

Republic of Iraq
Ministry of Higher Education and
Scientific Research
Thi-Qar University
College Of Science



Clinical Study for Oxidative Stress , Lipid Profile and Some Trace Elements in Sera of Patients with Heart Failure in Thi-Qar province

**A Thesis
Submitted to the College of Science
University of Thi-Qar
In Partial Fulfillment of the Requirements
for the Master Degree of Science in Chemistry / Biochemistry**

By

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B.Sc. in Chemistry (Al-Muthanna University)

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1438 A.H



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

﴿وَمَا أُوتِيتُمْ مِنَ الْعِلْمِ إِلَّا قَلِيلًا﴾

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الدراسات العليا
وحدة الدراسات العليا

الى / رئاسة قسم الكيمياء

م/ استلال الكتروني

تحية طيبة...

اشارة الى طلبكم الصادر بتاريخ (2017/11/12) نحيل اليكم تقرير الاستلال لرسالة طالب الماجستير(علي عادل عجيل) قبل المقوم العلمي ،الموسومة بـ (Clinical,Study for,Oxidative Stress , Lipid Profile,and Some Trace,Elements in Sera,of Patients,with Heart,Failure)، والذي بلغت نسبته (4%) فقط.

.....مع التقدير.....

أ.م.د. هيثم عبد الأمير مينا
معاون العميد للشؤون العلمية
والدراسات العليا

المرفقات
تقرير ورقي
قرص CD

نسخة منه الى //

- مكتب السيد العميد المحترم / للفضل بالاطلاع..... مع التقدير.
- مكتب السيد معاون العميد العلمي المحترم / للفضل بالاطلاع..... مع التقدير
- ملف الاستلال
- الصادرة.

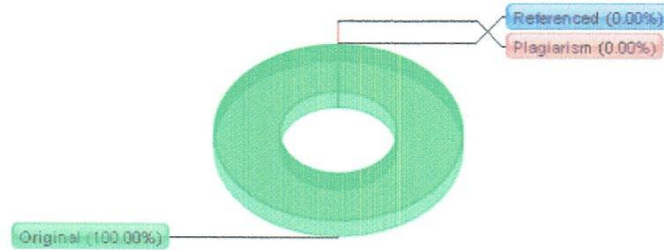
Plagiarism Detector v. 1041 - Originality Report:

Analyzed document: 11/27/2017 1:58:44 PM

علي عادل عجيل، العنوان، دراسة سريرية لحالة الإجهاد التأكسدي و نمط "الدهون وبعض العناصر النزرة في مصل دم مرضى عجز القلب.doc"

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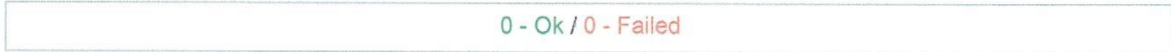


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Detailed document analysis:

Clinical, Study for, Oxidative Stress , Lipid Profile, and Some Trace Elements in Sera, of Patients, with Heart Failure

دراسة سريرية لحالة الإجهاد التأكسدي و نمط الدهون وبعض العناصر النزرة في مصل دم مرضى عجز القلب





وزارة التعليم العالي
والبحث العلمي
Ministry of Higher Education & Scientific Research

استمارة تعهد الالتزام
بأخلاقيات البحث العلمي



جامعة ذي قار
كلية العلوم



نتعهد بالتقيد التام بما جاء في مضمون كتاب وزارة التعليم العالي والبحث
العلمي/جهاز الاشراف والتقويم المرقم ج ت/425 الصادر بتاريخ 2014/3/24،
والمبلغ الينا بكتاب رئاسة جامعة ذي قار/قسم البحث والتطوير المرقم 4704/54/7
والصادر بتاريخ 2014/3/31، عند أعداد الرسالة أو الاطروحة الموسومة:

دراسة سريرية لحالة الإجهاد الكلي وفحص
الرهيون وبعض المعايير النزوية في مصل دم مرضى
عجز القلب

وبخلافه نتحمل نحن الموقعون أدناه المسؤولية القانونية حال وجود ما
يخالف مضمون الكتاب أعلاه أو ما ينافي أخلاقيات البحث العلمي.

الاسم	القسم والكلية أو المعهد	التوقيع	التاريخ
1- المشرف الاول: أ.د. محمد علي حسن	الطب / البصرة		2014/3/24
2- المشرف الثاني: أ.م.م. محمد كرم محمد	الطب / ذي قار		2014/3/24
3- طالب الدراسات: كمال ناظم علي	الطب / البصرة		2014/3/24

ملاحظات هامة:

- 1- تعتبر استمارة التعهد هذه جزء من متطلبات اعتماد مشاريع طلبة الدراسات العليا وتوزيع المشرفين على الطلبة.
- 2- تطبق استمارة التعهد هذه على السادة المشرفين على الرسالة أو الاطروحة وعلى طلبة الماجستير والدكتوراه.
- 3- السطو العلمي هو سرقة نتاج فكري، وعند الاقتباس ضرورة الإشارة للمصدر، وفي حالات الاقتباس ضرورة إعادة صياغة الفقرة المقتبسة دون الخروج من حدود فكرة الفقرة الاصلية المقتبسة والمشار لمصدرها في متن الرسالة أو الاطروحة.
- 4- تشمل استمارة التعهد هذه الرسائل والاطاريح التي لم تنجز حتى تاريخ كتاب جهاز الاشراف والتقويم أدناه.
- 5- أعدت استمارة التعهد هذه استناداً للفقرة 4 من كتاب وزارة التعليم العالي والبحث العلمي/جهاز الاشراف والتقويم المرقم ج ت/425 الصادر بتاريخ 2014/3/24 والمبلغ اليها عن طريق كتاب رئاسة جامعة ذي قار/قسم البحث والتطوير المرقم 4704/54/7 بتاريخ 2014/3/31.



ملاحظات
وزارة التعليم العالي والبحث العلمي
حول الحد من ظاهرة انتهاك حقوق الملكية الفكرية

- 1- تعد السرقعة العلمية سرقة فكرية وانتهاك لحقوق الملكية الفكرية لاخرين، لذا يجب أن تظافر الجهود مع أقسامنا العلمية لايلاء الموضوع أهمية قصوى لمنع ظهورها في كينفتنا والحد من وجودها وانتشارها، وذلك من خلال ما يلي:
- 2- على جميع الباحثين وطلاب الدراسات العليا والدراسات العليا التحلي بأخلاقيات البحث العلمي وعدم نقل النصوص من البحوث والأطاريح، والتحلي بالإنصاف العلمية.
- 3- على الباحثين وطلاب الدراسات العليا والدراسات العليا بالوعي الكافي بالأضرار الناتجة من اقتباس أو استنساخ معلومات عن بحث منشور أو أطروحة دون الإشراف عليها كمنع.
- 4- التزام الباحثين وطلاب الدراسات العليا والدراسات العليا والتدريسيين بتقافة الرصانة العلمية ورفض أي حالة محاولة لأخلاقيات البحث العلمي، متجنبين بذلك أثار السرقعة العلمية والحد منها.
- 5- السرقعة العلمية عواقبها وخيمة على الباحثين والمجلات العلمية على حد سواء، وعليه تم الشروع بوضع ضوابط رادعة تحذر من عواقب السرقعة العلمية.
- 6- تم استخدام برامج حديثة للكشف عن حالات الاقتباس الجزئي والكلي من بحوث وأطاريح منشورة سابقا، بحيث تؤثر السرقعة العلمية بالآثار ومضرات واضحة.
- 7- تم وضع أسس عامة تهدف برفع علميا الباحث والمؤلف على الأضروحة، تتضمن التقيد الكام في عملية الاقتباس والالتزام عن أي سرقة علمية أو اقتباس فيه شبه السرقعة العلمية، وتضمن المسؤولية القانونية في حالة وجود سرقة علمية.
- 8- على الباحثين التدقيق بين الاقتباس العلمي السليم والنسب العلمي فالنسب العلمي هو سرقة نتائج فكري، بينما الاقتباس العلمي السليم هو نقل الفكرة أو النص مع إشارته إلى المصدر (أسم الكاتب والكاتب أو البحث).
- 9- الإهتمام بالبحوث المتوافقة مع الاختصاص الدقيق للباحث، حيث تم حصر بحوث الفرق في المجال الاختصاص لكي يسهل التتبع عنها، ومتابعتها بواسطة اللجان المختصة وباستخدام برامج علمية خاصة على الحاسوب تقوم بعمل مسح للأشرف وما يتوفر في رتيب مكتبة الكلية والجامعة والجامعات الأخرى للوقوف على أعضائها وجود مطابقة ما لا ي بحث مع أي تشابه موجود على الإنترنت.
- 10- يتشاور أن لا تتجاوز نسبة الاستنساخ البحثي المثلث عشر في المئة بين الكليات العلمية 15%.
- 11- استمارة المتولين المتولين ولجان الاستنساخ المركزية في الكلية واللجان العلمية في الأقسام العلمية بالمكتبة الافتراضية، من شأنه توفير مساعدة كبيرة في معرفة ما تقدمه دور النشر العلمية من بحوث ودراسات علمية بالشكل الذي يتكهنه ويساعد على كشف وتحديد البحث العلمي.
- 12- سيتم نشر أسماء المخالفين والمتخلفين على الجامعات العراقية والعلمية واتخاذ أقصى العقوبات الإدارية والعلمية لردعهم عن هذا السلوك المنافي لأخلاقيات البحث العلمي.
- 13- تم نشر الرسائل والأطاريح الإلكترونية في خلال اكتشافات السلوة بين الجامعات، مع وضع في المستقبل القريب خطط وأفاق للتعاون الإقليمي والدولي بهذا الصدد.
- 14- وضعت آليات لمراقبة ومحاسبة المكاتب التي تمثل على بيع الرسائل دون الموافقات الأسبوعية من قبل الجامعات والباحثين.
- 15- تقلصت أعداد المجلات العلمية الصادرة في الجامعات والأساط العلمية، وذلك لحدوث العديد من المجلات الضعيفة والتي نشرت أكبر قدر من البحوث حفاظا على ديمومة أصدورها دون تدقيق البحوث المقدمة للنشر.
- 16- شُكلت وباتت بالعمل لجنة مركزية تتولى متابعة الرسائل والأطاريح والبحوث العلمية والتأكد من عدم سرقتها بأي شكل من الأشكال، تضم هذه اللجنة من بين أعضائها من يجيد اللغة الإنجليزية.
- 17- ومن تم عرض البحث أو الدراسة التي يحمل سرقتها على خبراء متولين للتأكد والمؤازرة ومعرفة الأصل إذا كانت الدراسة مترجمة أو من نتائج البحوث.
- 18- جمع الأبحاث العلمية التي يتناولها كل مجال علمي على حدة في داخل الكلية والجامعة وعمل أرشيف إلكتروني خاص بها، وفي حالة تقدم ببحث لأحد موضوعات البحث يتم فحص الأبحاث الموجودة والتعرف إذا كان البحث قد تم تقديمه من قبل أو لا، وهكذا لجميع الجامعات، وتتميز بربطها.
- 19- استخدام برامج خاصة على الحاسوب تقوم بعمل مسح للأشرف وعملية مطابقة لأي بحث مع أي تشابه موجود على الإنترنت فمثلا يوجد موقع على الإنترنت عنوانه (Copy escape) يساعد في اكتشاف المقالات المسروقة ويقدم خدمة مجانية ومن وسائل حماية البحث من السرقة نشره على الإنترنت.
- 20- يوضع صيغ هوية التدریس للطلاب عدم قوله بالبحرء إلى المكاتب التي تقوم بتجهيز هذه البحوث لحساب الطالب ويحرص بعض النماذج من البحوث ويتناقش مع الطالب نقاط القوة والضعف فيها، حتى يدرك الطالب أن المدرس على علم بما هو موجود موضعا أن معظم هذه البحوث لا ترفي إلى المستوى المطلوب، ومن أكثر أسباب البحوث للسرقة العلمية قسر الوقت وتأجيل إنجاز المهام إلى أجل الموعود النهائي لتقسيم البحث أو لصورة البحث المطلوب.
- 21- تشكيل فريق عمل لأعداد (وثيقة لأخلاقيات البحث العلمي) من خلال الإطلاع على مجموعة من الوثائق الصادرة عن جامعات أخرى (عراقية عربية أجنبية) لاستشارة بها عما فيها مضمونها واسلوبها والتركيز على المحاور الأمية والأوزاع البنيي سمعة الوطن بشكل عام والمؤسسة التعليمية بشكل خاص.
- 22- مراعاة أخذ الموافقات في عملية التسجيل الرقمي (النقاط الصور وتسجيل صوتي أو مرئي) للكتابات المستفيدة من البحوث وأن تكون الموافقة قبل الشروع بالبحث وليس بعدهم.
- 23- وضع آليات لتتبع ومراقبة أخلاقيات البحث العلمي وتفعيل الشكاوى الخاصة بالسرقات العلمية وسماجة المخالفين وفق القوانين المعمول بها في العراق (قانون الخدمة المدنية، قانون التصنيط موظفي الدولة، قانون حماية حق المؤلف).
- 24- أن البعثات الجامعية المختصة بقرصنة أن تقوم بمسح هذه الظاهرة بحزم وصرامة كلما تم ضبطها، سواء عبر التوقيف عن العمل أو الدراسة، أو المنع من النشر أو المشاركة في المؤتمرات أو منع مناقشة الرسائل والأطاريح الممنوعة بهذه الممارسات.
- 25- دعم هيئة الإقتصاد والحث عليها كمدخل أساسي ومهم للحد من القيم الثقافية لقيمة طلب العلم، ومنها ظاهرة الغش في الامتحانات والتي يعتبر إعداد البحوث الخفية وغيرها جزءا منها.
- 26- الحكم القضائي بتخاذل إراءات تأديبية تمنع الجناة من مزاولة مهام البحث والتعليم بشكل نهائي أو لفترات محددة، أو الحرمان من المشاركة في التواتات واللقاءات في المؤسسات العلمية.
- 27- شمول السرقعة العلمية بتقارير التدریس في المحاكم العراقية.
- 28- السماح لطالبة الدراسات العليا بنشر بحوثهم في المجلات المحكمة داخل الجامعات بحصرف النظر عن لنتهم العلمي.
- 29- إلزام التدریس بالكتابة باختصاصه الدقيق وليس العام كون هذه البحوث جزء من برنامج مؤسسية ويمكن له تكبير اختصاصه في حالة الرغبة وبذلك ضمن الضوابط.
- 30- إلزام المجلات بطلب توافيق المشاركين في كل بحث على تعهد بعدم عائلية ذلك البحث لغيرهم، على أن تشارك المجلة من صحة التوافيق المقدمة لها، وتقترض عقوبات رادعة والإحالة إلى لجنة انضباطية في تأكد ما من حصول المكس.
- 31- تشكيل لجان علمية متخصصة بمعايير السلوك العلمي وأخلاقيات البحث العلمي للنظر في كافة البحوث المقترحة وتقييمها قبل النشر.
- 32- إلغاء الترقية العلمية لحصر الهيئة التدريسية وتكملة كل القضاة المالية المترتبة عن ترقية السابقة غير المستحقة، عند ثبوت سرقة لأي من البحوث التي أشتاد منها في ترقية.
- 33- تشكيل لجنة استنساخ مركزية تخاصد لجان الاستنساخ العلمية في كل قسم علمي لفحص ما إذا كانت البحوث مسروقة أو مسئلة بنسبة لا تؤثر في أبحاث البحث وعدم التسامح بأي نسبة استنساخ من غيره لم تتم الإشارة إليه.
- 34- زيادة الدرجة المخصصة للامانة العلمية في استمارة تقييم رسائل الماجستير والدكتوراة لتكون متعة من منح الدرجة في حال ثبوت السرقعة العلمية.
- 35- التأكد على ضرورة وجود ملخص للبحث المراد نشره باللغة الإنكليزية إذا كان البحث باللغة العربية إذا كان البحث باللغة الإنكليزية.
- 36- التأكد على المجلات العلمية بأحالة التقييم حصرا إلى صاحب الاختصاص في موضوع البحث المطلوب نشره، وكذا بالتسليم لتقييم أطاريح رسائل الدراسات العليا.
- 37- ضرورة أن يأخذ المشرف دوره في مطالبة الطالب بالمصادر المستخدمة والإطلاع عليها بين الحين والآخر.
- 38- عرض الرسالة أو الأطروحة على لجان الاستنساخ (لجنة الاستنساخ العلمية في القسم العلمي ومن ثم لجنة الاستنساخ المركزية في الكلية) من خلال إعطاء فرص CD للرسالة أو الأطروحة (مكتوبة بصيغة pdf ملف واحد غير مجزء) لكشف الاستنساخ الموجود فيها على غرار الترتيبات العلمية وذلك باستخدام برامج متخصصة، ويكون كشف الاستنساخ قبل إرسال الرسالة أو الأطروحة إلى المقوم العلمي.
- 39- ضرورة تحلي المشرف والطالب على حد سواء بالحاف والوعي الكافي للالتزام بأخلاقيات البحث العلمي.
- 40- فصل اتصال أة السرقعة العلمية والنسب العلمي والاقتباس الغير الشرعي يتم توفير برنامج شرطي السرقعة العلمية باللغة العربية للوقوف على أهم الخروقات في هذا المجال.
- 41- فصل كتابة الرسائل والأطاريح بتسجيل الباحث الخاص به وعدم نقله نصا كاملا منها وأدخال أفكاره الجديدة وتطويرها أثناء المناقشة مع أكل الباحثين الأخرين.
- 42- ضرورة توعية التدریس والباحثين بالأسلوب الصحيح للاقتباس ومخاطر الاقتباس غير الشرعي.
- 43- أن يكون للمكتبة الافتراضية أشرافه في مواقع عالمية للنشر والكتب بحيث تتمكن لجان الترقين من الإطلاع عليها من خلال البحوث المقدمة للترقية للتأكد من صحتها.
- 44- يجب أن يكون البحث التطبيقي مرافقا منه مكان وزمان التجربة التي أشتد عليها البحث وتكون موقنة بصورة أو كتاب رسمية.
- 45- إرسال بحوث المجلات العلمية إلى مقومين في الاختصاص الدقيق حصرا.
- 46- بوجوب العلمي والاقتباس غير السليم يعد اعتداء على ملكية فكرية محمية بموجب قانون حماية حق المؤلف (3 لسنة 1971 بدلالة المادة 49 منه) وهو ما يشكل مخالفة جزائية يعاقب عليها القانون بموجب المادة 476 من قانون العقوبات والتي تستوجب أحالة مرتكب هذا الفعل إلى هيئة الزاخرة العامة لاتخاذ العقوبات بطفه.
- 47- إقتاء برامج خاصة لمعرفة أصالة البحوث والكشف عن نسب الاستنساخ ومنها البرنامج التدريبي المدع لحماية الإنسان والبيئة من قبل بعض كوارها من لجان الترقين ولجان تحرير المجلات.
- 48- الحد من ظاهرة السرقعة العلمية وإنهاؤها تمام في مجتمع الجامعات الأكاديمية وغيرها من المجتمعات الأكاديمية الرصينة، بل يجب تطبيق الشريعات الخاصة بحماية حقوق المفكرين والعلماء ويتضمن ذلك عقوبات صارمة منها:
- أ- سحب الشهادة.
- ب- إبطال الترقية العلمية.
- ج- اعتبار قدم أو جريمة السرقعة أو مضي زمن بعيد عليها لا يؤثر بقاء بالعقوبة.
- د- اعتبار مكتبة السارق الوطنية كطرف مخصص يتنا.
- 49- ضرورة تدريب الكوادر الأكاديمية (أثناء من مدرسين مساعدين) من قبل الباحثين الذين لديهم الخبرة والامكانية على كلفة البحوث العلمية بالطرق الصحيحة وتبنيهم لعدم اللجوء مطلقا وبوقت مبكر إلى الاستنساخ أو النسخ من رسالة الماجستير أو أطروحة الدكتوراه.
- 50- نشر تلك البحوث والرسائل والأطاريح من قبل المجلات العلمية بالنسبة للبحوث أو من قبل الكليات بالنسبة للرسائل والأطاريح وأن يكون ذلك النشر عبر المواقع الإلكترونية الخاصة بتلك المجلات، أو الكليات ليتسنى معرفة كل الشخصيين بها من جانب وليكون لدى الباحث علم مسبق بأن عمله سوف يعلم به الجميع وبالتأكيد يكون وسيلة رادعة لم يفكر بسرعة التناجات العلمية للأخرين.
- 51- اختيار موضوع الطالب (البحث / الرسالة / الأطروحة) خلال السنة التحضيرية وتفعيل السيمانر للطلبة كل ثلاثة أشهر.
- 52- توجب على المشرف أخذ الدور المسند له من خلال متابعة الطلبة المشرف عليهم لمعرفة أكتيبتهم على الكتابة وتدريبهم بأخلاقيات البحث العلمي وتوجيههم التوجه الصحيح وصولا إلى تشخيص الأخطاء وتصويبها لكافة الطالب.
- 53- عقد الأساتذة الذين يقومون بدور الإشراف مسالة الزامهم بالتعهد بمنع الطالب من التعامل مع المكاتب التي تقوم بمسمة طبع وبيع البحوث والرسائل والأطاريح لطالبة الدراسات العليا، ووضع صيغته من قبل الكليات بعد توجيهاها من خلال الجامعة.
- 54- تقديم تقرير كل ثلاثة أشهر عن عملية سير الإشراف من قبل المشرف ولكل طالب على حدة ويكون ملزما بإلقاء الأستاذ مشرفا على طلبته، لينين من خلاله أكتيبة الطالب على الكتية ومستوى أكتيبيه للموضوع المختار للكتابة فيه ومدى معرفته لأخلاقيات البحث العلمي ليستخلص من هذه التقارير تقريراً نهائيا يقدم إلى المقوم العلمي لدى تقييم (الرسالة أو الأطروحة)، (ترسل نسخة من كل تقرير دوري إلى مكتب معاون العميد للشؤون العلمية والدراسات العليا لاعتماده وأرسل نسخة منه إلى ملف الطالب في مكتب الدراسات العليا والقسم العلمي).

ت	اسم الخبير الاحصائي	نوع المشورة	الملاحظات
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3	الد. محمد عبدالله	✓	✓

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عنوان الرسالة أو الاطروحة: Clinical study For oxidative stress, Lipid profile and some trace Elements in sera of patients with Heart failure

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أتعهد بتولي وتنظيم الدراسة الاحصائية بنفسني من دون
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CERTIFICATE

We certify that this thesis, entitled *Clinical Study for Oxidative Stress , Lipid Profile and Some Trace Elements in Sera of Patients with Heart Failure*, was prepared by *Ali Adil Ajeel* under our supervision at the Department of Chemistry, College of Sciences , University of Thi-Qar (Iraq) in partial fulfillment of the requirements for the Master degree of science in chemistry.



