

The Relationship between Some Bacterial Species Isolated from Wounds with the Immunoglobulin-G (Igg)

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Abstract

Samples were collected from patients with wound infection 38 samples of both sexes, males and females, their ages ranged between (4-60) years from patients who were admitted to Salah El-Din General Hospital, Tikrit Emergency Hospital, and outpatient clinics for both sexes. A period from the publication of space sciences from mid-October 2021 until March 2022, after which samples were transferred to the competent laboratory. This study was conducted on patients suffering from wound infection in Salah El-Din General Hospital and Tikrit Emergency Hospital, for the period from the beginning of October 2021 until March 2022. 38 urine samples were collected for both sexes, 20 samples (52.63%) Female samples and 18 (47.36%) male samples were taken. These samples were collected to check for bacterial infection associated with inflammation. It was found that 24 (63.15%) samples were growth-positive and 14 (36.84%) growth-negative samples, and during laboratory diagnosis 34 bacterial isolates were obtained from the growth-positive samples. Staphylococcus aureus and Staphylococcus epidermidis had the highest rate among all bacterial isolates isolated from patients with wound infections and amounted to 12 (35.29%) and 10 (29.41%) respectively, followed by Escherichia coli 6 isolates (17.64%), while pseudomonas aeruginosa and klebsiella pneumoniae, with a lower percentage and the same rate in 3 isolates for each (8.82%). Most of the bacterial isolates (Staph aureus, Staphylococcus epidermidis, Ecoli, Klebsiella pneumoniae, Pseudomonas aeruginosa) were resistant to antibiotics, (Amikacin 30 µg, Erythromycin.10 µg, Ceftriaxone 10 mcg, Azithromycin15 µg Trimethoprim - sulfamethoxazole 25 µg1.25/23.75mcg). also shown the largest percentage of isolation of positive bacteria was in the group between (25-34 years), followed by the groups (15-24 years) and (35-44 years) equally. Followed by the age group between (1-14 years), and the lowest isolation rate in the two categories (45-54 years) and (55-65 years) equally. Studies have shown that IgG plays an important role in controlling infection of body tissues, and protects the body from various infections, including bacterial infections. The results of our current study showed a significant increase in IgG in wound infection patients, and the results of this study agreed. The study with the findings of the researcher where he found that IgG increases in microbial infection.

Keywords: Antibiotics resistant, IgG, SKIN, WOUND INFECTION

1. Introduction

The skin is the layer that covers and protects the body and acts as a physical barrier. It is impossible for pathogens to penetrate healthy skin. Despite this, microbes can enter from different places, and it is also the body's first line of defense from microbes, as it is possible for some parasites to penetrate healthy skin (1). The healthy skin is the main line of defense against bacterial pathogens, and the occurrence of damage or damage to the skin increases the possibility of infection, and the greater the damage in the skin increases the possibility of infection with bacteria on the surface of the skin and the types found on the surface of the skin (Staphylococcus aureu) (2). The skin is the main innate barrier that protects internal tissues from infection, and its disruption leads to wound formation, and these wounds can become contaminated with pathogenic bacteria, hindering the healing process (3). There are two main parts to the skin: the epidermis and the dermis (4), The layers of the skin are shown In Figure (1) the cross-section

of the skin (5).

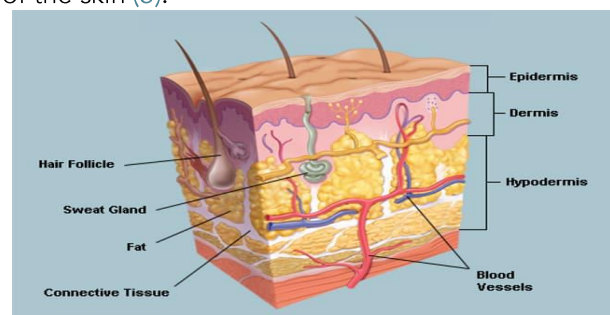


Figure (1) cross-section (A) layers of human skin

There are many definitions of wounds, as it can be defined as any cut or breach in the natural tissue that occurs to the skin for mechanical, physical, chemical or biological reasons, allowing the entry of pollutants into the blood and tissues, which leads to the occurrence of cellular disorders (6).

