مجلة كلية الإسراء
الجامعة للعلوم الطبية

مجلة علمية محكمة تصدر عن جامعة الإسراء

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بسم الله الرحمن الرحيم

جمهورية العراق
وزارة التعليم العالي والبحث العلمي
دائرة البحث والتطوير

Republic of Iraq
Ministry of Higher Education & Scientific Research
Research & Development Department

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Date:

كلية الاسراء الجامعة / السيد العميد المحترم

م/ مجلة كلية الاسراء الجامعة للعلوم الطبية

السلام عليكم ورحمة الله وبركاته ...

أشارة الى كتابكم المرقم ع/١٩٥٠ في ٢١/ ١١/ ٢٠٢٠ بشأن اعتماد مجلتهم التي تصدر عن جامعتكم الموقرة واعتمادها لأغراض النشر والترقيات العلمية وتسجيلها ضمن موقع المجلات العلمية الاكاديمية العراقية ، حصلت موافقة السيد وكيل الوزارة لشؤون البحث العلمي بتاريخ ٢٠٢١/٢/١٤ على أعتماد المجلة المذكورة في الترقيات العلمية والنشاطات العلمية المختلفة الاخرى وتسجيل المجلة في موقع المجلات الاكاديمية العلمية العراقية ، وحسب ما جاء بأعمامنا المرقم ب ت ١٠٩٨٨/٤ في ٢٠١٩/١١/٢٤ **(تقرر اعطاء موافقة مؤقتة لمدة ٦ أشهر على ان يتم تزويدنا بالرقم المعياري الدولي المطبوع والالكتروني وانشاء موقع الكتروني للمجلة وبخلافة تلغى الموافقه وأعلامنا الاجراءات لاحقاً).**

للتفضل بالاطلاع وابلاغ مخول المجلة لمراجعة دائرتنا لتزويده باسم المستخدم وكلمة المرور ليتسنى له تسجيل المجلة ضمن موقع المجلات العلمية العراقية وفهرسة اعدادها ... مع التقدير.

السيد المدير العام المحترم

للتفضل بالتوقيع مع التقدير

د.هناء /المعاون

٢/١

أ.د. غسان حميد عبدالمجيد
المدير العام لدائرة البحث والتطوير
٢٠٢١/٣/ ١

نسخة منه الى:
- مكتب السيد وكيل الوزارة لشؤون البحث العلمي / أشارة الى موافقة سيادته المذكورة أعلاه والمثبتة على اصل مذكرتنا المرقم ب ت م/٤ ١٠٩٣ في ٢٠٢١/٢/١٧ / للتفضل بالاطلاع ... مع التقدير .
- قسم المشاريع الريادية / شعبة المشاريع الالكترونية / للتفضل بالعلم واتخاذ مايلزم ... مع التقدير
- قسم الشؤون العلمية / شعبة التاليف والنشر والمجلات / مع الاوليات .
- الصادرة .

مهند ، أنس
٢٤/ شباط

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تعليمات النشر

في مجلة كلية الإسراء الجامعة للعلوم الطبية

- تصدر جامعة الإسراء (مجلة كلية الإسراء الجامعة للعلوم الطبية) في مجلد سنوي يضم عددين.
- تقوم المجلة بنشر البحوث العلمية للباحثين في تخصصات العلوم الطبية التالية:
  - الطب العام وطب الأسنان
  - العلوم الصيدلانية
  - تقنيات المختبرات الصحية والطبية
  - تقنيات الطب الحيائي
  - التمريض
  - العلوم البيولوجية.
- يشترط في البحث المقدم للنشر أن لا يكون قد نشر أو أرسل لجهة أخرى للنشر .

تخضع البحوث المقدمة للنشر في المجلة للتقييم حسب الأصول العلمية المتبعة من قبل اثنين من المختصين في موضوع البحث ومن ذوي الكفاءة، وقد يستشار بثالث عند الضرورة مع حجب أسماء المقيّمين عند إرسال الملاحظات للباحثين.

- يلتزم الباحث بإجراء جميع التعديلات التي يراها المقيّمان ضرورية ويُرفض البحث إذا اتفق المقيّمان على رفضه، أو رفض من أحدهما وتعديلات جوهرية من الآخر، أو تعديلات جوهرية من كلا المقيّمين.
- يلتزم الباحث عند النشر في هذه المجلة بمليء استمارة التعهد الخاص يبين فيها ملكيته الفكرية للبحث وعدم نشره سابقاً في أي مجلة علمية أو مؤتمر علمي.
- تخضع البحوث المقدمة للنشر لتحديد نسبة الاستلال (الانتحال) Plagiarism باستعمال برنامج Turnitin.

- يعرض البحث قبل النشر للتدقيق من قبل مقيّم لغوي (اللغة العربية واللغة الانكليزية) ويجب على الباحث الالتزام بتعديلاتهما.

تلتزم المجلة بسياسة نشر تعكس التزامها بأخلاقيات البحث العلمي وبنود لجنة أخلاقيات النشر Committee of Publication Ethics

- تلتزم المجلة بجميع الضوابط الصادرة من وزارة التعليم العالي والبحث العلمي / دائرة البحث والتطوير الخاصة بالمجلات العلمية.
- تحتفظ هيئة التحرير بحقها بإجراء التعديلات الشكلية واللغوية اللازمة.
- تحتفظ هيئة التحرير بحقها في عدم نشر أي بحث دون إبداء الأسباب وتعتبر قراراتها نهائية.
- لا ترد البحوث لأصحابها سواء قبلت للنشر أو لم تقبل.
- يزود صاحب البحث بنسخة ورقية واحدة من العدد الذي نشر فيه بحثه.

شروط النشر

1. يطبع البحث بواسطة الحاسوب بمسافات مفردة بين الاسطر وبحجم خط 12 ونوع (Simplified Arabic)، اما العنوان باللغتين العربية والانكليزية فيكون بحجم خط 14 شريطة ألا يزيد عدد صفحاته عن 15 صفحة بما في ذلك الجداول والأشكال والمراجع وعلى وجه واحد على ورق قياس A4 مع ترك هامش في حدود 2 سم من الاعلى والاسفل وهامش بحدود 3 سم من الجانبين الايمن والايسر.
2. لا يفضل نشر البحوث من قبل رئيس وأعضاء هيئة التحرير في المجلة سواء كان البحث منفرداً أو مشتركاً.
3. يقدم البحث بثلاثة نسخ ورقية عند تقديمه للنشر ونسخة محدثة وأخرى إلكترونية بعد قبول البحث للنشر، يسلم البحث بشكله النهائي مطبوعاً **بالنظام الاعتيادي** بمسافة منتظمة لكافة الصفحات عدا الصفحة الأولى **التي تتضمن عنوان البحث وأسماء الباحثين وعناوينهم والبريد الإلكتروني للباحث الأول باللغتين العربية والإنكليزية** وعلى قرص مدمج CD ببرنامج Microsoft Word 2010 .
4. تقبل البحوث باللغتين العربية والإنكليزية ويفضل كتابة البحث باللغة الإنكليزية.

دليل المؤلف Author Guidelines

أدناه الشروط والمتطلبات الواجب مراعاتها من قبل الباحث للنشر في هذه المجلة بشرط أن لا يكون البحث قد نشر أو سينشر في أية مجلة علمية أخرى ولم يمضِ على إنجازه أكثر من أربع سنوات.

1. يجب أن يكون عنوان البحث موجزاً قدر الإمكان ومعبر عن البحث.
2. أسماء الباحثين: تكتب أسماء الباحثين وعناوين عملهم بصورة واضحة مع البريد الإلكتروني للباحث الأول.
3. **يجب أن يتضمن المستخلص موجزاً واضحاً عن البحث مكون من 250-300 كلمة متبوعاً بكلمات مفتاحية 4-6. إذا كان البحث باللغة العربية فيكون المستخلص متبوعاً بالكلمات المفتاحية أولاً، ثم المستخلص متبوعاً بالكلمات المفتاحية باللغة الإنكليزية ثانياً والعكس صحيح.**
4. **المقدمة:** تتضمن مراجعة المعلومات وثيقة الصلة بموضوع البحث الموجودة في المصادر العلمية وتنتهي المقدمة بأهداف الدراسة وأساسها المنطقي.
5. **المواد وطرائق العمل:** تذكر طرائق العمل بشكل مفصل إن كانت جديدة، أما إذا كانت منشورة فتذكر بشكل مختصر مع الإشارة للمصدر، يستعمل النظام العالمي للوحدات Standard International of Units (S.I.Us) بكتابة الوحدات فضلاً عن استخدام مختصرات المصطلحات العلمية المعتمدة عالمياً، على أن تكتب بشكل كامل في أول مرة ترد في النص.
6. **النتائج والمناقشة:** تعرض بشكل موجز وهادف وبنظام متوالي وتعرض النتائج بأفضل صورة معبرة وتوضع الجداول والأشكال في أماكنها المخصصة بعد الإشارة إليها في النتائج.
7. يستعمل نظام الأرقام العربية وهكذا في البحوث المرسلة للنشر وتمثل مناقشة النتائج تعبيراً موجزاً عن النتائج وتفسيراتها.
8. تكون كتابة المصدر في **قائمة المصادر** متضمنة الآتي: اسم أو أسماء الباحثين، سنة النشر وعنوان البحث كاملاً واسم المجلة ورقم المجلد والعدد وعدد الصفحات، مثال:

حمزة، عصام شاكر و جارالله، عزيز لطيف ورشيد، فرقد عبدالله وسلمان، سرحان علي (2018)، تقدير مستويات الزئبق في مصل دم مستخدمين لحشوات الأسنان. مجلة كلية الإسراء الجامعة، المجلد الأول\العدد الأول: 281-294.

9. المستخلص الإنكليزي يجب أن يكون وافياً ومعبراً عن البحث بصورة دقيقة، وليس بالضرورة أن يكون ترجمة حرفية للمستخلص العربي و**متبوعا بكلمات مفتاحية 4-6**.

دليل المقيّم Reviewer Guidelines

أدناه الشروط والمتطلبات الواجب مراعاتها من قبل المقيم للبحوث المرسلة للنشر في هذه المجلة

1. ملء استمارة التقويم المرسلة رفقة البحث المطلوب تقييمه بشكل دقيق وعدم ترك أي فقرة بدون إجابة.
2. على المقيّم التأكد من تطابق وتوافق عنوان البحث باللغتين العربية والإنكليزية وفي حالة عدم تطابقهما اقتراح العنوان البديل.
3. أن يبين المقيّم هل أن الجداول والأشكال التخطيطية الموجودة في البحث وافية ومعبرة.
4. أن يبين المقيّم هل أن الباحث اتبع الأسلوب الإحصائي الصحيح.
5. أن يوضح المقيّم هل أن مناقشة النتائج كانت كافية ومنطقية.
6. على المقيّم تحديد مدى استخدام الباحث للمراجع العلمية الرصينة وحداثتها.
7. أن يؤشر المقيّم بشكل واضح على واحد من ثلاث اختيارات وهي:
   - البحث صالح للنشر بدون تعديلات.
   - البحث صالح للنشر بعد إجراء التعديلات.
   - البحث غير صالح للنشر.
8. يجب أن يوضح المقيّم بورقة منفصلة ما هي التعديلات الأساسية التي يقترحها لغرض قبول البحث.
9. للمقيّم حق طلب إعادة البحث إليه بعد إجراء التعديلات المطلوبة للتأكد من التزام الباحث بها.
10. على المقيّم تسجيل اسمه ودرجته العلمية وعنوانه وتاريخ إجراء التقييم مع التوقيع على استمارة التقييم المرسلة له رفقة البحث المرسل له للتقييم.

المصادر

1. يشار إلى المصادر في متن البحث كما يلي:

اللقب او الاسم الثالث للمؤلف والسنة إذا كان البحث بإسم باحث واحد، وإذا كان مؤلفين فيذكران والسنة وإذا كانوا ثلاثة فأكثر فيذكر اسم الأول وآخرون والسنة.

2. ترتب المصادر حسب الصيغة العالمية (APA) وكما بالأمثلة المذكورة :

أ. بحث في مجلة.

اسم الباحث أو الباحثون، (السنة)، عنوان البحث، اسم المجلة، المجلد، العدد وصفحتي البدء والانتهاء للبحث.

ب. كتب.

اسم المؤلف أو المؤلفون، (السنة) عنوان الكتاب، الطبعة، دار النشر وعدد الصفحات.

ج. الرسائل والأطاريح الجامعية.

اسم الباحث، (السنة)، عنوان الرسالة أو الأطروحة، العنوان (الكلية والجامعة) وعدد الصفحات.

د. بحث في وقائع مؤتمر أو ندوة علمية.

اسم الباحث أو الباحثون، (السنة)، عنوان البحث، اسم المؤتمر أو الندوة العلمية، مكان الانعقاد، صفحتي البدء والانتهاء للبحث.

ترسل البحوث إلى مجلة كلية الإسراء الجامعة للعلوم الطبية على العنوان الآتي:

جامعة الإسراء – قسم التوثيق والنشر

بغداد \ العراق

البريد الإلكتروني :

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(تعهد الملكية الفكرية)

إني\إننا الباحث\الباحثين ..... صاحب\أصحاب البحث الموسوم

(.....

.....)

أتعهد\نتعهد بأن البحث قد أنجز من قبلي\قبلنا ولم ينشر في أي مجلة أخرى في داخل وخارج العراق وأرغب بنشره في مجلة (**مجلة كلية الإسراء الجامعة للعلوم الطبية**) في جامعة الإسراء.

التوقيع:

التاريخ:

(تعهد نقل حقوق الطبع والتوزيع)

إني\إننا الباحث\الباحثين ..... صاحب\أصحاب البحث الموسوم

(.....

.....)

أتعهد\نتعهد بنقل حقوق الطبع والتوزيع والنشر إلى مجلة (**مجلة كلية الإسراء الجامعة للعلوم الطبية**) في جامعة الإسراء.

التوقيع :

التاريخ :

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study's findings demonstrated that bacterial isolates from various clinical sources had genetic relationships with one another.

Conclusions

This study emphasizes the serious threat that *S. aureus* poses due to its high level of antibiotic resistance and its widespread in hospitals and public settings. The study identifies the *Agr* gene types (*Agr1*, *Agr2*, *Agr3*, and *Agr4*) and provides insight into the molecular mechanisms underlying *S. aureus* pathogenicity. The research discovered no significant correlation between sample sources and antibiotic-resistant patterns, despite the fact that more than half of the isolates had high levels of multidrug resistance (MDR). This suggests that the origin of the illness may not have an effect on how well treatments work. The results highlight the significance of continuous monitoring of antibiotic resistance and the importance of molecular methods such as *Agr* typing to comprehend the genetic connections among bacterial strains and direct the creation of more potent treatment approaches to stop the spread of this infection.

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3 (10.7%), *Agr*3 was 10 (35.8%), and *Agr*4 was 1 (3.5%) of a total of 28 isolates. Furthermore, the current result differed from the research carried out by (Bibalan *et al.*, 2014), who showed that the percentage of *Agr*1 presence in bacteria was 5% and the percentage of *Agr*3 presence was 55%. But in the investigation of (Abbasian *et al.*, 2018) the presence rate of *Agr*1 was 131 isolates (78.4%), *Agr*2 was 17 isolates (10.2%), and *Agr*3 reached 8 isolates (4.8%). A finding from the study of (Ahmed *et al.*, 2022)2022 provide evidence that the presence rate of *Agr*1 reached 82 isolates (55%), *Agr*2 was 37 isolates (25%), *Agr*3 reached 10 isolates (7%) and *Agr*4 was 21 isolates (14%).

Multiple genes involved in *S. aureus* bacterium pathogenicity, including coagulase, lipase, toxic shock syndrome type T, leucocidin, a and β-hemolysin, and fibronectin-binding protein, have been linked to the *Agr* regulator, according to the study of (Enwuru *et al.*, 2023). Based on research findings, each group of Agr regulators mediates a number of diseases, including impetigo and exfoliative toxin (eta etb) encoded by *Agr*4, enterotoxins (Seg, Sei, Sem, and Seo) encoded by *Agr*1 and *Agr*2, leukotoxic-lethal genes LukF-PV and LukS-PV, and toxic shock syndrome genes (TST) regulated by *Agr*1, *Agr*2, and *Agr*3 (Horswill *et al.*, 2019). According to study, the typing method is now crucial for determining the genetic relationships between bacterial strains, categorizing bacteria according to their epidemiology, locating infection sources and methods, identifying high-virulence bacterial strains, and treating them to stop them from spreading (Furuya *et al.*, 2023). By using the *Agr* technique to type the *S. aureus* under investigation, the genetic link was discovered and recognized. The *Agr* method sequences were discovered to be distributed across several areas of the bacterial genome, including *Agr*1, *Agr*2, *Agr*3, and *Agr*4 (Pereira *et al.*, 2022). The present

The current study is closely agreed with the results of (Derakhshan *et al.*, 2021), who showed that the percentage of the *Agr*1 presence in *staphylococcal* bacteria was 20%, which is in close agreement with the 10 (21.27%). *Agr*2 was 1 (2.12%), but in another research the prevalence was found to be 53%, which is significantly higher. And the prevalence of *Agr*3 was 21 (44.68%), which is greater than the 35% reported in a different study (Ahmed *et al.*, 2024). This indicates a variability in the distribution of *Agr* system among different *S. aureus* isolates. *Agr*4 was 3 (6.36%), slightly lower than the 8.3% observed in the previous study (Maleki *et al.*, 2019). Some factors, like the regional variance and the sample size, influence the fluctuations (Yoon *et al.*, 2007). The classification levels (MDR and XDR) are substantially correlated with the presence of *Agr* gene types, according to the chi-square test, which yields highly statistical significance with an overall p-value of 0.01. Table (4) presented the correlation between the antibiotic classifications and gene type.

Table 4: The correlation between the antibiotic classifications and gene type.

Classification	*Agr*1	*Agr*2	*Agr*3	*Agr*4	no *Agr*
MDR	9	0	14	1	8
XDR	1	1	7	2	3
Total (N=46)	10	1	21	3	11
P-value	0.01**				

The study conducted by latifpour *et al* (Latifpour *et al.*, 2022) showed that *S. aureus* had *Agr*1 of 16 isolates (29.09%), *Agr*2 of 30 isolates (54.54%), *Agr*3 of 6 isolates (10.9%), and *Agr*4 of 3 isolates (5.45%) out of 55 isolates. Najafi Olya *et al* (Najafi Olya *et al.*, 2021) found that the rate of regulation of the virulence genes *Agr*1 in the resistance *S. aureus* was 14 (50%), *Agr*2 was

The statistical analysis evaluates the relationship between the sample sources and the different types of Agr genes (*Agr*1, *Agr*2, *Agr*3, and *Agr*4). The Chi-square test results indicate no statistically significant association between the sample sources. All p-values for the tests exceeded 0.05. And this result corroborates previous research (Xu *et al.*, 2021)

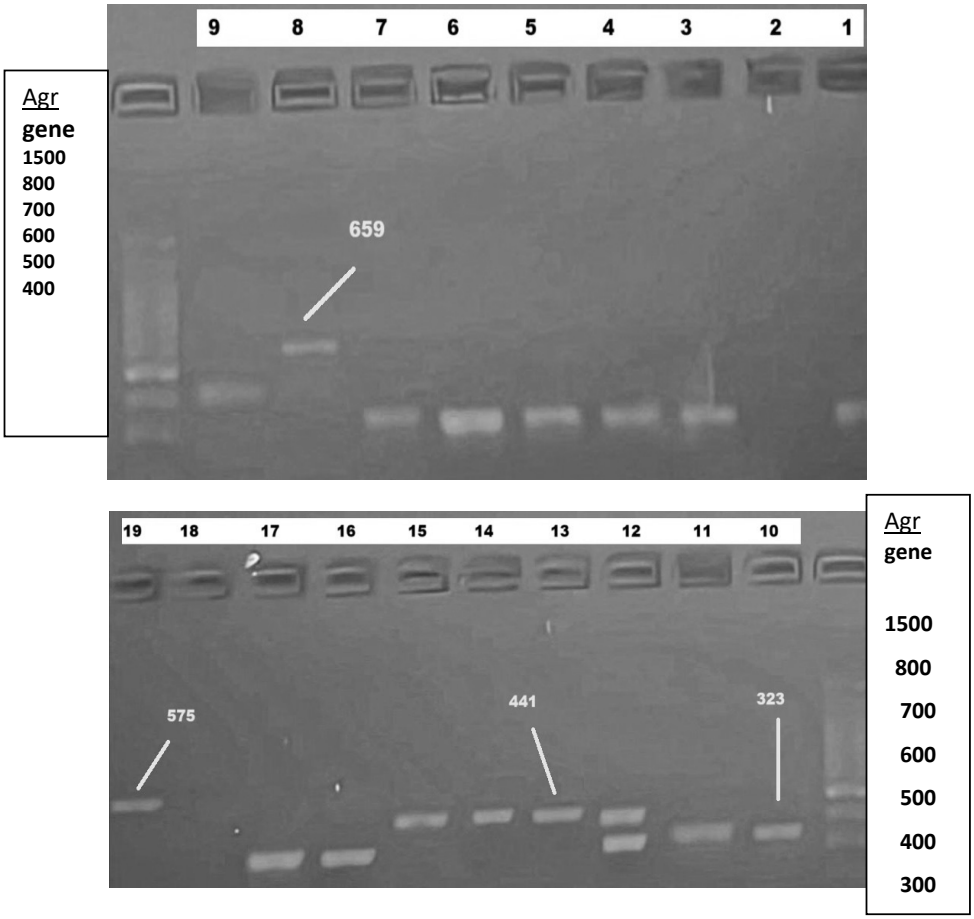

Figure 1: Electrophoresis of the *Agr*1, *Agr*2, *Agr*3, and *Agr*4 genes of *S. aureus* PCR reaction outcomes at a 441 bp, 575 bp, 323 bp, and bp product size. A DNA marker ladder (100-1500 bp) and a 2% agarose gel were utilized at 70 volts for 60 min.

2019). Conversely, *S. aureus* displayed high levels of resistance to antibiotics that target the formation of proteins and cell walls, such as erythromycin, tetracycline, and oxacillin. Multi-drug resistance (MDR) was found in 32 (51.61%) of the 62 *S. aureus* isolates, which is in good agreement with the 55% MDR found in earlier research (Suma *et al.*, 2023).

The percentage of *Agr*1, *Agr*2, *Agr*3, and *Agr*4 presence for *S. aureus* bacteria was 10 (21.27%), 1 (2.12%), 21 (44.68%), and 3 (6.38%) as presented in Table (3). According to the results of the electrophoresis, the generated bands had a molecular weight of 441, 575, 323, and 659 base pairs, according to a comparison of the multiplied bands and the volumetric index as demonstrated in Figure (1).

Table 3. The prevalence of genes among sample sources

Source	*Agr1*	*Agr*2	*Agr*3	*Agr*4	no *Agr*
Abscess	3	0	1	0	2
Aspiration	0	0	0	0	1
Blood	0	0	0	0	1
Burns	1	0	1	1	2
Csf	0	0	1	1	0
ear swab	0	0	3	0	0
Fluid	0	0	2	0	0
Nasal swab	0	0	1	0	0
Pus	2	0	0	0	2
Sputum	1	0	2	0	0
Tissue	1	0	2	0	0
Urine	2	0	3	0	1
vaginal swab	0	0	1	0	0
Wound	0	1	4	1	3
Total (N=47)	10	1	21	3	12
P-value	0.3NS	0.3NS	0.4NS	0.4NS	0.3NS

bacteria to produce the plasma coagulant enzyme and work to convert fibrinogen to fibrin. These biochemical tests were approved for the diagnosis of *S. aureus* bacteria (Petrillo *et al.*, 2021). Because it may spread illness and has many drug resistances, *S. aureus* is one of the most harmful bacteria that can infect hospitals and the general public (Vittorakis *et al.*, 2023).

The results of the study demonstrated that among antibiotics, ciprofloxacin (79.03%), nitrofurantoin (59.67%), and cefoxitin (54.83%) have the greatest percentages of inhibitory activity against *S. aureus.* On the other hand, the lowest percentages were for tetracycline (24.19%) and erythromycin (12.90%). Among the antibiotics that *S. aureus* tested, erythromycin (77.41%), oxacillin (75.80%), and tetracycline (75.80%) exhibited the highest levels of resistance, while the lowest percentages were found for ciprofloxacin (19.35%) and nitrofurtoin (14.51%).

Penicillin-binding proteins, such as penicillin's and cephalosporins, are altered by the expression of the *mecA* gene, which causes methicillin resistance. Antibiotic resistance can also result from other processes, such as the synthesis of beta-lactamases, which degrade beta-lactam antibiotics (Ali *et al.*, 2021).Nevertheless, no statistically significant correlation was found between the types of samples and the antibiotic resistance pattern examined, indicating that the source of infection may not have an impact on the effectiveness of the antibiotic in this particular study, and the outcomes supports this research (Hanif *et al.*, 2019).Ciprofloxacin and nitrofurantoin were shown to have the lowest level of resistance to *S. aureus* in this specific study. In our investigation, the resistance rate to ciprofloxacin was 19.35%; this is in close agreement with the 14.6% found in another study (Patoli *et al.*, 2018). However, our study's 14.51% nitrofurantoin resistance rate deviates from another study's 8.3% reported resistance rate (Singh *et al.*,

Statistical analysis section

Every experiment was carried out and recorded in triplicate. The standard deviation numbers were provided alongside the average mean values. After confirming that the data was homogeneous and normal, the Chi-square test was performed to compare the means and determine the significance of the data (significant * <0.05; high significant ** <0.01; very high significant *** <0.001). R Studio 4.5 was used by OriginLab 2021Software for the correlations and the figures in the statistical study.

Results and Discussion

when culturing *S. aureus* on 7.5% NaCl-containing mannitol salt agar. Bacterial colonies are circular in shape, have a non-zigzag edge, and are golden in color (Socohou *et al.*, 2021). They undergo fermentation to mannitol, producing acidic byproducts that lower pH, which causes the material to turn yellow. This is regarded as a differential analysis between the *staphylococcus* species (Obanda *et al.*, 2022). In addition, The physical traits of the isolates grown on blood agar were used to make the identification (Abdulbaqi *et al.*, 2023). The bacterial colonies had a convex shape, were shiny, smooth, had rounded edges, and were white in appearance. They were also starting to turn golden yellow and totally β-hemolysis type (Tang *et al.*, 2024). Microscopic analysis of slides containing colonies stained with gram-stain revealed that gram-positive bacteria create non-spore-forming, dark purple clusters that resemble bunches of grapes (Cao *et al.*, 2021). Additionally, all isolates yielded negative results for the oxidase test, positive results for the catalase test, and initial positive results for the coagulase test, which was conducted using the tube method when a layer appeared inside the tube, indicating the ability of

Table 1. Oligonucleotide primer sequence and Size amplicon.

Target gene	Initial Sequence from 5′ to 3′	Product Size(bp)	Reference
Agr1	F-5′- GTCACAAGTACTATAAGCTGCGA-3 R-5′-ATGCACATGGTGCACATGC -3	441	(R. Z. T. Ahmed *et al.*, 2024)
Agr2	F-5′-TATTACTAATTGAAAAGTGGCCATAGC -3′ R-5′-ATGCACATGGTGCACATGC -3	575	(R. Z. T. Ahmed et al., 2024)
Agr3	F-5′- GTAATGTAATAGCTTGTATAATAATACCCAG -3	323	(R. Z. T. Ahmed et al., 2024)
Agr4	R-5′-ATGCACATGGTGCACATGC -3 F-5′-GTAATGTAATAGCTTGTATAATAATACCCAG -3 R-5′-CGATAATGCCGTAATACCCG -3	659	(R. Z. T. Ahmed et al., 2024)

As per the instructions provided by the manufacturer, 12.5 µl of 2x EasyTaq® PCR SuperMix, 1 µl each of forward and reverse primers, 4 µl of DNA template, and 6.5 µl of nuclease-free water were used to prepare 25 µl of the reaction mixture, as illustrated in Table (2), with the given reaction conditions, this combination was utilized to carry out the PCR for gene amplification.

Table 2. The optimum condition of detection *Agr* gene.

No.	Phase	Tm (°C)	Time	No. of cycle
1-	Initial Denaturation	94°C	5 min.	1 cycle
2-	Denaturation -2	94°C	30 sec.	
3-	Annealing	57 °C	90 sec.	40 cycle
4-	Extension-1	72°C	60 sec.	
5-	Extension -2	72°C	7 min.	1 cycle

Agarose gel electrophoresis

Following ethidium bromide staining, the extracted DNA and amplified PCR fragments were separated on an agarose gel and seen under UV light.

traditional methods including coagulase testing, catalase, mannitol fermentation assays and vitek 2 compact system assay.

Antibiotic Susceptibility Testing

The disc diffusion technique on Mueller-Hinton agar and the antibiotic resistance of the 62 isolated bacteria were performed according to CLSI criteria. Concerning clindamycin (CD) 2µg, oxacillin (OX) 1µg, ciprofloxacin (CIP) 5µg, gentamycin (CN) 10µg, tetracycline (TE) 10µg, cefoxitin (FOX) 30µg, nitrofurantoin (F) 300µg, and erythromycin (E) 15µg. Data analysis and interpretation were done based on CLSI, 2023 (Bhagaskara *et al.*, 2023).

DNA isolation

A genomic DNA extraction kit prepared by EasyPure® Genomic DNA Kit (TransGen, biotech. EE101-01) was used to extract DNA for the bacterial isolates under study according to the manufacturer's instructions.

DNA examination

In order to determine DNA purity, a nanodrop spectrophotometer was used to assess the concentration of DNA samples that demonstrated acceptable integrity at two wavelengths (260 and 280 nm) (Bruijns *et al.*, 2022).

Molecular diagnosis of the *Agr* genes in *Staphylococcus aureus*

PCR technology was used in this investigation to identify the *Agr* genes (*Agr*1, *Agr*2, *Agr*3, *Agr*4). As shown in Table (1).

survival under antibiotic pressure (Raghuram *et al.*, 2022). Understanding the distribution of *Agr* types in MDR and XDR *S. aureus* is crucial for identifying genetic markers that predict resistance patterns and guiding therapeutic strategies (Raghuram *et al.*, 2022). Targeting the *Agr* system could reduce virulence and combat resistance. Studies on highly resistant strains have highlighted the need for molecular surveillance and deeper exploration of how regulatory mechanisms influence treatment outcomes (Horswill *et al.*, 2019). The study investigates the molecular characteristics of the *Agr* gene in MDR and XDR strains, focusing on the prevalence of *Agr* 1, *Agr* 2, *Agr* 3, and *Agr* 4 in resistant populations. It seeks to understand the role of *Agr* in MDR persistence and pathogenicity in *S. aureus.*

Ethical approval

This study was carried out in accordance with the principles outlined in the Declaration of Helsinki. The ethics committee of Health and Medical Techniques College (173/3) granted approval for the research before any interventions were made, as did the agreements of Ghazi Al-Hariri Hospital (No.2643), Al-Kindi Hospital (No.255/3), and Ibn Al-Baladi Hospital (No.850/3).