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الإهداء

إلى من وصفه أعداؤه... الصادق الأمين ووصفه ربه... وأذكى لخلق عظيم
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List of Abbreviations

4- HNE	4-hydroxyalkenals
A	Absorbance
ABG	Arterial blood gas
ACE	angiotensin-converting enzyme
AF	Atrial fibrillation
ATP	Adenosine tri phosphate
CAD	Coronary Artery Diseases
CBC	Complete blood count
CCU	Coronary Care Unit
CHD	Congenital Heart Disease
CHF	Chronic Heart Failure
CM	Chylomicrons
Cp	Ceruloplasmin
CO	Cholesterol oxydase
CE	Cholesterol esterase
CKD	Chronic Kidney Disease
CVD	Cardiovascular disease
DM	Diabetes Mellitus

DNA	Deoxyribonucleic acid
D .W	Distilled Water
ECG	Electro Cardio Graphic
Echo	Echocardiography
EF	Eject Fraction
GPO	Glycerol-3-phosphate oxidase
GK	Glycerol kinase
GUE	General Urine Exam
HIV	human immunodeficiency virus
HDL	High density lipoprotein
HF	Heart Failure
HFpEF	Heart Failure with preserved Ejection Fraction
HFrEF	Heart Failure with reduced Ejection Fraction
HTN	Hypertension
ID	Iron deficiency
IHD	Ischemic heart disease
LA	Left atrial
LH	lipid hydroperoxides
LVEF	Left Ventricular Eject Fraction
LVSD	Left Ventricular Systolic Dysfunction
LV	Left ventricular
LDL	Low density lipoprotein

LPO	Lipid peroxidation
LSD	Least Significant Difference
MAGGIC	Meta-Analysis Global Group in Chronic Heart Failure
MDA	Malondialdehyde
MI	Myocardial Infarction
NYHA	New york heart association
PAP	4-Amino-antipyrine
POD	peroxidase
PPD	Para-phenylene diamine
PTA	Phosphotungstic acid
PUFA	Poly Unsaturated Fatty Acid
RAAS	renin–angiotensin–aldosterone system
RV	Right ventricular
ROS	Reactive Oxygen Species
RNS	Reactive Nitrogen Species
RF	Renal Failure
rpm	Rotor per minute
SD	Standard deviation
SOD	Superoxide dismutase
TBARS	Thio barbituric acid reactive substance
TCA	Tri chloro acetic acid
TCH	Total cholesterol

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Tf	Transferrin
TG	Triglyceride
TIBC	Total Iron Binding Capacity
UV	Ultra-Violate
VHD	Valvular Heart Disease
VLDL	Very low density lipoprotein
WR	Working reagent

Summary

Heart failure is a chronic progressive clinical syndrome where the heart is unable to provide the different organs with adequate circulation of blood due to abnormality in the heart and changes in the hemodynamic , kidney , nerve and hormone system .

This study is conducted to elicit the role of oxidative stress status (malondialdehyde) (MDA) , (ceruloplasmin , transferrin) (Cp , Tf) , lipid profile (cholesterol , triglyceride , high density lipoprotein , low density lipoprotein , very low density lipoprotein) (TCH , TG , HDL-C , LDL-C , VLDL) and some trace elements (copper , iron) in patients with systolic heart failure (HF)

The study includes 74 patients , who were attending AL-hussein teaching hospital in Thi-Qar,Iraq especially, in the coronary care unit (CCU) , with 74 healthy persons as a control group . The diagnosis was made by the consultant medical staff based on medical history , symptoms , clinical examination and other investigations .

Measuring parameters besides the general comparison , were studied on the basis of four variables types of disease (mild , moderate , severe) , sex (male , female) and age into four groups (40-49, 50-59, 60-69 and 70-79 year) (A , B , C , D) respectively , as well as smoking .

Throughout the general comparison between the patients and the control group , the results show a significant increase in the serum levels of (MDA) , (Cp) , (TCH) , (TG) , (LDL-C) , (VLDL) and (copper) ($P \leq 0.05$) , and a significant decrease in the serum level of the (Tf) , (HDL-C) and (iron) ($P \leq 0.05$) .

According to the types of disease , there is only a significant increase in severe heart failure in both MDA and copper in patient group in comparison with mild and mod heart failure , and significant increase in concentration of serum TCH in patients of (HF severe , HF mod) group in comparison with patient of (HF mild) ($P \leq 0.05$) . Also there is a presence of a significant decrease in HDL-C and iron in patient of (HF severe) group in comparison with patient of (HF mild and HF mod) ($P \leq 0.05$) , and no significant differences in (TG) , (VLDL) , (LDL-C) , (Cp) and (Tf) with types heart failure.

According to sex , the study shows a significant increase in serum copper levels in female in comparison with male ($P \leq 0.05$) and a significant decrease in serum iron levels in female in comparison with male ($P \leq 0.05$) , and no effects of sex on remaining parameters .

According to age , there is a significant increase in (iron) in (D,C) patients group in comparison with (A,B) patients group , and there is a significant increase in (TCH , MDA) and a significant decrease in (HDL-C) in (B,C,D) patients group in comparison with (A) patient group , and there is a significant increase in (LDL-C) and a significant decrease in (Tf) in (D) patient group in comparison with (A,B,C) patients group , and show no significant differences in concentration of serum Cp ,TG,VLDL and copper in all patient age groups

According to smoking , the study shows smokers have significant increase in concentrations of serum (TCH , TG , LDL-C , VLDL , MDA , Cp and iron) and significant decrease in concentrations of serum (HDL-C and copper) . and no significant differences in concentration of serum Tf compared to non-smoking group .

CHAPTER ONE

INTRODUCTION

1-1: Heart Failure :

Heart failure (HF) , also called congestive heart failure (CHF) , occurs when the heart is unable to pump sufficiently to maintain blood flow to meet the body's needs , ultimately , significant morbidity and mortality (Task, F *et al.*, 2012 ; McMurray *et al.*, 2012 ; Mazurek and Jessup, 2017) . HF is a progressive , clinical syndrome (Mazurek and Jessup, 2017) .

In many countries , (1-2) % of adults and more than 10 % of elderly people have HF (Mosterd and Hoes, 2007) . With a 1-year survival rate of only (30-40) % (Mozaffarian *et al.*, 2015) . Furthermore , the number of people with HF has rapidly increased in the past few decades , and is estimated to continue increasing until 2035 (Mozaffarian *et al.*, 2015) .

About 5.7 million adults in the united states have HF. One in nine deaths in 2009 included HF as contributing cause . About half of people who develop HF die within 5 years of diagnosis (Writing Group Members *et al.*, 2016) .

CHF is common , with approximately 900,000 people living with the condition in the United Kingdom (Mant, Al-Mohammad and Davis, 2010) . HF affects 26 million people globally (Ambrosy *et al.*, 2014) .

CHF can occur in all age groups ; however , its prevalence increases with age (Ponikowski *et al.*, 2016) , with an average age of 77 years (Mosterd and Hoes, 2007) . One in ten patients dies in hospital , and between one quarter and one third of those who survive die within one year of admission (Mcdonagh *et al.*, 2013) .

In spite of the availability of a number of therapeutic strategies to treat patients with HF, the disheartening fact about HF is that , within 5 years of diagnosis , the mortality is a whopping 50% (Goenka *et al.*, 2017) .

HF is an increasing public health problem accelerated by a rapidly aging global population (Deng *et al.*, 2011 ; Qing lou , Ajit janardhan, 2012) . HF develops secondary to another disease process and is not a disease in itself (Butler, 2012) .

The terms chronic heart failure (CHF) or congestive cardiac failure (CCF) are often used interchangeably with congestive heart failure. CHF is a dynamic and progressive syndrome , which develops secondary to structural or functional abnormalities of cardiac tissue (Ponikowski *et al.*, 2016) .

1-2 : Classification of Heart Failure :

Depending on the time of onset , HF is classified as acute or chronic . There is a difference between acute and chronic HF , acute HF is characterized by a rapid onset of symptoms and insufficient cardiac function , in contrast to chronic HF which seldom presents with acute exacerbations (Nieminen *et al.*, 2005) .

HF previously classified as either low-output or high-output failure, where low-output failure predominates . Low-output failure is characterized by a decreasing volume of blood that is being pumped by a weakened heart in patients . Low-output failure is divided into left ventricular (LV) , right ventricular (RV) and biventricular failure based on the location of the deficit (Nieminen *et al.*, 2005) . Since the left ventricle is the major pumping chamber of the heart , left ventricular failure is most common . Left ventricular failure is divided into systolic

or diastolic dysfunction , where systolic is more common (Brian *et al.*, 2013) .

In high-output failure the heart itself is healthy and often pumps a normal or even higher than normal volume of blood . Because of high metabolic demands caused by other underlying medical disorders (e.g., hyperthyroidism , anaemia) (Brian *et al.*, 2013) .

Current guidelines support the use of HFrEF and HFpEF to replace systolic HF and diastolic HF, respectively (Mazurek and Jessup, 2017) .

Clinically, it is typically classified into two major types based on the functional status of heart : heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF) (Mitter and Yancy, 2017) .

HFrEF , Left ventricular systolic dysfunction results from the impaired contraction of the left ventricle , in the systolic or ‘pumping phase’ of the cardiac cycle . It is usually associated with a reduction in left ventricular ejection fraction , and is referred to as HFrEF or systolic dysfunction . This is the usual pattern of acute and chronic HF (Nicholson, 2008) .

HFpEF , HF with preserved or ‘normal’ ejection fraction results from impaired left ventricular relaxation , which occurs in the diastolic or ‘relaxation phase’ of the cardiac cycle . This is known as diastolic dysfunction (Nicholson , 2008) .

Left Ventricular Ejection Fraction (LVEF) , often referred to as Ejection Fraction (EF) , is a calculation used to measure the percentage of blood forced out of the left ventricle with each contraction . It is used to classify the severity of Left Ventricular Systolic Dysfunction (LVSD) (Table 1-1) (Brake and Jones, 2017) .

Table (1-1) : Left ventricular ejection fraction and systolic Function .

Left Ventricular Ejection Fraction (%)	Systolic Function
≥ 55	Normal
45 - 54	Mild left ventricular dysfunction
36 - 44	Moderate left ventricular dysfunction
≤ 35	Severe left ventricular dysfunction

1-3 : Symptoms of Heart Failure :

The clinical symptoms of HF are generally the result of reduced cardiac output and the accumulation of excess fluid; for example , breathlessness (Clyde W. Yancy, 2017) , orthopnoea , paroxysmal nocturnal dyspnoea , peripheral oedema (Butler, 2012) , fatigue and exercise intolerance (Ikram, 1995; Badgett *et al.*, 1996) . However , such symptoms are not exclusive to HF and it can be difficult for less experienced practitioners to identify the signs of the condition , leading to challenges in its recognition (Brake and Jones, 2017) .

As well as physical symptoms , patients with HF can also experience mental health problems , including low mood , anxiety and depression . A study by Jiang et al (2001) demonstrated that 13.9 % of the patients hospitalised with HF had major depressive disorder , irrespective of age , ejection fraction and New York Heart Association classification .

1-4 : Causes of Chronic Heart Failure :

There are many possible causes of HF (show in table (1-2)). Myocardial ischaemia is the most common cause in patients , with many patients having a history of myocardial infarction (MI) (NICE Guideline, 2010) .

Table (1-2) : Causes of Heart Failure (Butler, 2012) .

- | |
|--|
| <ol style="list-style-type: none">1- Coronary heart disease : ischaemia , myocardial infarction (Department of Health, 2009) .2- Hypertension (Cunha, 2011) .3- Valvular heart disease : mitral or aortic (Cowie <i>et al.</i>,1999) .4- Arrhythmias : atrial fibrillation , complete heart block .5- Congenital heart disease : atrial or ventricular septal defects (Cowie <i>et al.</i>,1999) .6- Cardiomyopathy : dilated , hypertrophic , viral , myocarditis , familial , post-partum (Lewis <i>et al.</i>, 2007) .7- Toxins : chemotherapy , alcohol .8- Hypothyroidism .9- Infection : viruses , human immunodeficiency virus (HIV) , bacteria , post-partum . |
|--|

1-5 : Diagnosis of Heart Failure :

Early diagnosis of HF in patients without clinical symptoms is often difficult due to the lack of universal access to screening echocardiography and the costs associated with it (Ky *et al.*, 2012 ; Richter *et al.*, 2013) .

The diagnosis of HFpEF is more challenging than the diagnosis of HFrEF . Patients with HFpEF generally do not have a dilated LV, but

instead often have an increase in LV wall thickness and / or increased left atrial (LA) size (Ponikowski *et al.*, 2016) .

However , most patients with HFrEF (previously referred to as ‘systolic HF’) also have diastolic dysfunction, and subtle abnormalities of systolic function have been shown in patients with HFpEF (Ponikowski *et al.*, 2016) .

Patients’ prognosis remains poor and few conditions can compare with HF for its diverse effects on patients and its high morbidity and mortality (Metra *et al.*, 2017) , Diagnostic test methods include (Maisel, 2002) :-

- 1- Patient history and physical examination including the findings of edema abnormal heart sounds , and the presence of crackles with dyspnea .
- 2- Chest x-ray examination .
- 3- Electro cardiography (ECG) .
- 4- Arterial blood gas test (ABG) .
- 5- Liver function studies .
- 6- Renal function studies .
- 7- Complete blood count (CBC) .
- 8- Echocardiography (Echo) .
- 9- S . Lipid profile .

1-6 : Treatments of Heart Failure :

The last year have witnessed major advances in treatment of HF (Metra *et al.*, 2017) . The treatment goals for patients with HF are to relieve symptoms and signs , prevent hospital admission (Masson *et al.*, 2008) . Reduction in mortality and hospital admission rate reflects the ability of effective treatments to slow down worsening HF .

Pharmacological therapy is based on the use of angiotensin-converting enzyme inhibitors (ACE inhibitors) , and / or angiotensin II receptor blockers , beta-blockers , mineral corticoid receptor antagonist and diuretics (Mcmurray *et al.* 2012) . Sometimes , surgical therapy is warranted in cases where HF is caused by a surgically correctable condition , such as valve or coronary artery disease . Furthermore , surgery with left ventricular devices or heart transplantation can be done in severe cases of cardiomyopathy (Nicolini and Gherli, 2009) .

Non-pharmacological treatment is based on education and counselling to promote patients self-care behaviour in order to improve or maintain health . Important topics for education are HF pathophysiology , monitoring of symptoms , daily weight , pharmacological treatment , prognosis , advice about lifestyle changes such as dietary changes , fluid restrictions and exercise recommendations (Riegel *et al.*, 2011 ; Moser *et al.*, 2012 ; Sears, 2013) .

The World Health Organisation report that up to 50 % of individuals with chronic diseases do not adhere to their medication and when it comes to exercise and diet advice the numbers are even lower (Van Der Wal *et al.*, 2006 ; Van Der Wal *et al.*, 2010) .

Factors that influence adherence are related to the disease effects of the treatment , personality of the patient , social and economic context , the patient-physician communication , and the healthcare system

(Vermeire *et al.*, 2001 ; Krueger *et al.*, 2005) . Nonadherence can be regarded as unplanned relating to issues of cognition (e.g. forgetfulness) , ability to read and write , or intentional where beliefs about a medicine (side effects) or costs of the medicine result in not taken the medication (Vermeire *et al.*, 2001) .

1-7 : Complications of Heart Failure :

In advanced HF a number of non-specific complications may occur.

1-7-1 : Arrhythmias :

Atrial and ventricular arrhythmias are very common and may be related to electrolyte changes (e.g. Hypokalemia , hypomagnesaemia) . Atrial fibrillation (AF) can be either a cause or a consequence of HF (Maisel and Stevenson, 2003) . Sudden death occurs in up to 50 % of patients with HF and is often due to a ventricular arrhythmia (Maisel and Stevenson, 2003 ; Urden *et al.* , 2014) .

1-7-2 : Depression :

Depression is associated with poor quality of life , functional limitations , suboptimal self-care behaviours , higher healthcare costs and poorer outcomes for all patients with cardiovascular disease (CVD) (Thombs *et al.*, 2008) and up to a third of people with HF developed severe and prolonged depression (Maisel, 2002 ; Rutledge *et al.*, 2006) .

1-7-3: Cachexia (Wasting) :

Wasting is a serious complication of HF and affects (10 to 15) % of HF patients . An important predictor of reduced survival , malnutrition is

common in patients with severe HF . It usually occurs with severe dyspnoea (breathlessness) and weakness (Dickstein *et al.*, 2008) .

1-7-4 : Sexual dysfunction :

Sexual dysfunction is a common complication in HF (Dickstein *et al.*, 2008) . This may be related to cardiovascular disease , fatigue , weakness , medications (such as beta-blockers) , depression and anxiety (Mahdi M *et al.* , 2014) .

1-7-5 : Stroke and Thromboembolism :

HF predisposes patients to thromboembolism (including stroke, deep vein thrombosis and pulmonary embolism) . Factors contributing to this increased risk include low cardiac output (with relative stasis of blood in dilated cardiac chambers) , AF and patient immobility (Davis, R *et al.*, 2006) . Eighteen of every 1,000 HF patients suffer a stroke during the first year after their diagnosis . The stroke rate increases to a maximum of 47.4 per 1,000 at five years (Mahdi M *et al.* , 2014) .

1-8 : Risk Factors :

The MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) database has played a major role because of the large number of patients included , the accuracy of the entry criteria and of the follow-up . The final model included independent predictors of mortality which are , in order of strength : age , lower EF, NYHA class , serum creatinine , diabetes , not being prescribed a beta blocker , lower systolic blood pressure (BP) , lower body mass , time since diagnosis , current smoker , chronic obstructive pulmonary disease and not being prescribed an ACE inhibitor or angiotensin-receptor blockers (Pocock *et al.*, 2013) , this

score has been then validated in an independent patient population from sweden (Sartipy *et al.*, 2014) .

As well as from risk factors Olmstead County found that CHD (coronary heart disease) , hypertension (management of hypertension is the most important) . Early work recognized the benefits of diuretics for hypertension treatment in preventing HF (Sciarretta *et al.*, 2011) , obesity (treatment hyperlipidemia according to contemporary guidelines in order to lower the risk for developing HF) (Alan S. *et al .*, 2014) , Valvular Heart Disease (VHD) (Nkomo *et al.*, 2006) , Dietary sodium intake (He , j *et al.*, 2002) .

1-9 : Oxidative Stress :

Oxidative stress , an impaired balance between free radical production and the endogenous antioxidant defense system , mainly leads to accumulation of oxidative damage and development of pathologic conditions such as cardiovascular disease (Jenkinson *et al .*, 1999 ; Cruz *et al.*, 2015) . Oxidative stress has been implicated in the pathophysiology of HF as well as other disease states (Hammadah *et al.*, 2017) .

Oxidative stress is defined in general as excess formation and insufficient removal of highly reactive molecules such as Reactive Oxygen Species (ROS) (The latter can be classified into oxygen-centered radicals and oxygen-centered non radicals . Oxygen-centered radicals are superoxide anion ($O_2^{\bullet -}$) , hydroxyl radical ($\cdot OH$) , alkoxyl radical ($RO\cdot$) , hydroperoxyl (HO_2) , and peroxy radical ($ROO\cdot$) . Oxygen centered nonradicals are hydrogen peroxide (H_2O_2) , hydrochlorous acid ($HOCl$) , and singlet oxygen ($^1O_2$)) (Fang *et al.*, 2002 ; Lee *et al.*, 2004) , and Reactive Nitrogen Species (RNS) (The latter can be classified into free radicals like nitric oxide ($\cdot NO$) and nitric dioxide ($\cdot NO_2$) and non radicals

such as peroxynitrite (ONOO^-) , nitrous oxide (HNO_2) and alkyl peroxynitrates (RONOO) (Evans *et al.*, 2002) .

Chemically , oxidative stress is associated with increased production of oxidizing species or a significant decrease in the effectiveness of antioxidant defenses, such as glutathione (Schafer and Buettner, 2001) . Production of ROS is a particularly destructive aspect of oxidative stress (Valko *et al.* , 2005) .

ROS are generated inside the body, it works to attack cells and destroy their protein , lipid , DNA , carbohydrate and other components in the cell and lead to cell wall damage (Bartosikova, 2003) .

The effect of ROS on proteins through the effect on the double bond, as it works on oxidation of thiol group (SH group) and then will change the synthesis of proteins and the occurrence of mutations on them and then will affect their work and inhibit the effectiveness of enzymes (Jacob, 1995; Ambrosio and Tritto, 1999) .

1-10 : Lipid Peroxidation (LPO) :

Peroxidation is defined as the damage to unsaturated fatty acids found in the cellular membranes due to the presence of oxygen and the effect of free radicals (Aust *et al.*, 1993) . Lipid peroxidation oxidizes polyunsaturated fatty acids (PUFAs) (Gaschler and Stockwell, 2017) . The lipid molecules are important cellular molecules that enter into the cellular membranes (Aguilera *et al.*, 2004) .

The fatty acids are divided into saturated fatty acids and unsaturated fatty acids , unsaturated fatty acids divided mono unsaturated fatty acids and poly unsaturated fatty acids . Unsaturated fatty acids have two or more double bonds that are the main target of free radical reactions

(Aguilera *et al.*, 2004) , and the presence of double bonds in the polyunsaturated fatty acids (PUFA) weakens the bond between (carbon hydrogen) located on the carbon atom content to the double bond and easy the removal of hydrogen from them (Halliwell, B., & Gutteridge, 1985) .

Free radicals and ROS destroy cellular membranes through the over-oxidation of unsaturated fatty acids (PUFA) in these membranes (Dubey *et al.*, 2000) , and the process of lipid peroxidation show in figure (1-1) (yin *et al.* , 2011) .

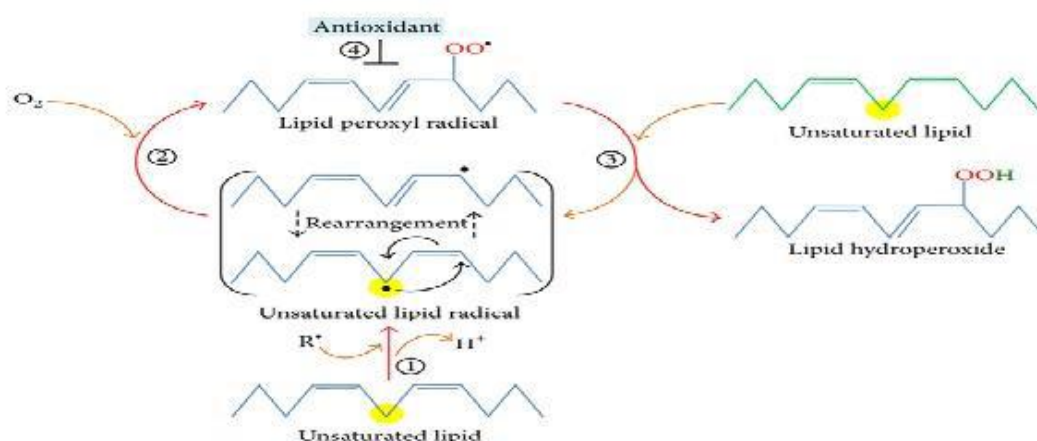


Figure (1-1) : The process of lipid peroxidation .

