive to amikacin and imipenem (100%) while most isolates were resistance to ticarcillin and piperacillin 92.8%, aztreonam 78.5%, ciprofloxacin72.7%ticarcillin/clavulanicacid71.4%, cefepime60%, gentamicin50%, tobramycin57.1%, trimethoprim/sulfamethoxazole 55.5%, piperacillin/tazobactam55% as shown in Fig.5.

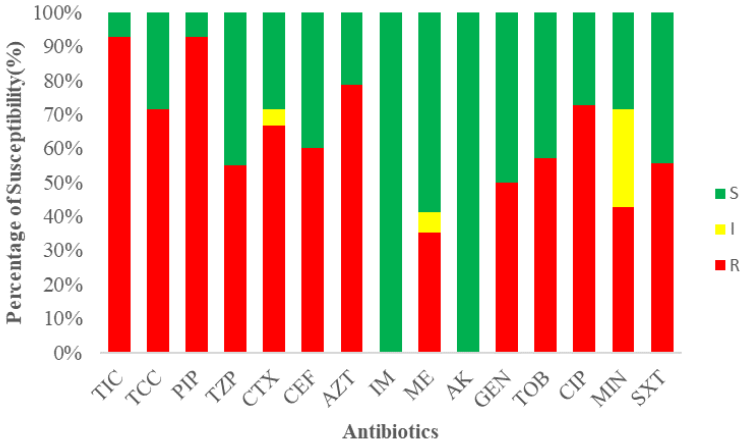

Figure5: Percentage of Bacterial Susceptibility to Various Antibiotics

This bar chart illustrates the susceptibility profiles of bacterial isolates tested against multiple antibiotics. Susceptibility (S) is shown in green, intermediate resistance (I) in yellow, and resistance (R) in red. High resistance rates were observed for several antibiotics, including ticarcillin (TIC), piperacillin (PIP), cefotaxime (CTX), ciprofloxacin (CIP), minocycline (MIN), and trimethoprim-sulfamethoxazole (SXT). In contrast, carbapenems such as imipenem (IM) and meropenem (ME) exhibited 100% susceptibility. These findings emphasize the prevalence of multidrug-resistant strains and the critical need for targeted antimicrobial therapy based on

our results showed that both Imipenem and Amikacin are more effective antimicrobial against all gram-negative bacteria. Our results agreement with a new study where both imipenem and Amikacin were well effective against gram negative bacteria. gram positive bacteria in our study showed sensitivity to penicillin, vancomycin, rifampicin and ticarcillin which agree with a recent study (Heo, 2021; Sahra *et al.*, 2021). gram positive bacteria which have been characterized to be sensitive to most common antibiotics in comparison with gram negative bacteria due to the difference in the outer membrane structure which looks to be permeable to most antibiotics in gram positive bacteria than gram negative bacteria. Our study found that all species of gram-positive bacteria had be isolated were resistance to benzylpenicillin and oxacillin, most gram-negative isolates were resistance to ticarcillin and piperacillin 92.8%. Gram negative bacteria have broad spectrum resistance for antimicrobial agent, the production of β lactamase is the main mechanism for this resistance (Bryskier, 1997; Jubeh, Breijyeh and Karaman, 2020). Resistance may be attributed to the continuous and excessive intake of the antimicrobial by the patient that results in the development of the bacterial resistance. Iraqi patients are well known for taking antimicrobial for everything without doctor consultation so this is a very strong reasons for this resistance. In some time use lower dose of antimicrobial gives the appearance that bacteria are resistant whereas in actual fact they are not affected by lower doses of antimicrobial given or use higher doses of antimicrobial to patient with low immunity. Generally, combination of antimicrobial can lead

to declined efficiency of drugs or sometimes increased effect on bacteria as it was by (Leus *et al.*, 2023; Salam *et al.*, 2023). Also, problems of resistance occur in patients susceptible to colonization as in hospital which associated to presence of drug resistant bacteria that may originate in hospital. Scientists observed that acquired drug resistant can also be the result of therapy failure. The importance of the use of prophylactic antimicrobial before operation has been demonstrated in a number of studies who found the aim of this treatment line is to prevent post-surgical infections following open appendectomy. The optimum type and dose of antimicrobial is unknown, so this carries the possibility of either under treatment with increased risk of post-operative infection or over treatment which could result in the microbial resistance. There are many reasons to which the differences in the antimicrobial sensitivity reported in our study can be attributed. The unnecessary prophylactic use of antimicrobial should be discouraged since this may result in increased selection of resistant variants or super infection with resistant flora, the poor quality of the antimicrobial source, absence quality control for imported antimicrobial and poor storage conditions all these participate in change of results (Andersen, Kallehave and Andersen, 2005). Antibiotic resistance significantly affects the management of bacterial infections in appendicitis, leading to increased complications and necessitating careful selection of empirical antibiotic therapy. Ongoing surveillance of resistance patterns and adaptation of treatment protocols are crucial to improving patient outcomes (Andersen, Kallehave and Andersen, 2003).

4. Recommendations

Conduct an extensive study on pathogens from other microorganisms and determine their proportion in causing appendicitis and study the possibility of the present of human leukocyte antigen (HLA) that may determine susceptibility of persons for acute appendicitis.

5. Acknowledgements

We express our genuine appreciation to the hospital staff and study participants.

6. Ethical Approval

Before the specimen was collected, written permission was obtained from each study participant, and all subjects involved in this experiment were informed. The university of Kerbala, College of Education for Pure Science Ethics Committee gave its approval to this work.

7. Conflict of Interest

The authors declare there is no conflict of interests

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