Relation betweenC3 &C4 Complement andHeart DiseasesamongLibyans

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Abstract:
Background:The complement system is part of the host defense response. However, considerable evidence suggests that complement plays an important role in the pathophysiology of ischemic heart disease. The relationship between C3, C4 levels and acute coronary syndromes, further suggests that the complement activation is related to myocardium necrosis. ***Methods:*** Samples were collected from cardiac patients admitted to CCU atTripoli Medical Centreand analyzed for both C3 and C4 components. Venous blood has been collected from patients and their sera were separated. The principle of assay depends on Immunoturbidimetric method .***Results:***Of 130 cardiac patients with different cardiac diagnoses; 57 (43.8%) generally showed high C3 levels, and 30 (23%) of patients showed high levels of C4.C3 was high among cardiac diseases as represented here: IHD (48%), Valvular diseases (44%), while it was high in (27%) of Arrythmia patients, though it was high also amGong hypertensive patients (44%), on the other side C4 was high among (18%) of IHD patients, (28%) of Valvular diseases, (33%) of Arrythmia and (19%) of hypertensive patients. Both C3 and C4 represented high levels among females than males, and generally increased as age increase.***Conclusion:***C3, C4 in this study was shown to be high with coronary artery diseases and might work as diagnostic factors for Myocardial infarction, this study presented that C3 is better marker indicating that it could be a diagnostic factor for cardiac diseases than C4 as it always giving higher levels compared to C4

Keywords:Cardiac patients, Complement, C3, Immunoturbidimetric, Libya

I.   Introduction

Complement is a complex system composed of more than 25 proteins including C3, C4, properdine, etc. (1). The protein components (inactive form) of the system undergo sequential activation ultimately cause their biological effects (2). The complement component C3 acts as the centrally important component of the classical pathway as well as alternative and mannose-binding lectin mediated (MBL) pathways of complement activation. All pathways generate C3-convertase which converts C3 into C3b and C3a. This is the central event in the activation of complement sequence C5-C9 (3). Additional differentiation can be obtained by the determination of C4 when the level of complement factor C3 is low. If in such cases the concentration of C4 is normal, then an activation of the alternative route is likely (11).

The complement components have the potential to be involved and implicated in the immunopathogenesis of diseases (4,5). The body may be exposed to an excess of antigen in a number of circumstances which can cause formation of immune complexes at fixed sites, they can interact with the complement system leading to tissue damage and hence disease (7,8). Considerable evidence suggests that complement plays an important role in the pathophysiology of ischemic heart disease. The relationship between C3, C4 levels and acute coronary syndromes, further suggests that the complement activation is related to myocardium necrosis (9).

There are no sufficient studies in Libya concerning the role of complement components C3 and C4 in cardiac patients, However a study in Benghazi concluded that serum C3 and C4 levels were more profoundly elevated in Myocardial Infarction compared to angina pectoris patients suggestive of an acute phase and inflammatory response.(18). The purpose of this work is to determine the levels of C3 and C4 complement in patients with different cardiac diseases, and to assess the relationship between C3, C4 levels and cardiac patients' age, sex and occupation as well.

II.   Materials And Methods

2.1 Study population:

130 patients suffering from different heart disease were included in this study, their samples were collected from coronary care unit at Tripoli Medical Centre (TMC) in the period from June 6th to August 15th 2008, Patients' ages ranged between 22 to 90 years old (mean age 56).

2.2 Collection of specimens:

About 5 ml of blood was collected from each patient in a blank tube , then allowed to clot at room temperature,andsera separated and finally stored frozen until required for analysis.

2.3 Questionnaires and data collection

Study questionnaire contains patient data including personal data (name, sex, age, address and occupation), in addition to the medical history (diagnosis, surgical history, blood transfusion and medications).

2.4 Serological assays:

Assay of complements was done in Al Khadra hospital in Tripoli, Libya using Immunoturbidimetric assay done by COBAS INTEGRA systems (USA) using C3 and C4 provided cassettes.

