ORIGINAL PAPER

# B-type natriuretic peptide and high sensitivity C-reactive protein in patients with rheumatic fever and rheumatic heart disease: relationship to mitral regurgitation

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## ABSTRACT

**Introduction:** Rheumatic fever (RF) is one of the leading causes of cardiac disease in developing countries. Brain natriuretic peptide (BNP) is a cardiovascular hormone emitted from the myocardium of the ventricles as a reaction to pressure overload and the expansion of ventricular volume. High sensitivity C reactive protein (hsCRP) levels are increased in several inflammatory and cardiac diseases. We aimed to study the relationship between BNP and hsCRP levels and the presence of rheumatic heart disease (RHD) and to investigate their levels as indices of the severity of chronic rheumatic mitral regurgitation (MR).

**Material and methods:** Seventy-seven Egyptian patients with RF and 43 age and gender-matched healthy controls were included in the study. The two groups of the RF patients were: RHD, group ($n = 62$) diagnosed by transthoracic echocardiogram detecting the rheumatic involvement of the mitral valve, and rheumatic fever only (RFo) group ($n = 15$) had a history of RF without the presence of RHD. Serum BNP levels were measured by enzyme-linked immunoassay, while hsCRP levels were measured by the immunometric assay.

**Results:** Both serum BNP and hsCRP levels were higher in RHD groups than in the controls ($p = 0.001$ and $p = 0.018$, respectively). Serum BNP levels were elevated in the RHD patients than in the RFo patients ($p = 0.01$). Both BNP and hsCRP levels were correlated positively with echocardiographic parameters of the severity of MR ($p = 0.001$). The cut-off value of BNP levels of 9.02 ng/ml with sensitivity 67.7% and specificity 85.4% was associated with the risk of RHD. No correlation was found between BNP levels and the duration of RHD.

**Conclusions:** The serum BNP levels and hsCRP levels appear to be significantly associated with the RHD and the MR severity.

KEY WORDS:

**rheumatic fever, rheumatic heart disease, brain natriuretic peptide, hsCRP, mitral regurgitation.**

## INTRODUCTION

Acute rheumatic fever (RF) and chronic rheumatic heart disease (RHD) remain major causes of cardiovascular disability in school children and young adults from developing countries [1]. Cardiac involvement in the first attack and/or in recurrent episodes is determinant because it results in cumulative injury and permanent

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heart valve damage [2]. Rheumatic valve disease is the most severe sequel of RF which occurs in approximately 30 percent of patients with RF [3]. RHD presents with varying degrees of pancarditis and is associated with valve dysfunction.

The suggested pathophysiology for RHD production is that cross-reactive antibody attaches to cardiac tissue, stimulating infiltration of streptococcal-primed CD4+ T cells, which causes an autoimmune response and inflammatory cytokines (including tumor necrosis factor α [TNF-α] and interferon γ [IFN-γ]) are released. Since there are few IL-4 producing cells in the valvular tissue, inflammation continues, causing valvular lesions [4]. So, the increased levels of some inflammatory markers are expected in these patients.

RHD is the most common cause of severe mitral regurgitation (MR) in developing countries [1]. MR leads to progressive systolic and diastolic left ventricular (LV) failure, with an increased risk of sudden death [5].

Echocardiography-based surveys conducted in some developing countries showed that the prevalence of RHD was 3–10 times greater than previous assessments which were based only on clinical examination [6]. The echocardiographic indices of significant regurgitation of mitral valves are the basis for the diagnosis of MR and LV systolic and diastolic dysfunction. Markov modelling study has shown the echocardiographic screening to be a cost-effective strategy for early diagnosis of RHD and LV dysfunction but it is still relatively costly for widespread deployment in countries with limited resources [7]. Blood biomarker techniques could be alternative modalities for population screening of RHD with less resource-intense as respect to staff, equipment, and time and therefore able to be scaled [8].

The B type natriuretic peptide (BNP) system is ubiquitously and sensitively elevated in clinical circumstances including cardiomyopathies, valvular regurgitation, and congestive heart failure (CHF) in adult studies [9–11]. The plasma level of BNP is known to increase with LV dysfunction from many causes, and elevated plasma levels of BNP have been shown to indicate early stages of myocardial deterioration in various diseases [12–14]. BNP had several effects including antifibrotic remodelling and diuresis induction both of them might be adaptive in RHD [15]. BNP was higher in adults with severe rheumatic mitral disease and the levels reduced after mitral valve surgery [14]. These results increase the chance that BNP may also be beneficial in RHD [16]. So that, utilizing the combination of hormonal and echocardiographic parameters could provide a rigorous assessment of the severity of MR in these patients.