Malonaldehyde (MDA) , thiobarbituric acid reactive substance (TBARS) , lipid hydroperoxides (LH) , and 4-hydroxyalkenals (4-HNE) used as biomarker of lipid peroxidation level . Many investigations have shown that MDA , TBARS , LH and 4-HNE are directly linked to increase the rates of lipid peroxidation (La Monte *et al.*, 2000) . ROS has been linked to cardiac contractile dysfunction , potentially leading to arrhythmia and heart attack (Vincent *et al.*, 1999) .

1-11 : Antioxidants :

Antioxidant molecule can prevent the oxidation of other molecule (Bjelakovic *et al.*, 2013) . And terminate the chain reaction by removing the free radical species and inhibit other oxidation reactions by oxidizing themselves (La Monte *et al.*, 2000) .

The classification of antioxidants , including endogenous antioxidants and exogenous antioxidant (Jeppsson *et al.*, 2007) .

Endogenous antioxidants include Bilirubin , glutathione , lipoic acid , N-acetyl cysteine , NADPH and NADH , ubiquinone (coenzyme Q 10) , uric acid . Enzyme :- Iron-dependent catalase , selenium-dependent glutathione peroxidase , copper/zinc and manganese-dependent superoxide dismutase (SOD) and metal binding proteins such transferrin (iron) , ferritin (iron) , myoglobin (iron) , ceruloplasmin (copper) and albumin (copper) . Exogenous antioxidants such as beta carotene and other carotenoids and oxycarotenoids , vitamin C , vitamin E , lipoic acid and polyphenols , e.g. flavonoids (Cruz *et al.*, 2015) .

The endogenous antioxidant system plays a crucial role in controlling ROS levels and maintaining the balances of the oxidation reduction (redox) status of the body (Cruz *et al.*, 2015) .

However , when the endogenous antioxidants fail to counteract the excessive production of ROS , the exogenous antioxidants would be useful in synchronizing the redox balance status (Cruz *et al.*, 2015) .

1-11-1 : Ceruloplasmin (Cp) :

Cp is a blue multi-copper oxidase which is found in the plasma as a major copper ion transporter . The protein is synthesized mainly in the liver as a single-chain polypeptide and secreted into the plasma as a α_2 -glycoprotein (De Domenico *et al.*, 2007) . It is a protein associated with the metal . It consists of a single peptide series containing 1046 amino acids and three amino-glucose molecules associated with a side chain of multiple sugars and the molecular weight of the peptide series with sugars 132 KD and that each molecule of Cp contains 6 to 8 copper atoms (Tietz, 1999) .

The efficacy of Cp as an antioxidant depends on the level of Cu^{+2} in the protein , as the Cp works to remove the $\text{O}_2^{\cdot-}$ superoxide radical by reducing the copper atom in the protein (Halliwell and Gutteridge, 1985) .

During exposure to oxidative stress , substantial inactivation of Cp may occur and free copper ion may be released (Swain, Darley-Usmar and Gutteridge, 1994 ; Choi *et al.*, 2000) . Therefore , the damaged Cp may cause the augmentation of free radical-mediated damage to other macromolecules upon exposure to oxidative stress , thus , Cp is a very important component of the cellular defense mechanism against toxicity (Kang, 2006) .

1-11-2: Transferrin (Tf) :

Tf is the most important iron transporting protein , is a glycoprotein with a molecular mass of about 79.57 Daltons that consists of a single peptide chain of 679 amino acids (Herruzo and Muñoz, 2005) . It is fundamentally synthesized in the liver (Koeller *et al.* , 1994) .

Transferrin synthesis and storage are regulated by iron levels , estrogens , and nutritional status (Morgan, 1983) .

Transferrin transports ferric iron into cells by receptor-mediated endocytosis , a unique process by which transferrin and its receptor are reutilized repeatedly in iron delivery (Vostreis *et al.*, 1988) .

1-12 : Lipids and Lipoproteins :

Lipid is one of the insoluble Bio- molecules in water and dissolved in organic solutions . It is used as a source of energy (King, 2004) .

Cholesterol , cholesterol esters , triglycerides and phospholipid are ones of the most common lipids in humans (Montgomery, R *et al .*, 1996).

It is transmitted through the blood linked with special proteins called (Apoportion) complex result is a called (Lipoprotein) , and the type and amount of lipid within these complex depend on the nature of nutrition and various metabolic processes in the body (Montgomery, R *et al .*, 1996) .

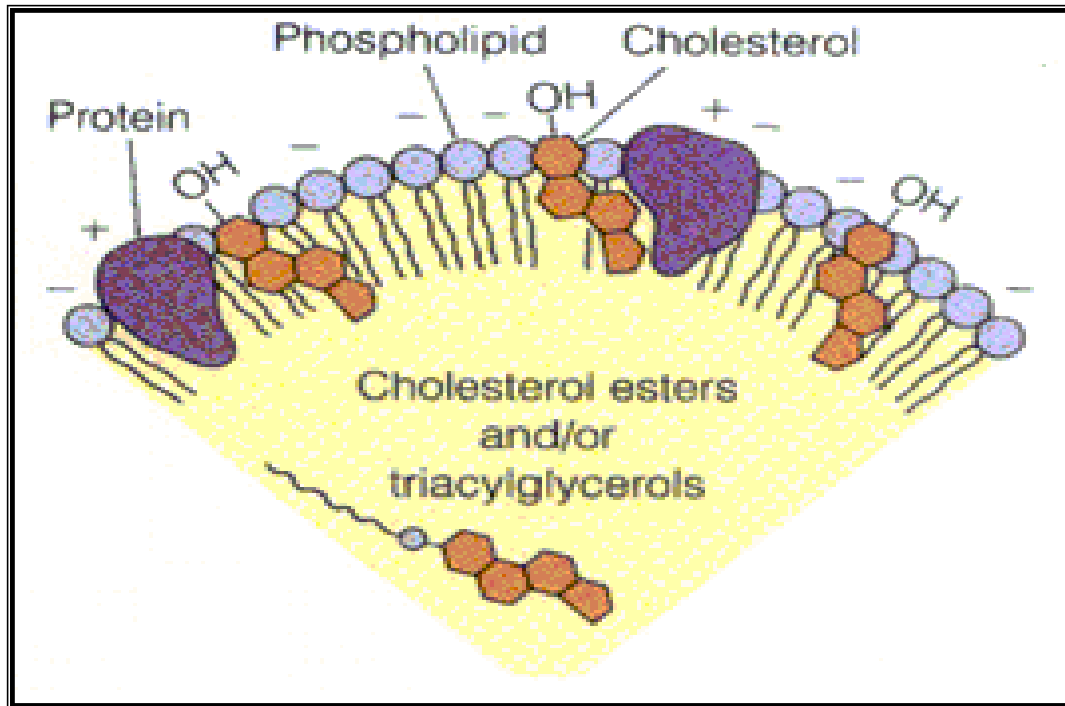


Figure (1-2) : The generalized structure of plasma lipoprotein (Aisen, 1989) .

Plasma lipids consist of triacylglycerol (triglycerides) 16% , phospholipids 30 % , cholesterol 14 % , cholesterol esters 36 % and a much smaller fraction of un esterified long-chain fatty acids or free fatty acids 4 % (Murray, R.K *et al.*, 2003) .

Hyperlipidemia play important roles in the development of atherosclerosis and are strong risk factors for cardiovascular events (Nakamura *et al.*, 2017) , and coronary artery disease , obstructive sleep apnea (Ng , G *et al.*, 2017) .

1-13 : Heart Failure with Trace Elements :

Trace elements are primary nutrients , chemicals with functions of regulatory , immunologic , and antioxidant as they act as essential components or cofactors of some enzymes throughout metabolism (Lobo *et al.*, 2010) .

Every one of trace element contributes differently in many important physiological and biochemical processes in the body , the interaction between trace elements in biological processes play a role in mediating biological and chemical reactions which could be applied to the management of human health (Rasdi *et al.*, 2013) .

Trace elements are being increasingly recognized as essential mediators of the development and progression of heart diseases . It is well known that level of trace elements in serum can affect certain heart diseases such as keshan disease , HF , cardiomyopathy and atherosclerosis (Topuzoglu G, *et al.*, 2003) .

Trace elements may be protective against free radicals in the development of cardiovascular disease (Marin J *et al.*, 1995) .

1-13-1: Iron (Fe) :

Iron is an essential micronutrient in many cellular processes (Wong *et al.*, 2016) . Iron is an element necessary for cells due to its capacity of transporting oxygen and electrons . Iron has biological functions , for example , the formation of haemoglobin , myoglobin and numerous enzymatic groups (Ebner *et al.*, 2013) .

The changes in iron status occurring during the course of HF and the underlying pathomechanisms are largely unknown . Hepcidin , the major regulatory protein for iron metabolism , may play a causative role (Jankowska *et al.*, 2013) .

Iron deficiency (ID) , is common in patients with HF . Observational studies have shown ID to be associated with worse clinical outcomes and mortality . The treatment of ID in HF patients using intravenous iron (Wong *et al.*, 2016) .

In patients with HF , ID correlates with decreased exercise capacity and poor health-related quality of life . Intravenous iron therapy in iron-deficient patients with HF and reduced EF has been shown to alleviate HF symptoms and improve exercise capacity and quality of life (Drozd *et al.*, 2017) .

1-13-2 : Copper (Cu) :

Copper is an essential trace element necessary for many vital functions in the body . Free copper is toxic , however , due to the potential to create ROS . Therefore , copper uptake , distribution , and excretion are tightly regulated (Kim *et al.*, 2008) . (90-95) % of human plasma copper is associated with the Cp the remaining (5-10) % of plasma copper is fairly loosely attached to albumin and histidine , but only a trace of copper is present as free copper (Burtis, C.A. , and Ashwood, 1996) .

Copper plays key catalytic and regulatory roles in biochemical processes essential for normal growth , development , and health (Chun *et al.*, 2017) .

Defects in copper metabolism cause Menkes and Wilson's disease myeloneuropathy , and cardiovascular disease and are associated with other pathophysiological states (Chun *et al.*, 2017) .

1-14 : Aims of Study :

This study is designed to provide information on the following aims :

- 1- Investigation the role of oxidative stress in HF .
- 2- Evaluation of lipid profile in the HF patients .
- 3- Evaluation the levels of iron and copper in HF.
- 4- Investigation the role of some variables (types of disease , sex and age , as well as smoking) on the mentioned parameters in HF.

CHAPTER TWO

METHODS AND MATERIALS

2.1 : Design of study :

This study conducted at AL-Hussein Teaching Hospital in Thi-Qar , Iraq , in the coronary care unit (CCU) , biochemistry laboratory at the period between 1/11/2016 and 1/8/2017 .

The study include (148) subjects , (74) patients with Heart Failure (mild , moderate and severe) [37 males and 37 females] with age range (40—79) years . While the control group , consists of (74) apparent healthy subjects [37 males and 37 females] with no history of systematic illness at age range (40 –79) years .

Table (2-1) : Data of patients HF and controls groups .

Groups	NO
Patients	74
Controls	74

Subjects are divided according to several variables as the following

I: According to type of disease (Type of HF) :

A Group HF mild :- including (25) patients .

A Group HF mod :- including (24) patients .

A Group HF severe :- including (25) patients .

as shown in Table (2-2) .

Table (2-2) : Data of the studied groups .

Type of disease	NO
HF mild	25
HF mod	24
HF severe	25

II: According to the sex as shown in Table (2-3) .

Table (2-3) : Data of all sex groups .

Sex groups	NO	
	Control	Patient
Male	37	37
Female	37	37

III: According to the age

Table (2-4) : Data of all age groups .

groups	Age (year)	NO	
		Control	Patient
A	(40-49)	15	15
B	(50-59)	15	15
C	(60-69)	20	20
D	(70-79)	24	24

III : According to the smoking

Table (2-5) : Data of smoking groups .

<i>Smoking group</i>	<i>HF</i>	control
Smokers	37	37
Non-smokers	37	37

2-2: Collection of blood samples :

Blood samples are collected after the echocardiogram had been recorded . About (8 mL) of blood samples of HF patients and controls are taken and allowed to clot at room temperature in empty disposable tubes and centrifuged to separate it at 3000 rotor per minute (rpm) for 10 min , the serum samples are separated and stored at (-20°C) for later measurement of biochemical parameters , unless used immediately.

The clinical chart and biochemical tests of this study describes experimental parameters in the following Table (2-6 a) and (2-6 b) .

Table(2-6 a) : The clinical chart of the study .

Patient profile	
Name:-	
Age:-	
Sex:-	
Drug:-	
Other disease	IHD HTN RF DM
Others:-	
Smoking:-	
ECG:- Normal abnormal	
Echo HF:- Positive (+) Negative (-)	
Systolic HF Diastolic HF	
mild mod severe	

Table(2-6 b) : Biochemical tests of the study .

Biochemical tests	
Lipid peroxidation:-	Serum Malondialdehyde (MDA)
Antioxidants:-	Serum Ceruloplasmin
	Serum Transferrin
Lipid Profile:- (TCH , TG , HDL-C , LDL-C , VLDL)	
Trace Elements:-	Serum Iron
	Serum Copper

2-3: Chemicals :

The chemicals used in this study with their companies are shown with suppliers in Table (2-7) .

Table (2-7) : Chemicals and their suppliers .

Chemicals	Suppliers
Cholesterol Kit	Biolabo , France
Copper Kit	LTA , Italia
Glucil acetic acid	BDH , England
HDL-C Kit	Biolabo , France
Iron Kit	Biolabo , France
Para pheneline di amine (PPD)	BDH , England
Sodium acetate	BDH , England
Sodium azide	Reidledenhain , Germany
Tri chloro acetic acid (TCA)	BDH , England
Thio bar bituric acid (TBA)	BDH , England
Total Iron Binding Capacity (TIBC) Kit	Biolabo , France
Triglyceride Kit	Biolabo , France

2-4: Instruments :

The instruments are available in the laboratories of chemistry department in the college of science (University of Thi-Qar) which are shown in Table (2-8) .

Table (2-8) : The instruments and their manufacturers .

Instruments	Manufacturers
Centrifuge	Universal 16A , Germany
Incubator	Jard , Japan
Sensitive balance	MO.12307078 , Japan
Shacking water bath	SW23 , Germany
UV/VIS spectrophotometer	CECiL CE 1011, England
Water bath	L513-0814 , French

2-5: Biochemical parameters :

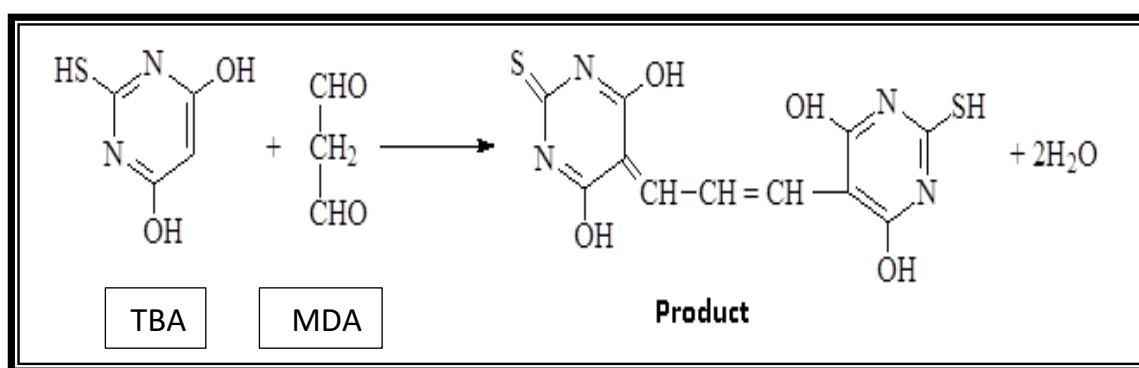
Several considerable methods are used to measure the studied parameters . It is notable that all measurements are duplicated for each sample .

2.5.1 : Determination of Serum Malondialdehyde ($\mu\text{mol/L}$) Concentration :

Principle :

Malondialdehyde (MDA) is an end-product formed during lipid peroxidation , due to degradation of cellular membrane phospholipids . MDA is released into extracellular space and finally into the blood ; it has been used as an effective biomarker of lipid oxidation (Lorente *et al.*, 2015) . MDA formed from the breakdown of polyunsaturated fatty acids are identified as the product of LPO that react with thiobarbituric acid

(TBA) , in coexisting trichloro acetic acid (TCA) , to give a red chromophore absorbing at 532 nm (Fong *et al.*, 1973) . MDA concentration are calculated , using the molar extinction coefficient of MDA ($\mathcal{E}_{MDA}$) equal to $1.56 \times 10^5 \text{ mol}^{-1} \cdot \text{cm}^{-1}$ (Wills, 1969) . MDA formed from breakdown of polyunsaturated fatty acid , serves as a convenient index of peroxidation reaction (Emad, A. and Sanaa, M. 2013)



Procedure :

The level of serum MDA is determined spectrophotometrically with a thiobarbituric acid (TBA) solution . In brief , to 150 μl serum sample the following are added : 1ml (17.5%) trichloroacetic acid (TCA) and 1ml of 0.66 % TBA , mixed , incubated in boiling water for 15 minutes , and then allowed to cool . One ml of 70 % TCA is added and the mixture allowed to stand at room temperature for 20 minutes , centrifuged at 2000 rpm for 15 minutes , the supernatant is taken out for scanning spectrophotometrically at (532nm) (Muslih R D, 2002) . The concentration of MDA calculated as follows :-

$$\text{MDA} \left(\frac{\mu\text{mol}}{L} \right) = \frac{\text{absorbance at } 532\text{nm}}{L \times E_0} \times D \times 10^6$$

L : light path (1cm)

E0 : Extinction coefficient $1.56 \times 10^5 \text{ M}^{-1} \cdot \text{Cm}^{-1}$

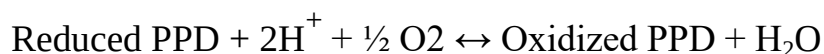
D : Dilution factor = $3.15 \text{ ml Vol. Used in ref.} / 0.15 = 21$

2.5.2 : Determination of Ceruloplasmin (Cp) (g/L)

Concentration :

Principle :

Plasma Cp concentration is measured by the method of (Menden, C *et al.*, 1977) . It is based on the Cp-catalyzed oxidation of color less para-phenyl ene diamine (PPD) to blue-violet oxidize form . The reaction is followed photometrically and the blank value is determined after inhibition of the enzyme with sodium azide at (0C^0) .



(Colorless)

(Blue)

A mixture of serum , substrate and acetate buffer at pH = 6.0 is incubated at 37°C for 15 min . The reaction is stopped by the addition of sodium azide , and the absorbance of the purple color formed (Oxidized PPD) in the diluted test mixture is read at 525 nm against blank solution. The corrected absorbance is directly related to the concentration of Cp (Herbert A. Ravin, 1961) .

Reagents :

● Substrate solution :

Fifty mg of PPD is dissolved in 5 mL (4 mL of distilled water (D.W) and 1 mL of glacial acetic acid). In another container 8.15gm sodium acetate tri hydrate is dissolved in 30 mL of D.W then added to the first solution , mixed and completed the volume to 50 mL with D.W. This solution is stable for three hours and its kept refrigerated in a dark bottle (Menden, C *et al.*, 1977) .

● Inactivating solution :

One hundred mg of sodium azide was dissolved in (500 mL) of D.W then is kept cold in refrigerator prior to use , this solution must be prepared every week .

Procedure :

- One mL of substrate is pipetted into test tubes , incubated at 37 °C for 1 min .
- One hundred µL of plasma is added , incubated at 37 °C for 15 min , then tubes are removed and placed in iced-bath for 30 min .
- Five mL of cold inactivating solution was added , mixed and the temperature is brought to 25 °C in water bath .
- Blank was prepared by combining the substrate , inactivating solution , and 0.1 mL of D.W, then the mixture is incubated as above .
- The absorbance of test and blank was read in spectrophotometer at 525nm .

- The concentration of Cp is calculated using the extinction coefficient of Cp (ϵ_{Cp}) equal to (0.68) .

$$\text{Serum Cp (g/L)} = \frac{A_{test} - A_{blank}}{\epsilon_{Cp}} \times 10 = \frac{\Delta A \times 10}{0.68}$$

2.5.3 : Determination of Transferrin (g/L) Concentration :

2.5.3.1 : Determination of Serum Iron Concentration :

Principle : (Hennessy *et al.*, 1984)

After dissociation of iron-transferrin bound in acid medium , ascorbic acid reduces Fe^{+3} iron into Fe^{+2} iron . Fe^{+2} iron then forms a coloured complex with 3-(2-pyridyl) -5, -6 difuryl-1, -2,-4triazine-disulfonate (Ferene) . The absorbance thus measured at 600nm (580-620) is directly proportional to the amount of iron in the specimen . Thiourea is added in the reagent to prevent the copper interference .

Reagents Composition :

Reagent	Composition
R1: Reductant	Citric acid 150 mmol/L Ascorbic acid 30mmol/L Thiourea 27mmol/L
R2: Chromogen	Ferene 600 μ mol/L
R3 : Standard	Iron 200 μ g/dL (35.8 μ mol/L)

Reagents Preparation :

- 1- Working reagent is prepared as follows : R1 + R2 .
- 2- Used carefully cleaned material with HCl 0.1 N and well rinsed with distilled water .

Manual procedure :

Stand reagents and specimens are let at room temperature . Two set of tubes were prepared according to following boards :

Blank- Tubes	Blank	Standard	Assay
Reagent R1	1mL	1mL	1mL
Specimen			200µL
Standard		200µL	
Distilled water	200µL		
All tubes mixed and let stand for at least 3 mins at room temperature . Recorded A1 absorbances at 600 nm (580-620) against blank			

Assay- Tubes	Blank	Standard	Assay
Working Reagent	1mL	1mL	1mL
Specimen			200µL
Standard		200µL	
Distilled water	200µL		
All tubes mixed and let stand for 5 mins at room temperatur Recorded A2 absorbances at 600 nm (580-620) against blank . Colour was stable for 1h			

Calculation :

$$\text{Serum Iron conc}(\mu\text{mol/L}) = \frac{(\text{A2-A1}) \text{ Assy}}{(\text{A2-A1}) \text{ Standard}} \times \text{Conc. Stand (200}\mu\text{g / dL)}$$

2.5.3.2 : Total Iron Binding Capacity (TIBC) ($\mu\text{g/L}$)

Concentration (Ramsay, 1958 ; Burtis C.A. and Ashwood E R, 1999).

Principle :

Total iron-binding capacity (T.I.B.C.) is determined by addition of sufficient Fe^{+3} to saturate iron binding sites on apo transferrin . The excess Fe^{+3} is removed by adsorption with basic magnesium carbonate powder .