A wound is a tear in the epithelial layer of the skin or mucous membrane as a result of exposure to physical or thermal damage, and the wound is classified as acute and chronic depending on the nature of the wound and the duration of healing (7,8). Chronic

wounds refer to wounds that have not been regularly treated and healed to achieve functional and anatomical integrity after three months (9). Whereas in acute wounds there is a delicate balance between production and degradation of molecules such as collagen. In chronic wounds this balance is lost, and deterioration plays a large role in wound healing (10,11). In patients with wound complications resulting from the spread of pathogenic microorganisms, septicemia, bacteremia, and shock are usually associated with, and prolonged hospital stay increases the likelihood of developing drug resistance, and this resistance may lead to long-term epidemics (12). Common bacterial pathogens associated with wound infections include:

(Staphylococcus aureus, Enterococcus spp., Streptococcus spp., Klebsiella pneumoniae, Proteus spp., Escherichia coli and Pseudomonas aeruginosa (13). And the occurrence of bacterial infection in wounds includes several initial stages Contamination, The second stage is colonization, the third stage is Critical colonization, and the last stage is infection (14). Immunoglobulins, Also known as antibodies, they are glycoproteins, which are produced by plasma cells in response to an immune reaction to antigens such as bacteria, viruses and fungi. Several types of immunoglobulins IgM, IgD, IgE, IgA, IgG (15). IgG, it is one of the types of immunoglobulins and the most abundant species, in the blood and extracellular fluids, which leads to the control of infection of the body tissues, and IgG protects the body from viral, fungal and bacterial infections, as it has a humoral response (16). It is monomer, i.e. it consists of two light chains and two heavy chains, and it is bivalent because it contains two regions that bind to the antigen and the immune antibody IgG, and it is found in the serum of the mother, and this type can cross to the fetus through the placenta, and it has receptors that facilitate its passage through the placenta to provide Protecting the fetus, it is secreted in the mother's milk and provides the fetus with humoral immunity before the immune system develops, and it constitutes about 85% of the total level of immunoglobulins (17,18). It has many functions, including complement activation and opsonization, and neutralizing toxins (19).

2. Methods and Materials

1- Collect samples

collected 38 samples were from patients with wound infections of both sexes, males and females, their ages ranged between (4-60) years from patients who were admitted to Salah El-Din General Hospital, Tikrit Emergency Hospital, and outpatient clinics for both sexes. A period from the publication of space sciences from mid-October 2021 until March 2022, after which samples were transferred to the competent laboratory.

2- Samples culture

After performing a microscopic examination confirm

the inflammation of the wounds on different media such as nutrients, blood and McConkey agar. In addition to some characterization media such as cetramide, Eosin methylene blue (EMB) and mannitol salt agar, these plates were then incubated at 37°C for 18-24 hours.

3- Diagnosis

The cultures were diagnosed after incubation and microscopic examination with biochemical tests, as well as based on the morphology of the growth of bacterial colonies. Some biochemical tests such as (catalase, oxidase, coagulation, and IMVC tests) were also performed for the isolates that help to identify the bacterial species, and to confirm the diagnosis was used a strip of (API 20 E, and API STAPH).

4- Antibiotic sensitivity test

An antibiotic sensitivity test was done for all isolated bacteria, and this test was performed on 6 antibiotics (Amikacin 30 µg, Azithromycin 15 µg, Ceftriaxone 10 µg, Erythromycin 10 µg, Trimethoprim - sulfamethoxazole 25 µg/1.25/23.75mcg, Co-trimoxazole 30 µg). the tablets were approved by the Turkish company BIOANALYSE. Sensitivity was measured based on the diameter of the area of inhibition around the disc.