This study aimed to study the relationship between plasma levels of BNP and hsCRP and the RF and its complication, RHD, and to study their levels as indices of the severity of chronic rheumatic MR.

## MATERIAL AND METHODS

Ethical approval of this prospective study was obtained by the local ethics committee of the National Research Centre (NRC) in Egypt (May 2017). All subjects signed a free informed consent form. The study was conducted from June 2017 to March 2018.

Seventy-seven patients with a history of RF diagnosed according to Jones' modified criteria [17] together with 43 healthy subjects (age and gender-matched with the patients) served as controls were included in the study. Patients were collected from the out-patients cardiology clinic, a specialized paediatric hospital, Cairo University, Egypt, and from the out-patient cardiology clinic of Medical Research Centre of Excellence (MRCE) at NRC, Egypt. The controls were collected from the outpatient paediatric clinic of MRCE at NRC, Egypt.

A health questionnaire; including the name, the age, the gender, the family history, and the given medications were recorded for each patient. The medical history and the physical examination were done for all participants to determine their specific health status.

The RHD was diagnosed according to the clinical history and the cardiac examination of all patients and was confirmed by the transthoracic echocardiographic examination. Patients presented with other inflammatory diseases, neoplasia, infective endocarditis, or other infections were excluded from the study.

Echocardiography studies were carried out on a GE Vivid 6 machine using classical interrogation modalities. The diagnosis of valvular involvement was based on the revised 2015 Jones criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association [17]. Pathological MR was diagnosed according to the following criteria (all four criteria met): 1. Viewed in at least two images. 2. Jet length of greater than or equal to 2 cm in at least one image. 3. Peak velocity of greater than 3 m/s. 4. Pansystolic jet in at least 1 complete envelope. Chronic mitral valve changes were in the form of thickening of leaflets, chordal thickening and fusion, restricted motion of leaflets, and calcification.

Assessment of the severity of MR was determined according to the recommendation of the American society of echocardiography [18]: a) vena contracta: the severity of MR was determined according to the vena contracta width into mild MR with vena contracta less than 0.3 cm, moderate MR with vena contracta from 0.3 to 0.7 cm and severe MR with vena contracta more than 0.7 cm. b) regurgitation jet area: the severity of MR was determined according to jet area into mild MR with a jet area less than 4 cm$^2$, moderate MR with a jet area from 4 to 8 cm$^2$, and severe MR with a jet area more than 8 cm$^2$. c) effective regurgitation orifice area (ERO): mild MR with an ERO less than 0.2 cm$^2$, moderate MR with an

**TABLE 1.** The demographical and clinical characteristics of the studied groups

| Variable | RHD (n = 62) | RFo (n = 15) | Controls (n = 43) | p-value |
|---|---|---|---|---|
| Age (years) | 15.23 ±4.60 | 11.88 ±4.05 | 13.33 ±4.01 | 0.01[a]/0.05[b] |
| Sex (M/F) | 30 (48.4%)/ 32 (51.6%) | 10 (66.67%)/ 5 (33.33%) | 19 (44.2%)/ 24 (55.8%) | 0.314[a]/0.457[b] |
| Duration (years) | 6.15 ±4.43 | 4.69 ±3.64 | – | 0.313 |
| BMI (kg/cm²) | 19.69 ±3.74 | 19.10 ±5.31 | 20.60 ±1.45 | 0.243[a]/0.238[b] |
| SBP (mm Hg) | 103.33 ±14.74 | 93.08 ±14.22 | 95.54 ±9.71 | 0.012[a]/0.001[b] |
| DBP (mm Hg) | 66.56 ±11.77 | 65.00 ±6.77 | 61.55 ±10.11 | 0.491[a]/0.065[b] |