After centrifugation , bound iron remaining in supernatant is measured with direct method (Ferene) or with deproteinization method .

Reagents :

Contents	Concentration
R1: Iron solution	Hydrochloric acid 5mmol/L. Ferric chloride $\geq 502 \mu\text{g/dL}$ ($\geq 90\mu\text{mol/L}$)
R2 : Precipitant	Magnesium carbonate 150 mg/capsule

Manual Procedure :

Reagent and sample are left stand at room temperature .

The following components are pipetted in centrifuge tube	
Specimen	1mL
Iron solution (vialR1)	2mL
Mix , wait 10 minutes then add :	
Precipitant (capsule R2)	150mg (The contents of a capsule)
All tubes mixed and let stand at room temperature for 30 min . shaking on a rotary or swinging agitator . Centrifuge 10 min at 3000 rpm .	

Calculation:

1- The result is calculated as in the reagent technical data sheet used for iron determination .

2- TIBC is calculated as follows :

TIBC = Iron concentration measured in supernatant x5

Calculate Transferrin concentrations :

$$\text{Tf (g/L)} = \text{TIBC } (\mu\text{g/L}) \times 0.007$$

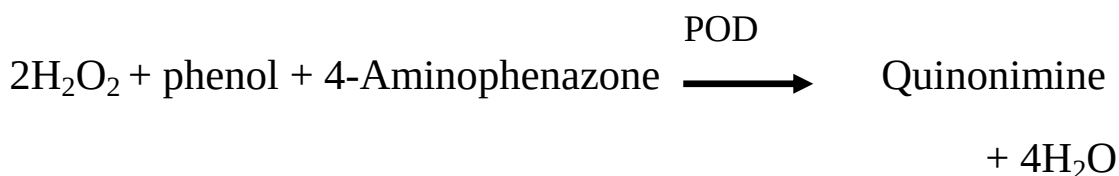
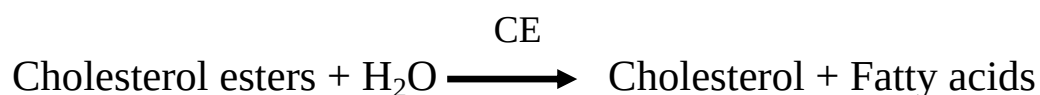
2.5.4: Determination of Serum Lipid Profile :

2.5.4.1: Determination of Serum Cholesterol :

Concentrations: (Meiattini *et al.*, 1978 ; Naito, H.K. , and Kaplan, 1984)

Principle :

The cholesterol present in the sample originates a colored complex , according to the following reaction :



The intensity of the color formed is proportional to the cholesterol concentration in the sample .

Reagents :

R1: Buffer	Phosphate buffer 100 mmol /L Chloro-4-phenol 5 mmol /L Sodium Cholate 2.3 mmol/L Triton *100 1.5 mmol /L
R2: Enzymes	Cholesterol oxydase (CO) ≥ 100 IU/L Cholesterol esterase (CE) ≥ 170 IU/L peroxydase (POD) ≥ 1200 IU/L 4-Amino-antipyrine (PAP) 0.25 mmol/L PFG 6000 167 μ mol/L
R3: Standard	Cholesterol 200 mg/dL (5.17 mmol/L)

Preparation :

Working reagent (WR) : The contents are dissolved of one vial R2 enzymes in one bottle of R1 buffer .

The contents are capped and mixed gently .

Procedure :

	Blank	standard	Assay
Working reagent	1 mL	1 mL	1 ml
D.W	10 μ L	...	...
Standard	...	10 μ L	...
specimen	...	...	10 μ L

1. Mixed and incubated for 5 minutes at 37 °C or 10 minutes at room temperature .
2. The absorbance (A) of the samples and standard, are read against the blank at wavelength 500 nm .

Calculation :

$$\text{Conce of TCH. (mg/dL)} = \frac{\text{Abs (Assay)}}{\text{Abs (standard)}} \times 200$$

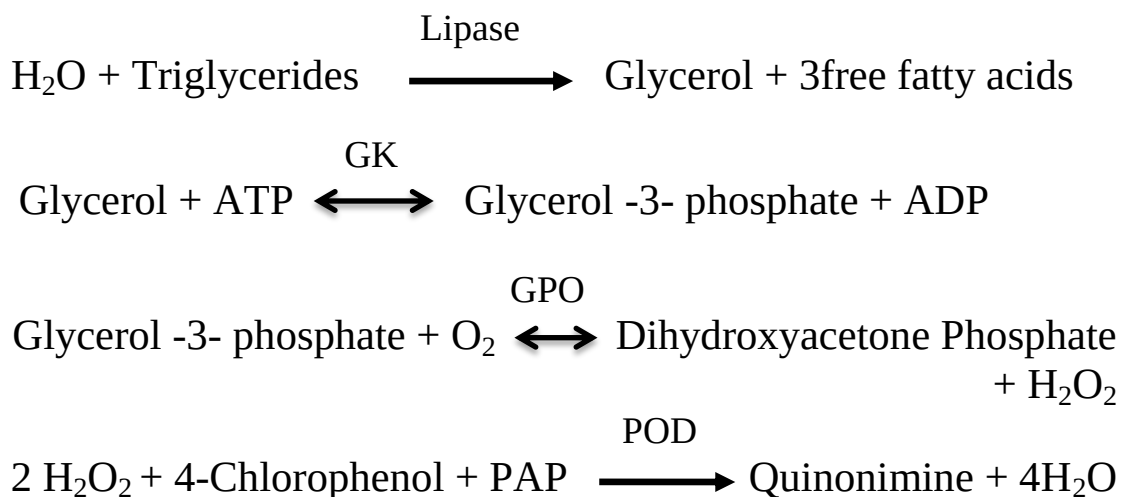
2.5.4.2 : Determination of Serum Triglyceride (mg/dL)

Concentrations :

The used reagents are supplied via Biolabo (France) , and Serum TG are measured according to (Tietz, 1999) .

Principle : (Trinder, P. , and Prencipe, 1969 ; Fossati and Prencipe, 1982)

Fossati and Prencipe method associated with Trinder reaction .
Reaction scheme is as follows :



Reagents composition :

Reagent	Composition
R1: Buffer	Pipes 100 mmol/L Magnesium chloride 9.8 mmol/L Chloro-4-phrnl 3.5 mmol/L
R2: Enzymes	Lipase ≥ 1000 IU/L Peroxidase (POD) ≥ 1700 IU/L, Glycerol-3-phosphate oxidase (GPO) ≥ 3000 IU/L Glycerol kinase (GK) ≥ 660 IU/L 4-aminoantipyrine (PAP) 0.5 mmol/L ATP 1.3 mmol/L
R3: Standard	2.28 mmol/L (200mg/dL)

Manual procedure :

- 1- R1 + R2 = Reagent
- 2- Reagent and sample are left stand at room temperature .

	Blank	Standard	Assay
Reagent	1 mL	1 mL	1 mL
D.W	10 μ L		
Standard		10 μ L	
Specimen			10 μ L

All tubes mixed and let stand for 5 minutes at 37°C or 10 minutes at room temperature

Absorbance are recorded at 500 nm against reagent blank .

Calculation :

The result is calculated as follows :

$$\text{Conce of Tg. (mg/dL)} = \frac{\Delta A_{\text{Assay}}}{\Delta A_{\text{standard}}} \times 200$$

Standard concentration = 200 mg/dL

2.5.4.3: Determination of Serum VLDL Concentration :

VLDL is calculated through the following equation :

$$\text{VLDL (mg/dL)} = \text{Triglyceride}/5$$

2.5.4.4: Determination of Serum HDL-C Concentration :

Principle :

Chylomicrons (CM) , very low density lipoproteins (VLDL) and low density lipoproteins (LDL) contained in the specimen are precipitated by the addition of phosphotungstic acid in the presence of magnesium ions (Burstein *et al.* , 1970 ; Lopes Virella *et al.*, 1977) . The supernatant is obtained after centrifugation contains high density lipoproteins (HDL) . The cholesterol bound to the HDL is determined using the cholesterol RTU reagent .

Reagents composition :

R1: precipitant	Phosphotungstic acid (PTA) 1.39 mmol/L Magnesium chloride 570 mmol/L
R2: Standard	Cholesterol 100mg/dL (2.58 mmol/L)

Procedure

- 1- Add 500 µL (0.5mL) from serum .
- 2- Add 50 µL from Precipitant .
- 3- Mixed . Wait 10 minutes in room temperature .
- 4- Centrifuge for 15 minutes at 3500 – 4000 rpm .

After centrifugation , the supernatant must be clear . Where the leachate is formed is Supernatant

	Blank	standard	Assay
Reagent(From Cholesterol)	1mL	1mL	1mL
D.W	25 µL	–	–
Standard 100 mg/dL		25 µL	
Supernatant (from above)			25 µL
All tubes mixed. Incubated for 5 mins at 37°C or 10 mins at room temperature Record absorbance at 500 nm against reagent blank .			

Calculation :

$$\text{Conce of HDL (mg/dL)} = \frac{\text{Abs}_{\text{Assay}}}{\text{Abs}_{\text{standard}}} \times \text{standard concentration} \times 1.1$$

standard concentration = 100 mg/dL

2.5.4.5: Determination of Serum LDL Concentration :

LDL is calculated through the following equation :

$$LDL = \text{Cholesterol con.} - (Tg \times 5) - HDL \text{ con.} = (\text{mmol/L})$$

2.5.5: Determination of Trace Elements Concentrations :

2.5.5.1: Determination of Serum Iron ($\mu\text{mol/L}$) Concentration :

The procedure of determination of iron in serum is show in section (2-5-3-1) .

2.5.5.2: Determination of Serum Copper ($\mu\text{mol/L}$) Concentration :

Principle :

The cupric ions react with the chromogen Di-BrPAESA forming a blue compound , which intensity is proportional to the concentration present in the sample (Pasquinelli F, 1984 ; Ciuti R. and Galli A., 1987 ; Abe , A *et al* ., 1989) .

Reagents :

Reagents	Concentration
Reagent A :	Acetate buffer PH 4.9 reducing agents and preservatives. 0.1M
Reagent B :	3,5 Di-Br-PAESA
Standard	Ion copper ($200\mu\text{g/dL}$) ; preservatives

Preparation Reagent :

The work reagent is prepared by mixing in equal quantity the reagent A with reagent B .

Procedure :

Reagent	Blank	Standard	Sample
Working Reagent	1mL	1mL	1mL
Distilled Water	66 µL		
Standard		66 µL	
Sample			66 µL

All tubes mixed and waited for 10 minutes then is read the absorbances against the blank at 580 nm . The colour is stable for 30 minutes .

Calculation :

$$\text{Copper conc. (}\mu\text{mol/L)} = \frac{\Delta A_{\text{sample}}}{\Delta A_{\text{standard}}} \times \text{Conc. of standard (3.15)}$$

2-6: Statistical Analysis :

The statistical analysis used in this study is done using Microsoft Excel 2010 , the results are expressed as mean $\pm$ standard deviations (mean $\pm$ SD) with LSD test . One way ANOVA-test is used to compare parameters in different studied groups . P-values ($P \leq 0.05$) are considered statistically significant .

CHAPTER THREE

RESULTS AND DISCUSSION

3.1 : General Comparison for all Studied Parameters :

3.1.1 : Serum Malondialdehyde Concentration :

Table (3-1) and Figure (3-1) show a significant increase in concentrations of serum MDA in patients HF group in comparison with control group ($P \leq 0.05$) . This result is approach to the result of (Rajesh *et al.*, 2011) .

MDA is the final product of lipid peroxidation , by converting the peroxidation of unsaturated fatty acids to MDA , which reflects cases of increased free radical generation and oxidative stress (Slatter *et al.*, 2000) . Serum MDA levels is frequently used to establish oxidative stress , and it is useful as an oxidative stress marker (Bulut *et al.*, 2007) .

Lipid peroxidation and oxidative damage which is caused by ROS and free radicals often associate with the emergence of many disease (Del Rio *et al.*, 2005) .

Also , higher levels of MDA have been observed in atherosclerotic patients compared to control patients (Cavalca *et al.*, 2001 ; Tamer *et al.*, 2002) .

Table (3 – 1) : Serum MDA concentrations in control and HF group .

Group	NO	MDA concentration ($\mu\text{mol/L}$) mean $\pm$ SD
control	74	1.77 $\pm$ 0.22 ^b
HF	74	3.19 $\pm$ 0.68 ^a
LSD		0.87

Note :- Each value represents mean $\pm$ S.D values with non-identical superscript (a , b or c...etc.) for vertical comparison and (*) for horizontal comparison , are considered significantly differences ($P \leq 0.05$) .

- HF : Patients with Heart Failure group .
- N : Number of subjects .
- SD : Standard deviation .
- LSD : Least Significant Difference .

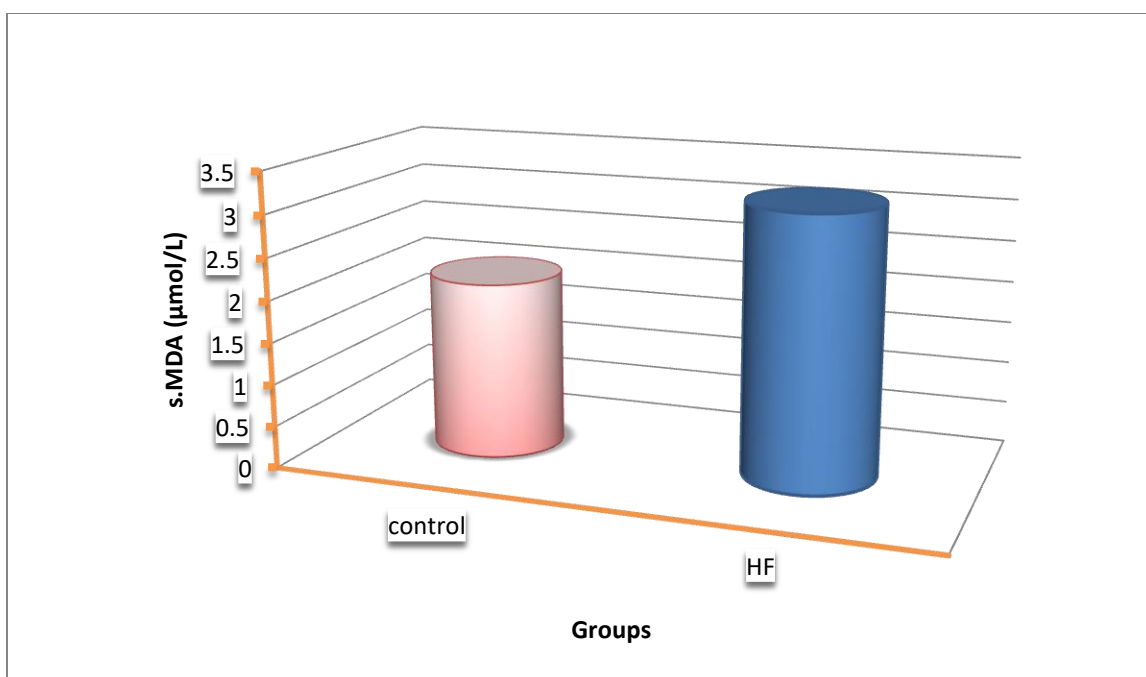


Figure (3-1) : Serum MDA levels of control and HF groups .

3.1.2 : Antioxidant System :

3.1.2.1: Serum Ceruloplasmin Concentrations :

Table (3-2) and Figure (3-2) show a significant increase in concentrations of serum Cp levels in HF patients group in comparison with control group ($P \leq 0.05$) .

Increasing the Cp levels in HF patients due to impairment of the oxidant-antioxidant balance in favour of the oxidants .

Lipid peroxidation and antioxidant change and their significance during myocardial injury have provided a new insight in the pathogenesis of heart disease (Yogeeta *et al.*, 2006) .

Antioxidant , including Cp , terminates the chain of the reaction by removing free radicals and inhibits other oxidation reaction by oxidizing themselves . The imbalance between free radicals formation and antioxidant activity is called oxidative stress . When the oxidative stress is unbalanced in favor for free radicals , such as acute and chronic exercises , damage occurs to many cellular membranes of tissues such as the heart and skeletal muscles (Jenkinson *et al.*, 1999) .

Table (3 -2) : Serum Cp concentrations of control and HF groups .

Group	NO	Cp concentration (g/L) mean± SD
control	74	2.35±0.66 ^b
HF	74	3.97±0.7 ^a
LSD		0.52

- Legend as in table (3- 1)

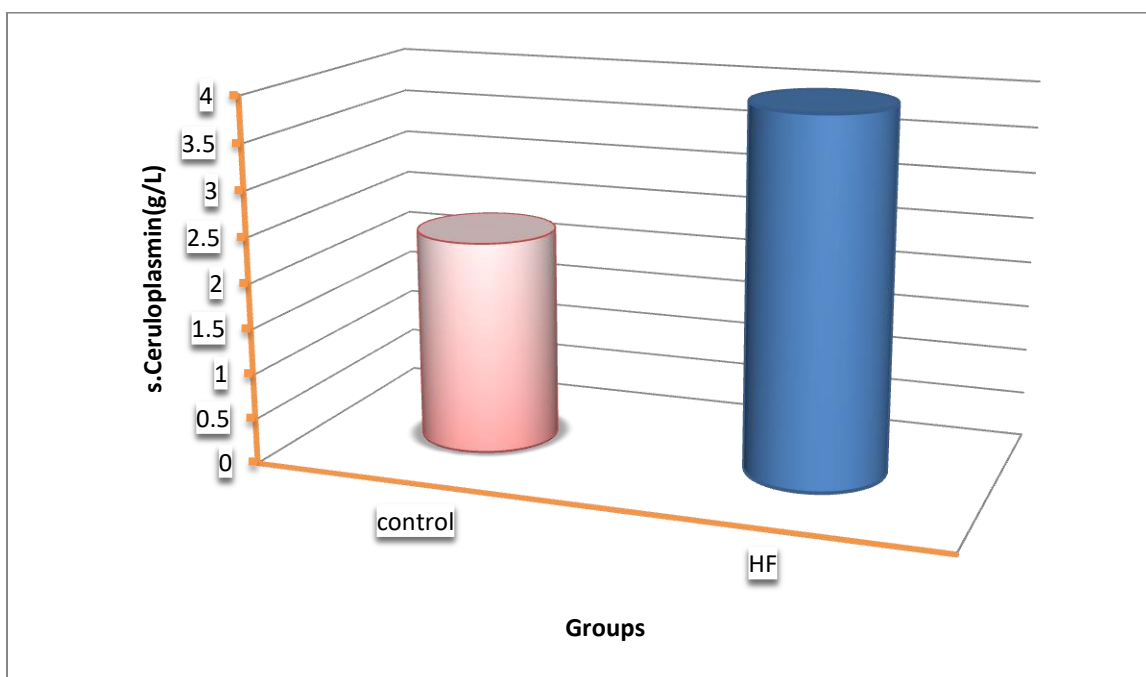


Figure (3-2) : Serum Cp levels of control and HF groups .

3.1.2.2 : Serum Transferrin Concentrations :

Table (3-3) and Figure (3-3) show a significant decrease in concentration of serum Tf in HF patients group when compared with control group ($P \leq 0.05$) . This result is approach to the result of (Hadeel *et al.*, 2012) .

Tf is one of protective antioxidants that prevent the formation of free radicals . It prevents the associated metal iron from interacting with the H_2O_2 to form free radicals , as well as Tf works to remove $O_2^{\cdot -}$ the root of superoxide negative . The Tf works to reduce oxidative stress that occurs in patients with HF , so its levels will be decreased (Sarah *et al .*, 2017) .

Table (3 – 3) : Serum Tf concentrations of control and HF groups .

Group	NO	Tf concentration (g/L) mean± SD
control	74	3.8±0.58 ^a
HF	74	2.53±0.29 ^b
LSD		0.13

- Legend as in table (3- 1)

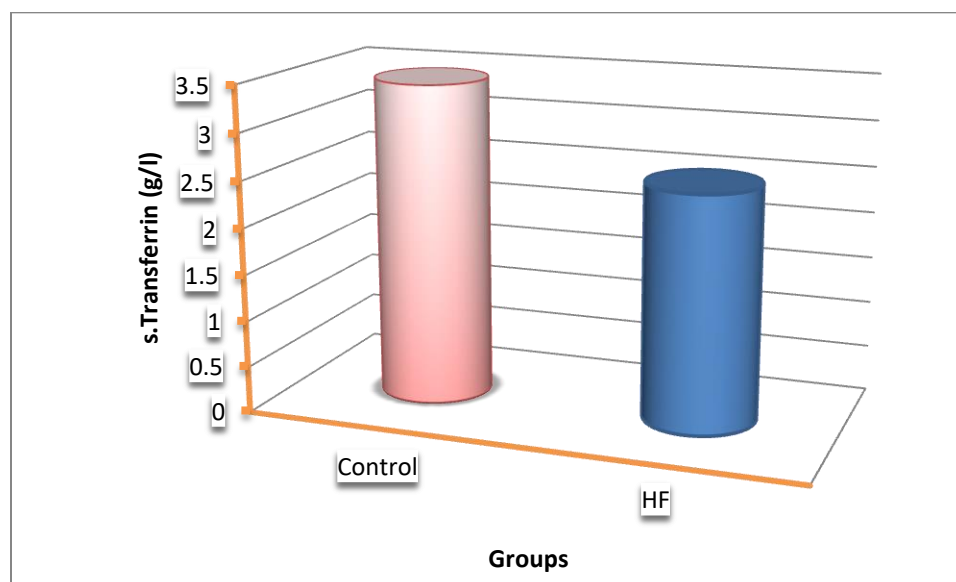


Figure (3-3) : Serum Tf levels of control and HF groups .

3.1.3 : Serum Lipid Profile Concentrations :

Table (3-4) and Figure (3-4) show the levels of lipid profile in HF and control groups . TCH , TG , LDL-C and VLDL levels are significantly increased ($p \leq 0.05$) while the HDL-C level is significantly decreased in HF compared with the control groups . This result is approach to the result of (Rajesh *et al.*, 2011) .

High levels of TCH , LDL-C and TG and low levels of HDL-C cause deposition of lipid in arteries thus causing atherosclerosis . So lipid profiles are routinely measured for risk assessment in preventing (Coronary Artery Diseases) CAD (Wattanasuwan *et al.*, 2001) .

The lipids and lipoproteins which are central in the metabolism of the body have become increasingly important in clinical practice , primarily because of their association with coronary heart disease (Nicholas *et al.*, 2006) .

Abnormal lipid profile is reported to be an important risk factor for atherosclerosis and ischemic heart disease (Fox, 2002) . High plasma concentrations of cholesterol are ones of the principal risk factors for atherosclerosis (Shepherd *et al.*, 1995) .

Triglyceride elevation has a questionable role in CAD etiology . It has been shown that high triglyceride levels are linked to the progression of CAD (Assmann *et al.*, 1996) .