5- IgG test

Blood samples were also taken from the same patients with wound infection for IgG test, where the IgG concentration was determined using the (Fincare plus) technology and according to the instructions in the manufacturer's test kit (mybiosource) to detect IgG levels in the patients' serum.

3. Results and Discussion

1-Samples distribution according to the bacterial growth

From patients with wound infection, 38 samples were collected from both sexes, males and females, their ages ranged between (4-60) years from patients who were admitted to Salah El-Din General Hospital. The results in Figure (1) showed that 24 samples (63.15%) out of 38 samples showed growth in the culture medium, and 14 samples (36.84%) did not show bacterial growth in the culture medium, shown in figure (2).

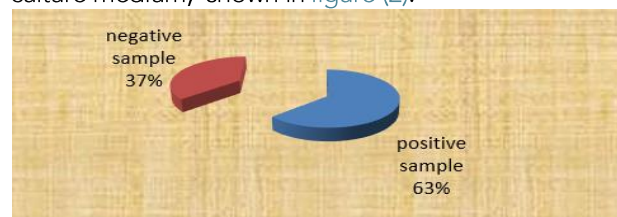


figure (2), Samples distribution according to the bacterial growth

The current study was approached to the study (20), where the percentage of isolates that showed growth on different culture media was (78.9%) and Samples that showed a negative growth on the media by (21.1%) of the total samples. This study

agreed with (21), where the percentage of samples that showed growth on the culture media (47.27%) was higher than the percentage of samples that showed negative growth, where the percentage was (25.45%). Perhaps the reason for the growth is the presence of bacteria in a normal flora

On the skin, and it can become opportunistic in the case of wound infection. As for the reasons for the lack of growth on the culture media, it may be due to the difference in the environment and the nature of the samples or the patients taking antibiotics before taking the sample (22).

Table (1), Arrangement of numbers and percentages of isolates extracted from wounds, distributed according to age groups

age classes	Gram Positive Isolate		Gram negative Isolate		The total (%)
	NO	%	NO	%	
1 – 14 years	3	2.542%	0	0%	3(2.542%)
15 – 24year	4	3.389%	1	0.847%	5(4.236%)
25 -34year	13	11.016%	2	1.694%	15(12.711%)
35 -44year	4	3.389%	4	3.389%	8(6.778%)
45 -54year	1	0.847%	1	0.847%	2(1.694%)
55 -65year	1	0.847%	0	0%	1(0.847)
Total (%)	26	22.031%	8	6.777%	34(28.81%)

2- Arrangement of numbers and percentages of isolates extracted from wounds, distributed according to age groups

Table (1) shows the number of isolates obtained from wound infections and distributed according to age groups, and that the largest isolation rate of bacteria was in the group confined between (25-34 years), where the largest isolation rate of negative bacteria was in the group between (35-44 years old).) followed by the category (25-34 years) and the two categories (15-24 years) and (45-54 years) equally and the lowest percentage of isolation in the two categories (1-14 years) and (55-65 years) if no bacterial species were isolated, and it is also shown The largest percentage of isolation of positive bacteria was in the group between (25-34 years), followed by the groups (15-24 years) and (35-44 years) equally. Followed by the age group between (1-14 years), and the lowest isolation rate in the two categories (45-54 years) and (55-65 years) equally, and these results were in agreement with the study (23) where the isolation rate in this study was the highest in The age group is confined between (15-35) and the rate of isolation decreases with age, and this may be due to the fact that during adolescence there is high physical and hormonal activity with continuous movement and constant exploration and mixing, and this may make them more susceptible to infection with different pathogens and at a higher rate than the groups Other age (24).

3- Frequency of bacterial isolates between

wound infection patients

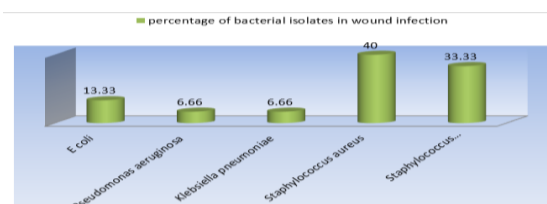


Figure (3): percentage of bacterial isolates in wound infection.