Data presented as mean ±SD, percentages, or (range) where appropriate. RHD – rheumatic heart disease, RFo – rheumatic fever only, BMI – body mass index, SBP – systolic blood pressure, DBP – diastolic blood pressure. [a] between RFo vs. RHD, [b] among different groups by ANOVA p < 0.05 was considered significant.
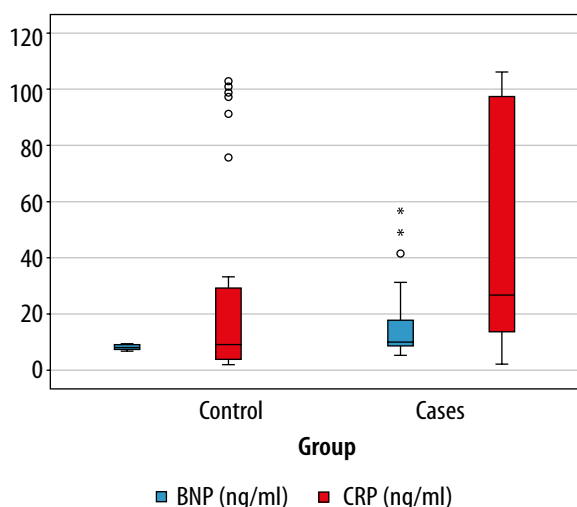


**FIGURE 1.** Comparisons of serum BNP and hsCRP levels in the total RF (n = 77) patients and the controls (n = 43)

ERO from 0.2 to 0.39 cm², and severe MR with ERO more than 0.4 cm².

Serum levels of BNP were measured by using enzyme-linked immunoassay (ELISA) kit (Cat No E1907h) as provided by the manufacture instructions. The reference range was defined as 0.125 ng/ml to 0.45 ng/ml. Serum hsCRP levels were measured by the chemiluminescent immunometric assay (the solid-phase) (Immulite/Immulite 1000) (Siemens Medical Solution Diagnostics, Eschborn, Germany). The reference range was up to 0.3 mg/l.

### STATISTICAL ANALYSIS

The statistical package SPSS (Statistical Package for the Social Sciences) version 25 was used for the statistical analysis of data. Quantitative data were shown as mean, standard deviation, median, minimum, and maximum. The non-parametric Kruskal-Wallis and Mann-Whitney tests were used for comparisons between quantitative variables. The Spearman correlation coefficient test was used to make relationships between quantitative variables. The receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off value of BNP and hsCRP levels for the detection of the severity of the disease. P-value < 0.05 was considered statistically significant.

## RESULTS

Our study included 77 RF patients and 43 healthy controls. The patients mean age was 14.54 ±4.67 (range = 4–28 years), males to females ratio, 40 (51.95%)/ 37 (48.05%). A secondary prophylaxis with three-weekly injections of benzathine penicillin was given to all RF patients. RHD group: Sixty-two (80.52%) showing rheumatic mitral regurgitation (MR), diagnosed by transthoracic echocardiographic examination. Rheumatic fever only (RFo) group: 15 patients (19.48%) had a history of RF without the presence of RHD. Among the RHD group, mild MR was found in 37 (63.8%) patients, moderate MR in 13 (22.4%) patients, and severe MR in 8 patients (13.8%). The mean age of the controls (n = 43) was 10.0 ±03.81, range 4–16 years, males to females ratio, 19 (44.2%)/24 (55.8%). The mean duration of the disease was 6.15 ±4.43 years in RHD vs. 4.69 ±3.64 years in RFo, p = 0.313.

The demographical and clinical characteristics of the studied groups are shown in Table 1.

### SERUM BNP AND HSCRP LEVELS IN THE STUDIED GROUPS

Serum BNP levels were higher in the total RF group than in the controls (median, 9.39 ng/ml [5.23–56.65] vs. 7.91 ng/ml [6.89–8.95], respectively, p < 0.001). Also, serum hsCRP levels were higher in the total RF group than in the controls (median, 26.55 ng/ml [2.30–105.90] vs. 9.00 ng/ml [2.00–102.70], respectively, p = 0.001) (Fig. 1).