Materials and Methods

Bacterial isolation

During the period from January 2024 to April 2024, 62 *S. aureus* isolates were collected from various clinical sources, from patients in selected hospitals in Baghdad city, the bacterial identification was performed using

Introduction

The rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) *Staphylococcus aureus* (*S. aureus*) poses a significant global health challenge (Jiang *et al.*, 2024). This pathogen can cause severe infections, including skin abscesses and systemic diseases like bacteremia and endocarditis (Linz *et al.*, 2023). Antibiotic resistance in *S. aureus* complicates infection management, leading to higher treatment failures, prolonged hospitalizations, and increased mortality. MDR and XDR strains are particularly significant due to their resistance to most available antibiotics. MDR strains exhibit resistance to multiple antibiotic classes, while XDR strains are resistant to all available antimicrobial agents, leaving limited therapeutic options (Marciniak *et al.*, 2024). Genetic factors like horizontal gene transfer, chromosomal gene mutations, and virulence factor regulation contribute to this resistance (Mlynarczyk-Bonikowska *et al.*, 2022). The accessory gene regulator (*Agr*) system plays a crucial role in controlling virulence and antibiotic susceptibility in these resistant strains. The *Agr* gene in *S. aureus* regulates the expression of virulence factors, including hemolysins, proteases, and toxins. It is part of four genetic groups: *Agr*1, *Agr* 2, *Agr*3, and *Agr*4. The system produces and senses autoinducing peptides (AIPs) that trigger virulence gene expression when bacterial populations reach a certain threshold (Fang *et al.*, 2024). The study of the *Agr* gene in resistant *S. aureus* strains has revealed a complex link between quorum sensing, virulence regulation, and antibiotic resistance (Cella *et al.*, 2023). Mutations or polymorphisms in the *Agr* locus in MDR and XDR strains may alter resistance gene expression and enhance resistance evasion. This disruption could contribute to infection persistence and spread, as this system promotes

المستخلص

تُعَدّ المكورات إلعنقودية من البكتيريا الانتهازية التي يمكن أن تؤدي إلى العدوى المكتسبة في المستشفيات. لذا تهدف هذه الدراسة إلى اكتشاف توزيع وانتشار جينAgr في السلالات المقاومة المتعددة للأدوية (MDR) والسلالات المقاومة للأدوية بشكل واسع (XDR) من المكورات العنقودية. تم أجراء اختبار حساسية المضادات الحيوية على 62 عزلة، حيث أظهرت العزلات مقاومة بنسبة 66.12% للكلايندامايسين وكان الحد الأدنى من التركيز المثبط (MIC) في نطاق ≤4، و77.41% للإريثروميسين مع (MIC) في نطاق ≤8، و19.35% للسيبروفلوكساسين مع (MIC) في نطاق ≤4، و75.80% للأوكساسلين مع (MIC) في نطاق ≤4، و45.16% للسيفوكسيتين مع (MIC) في نطاق ≤8، و29.03% للجنتاميسين مع (MIC) في نطاق ≤16، و14.51% للنيتروفورانتوين مع (MIC) في نطاق ≤128، و75.80% للتتراسايكلين مع (MIC)في نطاق ≤16. وتم عزل الحمض النووي الجيني من العزلات البكتيرية، وتم تاكيد وجود جين Agr باستخدام بادئات محددة، و أخيرا شخصت جينات Agr1 وAgr2 وAgr4 Agr3 بنجاح في المكورات العنقودية في هذه الدراسة.

الكلمات المفتاحية: المكورات العنقودية, جين Agr, مقاومة متعددة الادوية (MDR), مقاومة واسعة النطاق للادوية (XDR), اختبار الحساسية للمضادات الحيوية.

Abstract

Staphylococcus aureus a gram-positive coccus and one of the most important opportunistic bacteria that can lead to nosocomial infections. The purpose of this study is to explore the distribution and prevalence of the *Agr* gene in multidrug-resistance (MDR) and extensively drug-resistant (XDR) *S. aureus*. 62 isolates performed antibiotic sensitivity test. The isolates showed 66.12% resistance to clindamycin with MIC at range≥4, erythromycin 77.41% with MIC at range≥8, ciprofloxacin 19.35% with MIC at range≥4, oxacillin 75.80% with MIC at range≥4, cefoxitin 45.16% with MIC at range≥8, gentamycin 29.03% with MIC at range≥16, nitrofurantoin 14.51% and MIC at range≥128, and tetracycline 75.80% MIC at range≥16. Following the extraction of genomic DNA from the bacterial isolates, the presence of the *Agr* gene was confirmed. Using specific primers, the *Agr* genes (*Agr*1, *Agr*2, *Agr*3, and *Agr*4) were successfully amplified and detected in *S. aureus*.

Keywords: *Staphylococcus aureus***, Agr gene, Multi-drug-resistant (MDR), Extensively drug-resistant (XDR), Antibiotic sensitivity test.**

Molecular Study of the *Agr* Gene in Multidrug-Resistant (MDR) and Extensively Drug-Resistant (XDR) in the *S. aureus*

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دراسة جزيئية لجين *Agr* في بكتريا المكورات العنقودية الذهبية ذات المقاومة المتعددة للادوية (MDR) والمقاومة الشديدة للادوية (XDR).

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(Santacruz *et al.*, 2022). This finding agrees with Soliman's study of ESR and platelets. ESR evaluated in SLE patients (42.75±28.010) more than the control (10.53±4.447) similar to his study (39.4 ± 27.0),(7.8 ± 2.8), respectively and P=0.001. Platelets in SLE patients (262.62 ±80.820) while in control (281.73±99.168) and no significant, similar to his study (290.5 ± 100.6), (302.9 ± 93.4), respectively and P>0.05 (Soliman *et al.*, 2023).

SLE patients with anti-dsDNA positive were significantly higher in with Oral mucosal ulcer (Esquivel-Pedraza *et al.*, 2021 ; Xingguo *et al.*, 2008) and with Arthralgia or arthritis (Iaremenko and Koliadenko, 2022). Antibody levels are higher in SLE patients with positive anti-dsDNA antibodies compared to those with negative antibodies (P<0.05). Anti-Sm antibodies showed significant associations with serositis, renal involvement, psychosis, vasculitis, Raynaud's phenomenon, hemolytic anemia, leukopenia, lymphopenia, and arterial hypertension in the multivariable analysis. (Arroyo-Ávila *et al.*, 2015). In this study, there was no significant difference found for damage accumulation.

Conclusions

ANA and anti-dsDNA that commonest antibodies in SLE followed by anti-SSA and SSB. Anti-dsDNA is a commonest antibody responsible for active diseases. Arthralgia and arthritis are most affected by SLE disease. No association was found between auto antibodies and major clinical features.

Amongst anti-dsDNA unlike with study (Homa-Mlak), In SLE, the anti-dsDNA assay has a sensitivity of 40.74% and a specificity of 81.25%, with no significant difference found (p=0.399) (Homa-Mlak *et al.*, 2022).

Anti-Sm is widely recognized as a marker antibody of SLE in retrospect. In contrast to the low sensitivity and high specificity typically seen in SLE diagnosis, anti-Sm had a specificity of 100.0% and sensitivity of 45.0% when detected by ELISA, indicating a strong positive predictive value for diagnosing SLE. Yet, the diagnostic usefulness for the majority of negative patients is restricted because of its high specificity. The finding in this result the Specificity for all markers are 100% this agrees with Li results in ANA (99.3), anti-ds-DNA(98.87%), anti-SSA(87.47%), anti-SSB(97.21%), anti-Smith(99.74%), and anti-RNP (99.56%) (Li, Hejun *et al.*, 2022).

Arthritis was the predominant clinical manifestation, observed in 85% of the individuals, which was also observed in other study (Metry *et al.*, 2019). SLE-related arthritis which it usually appears as non-erosive arthritis and was found in 51 out of 60 patients, closely matching our results. (85.0%) (Csóka *et al.*, 2024). Even though conditions such as arthritis or arthralgia are typically temporary, they can exhibit symptoms resembling those of rheumatoid arthritis (RA), such as long-lasting stiffness, swelling, pain, and decreased mobility. Though tendonitis or tenosynovitis may also be present, the metacarpophalangeal and interphalangeal, wrist, and knee joints are the most commonly afflicted (Ceccarelli *et al.*, 2022).

Hematologic abnormalities, including lymphopenia, anemia, and thrombocytopenia, are commonly found in SLE patients reflecting the activity of the disease over time. Anemia may result from lupus medication usage through either an idiosyncratic response or a dose-dependent mechanism

Discussion

A higher proportion of patients resided in urban areas, primarily because the majority of samples were collected from Baghdad city. In these studies, autoantibodies similar to ANA, anti-dsDNA, anti-Sm, anti-SSA, and anti-SSB were identified with percentages of 90%, 85%, 32%, 65%, and 23%, respectively (Olferiev *et al.*, 2022). A high percentages of SLE may be consistently identified through the anti-ANA antibody (Anis *et al.*, 2023). Accurate identification and diagnosis of systemic lupus erythematosus requires specific testing for anti-dsDNA (Orme *et al.*, 2022). In this study discovered that the presence of the anti-dsDNA antibody correlated with disease activity, low white blood cell count, low red blood cell count, and elevated ESR levels, in line with earlier research (Correa-Rodríguez *et al.*, 2021). Kidney damage tends to lead to higher ESR levels, consequently reducing Alb levels. (Aringer, 2020). Anti-dsDNA and anti-Sm autoantibodies play a crucial role in the production of immune complexes and inflammatory damage on several organs, including the kidney, skin, and central nervous system (CNS). They are particularly specific to SLE (Lou *et al.*, 2022).

Within ANA testing, the anti-nuclear antibody assay holds greater diagnostic and prognostic significance. In systemic lupus erythematosus, the ANA test shows a sensitivity of 60-80% and an impressive specificity of 95-99%, giving it a strong predictive value. Autoantibodies can be detected in the early stages of SLE, including the preclinical phase (Li, H. *et al.*, 2022). this agrees with Jassim's study in ANA and dsDNA (with AUC 1.00, had a sensitivity and specificity of 100%), and the presence of double-strand DNA antibodies at a level of AUC ≥ 1.706 U/ml, had 100% sensitivity and 100% specificity) (Jassim *et al.*, 2023).

with P(0.010, 0.040, and 0.022 respectively). Arthralgia was correlated with anti-dsDNA antibodies, with a P value of 0.023. The occurrence of C3 (P=0.010) and C4 (P=0.002) were associated with an increased likelihood of developing Lymphadenopathy. Avascular necrosis showed a significant association with an anti-SSB antibody (P = 0.016) and C3 (P = 0.010). Furthermore, patients who had C4 (P = 0.045) were found to have developed Discoid lupus. The various autoantibodies had no correlation with other clinical symptoms.

Table 5: Correlation between clinical manifestations and autoantibodies among SLE group

clinical manifestations	ANA	dsDNA	SSA	SSB	Sm	RNP	Scl70	Jo-1
	P	P	P	P	P	P	P	P
Seizure	0.817	0.692	0.329	0.672	0.362	0.652	0.692	0.737
Visual disturbance	0.476	0.577	0.073	0.885	0.405	0.064	0.577	0.301
Cranial Nerve Disorder	0.741	0.573	0.137	0.546	0.193	0.520	0.121	0.001
Lupus Headache	0.950	0.339	0.244	0.909	0.765	0.069	0.873	0.417
CVA	0.741	0.573	0.962	0.546	0.193	0.520	0.573	0.055
Vasculitis	0.374	0.704	0.071	0.857	0.697	1	0.704	0.197
Arthritis	0.455	0.056	0.800	0.723	0.971	0.146	0.202	0.278
Myositis	0.764	0.072	0.315	0.582	0.895	0.026	0.797	0.029
New Rash	0.120	0.721	0.821	0.511	0.228	0.641	0.683	0.602
Alopecia	0.086	0.156	0.993	0.233	0.979	0.419	0.389	0.071
Mucosal Ulcers	0.764	0.010	0.040	0.199	0.693	0.412	0.797	0.190
Pleurisy	0.635	0.417	0.334	0.384	0.405	0.355	0.477	0.301
Pericarditis	0.057	0.417	0.945	0.384	0.835	0.355	0.417	0.490
Fever	0.809	0.163	0.752	0.238	0.916	0.157	0.088	0.725
Fatigue	0.400	0.601	0.379	0.123	0.169	0.881	0.647	0.221
Arthralgia	0.374	0.023	0.245	0.857	0.697	0.386	0.569	0.389
Lymphadenopathy	0.817	0.692	0.297	0.679	0.362	0.652	0.010	0.002
Avascular necrosis	0.817	0.692	0.329	0.016	0.362	0.652	0.010	0.737
Raynaud's phenomenon	0.844	0.822	0.204	0.718	0.708	0.522	0.286	0.504
Discoid lupus	0.554	0.129	0.931	0.278	0.795	0.248	0.129	0.045
Photosensitivity	0.327	0.905	0.451	0.104	0.668	0.172	0.905	0.684

Clinical features of SLEDAI in SLE patients

The most common clinical components observed in SLEDAI included arthritis/arthralgia (85.0%), lupus headache (65.0%), fever (60.0%), new rash (56.7%), alopecia (48.3%), visual disturbance (46.7%), myositis (41.7%), mucosal ulcers (41.7%), pyuria (35.0%), vasculitis (20.0%), pleurisy (6.7%), pericarditis (6.7%), cranial nerve disorder (3.3%), CVA (3.3%), seizure (1.7%), with organic brain syndrome and psychosis at (0.0%) as shown in Figure (2).

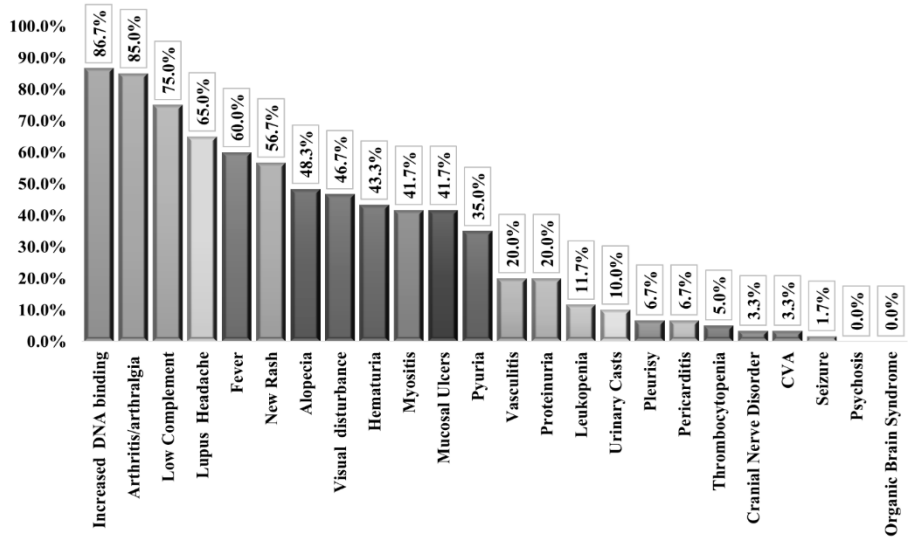

Figure (2). The frequency of SLEDAI clinical features components among 60 patients with SLE.

The association of autoantibodies with clinical manifestations of SLE

The relationship between various autoantibodies and clinical symptoms is summarized briefly in Table (5). Cranial nerve disorder showed a strong significance with anti-Jo1 (P=0.001). Myositis was linked to anti-RNP antibodies and C4 levels, with a correlation of P(0.026 and 0.029, respectively). Mucosal ulcers were associated with anti-dsDNA, and anti-SSA antibodies,

Table 4: Correlation levels of biomarkers in the serum of SLE patients

Parameters	Cutoff Point	Area under curve (AUC)	Asymp. Sig.	Asymptotic 95%C.I.		Specificity	Sensitivity
				L.B.	U.B.		
ANA	37.3	0.974	0.0001**	0.927	0.994	100.0	95.00
dsDNA	22.0	0949	0.0001**	0.893	0.981	100.0	86.67
Anti-SS-A	17.7	0.765	0.0001**	0.679	0.837	100.0	51.67
Anti -SS-B	49.42	0.541	0.5163	0.432	0.646	100.0	15.00
Anti -Sm	28.9	0.711	0.0001**	0.621	0.790	100.0	45.00
Anti -RNP	32.2	0.501	0.982	0.394	0.609	100.0	16.67
Anti-Jo1	39.5	0.503	0. 9690	0.395	0.610	100.0	10.00
Anti Scl-70	45.2	0.522	0.7352	0.414	0.628	100.0	13.33

**:(**) Highly Sig. at P<0.01; C.I.: Confidence Interval; L.B.: lower bound; U.B.: upper bound

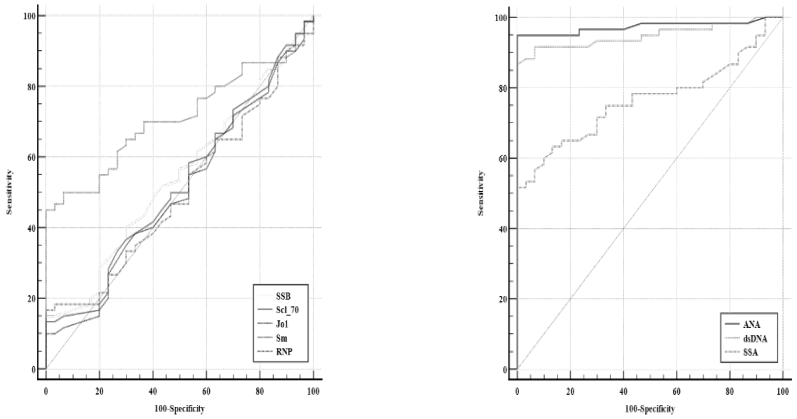

Figure (1): ROC Curve Chart for the association autoantibodies markers distributed of SLE group.

Table 3: Investigations laboratory among different SLE groups

	Patient		Control		P-Value
	Means ± SD	SE	Means ± SD	SE	
Blood tests					
WBCx109/L	8.24±3.35	0.433	7.75±1.41	1.415	0.306
LYM%	25.96±11.44	1.477	29.93 ±6.15	0.794	0.020*
NEU%	62.46 ±16.88	2.180	61.16±8.74	1.129	0.598
MON%	6.04±2.17	0.281	6.15±2.02	0.261	0.783
BASO%	0.31±0.15	0.020	0.27±0.12	0.016	0.163
EOS%	1.31±1.17	0.152	1.30±1.49	0.192	0.986
HGB g/dl	11.35±1.66	0.215	12.85±0.40	0.052	0.001**
HCT %	35.43±4.98	0.643	37.74 ±0.71	0.092	0.001**
PLTx109/L	262.62±80.82	10.434	281.73±99.16	12.802	0.249
ESR mm/hr	42.75 ±28.01	3.616	10.53±4.44	0.574	0.001**
Urine tests					
RBC/µl	31.96 ±27.77	3.585	3.92±2.33	0.302	0.001**
WBC/µl	28.05 ±25.95	3.351	3.77±1.94	0.250	0.001**
PRO g/l	0.27±0.57	0.075	0.00±0.00	0.000	0.001**
Cast/µl	0.12±0.37	0.048	0.00±0.00	0.000	0.017*

SD: Standard Deviation; SE: Standard Error

Receiver operative curve of autoantibodies markers among SLE group

Receiver Operative Curve (ROC) analysis was also used to determine the optimal cutoff point for medical tests. Table (4) and Figure (1) demonstrate the cutoff where sensitivity and specificity values intersect, including critical levels for evaluating area parameters below fifty percent, with a 95% confidence interval pertaining to ANA testing., dsDNA, SS-A, SS-B, Sm, RNP, Scl-70, and Jo1 antibody markers within diagnosis SLE patients concerning. this is shown in Table (4).

The anti-C3 antibody had a positive rate of 73.3% and C3 antibodies at 48.3%. This is shown in Table (2),

Table 2: Distributions of autoantibodies prevalence in the patient group

Parameters	Positive		Negative	
	No.	%	No.	%
ANA	57	95.0	3	5.0
Anti-dsDNA	52	86.7	8	13.3
Anti-SSA	31	51.7	29	48.3
Anti-SSB	9	15.0	51	85.0
Anti-Smith	27	45.0	33	55.0
Anti-RNP	10	16.7	50	83.3
Anti-Jo1	6	10.0	54	90.0
Anti-Scl-70	8	13.3	52	86.7
C3	44	73.3	16	26.7
C4	29	48.3	31	51.7

Laboratory investigation of study groups

Parameters like WBC count, Hemoglobin level, platelet count, lymphocyte count, monocyte count, neutrophils, eosinophil count, basophil count, and ESR were examined in both patients and controls for investigation purposes. Data shown as mean± SD demonstrated that there was a difference in the mean investigation parameters between SLE patients and the control group. Independent T-test statistical analysis demonstrated a significant disparity in Hb, Hct, ESR, CRP, and urine test (RBCs, pus cell, and Alb) between the healthy controls and SLE patients in the groups. Finally, the analysis of WBC, neutrophils, monocytes, eosinophils, basophils, and platelets, in the different groups revealed no significant variance, as shown in the Table 3.

Table 1: Demographical characteristics of the study groups

Parameters study		Patients (N=60)		Controls (N=60)	
		No.	%	No.	%
Age (Year)	15-24	15	25.0	20	33.3
	25-34	22	36.7	16	26.7
	35-44	14	23.3	15	25.0
	45-55	9	15.0	9	15.0
Residency	Urban	50	83.3	52	86.7
	Rural	10	16.7	8	13.3
Occupation	Employed	4	6.7	8	13.3
	Unemployed	56	93.3	52	86.7
Martial state	Single	17	28.3	28	46.7
	Married	40	66.7	30	50.0
	Divorced	3	5.0	2	3.3
Education	Illiterate	2	3.3	4	6.7
	Primary	15	25.0	18	30.0
	Intermediate	7	11.7	10	16.7
	Secondary	19	31.7	8	13.3
	College	17	28.3	16	26.7
	High college	0	0	4	6.7
BMI	Under Weight	5	8.3	0	0.0
	Normal	19	31.7	32	53.3
	Over Weight	15	25.0	12	20.0
	Obese	17	28.3	14	23.3
	Extremely Obese	4	6.7	2	3.3

Prevalence of autoantibodies

95.0% of 60 patients showed a positive result for the ANA. Additionally, the anti-dsDNA antibody showed a high positive rate of 86.7%, with anti-SSA following at 51.7%, anti-Sm at 45.0%, anti-RNP at 16.7%, anti-SSB at 15.0%, anti-Scl-70 at 13.3%, and anti-Jo-1 at 10.0%.

Materials and Methods

The case-control study included 60 patients and 60 controls. The research was done from 25th January 2024 until 25th April 2024. The patient reports are based on the criteria set by the European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR). ANA detection and pattern determination were conducted through IIF using HEp-20. Additionally, an ELISA immunoassay was conducted using an Enzyme-linked immunosorbent assay (ELISA, Sunlongbiotech), and the antibodies of each sample were obtained. Statistical analysis the results of this research were translated into a computerized database structure. Statistical analysis was carried out using the Social Sciences (SPSS) version 26.0. Mean, SD were used to express variables. Cross-tabulation was utilized to investigate a relationship between 2 categorical variables. The significance of these associations was evaluated using the Chi-square test (X^2) test. MedCalc software is utilized for ROC analysis, measuring parameter differentiation between two groups. AUC determines the test value. ROC also helps compare parameters and find the optimal cutoff for sensitivity and specificity.

Result

Demographics of the study groups

Based on the demographics of the groups being studied, it was shown in Table (1) that a central percentage of patients with SLE fell within the age group of 25-34 year at (36.7%). About 93.3% of individuals were unemployed, while 31.7% had completed secondary education. Martial state that has married more affected (66.7%). Furthermore, 31.7% of the individuals had a normal body mass index.

Introduction

Systemic lupus erythematosus is an autoimmune disease that is not well understood cause. Mostly seen in women, it presents with a range of symptoms (Emorinken *et al.*, 2021). It is identified by clinical and serological signs that, although distinctive, are insufficient to meet the classification criteria (Piga *et al.*, 2023). It is more prevalent among women than men at a ratio of 9:1 and is frequently seen in the age group of 15-40 years (Barber *et al.*, 2021). The frequency of SLE is between 72.1 and 74.4 per 100,000 individuals, with annual incidence rates of 5.6 per 100,000 individuals in predominantly Caucasian and African-American groups. African Americans experience elevated rates, while the disease is more common among Asian and Hispanic populations in comparison to Caucasians. The disease typically appears at a younger age and is more noticeable in African Americans (Tsai *et al.*, 2022). Linked to genetic and environmental influences such as viral infections and medications, triggering the creation of particular autoantibodies. The autoantibodies combine with autoantigens to create immunocomplexes that are then deposited in capillaries, resulting in systemic damage (Gong *et al.*, 2023). That affects numerous tissues and organs (Hasegawa *et al.*, 2023). The most recent clinical guidelines introduced by the European League Against Rheumatism/American College of Rheumatology in 2019 mandated a positive antinuclear antibody titer of 1:80 or higher as an entry requirement (Lam *et al.*, 2023). The aim of this investigation is to study the prevalence and the type of hematologic manifestations in SLE from pathologist's perspective

المستخلص

المقدمة: داء الذئبة الاحمراري هو مرض مناعي معقد غير معروف الاسباب ,النساء يصابون به بصورة اكثر. يمكن تشخيصة عن طريق العلامات السريرية والسيرولوجية . **الهدف**: دراسة تنبأ كميات المظاهر المناعية ومعلمات الدم لتقييم الحالة المرضية للنساء المريضات. **طريقة العمل**: اجريت الدراسة على (60) مريضة مصابة بداء الذئبة من العيادة الاستشارية في مستشفى بغداد وحدة امراض المفاصل و 60 امرأه سليمة في النصف الاول من عام 2024 للفتره من يوم 25 كانون الثاني الى يوم 25 نيسان . **النتائج**: المتزوجات من النساء المصابة كانت اكثر نسبة (66.7 ٪). نسبة (95 ٪) من المصابات كان لهن الاجسام المضادة للنواة ذات نتيجة ايجابية و الأجسام المضادة للحمض النووي المضاعف بنسبة (86.7 ٪) .اما قياس الهيموغلوبين و تحليل سرعة ترسيب كريات الدم الحمراء فكان ذات دلاله معنوية عالية (0.001) عند المقارنة بين المرضى والاصحاء . التهاب في المفصل أو مجرد ألم بالمفصل من دون وجود التهاب كانوا بنسبة(85 ٪) في تقييم نشاط المرض في وقت التقييم. **الاستنتاجات**: الأجسام المضادة للحمض النووي المضاعف اكثر شيوعا في قابلية نشاط المرض. آلام المفاصل قد يكون بوجود الالتهاب او بدونه هو اكثر تأثيرا.

الكلمات المفتاحية: داء الذئبة الاحمراري ، الأجسام المضادة الذاتية، الأجسام المضادة للنواة، المناعة غير المباشرة بواسطة الصبغة الفلورية.

Abstract

Background: Systemic Lupus Erythematosus is a complicated condition caused by the immune system attacking disease with unclear causes, affecting mainly women. It manifests with various symptoms and is diagnosed based on clinical and serological signs. **Aims**: To investigate the prevalence and the type of immunological and hematologic manifestations in SLE from pathologist's perspective. **Methods**: The study was done on 60 SLE patients and 60 controls from the Consulting Rheumatology Clinic in Baghdad Teaching Hospital in Baghdad City during the first half of the year 2024, from 25th January 2024 until 25th April 2024. **Results**: Marital state that has married more affected (66.7%). 95% of patients tested positive for the anti-nuclear antibody and the anti dsDNA antibody also showed a high rate of positivity 86.7%. Hb and ESR highly significant difference (P=0.001) compared between patients and controls. The Arthralgia and arthritis were most common clinical features observed in SLEDAI and included (85%). **Conclusions**: Anti-dsDNA is a common antibody responsible for active diseases. Arthralgia and arthritis are most affected by SLE disease.

Keywords: SLE, Autoantibodies, Antinuclear antibodies, Indirect immunofluorescence

Abbreviations

SLE: Systemic Lupus Erythematosus

ANA: Antinuclear antibodies

HEp-20: Human epithelial cell tumor line

ELISA: Enzyme-linked immunosorbent assay

IIFT: Indirect immunofluorescence tests

التحري عن المعلمات المناعية والاعراض السريرية لمرضى داء الذئبة الاحمراري بين النساء العراقيات المصابات

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Immunological Markers and Clinical Features with Systemic Lupus Erythematosus in Iraqi Women Patients

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Traditional risk factor and their influence on core study biomarkers levels in ACS patients

When the major conventional risk variables were examined for their impact on the significant variations in CPP levels between ACS patients and controls, the results remained significant whether any of the risk factors under study was present or not. Nevertheless, this does not rule out the possibility that these risk variables have an impact on CPP levels. Then there are circumstances other than ACS presentation; these pertain to a predominance of alterations brought on by the existence of ACS and its underlying disease or effects.

In the present study, there was a significantly high level of copeptin in ACS patients with presence or absence of any of the studied risk factors when compared with controls in the first few hrs. after onset of chest pain (by LSD TEST) (10). Copeptin level may even be raised within 30 min after the onset of chest pain in patients with AMI as a result of endogenous stress response and so it does not need serial sampling like troponin and may signify an accurate anchor point to diagnose AMI in ACS patients on time of their admission emergency department (8). Hence, a diagnosis of AMI based on copeptin level may help to enable someone to approve or to rule-out ACS with higher sensitivity and specificity which could serve to decrease mortality rate and to reduction the economic costs of management of “ACS” patients and AMI patients in particular , this agree with (9) due to acute endogenous stress response (copeptin) seems to be real and effective .

Table 6: Comparison of copeptin levels between of STEMI patients and controls according to smoking status.