During culture of samples, 30 bacterial isolates were obtained from wound infections shown in Table (3), where the highest percentage of Gram-positive bacteria was *Staphylococcus aureus* 12 isolates (40%), followed by *Staphylococcus epidermidis* 10 isolates with a percentage of (29.41%). as for the Gram-negative bacteria, *Escherichia coli* was the highest bacterial isolate, as 4 isolates were obtained with a percentage of (13.33 %), followed by bacterial species *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are the least bacterial isolates, as 2 isolates were obtained with a percentage of (6.66 %) for both. These bacteria are the most common in wound infections because of their spread and that they are responsible for hospital-acquired nosocomial infections and are characterized by their resistance to disinfectants used in hospitals and to commonly used antibiotics, where the results of this study converged with studies (20) and (21), as a result of the presence of some isolates bacterial with the results obtained by the researchers.

4- The resistance of some bacterial isolates toward some antibiotics

Table (2) The resistance of some bacterial isolates toward some antibiotics

Bacterial type	NO	Amikacin 30 µg		Erythromycin 10 µg		Azithromycin 15 µg		Ceftriaxone 10 µg		Trimethoprim - sulfamethoxazole 25 µg 1.25/23.75mcg	
		R	%	R	%	R	%	R	%	R	%
		<i>Staphylococcus aureus</i>	12	3	25	12	100	9	75	12	100
<i>Staphylococcus epidermidis</i>	10	3	30	12	100	7	70	5	50	7	70
<i>E. coli</i>	4	1	25	4	100	3	75	4	100	3	75
<i>Klebsiella pneumoniae</i>	2	0	0	2	100	2	100	2	100	2	100
<i>Pseudomonas aeruginosa</i>	2	0	0	2	100	1	50	2	100	2	100

The results shown in Table (2) showed that *Staphylococcus aureus* showed 100% resistance to Erythromycin, and the reason for the resistance might be due to its possession of plasmids carrying genes that encode changes in the genetic structure, which prevents its association with this antigen (25), also matching the study (25). (21), and this study does not match with the results reached by the researcher (26), where the percentage of resistance was 30%. About the antibiotic Ceftriaxone, where the resistance of bacteria was 100%, where the study (21) completely matched the ratio, and somewhat converged with (27), where the resistance rate was 77.3%. As for the anti-Amikacin, where the bacteria showed weak resistance by 25%, and it matched with (21) In terms of the same percentage, as well as with the study (28). As for the anti-Azithromycin, the percentage of resistance to the antibody was 75% where it matched with (21), while for the anti-trimethoprim - sulfamethoxazole, the resistance percentage was 25% where it differed with the study (29) and the resistance was by 60%, and perhaps the reason for the great difference in the resistance rates is due to the difference in the isolation environment and sample size between the current study and that study.

As for *Staphylococcus epidermidis* bacteria, they showed 100% complete resistance to Erythromycin, and this result was not identical with (26), where the percentage was 33%, and this result agreed with (21). As for the antagonist Trimethoprim - sulfamethoxazole, the resistance was 70%, which is close to the study (30), where the resistance rate was 49.1%, also in the study (31). The resistance was high towards the anti-Azithromycin, the resistance was 70%, and this result is close to the study (21). As for Ceftriaxone antagonist, the resistance rate was 100%, which is somewhat close to study (20), where the ratio was 82.3%, and the anti-amikacin was 30%, and it was close to study (20), where the resistance rate was 35.2%.

As for *Escherichia coli*, the results showed 100% resistance to Erythromycin.

Ceftriaxone and this study were close to (32) for Ceftriaxone, where the resistance rate was 66.58%, and for Erythromycin, where the results were close to study (33) and the resistance rate was 88%. Where the bacteria were completely sensitive and there is no resistance. As for the anti-Azithromycin, the resistance was 75%, and it was close to (21) where the ratio was 75.86%, and for the anti-trimethoprim - sulfamethoxazole, the resistance was 75% and it agreed with (34), the ratio was 65%.