On the other hand , several studies have confirmed the association between a low HDL-C and an increased risk of coronary heart disease (Gordon *et al.*, 1989; Thombs, *et al.*, 2008) .

HDL-C may be protective by reversing cholesterol transport , inhibiting the oxidation of LDL-C and by neutralizing the atherogenic effects of oxidized LDL-C . A greater increase of LDL-C may also cause a greater decrease of HDL-C as there is a reciprocal relationship between the concentrations of LDL-C and HDL-C (Kaviarasan *et al.*, 2005) .

Table (3 – 4) : Serum Lipid Profile concentrations of control and HF groups .

Groups	NO	TCH mg/dL	TG mg/dL	HDL-C mg/dL	LDL-C mg/dL	VLDL mg/dL
control	74	172.5±11.2 ^b	106.32±19.3 ^b	50.02±6.0 ^a	101.2±14.0 ^b	21.26±4.2 ^b
HF	74	245.55±34.4 ^a	155.75±31.4 ^a	32.59±7.7 ^b	182.7±57.7 ^a	31.15±5.4 ^a
LSD		10.55	15.35	8.15	16.26	8.32

- Legend as in table (3- 1)

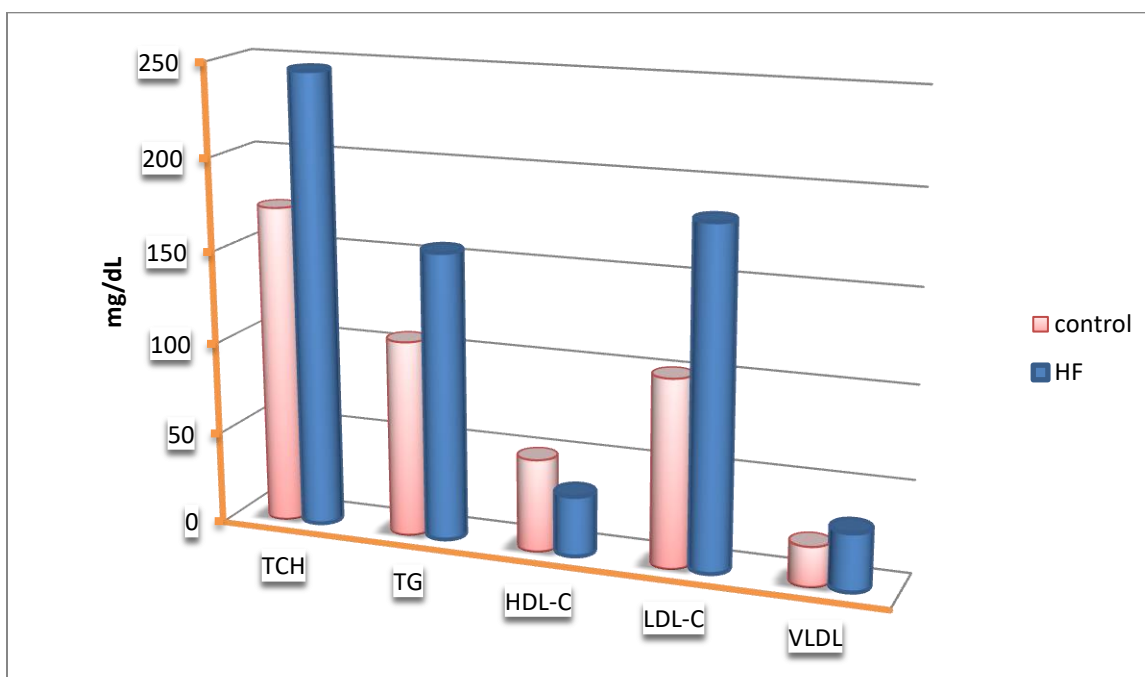


Figure (3-4) : Lipid profile levels of control and HF groups .

3.1.4 : Serum Trace Elements Concentrations :

Table (3-5) and Figure (3- 5) show a significant decrease in Iron level in patients group in comparison with control group ($P \leq 0.05$) . This result is approach to the result of (Ebner and Haehling, 2013 ; Wang *et al.*, 2016) . And serum copper concentrations in HF patients are significantly higher than in controls ($P \leq 0.05$) ,

The sequence of changes in iron status occurring during the natural history of HF and the pathomechanisms triggering ID in these patients still remain enigmatic . Hepcidin as the major regulatory protein of iron metabolism may play a causative role in HF (Nemeth and Ganz, 2009) . The hepatic upregulation of hepcidin has been shown to be centrally involved in the pathogenesis of ID and

anaemia associated with chronic inflammatory diseases , including chronic kidney disease (CKD) , infections , cancer , autoimmune diseases (Rumjon *et al.*, 2012) . Available evidence on detailed iron status in HF is scarce and equivocal (Jankowska, E *et al.*, 2013) .

Table (3 – 5) : Serum (Iron , Copper) concentrations of control and HF groups .

Groups	NO	Iron $\mu\text{mol/L}$ Mean $\pm$ SD	Copper $\mu\text{mol/L}$ Mean $\pm$ SD
control	74	21.79 $\pm$ 7.02 ^a	18.22 $\pm$ 2.8 ^b
HF	74	12.20 $\pm$ 7.25 ^b	23.5 $\pm$ 3.6 ^a
LSD		6.45	1.8

- Legend as in table (3- 1)

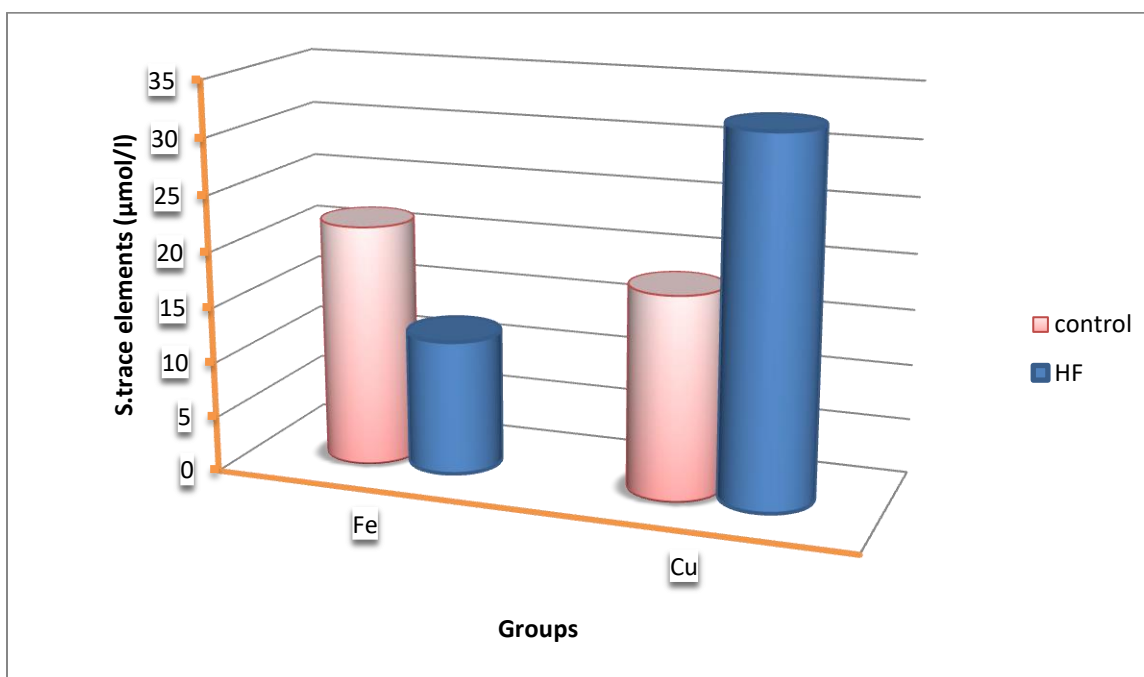


Figure (3-5) : Serum (Iron , Copper) levels of control and HF groups .

3.2 : The Studied Parameters According to Types of HF :

3.2.1 : Serum Malondialdehyde Concentration :

Table (3-6) and Figure (3-6) show a significant increase in concentration of serum MDA in all HF groups in comparison with control group ($p \leq 0.05$) . In the same table , It is find a significant increase in concentration of serum MDA in (HF severe) group in comparison with (HF mild and HF mod) group .

Oxidative degradation of lipids is known as lipid peroxidation , and one of the most abundant carbonyl products of lipid peroxidation is MDA , which is an index of oxidative damage (Cavalca *et al.*, 2001) . Increased lipid peroxidation may occur as a result of increased free radical generation (Jayakumari *et al.*, 1992) .

A correlation between MDA and LVEF is found and several further studies imply the causative role of oxidative stress in decreased cardiac output , renin–angiotensin–aldosterone system (RAAS) activation , salt and water retention and progression to more severe cardiac failure (Diaz-Velez *et al.*, 1996 ; Radovanovic *et al.*, 2008).

Table (3 – 6) : Serum MDA concentrations of control , HF mild , HF mod and HF severe groups .

Group	NO	MDA concentration ($\mu\text{mol/L}$) mean $\pm$ SD
Control	74	1.77 $\pm$ 0.22 ^c
HF mild	25	2.504 $\pm$ 0.626 ^b
HF mod	24	2.83 $\pm$ 1.15 ^b
HF severe	25	3.27 $\pm$ 0.82 ^a
LSD		0.44

HF mild :Patients with Heart Failure Mild .

HF mod :Patients with Heart Failure Moderate .

HF severe :Patients with Heart Failure Severe .

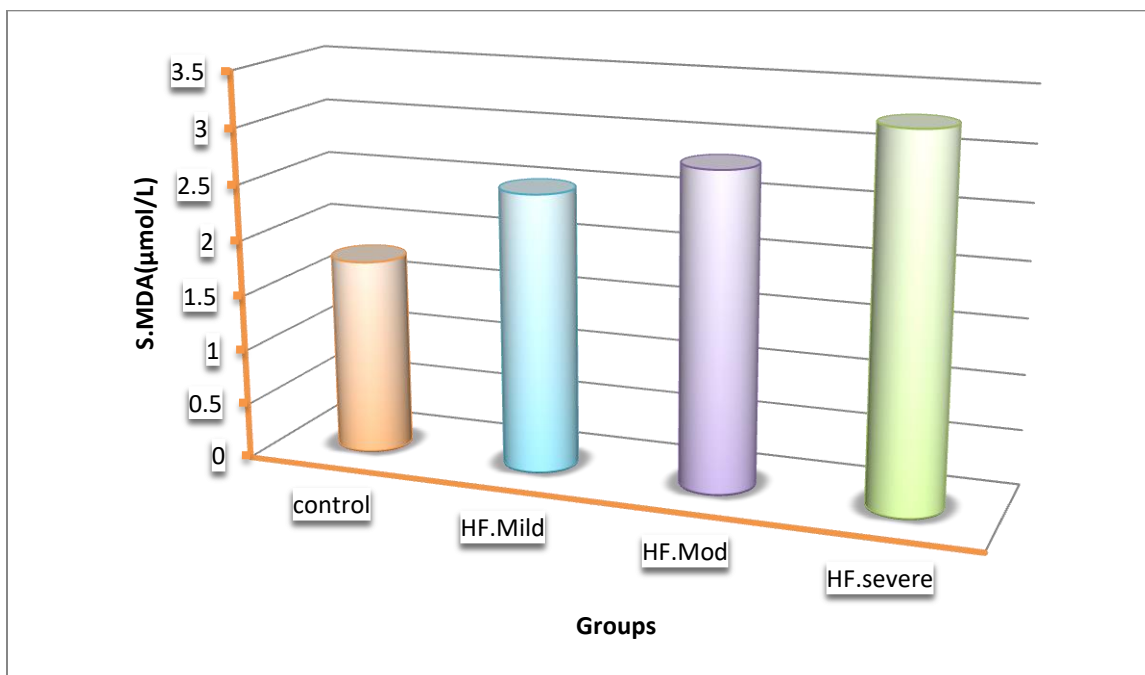


Figure (3-6) : Serum MDA levels of control and Type of HF groups .

3.2.2 : Antioxidant system :

3.2.2.1 : Serum Ceruloplasmin Concentrations :

Table (3-7) and Figure (3-7) show a significant increase in concentration of serum Cp in all patients group in comparison with control group ($p \leq 0.05$) . In the same table , it is find no significant differences in concentration of serum Cp in all patients group .

Many studies have shown that Cp levels are elevated in patients with cardiovascular disorders including arteriosclerosis (Bustamante *et al.*, 1976) , coronary heart disease (Reunanen *et al.*, 1992) , and myocardial infarction (Klipstein *et al.*,1999) . In the IHD , CP is recognized as an inflammation-related marker protein for its predictive value (Ridker *et al.*,1997) .

Considerable research has indicated that increased Cp concentrations are associated with an increased risk of myocardial infarction and stroke (Shukla *et al.*, 2006) .

Table (3 – 7) : Serum Cp concentrations of control , HF mild , HF mod and HF sever groups .

Group	NO	Cp concentration (g/L) mean± SD
Control	74	2.35±0.66 ^b
HF mild	25	3.69±0.66 ^a
HF mod	24	4.233±0.726 ^a
HF severe	25	4.04±0.76 ^a
LSD		0.66

- Legend as in table (3- 6)

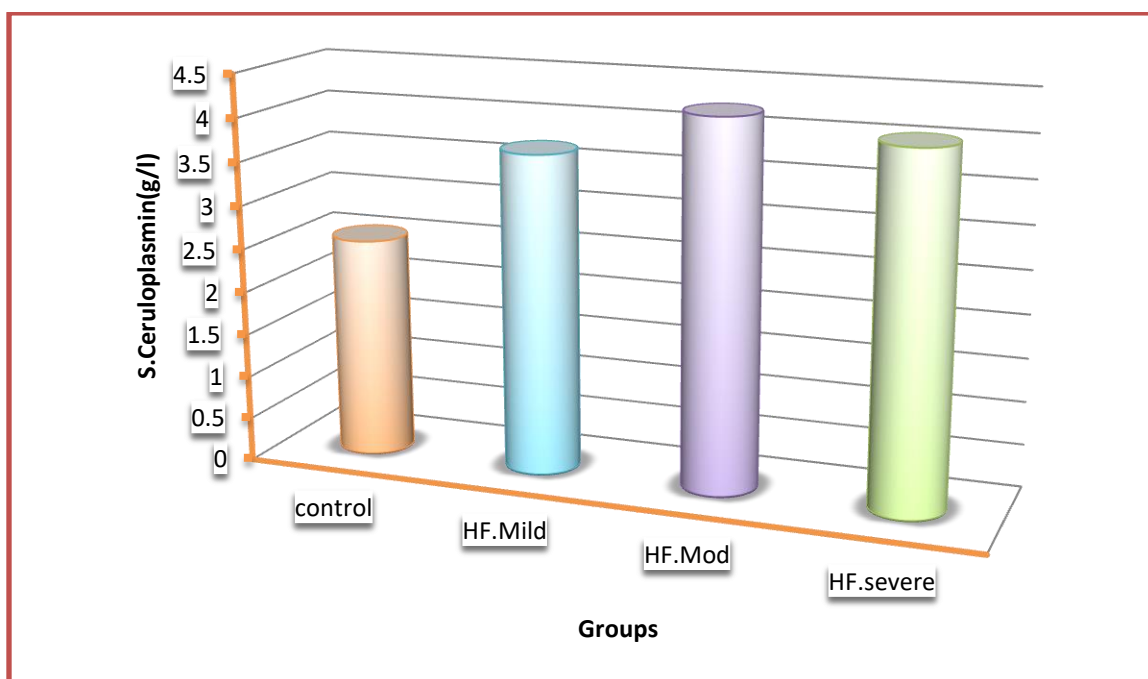


Figure (3-7) : Serum Cp levels of control and Type of HF groups.

3.2.2.2 : Serum Transferrin Concentrations :

Table (3-8) and Figure (3-8) show a significant decrease in concentration of serum Tf in all groups in comparison with control groups ($p \leq 0.05$). In the same table, there are no significant differences in concentration of serum Tf in all patients group ($p \leq 0.05$).

Table (3 – 8) : Serum Tf concentrations of control , HF mild , HF mod and HF severe groups .

Group	NO	Tf concentration (g/L) mean $\pm$ SD
Control	74	3.8 $\pm$ 0.58 ^a
HF mild	25	2.5 $\pm$ 0.31 ^b
HF mod	24	2.6 $\pm$ 0.30 ^b
HF severe	25	2.55 $\pm$ 0.29 ^b
LSD		0.56

- Legend as in table (3- 6)

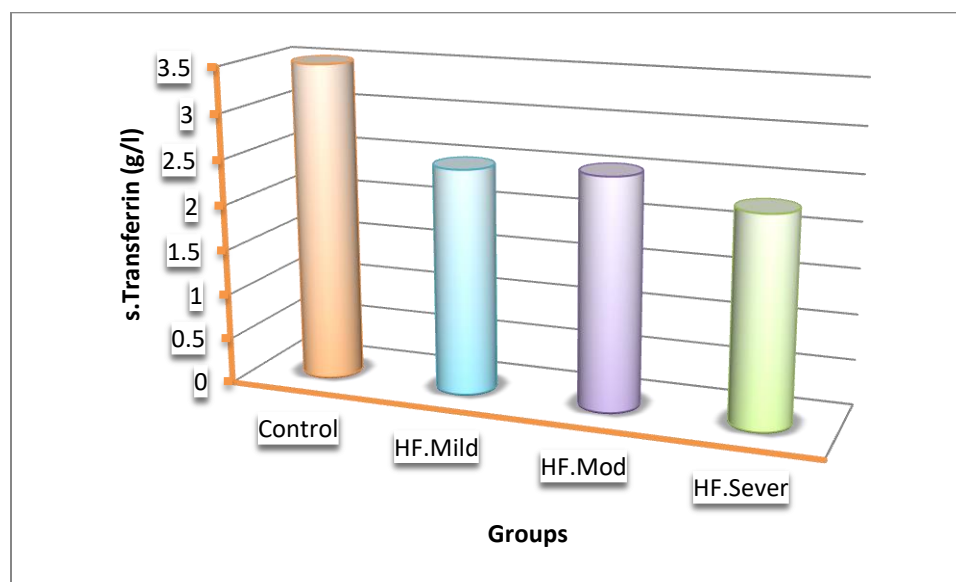


Figure (3-8) : Serum Tf levels of control and Type of HF groups .

3.2.3 : Serum Lipid Profile Concentrations :

Table (3-9) and Figure (3-9) show a significant increase in concentration of serum lipids and lipoproteins except HDL-C in all patients group in comparison with their control group ($p \leq 0.05$) . In the same table , There is a significant decrease in concentration of serum (HDL-C) in patients of (HF severe) group in comparison with patients of (HF mild) group , and significant increase in concentration of serum TCH in patients of (HF severe , HF mod) group in comparison with patients of (HF mild) group ($p \leq 0.05$) , and no significant differences in concentration of serum (TG , VLDL and LDL-C) among all patients groups .

The elevation of blood cholesterol level play important role in the pathogenesis of atherosclerosis , due to precipitation of it on the vascular walls leading to an increase in the shear stress on the vessels , decreasing the lumen size and increasing in the vascular resistance (Stampfer *et al.*, 1991; Erhardt *et al.*, 2002) .

The lipid abnormality is one important risk factor for ischemic heart disease (Rama *et al.*,2012) .

Table (3 – 9) : Serum Lipid Profile concentrations of control , HF Mild ,HF Mod and HF Severe groups .

Groups	NO	TCH mg/dL	TG mg/dL	HDL-C mg/dL	LDL-C mg/dL	VLDL mg/dL
Control	74	172.5±11.2 ^c	106.32±19.30 ^b	50.02±6.0 ^a	101.2±14.0 ^b	21.26±4.2 ^b
HF mild	25	223.82±18.86 ^d	152.34±38.89 ^a	34.85±14.34 ^b	158.49±44.4 ^a	30.46±7.77 ^a
HF mod	24	256.43±24.3 ^a	148.71±29.07 ^a	32.03±18.19 ^{bc}	199.59±64.9 ^a	29.74±5.81 ^a
HF severe	25	267.27±21.85 ^a	168.1±24.34 ^a	29.63±13.12 ^c	204.02±60.3 ^a	33.62±4.86 ^a
LSD		16.42	25.102	2.8	20.98	4.99

- Legend as in table (3- 6)

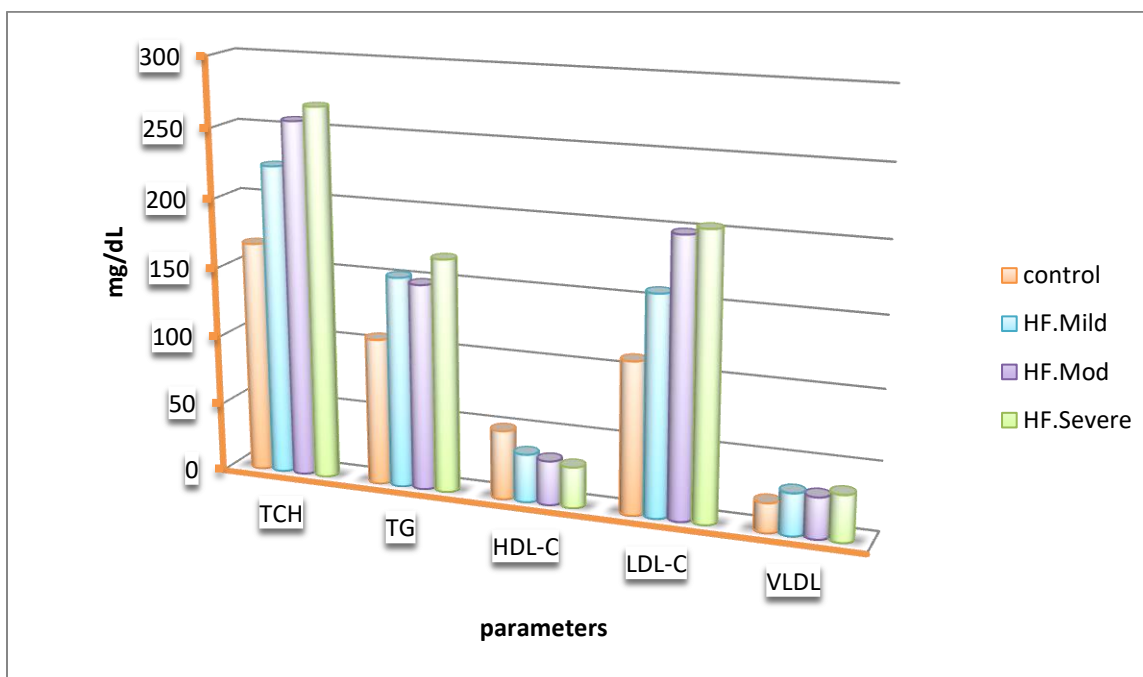


Figure (3-9) : Lipid profile levels of control and Type of HF groups .