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	SMO	Patients	16	344.84 ± 24.55	<0.001
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	24	339.13 ± 16.24	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	SMO	Patients	20	219.28 ± 11.65	<0.001
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	20	209.07 ± 11.21	<0.001
		Control	80	162.65 ± 3.19	
UA	SMO	Patients	12	187.28 ± 11.03	0.294
		Control	80	162.65 ± 3.19	
	Non-SMO	Patients	28	185.2 ± 6.74	0.004
		Control	80	162.65 ± 3.19	

Discussion

Early identification of ACS patients among those presenting with chest pain to the emergency department in real-life daily clinical practice is important. Accelerated and intensive medical and interventional therapy can be beneficial for patients with ACS. Copeptin evaluation is therefore a useful diagnostic technique for AMI patients. Excluding healthy people who report having at least chest pain should improve the efficiency of emergency department operations. Nevertheless, when copeptin and hs-cTn-I are combined, the ACS patient exclusion rate is much higher than when those two markers are examined separately (9).

Table 4: Comparison of copeptin level between ACS patients and controls according to hypertension

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	HT	Patients	20	366.59 ± 19.38	<0.001
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	20	316.23 ± 17.96	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	HT	Patients	30	212.6 ± 9.14	<0.001
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	10	218.9 ± 17.41	<0.001
		Control	80	162.65 ± 3.19	
UA	HT	Patients	20	187.16 ± 8.12	0.004
		Control	80	162.65 ± 3.19	
	Non-HT	Patients	20	184.48 ± 8.17	0.004
		Control	80	162.65 ± 3.19	

Table 5: Comparison of Copeptin between STEMI patients and controls according to diabetic

		Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	DM	Patients	24	345.93 ± 18.37	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	16	334.64 ± 20.72	<0.001
		Control	80	162.65 ± 3.19	
NSTEMI	DM	Patients	16	216.88 ± 11.24	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	24	212.37 ± 11.25	<0.001
		Control	80	162.65 ± 3.19	
UA	DM	Patients	18	176.71 ± 8.61	<0.001
		Control	80	162.65 ± 3.19	
	Non-DM	Patients	22	193.28 ± 7.37	<0.001
		Control	80	162.65 ± 3.19	

controls is presented in tables (3-6). The changes in this study biomarker among patients and controls stayed significant in CPP above and below age of 50 years (Tables 3), with or without of systemic hypertension (Tables 4), in the presence or not of diabetes mellitus (Tables 5), and in smokers and non-smokers (Tables 6).

Table 3: Comparison of Copeptin between ACS patients and controls according to age

	Age (years)	Groups	N	Mean ± S.E. CPP (pg/ml)	P value
STEMI	≤ 50 years	Patients	12	332.74 ± 23.51	<0.001
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	28	345.13 ± 16.92	<0.001
		Control	52	162.26 ± 3.55	
NSTEMI	≤ 50 years	Patients	8	195.01 ± 13.34	0.024
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	32	218.97 ± 9.35	<0.001
		Control	52	162.26 ± 3.55	
UA	≤ 50 years	Patients	8	182.55 ± 9.37	0.05
		Control	28	163.36 ± 6.34	
	> 50 years	Patients	32	186.64 ± 6.77	0.001
		Control	52	162.26 ± 3.55	

The result of comparison of levels of study parameters among subgroups of ACS patients (STEMI, NSTEMI and UA) and controls is shown in Table 2. The comparison revealed significant differences among the study groups or subgroups in regard to the CPP mean level as well as to the mean levels of cholesterol, GOT, and FBS.

Table 2: Demographic, clinical Characteristics, baseline laboratory tests and copeptin level in subgroups of ACS patients and controls

Characteristic	STEMI N= 40	NSTEMI N = 40	UA N= 40	Controls N= 80	P-value
	Mean ± S.E.				
Age (years) Range Mean	45-75 years 59 ± 2	45-78 years 60 ± 3	47-80 years 61 ± 3	34-77 years 57 ± 2	0.065 NS
BMI (kg/m2)	28.53±0.57	28.17±0.53	27.53±0.57	23.37±0.46	0.032 Sig.
FBS (mg/dl)	194.27 ± 8.78	173.79 ± 11.32	152.77 ± 6.81	92.67 ± 2.37	0.001> Sig.
Cholesterol (mg/dl)	211.42 ± 5.2	173.87 ± 5.93	153.18 ± 4.58	141.64 ± 2.73	0.001> Sig.
GOT (IU/l)	146.1 ± 14.86	58.69 ± 3.17	15.74 ± 1.2	14.42 ± 0.56	0.001> Sig.
Copeptin (pg/ml)	341.41 ± 13.65	214.18 ± 8.02	185.82 ± 5.69	162.65 ± 3.19	0.001> Sig.

ANOVA test was performed, STEMI: ST-segment elevation myocardial infarction, NSTEMI: non ST-segment elevation myocardial infarction, UA: unstable angina, BMI: body mass index, FBS: fast blood sugar, GOT: glutamate oxaloacetate transaminase

The outcome of traditional CHD risk factors “age, hypertension, smoking and diabetes mellitus” on CPP in patients and compared with

Statistical analysis

Data were analyzed by the statistical package of SPSS-24. After assuring that the data was normally distributed, data presentation was done by mean, standard error or standard deviation of the mean, and percentage. LSD test was used for the difference between two means. A P-value of "< 0.05" was measured as statistically significant.

Results

The clinical characteristics of study subjects are shown in Table 1. The patients and the control subjects had a similar sex distribution (60 % males, 40% females). The study patients who were ≤ 50 years in age constituted 33.3% and persons were > 50 years constituted 66.66%. In regard to BMI, 20% normal weight of patients, "47.5%" overweight and "32.5% " were within the obese. The ACS patients included those with STEMI (40 patients), NSTEMI (40 patients) and UA (40 patients).

Table 1: Clinical characteristics of study subjects

Characteristic	Patients N= 120	Controls N=80
Age (years) ≤ 50 y > 50 y	 N= 40 (33.3%) N= 80 (66.66%)	 N = 27 (33.75%) N = 53 (66.2%)
BMI (kg/m2) Normal weight Over weight Obese	 N=24 (20%) N= 57 (47.5%) N= 39 (32.5%)	 N=16 (20%) N= 38 (47.5%) N= 26 (32.5%)
Sex Male Female	 N= 72 (60%) N= 48 (40%)	 N= 48 (60%) N= 32 (40%)
ACS subgroups STEMI NSTEMI UA	 N= 40 (33.3%) N= 40 (33.3%) N= 40 (33.3%)	 80 (100%)

"N: Number, BMI: Body mass index, STEMI: ST-elevation myocardial infarction, NSTEMI: non ST-elevation myocardial infarction, UA: Unstable angina".

Hence, CPP level may confirm or rule-out ACS in patients admitted to emergency department an early time if it were of high sensitivity and specificity, a property that would reduce mortality rate and decrease the economic costs of ACS treatment. The aim of this study is to explore the relationship of serum copeptin level with traditional risk factors for acute coronary sydrome in Iraqi patients.

Materials and Methods

Study patients were recruited from the coronary care unit "CCU" at "Al-Yarmouk Teaching Hospital" during the period among the "1st of November 2022 to the 1st of Septemper 2023". 120 patients "72 males and 48 females", aged ≥ 30 years were consecutively selected from those who were admitted and diagnosed as "ACS" by specialist cardiologists. The diagnosis of ACS was based on the presence of two available of three criteria:

- Clinical presentation of the patients
- ECG changes
- A positive troponin test

Based on the same adopted criteria, ACS patients comprised three subgroups; namely, STEMI, NSTEMI and UA. The apparently healthy subjects as a controls group were recruited from those who had no current illness with consideration of age and sex matching with the ACS patients. They had no history of CHD or other systemic diseases and have had normal ECG recording.

Blood analysis

Blood samples were collected from patients and controls. Serum was separated, divided into aliquots, and used for measurement of CPP. The assays of CPP depended on use of enzyme linked immune sorbent assay kits that were supplied by MyBioSource Company, USA. Serum cholesterol, glutamate oxaloacetate transaminase (GOT), and fasting blood sugar (FBS) were measured by fully automated cobas c111 analyser.

Introduction

Coronary heart disease (CHD) is caused by an poor myocardial oxygen supply because of narrowing or block of the coronary arteries and is the commonest reason of death worldwide(1). Clinically, the major acute clinical appearance of CHD is called Acute Coronary Syndrome (ACS ((2). The ACS could be manifested as one of three subtypes. These subtypes of ACS include myocardial infarction (MI) with the electrocardiogram (ECG) is showing ST-segment elevation (STEMI), the another is MI with the ECG is showing no ST-segment elevation (NSTEMI) and the third type is unstable angina (UA) (3).

Certain risk factors lead to increase occurrence of acute coronary syndrome like (Age , Being overweight or obese , Diabetes , Smoking , High blood pressure , High cholesterol , Family history of heart disease , chest pain, or stroke and Not being physically active may be altered by pharmacological treatment or behavioral adjustments, making them suitable goals for interventional efforts to reduce the risk of developing or slow down the development of CHD..(4)

A person with a high risk of developing CHD may still benefit from more aggressive and successful therapies for other risk factors, even while some risk variables are unmodifiable(5).

Copeptin (CPP) a polypeptide molecule that is derived from the precursor peptide prepro-vasopressin (164 amino acids) which consists of arginine vasopressin (AVP), neurophysinII, and copeptin(6) .

It has recently been stated that the level of copeptin, the “C-terminal part of AVP precursor” was **raised within 30 min after the onset of chest pain in patients with MI as an outcome of endogenous stress response** (7). The CPP level **did not required serial sampling** in contrast to troponin and so may signify an accurate anchor point to diagnose AMI in patients admitted to ED (8).

المستخلص

الخلفية: لا تزال متلازمة الشريان التاجي الحادة (ACS) واحدة من الأسباب الرئيسية للمرض والوفيات في جميع أنحاء العالم، ويهدف التشخيص المبكر لاحتشاء عضلة القلب (MI) إلى تقليل الوفيات لدى مرضى احتشاء عضلة القلب. تتجلى متلازمة الشريان التاجي الحادة كواحد من ثلاثة أنواع فرعية. تشمل هذه الأنواع الفرعية احتشاء عضلة القلب مع تخطيط كهربية القلب (ECG) يظهر ارتفاع القطعة ST (STEMI)، والآخر احتشاء عضلة القلب مع تخطيط كهربية القلب لا يظهر ارتفاع القطعة ST (NSTEMI) والنوع الثالث هو الذبحة الصدرية غير المستقرة (UA).. **الأهداف:** استكشاف العلاقة بين مستوى الكوبتين في المصل وعوامل الخطر التقليدية لمتلازمة الشريان التاجي الحادة في التشخيص المبكر لهذه المتلازمة لدى المرضى العراقيين. **المنهجية:** تم اختيار 120 مريضًا "72 من الذكور و 48 من الإناث"، تتراوح أعمارهم بين 30 عامًا أو أكثر على التوالي من أولئك الذين تم إدخالهم وتشخيصهم على أنهم متلازمة الشريان التاجي الحادة. كان مرضى متلازمة الشريان التاجي الحادة من ثلاثة أنواع فرعية؛ تم تجنيد مرضى احتشاء عضلة القلب الحاد (STEMI) واحتشاء عضلة القلب الحاد (NSTEMI) واالذبحة الصدرية (UA) و أصحاء ظاهريًا كضوابط لهذه الدراسة. لكل مريض في الدراسة، تم قياس مستويات كوبتين في المصل، وFBS، والكوليسترول، وGOT.. **النتائج:** ظل مستوى كوبتين أعلى بشكل ملحوظ في وجود أو غياب أي من عوامل الخطر المدروسة. أظهر متوسط مستوى CPP فرقًا كبيرًا بشكل عام بين مجموعات الدراسة، وكان متوسط مستوى كوبتين أعلى بشكل ملحوظ في كل مجموعة فرعية من ACS مقارنة بمجموعة الضوابط ($P < 0.001$).

الاستنتاج: ظل مستوى كوبتين في المصل أعلى بشكل ملحوظ في المجموعات الفرعية من ACS مقارنة بمجموعة الضوابط في الساعات الأولى بعد ظهور ألم الصدر في وجود أو غياب أي من عوامل الخطر المدروسة لـ ACS.

الكلمات المفتاحية: متلازمة الشريان التاجي الحادة، احتشاء عضلة القلب الحاد مع ارتفاع المقطع اس تي (STEMI)، كوبتين، عوامل الخطر التقليدية، ال (UA)، الذبحة الصدرية , احتشاء عضلة القلب الحاد مع عدم ارتفاع المقطع اس تي (NSTEMI).

Abstract

Background: Acute coronary syndrome (ACS) is still one of the main causes of morbidity and mortality worldwide and an early diagnosis of myocardial infarction (MI) aims to decrease mortality in MI patients. The ACS is manifested as one of three subtypes. These subtypes include MI with the electrocardiogram (ECG) is showing ST-segment elevation (STEMI), the other is MI with the ECG is showing no ST-segment elevation (NSTEMI) and the third type is unstable angina (UA). **Objectives**: To explore the Relationship of serum copeptin level with traditional risk factors for acute coronary syndrome in early diagnosis of this syndrome in Iraqi patients.

Methodology: 120 patients "72 males and 48 females", aged ≥ 30 years were consecutively selected from those who were admitted and diagnosed as ACS. The ACS patients were of three subtypes; STEMI, NSTEMI and UA and apparently healthy subjects were recruited as controls for this study. For each study subject, serum Copeptin, FBS, cholesterol and GOT levels were measured. **Results**: The copeptin level remained significant higher level in presence or absence of any of the studied risk factors .The CPP mean level showed an overall significant difference among study groups, copeptin mean level was significantly higher in each ACS subgroup than in controls group ($P < 0.001$).

Conclusion: Serum copeptin level remained significantly higher in ACS subgroups than in controls group in the first hurs. After onset of chest pain in presence or absence of any of the studied risk factors of ACS.

Keywords: Acute coronary syndrome, STEMI, Copeptin, Traditional risk factors, UA, NSTEMI.

علاقة مستوى الكوببتين في المصل بعوامل الخطورة لمتلازمة الشريان التاجي الحادة في التشخيص المبكر لهذه المتلازمة لدى المرضى العراقيين

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Relationship of Serum Copeptin Level with Traditional Risk Factors for Acute Coronary Syndrome in Early Diagnosis of this Syndrome in Iraqi Patients

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was daily use drugs, while (12.0%) 1–6 days/week, and (6.8%) few days/ month. The number of drugs taken by the addicted patient in this study was maximum (56.3%) only one drug, while (42.3%) two drugs at same time, and (1.3%) three or more drug. This finding is conformed with other study (Batool *et al.,* 2017) in Pakistan, were the percentage of patient using single drug was (53.8%) while others using multiple drugs was (46.2%).The DAST-20 score is a measure of drug dependence severity; the mean score and (SD) was 12.7±2.2 in this study, and highest proportion at "substantial" was (73.3%), while (15.0%) "intermediate", (11.0%) "sever", and (0.7%) "low" severity categories. This finding is conformed with study result (Harada *et al.,* 2023) conducting in Philippines were mean and standard division of DAST-20 Score was (10.1± 4.1)

Conclusions

The majority of addicted patient was male. the main symptoms were poor performance and/or attendance at work or school and mood swing. The highly complication was fatigue. Regarding the way of addiction, the tablets is vast majority and enjoyment is the most common cause of addiction.

Limitations

There are some limits that stand out. Even though the study only looked at one center, the sample size is about the smiler as in a number of other studies.

Recommendations

It's possible that other important differences between the factors seen in this study would become clearer if multicenter study, the sample size was larger and the duration of the addiction study had been longer.

findings of a past study in Iran (Pourallahvirdi *et al.,* 2016) was (36.4%) married, (58.7%) single, and (3.2%) divorced; (Abdelrehim *et al.,* 2022) in Egypt were (40.0%) married, (51.3%) single, and (8.0%) divorced;(Ma *et al.,* 2022) in China were married (29.7%), single or divorce (70.3%); (Ibrahim *et al.,* 2018) in Saudi Arabia were married (35.0%), single (54.9%), and divorced (9.5%). And also disagree by study (Farook *et al.,* 2022) in Afghanistan were (50.6%) were married, (34.3%) were single; (Chaman *et al.,* 2020) in Iran were (77.5%) were married, (22.5%) were single.

The majority of study sample were reported to have free business (76.3%), while unemployed (14.3%), and only (9.3%) was employed. This agree with what had been reports in study done in Iran (Pourallahvirdi *et al.,* 2016) was (5.5%) had employed, (67.8%) were free business.

The mean and (SD) of age using drugs for the first time in this study was 25.2 ± 9.0 at percentage was 0.7% is below 10 years, 29.3% (10-19), 44.7% (20-29), 17.0% (30-39), 6.7% (40-49), and ≥ 50 years was 1.7%. These findings were consistent with the findings of a past studies including; (Abazid *et al.,* 2020) in Syria were the mean and (SD) was 21.4 ± 5.3; (Goyal *et al.,* 2022) in India were the mean and (SD) was 19.7 ± 6.66; (Farhat *et al.,* 2015) in India also were the mean and (SD) was 25.5 ± 7.6

This result is disagreed with other study like (Rather *et al.,* 2013) in India were (10.1%) in age group below 10 years, while (76.8%) in age group (11-20) years, and (13.1%) in age group (21-30);

Regarding to times of using drug in this study was (47.0%) more than once time/day, (41.0%) only one time/day, (8.7%) once time/week, (2.0%) more than once time/week, and (1.0%) only once time/month. This result is conformed with other study (Al-Kandari *et al.,* 2007) in Kuwait were (80.9%)

Discussion

Many individuals were in the third decade of their life with mean age and standard division was (29.3±8.7). This result is agreed with several studies carried out in different countries including; (Sahar, 2019) in Iraq were 36.94 ±11.93 years; (Mohamed *et al.,* 2020) in Egypt was 28.1 ± 6.5 year among addicted patient; (Farook *et al.,* 2022) in Afghanistan was 30.7 ± 11.4 years.

Other studies that disagree with this study include; (Chen *et al.,* 2022) that conducted in Taiwan was 17.25 ± 1.33 years.

Male patients were (89.3 %) of studied sample while Females only (10.7%) of included patients with a ratio 8.4:1. This study showed a high male to female ratio and these results were confirmed with other studies; (Sahar, 2019) in Iraq were (88.0%) male and (12.0%) female; (Abdelrehim *et al.,* 2022) in Egypt was (96.7%) male and (3.3%) female. While in other study (Ma *et al.,* 2022) in China the result disagree with sex in this study were the male (70.3%) and female was (29.7%); (Chen *et al.,* 2022) In Taiwan were (71.7 %) male and (28.3%) female. Unlike their male counterparts, females may experience more difficulties in trying to acquire drugs in an Islamic society, because of restrictions on female socializations. (Al-Kandari *et al.,* 2007)

The majority of study sample were reported to have primary education (38.7%), while secondary (33.0%), illiterate (16.0%) and only (12.3%) had college or higher degree. The present findings also support (Abdelrehim *et al.,* 2022) in Egypt were primary education (29.3%), illiterate (14.0%) and only (13.3%) had college or higher degree. While the same study secondary education (43.3%) is disagreed to this study.

In terms of marital status, were (36.0%) married, while (51.7%) single, and 17 cases (12.3%) divorced. These findings were consistent with the

Table (3): Drug Abuse Screening Test (DAST-20).

Drug Abuse Screening Test (DAST-20)		No.	%
Lose time from work due to drinking or drug use		271	90.3
Drinking or drug use making your home life unhappy		225	75.0
Drink or use drugs because he/she is shy with other people		147	49.0
Is drinking or drug use affecting reputation		299	99.7
Have ever felt remorse after drinking or drug use		299	99.7
Have gotten into financial difficulties as a result of drinking or drug use		103	34.3
Turn to lower companions and an inferior environment when drinking or using drugs		94	31.3
Drinking or drug use make you careless of family's welfare		178	59.3
Has ambition decreased since drinking or using drugs		286	95.3
Crave a drink or a drug at a definite time daily		293	97.7
Want a drink or drug the next morning		182	60.7
Drinking or drug use cause him/her to have difficulties in sleeping		180	60.0
Has efficiency decreased since drinking or using drugs		129	43.0
Drinking or drug use jeopardizing job or business		68	22.7
Drink or use drugs to escape from worries or troubles		285	95.0
Drink or use drugs alone		233	77.7
Have ever had a complete loss of memory		75	25.0
Has physician ever treated you for drinking or drug use		135	45.0
Drink or use drugs to build your self-confidence		251	83.7
Have ever been in a hospital or institution on account of drinking or drug use		82	27.3
DAST 20 score	None	-	-
	Low (1-5)	2	0.7
	Intermediate (6-10)	45	15.0
	Substantial (11-15)	220	73.3
	Sever (16-20)	33	11.0
	Mean±SD (Range)	12.7±2.2 (5-18)	

Table (3) represent the answer of addicted patient according to John Hopking Addiction Questionnaire- Drug Abuse Screening Test (DAST-20) at the highly answer 99.7% for each two question as, is drinking or drug use affecting your reputation, and have you ever felt remorse after drinking or drug use, while 97.7% do you crave a drink or a drug at a definite time daily, 95.3% has your ambition decreased since drinking or using drugs, 95.0% has your ambition decreased since drinking or using drugs, 90.3% do you lose time from work due to drinking or drug use, 83.7% do you drink or use drugs to build your self-confidence, 77.7% do you drink or use drugs alone, 75.0% is drinking or drug use making your home life unhappy, 60.7% do you want a drink or drug the next morning, 60.0% does your drinking or drug use cause you to have difficulties in sleeping, 59.3% does your drinking or drug use make you careless of your family's welfare, 49.0% do you drink or use drugs because you are shy with other people, 45.0% has your physician ever treated you for drinking or drug use, 43.0% has your efficiency decreased since drinking or using drugs, 34.3% have you gotten into financial difficulties as a result of your drinking or drug use, 31.3% do you turn to lower companions and an inferior environment when drinking or using drugs, 27.3% have you ever been in a hospital or institution on account of drinking or drug use (second addition for addiction cause), 25.0% have you ever had a complete loss of memory, and minimum answer of addicted patient 22.7% on is your drinking or drug use jeopardizing your job or business.

According to John Hopking Addiction Questionnaire - Drug Abuse Screening Test (DAST-20) Mean ± SD (Range) 12.72±2.2 (5-18), at highly answered 73.3% Substantial/Intensive, while minimum answered 0.7% Low / Brief Counseling, and 0.0% None/ Monitor.

In Table (2) the mean and standard deviation of age using drug at first time was 25.2±9.0 and patient received any information about drug use was 76.0%. Furthermore, 47.0% of drug addicted patient use drugs more than once a day, majority of them 56.3% use only one drug every time. And 93.3% from patients were addicted to drug just before admitted and majority of them (52.0%) take drug at home.

Table (2) Epidemiological characteristic of the drug addiction patient.

Epidemiological characteristic		No	%
age using drug at first time	<20	103	34.3
	21-29	119	39.7
	30-39	52	17.3
	40-49	21	7
	50-59	3	1.0
	>=60	2	0.7
	Mean ± SD (Range)	25.2±9.0 (9-61)	
How often do you use drugs	Once a day	124	41.3
	More than once a day	141	47
	Once a week	26	8.7
	Several times a week	6	2
	Other	2	0.7
	monthly	1	0.3
How much drug do you use every time?	1	169	56.3
	2	127	42.3
	3	4	1.3
In what occasions do you use drugs	Before exams	3	1
	in friend home	134	44.7
	At home	156	52
	at work	7	2.3

42.7%. Conversely, the age group with the lowest frequency, people at aged 50-59 years was 0.7%, 89.3% of the participants were male, while 10.7% were female. The majority of patients had 51.7% unmarried, with only 36.0% being married and 12.3% was divorced. The main rate among drug addiction patients was 38.7% primary education ,33.0% secondary education, and 16.0% was illiterate patient, while lowest patient 12.3% at collage. According to the statistics in the table,76.3% of the participants were free business, while 14.3% unemployed, and minimal 9.3% employed. As illustrated in Table (1)

Table 1: Distribution of demographic characteristic among drug addiction patients

Demographic characteristic		No	%
Age (years)	≤20	38	12.7
	20-29	128	42.7
	30-39	94	31.3
	40-49	33	11
	50-59	2	0.7
	≥60	5	1.7
	Mean ± SD (Range)	29.33±8.74 (18-68)	
Sex	Male	268	89.3
	Female	32	10.7
Educational level	Illiterate	48	16
	Primary	116	38.7
	Secondary	99	33
	College	37	12.3
Current marital status	Married	108	36
	Unmarried	155	51.7
	Divorced	37	12.3
Occupation	Employed	28	9.3
	Unemployed	43	14.3
	Free Business	229	76.3

The sites' exclusion criteria included patients less than 18 years old, and addicted on alcohol or other substance not drug.

Statistical analysis

The coding of the responses was done, entered into IBM SPSS-29 and data presentation and analysis conducted. The descriptive analysis used frequency, percentage, added mean standard deviation, and range which is the difference in the minimum and maximum values.

Students-t-test, Paired-t-test, or ANOVA tests were used to determine the significance of difference of means (quantitative data). The differences in categorical data were determined by Pearson Chi-square test (χ2-test) with Yate's correction or Fisher Exact test where appropriate. P values of 0.05 or less indicated statistical significance.

Ethics

The participants in this study signed informed consent form and ethical clearance was sought from the medical department at Alqana Center for Social Rehabilitation as well as the College of Health and Medical Techniques in Baghdad. The subjects' consent was sought and obtained prior to the study as per the standards recommended in the Declaration of Helsinki on use of human subjects for research in 1964.

Results

This cross-sectional study comprised 300 patients addicted to drug, with a mean and a standard deviation (SD) of age of 29.33±18.68. Individuals aged 20-29 year had the highest proportion to addiction, with a rate of

According to the National Institute of Health, adolescents might start using or continue to use drugs for a number of different reasons. These include:

1) To fit in or due to peer pressure
2) To experiment and have new experiences
3) Self-medicating for mental health conditions
4) To experience the positive feelings associated with substances
5) To keep up with intense pressure to perform athletically or academically (for example, using prescription or illegal stimulants)

Drug addiction is now best defined as the outcome of a series of allostatic alterations, similar to other chronic illnesses such as diabetes, hypertension, and obesity. This is worth highlighting since allostatic changes indicate increasing stability via change, rather than just returning to the original homeostatic state (Ruisoto and Contador, 2019).

Drug addiction represents a significant public health concern that has high rates of relapse despite optimal medical therapy and rehabilitation support. (Wang *et al.,* 2018) combining treatment medications (where available) with behavioural therapy is the best way to ensure success for most patients. Treatment approaches must be tailored to address each patient's drug use patterns and drug-related medical, psychiatric, and social problems. (Volkow, 2010)

Materials & Methods

The study adopted a cross-sectional design to recruit (300) subjects diagnosed as drug addiction in the Baghdad governorate, consistent with American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

Sampled data were collected during the patients' admitted to Alqana Center for Social Rehabilitation; variables included socio-demographic, clinical, and epidemiological.

Introduction

Drug Addiction is a multifaceted condition characterized by repeated psychological and physiological dysfunction resulting from prolonged use of psychoactive substances. The phenomenon is marked by a shift in behavior from seeking the pleasurable benefits of a substance to attempting to alleviate the unpleasant symptoms of withdrawal (Koijam *et al.,* 2024).

Drug addiction is a worldwide issue; 5.6% of the world's population aged 15 to 64 took drugs at least once in 2016. For the majority of medicines, younger individuals use them more than older people do (Nations, 2018). Drug abuse seems to be on the increase in several ASEAN (Association of Southeast Asian Nations) countries, particularly among young men aged 15 to 30. The Global Burden of Disease (GBD) research published in 2013 demonstrated the growing burden of drug addiction among adolescents and young adults. Illicit drug abuse account for around 14% of the overall health burden among young males. Younger individuals are also more prone to die from drug abuse issues. (Nawi *et al.,* 2021)

Teenagers are the group of persons most susceptible to addiction. (Luikinga *et al.,* 2018). Teenagers throughout this time have a high tendency toward experimenting, curiosity, sensitivity to peer tension, disobedience against authority, and low self-esteem, all of which make them prone to drug addiction. (Degenhardt *et al.,* 2016). Adolescent drug addiction has significant health consequences, including acute intoxication, long-term health impacts, unsafe sexual behaviors, unwanted pregnancy, sexual violence, and limited key social and psychological transitions to adults roles and responsibilities. (Chen *et al.,* 2022). Addiction is a complicated neuropsychiatric condition that affects a portion of those who use drugs. It has characteristics by maladaptive drug-seeking practices that are sustained despite negative consequences and high drug desire. (Belin-Rauscent *et al.,* 2016)

من القسم الطبي في مركز القناة للتأهيل الاجتماعي في بغداد. نفذ البحث في الفترة من 25/ديسمبر/2023 إلى 30/يونيو/2024. **النتائج:** جميع الأفراد في هذه الدراسة مدمنون على المخدرات. المتوسط والانحراف المعياري (SD) للعمر 29.33 ± 18.68. وكان الأفراد الذين تتراوح أعمارهم بين 20–29 سنة لديهم أعلى نسبة للإدمان، بمعدل 42.7%. وعلى العكس من ذلك، كانت الفئة العمرية ذات التردد الأقل، وهي الأشخاص الذين تتراوح أعمارهم بين 50 و59 عامًا، 0.7%. 89.3% من المشاركين ذكور. كان غالبية المرضى 51.7% غير متزوجين، و36.0% فقط متزوجون و12.3% مطلقون. وكان المعدل الرئيسي بين مرضى إدمان المخدرات هو 38.7٪ في التعليم الابتدائي. و 76.3% من المشاركين كانوا من أصحاب الأعمال الحرة. المتوسط والانحراف المعياري لعمر تعاطي المخدرات لأول مرة 25.2 ± 9.0 وتلقى المريض أي معلومات عن تعاطي المخدرات 76.0% كان 47.0% من المرضى المدمنين يستخدمون المخدرات أكثر من مرة في اليوم، وأغلبهم 56.3% يستخدمون عقارًا واحدًا فقط كل يوم. وقت.إجابة المريض المدمن وفقًا لاستبيان جون هوبكنج للإدمان – اختبار فحص تعاطي المخدرات (DAST-20) بإجابة عالية 99.7% لكل سؤالين، هل يؤثر شرب الخمر أو تعاطي المخدرات على سمعتك، وهل شعرت يومًا بالندم بعد الشرب أو تعاطي المخدرات، والحد الأدنى لإجابة المريض المدمن 22.7% هو أن شرب الخمر أو تعاطي المخدرات يعرض وظيفتك أو عملك للخطر. **الاستنتاجات:** غالبية المرضى المدمنين كانوا من الذكور. الشباب الذين تتراوح أعمارهم بين 20–29 سنة لديهم أعلى نسبة للإدمان ونفس العمر يتعاطون المخدرات لأول مرة .