2.5 Statistical analysis:

Data analysis was performed with computer software (SPSS, Version 10.0, SPSS Inc., Chicago, IL). Frequencies, percentages were computed and the comparison was made by Chi squire analysis to examine significant relationship between different variables in the data. Statistical significance was taken at a p value of less than 0.05.

III.   Results

Of 130 cardiac patients 57 (43.8%) showed high C3 levels, and 30 (23%) showed high levels of C4.Both C3 and C4 represented high levels among females than males, but this increase was significant regarding C3. C3 was increased even beyond 90 years of age (Fig. 1), while this increase was also noticed in case of C4 but it decreases in patients who exceed 60 years old.(Fig. 2)
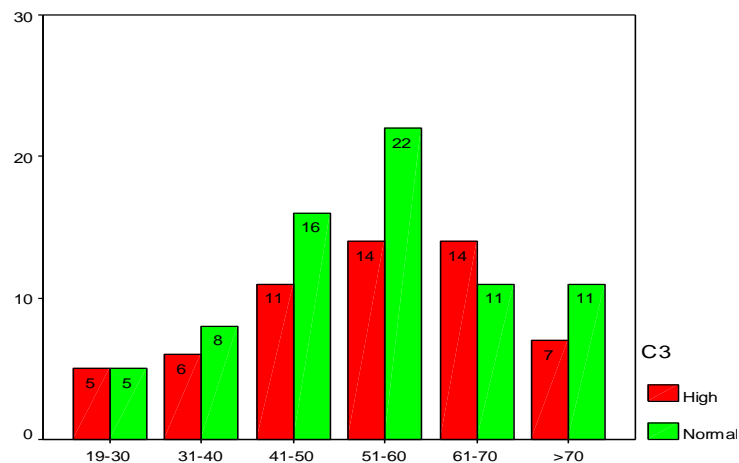
Figure 1.C3levels among different age groups of cardiac patients included in the study
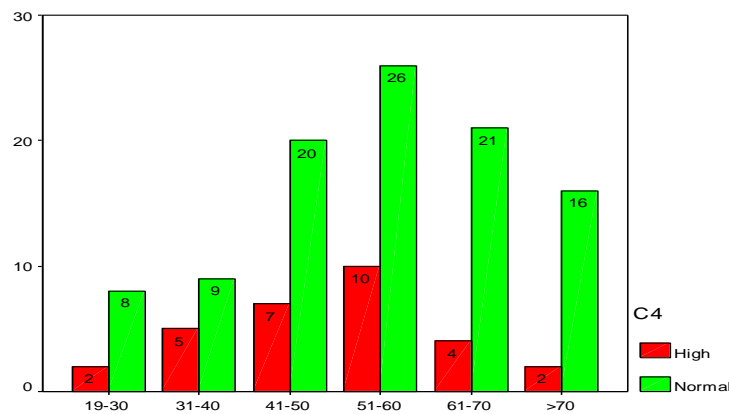
Figure 2.C3 levels among different age groups of cardiac patients included in the study

Concerning C3 most occupation affected was civil servants (employees, retired) (54%) and house wives (52%), mentioned occupations were affected significantly more than others (P <0.05), and in C4 employees also represented higher levels with the same percentage to student group (33%) followed by house wives (25%) with no significant difference among occupations (>0.05).

C3 level was high among cardiac diseases as represented here:Ischemic heart disease (IHD) (48%), Valvular diseases (44%), Arrhythmia patients (27%), and hypertensive patients (44%) (Fig. 3)