3.2.4 : Serum Trace Elements Concentrations :

Table (3-10) and Figure (3- 10) show a significant increase in concentration of serum (Copper) and significant decrease in concentration of serum (Iron) in patients (HF severe) group in comparison with patients (HF mild) group ($p \leq 0.05$) . This result is approach to the result of (Málek *et al.*, 2003 ; Ebner and Haehling, 2013) .

The prevalence of iron deficiency (ID) increases with the severity of HF (Ebner *et al.*, 2013) . Iron deficiency (ID) is frequent among patients with HF , and has serious unfavourable clinical consequences (Okonko *et al.*, 2011) .

Trace elements are known to have a key role in myocardial metabolism . Trace elements including copper , iron may be protective against cardiovascular disease (Clayton BE., 1980) .

Table (3 – 10) : Serum (Iron , Copper) concentrations of control , HF Mild, HF Mod and HF Severe groups .

Group	NO	Iron $\mu\text{mol/L}$ Mean $\pm$ SD	Copper $\mu\text{mol/L}$ Mean $\pm$ SD
Control	74	21.79 $\pm$ 7.02 ^a	18.22 $\pm$ 2.8 ^c
HF Mild	25	13.02 $\pm$ 8.65 ^b	20.88 $\pm$ 1.9 ^b
HF Mod	24	11.20 $\pm$ 6.64 ^{bc}	20.5 $\pm$ 2.4 ^{ab}
HF Severe	25	8.82 $\pm$ 3.34 ^c	27.38 $\pm$ 2.2 ^a
LSD		2.03	3.46

- Legend as in table (3- 6)

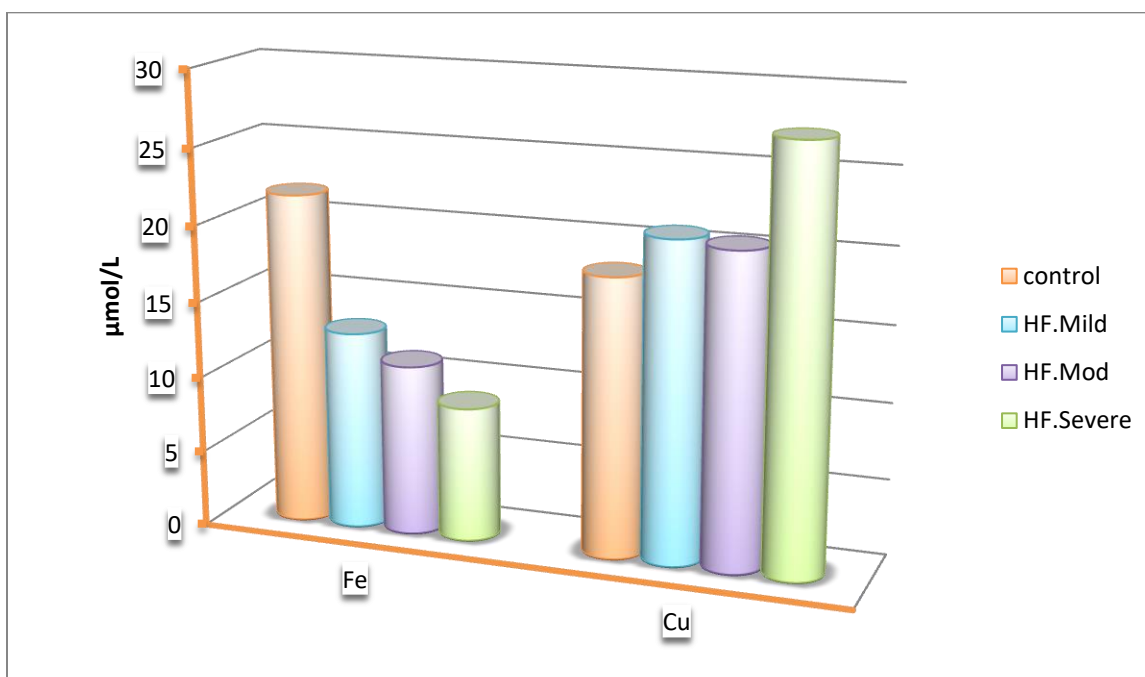


Figure (3-10) : Serum (Iron , Copper) levels of control and Type of HF groups .

3.3 : The Studies Parameters According to the Sex :

3.3.1 : Serum Malondialdehyde Concentration :

Table (3-11) and Figure (3.11) show serum MDA level according to the sex groups . There are no significant differences in concentrations of serum MDA in male group compared with female group ($P \leq 0.05$) . But it show there is a significant increase in concentrations of serum MDA in patients group compared to control group ($P \leq 0.05$) .

Table (3 – 11) : Serum MDA concentrations of all sex groups .

Group	NO		MDA concentration ($\mu\text{mol/L}$) mean $\pm$ SD		LSD
	Male	Female	Male	Female	
Control	37	37	1.523 $\pm$ 0.82 ^b	1.597 $\pm$ 0.97 ^b	0.83
HF	37	37	2.769 $\pm$ 0.79 ^a	2.814 $\pm$ 1.04 ^a	0.99
LSD			0.5	0.42	

- Legend as in table (3- 1)

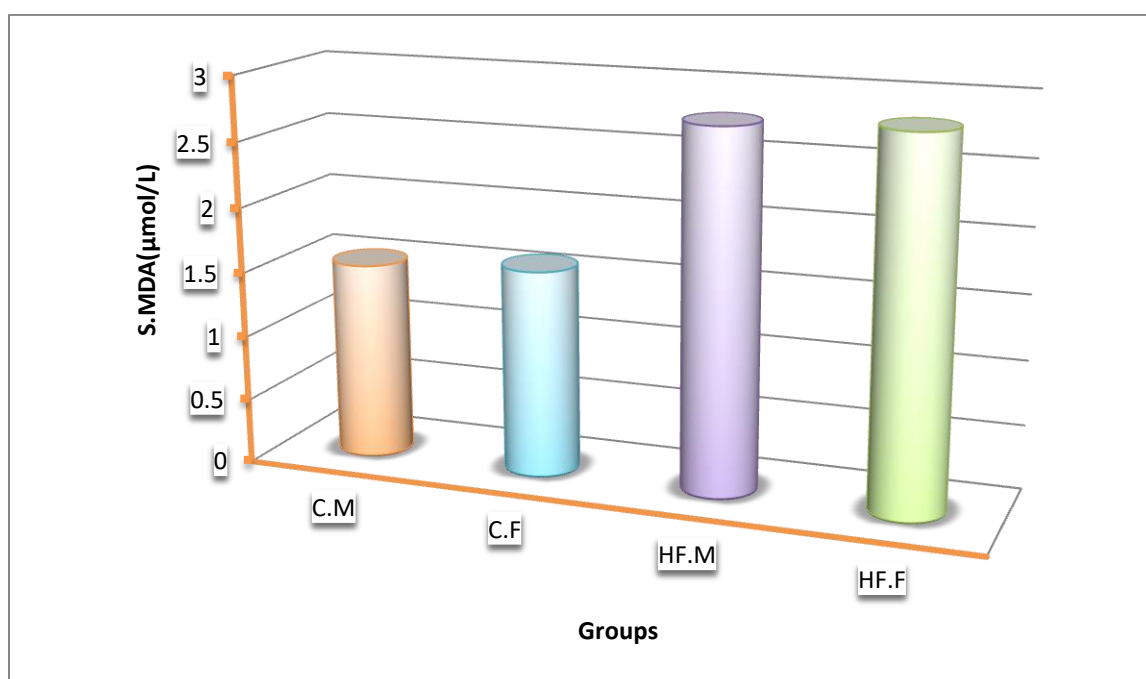


Figure (3-11) : Serum MDA levels of all sex groups .

-C.M : Control-Male

-C.F : Control-Female

-HF.M : Heart Failure-Male

-HF.F : Heart Failure-Female

3.3.2 : Antioxidant system :

3.3.2.1 : Serum Ceruloplasmin Concentrations :

Table (3-12) and Figure (3-12) show serum Cp level according to the sex groups . There are no significant differences in concentrations of serum Cp in male group compared with female group ($P \leq 0.05$) . But they shows there is a significant increase in concentrations of serum Cp in patients group compared to control groups ($P \leq 0.05$) .

This study finds non differences in serum Cp among all sex groups to be approach to the result of (Razvan *et al.*, 2013) .

Table (3 – 12) : Serum Cp concentrations of all sex groups .

Group	NO		Cp concentration (g/L) mean± SD		LSD
	Male	Female	Male	Female	
Control	37	37	2.79±0.53 ^b	2.76±0.52 ^b	0.43
HF	37	37	4.04±0.77 ^a	3.82±0.626 ^a	0.51
LSD			1.03	0.91	

- Legend as in table (3- 1)

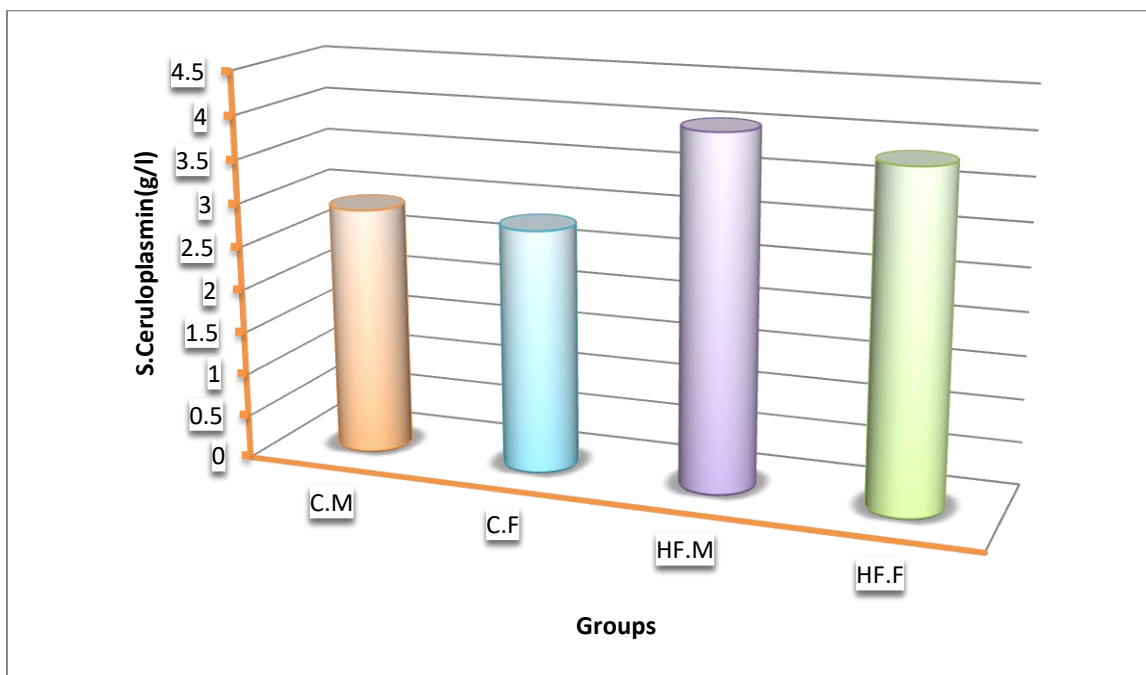


Figure (3-12) : Serum Cp levels of all sex groups .

- Legend as in Figure (3- 11)

3.3.2.2 : Serum Transferrin Concentrations :

Table (3-13) and Figure (3-13) show serum Tf level according to the sex groups . There are no significant differences in concentrations of serum Tf in male group compared with female group ($P \leq 0.05$) . But it show there is a significant decrease in concentrations of serum Tf in all patients group compared to control groups ($P \leq 0.05$) .

Table (3 – 13) : Serum Tf concentrations of all sex groups .

Group	NO		Tf concentration (g/L) mean± SD		LSD
	Male	Female	Male	Female	
Control	37	37	3.63±0.57 ^a	3.58±0.56 ^a	0.55
HF	37	37	2.58±0.24 ^b	2.49±0.28 ^b	0.68
LSD			0.89	0.73	

- Legend as in table (3- 1)

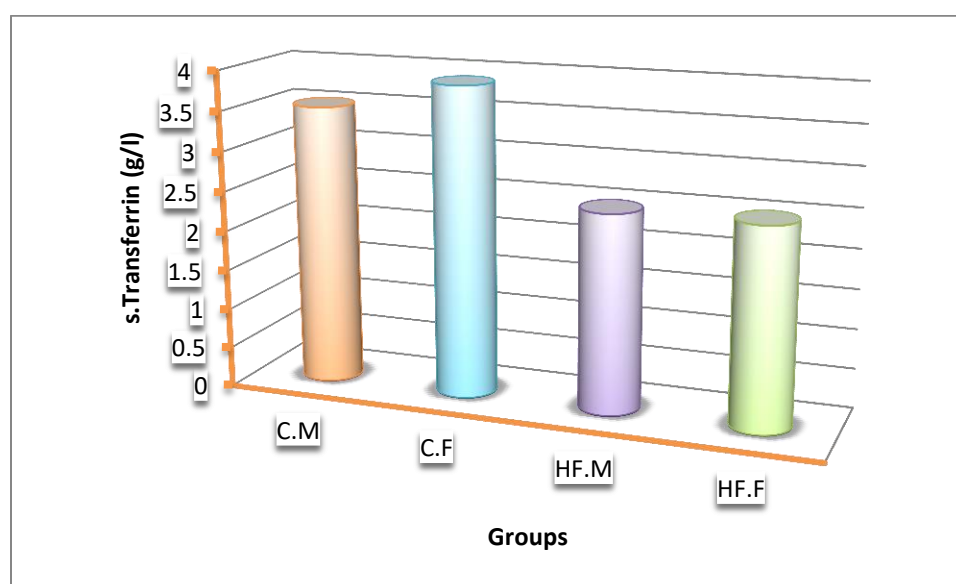


Figure (3-13) : Serum Tf levels of all sex groups .

- Legend as in Figure (3- 11)

3.3.3 : Serum Lipid Profile Concentrations :

Serum (TCH , TG , HDL-C , LDL-C and VLDL) levels are shown in Table (3-14) and Figure (3-14) according to the sex groups . There are no significant differences in concentrations of serum (TCH , TG , HDL-C , LDL-C and VLDL) in male groups compared with female groups ($P \leq 0.05$) . But it show there is a

significant increases in (TCH , TG , LDL-C and VLDL) and significant decrease in (HDL-C) in patients group compared to control groups ($P \leq 0.05$) .

Table (3 – 14) : Serum (TCH , TG , HDL-C , LDL-C and VLDL) concentrations of all sex groups .

Parameters (mg/dl)		NO		Control	HF	LSD
		Control	HF			
TCH mean±SD	Male	37	37	172.04±13.4 ^a	240.46±37.0 ^{a*}	16.46
	Female	37	37	174.82±7.58 ^a	242.58±27.71 ^{a*}	15.66
LSD				6.88	9.95	
TG mean±SD	Male	37	37	102.57±19.5 ^a	160.35±30.23 ^{a*}	18.32
	Female	37	37	108.69±18 ^a	163.11±29.9 ^{a*}	19.56
LSD				15.62	19.22	
HDL-C mean±SD	Male	37	37	47.49±8 ^{a*}	32.41±15.79 ^a	5.02
	Female	37	37	50.64±4.5 ^{a*}	32.86±14.03 ^a	4.39
LSD				9.28	5.45	
LDL-C mean±SD	Male	37	37	101.3±15.6 ^a	182.97±25.2 ^{a*}	15.82
	Female	37	37	99.23±10.2 ^a	182.51±29.4 ^{a*}	12.35
LSD				10.8	9.09	
VLDL mean±SD	Male	37	37	20.55±3.1 ^a	32.35±6.04 ^{a*}	5.02
	Female	37	37	21.73±2.5 ^a	32.62±5.98 ^{a*}	4.82
LSD				8.01	4.07	

- Legend as in table (3- 1)

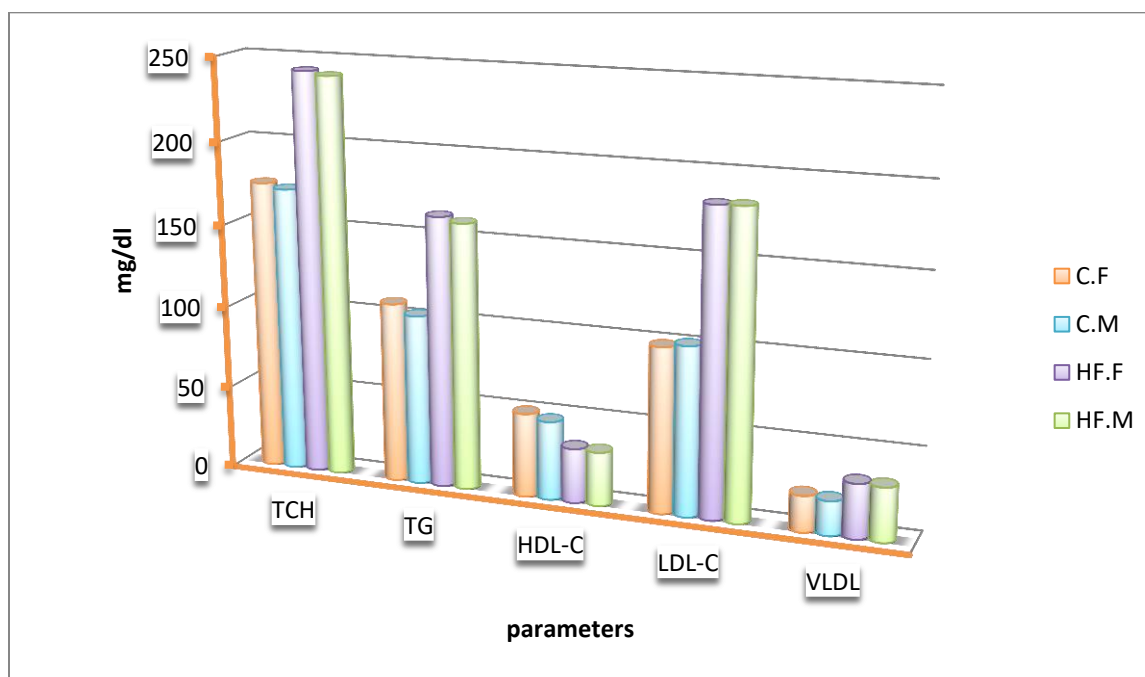


Figure (3-14) : Lipid profile levels of all sex groups .

- Legend as in Figure (3- 11)

3.3.4 : Serum Trace Elements Concentrations :

Table (3-15) and Figure (3- 15) show a significant decrease in iron levels in female in comparison with male in both patients and control groups ($P \leq 0.05$) . This result is approach to the result of (Divakaran *et al.*, 2011) . The mentioned Table and Figure also show a significant increase in copper levels in female in comparison with male in both patients and control groups ($P \leq 0.05$) .

Table (3 – 15) : Serum (Iron , Copper) concentrations of all sex groups .

Group	NO		Iron $\mu\text{mol/L}$ Mean $\pm$ SD		LSD	Copper $\mu\text{mol/L}$ Mean $\pm$ SD		LSD
	M	F	Male	Female		Male	Female	
Control	37	37	20.30 $\pm$ 6.9 ^{a*}	18.125 $\pm$ 8.2 ^a	1.15	16.19 $\pm$ 0.9 ^b	19.67 $\pm$ 0.06 ^{b*}	1.15
HF	37	37	13.28 $\pm$ 5.19 ^{b*}	11.33 $\pm$ 6.53 ^b	0.99	21.98 $\pm$ 0.27 ^a	25.02 $\pm$ 0.23 ^{a*}	1.30
LSD			5.69	4.34		1.95	2.47	

- Legend as in table (3- 1)

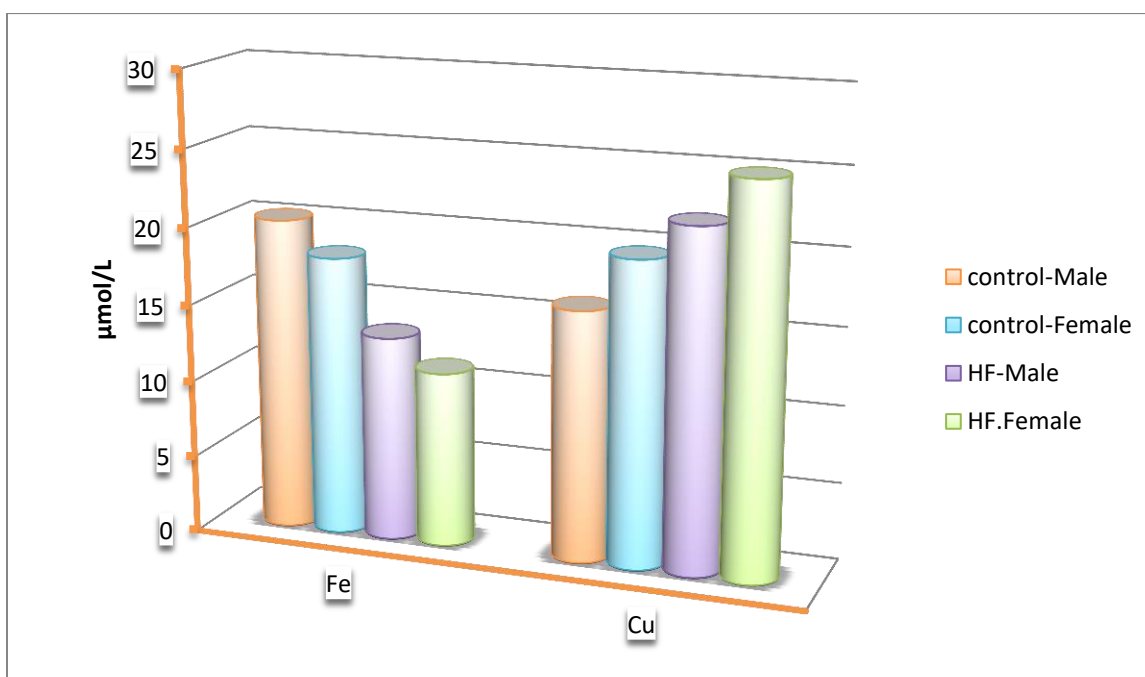


Figure (3-15) : Serum (Iron , Copper) levels of all sex groups .

3.4 : The Studies Parameters According to the Age :

3.4.1 : Serum Malondialdehyde Concentration :

Table (3-16) and Figure (3-16) show a significant increase in concentration of serum MDA in all patients age group in comparison with control group ($P \leq 0.05$). In the same table , there is a significant decrease in concentration of serum MDA in patients group (A) in comparison with patients group (B,C,D) ($P \leq 0.05$) .

Aging is a process of irreversible physiological and morphological changes associated with an increasing susceptibility to disease (Kasapoglu and Ozben, 2001) . The free radical theory of aging provides an attractive mechanistic view point that may explain molecular changes associated with the aging process (Granot and Kohen, 2004) .

The excessive production of free radicals in the organism , and the imbalance between the concentrations of these and the antioxidant defenses may be related to aging (Afanas, 2005) . This is due to oxidative damage to lipids induced by the over production of reactive oxygen species (ROS) accumulated with age and contributes to degenerative diseases and the aging phenomenon by disrupting cellular homeostasis (Mahdi *et al* ., 2014) .