الكلمات المفتاحية: إدمان المخدرات، الاعتماد، علم الأوبئة، تعاطي المخدرات.

47.0% of drug addicted patient use drugs more than once a day, majority of them 56.3% use only one drug every time.

The answer of addicted patient according to John Hopking Addiction Questionnaire- Drug Abuse Screening Test (DAST-20) at the highly answer 99.7% for each two question as, is drinking or drug use affecting your reputation, and have you ever felt remorse after drinking or drug use, and minimum answer of addicted patient 22.7% on is your drinking or drug use jeopardizing your job or business. **Conclusions**: The majority of addicted patient was male. Young person aged 20-29 year had the highest proportion to addiction and same age used drug at first time.

Keywords: Drug addiction, Dependence, Epidemiology, Drug abuse.

المستخلص

المقدمة: يعد إدمان المخدرات مشكلة عالمية؛حيث يتعاطى 5.6% من سكان العالم الذين تتراوح أعمارهم بين 15 و64 عامًا المخدرات مرة واحدة على الأقل في عام 2016. وبالنسبة لغالبية الأدوية، يستخدمها الأفراد الأصغر سنًا أكثر من كبار السن. ويبدو أن تعاطي المخدرات في ازدياد في العديد من دول (ASEAN)رابطة دول جنوب شرق آسيا، وخاصة بين الشباب الذين تتراوح أعمارهم بين 15 إلى 30 عاما. ويمثل تعاطي المخدرات غير المشروعة نحو 14% من العبء الصحي الإجمالي بين الشباب الذكور. الأفراد الأصغر سنا هم أيضا أكثر عرضة للوفاة بسبب مشاكل تعاطي المخدرات. **الهدف**: هو تقييم مدى خطورة المشاكل المتعلقة بإدمان المخدرات. في مدينة بغداد ودراسة المظاهر الوبائية لإدمان المخدرات لدى المرضى المقبولين في مركز القناة للتأهيل الاجتماعي. **طريقة العمل**: دراسة مقطعية تحليلية لـ 300 فرد شخصوا على أنهم مرضى إدمان المخدرات وفقًا للمعايير التي وضعها "الدليل التشخيصي والإحصائي للاضطرابات العقلية"، الطبعة الخامسة، مراجعة النص، والتي تسمى غالبًا DSM-V-TR أو DSM-5 -TR.

Abstract

Background: Drug addiction is a worldwide issue; 5.6% of the world's population aged 15 to 64 took drugs at least once in 2016. For the majority of medicines, younger individuals use them more than older people do. Drug abuse seems to be on the increase in several ASEAN (Association of Southeast Asian Nations) countries, particularly among young men aged 15 to 30. Illicit drug abuse account for around 14% of the overall health burden among young males. Younger individuals are also more prone to die from drug abuse issues. **Aim**: To assess the severity of problems related to drug addiction. in Baghdad city and to study epidemiological features of drug addiction among Patients Admitted to the Alqana Center for Social Rehabilitation. **Methods**: An analytical cross-sectional study of 300 individuals diagnosed as a drug addiction patient according to the criteria established by the "Diagnostic and Statistical Manual of Mental Disorders", Fifth Edition, text revision, often called the DSM-V-TR or DSM-5-TR. From the medical Department at Alqana Center for Social Rehabilitation in Baghdad. The research was carried out from 25/ December/2023 to 30/June/2024.**Results**: All individuals in this study are addicted to drug. The mean and a standard deviation (SD) of age 29.33±18.68. Individuals aged 20-29 year had the highest proportion to addiction, with a rate of 42.7%. Conversely, the age group with the lowest frequency, people at aged 50-59 years was 0.7%. 89.3% of the participants were male. The majority of patients had 51.7% unmarried, with only 36.0% being married and 12.3% was divorced. The main rate among drug addiction patients was 38.7% primary education. And 76.3% of the participants were free business.

The mean and standard deviation of age using drug at first time 25.2±9.0 and patient received any information about drug use 76.0% were

توزيع الخصائص الوبائية بين مرضى إدمان المخدرات المقبولين في مركز القناة للتأهيل الاجتماعي

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2 كلية التقنيات الصحية والطبية-بغداد ، الجامعه التقنية الوسطى ، بغداد \ العراق
3 معهد طبي المنصور-بغداد ، الجامعه التقنية الوسطى ، بغداد \ العراق

Distribution of Epidemiological Characteristics among Drug Addiction Patients Admitted to Alqana Center for Social Rehabilitation

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of this study found no significant changes in WBCs between patients and healthy persons or between forms of IBS, implying that there are no physiological abnormalities and all of which are within the normal range.

The significance of these findings opens the door to investigate whether this trait was considered as a genetic risk factor for GITs disease including IBS, because previous studies found that secretor status can introduces a proof of exposure to numerous dangerous agents, and as health and disease biomarkers to diagnose systemic disorders (Schipper *et al.,* 2007; Motamayel *et al.,* 2018). It has been reported that the absence of ABH soluble substances in intestinal secretions (non-secretors) decrease hydrolase enzyme activity, which has a significant influence on bacterial and lectin adherence to the intestine microvilli. As a result, non-secretors have higher risk of infection because the absence of ABH compounds in intestinal secretions stimulates microbe adherence, increasing the risk of duodenal ulcers, colitis ulcerative, sclerosing cholangitis and pancreatitis (Azevedo *et al.,* 2008; Folseraas *et al.,* 2012; Weiss *et al.,* 2016).

According to these findings, it can be concluded that people who are non-secretors and having experience of severe anxiety may be at higher risk for getting IBS.

growth influences the disease's symptoms (Sadik *et al.,* 2010). It was hypothesized that obesity plays a significant part in its pathogenesis since the condition is more prevalent in obese persons than in non-obese ones (Pickett-Blakely, 2014).

Since there is no previous study focused on the link between the blood groups and IBS, the above results can be interpreted that this significant correlation is due to indirect influence of blood group on initiation of IBS via their specific effect on blood pressure disorders and atherosclerosis, both of which can indirectly induce a state of stress and anxiety that leads to IBS disease. To confirm this interpretation, previous studies found that ABO antigens indirectly influencing arterial pressure and cardiovascular diseases by influencing renin levels and affecting plasma angiotensin and aldosterone secretion (Nemesure *et al.,* 2006; Nishi *et al.,* 2012).

Few studies have examined the relationship between RBC count and IBS in the current results compared to the results of others. According to Cakal *et al.* (2009), and Song *et al.* (2012) refer that RDW was associated with disease severity in patients with IBD, not IBS. As indicated by Aktas *et al.* (2014) MPV has not been examined in functional gastroenterology but has been an inflammatory marker in IBD patients not in IBS. Also, according to Ratnakumaran *et al.* (2018) refers to hemoglobin having no association with IBS. Furthermore, in a study in Iran by Vaghari-Tabari *et al.* (2020), IBS patients and RBC count also found no relationship between them.

The white blood cell count (WBC) is a nonspecific measure of inflammation that commonly rises after acute or chronic infections and some research show that WBC spikes within the clinically normal range may be indicative of chronic nonspecific inflammation (Erlinger *et al.,* 2004). Result

Discussion

It is well known that IBS patients have experience of severe anxiety when coincided with GAD-7. Lee *et al.* (2009) revealed a probable link between IBS and some psychiatric diseases and that IBS and GAD are linked to both symptoms and disease. Also, several studies reported a high presence of anxiety in IBS patients compared to healthy people who was also significantly associated with poor quality of life (QOL) (Lee *et al.,* 2017; Üçüncü *et al.,* 2020; Rijnaarts *et al.,* 2021). It is suggested that stress stimulates mucosal neuroendocrine secretion, autonomic efferent neurons, and afferent neuron sensitization, resulting in GIT motility problems and visceral hypersensitivity leading to worsening the brain-gut connection (Kosako *et al.,* 2018). As a result, serotonin indirectly impacts the occurrence of systemic illnesses in IBS patients via brain-gut interactions because the central nervous system has a considerable effect on blood flow, secretion, and motility of GIT, so emotions (fear, anger, and anxiety), unpleasant stimuli, and physical stress can all cause stomach emptying and intestinal transit to be delayed (Mayer, 2000). Recent studies suggested that the displacement of bacteria as a result of changing the secretion of the mucous membrane and the function of the barrier causes discomfort in the GIT and thus causes anxiety and depression (Kosako *et al.,* 2018; Niewinna *et al.,* 2020).

Comparing these findings with those attained by other researchers, the majority of previous studies found no link between BMI and the risk of IBS (Guo *et al.,* 2014; Arasteh *et al.,* 2018; Akhondi *et al.,* 2019). In disagreement with these findings, IBS was shown to be substantially linked to obesity (Foster *et al.,* 2003). Other researchers have shown that there is a link between BMI and digestive illnesses particularly IBS and that weight

Table-5: Platelet indices in patients and control groups

Platelet's indices	Normal range	Patients (n= 50)	Control (n= 20)	P value
Count (x 103/µl)	150 - 450	247 ± 58	242 ± 49	0.690
MPV (fl)	7.2 – 11.7	9.3 ± 1.1	8.8 ± 0.9	0.058
PDW (%)	9 – 17	13.8 ± 2.4	13.2 ± 2.6	0.399
Pct (%)	0.20 – 0.24	0.22 ± 0.06	0.21 ± 0.04	0.359
PLR	NA	114 ± 40	129 ± 38	0.161

Based on a 95% confidence interval (95% CI), the normal range of non-secretors' proportion in the general population is 0.13 up to 0.29. Figure-4 shows that 16/50 are non-secretors in the patient's group with a proportion of 0.32, which is significantly higher than the upper limit of normal range, while only 5/20 are non-secretors in the control group with a proportion of 0.25, which is within the normal range.

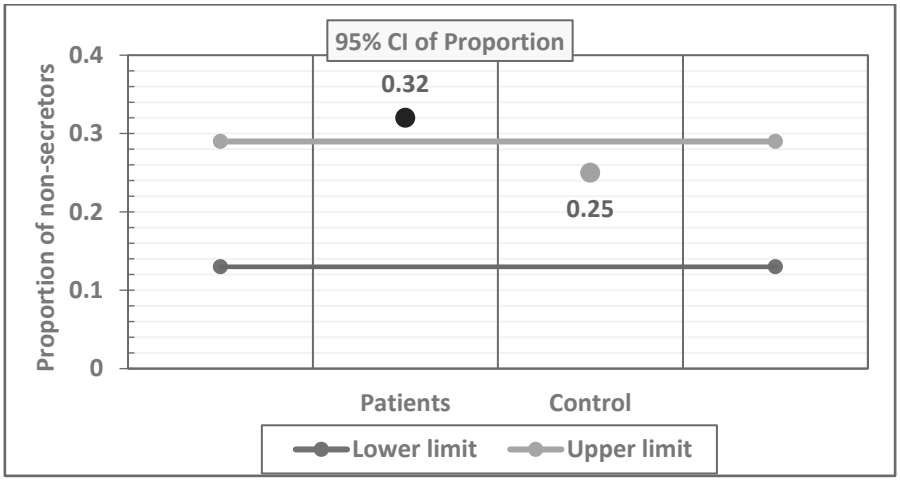

Figure-4: Proportion of non-secretors in patients and control group based on 95% confidence interval.

Table-3: The values of RBCs indices in patients and control groups

RBCs indices		Normal range	Patients (n=50)	Control (n=20)	P value
Count (x106/µl)	M	4.2 - 5.9	5 ± 0.6	4.9 ± 0.5	0.843
	F	3.5 - 5.5	4.3 ± 0.5	4.2 ± 0.7	0.641
Hb (g/dl)	M	13.2 - 16.5	14.3 ± 1.4	13.8 ± 1.5	0.439
	F	11.5 - 15.5	11.9 ± 1.3	12.1 ± 1.5	0.778
Hct (%)	M	40 - 50	43.8 ± 4.1	42.1 ± 4	0.332
	F	36 - 48	36.4 ± 4	36 ± 6	0.710
MCV (fl)		80 - 97	86.2 ± 6.6	84.7 ± 5.1	0.377
MCH (pg)		27 - 31	28.2 ± 2.4	27.5 ± 2.3	0.245
MCHC (g/dl)		32 - 36	32.7 ± 1.1	32.5 ± 1.2	0.395
RDW (%)		11.5 - 14.5	13.8 ± 1.9	14.3 ± 1.3	0.283
M= male; F= female					

The total and differential counts of WBCs in both groups are within their normal range and without significant difference between patients and control groups as shown in Table-4.

Table-4: Total and differential count of WBCs in patients and control groups

WBCs count (x103/µl)	Normal range	Patients (n= 50)	Control (n=20)	P value
Total	4 - 11	6.9 ± 1.7	6.6 ± 2.5	0.437
Granulocyte	2 – 7.8	4.2 ± 1.3	4 ± 1.9	0.561
Lymphocyte	1 – 4.1	2.2 ± 0.7	2 ± 0.6	0.169
Monocyte	0.2 – 0.8	0.49 ± 0.21	0.57 ± 0.22	0.171

The values of platelets count and their indices such as mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (Pct), and platelet-lymphocyte ratio (PLR), all of them in both groups are within their normal range and without significant difference between patients and control groups as shown in Table-5.

patients and control groups. This figure also shows the non-significant difference in the distribution of positive and negative groups based on the Rh system, and Rh +ve group is the most common in both groups (90%, and 85% respectively).

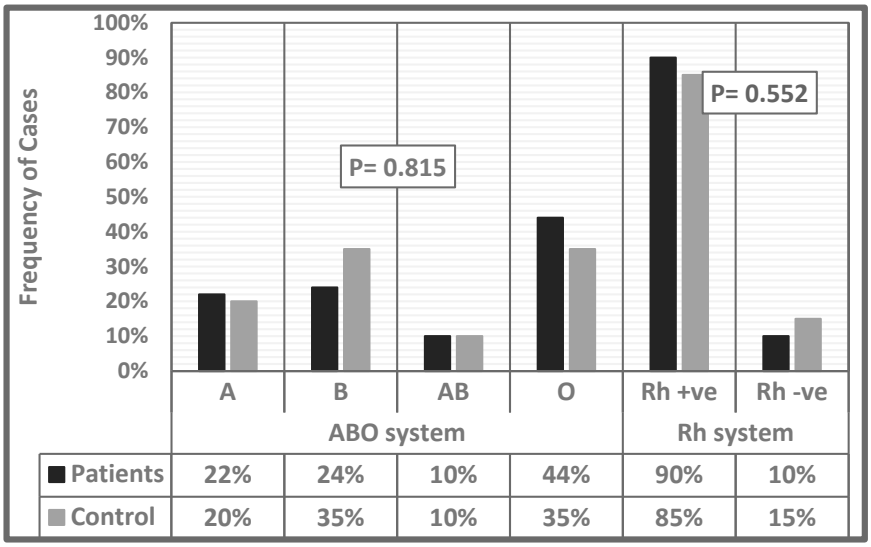

Figure-3: Distribution of blood groups in patients and control groups based on ABO and Rh systems

The values of RBCs count, hemoglobin content (Hb), hematocrit (Hct), as well as all RBCs indices including mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and RBC distribution width (RDW) in both groups are within their normal range and without significant difference between patients and control groups (Table-3).

Table-2 shows non-significant difference in the BMI between patients (27.7 ± 5.6 Kg/m2) and control group (26.2 ± 3.9 Kg/m2). By calculating the frequency of cases with different categories of BMI, Figure-2 also shows non-significant difference between two groups, in which only 24% and 20% of cases are obese in patients and control groups respectively.

Table-2: Body mass index (BMI) in patients and control groups

Parameter	Patients	Control	P value
Weight (Kg)	76.2 ± 15.3	73.2 ± 14.4	0.452
Height (m)	1.65 ± 0.09	167 ± 0.1	0.664
BMI (Kg/m2)	27.7 ± 5.6	26.2 ± 3.9	0.275

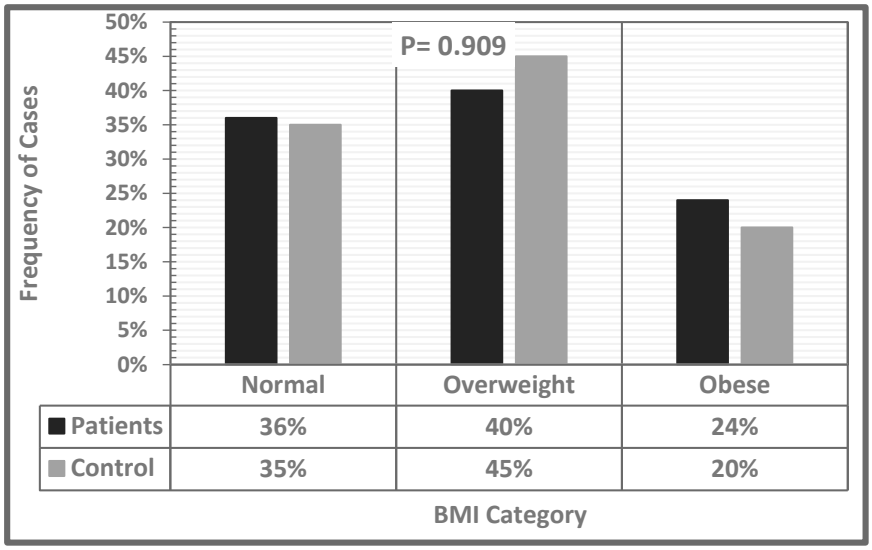

Figure-2: Frequency of cases with different categories of BMI in patients and control groups.

According to the ABO system, Figure-3 shows a non-significant difference in the distribution of A, B, AB, and O blood groups between

Results

Several parameters were investigated in two groups of subject; the first group includes 50 patients with different types of IBS, while the second group includes 20 normal subjects to act as control group. Table-1 shows that gender and age of subjects in both groups are matched and without significant difference.

Table-1: Matched age and gender in patients and control groups

Character		Patients (n=50)	Control (n=20)	P value
Age (year)	Range	20 - 70	20 – 60	1.0
	M ± SD	33.1 ± 13	33 ± 10.3	
Gender (n, %)	Female	33 (66%)	12 (60%)	0.636
	Male	17 (34%)	8 (40%)	

Among all factors of questioners list, only anxiety score reveals significant difference ($P < 0.0001$) between patients and control groups. Figure-1 shows that the majority of patients (64%) suffer from severe anxiety, while the most subjects in control group (75%) have mild anxiety. This result indicates that anxiety score may act as risk factor for getting IBS.

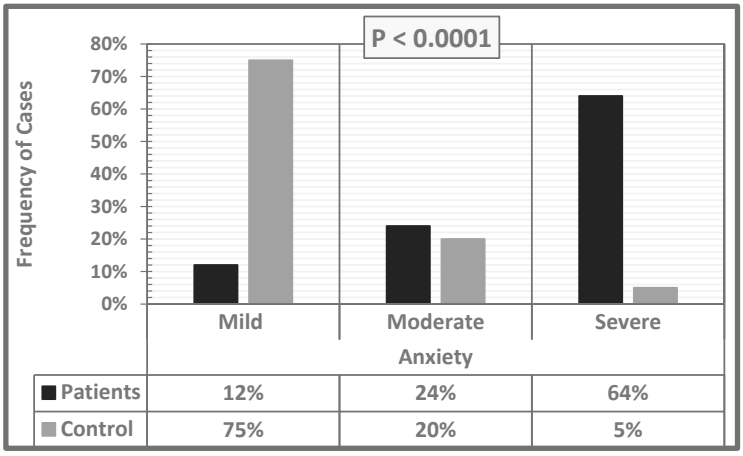

Figure-1: Anxiety categories in patients and control groups.

and H, and secretes blood group "B" both substances B and H (Smart and Armstrong, 2008; Kazmi, 2019). Accordingly, the present study is aimed to investigate whether the hematological indices, anxiety, and secretor status in Iraqi people can act as risk factors for getting IBS.

Materials and Methods

Case-control study was carried out on 50 Iraqi patients with IBS and 20 normal individuals who were matched in age and gender to the patients to act as the control group during the seven months from November 2021 to May 2022. All patients (males and females) with IBS were collected from private clinics specialized in GIDs in Baghdad / Iraq, while those in control group were collected from educational institutions and from outside the framework of private clinics. The height and weight of all subjects are measured to calculate body mass index (BMI). Blood samples are obtained from all subjects to determine many parameters including blood groups, complete blood count (CBC). Saliva samples also are obtained from all subjects to determine their secretor status (Bercher, 2005). All subjects (patients and control) determined their degree of anxiety by using the Generalized Anxiety Disorder Assessment (GAD-7). Body mass index (BMI) was calculated from dividing the body weight (in kg) by the square height (in meter), so its unit is kg/m2. The hemagglutination slide method was used to determine blood groups based on the ABO and Rh systems (Rowley *et al.,* 2012). WBCs, RBCs, Hb, PLT, Granulocyte, Monocyte, and Lymphocyte are measured immediately and in different percentages by the Samsung analyzer (Koepke, 1991), while platelets-lymphocyte ratio (PLR) was calculated from dividing platelet count by absolute count of lymphocyte.

Introduction

The irritable bowel syndrome (IBS) is a functional gastrointestinal tract (GIT) disorder that affects 10% to 20% of the population and is characterized by abdominal pain/discomfort, as well as changes in bowel habits. The natural history of the condition is relapse and recovery (Giuseppe *et al.,* 2020). Anxiety in general people is widespread with IBS, and it is linked to a worsening of GIT symptoms. Adults with IBS have significant rates of anxiety and depression, which may be linked to visceral hyperalgesia and autonomic nervous system dysfunction (Black *et al.,* 2020). Furthermore, fresh evidence reveals that in around two-thirds of IBS cases, psychological distress develops after the beginning of GIT symptoms (Pimentel and Lembo, 2020). On the other hand, people can all be classed as "secretors" or "non-secretors" depending on their capacity to secrete ABO blood group antigens in body fluids (Kim *et al.,* 2002). According to the presence or lack of A, B, and H antigens on the surface of RBCs, the ABO system separates blood types into A, B, AB, and O (Yazer, 2005). In the fluids, the "O" blood type secretes just H element, both A and H substances are secreted by blood group "A", and both B and H substances are secreted the blood group "B" (Kim *et al.,* 2002; Yazer, 2005). Approximately 80% of the population is secretors, meaning they secrete H-substance regardless of their ABO blood group (Ndeh *et al.,* 2022). ABH secretions are regulated by the fucosyltransferase-2 secretor gene, which is found on the short arm of chromosome 19 and has two alleles: dominant "Se" and recessive "se." (Se Se) and (Se se) have a dominant secretor phenotype in their inheritance pattern, whereas (se se) has a recessive non-secretor phenotype. As a result, secretes blood group "O" only material H in the fluids, while secretes blood group "A" both substances A

المستخلص

متلازمة القولون العصبي (IBS) هو مرض وظيفي في الجهاز الهضمي (GIT) يصيب 20-10٪ من السكان في جميع أنحاء العالم ويتميز بألم / انزعاج في البطن وتغيرات في عادات الأمعاء المصحوبة بالإسهال أو الإمساك أو عليهما. أجريت دراسة قائمة على التحكم على 50 مريضًا عراقيًا مصابًا بمتلازمة القولون العصبي والذين تم تقديمهم إلى عيادات خاصة لأمراض الجهاز الهضمي (GIDS) ، إلى جانب 20 فردًا سليمًا مطابقين في العمر والجنس ليكونوا مجموعة تحكم. استمرت الدراسة من نوفمبر 2021 إلى مايو 2022 وهدفت إلى تحديد تواتر الأنواع الفرعية لمتلازمة القولون العصبي بين المرضى العراقيين ، بالإضافة إلى تأثير العديد من العوامل على بدء المرض ونوعه وشدته مثل العمر والجنس والقلق والسمنة ومؤشرات الدم وحالة الإفراز. بالمقارنة مع مجموعة التحكم ، أظهر المرضى تواترًا أعلى بكثير من القلق الشديد وحالات عدم الإفراز خاصة في أولئك الذين يعانون من النوع C من متلازمة القولون العصبي. ومع ذلك، كشف مؤشر كتلة الجسم وفصائل الدم وجميع معايير تعداد الدم الكامل عن وجود فروق غير مهمة بين المرضى ومجموعات المراقبة. بين مرضى أنواع مختلفة من القولون العصبي، أظهرت النتائج أن فصيلة الدم A ترتبط ارتباطًا وثيقًا بمرضى القولون العصبي من النوع d و BS-m]، في حين أن فصيلة الدم 0 ترتبط ارتباطًا وثيقًا بمرضى القولون العصبي من النوع C. أيضًا، ترتبط نسبة الصفائح الدموية إلى الخلايا الليمفاوية بشكل كبير بأنواع القولون العصبي، والتي ترتفع لدى مرضى القولون العصبي من النوع ع مقارنة بأنا)) أخرى من الأمراض. يمكن أن نستنتج أن الأشخاص الذين لا يفرزون الصفائح الدموية ولديهم خبرة في القلق الشديد قد يكونون أكثر عرضة للإصابة بالقولون العصبي.

الكلمات المفتاحية: حالات الافراز، القلق، الاصابة بالقولون العصبي

Abstract

Irritable Bowel Syndrome (IBS) is a functional disease of gastrointestinal tract (GIT) that affects 10-20% of the population worldwide and is distinguished by abdominal pain/discomfort and changes in bowel habits that is accompanied by diarrhea, constipation, or both. Control-based study was conducted on 50 Iraqi patients with IBS who were presented at private clinics for gastrointestinal diseases (GIDs), along with 20 healthy individuals matched in their age and gender to act as control group. The study lasted from November 2021 to May 2022 and aimed to determine the frequency of IBS subtypes among Iraqi patients, as well as the influence of several factors on disease's initiation, type and severity such as age and gender, anxiety, obesity, hematological indices, and secretor status. In comparison with control group, patients showed significant higher frequency of severe anxiety and non-secretor cases particularly in those with IBS-c type. However, BMI, blood groups, and all complete blood count parameters revealed non-significant difference between patients and control groups. Among patients of different types of IBS, results showed that blood group A is highly correlated with IBS-d, and IBS-m patients, while blood type O is highly correlated with IBS-c. Also, platelet-lymphocyte ratio (PLR) is significantly associated with IBS types, which is elevated in patients with IBS-c in comparison with other types of disease. It can be concluded that people who are non-secretors and having experience of severe anxiety may be at higher risk for getting IBS.

Keywords: Anxiety, BMI, IBS, Non-secretor, PLR

Secretor Status and Anxiety Are Risk Factors for Getting Irritable Bowel Syndrome

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حالة الإفراز والقلق
من عوامل الخطر للاصابة بمتلازمة القولون العصبي

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5. Conclusion

The study revealed that individuals with HT and Hypothyroidism have a higher Body Mass Index (BMI) compared to healthy people. At the same time, there were statistically significant changes in C-reactive protein, as well as in other biochemical markers (Ca and Cholesterol).

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4. Discussion

The BMI was significantly difference between HT and hypothyroidism patient than those in control group (p≤0.001). Women with Hashimoto disease exhibited noticeably elevated body weight, resulting in an increased BMI (Chao *et al*., 2020). A study conducted by (Wagh *et al.,* 2020) observed a correlation between BMI and thyroid function in women. CRP also was elevated in both HT and Hypothyroidism than in Control group (p≤0.001), acute-phase protein frequently researched, has been found to promote the secretion of inflammatory cytokines in monocytes. One more significant protein during the inflammatory response (Erden e*t al.*, 2008),therefor, the CRP median in HT was higher than Hypothyroidism patient . In addition, Ca and Cholesterol serum level also extremely significant difference (p≤0.001) when comparing the levels of the HT group, Hypothyroidism group, and Control group. In current study we demonstrated low levels of Serum levels of calcium, it also was decreased notably in patients with Hypothyroidism in the other study (Sultana *et al.*, 2024). Cholesterol in our study was higher in HT patient (p≤0.001) as in (Kurtkulagi *et al.*, 2021) who show elevation in Cholesterol in inflammatory conditions diseases ,while in Hypothyroidism it was elevated more than the Control group and less than the HT with median for HT (54.7) , Hypothyroidism (47.9)) as (Song *et al*., 2021) who mentioned that, individuals with Hypothyroidism and baseline total cholesterol levels above 200 and 240 mg/dL have a 6 and 15 times higher chance of increasing, respectively. Rats fed a high-cholesterol diet indicated high cholesterol but without high triglycerides, along with increased serum TSH. The rise in serum TSH due to excess cholesterol is gradual and time-dependent, and is not related to changes in triiodothyronine or thyroxine levels.

3.4. Ca and Cholesterol test.

Cholesterol and CRP are important markers. The findings indicated an extremely significant difference (p≤0.001) when comparing the levels of these parameters between the HT group, hypothyroidism group, and control group. Calcium median results were (0.86) for HT, (0.91) for hypothyroidism patients while (0.95) for control group all were highly significant statically (≤0.001), median for cholesterol serum levels in HT (54.7) while in hypothyroidism (47.9) and the control group (15.1), the P-value for the three groups was (≤0.001) highly significant. Figure (2) below illustrate the pairwise comparisons between groups to assess the significance level and identify the specific differences between groups. Each node displays the average ranking of the group's samples. Blue lines show a significant difference at p≤0.05 of lower; green lines show no significant difference at p≥ 0.05.

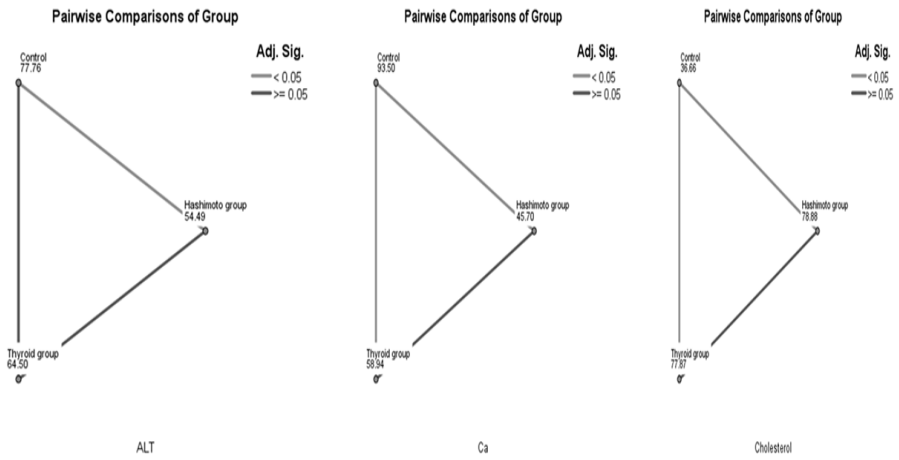

Figure (2) Pairwise comparisons for Cholesterol and CRP between groups

Table 2: Comparison between BMI (Mean ± SD) for the studied groups.