The current study showed a high resistance by *Klebsiella pneumoniae* to each of the following antibiotics: Erythromycin, Azithromycin, Ceftriaxone, Trimethoprim - sulfamethoxazole, where the resistance was 100%, and it matched with study (20) for the anti-Ceftriaxone, where the resistance was 94.4%, and it was similar to the study (33) with regard to Erythromycin, where the resistance was 100%, and with regard to Trimethoprim - sulfamethoxazole, the

ratio was 100%, and this The study with (21) and the resistance was identical. This may be due to its possession of the beta-lactamase enzyme, and it may also be due to its widespread presence, which makes it constantly exposed to antibiotics. As for the anti-Amikacin, the bacteria were completely sensitive to it, and this result matched with (35) where it was completely sensitive to the antibacterial, and it was close to (21) where the resistance rate was 25%.

Where the bacteria *Pseudomonas aeruginosa* showed high resistance to many antibiotics such as Erythromycin, Ceftriaxone, Trimethoprim - sulfamethoxazole, where resistance was 100%. This resistance may be since bacteria can show resistance to different types of antibiotics, and possess many virulence factors, and it is also an opportunistic species that exploits the weakness of the immune system, especially in hospitalized patients (21).

This percentage corresponded to (33) where the resistance was 100% for Erythromycin, and 94% for Trimethoprim - sulfamethoxazole. As for the anti-Amikacin, the resistance percentage was completely non-existent, as it approached (21) where the percentage was 4.5%, and approached (33) where the resistance rate was 17%, and it differed from the study () where it was 77.77%, and the current study showed a resistance of 50%, which is identical With (21), one of the causes of bacterial resistance is their production of beta-lactamase enzyme or because they have a permeable barrier represented by the outer membrane layer, and it is one of the most important reasons for the resistance that bacteria possess against disinfectants and antibiotics.

5-The relationship between IgG levels and bacterial types

Bacterial types	IgG Levels
control	98.299 ± 0.443 b
<i>Staphylococcus aureus</i>	290.411 ± 16.070 a
<i>Staphylococcus epidermidis</i>	273.598 ± 14.895 a
<i>Escherichia coli</i>	255.028 ± 26.529 a
<i>Klebsiella pneumoniae</i>	294.413 ± 25.701 a
<i>Pseudomonas aeruginosa</i>	229.871 ± 38.840 a
P VALUE > 0.05	

Studies have proven that IgG immunoglobulin plays an important role in controlling infection of body tissues, and protects the body from various infections, including bacterial infections (37). The results of our current study showed very large differences at the level of probability. (p value > 0.05) a significant increase in IgG in patients with wound infections, and the results of this study agreed with the results of the researcher (38) where it was found that IgG increases in microbial infection.

References

- Gerard J.T.; Berdell R.F. and Christine L.C. (2016). Microbiology An Introduction 12th.21:580-581.
Singhal, H. and Zammit, C. (2002). Wound infection emedicine speciattie.