Serum BNP levels were higher in RHD group than in the RFo group (median, 9.44 ng/ml [5.78–56.65] vs. 8.86 ng/ml [5.23–18.87], respectively, p = 0.01). Serum BNP in RHD and RFo groups were higher than those in the controls (median, 9.44 ng/ml [5.78–56.65] and 7.86 ng/ml [6.89–8.95] vs. 7.86 ng/ml [6.89–8.95], p < 0.001, p = 0.022 respectively). hsCRP levels were

**TABLE 2.** Comparison among the studied groups as regards to BNP and hsCRP levels

| Variable | RHD (n = 62) | RFo (n = 15) | Controls (n = 43) | p-value by ANOVA | p-value RFo vs. RHD | p-value RFo vs. controls | p-value RHD vs. controls |
|---|---|---|---|---|---|---|---|
| BNP (ng/ml) | 9.44 (5.78–56.65) | 8.86 (5.23–18.87) | 7.86 (6.89–8.95) | < 0.001* | 0.010* | 0.022* | < 0.001* |
| hsCRP (ng/ml) | 27.35 (2.50–105.90) | 17.05 (2.30–102.30) | 15.00 (2.00–102.70) | 0.047* | 0.192 | 0.172 | 0.018* |

*Data presented as a median and minimum-maximum. RHD – rheumatic heart disease, RFo – rheumatic fever only, BNP – pronatruritic peptide, hsCRP – high sensitivity C-reactive protein. P < 0.05 was considered significant.*

higher in RHD than in the controls (median, 27.35 ng/ml [2.50–105.90] vs. 15.00 ng/ml [2.00–102.70], $p = 0.018$, respectively) (Table 2).

Both BNP and hsCRP levels were correlated positively with echocardiographic parameters of MR severity: width of the vena contracta ($r = 0.431$, $p < 0.001$ and $r = 0.606$, $p = 0.0001$, respectively), the regurgant jet area ($r = 0.430$, $p = 0.001$ and $r = 0.450$, $p = 0.001$, respectively), effective regurgitant orifice area (ERO) ($r = 0.471$, $p = 0.001$ and $r = 0.423$, $p = 0.001$, respectively), regurgitant volume ($r = 0.480$, $p = 0.001$ and $r = 0.462$, $p = 0.007$, respectively) and the severity of MR ($r = 0.570$, $p < 0.0001$ and $r = 0.460$, $p < 0.0001$, respectively).

Also, BNP and hsCRP levels were correlated positively with left atrial (LA) dimensions ($r = 0.329$, $p = 0.004$ and $r = 0.327$, $p = 0.004$, respectively), left ventricular end systolic dimensions (LVESD) ($r = 0.0440$, $p < 0.001$ and $r = 0.347$, $p = 0.002$, respectively) and left ventricular end diastolic dimensions (LVEDD) ($r = 0.402$, $p < 0.001$ and $r = 0.392$, $p < 0.001$, respectively). hsCRP levels were correlated positively with left ventricular posterior wall in diastole (LVPWd) ($r = 0.275$, $p = 0.015$) and the deceleration time of E of mitral inflow ($r = 0.232$, $p = 0.047$). Serum BNP levels were correlated positively and mitral valve area ($r = 0.337$, $p = 0.009$) (Table 3). There were no significant correlations between the duration of the RHD and both of BNP and hsCRP levels ($r = 0.002$, $p = 0.990$, $r = 0.180$, $p = 0.152$, respectively). Also, no significant correlations were found between age of patients and both of BNP and hsCRP levels ($r = -0.041$, $p = 0.719$ and $r = 0.112$, $p = 0.328$, respectively).

For comparison of row biomarkers performance, typical of the pre-defined threshold level samples, we tested a wide range of test performance using the ROC. The area under the curve (AUC) of serum BNP levels in RFo patients vs. controls were 0.714 with a cut-off value of 8.01 ng/ml associated with the risk of RFo (sensitivity 81.3% and specificity 58.1% [95% CI: 0.546–0.881; $p < 0.012$]). While in RHD group vs. controls, the AUC of serum BNP levels were 0.786 with a cut-off value of 9.02 ng/ml associated with the risk of RHD (sensitivity 67.7% and specificity 85.4% [95% CI: 0.702–0.871; $p < 0.001$]). Also, AUC of serum hsCRP levels were 0.635 with a cut-off value of 20.15 ng/ml associated with the risk of RHD (sensitivity 62.9% and specificity