Variable	Mean ± SD			
	Hashimoto group (n=50)	hypothyroidism group (n=50)	Control (n=50)	P-value
BMI	33.07±4.6	31.92±3.0	21.72±1.43	≤0.001***

***** Highly statistically significant at p≤0.001**

3.3. CRP acute-phase protein measurement.

CRP statically measured by the Kruskal-Wallis test, by calculating the median for each studied group, CRP median in HT was (11.2), hypothyroidism (6.2) while control group (1.91). The results showed very highly statistically significant differences (p≤0.001) when the levels of these parameters were compared among Hashimoto group, Hypothyroidism group, and Control group. Figure (1) below illustrate the pairwise comparisons between groups to assess the significance level and identify the specific differences between groups. Each node displays the average ranking of the group's samples. Blue lines show a significant difference at p≤0.05 of lower; green lines show no significant difference at p≥ 0.05.

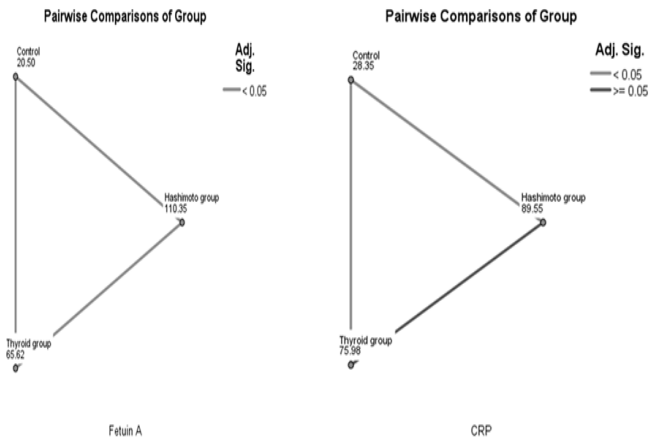

Figure (1) Pairwise comparisons for CRP between groups

2.4. Statistical analysis

The Statistical 26 program in SPSS was utilized for analyzing the impact of various parameters. Comparison between One-way ANOVA and Kruskal-Wallis test.

3.Results.

3.1. Characteristic of the study groups.

The studied groups were distributed as Hashimoto group (Female 34.3% , Male 27.5%) , Hypothyroidism (Female 31.3% , Male 38.0%) and the control group (Female 34.3% , Male 27.5%) , The distribution of the study groups and their gender by numbers and percentages were shown in Table (1).

Table 1: Categorical distribution for studied groups.

Gender	Frequency (%)			Total
	Hashimoto group	Hypothyroidism group	Control	
Female	34 (34.3)	31 (31.3)	34 (34.3)	99 (100)
Male	16 (27.5)	19 (38.0)	16 (27.5)	51 (100)
Total	50 (33.3)	50 (33.3)	50 (33.3)	150 (100)

3.2. BMI in studied group.

Conducting a one-way ANOVA test to assess the differences in BMI among the group, hypothyroidism group, and control group. A significant difference was observed between the studied groups, with a p-value of less than or equal to (≥0.001). The Bonferroni test was employed to ascertain the specific nature of these differences. This analysis found that the average BMI of the Hashimoto group (33.07±4.6) and hypothyroidism group (31.92±3.0) did not show a significant statistical difference (p=0.293), but both groups had a highly significant statistical difference (p≤0.001) in comparison to the control group's BMI (21.72±1.43) as illustrated in Table (2).

mmol/L), different laboratories may have variations in normal values and reference ranges up to 0.5 mg/dl (Goldstein, 1990). Cholesterol is a vital part of the human body, necessary for all cell membranes and the creation of various hormones, bile acids, fats, and fat-soluble vitamins. Furthermore, it helps to support the normal functioning of the brain (Gliozzi *et al*., 2021).

The aim of this study is to investigate the difference between inflammatory and biochemical test in Hashimoto patients.

2. Materials & Methods

2.1. Patients and samples.

The case-control study included 50 patients with Hashimoto, 50 Hypothyroidism patient and 50 control healthy. The patient reports are based on Clinical manifestation and laboratory investigation including (Tsh, T3, T4 and TPOAbs). A blood sample was obtained via vein puncture with disposable syringes, extracting 10 ml of blood from each individual. Blood was gathered in a glass tube without anticoagulant and an EDTA tube with anticoagulant. The serum was separated by centrifugation at 3000 rpm for 5-10 minutes after the gel tube was incubated at room temperature and clot formation occurred.

2.2. Evaluations of CRPL3, Ca and Cholesterol level

CRPL3 by Cobas C311while Ca and cholesterol test was measured by a manual test kit / Mindray BA-88A.

2.3. Ethical approval

The study was approved by the ethical committees of the Middle Technical University College of Health and Medical Techniques.

1. Introduction

Thyroid gland, initial endocrine gland to evolve in humans. It originates from the thyroid diverticulum situated on the middle ventral side of the pharynx *(Song et al.,* 2010). The thyroid gland is a hormone-producing organ that regulates metabolism, growth, and serum levels of electrolytes like calcium through the secretion of thyroid hormone and calcitonin (Fitzpatrick and Siccardi, 2018). Hypothyroidism, which is caused by insufficient thyroid function, can be the result of issues within the thyroid gland (primary thyroid disease) or, in rare cases, issues within the hypothalamus or pituitary gland (central hypothyroidism) or external causes, it is a common condition with possible harmful health effects that impact people all around the globe (Corbetta, 2021). Hashimoto's thyroiditis is an autoimmune condition that results in an underactive thyroid, individuals with Hashimoto's thyroiditis often develop autoantibodies against the thyroid's own antigens, such as anti-thyroid peroxidase (TPOAbs), anti-thyroglobulin (anti-Tg), and TSH receptor-blocking antibodies. These autoantibodies result in insufficient production of thyroid hormone as they destroy the thyroid gland tissue *(Phagoora et al.*, 2023). The primary roles of TSH, aside from stimulating the production of thyroid hormones through increased iodide absorption, include producing thyroglobulin and governing the function of thyroperoxidase (Pirahanchi *et al*., 2018). CRP, an acute-phase protein frequently researched, has been found to promote the secretion of inflammatory cytokines in monocytes, and one of significant protein during the inflammatory response (Erden *et al*., 2008). Calcium is the most plentiful mineral in the body, with 98% of the adult's 1200 g found as hydroxyapatite in the skeleton, the rest is distributed in the extracellular fluid (50%) and different tissues, primarily skeletal muscle, calcium levels are kept relatively stable between 8.5 and 10.5 mg/dl (4.3 to 5.3 mEq/L or 2.2 to 2.7

الهاشيموتو و (0.91) لمرضى قصور الغدة الدرقية و (0.95) للاصحاء وكانت نتيجة المتوسط الحسابي للثلاث مجاميع ذات دلالة معنوية عالية (≤0.001) ومهمة جدا احصائيا. اما بالنسبة لنتائج البروتين سي التفاعلي فكانت هي الاخرى مهمة جدا احصائيا وذات دلالة معنوية عالية (p≤0.001)) عندما قورن الوسيط الحسابي للثلاث مجاميع وكالتالي، مرضى الهاشيموتو (11.2) ومرضى قصور الغدة الدرقية (6.2) مع الوسيط الحسابي للاصحاء و الذي هو (1.91). **الاستنتاجات:** لم يكن هنالك فرق معنوي لمؤشر كتلة الجسم بين مرضى الهاشيموتو ومرضى قصور الغدة الدرقية. ولكن الفرق المعنوي كان عند مقارنة المجموعتين مع الاصحاء. بروتين سي التفاعلي والكولسترول والكالسيوم كانوا مختلفين بفرق معنوي مهم بين المجاميع الثلاثة.

الكلمات المفتاحية : مرضى الهاشيموتو,ثايروكسين,قصور الغدة الدرقية المناعي,التألق المناعي غير المباشر,بروتين سي التفاعلي,كالسيوم .

Abbreviations

HT: Hashimoto's thyroiditis

AITD: Autoimmune thyroid disease

TSH: Thyroid stimulating hormone

Ca: calcium

CRP: C-reactive protein

BMI: Body mass index

المستخلص

المقدمة: خمول الغدة الدرقية واحد من الامراض الشائعة الناتجة عن نقص هرمون الثيروكسين. الهاشيموتو واحد من أكثر الامراض شيوعا للغدة الدرقية يسمى ايضا بمرض الغدة الدرقية المناعي، ما يقارب 20 – 30 % من مرضى الهاشيموتو يعانون من قصور الغدة الدرقية بسبب تكرار الالتهاب في نسيج الغدة الدرقية. **الهدف:** دراسة الفرق بين مؤشر الالتهاب وبعض الفحوصات البيوكيماوية لمرضى الهاشيموتو (مرض الغدة الدرقية المناعي) ومرضى قصور الغدة الدرقية (غير المناعي) **طريقة العمل:** اجريت الدراسة على (50) مريض مصاب بالهاشيموتو و (50) مريض مصاب بقصور الغدة الدرقية غير المناعي المراجعين الى العيادة الاستشارية لأمراض الغدد الصماء في مستشفى بغداد وحدة المختبرات الاستشارية و50 شخص سليم في النصف الاول من عام ٢٠٢٤ أي للفتره من يوم ٧ كانون الثاني الى يوم ٢٥ اغسطس. **النتائج:** كان متوسط مؤشر كتلة الجسم لمرضى الهاشيموتو (4.6±33.07) ولمرضى قصور الغدة الدرقية (3.0±31.92)، لم يكن هذا الفرق ذو دلالة عالية ولا فرق مهم احصائيا لهاتين المجموعتين ($p=0.293$)، لكن بالمقارنة مع مجموعة الاصحاء (1.43±21.72) كان هنالك فرق احصائي عالي ($p\leq0.001$). المتوسط الحسابي للكولسترول في مرضى الهاشيموتو كان (54.7) ولمرضى قصور الغدة الدرقية (47.9) و للاصحاء (15.1)، كان المتوسط لكل المجموعات ذو دلالة معنوية عالية (≥0.001). الكالسيوم كان ايضا بمتوسط حسابي (0.86) لمرضى

Abstract

Background: Hypothyroidism is a common medical condition that occurs due to a lack of the hormone thyroxine. Hashimoto's thyroiditis (HT) is the most prevalent thyroid disorder, also known as autoimmune thyroid disease (AITD). Approximately 20-30% of people develop hypothyroidism due to ongoing inflammation of the thyroid tissue it triggers. **Aims**: To investigate the difference between inflammatory and biochemical test in Hashimoto autoimmune thyroiditis (AITD) and hypothyroidism patients (non-autoimmune) **Methods**: The study was done on 50 Hashimotos patients, 50 Hypothyroidism patients from the Endocrinology Unit at Baghdad Teaching Hospital and Educational Laboratories / Baghdad City, Iraq, and 50 control healthy subjects during the first half of the year 2024, from 7th January until 25th August 2024. **Results**: The mean BMI of the HT group was (33.07±4.6) and for hypothyroidism group was (31.92±3.0), did not show statistically significant differences (p=0.293). However, the mean BMI of both groups differed highly statistically significant (p≤0.001) when compared to that of the control group (21.72±1.43). Median serum levels of cholesterol in HT was (54.7) while in hypothyroidism was (47.9) while for the control group was (15.1), the p-value for the three groups was (≤0.001) and showed highly significant differences. Calcium median results were (0.86) for HT, (0.91) for hypothyroidism patients while (0.95) for control group all were highly significant statically (≤0.001). Finally, CRP showed highly statistically significant difference (p≤0.001) when the levels of these parameters were compared among Hashimoto group, hypothyroidism group, and control group with median range in HT (11.2), hypothyroidism (6.2) and control group (1.91). **Conclusions**: BMI had no significant differences between HT and hypothyroidism group but the two groups were different significantly from the control group, CRPL3, CA, Cholesterol all were different significantly between HT, Hypothyroidism and control group.

Keywords: HT, Thyroxine, AITD, Indirect immunofluorescence, CRP, Ca

Comparison between CRP Level and Some Biochemical Parameters in Hashimoto and Hypothyroidism Iraqi Patients

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المقارنة بين بروتين سي التفاعلي و الفحوصات الكيمياوية الحيوية لمرضى الهاشيموتو ومرضى خمول الغدة الدرقية في المرضى العراقيين

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result of the presence of antiphospholipid antibodies, which are frequently found in patients with SLE (Zhang *et al*., 2023, Garcia *et al.*, 2024). Platelets were within normal values in the studied group and there were no statistically differences between them, $p>0.05$.

Conclusion

Systemic lupus erythematosus is an autoimmune disease that affects multiple parts of the body. It is relatively common in adults but rare in children, and tends to be more severe in children than in adults. The study showed a decrease in complement C3 and C4 levels in all patients, but the decrease was more pronounced in children. This reduction in complement levels is associated with increased disease severity and exacerbation of systemic symptoms. Additionally, serum urea and creatinine levels were higher in children, as they are more prone to kidney damage. All patients also had anemia due to the disease.

Hypocomplementemia is an important indicator in adults and children with SLE, showing the presence of active disease, and organ damage, especially in lupus nephritis and helping to determine treatment plans (Sharma *et al.*, 2020). In current study we demonstrated low levels of C3 in (jSLE) patients were found to be strongly linked to higher disease severity (based on physician assessment), while low C4 showed no connection with disease severity, this implies that C4 could be a less accurate indicator of disease activity in patients with (jSLE). disease activity tends to be higher in (jSLE). However low levels of complement C3 and C4 in (jSLE) compared to (aSLE) is mainly due to immune system differences as the immune system of children may respond differently to immune triggers and accordingly (jSLE) would have a more aggressive course leading to rapid complement depletion (Afzali *et al.*, 2018). The WBCs count means were within the normal range it concurred with recent research on Iraqi individuals with SLE (Ali *et al.,* 2024) , indeed, there were cases in both groups of mild leukopenia, but some patients had leukocytosis, leading to this normal average result overall. Patients with systemic lupus erythematosus often exhibit leukopenia, neutropenia, and lymphopenia as common clinical manifestations, with a significant decrease seen in all blood cell counts (Lu *et al.*, 2021). Both study groups showed low levels of hemoglobin (anemia), with lower levels observed in the (jSLE) group, although there was no statistically significant difference between them, $p>0.5$. In (jSLE) autoimmune hemolytic anemia is observed more than adults as discussed in clinical features, according to (Kisaoglu *et al*., 2022), AIHA and anemia of chronic disease are most common with (jSLE), although iron deficiency is not uncommon, the seriousness of inflammation is linked to the seriousness of anemia. AIHA develops as a

Table 3 Comparison Between the Mean of WBC, Hb, PLT and ESR Among Studied Groups

Group	Mean ±SE		
	WBC (x103)	Hb (g/dl)	PLT (x103)
Juvenile-onset SLE n= (35)	9.73 ±0.96	10.19 ±0.45	288.77 ±19.54
Adult-onset SLE n= (35)	7.65 ±0.54	11.60 ±0.84	262.23 ±17.57
P-value	0.0497	0.167	0.317

WBC, white blood cells; Hb, hemoglobin; PLT, platelet; ESR, erythrocyte sedimentation rate. *P-value ≤0.05 is significant; P-value ≥0.05 is non-significant.

Discussion

Female gender is domain in the study groups (P≤0.01). Duo to SLE is an autoimmune disease that typically shows sexual dimorphism, with about 90% of patients being female (Bose and Jefferies, 2022). The ratio of males to females in the two age groups notably showed disparity that strongly suggests the impact of puberty (hormonal changes) witch increase adult females susceptibility to the disease (Margery-Muir *et al.*, 2017), same results observed in previous studies (Aggarwal and Srivastava, 2015, Aeschlimann et al., 2019). Creatinine and urea levels correlate with renal injury (Gounden *et al*., 2018). And renal damage is more frequent in child (Tektonidou *et al*., 2017). Since lupus nephritis is observed in approximately 50-82% of cases, while in adults it affects about 20-40% of cases (Samanta *et al*., 2017). Disease activity tends to be higher in (jSLE) as previously mentioned, it likely leads to greater organ damage, which in turn results in elevated urea and creatinine levels compared to (aSLE). In addition, research indicates a stronger connection between genetic loci linked to SLE susceptibility and LN in SLE diagnosed during childhood (Webber *et al.*, 2020).

high-significant between them p<0.01. But there was none statistical significance of C4 between the studied groups as presented in Table 1, (jSLE) had a greater level of both urea p<0.01 and creatinine p<0.05 compared to (aSLE) as presented in Table 2. Mean WBC count were non-significant changes among all patients, both study groups showed low levels of hemoglobin (anemia), with lower levels observed in the (jSLE) group, although there was no statistically significant difference between them, p>0.5, platelets were within normal values in the studied group and there were no statically differences between them, p>0.05 as presented in Table 3.

Table 1: Comparison Between the Mean Complement 3 (C3) & Complement 4 (C4)

Group	Mean ±SE	
	C3 (mg/dl)	C4 (mg/dl)
Juvenile-onset SLE n= (35)	67.66 ±6.91	16.74 ±1.93
Adult-onset SLE n= (35)	101.35 ±5.64	18.41 ±1.80
P-value	0.0004	0.531

*P-value ≥0.05 is non-significant; P-value ≤0.01 is highly-significant.

Table 2: Comparison Between the Mean of Urea and Creatinine Among Studied Groups

Group	Mean ±SE	
	Urea (mg/dl)	Creatinine (mg/dl)
Juvenile-onset SLE n= (35)	39.20 ±3.70	1.12 ± 0.12
Adult-onset SLE n= (35)	25.69 ±1.93	0.66 ± 0.04
P-value	<0.01	<0.05

*P-value ≤0.05 is significant; P-value ≤0.01 is highly-significant.

comprises 30 healthy volunteers who were matched with patients in age and sex, and had no previous history of lupus or other autoimmune diseases. Participants could be enrolled at any point after their diagnosis. Human C3 and C4 tests was measured by Immunoturbidimetric assay, in which form a precipitate with a specific antiserum determined turbidimetrically by using Roche/Hitachi cobas c 311 analyzer. Blood urea, serum creatinine tests done by Mindray BS-240 chemistry full-automated analyzer, China. While for CBC, Mindray BC-5000 Hematology analyzer, China, was used. The SAS program / 2018 was utilized to identify how various groups impacted study parameters. A t-test was employed to compare means for significance. Chi-square test was utilized to compare significance between percentages with probabilities (p-value). The study was done with the permission of the Middle Technical University, College of Health and Medical Technology, Baghdad. Furthermore, approval has been obtained by The General Directorate of The Medical City, Baghdad Hospital, Baghdad. And all participants submitted written, informed consent. Approval numberd:193/3; date:09/01/2024.

Results

The study included seventy patients, categorized by age. Individuals over the age of 20Y were classified as having adult-onset systemic lupus erythematosus (aSLE), (mean ± SD, 34.73 ±1.76 years); Male: Female 3:32 respectively, and those aged under 16Y were categorized as juvenile-onset systemic lupus erythematosus (jSLE) (mean ± SD, 10.44 ±0.59 years); Male: Female ratio is 8:27 respectively, and 30 healthy control (15 children, mean ± SD, 8.44 ±1.50 years, Male: Female 3:12 respectively), and (15 Adult, mean ± SD, 33.2 ±1.62 years, Male: Female 2:13 respectively. (jSLE) group experienced the lowest levels of C3 than (aSLE) and there are statistically

photosensitivity, alopecia, and malar rash (Connelly and Morand, 2021). Renal inflammation is considered to be the most common clinical presentation in SLE, compared to adult-onset disease, (jSLE) has a higher frequency of lupus nephritis which can result in severe morbidity (Smith *et al.,* 2019, Li *et al*., 2021). Complement activation is a key event in the pathogenesis of tissue inflammation and injury in systemic lupus erythematosus (Weinstein *et al*., 2021). In general, most patients typically experience decreased complement C3 and C4 levels during the stages of the disease, which is due to the consumption of these complements as part of the immunopathogenesis process (Weinstein *et a*l., 2021). C3 is included in the common cascade after the convergence of the three pathways, by contrast, C4 is included in the classical and lectin pathways. Therefore, low levels of both proteins indicate the activation of these two pathways, whereas low C3 and normal C4 indicate the activation of the alternative pathway (Sandhu and Quan, 2017). The study aimed to compare complement levels (C3) and (C4), blood urea, serum creatinine, and complete blood count among adult and juvenile SLE patients.

Patient and Methods

The present research was to recruit 70 participants from different ages, all of whom have been diagnosed with SLE according to the 1997 American College of Rheumatology (ACR) criteria (Hochberg, 1997). They went to the Rheumatology Unit at Baghdad Teaching Hospital (Adults) and the Welfare Teaching Hospital (children) between January and May 2024. Patients were categorized into two groups according to their age: Group I consisted of 35 individuals with adult-onset SLE, aged over 20 years, while Group II comprised 35 patients with juvenile-onset SLE, aged under 16 years. The control group

Introduction

Systemic lupus erythematosus (SLE) is a complicated autoimmune disorder that affects multiple body systems, it is complex and includes epigenetic, genetic, and environmental factors *(*Ameer *et al*., 2022a). Pathogenicity of SLE is heterogenetic, involving impaired removal of cells, increase in both innate and adaptive immune responses, activation of complement system, formation of immune complexes, and inflammation in tissues (Fava and Petri, 2019). Patients under 18 years old, they are often called to have juvenile-onset systemic lupus erythematosus (jSLE), which is uncommon, around 10% to 20% of youngsters with SLE diagnosed during childhood, and usually, (jSLE) demonstrates a more intense clinical progression compared to adult cases, often with a greater frequency of lupus nephritis and blood-related abnormalities (Harry *et al*., 2018). A combination of clinical criteria, laboratory testing, and sometimes imaging techniques are used to diagnose SLE, standardized guidelines regarding the diagnosis and classification of SLE are provided by the classification criteria created by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR), which incorporate both clinical and immunologic criteria (Aringer *et al*., 2019). Women *in 10 times risk of developing SLE compared to males,* men experience a more severe and aggressive course of the disease, which leads to a poor prognosis (Ameer et al., 2022b, Garcia et al., 2024). According to research, the prevalence of SLE worldwide is 43.7 (15.87 to 108.92) per 100,000 individuals, with 3.41 million persons affected (Tian *et al.*, 2023). SLE has a wide range of clinical features that can initially appear in almost any organ including the kidney (lupus nephritis) and a spectrum of mucocutaneous involvement including mouth ulcers,

المستخلص

المقدمة: داء الذئبة الاحمراري هو مرض مناعي ذاتي، وتشخيصه في الاطفال يُشكّل حوالي 15-20٪ من المرضى. تعود أسباب المرض إلى عوامل مختلطة بين الجينية والبيئية، تلعب المتممات 3 و4 دوراً مهماً في تشخيص المرض ومراقبة شدة الحالة. بالإضافة إلى ذلك، تعد اختبارات وظائف الكلى مهمة لمراقبة المرض، حيث يصيب المرض الكليتين في نسبة كبيرة من المرضى.

الهدف: أجريت هذه الدراسة لمقارنة مستويات المتممات 3 و4 , وظائف الكلى، صورة الدم الكاملة لدى المرضى العراقيين البالغين والأطفال المصابين بداء الذئبة الاحمراري. **المرضى وطريقة العمل:** تكونت الدراسة من 70 مريضاً، 35 طفلاً و35 بالغاً، بالإضافة إلى 30 فرداً كمجموعة ضابطة، أخذت العينات من المرضى خلال زيارتهم العيادة الاستشارية لأمراض المفاصل في مستشفى بغداد والعيادة الاستشارية لأمراض الكلى في مستشفى حماية الاطفال بمدينة الطب في بغداد، خلال الفترة من يناير إلى مايو2024، قيست المتممات بواسطة تقنية التعكر المناعي بواسطة جهاز./Roche Hitachi cobas c 311

النتائج: كانت مستويات المتممات 3 و4 منخفضة في كلا المجموعتين، لكنها كانت أكثر انخفاضاً لدى الأطفال وخاصة المتمم 3,

مع مستويات أعلى من اليوريا والكرياتينين في مجموعة الأطفال، $p<0.01$، $p<0.05$ على التوالي، لم يكن هناك فرق معنوي في تحليل صورة الدم لكلا المجموعتين. لكن جميع المرضى كانوا يعانون من فقر الدم كونه أحد اعراض الدموية الشائعة للمرض.

الاستنتاجات: يعد قياس مستويات المتممات ووظائف الكلى وتعداد الدم أمراً بالغ الأهمية في الفحوصات الدورية للمرضى، حيث ترتبط هذه الاختبارات بتقييم المرض وتطوير خطة علاج مناسب.

الكلمات المفتاحية: داء الذئبة الاحمراري لدى الكبار، داء الذئبة الاحمراري لدى الأطفال ونظام المتممات.

Abstract

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease, with about 15-20% of patients being children. The causes of the disease are a mix of genetic and environmental factors. Complement C3 and C4 play a significant role in the diagnosis and monitoring of disease severity. Additionally, renal function tests are important for monitoring the disease, as the disease affects the kidneys in a large percentage of patients. **Aim**: The study was primarily conducted to compare complement C3 and C4 levels in Iraqi adult and juvenile patients with systemic lupus erythematosus. **Patient and methods**: The study consisted of 70 patients, 35 children and 35 adults, in addition to 30 individuals as a control group. The patients visited the Rheumatology Clinic at Baghdad Hospital and the Nephrology Clinic at the Children's Welfare Hospital in Medical City, Baghdad, during the period between January and May 2024. Human C3 and C4 tests was measured by Immunoturbidimetric assay by using Roche/Hitachi cobas C311 analyzer. **Results**: Complement levels were low in both groups, but more notice in juveniles, particularly complement C3 $p<0.01$, with higher levels of urea and creatinine in the juvenile group $p<0.01$, $p<0.05$, respectively. There were no significant differences in blood counts between the two groups; however, all patients suffered from anemia, as it is one of the common hematological manifestations of the disease. **Conclusion**: Measuring complement levels, kidney function, and blood counts is crucial in the regular monitoring of patients, as these tests are related to disease assessment and the development of an appropriate treatment plan.

Keywords: Juvenile-onset SLE, Adult onset SLE, Complements system.

Complement Component C3 and C4 Levels in Juvenile and Adult SLE Iraqi Patients

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المتممات سي3 و سي4 في المرضى الأطفال والبالغين العراقيين المصابين بداء الذئبة الاحمراري

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Also a significant relationship between age, BMI, job, work experience, working hours per day, type of work shift, education level, type of occupational task, previous LBP, history of underlying diseases, and type of LBP in the subjects. Prior research has shown that these criteria are significant contributing variables to the chronicity of Low Back Pain. Research has shown that those who are older, have a higher body mass index (BMI) are more susceptible to Chronic Low Back Pain (CLBP).

Conclusion

LPB has a higher frequency among the female population, highest proportion chronic disease, highly significant between sex and BMI

Regarding association between sex and educational level, this study found High significant (p value=0.0001) and this conformed by study in Qatar too (Bener, *et al.*, 2014).

Occupation and marital status and smoking have significant associated with sex (p value =0.0001) and this conformed by the same study in Qatar (Bener, *et al.*, 2014), and in this study express significantly correlation between sex and BMI (p value = 0.0001) this conformed by study in Span, significant association between sex and BMI (Calais-Ferreira, *et al.*, 2023).

Regarding to this study significantly correlation between smoking and sex (p value =0.0001) and this conformed by study in Span, found significant association between sex and smoking (Calais-Ferreira, *et al.*, 2023) .

The most common symptom mentioned was increased pain with lifting and bending which affected 91.4% of individuals. stiffness in the morning upon rising that improves with exercise (55.5%), and back pain that comes and goes (60.7%). Less frequent symptoms were limitation of movement (45.7%), numbness or tingling, weakness in the legs or feet (42.3%), pain that radiates away from the back into the buttocks, leg, or hip (41.4%), weight loss that was (4.3%).

The mean and SD for Quebec disability score in this study was (57.5±15.6) and this is confirmed by many studies, e.g. in the Poland (Misterska, *et al.*, 2011a) was 50.2 ± 18.9, and in another studies disagreed such that in Turkey mean and SD (37.132 ±17.513) (Bicer, *et al.*, 2005), and In Marburg, Germany the mean and SD (43.58 ±18.08) (Riecke, *et al.*, 2016), and in Italy was (32.15 ±13.2) (Speksnijder, *et al.*, 2016).

In t,he present study a strong association was found between demographic characteristics and disease subtype. This finding is consistent with a study conducted in Iran (Sadeghi-Yarandi, *et al.*, 2021).

conducted in Poland by (Misterska, *et al.*, 2011))45.9(,and disagreed with the study in Colombo, Sri Lanka (Gamage & Ranasinghe, 2020) the duration of Low Back Pain less than one year (52.0). and by comparison with all group below 10 years in Canadian (48.17) (Zerriouh, *et al.*, 2024), in Portugal (22.7) (Cruz, *et al.*, 2013).

The disease subtype of Low Back Pain comprised from acute, subacute and chronic, in the current study acute (25.5%), subacute (5.5%), chronic (69.1%).

The finding of this research conformed with those of other study in Nigeria including in (20 %) of the patients recorded as acute LBP, (6.9%) as subacute while 73.1% recorded as chronic LBP (Eyichukwu & Ogugua, 2012) . other study in Nigeria showed that acute, subacute, and chronic LBP were 28.7%, 9.9%, and 61.4%, respectively.(Edomwonyi & Ogbue, 2017) .and in South Nigeria showed that the subacute was (7.8%) (Emorinken, *et al.,* 2023)

The disease subtype acute was (25.5) is disagreed with the study in Nigeria (12.2) (Emorinken, *et al.*, 2023) , and subacute is (5.5) disagreed with study in Amsterdam (17.4)(Pellekooren, *et al.*, 2022), and in Nigeria (7.8) (Emorinken, *et al.*, 2023)

Chronic disease in this study (69.1) disagree with study in Amsterdam (82.6) and in Nigeria (79.9) (Emorinken, *et al.*, 2023) ,and in Canda (28.4) (Benyamina Douma, *et al.*, 2019). Furthermore, the present investigation showed that the LBP was associated with sociodemographic factors, such as sex, age, education level, smoking, and occupation. This research also showed significant association between the frequency of LBP and socio-demographic factors, which is in accordance with previous studies.