C4 was high among (18%) of IHD patients, (28%) of Valvular diseases, (33%) of Arrhythmia and (19%) of hypertensive patients (Fig.4)
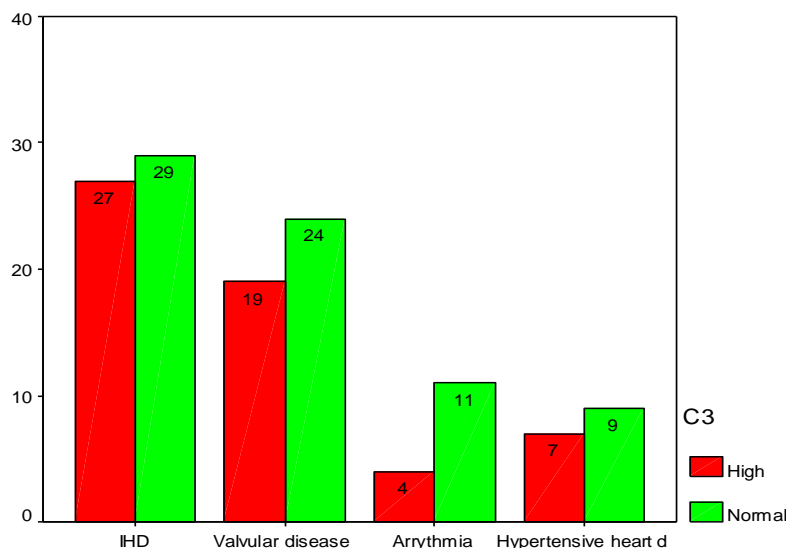

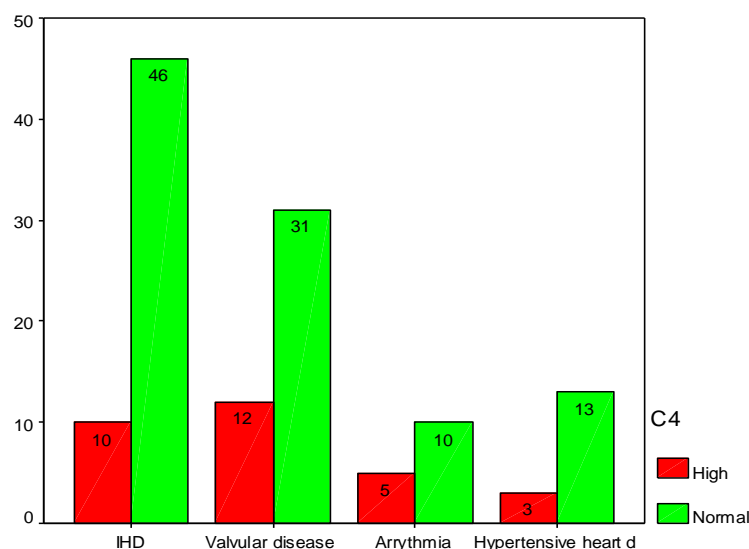**Figure 3.** High and normal C3 levels in patients suffering of different cardiac diseases

Figure 4. High and normal C4 levels in patients suffering of different cardiac diseases

C3 and C4 complement levels were compared in various diagnoses of patients included in the study, where;Ischemic heart disease (IHD) included Unstable Angina Pectoris (UAP), and Myocardial Infarction (MI), Valvular diseases included Aortic stenosis (AR), Mitral Regurgitation(MR), Mitral Stenosis(MS), Mitral Regurgitation (MR), and Combined Mitral Disease (CMD), while Arrhythmia included, Atrial Fibrillation (AF), Superior Ventricular Tachycardia (SVT), and finally Hypertension.

45% of UAP patients represented high levels of C3 and 23% represented high levels of C4, MI 50% represented high levels of C3 while all MI patients had normal C4 values, AS 66% represented high C3 levels and 33% represented high C4 levels, AR 100% of patients had high C3 levels and 50% represented high C4 levels, Both MS,SVT represented 20%, 50% high levels of C3 respectively, while both MS,SVT patients had normal C4

levels, MR 66% represented high C3 levels , but in C4 MR 55.5%, AF 23% represented high levels of C3, while 38.4% represented high levels of C4, MVD 25% represented high levels of both C3 and C4, LVH 100% represented high levels of C3 and 50% represented high levels of C4, CMD 100% represented high levels of C3 while 33% of CMD patients represented high levels of C4, and among hypertensive patients 44% represented high levels of C3 and 19% represented high levels of C4. (Table 1.), (Table 2.)