**TABLE 3.** Pearson's correlations between BNP and hsCRP levels with the clinical and the echocardiographic parameters

| Variable | BNP ( ng/ml) | | hsCRP (ng/ml) | |
|---|---|---|---|---|
| | r | p | r | p |
| Age (years) | −0.041 | 0.719 | 0.112 | 0.328 |
| Duration (years) | 0.002 | 0.990 | −0.180 | 0.152 |
| AO (mm) | −0.062 | 0.595 | 0.302 | 0.008* |
| LA (mm) | 0.329 | 0.004* | 0.327 | 0.004* |
| IVS d (mm) | −0.026 | 0.824 | 0.191 | 0.094 |
| LVEDD (mm) | 0.402 | <0.001* | 0.392 | < 0.001* |
| LVPW d (mm) | −.0003 | 0.981 | 0.275 | 0.015* |
| LVESD (mm) | 0.440 | <0.001* | 0.347 | 0.002* |
| EF (%) | −0.095 | 0.410 | −0.101- | 0.379 |
| FS (%) | −0.062 | 0.590 | −0.069 | 0.547 |
| E wave (cm/s) | −0.048 | 0.683 | 0.047 | 0.694 |
| A wave (cm/s) | −0.008 | 0.944 | 0.143 | 0.224 |
| E/A ratio | 0.061 | 0.604 | −0.082 | 0.487 |
| DC time of E (s) | −0.115 | 0.330 | 0.232 | 0.047* |
| MV area (mm²) | 0.337 | 0.009* | −0.151 | 0.514 |
| Vena contracta (mm) | 0.431 | < 0.001* | 0.606 | 0.0001* |
| Regurgitant jet area (cm²) | 0.430 | 0.001* | 0.450 | 0.001* |
| ERO (cm²) | 0.471 | 0.001* | 0.423 | 0.001* |
| RV (ml/beat) | 0.480 | 0.001* | 0.462 | 0.007* |
| Severity of MR | 0.570 | < 0.0001* | 0.460 | < 0.0001* |

*LA – left atrium, LVEDD – left ventricular end-diastolic dimension, LVESD – left ventricular end-systolic diameter, FS – fraction shortening, EF – ejection fraction, E – early peak diastolic velocity, A – late peak diastolic velocity, DC – deceleration time of E wave, MV area – mitral valve area, ERO – effective regurgitant orifice area, RV – regurgitant volume, MR – mitral regurgitation. P < 0.05 was considered significant.*

60.4%) [95% CI: 0.528–0.742; $p < 0.015$]) (Table 4 and Fig. 2).

## DISCUSSION

We found that the serum BNP and hsCRP levels were elevated in patients with RF and RHD than in healthy controls. Serum BNP levels were higher in the RHD group than in the RFo group. BNP is a cardiac hormone that is

**TABLE 4.** The ROC curves for the BNP and hsCRP levels and the severity of RFo and RHD

| Variable | Area under curve | P-value | 95% confidence interval | | Cut-off value | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|---|---|
| | | | Lower bound | Upper bound | | | |
| RFo | | | | | | | |
| BNP (ng/ml) | 0.714 | 0.012* | 0.546 | 0.881 | 8.01 | 81.3 | 58.1 |
| hsCRP (ng/ml) | 0.594 | 0.268 | 0.434 | 0.755 | – | – | – |
| RHD | | | | | | | |
| BNP (ng/ml) | 0.786 | < 0.001* | 0.702 | 0.871 | 9.02 | 67.7 | 85.4 |
| hsCRP (ng/ml) | 0.635 | 0.015* | 0.528 | 0.742 | 20.15 | 62.9 | 60.4 |