This study showed significant association between age group and sex (p= 0.003) and this conformed by study in Qatar (Bener, *et al.*, 2014) .

Among the other aspects of this research, it shows that female-to-male ratio of (1.4-1) within a percentage of 59.1% females; and 40.9 % were men. Furthermore, these findings were in consistent with previous study, in Iraq (Nayyef, *et al.*, 2022) observed that the male was 40.6% and female was 59.4%, in Taiwan (Lu, *et al.*, 2013) illustrated that the male was 35.5% and the female was 64.5%; and in other study in Iraq illustrated that the male (30.9%) and the female (69.1%) (Al-Bakri, *et al.*, 2024) . and in Iran conformed by male (66.8%) and female (33.2%) (Maghbouli, *et al.*, 2020).

The present study disagrees with another study, such as in Iran (Ibrahim, *et al.*, 2020)Male (2.8%) and female (97.2%)

This finding is conformed with another studies recording a greatest prevalence of Low Back P,ain, in women. Women, as compared with men, are more effected with the pain. tolerance, expression, and reporting of pain, have been attributed to biological, psychological, and sociocultural factors. (Makris, *et al.*, 2011).

In this study, the mean of BMI was (27.91±4.69). The findings were in Iraq indicated a mean (25.87 ± 3.65) (Professor *et al*., 2020), And another study in Iraq mean and SD of BMI (29.2 ± 4.1) (Sakr, *et al.*, 2016) . And in Saudi Arabia study that indicated a mean and SD of BMI of (24.94 ± 4.5) (Albasseet, *et al.*, 2023b) ,and in Thailand mean and SD of BMI (23.82±3.97) (Pajeemas, *et al.*, 2018) and in Indonesia that indicated a mean and SD of BMI (25,26 ± 3,8) (Novy, *et al.*, 2023).

In another study in Canada conformed the results of this study and showed that the mean and SD of BMI (29.3 ± 6.8) (Poder & Carrier, 2020) .

The duration of Low Back Pain for less than one year in this study was (41.1). This finding was conformed with of another study including a study

Figure (1) showed the sample distribution of Quebec Back Pain disability scale scores, the majority of participants had crippled 47%, severe (38.9%) disability, moderate (10.7%) or with only a small percentage (3.4%) having minimal disability and a mean ±SD (range) of 57.5±15.6

Discussion

All 440 patients in this study were diagnosed with Low Back Pain according to the 2010 ACR/EULAR criteria for Low Back Psain .The mean and SD of the age was (45.7 ± 14.8).Based on other studies in different countries, these results were in consistent with other study in Iraq were the mean and SD (51.4 ± 13.28) (Hassan, *et al.*, 2020), and in Saudia Arabia were the mean and SD (40.0 ± 13.5) (Alamam, *et al.,* 2019) , where in Taiwan (Lee, *et al*., 2017) illustrated that the mean age and SD was 40.7 ± 11.4 years, furthermore, study carried in Germany showed that the mean age and SD (53.31 ± 7.49) (Riecke *et al.*, 2016) , while study in Spain showed that the mean and SD of age (45.6 ± 9.9) (Gavira Pavón *et al.*, 2016), and study carried in Colombo showed that the mean age and SD (50.17± 11.20)(Gamage & Ranasinghe, 2020),The present study disagrees with several studies that previously carried out, as in Saudi Arabia (26.9 ± 7.69) (Albasseet, *et al.*, 2023a) , and in Turkey by (Bayar, *et al.*, 2003) (76.03 ± 5:89) , in Penang, Malaysia (Ibrahim, *et al*., 2020) (72 ± 50.7) years), in Taiwan (59.0±14.8) (Lu, *et al.*, 2013).

Older patients may be more likely to present with low back pain pathologies associated with age-related co-morbidities (e.g., cancer, osteoporosis, fractures), and may be less likely to present with non-specific low back pain than the middle-aged patient population (Federico, *et al.*, 2022)

Epidemiological characteristic		Disease subtype						P value
	Acute		Subacute		Chronic			
	No	%	No	%	No	%		
History of previous attack	Yes	29	25.9	4	16.7	304	100	0.0001*
	No	83	74.1	20	83.3	-	-	
Number of attacks	1	28	96.6	-	-	228	75.5	0.08
	2-3	-	-	-	-	38	12.5	
	≥4	1	3.4	-	-	38	12.5	
Lived with disability	Yes	29	25.9	4	16.7	304	100	0.0001*
	No	83	74.1	20	83.3	-	-	
Years lived with disability	No disability	83	74.1	20	83.3	-	-	0.0001*
	<1year	29	25.9	4	16.7	265	87.2	
	1---3	-	-	-	-	25	5.7	
	4---6	-	-	-	-	6	1.4	
	7---9	-	-	-	-	2	0.7	
	≥10years	-	-	-	-	6	1.4	
*Significant difference between percentages using Pearson Chi-square test (χ2-test) at 0.05 level.								

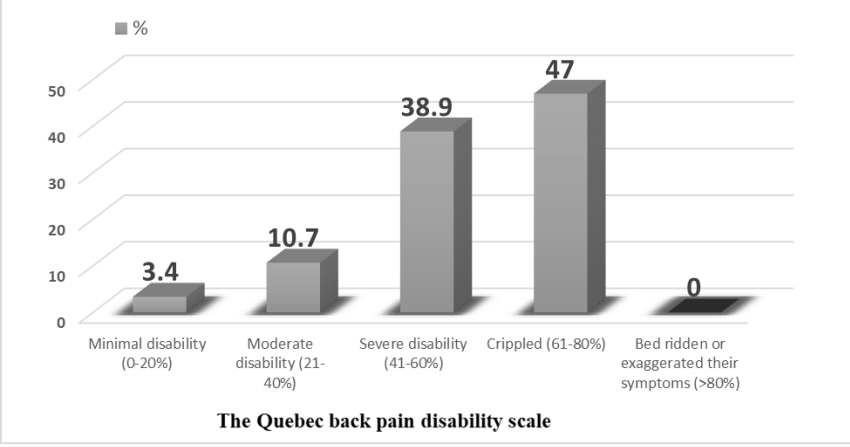

Figure (1), Sample distribution of Quebec Back Pan disability scale

Table 3: Associations between epidemiological characteristic and disease subtype

Epidemiological characteristic		Disease subtype						P value
	Acute		Subacute		Chronic			
	No	%	No	%	No	%		
Age at onset of disease (years)	<30years	32	28.6	8	33.3	44	14.5	0.010*
	30-39	25	22.3	2	8.3	72	23.7	
	40-49	24	21.4	9	37.5	68	22.4	
	50-59	21	18.8	3	12.5	63	20.7	
	60-69	8	7.1	1	4.2	44	14.5	
	≥70years	2	1.8	1	4.2	13	4.3	
Age at first visit (years)	<30years	32	28.6	8	33.3	42	13.8	0.006*
	30-39	25	22.3	2	8.3	72	23.7	
	40-49	24	21.4	9	37.5	69	22.7	
	50-59	21	18.8	3	12.5	63	20.7	
	60-69	8	7.1	1	4.2	42	13.8	
	≥70years	2	1.8	1	4.2	16	5.3	
Age at diagnosis (years)	<30years	36	32.1	9	37.5	52	17.1	0.002*
	30-39	21	18.8	1	4.2	62	20.4	
	40-49	24	21.4	9	37.5	66	21.7	
	50-59	21	18.8	3	12.5	64	21.1	
	60-69	8	7.1	1	4.2	44	14.5	
	≥70years	2	1.8	1	4.2	16	5.3	
Interval between onset of disease and diagnosis (years)	<1month	79	70.5	4	16.7	48	15.8	0.0001*
	1-3m	33	29.5	20	83.3	99	32.6	
	4-11m	-	-	-	-	47	15.5	
	1-3year	-	-	-	-	95	31.3	
	4-6y	-	-	-	-	9	3.0	
	7-9y	-	-	-	-	2	0.7	
	≥10years	-	-	-	-	4	1.3	

Demographic variables		Sex				P. value
		Males(n=180)		Females(n=260)		
		No	%	No	%	
Number of children	0	41	22.8%	28	10.8%	0.009*
	1	10	5.6%	14	5.4%	
	2	21	11.7%	25	9.6%	
	3	28	15.6%	43	16.5%	
	4	20	11.1%	27	10.4%	
	≥ 5	60	33.3%	123	47.3%	
menopause	Pre	0	0.0%	186	71.5%	
	Post	0	0.0%	74	28.5%	
occupation	Employed	82	45.6%	46	17.7%	0.0001*
	Unemployed	98	54.4%	214	82.3%	
smoking	non smoker	79	43.9%	260	100.0%	0.0001*
	ex-smoker	6	3.3%	0	0.0%	
	occasional smoker	6	3.3%	0	0.0%	
	current smoker	89	49.4%	0	0.0%	

Table (3) displays the results of statistical tests analyzing the association between socio-demographic characteristics (age, sex, education, BMI, etc.) and disease subtype, the results of the same Table indicated a statistically significant association between age and disease subtype of LBP (p value=0.0001). Current marital status (married) was significantly related to disease subtype of LBP (p value =0.0001), and menopause was significantly related with disease subtype of LBP (p value =0.027).

Table 2: Association between demographic characteristics and sex

Demographic variables		Sex				P. value
		Males(n=180)		Females(n=260)		
		No	%	No	%	
Age groups	<30	46	25.6%	37	14.2%	0.003*
	30-39	28	15.6%	46	17.7%	
	40-49	35	19.4%	65	25.0%	
	50-59	32	17.8%	69	26.5%	
	60-69	19	10.6%	30	11.5%	
	≥70	20	11.1%	13	5.0%	
	Mean ± SD	45.7 ±14.8				
BMI	Normal weight	63	35.0%	53	20.4%	0.0001*
	Over weight	85	47.2%	105	40.4%	
	Obese **I**	25	13.9%	74	28.5%	
	Obese **II**	6	3.3%	24	9.2%	
	Obese **III**	1	0.6%	4	1.5%	
residency	Urban	142	78.9%	192	73.8%	0.224
	Rural	38	21.1%	68	26.2%	
education level	Illiterate	11	6.1%	47	18.1%	0.0001*
	Primary	58	32.2%	96	36.9%	
	Intermediate	27	15.0%	41	15.8%	
	Secondary	24	13.3%	22	8.5%	
	Collage	60	33.3%	52	20.0%	
	higher educator	0	0.0%	2	0.8%	
marital status	Married	147	81.7%	238	91.5%	0.0001*
	Unmarried	33	18.3%	17	6.5%	
	Divorced	0	0.0%	5	1.9%	

Table 1: Socio-demographic and epidemiological characteristics

Socio-demographic and epidemiological characteristics		No	%
Age (years)	<30years	67	15.2
	30-39	90	20.5
	40-49	100	22.7
	50-59	101	23.0
	60-69	49	11.1
	>70years	33	7.5
	Mean ±SD (Range)	45.7±14.8 (18-88)	
Sex	Male	180	40.9
	Female	260	59.1
BMI (Kg/ m2)	Normal (18.5-24.9)	116	26.4
	Overweight (25-69.9)	190	43.2
	Obese (30-34.9)	99	22.5
	Obese II (35-39.9)	30	6.8
	Obese III >40)	5	1.1
	Mean ±SD (Range)	27.94±4.79 (18.1-51.4)	
Duration of disease (years)	<1yr	181	41.1
	1---4	178	40.5
	5---9	46	10.5
	10-14	22	5.0
	15-19	10	2.3
	≥20yr	3	0.7
Disease subtype	Acute	112	25.5
	Subacute	24	5.5
	Chronic	304	69.1

A significant correlation between age group and sex (p=0.003) was observed, BMI had significant correlation with sex (p = 0.0001), education level and marital status also had significantly correlation with sex (p = 0.0001), number of children had significant association with sex (p=0.009), occupation and smoking had significantly correlation with sex (p=0.0001. These results were illustrated in Table (2).

demographic, clinical and epidemiological variables. The sites' exclusion criteria included patients Less than 18 years old, malignancy and other autoimmune diseases. Statistical analysis the collected data were coded, entered, presented, and analyzed by computer using the available data base software program statistical package of IBM SPSS-29 (IBM Statistical Packages for Social Sciences- version 29, Chicago, IL, USA). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (Chi2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

Results

Table (1) Shows some of the demographic and epidemiological characteristics of the study sample with a mean and a standard deviation(SD) of age of 45.7±14.8, individuals aged 50–59 had the highest proportion of LBP, with a rate of 23%. Conversely, the age group with the lowest frequency at 7.5% was people aged ≥70 years, 59.1% of the participants were female, while 40.9% were men, 43.2% were overweight, and disease subtype consist from acute 25.5%, subacute 5.5%, chronic 69.1%.

Introduction

Low Back pain(LBP), especially in the lower and middle-income categories, affects a disproportionately high number of individuals around the world. Depending on the underlying medical condition, low back pain may be either acute or chronic. Mechanical injuries, such as sprains and strains, account for the bulk of abrupt low back pain. However, sciatica, a radiculopathy illness brought on by pressure, inflammation, or injury to the spinal nerve roots—is the most usual cause when it comes to persistent low back pain (Hassan, *et al.*, 2020).

LBP is commonly classified as non-specific (i.e., up to 90% of cases when the physio-pathological causes cannot be confirmed) or specific, the latter occurrences mainly due to hernias, osteoporosis, fractures, spondyloarthropathy, infections, or malignancy. LBP may alternatively be characterized as acute (i.e., lasting <6 weeks), sub-acute (i.e., lasting between 6 weeks and 3 months), or chronic (i.e., lasting for more than 3 months) (Mattiuzzi, *et al.*, 2020). The relevantly economic and social impact of low back pain is same to that of other common sever condition, such as immunological diseases, cardiovascular diseases, cancer, and mental health-related diseases (Yan, *et al.*, 2021). Therefore, the aim of this research is to study the epidemiological features of low back pain.

Patients and Methods

The total of 440 convenient samples diagnosed with Low back pain within the cross-sectional study who attended rheumatology clinics of Baghdad Teaching Hospital / Medical City. The collected data were socio-

المستخلص

المقدمة: آلام أسفل الظهر هي مشكلة صحية شائعة جدًا في جميع أنحاء العالم وخاصة في البلدان المنخفضة والمتوسطة الدخل. قد يكون الم اسفل الظهر حادًا أو مزمنًا بطبيعته بسبب العديد من الحالات الطبية. غالبية آلام أسفل الظهر الحادة ميكانيكية بطبيعتها بسبب الالتواء والإجهاد. من ناحية أخرى، يُعزى الم اسفل الظهر المزمن في الغالب إلى عرق النسا، وهو حالة اعتلال الجذور الناتجة عن الضغط و/أو الالتهاب و/أو إصابة جذور الأعصاب الشوكية . **الهدف**: دراسة السمات الوبائية لآلام أسفل الظهر. **طريقة العمل**: أجريت دراسة مقطعية لـ 440 فرداً تم تشخيص إصابتهم بآلام أسفل الظهر (LBP) من قسم الروماتيزم في مستشفى بغداد التعليمي – المدينة الطبية في محافظة بغداد. تكونت العينة من 180 رجلاً و260 امرأة، بمتوسط عمر 45.7±14.8 سنة. نفذ البحث للفترة من 12/اكتوبر/2023 الى 12/مارس/2024 . **النتائج**: شملت هذه الدراسة المقطعية 440 مريضًا مصابًا بـ LPB، بمتوسط عمر وانحراف معياري (14.8 ± 45.7 (SD، وكان الأفراد الذين تتراوح أعمارهم بين 50–59 عامًا لديهم أعلى نسبة من LBP، بمعدل ٪23. على العكس من ذلك، كانت الفئة العمرية ذات أقل تكرار بنسبة ٪7.5 هي الأشخاص الذين تتراوح أعمارهم بين ≤70 عامًا، وكان ٪59.1 من المشاركين من الإناث، بينما كان ٪40.9 رجالًا، وكان ٪43.2 يعانون من زيادة الوزن، ويتألف النوع الفرعي للمرض من الحاد ٪25.5 وتحت الحاد ٪5.5. ، مزمن 69.1%، أوضحت النتائج وجود ارتباط كبير بين الفئة العمرية والجنس (p=0.003)، مؤشر كتلة الجسم له ارتباط كبير بالجنس (p=0.0001)، مستوى التعليم والحالة الاجتماعية يرتبط ارتباطا كبيرا بالجنس (p=0.0001)، العدد من الأطفال لديهم ارتباط كبير بالجنس (P = 0.009)، والمهنة والتدخين لديهم ارتباط كبير بالجنس (P = 0.0001). الاستنتاجات: آلام أسفل الظهر له تكرار أعلى بين السكان الإناث، وأعلى نسبة للأمراض المزمنة، وعلاقه كبيرة بين الجنس ومؤشر كتلة الجسم.

الكلمات المفتاحية: آلام أسفل الظهر، علم الأوبئة، دراسة مقطعية، الإعاقة.

Abstract

Background: Low back pain (LBP) is a very common health problem worldwide especially in the low and middle-income countries. The LBP may be acute or chronic in nature caused by several medical conditions. The majority of acute low back pain is mechanical in nature due to sprains and strains. Chronic LBP, on the other hand, is most commonly attributed to sciatica, which a radiculopathy condition caused by compression, inflammation and/or injury to the spinal nerve roots. **Aims of study**: To study epidemiological features of low back pain. **Patients and Methods**: A cross-sectional study of 440 individuals diagnosed with Low back pain (LBP) from the rheumatology department at Baghdad Teaching Hospital-Medical City in Baghdad province were involved in the current cross-sectional investigation. The sample consisted of 180 men and 260 women, with an average age of 45.7±14.8 years. The research was carried out from 12/ October/2023 to 12 /March/2024. **Results**: This cross-sectional study comprised 440 patients with LPB, with a mean age and a standard deviation (SD) 45.7±14.8, individuals aged 50–59 had the highest proportion of LBP, with a rate of 23%. Conversely, the age group with the lowest frequency at 7.5% was people aged ≥70 years, 59.1% of the participants were female, while 40.9% were men, 4 3.2% were overweight, and disease subtype consist from acute 25.5% ,subacute 5.5% , chronic 69.1%, The results of this investigation expressed significant association between age group and sex (p=0.003) , BMI have significant association with sex (p=0.0001) , education level and marital status have significant association with sex (p= 0.0001) , number of children has significant association with sex (p=0.009) , occupation and smoking have significant association with sex (p=0.0001) **Conclusions**: LPB has a higher frequency among the female population, highest proportion chronic disease, highly significant between sex and BMI.

Keywords: Low back pain, Epidemiology, Cross Sectional Study, Disability.

توزيع الخصائص الوبائية لمرضى آلام أسفل الظهر المراجعين لمستشفى بغداد التعليمي

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Distribution of Epidemiological Characteristics of Low Back Pain Patients Attending to Baghdad Teaching Hospital

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of circulating CatD levels compared to control. The study revealed high sensitivity (95%) and specificity (96%) for CatD, making it a very good indicator for detecting and predicting the presence of atherosclerosis.

6. Recommendations

We recommended a study that addresses other types of cathepsins, like cathepsin A, B, and E, and their relationships with coronary atherosclerosis and comparing the results with this study to deduce the most predictive types of cathepsins for the disease.

7. Acknowledgements

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and stroke (Kuti *et al*., 2024). Two of the main causes of heart disease are high blood pressure and high cholesterol. When arteries become tight and restricted from deposited cholesterol, the heart needs to work hard to push blood through them. Consequently, blood pressure continually rises (Hui *et al.*, 2023). Elevated triglycerides frequently indicate other conditions that raise the risk of heart disease and stroke, such as obesity and metabolic syndrome (Shimizu *et al.*, 2015). On the other hand, the composition and function of HDL are changed by elevated blood pressure. However, it is unclear exactly how HDL contributes to the cardiovascular problems associated with hypertension (Aishah & Fawzi, 2022).

In a case-control study conducted in Jakarta, it was found that correlation between dyslipidemia and CHD varied according to hypertensive state. It was noticed that dyslipidemic individuals have an 18-fold higher risk of CHD incidence if they have a hypertension or a history of hypertension compared to those who are non-dyslipidemic. Whereas in dyslipidemic individuals who are not hypertensive or have no history of hypertension, it was found that there is 2.5-fold higher risk of developing CHD than non-dyslipidemic individuals. Dyslipidemia considered a predictor for CHD, and has a role in process of atherogenesis (Ariyanti & Besral, 2019).

5. Conclusion

At the end of this study, it was demonstrated that patients with atherosclerosis have higher levels of lipid profile parameters in comparison to healthy control, except for HDL levels, which have decreased levels in patients. This is due to possibility that some HDL particles have athero-protective ability. In addition, atherosclerosis patients have increased levels

4. Discussion

Findings obtained by this research agree with a study concerned with abnormal levels of lipid profile and obesity associated with coronary artery diseases (CADs) in Pakistani subjects. The study revealed the occurrence of hyperlipidemia in all cases for all lipid parameters except for HDL, which is decreased, and this can elevate predisposition to complications (Shabana *et al.*, 2020). Elevated levels of serum CatD were associated with endothelial dysfunction, atherogenesis, increased risk of coronary events, and carotid intima-media thickness (Gonçalves *et al.*, 2016). It was found in a previous studies that CatD concentrations were significantly higher in the CADs compared with healthy control, and this agrees with data displayed in the table (Amir *et al*., 2018). Moreover, increased CatD activation has been found in patients with cardiovascular events (Liu *et al.*, 2017). This study is the first that address the relationship of CatD levels with the progression and development of atherosclerosis in Iraq.

Epidemiological studies showed that elevated blood cholesterol level was associated with atherosclerotic cardiovascular diseases (ASCVDs) (Robinson *et al.*, 2018). Multiple clinical researches showed that number, size, and alterations in LDL can determine initiation and progression of atherosclerosis (Vekic *et al.*, 2022). The study showed that the values of HDL in control group was higher than the values in patients' groups. This findings lead to the belief that HDL may have an atheroprotective characteristics, and two recent MR studies found an independent association between HDL levels and CADs (Zhao *et al.*, 2021). According to the American Association for Clinical chemistry, a normal VLDL level is up to 30mg\dl. Measurements above this point indicate high VLDL levels which raise the risk of heart disease

equal to 1.0 (Joo *et al*., 2020). The area under curve (AUC) is primarily used to measure the accuracy of a diagnostic test. The closer the ROC curve is to the upper left corner of the graph, the higher the accuracy of the test as Nahm (Nahm, 2022) mentioned it, Furthermore, Fig. 1 illustrated this explanation.

Table (6) showed statistics of CatD. According to this study, AUC for CatD was 0.98, cutoff value was 10.123, the sensitivity of CatD was 95%, and specificity was 96%, with highly significant P value (<0.001). These findings suggest that CatD is very good indicator for detecting and predicting the presence of atherosclerosis. Further researches on cathepsin D are required to determine more pathological characteristics such as degree of disease progression and complications.

Table (6): ROC curve for Cathepsin D

AUC	cutoff	Sensitivity	Specificity	P Value
0.98	10.123	95%	96%	<0.001**

**** Highly significant P value (< 0.001)**

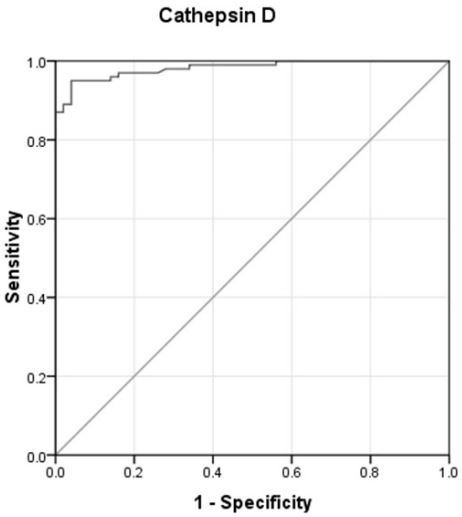

Figure (1): ROC curve of cathepsin D

3.5- Comparison of CatD level between control and patients groups according to blood pressure

Table (5) showed a significant difference between control and blood pressure categories (P value <0.001). In comparison to control, these differences were mostly demonstrated in all patients who have high and normal within the three patients groups. In contrast, there were non- significant differences between blood pressure categories and any patient group.

Table (5): Comparison of CatD level between control and patients groups according to blood pressure

Parameter	Groups	Blood pressure categories	Concentration (Mean ± S.E.)	P value
Cathepsin D	Control	NO	7.77±0.27	<0.001**
	First catheterization	NO	13.07±0.65 a	0.42 NS
		Yes	12.18±0.49 a	
	Previous catheterization	NO	15.54±0.60 a	0.5 NS
		Yes	16.21±0.44 a	
	CV transplantation	NO	15.89±1.51 a	0.3 NS
		Yes	17.26±1.32 a	

**** Highly significant P value, NS. Non-significant P value, a vs. control (NO)**

3.6. ROC curve for Cathepsin D

Receiver operating characteristic (ROC) curve is used for determining the existence or absence of a disease. ROC goal is to categorize disease condition as either positive or negative based on test results, and to detect the ideal cut-off value with the optimum diagnostic performance. Sensitivity is the percentage of people who actually have a target disease that are tested positive, while specificity is the percentage of people who actually do not have a target disease that are tested negative. The ideal test would have a sensitivity and specificity

Table (4): Comparison of lipid profile levels between control and patients' groups according to blood pressure

Parameter	Groups	Blood pressure categories	Concentration (Mean ± S.E.)	P value
Cholesterol	Control	NO (50)	166±1.75	<0.001**
	First catheterization	NO (12)	208.25±14.25 a	0.16 NS
		Yes (14)	188.79±9.40 a	
	Previous catheterization	NO (10)	189.50±16.30	0.42 NS
		Yes (42)	199.64±4.78 a	
	CV transplantation	NO (8)	205.38±23.21 a	0.9 NS
		Yes (14)	205.21±13.89 a	
Triglyceride	Control	NO	129.72±2.37	<0.001**
	First catheterization	NO	152.00±7.59	0.09 NS
		Yes	187.29±18.39 a	
	Previous catheterization	NO	204.00±19.83 a	0.1 NS
		Yes	174.40±6.75 a	
	CV transplantation	NO	242.25±55.61 a	0.017*
		Yes	186.14±11.36 a	
HDL	Control	NO	43.34±1.07	0.05*
	First catheterization	NO	33.83±3.81 a	0.087 NS
		Yes	43.93±7.69	
	Previous catheterization	NO	36.30±2.31	0.99 NS
		Yes	36.21±1.98 a	
	CV transplantation	NO	31.50±3.12 a	0.046*
		Yes	44.79±6.81	
LDL	Control	NO	94.51±1.27	<0.001**
	First catheterization	NO	147.73±13.94 a	0.2 NS
		Yes	134.33±8.63 a	
	Previous catheterization	NO	137.42±12.12 a	0.8 NS
		Yes	139.58±3.88 a	
	CV transplantation	NO	162.48±8.24 a	0.04*
		Yes	139.23±7.70 a	

*** Significant P value, ** Highly significant P value, NS. Non-significant P value, a vs. control (NO)**

differences between blood pressure categories and CV transplantation group (P value ≤0.05).

For the level of LDL, significant differences were found between control and blood pressure categories (P value <0.001). In comparison to control, these differences were observed especially in all patients who have normal and high blood pressure within all patients groups. Non-significant differences were noticed between blood pressure categories and both first and previous catheterization groups. In contrast, there was significant difference between blood pressure categories and CV transplantation group (P value ≤0.05). For the level of VLDL, there were significant differences between control and blood pressure categories (P value <0.001), particularly in patients with high blood pressure within first catheterization group, and in both patients categories who have normal and high blood pressure within previous catheterization and CV transplantation groups compared to control. Non-significant differences were demonstrated in blood pressure categories within both first and previous catheterization groups. Although that, there was significant difference between blood pressure categories and CV transplantation group (P value ≤0.05).

3.4. Comparison of lipid profile levels between control and different patients groups according to blood pressure

In Table (4), blood pressure patients are divided into 2 categories, those with high blood pressure (yes), and those with normal blood pressure (no). All control subjects are normal. Significant differences were found in the level of cholesterol between control and patients categories (P value <0.001), and these differences especially found in patients with high and normal blood pressure within first catheterization and CV transplantation groups, and also in patients with high blood pressure within previous catheterization group compared to control. However, insignificant differences were noticed between blood pressure categories and patients groups. For the level of triglyceride, significant differences between control and blood pressure categories were demonstrated (P value <0.001), especially in patients with high blood pressure within first catheterization group, and in blood pressure categories within both previous catheterization and CV transplantation groups in comparison to control. Although that, there were non-significant differences in blood pressure categories within both first and previous catheterization groups. In contrast, there was a significant difference between blood pressure categories and CV transplantation group (P value ≤0.05). In addition, significant differences were observed in the level of HDL between control and blood pressure categories (P value ≤0.05), mostly in patients with normal blood pressure within first catheterization and CV transplantation groups, and in patients with high blood pressure within previous catheterization group in comparison to control. Insignificant differences were found in blood pressure categories within both first and previous catheterization groups. Additionally, there were significant

3.2. Cathepsin D level in studied groups

Table (2) showed an increase in the level of CatD in patients with atherosclerosis. There was a significant difference between patients and control group in level of CatD due to highly significant P value (<0.001).

Table (2): Comparison between the level of CatD among patients and control

Parameter	Groups	Concentration (Mean ± S.E.)	P value
Cathepsin D	Control	7.77±0.27	<0.001**
	Patients	15.32±0.35	

**** Highly significant P value**

3.3. Comparison of CatD level between control and different groups of patients

As showed in Table (3), Patients were divided into 3 groups: first catheterization, previous catheterization, and cardiovascular (CV) transplantation. There was increasing in the level of CatD among patients groups compared to control. Also, there were significant differences between control and the three patients groups (P value <0.001), and the significant difference is also seen between patients groups (previous catheterization and CV transplantation) compared to first catheterization group (P value <0.001).

Table (3): Comparison of CatD between control and different groups of patients

Parameter	Patients groups	Concentration (Mean ± S.E.)	P value
Cathepsin D	Control	7.77±0.27	<0.001**
	First catheterization	12.59±0.40 b	<0.001**
	Previous catheterization	16.08±0.38 b	
	CV transplantation	16.77±0.99 b	

**** Highly significant P value, b vs. First catheterization**

Coefficient (r) was used to find the correlation between the studied parameters. ROC test also was performed for parameters to find AUC, sensitivity, and specificity of each studied parameter.