Table (3 – 16) : Serum MDA concentrations of all age groups .

Group Of Age		NO		MDA concentration ($\mu\text{mol/L}$) mean $\pm$ SD		
G	Age(year)	Control	HF	Control	HF	LSD
A	(40-49)	15	15	1.33 $\pm$ 1.55 ^b	1.65 $\pm$ 0.21 ^{b*}	3.52
B	(50-59)	15	15	1.75 $\pm$ 0.77 ^a	3.124 $\pm$ 0.46 ^{a*}	3.26
C	(60-69)	20	20	1.55 $\pm$ 1.42 ^a	2.86 $\pm$ 0.62 ^{a*}	2.79
D	(70-79)	24	24	1.74 $\pm$ 0.64 ^a	2.9 $\pm$ 1.08 ^{a*}	3.34
LSD				0.20	0.88	

- Legend as in table (3- 1)

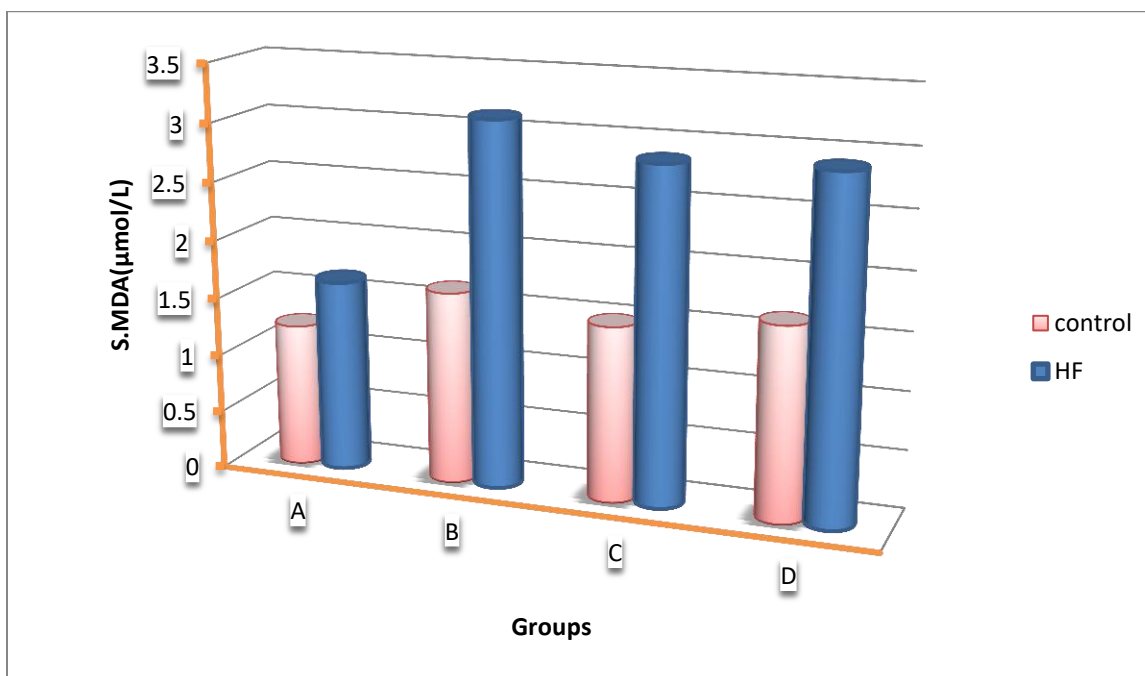


Figure (3-16) : Serum MDA levels of all age (control and patients) groups .

3.4.2 : Antioxidant system :

3.4.2.1 : Serum Ceruloplasmin Concentrations :

Table (3-17) and Figure (3-17) show a significant increase in concentration of serum Cp in all patients age group in comparison with control group ($P \leq 0.05$) . In the same Table , there are no significant differences in concentration of serum Cp in all age patients group ($P \leq 0.05$) .

Table (3 –17) : Serum Cp concentrations of all age groups .

Group Of Age		NO		Cp concentration (g/L) mean± SD		
G	Age(year)	Control	HF	Control	HF	LSD
A	(40-49)	15	15	2.66±0.63 ^a	3.65±0.50 ^{a*}	0.28
B	(50-59)	15	15	2.57±0.45 ^a	4.22±0.84 ^{a*}	0.92
C	(60-69)	20	20	2.95±0.34 ^a	4.22±0.63 ^{a*}	0.74
D	(70-79)	24	24	2.92±0.53 ^a	3.86±0.66 ^{a*}	0.38
LSD				0.65	0.74	

- Legend as in table (3- 1)

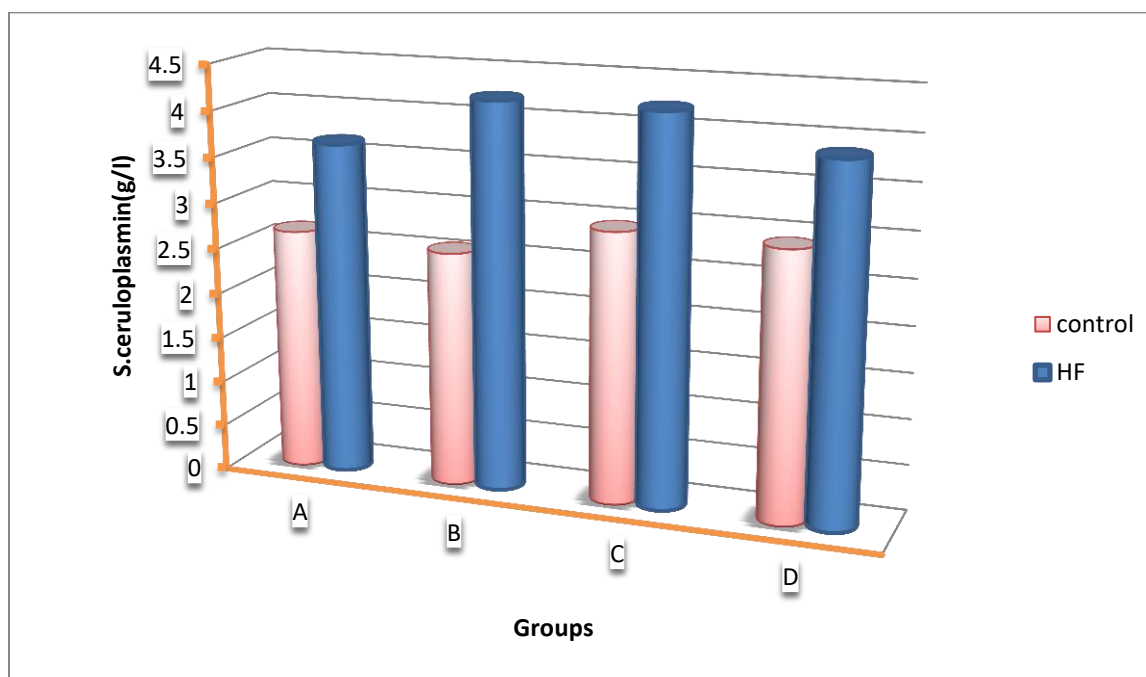


Figure (3-17) : Serum Cp levels of all age (control and patients) groups .

3.4.2.2 : Serum Transferrin Concentrations :

Table (3-18) and Figure (3-18) show a significant decrease in concentration of serum Tf in all age patients group in comparison with control group ($P \leq 0.05$) . In the same Table , there is a significant decrease in concentration of serum Tf in (D) patients group in comparison with (B,C,A) patients group ($P \leq 0.05$) .

The major carrier protein of iron is transferrin. Iron ions are delivered in the blood by the protein transferrin , each transferrin molecule can carry two iron ions (Attardo *et al.*,2006) . The antioxidant property of transferrin is its ability to bind with iron ions and storage it as a ferritin and prevent the oxidative role of iron which allows to generate free radicals by Fenton and Haber-Weiss reactions (De Feo *et al.*,2001) .

Table (3 – 18) : Serum Tf concentrations of all age groups .

Group Of Age		NO		Tf concentration (g/L) mean± SD		
G	Age(year)	Control	HF	Control	HF	LSD
A	(40-49)	15	15	3.88±0.16 ^{a*}	2.66±0.14 ^a	0.31
B	(50-59)	15	15	3.67±0.33 ^{a*}	2.53±0.34 ^a	0.28
C	(60-69)	20	20	3.72±0.42 ^{a*}	2.68±0.21 ^a	0.46
D	(70-79)	24	24	2.99±0.22 ^{b*}	2.41±0.21 ^b	0.24
LSD				0.30	0.10	

- Legend as in table (3- 1)

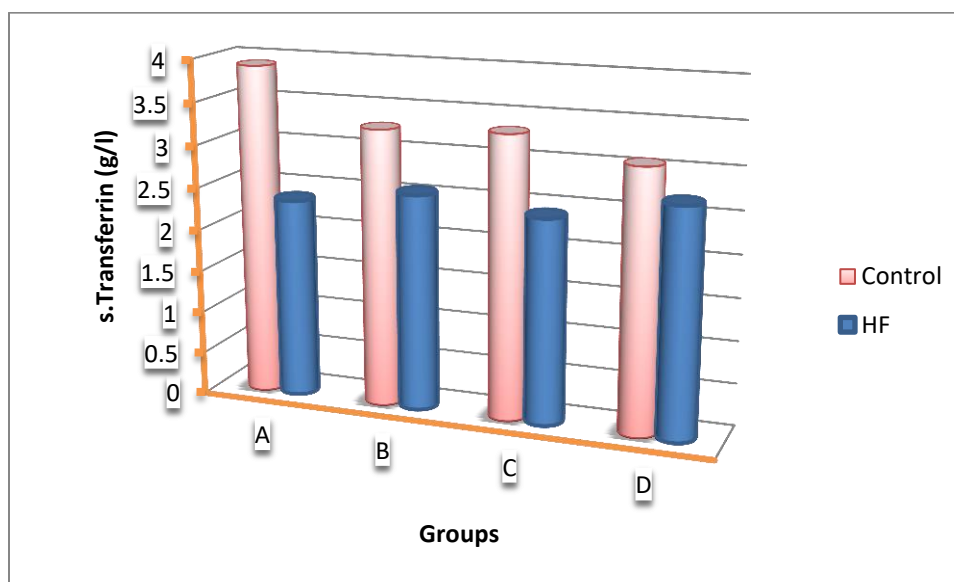


Figure (3-18) : Serum Tf levels of all age (control and patients) groups .

3.4.3 : Serum Lipid Profile Concentrations :

Tables (3-19) and (3-20) , as well as Figure (3-19) , show a significant increase in (TCH , TG , LDL-C and VLDL) as well as a significant decreases in (HDL-C) in all patients group compared to control groups ($P \leq 0.05$) . However there are a significant increase in (TCH) and a significant decrease in (HDL-C) in age patients group (B,C,D) in comparison with patients group (A) . Moreover there is a significant increase in (LDL-C) in patients group (D) in comparison with patients group (A,B,C) , no significant differences in concentrations of serum (TG,VLDL) are observed in all patients group can be observed . This result is approach to the result of (Adak and Shivapuri, 2010) .

The prevalence of dyslipidemia with advancing age and obesity is also reported worldwide . Adverse lipid and lipoprotein profile is recognized as independent risk factor for atherosclerosis and coronary artery disease (CAD) (Mahdi *et al* ., 2014) .

In addition , an elevated total cholesterol (TCH) , triglycerides (TG) , low-density lipoprotein-cholesterol (LDL-C) and lowered high-density lipoprotein-cholesterol (HDL-C) are conventional risk factor for heart disease as well as the major cause of atherosclerosis (Adak and Shivapuri, 2010) .

Table (3 – 19) : Serum (TCH and TG) concentrations of all age groups .

Group Of Age		NO		TCH (mg/dL) mean± SD		TG (mg/dL) mean± SD	
G	(year)	Control	HF	Control	HF	Control	HF
A	(40-49)	15	15	166.17±13.83 ^b	204.95±36.87 ^c	75.11±21.35 ^a	141.55±48.7 ^b
B	(50-59)	15	15	176.33±7.91 ^a	236.64±20.64 ^a	105.13±16.89 ^a	158.84±21.67 ^b
C	(60-69)	20	20	175.86±7.29 ^a	250.14±24.78 ^a	108.9±10.72 ^a	160.72±35.01 ^b
D	(70-79)	24	24	179.55±6.75 ^a	258.72±20.05 ^a	112.29±15.26 ^a	180.83±32.85 ^b
LSD				8.24	20.56	38.63	40.99

- Legend as in table (3- 1)

Table (3 – 20) : Serum (HDL-C , LDL-C and VLDL) concentrations of all age groups.

		NO		HDL-C (mg/dL) mean± SD		LDL-C (mg/dL) mean± SD		VLDL (mg/dL) mean± SD	
G	year	Cnt	HF	Control	HF	Control	HF	Control	HF
A	(40-49)	15	15	52.29±5.01 ^a	38.69±2.3 ^a	90.54±19.7 ^b	160.52±32.1 ^b	20.02±4.47 ^a	30.31±8.74 ^b
B	(50-59)	15	15	49.09±1.8 ^b	33.05±3.1 ^b	117.36±12.4 ^a	181.73±44.1 ^b	21.02±3.38 ^a	32.76±4.53 ^b
C	(60-69)	20	20	48.18±1.91 ^b	34.78±3.1 ^b	112.34±8.6 ^a	192.70±38.3 ^b	21.78±2.14 ^a	33.14±7.62 ^b
D	(70-79)	24	24	44.50±3.07 ^c	32.48±3.4 ^b	116.46±9.3 ^a	220.63±24.23 ^a	22.45±3.05 ^a	36.16±5.37 ^b
LSD				2.36	2.67	17.91	25.56	4.12	7.89

- Legend as in table (3- 1)

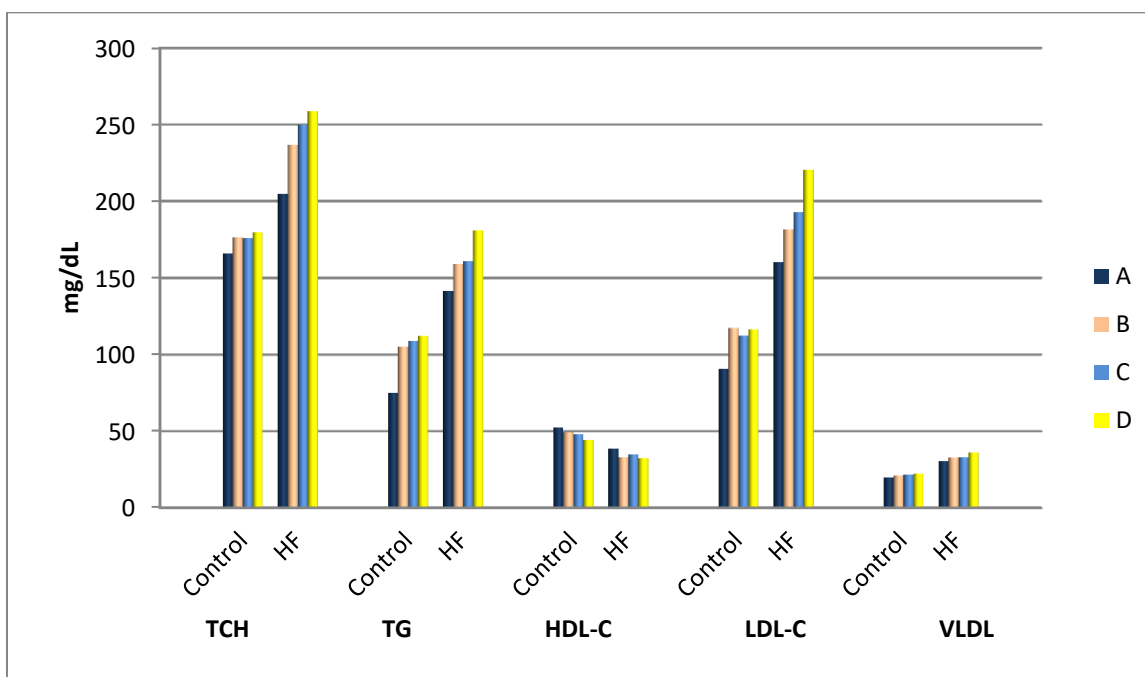


Figure (3-19) : Serum (TCH , TG , HDL-C , LDL-C and VLDL) levels of all age (control and patients) groups .

3.4.4 : Serum Trace Elements Concentrations :

Table (3-21) and Figure (3- 20) show a significant increase in concentration of serum copper and decrease in concentration of serum Iron in all patients age group in comparison with control group ($P \leq 0.05$) . The same Tables show a significant increase in iron levels in (A , B) groups in comparison with (C , D) groups ($P \leq 0.05$) . This result is approach to the result of (Jorde *et al* ., 2001 ; Wang *et al.*, 2016) . In the same Table , shows non significant differences in concentration of serum copper in all patients age group ($P \leq 0.05$) can be observed .

Table (3 – 21) : Serum (Iron , Copper) concentrations of all age groups .

Group	Age (year)	NO		Iron $\mu\text{mol/L}$ Mean $\pm$ SD		Copper $\mu\text{mol/L}$ Mean $\pm$ SD	
		Cntrol	HF	Control	HF	Control	HF
A	(40-49)	15	15	25.39 $\pm$ 8.2 ^a	16.49 $\pm$ 7.5 ^a	18.18 $\pm$ 2.8 ^a	23.47 $\pm$ 2.7 ^b
B	(50-49)	15	15	22.56 $\pm$ 7.7 ^a	15.46 $\pm$ 10.7 ^a	18.37 $\pm$ 2.2 ^a	23.48 $\pm$ 2.6 ^b
C	(60-69)	20	20	18.02 $\pm$ 2.32 ^b	10.5 $\pm$ 5.96 ^b	17.96 $\pm$ 2.0 ^a	23.54 $\pm$ 3.7 ^b
D	(70-79)	24	24	17.01 $\pm$ 5.27 ^b	9.48 $\pm$ 3.15 ^b	18.67 $\pm$ 2.3 ^a	23.35 $\pm$ 2.6 ^b
LSD				4.37	2.33	1.13	1.91

- Legend as in table (3- 1)

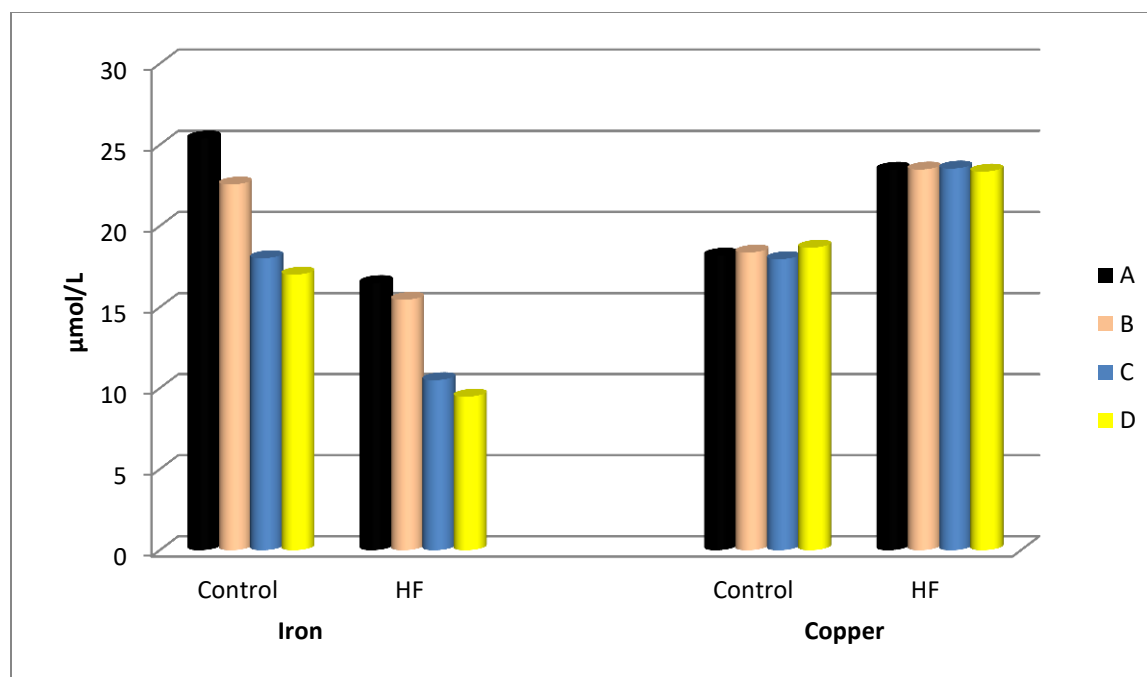


Figure (3-20) : Serum (Iron and Copper) levels of all age (control and patients) groups .

3.5 : The Studied Parameters According to smoking :

3.5.1 : Serum Malondialdehyde Concentration :

Table (3-22) and Figure (3-21) show a significant increase in concentrations of serum MDA in control and patients HF group smoking in comparison with control and patients group non smoking ($P \leq 0.05$) . This result is approach to the result of (Metta *et al.*, 2015) .

Smoking is a major contributor to all forms of cardiovascular disease (Ambrose and Barua, 2004) . In addition to vascular effects , smoking , via increased oxidative stress and inflammation (El-Menyar, 2008) , directly effects on the myocardium leading to systolic and diastolic dysfunction (Alam *et al.*, 2002) . It also promotes other heart failure (HF) risk factors including blood pressure , increased heart rate , diabetes , and atherosclerosis (Unverdorben *et al .*, 2009) .

The increase in concentration of MDA in smoking people indicates an enhanced lipid peroxidation in smokers . Our findings are concurrent with that of (Lykkesfeldt *et al.*, 2004) who have reported that , smoking induces lipid peroxidation significantly and thereby increases the plasma levels of MDA in comparison to non smokers (Lykkesfeldt J *et al .*, 2004) .

Table (3 – 22) : Serum MDA concentrations of smoking groups .