*RFo – rheumatic fever only, RHD – rheumatic heart disease, BNP – pronatruritic peptide, hsCRP – high sensitivity C-reactive protein. p < 0.05 was considered significant*
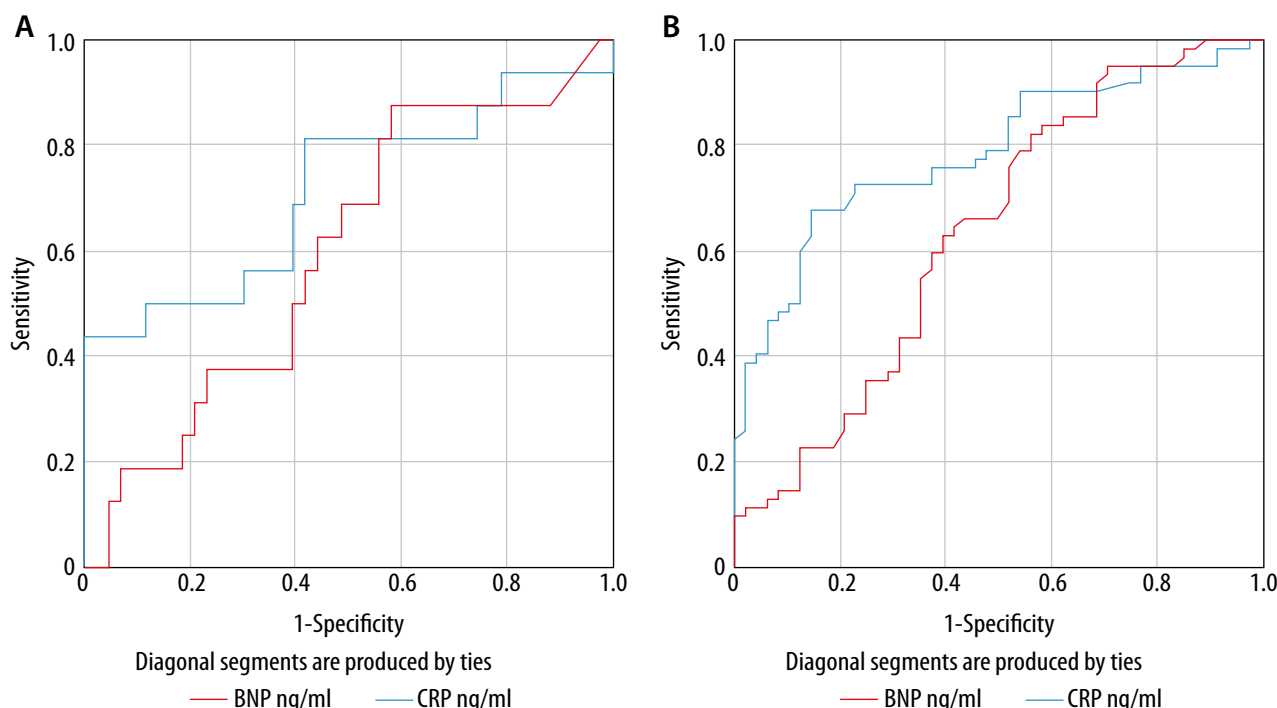


**FIGURE 2. A)** The ROC curves for serum BNP and hsCRP levels and the severity of the RFo. **B)** The ROC curves for serum BNP and hsCRP levels and the severity of the RHD

produced by atrial and ventricular myocytes in response to increased stress in the form of pressure or volume overload [19]. It is known that elevated BNP levels are correlated with LV systolic and diastolic dysfunction [20]. Also, the levels of BNP depend on the LV filling pressure [20]. In patients with CHF, the plasma level of BNP is elevated and increased proportionally with the degree of LV dysfunction and the severity of heart failure symptoms [21]. Suggesting that RHD disease, in contrast to myocardial dysfunction, is the mechanism of CHF in rheumatic carditis and represents a combined effect of elevated ventricular afterload, LV enlargement and right ventricular volume overload. These results suggest the possibility of broadening the investigation of BNP measurement to other diseases that gradually lead to LV dysfunction, such as RHD.

Chronic RHD of the mitral valve (MV) progresses over years and leads to a number of pathologic changes, which are the morphological diagnostic criteria for rheumatic valve disease: fusion of the leaflet commissures; thickening, fibrosis, and calcification of the leaflet cusps; and shortening of the chordae tendineae [17]. Chronic rheumatic MV changes are now considered as an activated and regulated molecular process that is related to injury, deposition of lipids, and inflammation [22]. Chronic rheumatic MR causes a volume overload of the LV with subsequent occurrence of a compensatory LV dilation and eccentric hypertrophy. The progressive increase in regurgitant volume, a decrease in contractility, an increase in afterload, or a combination of all these factors result in the occurrence of a decompensated state [1].

The plasma hsCRP levels have been described as a credible marker for oxidative stress and systemic inflammation [23, 24]. In our study, serum hsCRP levels were significantly higher in patients with RHD than in

the controls, with higher hsCRP levels were strongly associated with risk of RHD. These results may support the assumption that a chronic inflammation of cardiac valves will continue after an acute RF attack, a more rapid progression of valvular dysfunction will occur in patients with a more acute inflammatory reaction. Furthermore, it can be assumed that an abnormal antibody reaction leads to an autoimmune process that causes progressive and latent damage to the heart valves [25, 26].