Table 1. High and normal C3 levels among different cardiac diseases

	C3		
	High	Normal	Total
UAP	21	23	44
MI	6	6	12
AS	2	1	3
AR	2		2
MS	2	8	10
MR	6	3	9
CMD	3		3
MVD	4	12	16
AF	3	10	13
SVT	1	1	2
HTN	7	9	16
Total	57	73	130

UAP=Unstable Angina Pectoris, MI=Myocardial Infarction, AS=Aortic Stenosis, AR=Mitral Regurgitation, MS=Mitral Stenosis, MR=Mitral Regurgitation, CMD= Combined Mitral Disease, AF= Atrial Fibrillation, SVT=Superior Ventricular Tachycardia, HTN=Hypertension

Table 2. High and normal C4 levels among different cardiac diseases

	C4		
	High	Normal	Total
UAP	10	34	44
MI		12	12
AS	1	2	3
AR	1	1	2
MS		10	10
MR	5	4	9
CMD	1	2	3
MVD	4	12	16
AF	5	8	13
SVT		2	2
HTN	3	13	16
Total	30	100	130

UAP=Unstable Angina Pectoris, MI=Myocardial Infarction, AS=Aortic Stenosis, AR=Mitral Regurgitation, MS=Mitral Stenosis, MR=Mitral Regurgitation, CMD= Combined Mitral Disease, AF= Atrial Fibrillation, SVT=Superior Ventricular Tachycardia, HTN=Hypertension

IV. Discussion

This Libyan study done in Tripoli based on 130 cardiac patients, those are the only patients were obtained in this period of time in TMC. Another studies have been done in America and Turkey (9,15), also previous study was done in Benghazi-Libya and 42 patients were included.(18). C3, C4 in this study was shown to be high with coronary artery diseases and might work as diagnostic factors for them. This result was also confirmed by Palikhe et al (2007) (15) and by Giasuddin et al (2007) in Benghazi (18). The study age structure was 22-90 years, where other studies concentrated on age from 28-61 only (14).

Also this study presented that C3 is better marker indicating that it could be a diagnostic factor for cardiac diseases than C4 (as it always giving higher levels compared to C4), and this finding also found in other studies (18), where there was relative increase in serum C3 protein in cardiac patients and decrease in C4 protein.

Other studies measured C3, C4 with follow-up time as in Benghazi study (18) or in cohort study by Engsrtrom et al (14), but this study was only screening in type without follow up.Also very few studies done

investigating of C3,C4 based on cohort study with comparison of normal individual group, but in this small study was difficult to be done as cohort study in Libya as it needs time, financial support, and men power.

This study showed that C3, C4 were higher among female cardiac patients than males (50%, 30% for C3 and 24%, 15% for C4), but other study of Engstrom et al, 2007 (14) found that C3 & C4 increased among males with acute cardiac problems, and this may be explained by high incidence of cardiac disease among males in Sweden while the incidence among Libyan was found to be higher among females, where most of the females included in this study were house wives. The elevation of C3 and C4 complement could be attributed to social life style, where Libyan females are known for their lack of exercise which in turn could be the leading cause for obesity in that sector of society; bearing in mind that heart disease is well linked to obesity and lack of exercise.

This study showed that C3 is superior to C4 especially in acute cardiac diseases (MI) and this finding also found in other studies. (18). This study showed slight difference in C3 increase between UAP and acute MI (45% versus 50%) though other studies (9) showed that C3 levels in patients with SA, UAP where lower than those found in MI. (18)This study recommendsusing C3, C4 as diagnostic parameters in our Libyan laboratories with other in use as CRP (C - reactive protein).

V.   Conclusion

This study presented that C3 is a better marker indicating that it could be a diagnostic factor for cardiac diseases than C4, hence suggesting use of C3 as laboratory tool for diagnosis of cardiac problems especially acute MI, Further studies with follow up cohort study among Libyans are recommended to provide important answersregarding the role of C3, C4 in cardiac problems especially acute type.

Acknowledgements

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