- Tom, I. M. (2019). Infection of Wounds by Potential Bacterial Pathogens and Their Resistogram. *Open Access Library Journal*. 6(07): 1-13.
- Bolognia, J.L.; Jorizzo, J.L. and Schaffer, J.V. (2012). *Dermatology* 3rd ed, Volume (1).
- Hoffman, M. (2014). *The Skin (Human Anatomy): Picture, Definition, Function, and Skin Conditions*. Retrieved from: <https://www.webmd.com/skin-problems-and-treatments/picture-of-the-skin#2>.
- O'dell, M.L. (1998). Skin wound infections An over view American family physician .
- Robson, M. C., Steed, D. L. and Franz, M. G. (2001). Wound healing: biologic features and approaches to maximize healing trajectories. *Current problems in surgery*. 2(38): 72-140.
- Dubhashi, S.P. and Sindwani, R.D. (2015). A comparative study of honey and phenytoin dressings for chronic wounds. *Indian J. of Surgery*. 77(3): 1209-1213.
- Dhivya, S., Padma, V.V. and Santhini, E. (2015). Wound dressings—a review. *BioMedicine*, 5(4): 24-28.
- Edwards, J.; Howley, P. and Cohen, I.K. (2004). *In vitro* inhibition of human neutrophil elastase by oleic acid albumin formulations from derivatized cotton wound dressings. *International Journal of Pharmaceutics*. 284:1–2.
- Schönfelder, U., Abel, M., Wiegand, C., Klemm, D., Elsner, P., and Hipler, U. C. (2005). Influence of selected wound dressings on PMN elastase in chronic wound fluid and their antioxidative potential *in vitro*. *Biomaterials*. 26(33): 6664-6673.
- Nita, P., Nikita, S., Rajni, S., Saroj, H. and Rakesh, K.M. (2018) Prevalence of Multidrug (MDR) and Extensively Drug Resistant (XDR) Proteus Species in a Tertiary-Care Hospital, India. *International Journal of Current Microbiology and Applied Sciences*. 3: 243-252.
- Sani, R. A., Garba, S. A. and Oyewole, O. A. (2012). Antibiotic resistance profile of gram-negative bacteria isolated from surgical wounds in Minna, Bida, Kontagora and Suleja Areas of Niger State. *American Journal of Medicine and Medical Sciences*. 2(1): 20-24.
- Cook, L., and Ousey, K. 2011. Demystifying wound infection: identification and management. *Practice Nursing*, 22(8), 424-428.
- Edward, A. G. (2014). *Generating Monoclonal Antibodies*. Dana-Farber Cancer Institute, Boston, Massachusetts. 02115
- Vidarsson, G., Dekkers, G., & Rispen, T. (2014). IgG subclasses and allotypes: from structure to effector functions. *Frontiers in immunology*, 5, 520
- Abel, J.; Conklin, J.; Hunter, S. K.; Empey, R.; Tyler, E.; Christensen, A.; Talcott, K.; Ballas, Z. K.; Santillan, M. and Santillan, D. (2013). Defining normal IgG changes throughout pregnancy. *Proc. Obs. Gyn.*; 3 (2): 8-11.
- Finkelman, F. D. (2007). Anaphylaxis: lessons from mouse models. *J. Allergy. Clin. Immunol.*; 12: 506–15–qiz 516–7.
- 19) Harvey, R. A.; Doan, T.; Melvord, R.; Veselli, S. and Waltenbaugh, C. (2013). *Immunology* (2nd ed.) Williams and Wilkins, Philadelphia.; pp: 60-61.
- 20) Al-Danidel, Omar Ajmad Abdul Qadir. (2019). Determination of the inhibitory activity of some essential vegetable oils against some bacterial pathogens for infection of wounds and burns isolated from patients admitted to Salah El-Din General Hospital. Master's Thesis, College of Education - Tikrit University.
- 21) Al-Samarrai, Ahmed Abdel-Bari Abdel-Wahed Latif. (2021). Study of some virulence factors of bacteria isolated from inflammation of wounds and burns in the city of Samarra, Master's thesis, College of Science - Tikrit University.
- 22) Abdali, Yasser Adel Jabbar. (2010). Extraction and purification of the catechin compound from green tea (*Camellia sinesis*) and its synergistic effect on the bacteria causing urinary tract infection. Master's thesis, College of Science, Al-Mustansiriya University.
- 23) Al-Zoubi, M.; Al-Tayyar, S. I.; Ali, H. E.; Al Jabali, A. and Khudairat S. (2015). Antimicrobial susceptibility pattern of Staphylococcus aureus isolated from clinical specimens in Northern area of Jordan. *Iran. J. microbial*. 7 (5): 265-272.
- 24) Joshua, A.; Zeichner, M. D.; Billary, E.; Baldwin, MD.; Cfran, E. Cook, M.D.; Dlawrence, F.; Eichenfield, M.D.; Dsheila, S.; Fallon, M.D.; E David, A. and Rodriguez, M.D. (2017). Emerging Issues in Adult Female Acne. *J. of clinical and aesthetic dermatology* January. (10).
- 25) Nester, E.W., Anderson, D.G., Roberts, C.E., Pearsall, N.N. and Nestor, M.T. (2001). *Microbiology a human prespective*, 3ed ed. McGraw- Hill Higher Education., P.P.295-512, 691-712.
- 26) Jarzis, Khanzad Khader. (2006). Studying the resistance of some types of bacteria isolated from patients to some antibiotics and new chemical compounds. Master's thesis, College of Science/Al-Mustansiriya University.
- 27) Ogunleye, V.O.; Ogunleye, A.O.; Ajuwape, A.T.P.; Akande, K.A. and Adetosoye, A. (2009). Occurrence of Methicilin-resistant Staphylococcus aureus in a Nigerian tertiary Hospital *Afr. J. Biomed. Res.* Vol. 12, No.9:187-192.
- 28) Nwankwo, E.O. and Nasiru, M.S. (2011). Antibiotic sensitivity pattern of Staphylococcus aureus from clinical isolates in a tertiary health institution in Kano, Northwestern Nigeria. *The Pan African medical journal*, 8, 4.
- 29) Ahmed, Selda Saeed Yassin. (2008). Isolation and diagnosis of the causes of wound infections and study of their sensitivity to antibiotics and chemical disinfectants in Kirkuk hospitals. Master's Thesis, College of Education - Tikrit University.
- 30) Ali, Fatima, Abboudi and Hadi, Ali Abbas and Ali, Mujahid Khalaf. (2009). Sensitivity of coagulase-negative bacteria isolated from different pathological conditions to antibiotics, *Tikrit Journal of Pure Sciences*, 14(1), 245-253.
- 31) Al-Jumaily, Hanan Thamer Negm Abd Ali (2017). A comparative study of the virulence factors of bacteria isolated from urinary tract infections in patients with cardiac intensive care, Master's thesis, College of Education for Pure Sciences, University of Diyala.
- 32) Kulkarni, S.; Peerapur, B. and Sailesh, K. (2017). Isolation and antibiotic susceptibility pattern of Escherichia coli from urinary tract infections in a tertiary care hospital of Northeastern Karnataka.