The present study evaluated the RHD patients with various grades of severity of rheumatic MR. Significant associations were found between BNP levels and the echocardiographic parameters of MR severity. These results were in agreement with [27] who found a significant positive relationship between BNP level and severity of organic MR. Furthermore, in our study, BNP levels were correlated positively with LA dimensions, LVESD and LVEDD. BNP secretion in patients with MR and/or mitral stenosis seemed to be associated with the increases in LA more than LV wall stress. The anatomical or functional stretching of the LA should play an important function in the increased BNP secretion. This assumption is supported by the establishment of the BNP synthesis by atrial cardiomyocytes and the joint storage of A-type natriuretic peptide and BNP in atrial granules [28].

The currently recommended the guidelines for surgery of MR are (a) severe symptomatic MR or (b) chronic asymptomatic severe MR and mild to moderate LV dysfunction, ejection fraction (EF) 30% to 60%, and/or LVESD more than or equal to 40 mm [28]. The timing of surgery in MR is a very critical and challenging. It is generally accepted that the surgical intervention should be considered before the onset of symptomatology [28]. Pizarro *et al.* searched a group of isolated severe asymptomatic organic MR patients with normal LV function as expressed by EF of more than 60% [29]. They reported that patients with BNP levels more than 105 pg/ml had a worse prognosis, which provides an independent prognostic usefulness of BNP levels in patients with asymptomatic severe MR. All of these quarrels in the management of MR have led to the realization of a requirement for markers other than LV size and EF that might help in the determination of the approach or onset of LV dysfunction and could assist in optimizing the surgical timing.

BNP levels were stronger predictors than various echocardiographic parameters such as ERO and the LVESD [28]. From this point of view, it has been suggested that BNP can be used in combination with traditional imaging techniques for risk stratification of asymptomatic patients who may benefit from the early surgical intervention.

The present study revealed the increased serum hsCRP levels in RHD patients and significant associations were found between hsCRP levels and the echocardiographic parameters of MR severity. These results suggested that hsCRP testing may serve as a biomarker for remodelling of LV in chronic rheumatic MR and may have the utility of identification of the earliest stages of LV decompensation. The low hsCRP level indicate that MR is not severe, when the echocardiographic examination is technically difficult. Attar *et al.* [26] reported that RHD patients with high levels of hsCRP are more susceptible to atrial fibrillation. The idea of long-term treatment with anti-inflammatory drugs, such as aspirin could be highlighted as regards to the high level of hsCRP in the chronic stage of the disease. Also statins have been shown to inhibit the inflammatory and the non-inflammatory processes that cause the acute-phase response and can lower hsCRP levels [26].

In the present study, the critical serum level of BNP associated with the risk of RHD was 9.02 ng/ml with a sensitivity of 67.7% and a specificity of 85.4%. Abdel Fattah *et al.* [27] reported that the cut-off point of 61 pg/ml mm with 97% sensitivity and 89% specificity was detected for predicting patients with severe MR. Meneghelo *et al.* reported that [30] the cut-off value for BNP 15.40 pg/ml with 73% sensitivity and 74% specificity could be used for detecting patients with severe MR. Sutton *et al.* [31] used a cut-off point of BNP greater than 12 (pmol/l) with 75% sensitivity and 85% specificity for recognizing symptoms in patients with organic MR.

No correlations were found between the serum BNP levels and the age of the patient or disease duration. These results might be due to small sample size of the study. A further large study is required to estimate the effect of duration of the disease on the BNP levels.

## CONCLUSIONS

Serum BNP and hsCRP levels were higher in patients with RF than in the controls especially those associated with RHD. It also showed a significant association between the serum BNP and hsCRP levels and the severity of MR. BNP and hsCRP levels can be used as additional tools for the diagnosis and monitoring of RHD patients. Whether management of the ongoing inflammation can alter future treatment strategies is an issue of future large study. The cut-off values of BNP could be used to identify patient with severe MR. An assessment of BNP as a prognostic marker in patients with severe rheumatic MR needs larger studies.

## ACKNOWLEDGMENTS

## DISCLOSURE

The author declares no conflict of interest.

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