3. Results

3.1. Lipid profile levels in studied groups

Data illustrated in Table (1) showed that there is an increasing in the levels of lipid profile parameters, which include cholesterol, triglyceride, high density lipoprotein (HDL), LDL, and very low density lipoprotein (VLDL), in patients with atherosclerosis in contrast to control. Since the p value was highly significant (P-value <0.001), there was a significant difference between patients and control group in levels of lipid profile.

Table (1): Comparison between the levels of lipid profile parameters among patients and control

Parameter	Groups	Concentration (Mean ± S.E.)	P value
Cholesterol	Control	166±1.75	<0.001**
	Patients	199.38±4.21	
Triglyceride	Control	129.72±2.37	<0.001**
	Patients	183.55±6.57	
HDL	Control	43.34±1.07	0.008**
	Patients	37.84±1.76	
LDL	Control	94.51±1.27	<0.001**
	Patients	141.39±3.15	
VLDL	Control	27.25±0.56	<0.001**
	Patients	36.30±1.43	

**** Highly significant P value**

study aimed to find out if cathepsin D is a good indicator to diagnose atherosclerosis and cardiovascular diseases and its relation with lipid profile.

2. Materials and Methods

2.1. Patients and samples

This study comprised 150 participants, distributed into two groups, 100 patients (64 males and 36 females), and 50 healthy controls (26 males and 24 females). The ages of both groups are ranging from 40 to 70 years. Patients` samples of the study were collected in Iraqi Center of Heart Diseases in Ghazi Al-Hariri hospital in Baghdad city, while control samples were collected from medical staff and special laboratory during the time period from February to July, 2024.

2.2. Evaluations of CatD and lipid profile serum level

Serum CatD level was evaluated using Enzyme-Linked Immunosorbent Assay (ELISA), and lipid profile parameters by using manual kits.

2.3. Ethical approval

The ethical committees of the Middle Technical University, College of Health and Medical Techniques gave their approval for the study.

2.4. Statistical analyses

The data were analyzed using SPSS (V.20, IBM). The T-test and One Way ANOVA test were used as appropriate tests. One Way ANOVA test was used by obtaining least significant difference (LSD) to find p value between the studied groups. The data were presented as Mean ± S.E. and the p value ≤0.05 was considered as significant result. In addition, Pearson Correlation

1. Introduction

Cardiovascular diseases (CVDs) are one of the leading causes of mortality worldwide and significantly lower life quality (Harikrishnan *et al.*, 2018).

Atherosclerosis considered the root cause for many forms of CVDs. The term atherosclerosis derives from the Greek “athere” (gruel) and “skleros” (hard), which describes the waxy plaques inside blood arteries. This condition is well known to progress gradually for decades without causing any notable signs until the patient encounters serious complications. Hypertension, diabetes mellitus, hypercholesterolemia, obesity, and smoking are risk factors for atherosclerosis (Libby *et al.*, 2019). Hypercholesterolemia has been identified as the greatest attributable risk factor for atherosclerosis and subsequent coronary heart disease (CHD). Furthermore, it was demonstrated that progression from early-stage fatty streaks to advanced-stage, lipid-rich lesions was directly linked to continuous high levels of low density lipoprotein-cholesterol (LDL-C) (Nicholas *et al.*, 2019). Lysosomes are small cytoplasmic organelles containing a variety of acidic hydrolytic enzymes that are capable of degrading different biological polymers, such as proteins, lipids, carbohydrates, and nucleic acids (Ballabio and Bonifacino, 2020). Lysosomal cathepsins were shown to be implicated in the etiology of CVDs (Liu *et al.*, 2018). Cathepsin D (CatD) is a ubiquitous, lysosomal, aspartic endo-proteinase, which synthesized in rough endoplasmic reticulum, and proteolytically active in acidic pH. CatD is mostly released following oxidative stress, and it is essential for protein degradation, proteolytic activation of hormones and growth factors (Mijanovic *et al.*, 2021). Clinical observations have indicated a possible substantial involvement of cathepsin D (CatD) derangement in cardiovascular pathophysiology (Imanaka *et al.*, 2020). This

المستخلص

الخلفية: تصلب الشرايين التاجي هو مرض طويل الامد ومتطور باستمرار مع مظاهر سريرية متعددة تمتد من عدم وجود اعراض الى الذبحة الصدرية المستقرة، متلازمة الشريان التاجي الحادة، فشل القلب، والموت القلبي المفاجئ. يتأثر ظهور وتطور تصلب الشرايين التاجي بالعوامل الوراثية والبيئية على حدٍ سواء. **الاهداف:** هدفت الدراسة الى معرفة ما اذا كان الكاثبسين D مؤشراً جيداً لتشخيص تصلب الشرايين وأمراض القلب والاوعية الدموية وعلاقته بالدهون. **المواد والطرق:** أُجريت الدراسة بمشاركة 150 شخصاً (100 مريض يعانون من تصلب الشرايين التاجي و50 شخصاً اصحاء). كان العمر لجميع الاشخاص يتراوح بين 40 و 70 سنة. تم اخضاع جميع المشاركين للقياس المختبري لمستوى الكاثبسين D عن طريق الفحص المناعي المرتبط بالانزيم (ELISA)، ومُعلمات الدهون باستخدام الطرق اليدوية.

النتائج: هناك ارتفاع معنوي في مستويات كل من الكاثبسين D ($P = <0.001$) وجميع مُعلمات الدهون ($P = <0.001$)، باستثناء البروتين الدهني عالي الكثافة في المرضى الذين يعانون من تصلب الشرايين التاجي. **الخلاصة:** يُمكن استخدام الكاثبسين D كمؤشر جيد للكشف عن تصلب الشرايين التاجي الى جانب المستويات المرتفعة من مُعلمات الدهون (ومستويات منخفضة من البروتين الدهني عالي الكثافة) مقارنةً بالأشخاص الاصحاء.

الكلمات المفتاحية: تصلب الشرايين التاجي، الكاثبسين D، الدهون، القسطرة، أمراض القلب والأوعية الدموية.

Abstract

Background: Coronary atherosclerosis is a long lasting and continuously evolving disease with multiple clinical manifestations ranging from asymptomatic to stable angina, acute coronary syndrome (ACS), heart failure (HF) and sudden cardiac death (SCD). The onset and advancement of coronary atherosclerosis are influenced by both genetic and environmental factors. **Objectives**: The study aimed to find out if cathepsin D a good indicator to diagnose atherosclerosis and cardiovascular diseases and its relation with lipid profile. **Materials and Methods**: The study conducted with the participation of 150 subjects (100 patients with coronary atherosclerosis and 50 healthy control). Age for all subject was in range 40-70 years. All participants were subjected for laboratory measurement of cathepsin D level by Enzyme-Linked Immunosorbent Assay (ELISA), and lipid profile parameters by using manual kits. **Results**: There are significant elevation in the levels of both cathepsin D (P = <0.001) and all lipid profile parameters (P = <0.001), except for high density lipoprotein in patients with coronary atherosclerosis. **Conclusion**: Cathepsin D can be used as a good indicator for detecting coronary atherosclerosis along with high levels of lipid profile parameters (and low levels of high density lipoprotein) in comparison to healthy control.

Keywords: Coronary atherosclerosis, Cathepsin D, Lipid profile, Catheterization, Cardiovascular diseases.

Cathepsin D and Its Relation with Lipid Profile in Coronary Atherosclerosis Patients

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كاثبسين D وعلاقته بالدهون في مرضى تصلب الشريان التاجي

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5. Conclusion

The patients with N-*Hp* G.T2DM significant elevated levels (p-value<0.05) of *H.pylori* IgG Ab, hs-CRP, FBS, HbA1c, IL-18 concentration and gene expression. Furthermore, decrease IL-10 concentration and gene expression.

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concentration can used in predict abnormality (Al Bander *et al*., 2020). IL-10 level significant lower in N-*Hp* G.T2DM compare to G and control, indicator T2DM patients demonstrate a marked decrease in serum (IL-10) concentrations when juxtaposed with non-diabetic control subjects. There by indicating a possible involvement of this cytokine in the inflammatory mechanisms associated with the disease (Mitra *et al*., 2021). Moreover, IL-10 plays a pivotal role in modulating inflammatory responses, and its diminished levels may have implications for gastric pathologies however, there is a dearth of specific investigations focusing on non-*H.pylori* gastritis (Kim *et al*., 2012). While IL-18 level significant elevated in N-*Hp* G.T2DM than G and control, due to IL-18 linked to persistent inflammation, which serves as a significant determinant of insulin resistance and the advancement of Type 2 Diabetes Mellitus (Zatterale *et al*., 2020). Gene expression of IL-10 such concentration in ELIZA low in N-*Hp* G.T2DM and downregulation compare with G and control (Dos Santos Haber *et al*., 2022). Opposite gene expression of IL-18 gene that show upregulation in N-*Hp* G.T2DM patient (Bagheri *et al*., 2014). In ROC evaluations, IL-18 demonstrates robust diagnostic potential with elevated sensitivity and specificity. This makes it a dependable indicator for differentiating between N-*Hp* G.T2DM and control group, as well as the G group with control (Badr *et al*., 2021).On the other hand, IL-10 has a sensitivity of zero; therefore, it is not effective in correctly recognizing true positives, even though it has perfect specificity. This indicates that IL-10 is effective in correctly identifying negative results, but it is unable to detect any positive results in both the N-*Hp* G.T2DM and G groups in this particular scenario.

4. Discussion

Inflammation of stomach is common in this time due to infection, diet, spread epidemics that weak immunity, autoimmune disease and taking non-steroidal anti-inflammatory drug(Kamada *et al*., 2022).Since patient with diabetic mellitus have low immunity are more susceptibility to inflammation (Scheithauer *et al*., 2020). A plethora of research has underscored the significance of inflammatory pathways and biomarkers in the context of diabetes and metabolic disorders. A cytokine constitutes one of these essential inflammatory indicators(Mansoor *et al*., 2022). Our research investigates the association between *H. pylori* infection and the levels of three pro-inflammatory cytokines (specifically IL-18 and IL-10) along with high sensitive C-reactive protein (hs-CRP), additionally *H.pylori* IgG levels in individuals with gastritis negative *H. pylori* and T2DM.The N-*Hp* G.T2DM show significant elevated *H. pylori* IgG Ab when compare to G and control . This due to old infection with *H. pylori* induce an immunological response, resulting in the synthesis of autoantibodies, which may be detectable even in individuals devoid of infection. In the context of autoimmune gastritis, individuals frequently exhibit heightened levels of autoantibodies in the absence of *H. pylori* infection, indicating a unique immunological mechanism in operation (Rugge *et al*., 2023). The hs-CRP significant increase in both N-*Hp* G.T2DM and G indicator about inflammation with diabetic mellitus (Ibrahim *et al*.).Fasting blood sugar and HbA1c high elevated in N-*Hp* G.T2DM because the subjects have diabetic but BMI level in this group not increase compare to G that significant elevated from normal .This due to loss of appetite and malabsorption in N-*Hp* G.T2DM patient. Since the interleukin play important role in inflammatory process therefor variation in their

Table (3) and Figure (6) also revealed the relation of IL-10 and IL-18 in the G group by (ROC test). The area under the curve (AUC) for IL-10 was (.156), and (1.000) for IL-18 which is excellent according to (20), furthermore a highly significant (p-value <0.0001) in both interleukins. The cut-off for IL-10 was (73.5) and (96.2) for IL-18 as well as sensitivity (0% &100% respectively) and specificity (100% & 98%).

Table 3: Roc curve analysis of IL-10 and IL-18 between G and control group

Test	Area	cutoff	SE	P-value	Asymptotic 95% C.I		Sensitivity	Specificity
					Lower Bound	Upper Bound		
IL10	.156	73.5	.048	.000	.061	.250	0	100
IL18	1.000	96.2	.000	.000	1.000	1.000	100	98

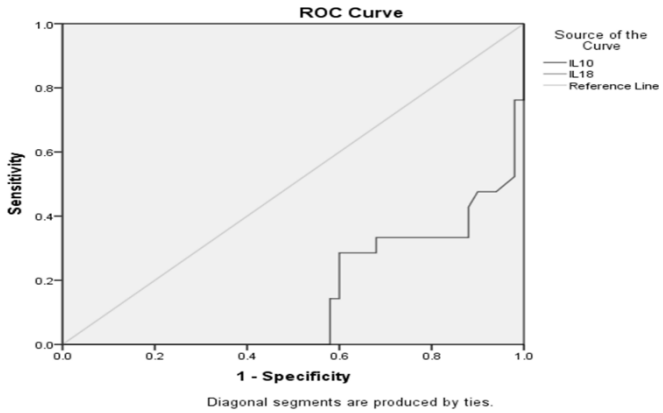


Figure 6: ROC for IL-10 and IL-18 in G group

The result of IL-10 and IL-18 Receiver Operating curve Characteristics: An evaluation of the link between IL-10 and IL-18 gene expression in N-*Hp* G. T2DM and the control group conducted using the Receiver Operating Characteristics (ROC) test. Findings the cut-off values of IL-10 were 72 and 98.7 for IL-18 and the p-value was very significant (p-value <0.0001. This suggests that the observed differences are not a consequence of random chance, additionally area under curve(AUC) very low in IL-10 (0.070) but excellent result in IL-18 (1), with a sensitivity of (0% and 100% respectively), and a specificity of (98% and 100% correspondingly) as illustrated in (Table 2) and (Figure 5).

Table 2: Roc curve analysis of IL-10 and IL-18 between N-*Hp* G.T2DM and control group

Test	Area Under Curve	cutoff	SE	P-value	Asymptotic 95% C.I		Sensitivity	Specificity
					Lower Bound	Upper Bound		
IL10	.070	72	.025	.000	.021	.120	0	98
IL18	1.000	98.7	.000	.000	1.000	1.000	100	100

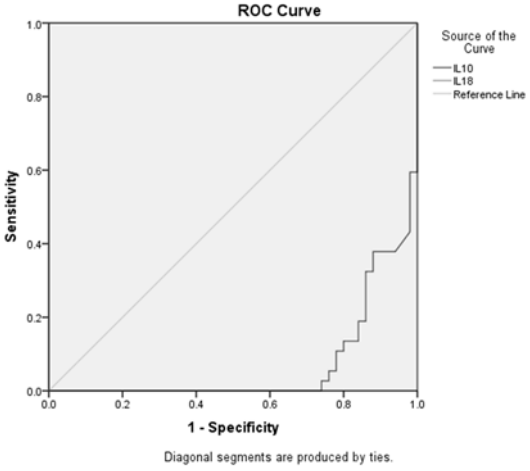
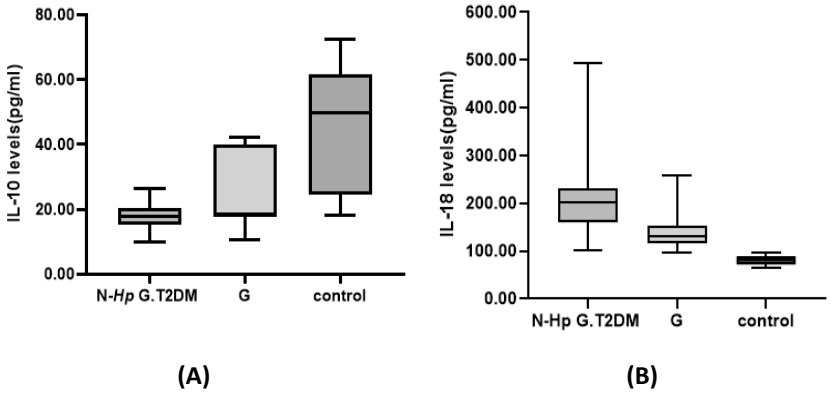


Figure 5: ROC for IL-10 and IL-18 in N-*Hp* G.T2DM



(A) **(B)**

Figure (3): Compare means of IL-10 (A) and IL-18(B) levels between study groups

The result of gene expression of the IL-10 and IL-18 between the studies groups performed by using RT-qPCR and quantitative 2–ΔΔCT show IL-10 expression significant differences across the groups ($p<0.05$). Relative fold gene of N-*Hp* G.T2DM lowered from 1 (control) to 0.90 and to 0.75 in G group. Conversely, it was found that participants N-*Hp* G.T2DM relative expression of IL-18 (2.1575) was increased (Figure 4) in comparison to the control group (1.0025) ($p<0.01$). Similar trend among G group also demonstrating an increase in IL-18 levels (1.245) from (1.0025) control.

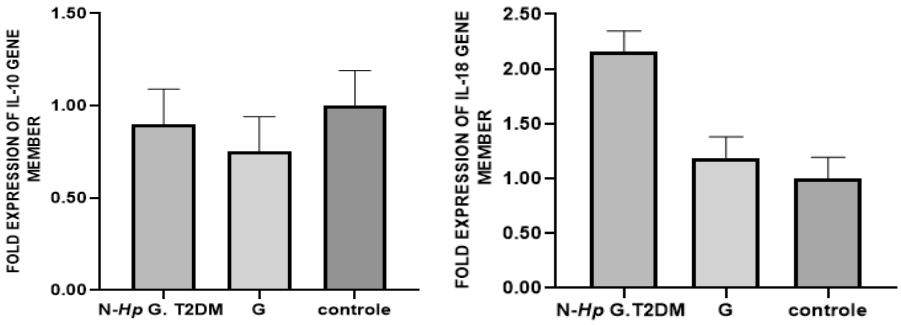


Figure (4): Comparison folding genes of IL-10 (left) and IL-18(right) gene expression between study groups.

T2DM estimation: via measure FBS and HbA1c in N-*Hp* G.T2DM (165.0±6.49, 8.85±0.24) statistically significant when compare with means of G (79.65±1.20, 5.37±0.27) and control (82.10±1.31, 4.56±0.04) p-value <0.0001 also HbA1C of G to control significant ($p < 0.05$).that indicator may be gastritis effect on metabolism and elevated sugar levels in blood. Furthermore BMI of N-*Hp* G.T2DM (25.23±0.39) significant with G (40.82=3.01) p-value< 0.0001 but not significant in comparison with control (22.62=0.35) p>0.05 (Figure 2).

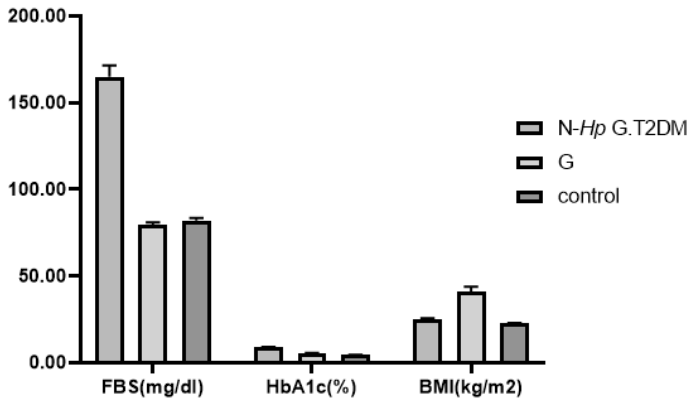


Figure (2): Histogram drown for FBS, HbA1C and BMI means observed samples of N-*Hp* G.T2DM, G and control groups

Interleukins estimated by ELIZA of all samples show opposite result. Found the anti-inflammatory IL-10 level decrease in N-*Hp* G.T2DM to (18.12±0.66) from (46.16±3.35) of control and group G also down to (25.28±2.46) p-value <0.05.On other hand IL-18 levels elevated in group N-*Hp* G.T2DM and G to (202.89±10.58 & 124.42±3.57) respectively from (81.00±1.80) of control p-value <0.0001. Figure 3 below showed the result.

One-way ANOVA tests employed to assess the statistical significance of the mean differences across the three groups. A ROC curve (receiver operating characteristic curve) conducted to evaluate the specificity and sensitivity of gene expression and to ascertain its role in the disease.

3. Results

Ninety participant in this study male (50%) and female (50%) dividing into 3 groups, N-*Hp* G 41.1%, G 25.6% and control 33.3%,median age 43 year . Non-significant different in age and gender between groups ($p > 0.05$).

Result of estimated gastritis: the *H. pylori* IgG antibody for N-*Hp* G.T2DM (215.72±3.57) high significant when compare to G (99.36±1.60) and control (98.02±0.98) the p-value <0.0001 that mean the patient have old infection with *H. pylori*. The level of hs-CRP following the same pattern of IgG. Hs-CRP levels found to be (8.04± 0.29 & 5.37±0.27) for N-*Hp* G.T2DM and G respectively ($p<0.0001$), control (5.33± 0.21) as shown in Figure 1 which demonstrated role of hs-CRP in N-*Hp* G T2DM.

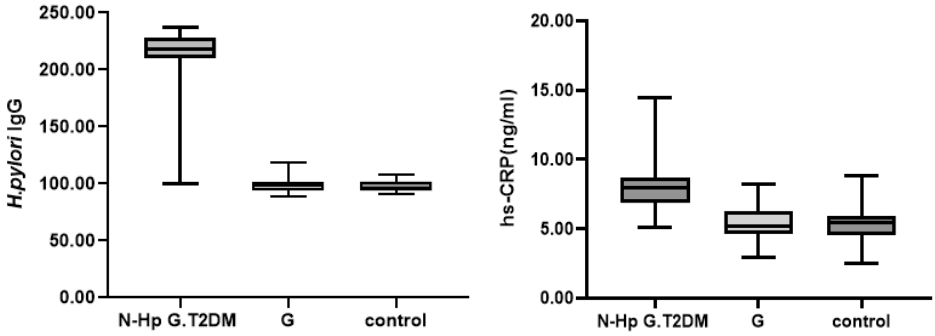


Figure (1): Means of *H.pylori* IgG (left) and hs-CRP (right) between study groups

cDNA (reverse transcription RNA), by utilising the Easy Script® One Step gDNA Removal and cDNA Synthesis Super Mix Kit from (Transgen, China). finally step including using the cDNA products, real-time PCR carried out after reverse transcription-PCR. Using a SYBR Green PCR two- cycling employed, comprising denaturation at 94°C for 10 sec , annealing at 64°C for 15 sec and extension step at 72 °C for 20sec. The reaction mixture comprised 10µl of SYBR Green PCR Master Mix, 2µl of primers, 2µl of template DNA or cDNA, and 6µl of RNase-free water. The parameters for real-time PCR were as follows: 30 sec of initial denaturation at 94°C, followed by 45 cycles of 10 seconds at 94°C and 15 seconds of annealing at 64°C. The expression of each gene was analysed relative to that of GAPDH. The genes encoding IL-10 and IL-18 evaluated. The primer and probe sequences utilised in this real-time PCR enumerated in Table (1). The 2-ΔΔCT method enables the use of real-time quantitative PCR to examine relative alterations in gene expression.

Table (1): Real time PCR Primers sequence for IL-10 and 1L-18 Gene

Gene	Primer Sequence 5`-3`
IL-10	Forward TCTCCGAGATGCCTTCAGCAGA Reverse TCAGACAAGGCTTGGCAACCCA
IL-18	Forward GATAGCCAGCCTAGAGGTATGG Reverse CCTTGATGTTATCAGGAGGATTCA
GAPDH	Forward GTCTCCTCTGACTTCAACAGCG Reverse ACCACCCTGTTGCTGTAGCCAA

2.5 Statistical analysis: The data of this study analysis by Statistical Package for Social Sciences (SPSS) version 26.0 for Windows. The data expressed as the mean ± standard error (SE). The p-value serves to denote statistical significance. Data are deemed significant when $p \leq 0.05$ or $p \leq 0.0001$.

from all participants' then two aliquots were prepared. An aliquot of direct blood sample used to assess the RUT, FBS, and Hb1Ac. A portion of the serum utilized for the ELISA assays and kept in the freezer. For gene expression, a second aliquot put into an anticoagulant tube containing Ethylene Diamine Tetra Acetic Acid (EDTA). For gene expression research, about 250µL taken out of the EDTA tube, added Trizol reagent, and utilized. The concept and procedures of the study approved by the Ethics Committee of the Middle Technical University/ College of Medical and Health Technologies/ Baghdad. Before collecting venous blood samples, written informed consents obtained from the patients.

2.2. Biochemical assay: Detected diabetic mellitus by estimated fasting blood sugar (FBS: 70–100 mg/dl) and HbA1C values (Normal Range: less than 5.7% -6.4%).Via Cobas INTEGRA-400 plus clinical chemistry automated system. .furthermore estimate body mass index (18.5-24.9 kg/m2) for every participant

2.3. Immunological assay: via using enzyme linked immunosorbent assay (ELIZA) kit (Elabscience, USA) to calculate the levels of *H. pylori* IgG Ab by indirect ELIZA and concentration of hs-CRP, interleukin 10 and 18 by sandwich ELIZA. According to the instructions of the kit manufacturer. The concentration of all tests calculate from read absorption by Human Read HS (company human, Germany). All biochemical and immunological assay applied for all participants.

2.4. Molecular assay: gene expression of interleukin 10 and 18 gene for 7 samples from N-*Hp* G.T2DM group, 13 from G group and 13 healthy control. First step extraction total RNA from blood sample that kept with Trizol, this process according to manufacture of kit TransZol up plus RNA Kit (Transgen, China). After that examination purity and concentration of RNA via Nano drop for all samples ranged (1.90-2.02). Second, convert RNA to

IL-10 plays an important role in regulating of immune response by down production of inflammatory cytokines in innate cells, including macrophages (MP) and dendritic cells (DCs). Immune response modulation through IL-10 demonstrated the important affect arrangement of allergy, inflammation, and autoimmune diseases (Rutz and Ouyang, 2016, Gabryšová *et al*., 2014). IL-18 considered pro-inflammatory have a crucial role in inflammatory response related to diabetes and impact on immunological responses. This interleukin involved in multiple metabolic disorder, for example type 1 and type 2 diabetes, by influencing insulin resistance and facilitating inflammation.(Chen *et al*., 2015, Zhuang *et al*., 2019). This study the investigated impact of these interleukins on N-*Hp* .T2DM by measuring concentration of these interleukins by ELIZA and their gene expression by real time polymerase chain reaction RT-qPCR.

2. Materials and methods

2.1. Specimen Collection: A total of (60) patients having dyspepsia and abdominal pain included in e study group. Every patient attended hospitals of Gastroenterology and Hepatology in Diyala and Baghdad, Iraq from January 2024 to April 2024. Total patients underwent upper gastrointestinal tract (GIT) endoscopy. Thirty healthy adult underwent standard medical examinations selected as controls. Patients with gastric cancer, type 1 diabetes, acute or chronic renal failure, cardiovascular diseases and pregnancy women excluded. The selected individuals divided into two categories: *N-Hp G* T2DM diabetic gastritis 37 and gastritis 23 (G). This classification was based on the results of gross endoscopic examination, rapid *H. pylori* urease test (RUT) and histological findings. The third group consisted of healthy individuals 30 (control). 5 ml of blood samples obtained

1. Introduction

Gastritis term commonly used, although incorrectly to describe a range of clinical symptoms associated with upper abdomen, namely epigastrium. Although endoscopy, gastritis is characterised as presence of redness or swelling in lining of the stomach. Moreover, it is important to note that these endoscopic findings are not exclusive or limited to mucosal inflammation(Okamura *et al*., 2018). Prominent reasons for gastritis involve extended consumption of alcoholic drinks that activates caspase-1, which leads to the release of pro-inflammatory cytokines such as IL-1β and IL-18, hence triggering inflammatory pathways (Li *et al*., 2018). In addition, non-steroidal anti-inflammatory medicines (NSAIDs), such as Aspirin, used by people with Rheumatoid arthritis and Osteoarthritis. Stress, chronic bile reflux, autoimmune illnesses, and positive helicobacter pylori infection that major cause chronic gastritis. The symptoms noticed in her include nausea, vomiting, indigestion, a burning feeling, and abdominal bloating. Diagnosis often involves the blood testing, stool tests, urea breath and gastro endoscopy(Elseweidy, 2017). Gastritis is a common and typically severe condition in persons with diabetes mellitus type 2 (T2DM), likely caused by the compromised state of their immune system (Ebule *et al*., 2017). T2DM a burgeoning worldwide health issue intricately connected to the widespread prevalence of obesity. Individuals diagnosed with T2DM face a significant likelihood of developing both microvascular problems (such as retinopathy, nephropathy, and neuropathy) and microvascular complications such as cardiovascular diseases(DeFronzo *et al*., 2015). Therefore, both gastritis and T2DM affect immunity of patients including interleukins that regulation inflammatory pathways, such as interleukin 10 and 18. Anti-inflammatory

المستخلص

التهاب المعدة هو أحد أكثر الأمراض شيوعاً في الجهاز الهضمي، وخاصة عند المرضى ذوي المناعة المنخفضة، بما في ذلك مرضى السكري. يعتبر مرض السكري احد امراض الغدد الصماء الذي يتميز بارتفاع سكر الدم بسبب خلل في تنظيم السكر في الجسم. كان الغرض من هذه الدراسة تقييم العلاقة بين التهاب المعدة غير الناجم عن البكتيريا الحلزونية البوابية ومرض السكري النوع الثاني بواسطة الانترليوكينات 10 و18. شملت هذه الدراسة 37 (41.1%) من مرضى التهاب المعدة غير الناتج عن جرثومة الملوية البوابية والسكري النوع الثاني (N-HP G.DM) , 23(25.6%)من مرضى التهاب المعدة فقط(G) و30 (33.3%) من المشاركين الاصحاء. تم تقييم المؤشرات الحيوية لمرض السكري من النوع الثاني والتهاب المعدة التي هي سكر الدم الصائم ,السكر التراكمي ومؤشر كتلة الجسم (FBS,HbA1C and BMI) إلى جانب تحليل جرثومة المعدة بالدم للاجسام المضادة من نوع الغلوبولين ج وتحليل البروتين المتفاعل عالي الحساسية (H.pylori IgG Ab & hs-CRP) بالإضافة إلى ذلك، تم تقييم مستويات الانترليوكينات 10 و18 بواسطة كل من الاليزا (ELIZA) وتفاعل البوليميراز المتسلسل (RT-qPCR). من خلال دراستنا لاحظنا وجود علاقة بين المرضى المصابين بالتهاب المعدة غير الناجم عن البكتريا الحلززونية والسكري النوع الثاني (N-Hp G.T2DM)مع مرضى التهاب المعدة(G). اكتشفنا أن مرضى (N-Hp G.T2DM) لديهم مستويات أقل من IL-10 مقارنة بمرضى (G) $p<0.0001$. بالإضافة إلى ذلك، تم التعبير عن IL-18 بشكل أكبر في (N-Hp G.T2DM)مقارنة ب(G) $p<0.0001$.