Journal of Natural Science, Biology and Medicine, 8(2), 176.

33) Al-Jubouri, Sami Hamad, Majeed Hamad. (2012). Isolation and identification of some bacteria causing wound infection from patients in Tikrit Teaching Hospital, Master's Thesis, College of Education, Tikrit University.

34) Hassan, Qusai Ali, S. (2009). Inhibitory effect of some plant extracts on pathogenic isolates resistant to antibiotics. Master Thesis. College of Science, Tikrit University.

35) Al-Harmazi, Muhammad Talib Tawfiq. (2016). Isolation and identification of bacteria from the corridors of Kirkuk General Hospital and the effect of some disinfectants on them. Master Thesis, College of Science, Tikrit University.

36) Madigen, M.T., Martinko, J.M. and Parker, J. (2003). Prick biology of microorganisms. 10th ed. Principle. Hill, Inc. London, Sydney, Pte, Ltd. Hong Kong, Toronto, S.A. Dec-V. Tokyo, 1td, Upper Sapper Saddle River, New Jersey .

37) Mallery, D.L.; McEwan, W.A.; Bidgood, S.R.; Towers, G.J.; Johnson, C.M.; James, L.C. Antibodies mediate intracellular immunity through tripartite motif-containing 21 (TRIM21). Proc. Natl. Acad. Sci. USA 2010, 107, 19985–19990.

38) Lighaam, L.; Rispens, T. The Immunobiology of Immunoglobulin G4. Semin. Liver Dis. 2016, 36, 200–215.