Group	NO		MDA concentration ($\mu\text{mol/L}$) mean $\pm$ SD		LSD
	Smokers	Non-Smokers	Smokers	Non-Smokers	
control	37	37	3.2 $\pm$ 0.69*	1.5 $\pm$ 0.7	0.34
HF	37	37	3.33 $\pm$ 0.95*	3.02 $\pm$ 1.04	0.12

- Legend as in table (3- 1)

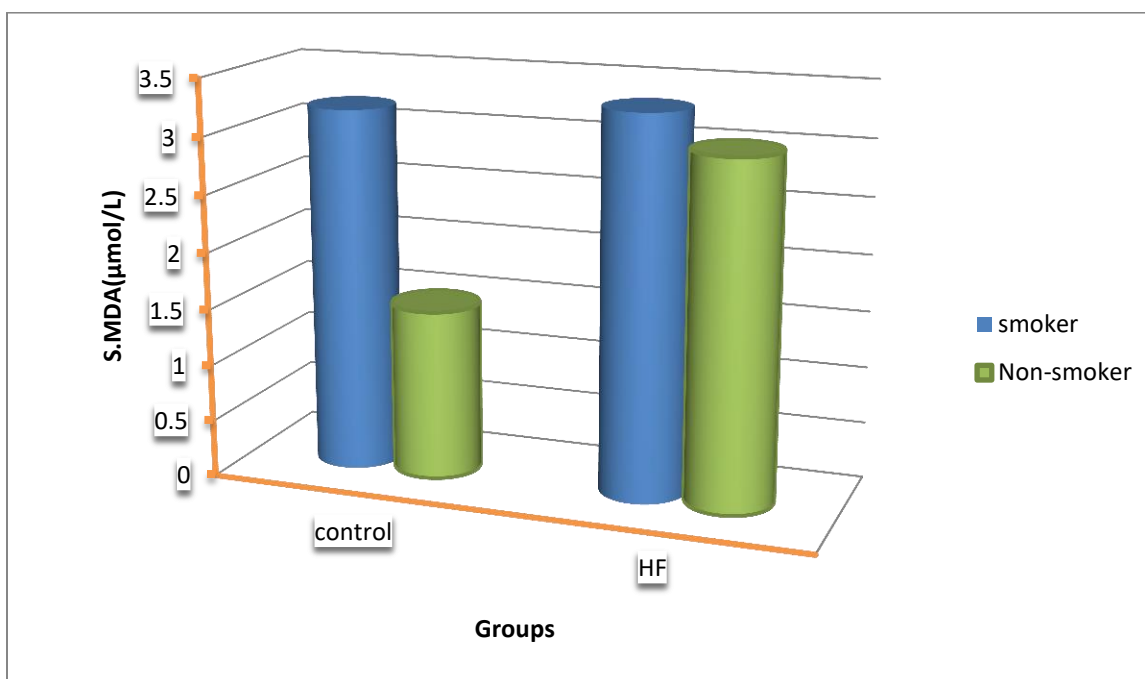


Figure (3-21) : Serum MDA concentrations of smoking groups .

3.5.2 : Antioxidant System :

3.5.2.1 : Serum Ceruloplasmin Concentrations :

Table (3-23) and Figure (3-22) show a significant increase serum ceruloplasmin concentration in smokers comparison with non smoking ($P \leq 0.05$) .

Several studies have documented that smoking may increase oxidative stress and impair oxidant defense system (Kim SH ., 2003) .

Table (3 – 23) : Serum Cp concentrations of smoking groups .

Group	NO		CP concentration (g/L) Mean $\pm$ SD		LSD
	Smokers	Non-Smokers	Smokers	Non-Smokers	
control	37	37	2.78 $\pm$ 0.15*	2.35 $\pm$ 0.11	0.31
HF	37	37	4.11 $\pm$ 0.85*	3.8 $\pm$ 0.86	0.12

- Legend as in table (3- 1)

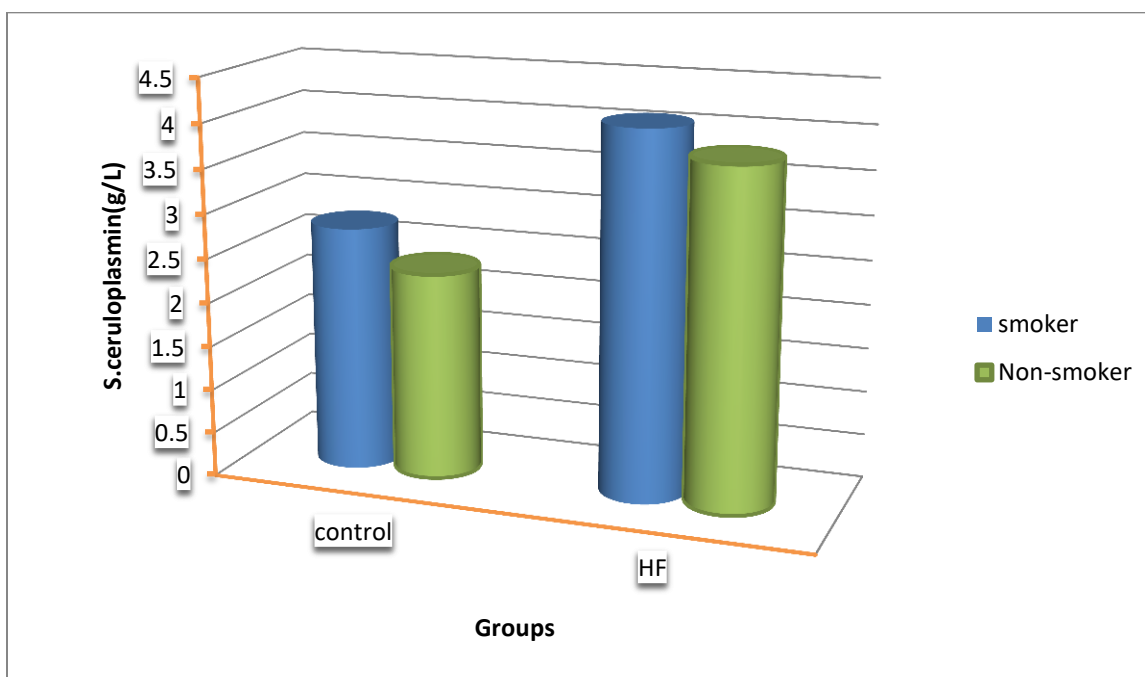


Figure (3-22) : Serum Cp concentrations of smoking groups .

3.5.2.2 : Serum Transferrin Concentrations :

Table (3-24) and Figure (3-23) show a no significant differences in concentrations of serum Tf between smoking and non smoking ($P \leq 0.05$) .

Table (3 – 24) : Serum Tf concentrations of smoking groups .

Group	NO		Tf concentration (g/L) Mean $\pm$ SD		LSD
	Smokers	Non-Smokers	Smokers	Non-Smokers	
control	37	37	3.33 $\pm$ 0.15	3.41 $\pm$ 0.11	0.65
HF	37	37	2.21 $\pm$ 0.85	2.8 $\pm$ 0.86	0.82

- Legend as in table (3- 1)

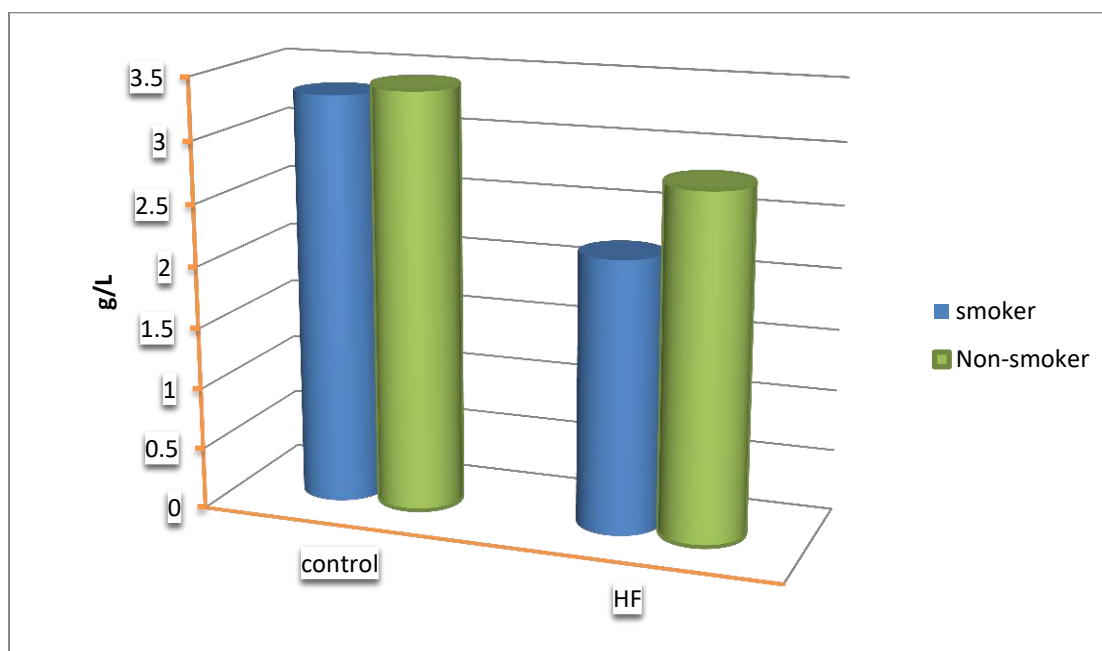


Figure (3-23) : Serum Tf concentrations of smoking groups .

3.5.3 : Serum Lipid Profile Concentrations :

As it is evident from table (3-25) and Figure (3-24) , the smoking shows a significant increase in levels of TCH , TG , LDL-C and VLDL in almost all the groups of cigarette smokers as compared to non smokers . Simultaneously a significant decrease in level of HDL-C is observed in cigarette smokers as compared to non-smokers ($P \leq 0.05$) .This result is approach to the result of (Wilma, 2011 ; Srinivasa Rao and Emmanuel Subash, 2013 ; Banihani, 2014) .

Smoking , or if we say more carefully , tobacco , has a very bad influence on the total health system of the human beings , not only effecting the arteries or the lung but almost all the functional systems of the body , from cell to cell (Srinivasa Rao and Emmanuel Subash, 2013) .

The nicotine in tobacco causes a decrease in the HDL-C level (good cholesterol) with an increase in the LDL-C level (bad cholesterol) and also an increase in the VLDL level , with an accumulation of lipids in the arterial wall . This is responsible for the greater risk of developing atherosclerosis in the tobacco users than in the non-tobacco users (Srinivasa Rao and Emmanuel Subash, 2013) .

Table (3 – 25) : Serum (TCH , TG , HDL-C , LDL-C and VLDL) concentrations of smoking groups .

Parameters (mg/dl)		NO		Control	HF
		Control	HF		
TCH mean±SD	Smokers	37	37	214.13±20.98 ^a	301.65±32.19 ^a
	Non-Smokers	37	37	155.28±24.09	237.82±47.32
LSD				20.31	31.24
TG mean±SD	Smokers	37	37	140.01±21.5 ^a	174.11±24.6 ^a
	Non-Smokers	37	37	106.02±16.6	153.13±14.7
LSD				11.71	16.51
HDL-C mean±SD	Smokers	37	37	32.04±4.4	29.56±13.34
	Non-Smokers	37	37	40±5 ^a	36.50±13.72 ^a
LSD				5.41	4.29
LDL-C mean±SD	Smokers	37	37	112±32.6 ^a	189.9±41.2 ^a
	Non-Smokers	37	37	84±39.4	172.49±46.5
LSD				13.18	12.29
VLDL mean±SD	Smokers	37	37	28.01±4.1 ^a	34.82±5.29 ^a
	Non-Smokers	37	37	21.20±3.9	30.62±6.54
LSD				5.28	1.17

- Legend as in table (3- 1)

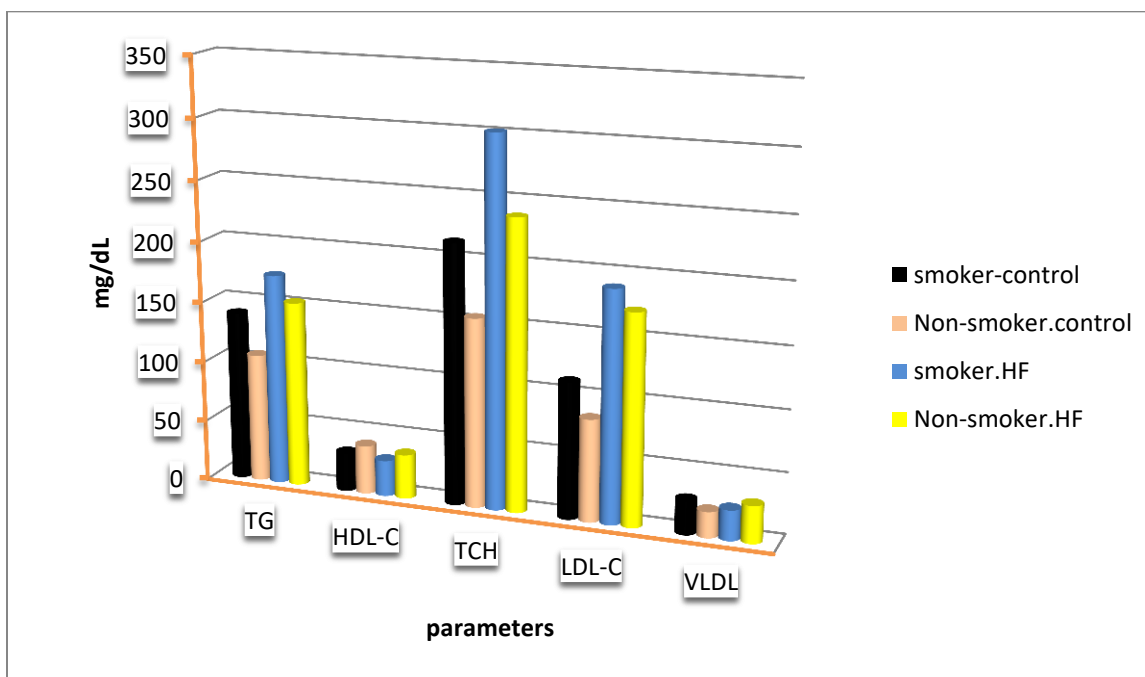


Figure (3-24) : Serum Lipid Profile concentrations of smoking groups .

3.5.4 : Serum Trace Elements Concentrations :

Table (3-26) and Figure (3- 25) show a significant increase serum iron concentration in smokers comparison with non smoking ($P \leq 0.05$) . This result is approach to the result of (Sulafa A *et al.*, 2013) , and show a significant decrease serum copper concentration in smokers comparison with non smoking ($P \leq 0.05$) . This result is approach to the result of (Hassan, 2015) .

Table (3 – 26) : Serum (Iron , Copper) concentrations of smoking groups .

	Iron $\mu\text{mol/L}$ Mean $\pm$ SD		LSD	Copper $\mu\text{mol/L}$ Mean $\pm$ SD		LSD
	Smokers	Non-Smokers		Smokers	Non-Smokers	
control	33.89 $\pm$ 8.11*	21.79 $\pm$ 7.0	5.21	16.37 $\pm$ 2.7	20.04 $\pm$ 3.5*	1.9
HF	16.93 $\pm$ 8.25*	8.71 $\pm$ 3.94	4.34	21.54 $\pm$ 2.2	25.43 $\pm$ 2.5*	2.0

- Legend as in table (3- 1)

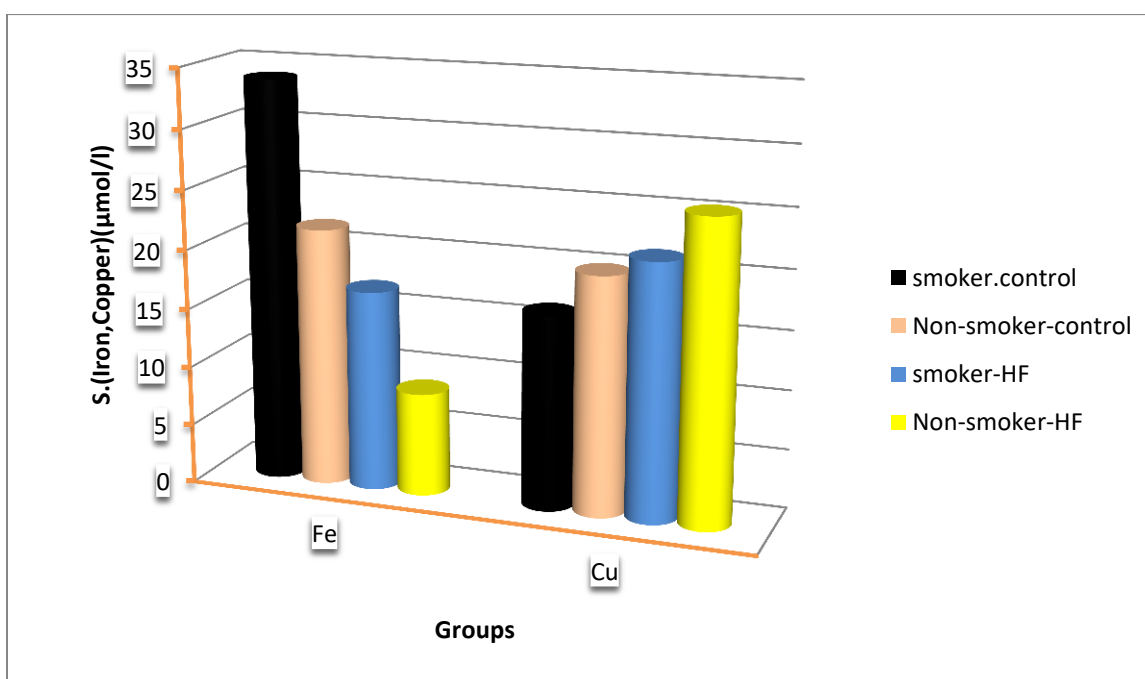


Figure (3-25) : Serum (Iron , Copper) concentrations of smoking groups .

Conclusions and Future Works

Conclusions :

From the data in this study we can conclude the following points relevant to patient with HF :-

- 1- Oxidative stress is a significant feature during heart failure .
- 2- Disorder the antioxidant system in patient with heart failure , according to the levels of (ceruloplasmin and transferrin) .
- 3- Dyslipidemia is present during heart failure .
- 4- Heart failure effect negatively on iron as well as positively on copper .
- 5- Gender has no effect on most studied parameters including (MDA , Cp , Tf , lipid profile) where as it effects significantly on iron and copper .
- 6- Age has effect on (MDA , Tf , TCH , HDL , VLDL , LDL , Iron) .
- 7- There is effect of smoking on all the studied parameters except for Tf .

Future Works :

It is important to design further studies relevant as indicated below :-

- 1- Effects of smoking on the response of heart failure patients to drug .
- 2- Study of another trace elements in patients with HF such as selenium ,
chrome .
- 3- The effect of drugs that use in HF on oxidant- antioxidant balance .
- 4- Study the effect of DM on the level of Parameters studied in patient heart
failure .

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الخلاصة

عجز القلب هو متلازمة سريرية تقدمية مزمنة اذ يكون القلب غير قادر على توفير ما يكفي من الدم للأعضاء المختلفة بسبب وجود خلل في القلب وتغيرات في النظام الدموي والكلية والأعصاب والنظام الهرموني .

تم تصميم هذه الدراسة لتقدير مستويات فرط الاكسدة متمثلة بالمالون ثنائي الايديهايد (MDA) وكل من السيرلوبيلازمين و الترانسفيرين (Tf , Cp) وكذلك لتقدير انماط الدهون (الكوليسترول ، الكليسيريدات الثلاثية ، البروتينات الدهنية عالية الكثافة ، البروتينات الدهنية واطئة الكثافة ، البروتينات الدهنية واطئة الكثافة جدا (VLDL , LDL-C, HDL-C , TG , TCH) وبعض العناصر النزرة متمثلة بالحديد و النحاس في مرضى عجز القلب الأنقباضي .

شملت الدراسة (74) مريض مصابين بالعجز القلبي و(74) شخص من المفترض اصحاء (مجموعة السيطرة) . وتمت المقارنة على اساس اربعة متغيرات بالإضافة الى المقارنة العامة (نوع المرض ، الجنس ، العمر و التدخين) .

تم تقسيم المرضى وفقا لنوع المرض إلى ثلاثة مجاميع (HF بسيط ، HF معتدل ، HF حاد) . وتم تصنيف المرضى تبعا لجنسهم (ذكور ، اناث) . وقسم إجمالي المرضى وفقا لأعمارهم إلى أربع مجاميع (المجموعة (A) تضم المرضى ذات الفئة العمرية بين (40-49) سنة ، المجموعة (B) بين (50-59) سنة ، المجموعة (C) بين (60-69) سنة والمجموعة (D) بين (70-79) سنة) .

أظهرت النتائج أن هناك ارتفاع معنوي في (MDA , Cp ,TCH,TG,LDL,VLDL) وانخفاض معنوي في مستوى مصل (copper , Tf ,HDL-C ,iron) ($P \leq 0.05$) من خلال المقارنة العامة بين مجموعة المرضى (74) و مجموعة السيطرة (74) .

بالنسبة لنوع المرض أظهرت النتائج زيادة معنوية في (MDA , copper) وإن هذه الزيادة كانت في المجموعة (HF الحاد) مقارنة بالمجموعتين (HF البسيط والمعتدل) كذلك وجود زيادة معنوية في (TCH) في (HF المعتدل والحاد) مقارنة مع (HF البسيط) كذلك وجد انخفاضا معنوياً في مستوى (HDL-C , iron) في مجموعة (HF الحاد) مقارنة

بالمجموعتين (HF البسيط والمعتدل) فيما أظهرت الدراسة عدم وجود اختلاف معنوي في مستويات (LDL-C , VLDL , TG , Tf , Cp) في انواع عجز القلب.
بالنسبة للجنس ، فأظهرت زيادة معنوية في مستوى copper لدى النساء مقارنة بالرجال . وكذلك انخفاض معنوي في iron لدى النساء مقارنة بالرجال . اما بقية المتغيرات لا تأثير للجنس عليها.

اما بالنسبة للعمر ، بينت النتائج وجود زيادة معنوية في مستوى (iron) في المجاميع (D , C) مقارنة مع المجاميع (A,B)، وكذلك هناك زيادة معنوية في مستوى (MDA , TCH) وانخفاض معنوي في مستوى (HDL-C) في المجاميع (B , C , D) مقارنة مع المجموعة (A) ، وكذلك وجد زيادة معنوية في مستوى (LDL-C) وانخفاض معنوي في مستوى (Tf) في المجموعة (D) مقارنة مع المجاميع (A , B , C) . ووجد انه لا يوجد تأثير للعمر على مستوى (TG , VLDL , copper) .

اما بالنسبة للتدخين ، بينت النتائج وجود زيادة معنوية في مستوى (TCH, TG, LDL-C) iron , Cp , MDA, VLDL) وكذلك وجود انخفاض معنوي في مستوى (HDL-C) copper) في الأشخاص المدخنين بالمقارنة مع الأشخاص الغير مدخنين ، كما أظهرت النتائج لوجود لفرق معنوي في مستوى (Tf) بين الأشخاص المدخنين والغير مدخنين .



جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة ذي قار

كلية العلوم

دراسة سريرية لحالة الإجهاد التأكسدي و نمط الدهون وبعض العناصر النزرة في مصل دم مرضى عجز القلب في محافظة ذي قار

رسالة

مقدمة الى مجلس كلية العلوم / جامعة ذي قار
كجزء من متطلبات نيل درجة الماجستير في الكيمياء الحياتية
من قبل

علي عادل عجيل

بكالوريوس علوم كيمياء (جامعة المثنى)

٢٠١٣-٢٠١٤

بإشراف

أ.م.د. عدنان طعان الخفاجي

أ.د. رائد معتك الصالح

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