الكلمات المفتاحية: التهاب المعدة غير الناتج عن جرثومة الملوية البوابية, مرض السكري النوع الثاني ,اليزا, تفاعل البوليميراز المتسلسل الكمي.

Abstract

Gastritis is one of the most common diseases in the digestive system, especially in patients with low immunity, including diabetic mellitus. Diabetic Mellitus considered one of an endocrine gland disease characterized by elevated blood sugar because of a defect in the regulation of sugar in the body. The purpose of this study was to assess the association between Non-*Helicobacter pylori* gastritis with type 2 diabetic mellitus (N-*Hp* G.T2DM), by interleukin IL-10 and IL-18. This study included 37(41.1%) N-*Hp* G.T2DM, 23 (25.6%) gastritis (G) only and 30 (33.3%) healthy participants. Biomarkers for T2DM and G (FBS, HbA1c and BMI) along with *H.pylori* IgG Ab and hs-CRP evaluated. Additionally, levels of IL-10 and IL-18 evaluated by both ELSIA and real time PCR .Through the study; we noticed a correlation between *N-Hp G.T2DM* patients and patients with G. We discovered that N-*Hp* G. T2DM associated had lower levels of Il-10 than gastritis ($p<0.0001$). In addition, that IL-18 was more highly expressed in gastritis linked to N-*Hp* G.DM than in gastritis ($p<0.0001$).

Keywords: Non-*H.pylori* gastritis, T2DM, ELISA, Real time Polymerase Chain Reaction.

دراسة مناعية وجزيئية لالتهاب المعدة غير الناتج عن جرثومة الملوية البوابية في مرضى السكري من النوع الثاني

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Immunological and Molecular Investigation of Non- *Helicobacter pylori* Gastritis within Type 2 Diabetes Mellitus

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substrata and environmental conditions. Biofilms are colonized by a variety of microorganisms, including bacteria, yeasts, protozoans, and algae. Usually, a few species dominate a specific environment. However, under certain conditions, opportunistic pathogens can also settle in biofilms (Gebreyohannes *et al*., 2019).

mind that current lock solutions have significant limitations. Consequently, a combination of different agents with specific activity against biofilms, like enzymes or antibodies, is proposed to improve patient treatment. Finally, healthcare professionals should be made aware of the aetiologic role of nonfermentative Gram-negative bacteria, namely Pseudomonas aeruginosa, in biofilm-associated UTIs.

Conclusion and Summary

Urinary tract infections (UTIs) are one of the most prevalent hospital-acquired infections globally. The continuous bladder drainage is performed using a urethral catheter for the management of various medical and surgical conditions. However, recurrent catheter-associated UTIs (CAUTIs) are among the most common types of nosocomial infections caused mainly by *Pseudomonas aeruginosa*. The central mechanism by which bacteria become resistant to antibiotic therapy inside implanted prosthetic devices is the formation of biofilms. This review aimed to summarize the novel, emerging, and innovative strategies, anti-biofilm compounds, and proposed mechanisms to manage *Pseudomonas aeruginosa* biofilm-associated antibiotic resistance in renal catheters.

Biofilms are sessile, well-organized, and structured colonies of microorganisms attached to biotic and abiotic surfaces embedded in an extracellular polymeric matrix secreted by the microorganisms. Biofilms can develop on different surfaces, including plastic and metal ligatures, which are frequently used in catheterized patients and artificial devices such as prosthetic heart valves, artificial joints, vascular grafts, and intrauterine devices. The architecture of biofilms is highly complex and varies on different

these studies, the potential applications of the results, the advantages that are highlighted, and any potential drawbacks.

The formation of biofilms on renal catheters or renal replacement devices is a commonly observed occurrence that leads to the development of complicated CA-UTIs. Biofilm-associated bacteria embedded in EPSs are protected from the action of several drugs, disinfectants, sanitizers, and also the immune system of the host (Anjum *et al*., 2017). Biofilm formation is a major challenge in hospital-acquired infections. The incidence of biofilm-associated infection, due to pathogenic bacteria, is rising at an alarming rate, in dialysis patients. Pseudomonas aeruginosa has infected indwelling renal replacement devices, leading to high morbidity and mortality. Understanding the unique physiology of biofilms is crucial to combating such infections. The review discusses the innovative strategies developed by great minds to avoid biofilm formation on the catheter surfaces. It discusses the mechanisms of action of the innovative strategies and how these non-bactericidal strategies have an impact on the biofilm physiology. Understanding the physiology of biofilms and combating them with innovative strategies will present new tools, technologies, and opportunities to solve the infection problem, which can be translated into clinical settings (Kamaruzzaman *et al*., 1970).

Recommendations for Clinical Practice

The following recommendations are proposed for practitioners: the close monitoring of catheterized patients, particularly those undergoing repeated irrigation. This should include tracker evaluation in newly implanted catheters, together with implementation and validation of biofilm eradication protocols in cases where impaction is detected. Clinicians should bear in

Clinical Implications and Future Directions

The review's conclusions have significant therapeutic ramifications for the treatment of antibiotic resistance linked to Pseudomonas aeruginosa biofilm in renal catheters. The review emphasizes the promise of novel approaches to reduce the formation of biofilms and antibiotic resistance, including the use of nanomaterials, quorum sensing inhibitors, bacteriophage treatment, and antimicrobial peptides. As these tactics are refined and tested, they may present fresh treatment alternatives for the management of P. aeruginosa-caused catheter-associated UTIs. (Reig *et al.*, 2022). (Anjum *et al.*, 2017) The study also covers a number of recently developed mechanisms of action, such as photothermal therapy, electrochemical methods, and the application of electric fields, for the treatment of biofilm-associated infections.

These processes could lead to the development of novel therapeutic modalities or improve the effectiveness of currently available ones. To completely comprehend their processes of action and create useful applications, more study is necessary. It is advised that physicians keep in mind the difficulties caused by biofilm-associated antibiotic resistance and take into account the possibilities of novel approaches and developing mechanisms in their clinical practice in light of the review's conclusions. To effectively prevent and treat catheter-associated UTIs, researchers and clinicians must work together to translate these results into therapies.

Translational Potential of Research Findings

The scientific results or innovations covered in this review's potential for translation into clinical settings. This covers talks about the necessity of

CRISPR-Cas Systems in Biofilm Eradication

The CRISPR-Cas systems, which are well-known for guarding prokaryotic cells from incoming nucleic acids, show potential in the removal of biofilms. They can be used to develop novel antimicrobials that can specifically target and eradicate microorganisms that form biofilms, either on their own or in conjunction with antibiotics. Preference must be given to CRISPR-Cas systems with optimized, manufactured protospacers that match virulence- or survival-enhancing genes, often known as "Fleet Attacks," rather than naturally occurring CRISPR-Cas systems. These genes may be linked to pathogenicity, virulence, persistence, biofilm development, and antibiotic resistance. CRISPR-Cas systems target the desired gene using a single adaptive spacer. When creating these strategies, a number of factors need to be taken into account (Mayorga-Ramos *et al.*, 2023). The development of biocontrol, barrier-building, and eradication-focused approaches

By neutralizing ARGs, the CRISPR-Cas system restores bacterial sensitivity to antibiotics, functioning as an antimicrobial agent. Researchers have resensitized drug-resistant bacteria to antibiotics by targeting genes on the plasmids of pathogenic bacteria, particularly ARGs, using the CRISPR-Cas system. Through a technique known as "Curing," the CRISPR-Cas system can be specially designed to target and destroy plasmids containing ARGs. Research has validated the function of the CRISPR-Cas system in resensitizing *S. aureus* to methicillin and kanamycin. Nevertheless, the method only eliminated high-copy plasmids from a few bacterial colonies, and treated cells regained sensitivity to resistance to ampicillin, cefazolin, cefuroxime, ceftriaxone, and cefotaxime. The CRISPR-Cas9 system is capable of eliminating resistance gene plasmids in their entirety (Wu *et al*., 2021).

systems (TCSs), quorum sensing (QS), and secretomics have all contributed to the biofilm-forming ability and antibiotic resistance. Therefore, more studies need to address existing knowledge gaps in the interaction of biofilms and plant or nanomaterial-based antimicrobials, as well as the identification and characterization of biofilm-associated protein targets (Pai *et al.,* 2023).

The clustered regularly interspersed short palindromic repeats (CRISPR) systems are prokaryotic defense mechanisms against foreign nucleic acids that are present in at least 50% of archaea and 40% of bacteria. Two classes of these CRISPR systems exist. Class 1 systems (types I, III, and IV) contain multiple proteins, while class II systems (types II, V, and VI) contain only one protein, called the CRISPR-associated (Cas) endonuclease. Initially believed to limit plasmid/naked DNA invasion, it has become clear that these systems can also target viruses (phages), as well as RNA-targeting systems. Biofilms are defined as a structured community of microorganisms attached to surfaces, typically encased in an extracellular polymeric substance. Biofilms are physiologically different from their planktonic counterparts. Biofilms can also be resistant to a variety of antimicrobials, including biocides and disinfectants. In particular, because of their high initial resistance, biofilm-encased bacteria can endure high concentrations of antimicrobials that would otherwise kill planktonic cells. The importance of biofilms in chronic human infections and their detrimental impact on human health and productivity have made them the fiercest battlegrounds in the war against microorganisms (Rao *et al*., 2021).

Quorum sensing is a process in which bacteria produce, detect and respond to signal molecules by which they send out a message to tell other bacteria to express their genes that will help them in biofilm formation. The bacteria will have higher confidence to form a biofilm when and only when the signal molecules they produce reach a density that is sufficiently high enough (Vogel *et al*., 2020). As biofilm formation is a cooperative process that is initiated only when a sufficient number of bacteria are present, quorum sensing is believed to be a requirement for biofilm establishment. Quorum sensing inhibitors are compounds that interfere with one of the steps in the quorum sensing process. Research efforts have been directed toward the discovery of natural and synthetic antibacterial combinations that likewise act as quorum sensing inhibitors. Common natural quorum sensing inhibitors are a compound name, furanones, that produced by a certain type the red alga named *Delisea pulchra* and halogenated furanones produced by certain marine bacterium known as *Phaeobacter inhibens* (Perković *et al*., 2023).

Emerging Mechanisms and Technologies

The emergence of new antibiotic-resistant pathogens, such as those that cause bladder infections, is becoming a serious global health challenge. Antibiotic-resistant strains of *Pseudomonas aeruginosa* were recently reported to cause a urinary tract infection (UTI) in a 1000-bed hospital in India that relied on indwelling catheters for a long-term placement (Pai *et al.,* 2023). These macromolecule- or metal-based (e.g., silver) antimicrobials that acquire inherent antibiotic resistance through biofilm formation and efflux pumps might enter the bloodstream, causing bacteremia, septic shock, and even death. Further, double negative gram bacteria, two-component

modifications of physical, chemical, or biological characteristics, thus enabling higher efficacy, and drug delivery systems that would release drugs selectively in treated areas. This review, having summarised the action mechanisms of various typical micro- and nanotechnologies, aims to explore current explorative and novel strategies involving micro- and nanotechnologies to target biofilms and mitigate biofilm-related drug resistance (Rao *et al.*, 2021).

Nanotechnology, defined as an area of science and engineering smaller than 100 nm, has gained substantial research momentum among the biomedical community in recent years, presenting an untapped avenue for combatting advanced multi-drug resistant bacteria and their biofilms. Above a certain size, nanoparticles exhibit particle size-dependent properties, which may involve the modifications of physical, chemical, or biological characteristics as size or dimension changes. Likewise, micro- and nanotechnologies make use of numerous types of physical, chemical, biological, or engineering responses, such as electrostatic, mechanical, adhesive, thermal reaction, or light-induced processes for the purpose of drug release. In biomedicine, there is a growing interest in the exploration of micro- and nanotechnology-based approaches, including micro- and nanoparticles, microgels, bioengineered moving devices, and novel coatings for the mitigation of biofilm-related infection (Vallet-Regí *et al.*, 2019).

Quorum Sensing Inhibitors

As biofilms protect bacteria from all kinds of antimicrobials, finding ways to dispel biofilms is one of the major problems that researchers are trying to get hold of. One innovative way to dispel biofilm bacteria is by disrupting their quorum sensing that biofilm bacteria depend on to live.

a planktonic population of the same strain. As a consequence of the above phenomena, bacteria like ESKAPE pathogens (*Staphylococcus aureus, Enterococcus faecium, Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and Enterobacter species) posing formidable threats to human life and health are already resistant against the currently available antibiotics. Hence, there is an imminent and dire need for the action plan to combat ABR if mankind desires to check the return of the preantibiotic days. In view of the above context, recent innovative strategies that are either multidisciplinary in nature or operate via unexplored mechanisms or target root causes of the problem have been collected together mostly emphasizing their scientific plausibility and efficacy against bacterial infections in general and Pseudomonas aeruginosa biofilm infection in renal catheters in particular.

Nanotechnology-based Approaches

Recent decades have seen a sharp rise in global antibiotic divergence, with multi-drug resistant strains blooming. As a result, drug-resistant bacteria and their corresponding infections have posed concerns across the world, thereby evoking the urgent need for alternative strategies to combat this escalating threat. Numerous micro- and nanotechnologies-based approaches have been, or are being, actively explored for this purpose. Nanotechnology, which was explicitly defined by the United States National Nanotechnology Initiative, refers to engineered structures, devices, or systems produced with specific properties at dimensions less than 100 nanometers (nm). Opportunities to improve the choice of intervention include the use of nanomaterials that exhibit particle size-dependent properties, allowing for

aeruginosa UTI and have been shown to harbor more drug-resistant Pseudomonas aeruginosa than a control group. Pseudomonas aeruginosa is particularly problematic in patients on chronic catheterization and patients with spinal cord injury (SCI). SCIs result in damage to central nervous tissue leading to loss of voluntary control of the bladder so the routine could be the insertion of an indwelling balloon-tip Foley catheter to drain urine from the urinary bladder and avoid CTs is better understood (Gaglione *et al*., 2022).

Innovative Strategies for Combating Antibiotic Resistance

The affection of bacteria and their inevitable resistance against antibiotics is threatening the well-being of mankind. No antibiotic has been added in the pharmaceutical chain since the last couple of decades to sustain the onslaught of superbugs (Anjum *et al*., 2017). The infections by bacteria are still dealt with the limited arsenal of antibiotics. The dramatic rise in Antibiotic Resistance (ABR) is largely attributable to the mutations in bacterial gene expression in succession to constant exposure to antibiotics. Occasional encounter with antibiotics employed in therapeutics allows the surviving population of micro-organisms to adopt genetic changes that are significant in enabling resistance against recurring attacks (Baptista *et al.*, 2018). Other than this, the appearance of acquired resistance is also suggestive of the lateral transfer of genetic material among bacteria. The emergence of biofilm colonies may provide another driving force for the development of resistance. The polymeric matrix not only provides protection to the resident bacteria against the engulfment of cleansing agents but also promotes local conditioning that makes them gradually resistant to antibiotics. The biofilm communities have been reported to be 1000 times resistant as compared to

used antibiotics in vitro. Understanding the consequences of antibiotic resistance on treatment success is central to treating biofilm-associated infections (Glen & Lamont, 2021).

Current Challenges in Managing Antibiotic Resistance in Renal Catheters

Catheter-associated urinary tract infection (CAUTI) remains the most prevalent hospital-acquired infection, accounting for approximately 80% of all UTIs in hospitalized patients leading to significant healthcare expenses. CAUTIs typically develop as a consequence of indwelling urinary catheters which act as persistent infection foci in the urinary tract for many years. Microorganisms attached to catheter surfaces can develop biofilms which are a community of microorganisms in a self-produced extracellular polymeric substances (EPS) matrix that adhere to each other and/or to a surface. Biofilms protect microorganisms against host immune responses and significantly reduce susceptibility against antibiotics thereby offering a selective environment for normal flora and pathogen coexistence. Although much progress has been made in understanding the pathogenesis of biofilm infections, their prevention remains a significant challenge (Anjum *et al.,* 2017).

Biofilms formed on urinary catheters are mainly composed of uropathogenic strains, of which Pseudomonas aeruginosa is one of the most common bacteria and is a highly problematic pathogen particularly in patients with an indwelling catheter. Pseudomonas aeruginosa is characterized by a diverse antibiotic resistance mechanism and it has been shown to gain multidrug resistance when exposed to β-lactams. Indwelling ureteral catheters significantly increase the risk of developing Pseudomonas

polysaccharides. Poor nutrient and oxygen distribution in biofilms leads to persister cells-cohort formation. *P. aeruginosa* biofilms also show reduced metabolic activity due to nitrogen starvation, iron depletion, alkaline phosphatase production, cell–cell signaling and downregulation of genes transcription for ribosomes, efflux pumps, enzymes, and phosphofructokinase (Abbas *et al*., 2018). These changes lead to tolerance even in susceptible phenotypes. Biochemical analyses reveal the mediation role of a complementary system, complemented with other oxido-reductive systems that endow biofilm cell types more resistance to antibiotics than their planktonic counterparts. Biofilms exhibit a low, yet significant, level of drug resistance in comparison to planktonic cultures even in the absence of cell–cell communication and metabolically inactive cells (Pai *et al*., 2023).

Impact on Treatment Outcomes

Resistance to therapy in *Pseudomonas aeruginosa* biofilms poses treatment challenges and has been associated with treatment failure since the 1980s. Resistance has been attributed to the reduced penetration of antibiotics within biofilms, the induction of resistance mechanisms, and the reduction in active cell division within biofilms.

Failure to eradicate biofilm infections can result in severe complications, such as septicemia related to the infected central venous catheter, resulting in high mortality. Treatment responses vary significantly, ranging from patients who are cured to those who are non-responsive. Antimicrobial resistance in Pseudomonas aeruginosa biofilms has been presented as a key mechanism of biofilm-associated treatment failure. Nevertheless, *P. aeruginosa* biofilm-associated infections are often susceptible to commonly

resistant to heavy doses of antibiotic drugs. Biofilms limit the diffusion of antibiotics into them by 100 to 1000 times more than the free organisms present in the same growth medium, an effect that is higher with larger molecules. Often biofilm-associated microorganisms show no efficacy of 1000 times the Minimum Inhibitory Concentrations (MIC) of antibiotics when tested as planktonic organisms. Accumulation of inactivating enzymes in high concentration in biofilm structure leads to the greater inactivation of antibiotics compared to non-biofilm-associated cells. It was also shown that biofilm exopolysaccharide gives an extra protective wall by trapping the antibiotic into their matrix, preventing it from reaching their target site (Sindeldecker & Stoodley, 2021). Biofilm-associated organisms show phenotypic heterogeneity in the form of metabolically less active and even dormant microorganisms, which do not show any effect of antibiotics and prevent their killing due to cessation of their target actions. Biofilm-associated *P. aeruginosa* widening the efflux pump activity of antibiotics is another mode of antibiotic resistance. There is discussion of selective pressure, a feature of biofilms associated with *P. aeruginosa* which increase the mutation frequency in biofilm cells, hence ultimately leading to enhanced multi-drug resistance.

Mechanisms of Resistance

Biofilm development drastically alters antibiotic resistance in *P. aeruginosa.* Biofilm-associated antibiotic resistance mechanisms encompass a variety of phenotypic adaptations. Low penetration of antibiotics into biofilm is caused by diffusive exclusion in hydrophobic biofilms due to the higher viscosity and exopolysaccharide (EPS) matrix consisting of

Jetz-type IV pili (T4P). Attachment triggers the biogenesis of T4P, which typically adhere bacteria to surfaces through a combination of twitching motility and pilus retraction. Surface adherence also triggers the regulation of biofilm-forming exopolysaccharides such as alginate and pel, resulting in the formation of a sugar-coated bacterial cluster that aggregates with other organisms within the aqueous solution (Silva *et al*., 2023).

P. aeruginosa has a proprietary application of virulence factors that are sub-classified into distinct activities and modes of action with different targets. The overall pathogenicity of *P. aeruginosa* is multifactorial, meaning that diseases arise from the interplay among all virulence factors and the host environment. The precise influence of each on specific pathologies is often difficult to untangle. *P. aeruginosa* possesses several protein secretion systems that have different activities against different hosts and competitors that vary depending on the biological context. This reduces their applicability as predictable virulence factors across different environments (Nolan & Behrends, 2021).

Antibiotic Resistance in *Pseudomonas aeruginosa* Biofilms

Biofilm-associated *Pseudomonas aeruginosa* shows increased antibiotic resistance and decreased efficacy of treatment with higher medicament concentrations (Abbas *et al*., 2018). Superior resistance is an intrinsic feature of *P. aeruginosa* owing to several antibiotic resistance mechanisms. In addition, the presence of biofilm around the microorganism makes this pathogen more dearly paid with antibiotics. Biofilm presents another structure, which in general protects the microorganism from injury, an important barrier to penetration of antibiotics, which can make them

planktonic counterparts (Thi *et al*., 2020). *P. aeruginosa* has long been recognized as a strong biofilm bacterium. Biofilm structure is polymicrobial and contains a diverse community of micro-colonies consisting of different bacterial species cooperating with one another.

Biofilm EPS matrix is a complex assortment that primarily involves polysaccharides, extracellular DNA (eDNA), proteins and lipids. It is commonly known that the main and most prevalent structural element is composed of polysaccharides. The physical barrier that this EPS matrix creates stops amikacin and imipenem from being transported, which adds to the antibiotic resistance of biofilms. Furthermore, it has been demonstrated that the EPS matrix is important in the architecture, upkeep, development, and structural integrity of biofilms. More importantly, depending on the types of EPSs the bacteria display, the EPS matrix can both positively and negatively affect how effective antibiotics are against biofilms. Gaining more insight into the makeup and structure of *P. aeruginosa* biofilms that grow on and inside indwelling medical devices is critically important. Only by learning this information can practical methods for managing and eliminating biofilm-associated (Luo *et al*., 2020).

Virulence Factors

To establish infection*, P. aeruginos*a must overcome early host immune response stages. When colonizing a surface, planktonic bacteria begin transitioning to biofilm growth mode, allowing them to resist immune attack (*P. aeruginosa* biofilms are particularly adept at resisting phagocytosis) and more effectively manage the external nutrient supply. This process begins with the attachment of motile, flagellated bacteria to surfaces, mediated by

to manage, prevent and more essentially eradicate biofilm-associated infections.

For clinical isolates, biofilms develop at any surface (medical devices, catheters) colonized by *P. aeruginosa*. Bacteria within a biofilm can escape host immune responses and resist antimicrobial treatments up to thousands of times more than their planktonic counterparts. Biofilms predictably evolve under external selective pressure (antibiotics, UV light) and are genetically less stable. Biofilm development is governed by a complex interplay of various biochemical, molecular, environmental, and physical factors, including surface properties, liquid streaming, circle flow, shear stress, and viscosity. It has been shown that *P. aeruginosa* biofilm matrix primarily encompasses polysaccharides, extracellular DNA (eDNA), proteins, and lipids.

Biofilm Structure and Characteristics

The biofilm is defined as a complex aggregate of bacteria (micro-colonies) encased in a self-generated matrix of extracellular polymeric substances (EPS). Most animal and plant-associated bacteria, including the human pathogen *Pseudomonas aeruginosa*, have the ability to form biofilms on biotic and abiotic surfaces. *P. aeruginosa* is an opportunistic pathogen that causes acute infections in immunocompromised patients and chronic infections in individuals with cystic fibrosis, burns or extensive skin injuries. It produces a polysaccharide pellicle that is tightly attached to the plastic inner surface of respiratory ventilators and can colonize, contaminating the expiratory airflow. Biofilms allow bacteria to escape from the host immune responses and resist antimicrobial treatments. Bacteria growing within biofilms can survive antimicrobials up to 1000 times more than susceptible

Pseudomonas aeruginosa Biofilm Formation

Pseudomonas aeruginosa is a Gram-negative, motile, and rod-shaped bacterium belonging to the pseudomonad group. It is known for its remarkable metabolic versatility, allowing it to thrive in various environments, including soil, water, and even on human tissues, as it can opportunistically infect patients with relatively intact immunity. Infection by *P. aeruginosa*, however, is of particular concern among immune-compromised individuals and in the management of lengthy diseases. It is an opportunistic pathogen categorized as a "critical priority" bacterium by the World Health Organization (WHO) due to its global threat. The most concerning factor about this bacterium is its hyper-resistance to antibiotics, which has been occluded primarily via biofilm production (Sindeldecker & Stoodley, 2021).

Biofilm is a multifaceted aggregate of bacteria covered in a self-generated matrix of extracellular polymeric substances (EPS). One of the key strategies for the existence of species against unpredicted changes of living environments such as temperature and nutrient accessibility. In a broad sense, biofilms are sticky, surface-attached aggregates of microbial cells, protecting cells against adverse conditions (e.g., grazing, predation, antibiotics) by producing EPS. *P. aeruginosa* is considered a well-known biofilm former, making it an excellent model for studying biofilm formation. Biofilms are regarded as the default mode of growth of bacteria in nature (Thi *et al.,* 2020). About 80% of chronic infections in humans are associated with biofilms, contributing to human mortality by 550,000 victims/annum. More understanding of the biofilm conformation and structure, and the molecular mechanisms essential for the antimicrobial tolerance of bacteria growing within a biofilm, are energetic for the design of effective strategies

Background and Significance

Biofilms are tightly clustered groups of bacteria that can develop on various surfaces, including biotic (inside the human body) and abiotic (such as medical devices, synthetic materials) locations. Biofilm formation starts with the reversible attachment of bacteria to the surface. This is followed by an irreversible adhesion, which involves the secretion of extracellular polymeric substances (EPS) and the formation of a three-dimensional structure. Biofilms can form in both natural and artificial environments, on the surface of abiotic materials, or on tissues or organs of a living organism.

Of special importance in medicine are biofilms generated in association with indwelling catheters, prostheses, heart valves, reconstructive joints, artificial devices, etc. Biofilm development on medical devices leads to persistent bacterial infections that are highly resistant to antibiotics and the host immune system. Chronic infections associated with biofilms can only be treated by the removal of the infected device. Urinary catheters that are indwelling inside the bladder are important biomedical devices used to manage surgeries, urinary tract diseases, and mental disorders. 815 million urinary catheters are estimated to be sold worldwide in 2018. Catheter-associated urinary tract infections (CAUTIs) are the most common healthcare-acquired infections globally and are associated with increased morbidity, mortality, and economic burden. Biofilm-associated antibiotic resistance (ABR) mechanisms in *Pseudomonas aeruginosa* are the topic of interest (Kamaruzzaman *et al*., 2018).

Introduction

Long-term indwelling medical devices that are biofouling run the risk of catheter-associated urinary tract infections (CAUTIs) and bloodstream infections as a result of the migration of microorganisms that form biofilms. Because biofilm-forming bacteria, such as Pseudomonas aeruginosa and Enterobacter cloacae, are lodged in biofilms, their infectiousogenicity endures despite antibiotic treatment and immunological response. By the middle of this century, biofilm-associated CAUTIs are predicted to become pandemic due to the increased appearance of hypervirulence and antibiotic-resistant strains. Thus, there is an urgent need for more concentrated study on novel approaches and their developing mechanisms for treating drug-resistant biofilm-associated bacterial infections in long-term indwelling medical catheters. (Mancuso *et al*., 2024).

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المستخلص

إن الاستراتيجيات والآليات المستخدمة في التحكم في مقاومة بكتيريا *P. aeruginosa* المرتبطة بالأغشية الحيوية Biofilm في حالات قسطرة الكلى تشكل مصدر قلق بالغ في هذا المجال. تُستخدم قسطرة الكلى على نطاق واسع في المستشفيات لعلاج العديد من الاضطرابات البولية. ومع ذلك، فهي السبب الرئيسي للعدوى البكتيرية، وخاصة بكتيريا *P. aeruginosa* ، عند استخدامها لفترة طويلة. إن آلية مقاومة تلك البكتيريا للمضادات الحيوية والمرتبطة بالأغشية الحيوية في قسطرة الكلى معقدة ولم يتم السيطرة عليها بشكل جيد.في هذه المراجعة يتم مناقشة بعض الاستراتيجيات والآليات المرتبطة بمقاومة البكتيريا *P. aeruginosa* للمضادات الحيوية في حالات القسطرة الكلوية، بما في ذلك منع تكوين الأغشية الحيوية، والقضاء على تلك الاغشية، والحد من مقاومة المضادات الحيوية المرتبطة بها وقدرتها على التسبب في الأمراض. التركيز على تلك الاستراتيجيات والطرق المطروحه في هذه الدراسة والتجارب السريرية لتحديد مدى فعاليتها في إدارة الأغشية الحيوية الكلوية لدى المرضى ممن لديهم أصابه ببكتريا *P. aeruginosa* مع كل طرق السيطرة على هذه الالتهابات التي تحدث نتيجة للأغشية الحيوية، سيسمح بشكل جيد لتعافي هؤلاء المرضى.

الكلمات المفتاحية: الزائفة الزنجارية، الأغشية الحيوية، مقاومة المضادات الحيوية ، قسطرة الكلى

Abstract

Strategies and mechanisms in controlling *Pseudomonas aeruginosa* resistance to biofilm-associated with renal catheters are a serious concern. Renal catheters are widely used in hospitals for numerous urological disorders. However, they are the main cause of bacterial infections, especially *P. aeruginosa,* when used for a long time. The mechanism of biofilm-associated antibiotic resistance of *P. aeruginosa* in renal catheters is complex and has not been efficiently managed. This review debates certain strategies and mechanisms associated with *P. aeruginosa* biofilm antibiotic resistance in cases with renal catheters, including the prevention of biofilm formation, eradication of biofilm, and reducing biofilm-associated antibiotic

resistance and virulence. Also, more focusing on strategies are presented in this review, in clinical trials to determine their effectiveness in managing renal biofilms in *P. aeruginosa* patients. With all the proper management of these infections that occur as a result of biofilms will promote the recovery of these patients.

Keywords: *Pseudomonas aeruginosa***, Biofilm, Antibiotic resistance, Renal catheters**

Strategies and Emerging Mechanisms in Managing *Pseudomonas aeruginosa* Biofilm-Associated Antibiotic Resistance in Renal Catheters /A Review Article

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استراتيجيات وآليات ناشئة في إدارة مقاومة المضادات الحيوية المرتبطة بالأغشية الحيوية لبكتيريا *Pseudomonas aeruginosa* في قسطرة الكلى: مقالة مراجعة

مدرس دكتور احمد فاضل كاظم
كلية العلوم – جامعة بغداد, بغداد\ العراق

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