

Profile of Native infective endocarditis at a tertiary care hospital in Tunisia

Profil de l'endocardite infectieuse sur valve native : A propos d'une série Tunisienne

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SUMMARY

Introduction : Despite recent advances in diagnosis and treatment, Native Infective Endocarditis (NIE) remains a serious disease especially in developed countries. The aim of the work is to evaluate recent changes in the profile of Native Infective Endocarditis at a tertiary care hospital in Tunisia over a 10-year period and to determine predictors of outcome.

Methods : We gathered prospectively the data from 110 patients who fulfilled the modified Duke's criteria for NIE during a 10-year period. The logistic regression model was used to identify predictive factors for death.

Results : The mean age of patients was 39.2 ± 14 years. A male predominance was noted with a sex ratio of 1.34. The median time from admission to diagnosis was 15 days. Rheumatic heart disease (RHD) was the predominant underlying heart condition (92%). The infective agent was identified in 40.9% of cases, and the most frequent causative agents were streptococci (46.6%), followed by staphylococci (42.2%). Echocardiography demonstrated vegetations in 90% of cases, abscesses in 12.7% and valvular mutilation in 21%. Complications were dominated by heart failure in 36% of patients. Surgery was performed during the acute phase of the infective endocarditis (IE) in 29% of cases. The overall in-hospital mortality was 21.8%. On multivariate analysis, staphylococci infection, heart failure, neurological complications and abscesses were predictors of in-hospital mortality.

Conclusion : NIE remains a severe disease affecting the young population in Tunisia. RHD continues to be the most common underlying heart condition and streptococci were the major causative agents. Its prognosis is still dark with a high rate of mortality.

KEYWORDS

Endocarditis, Rheumatic Heart Disease, Valvular Heart Disease, Echocardiography.

RÉSUMÉ

Introduction : Malgré les progrès récents dans le diagnostic et le traitement, l'endocardite infectieuse (EI) sur valve native reste une maladie grave, en particulier dans les pays développés. Le but de ce travail est d'évaluer les changements récents dans le profil de l'endocardite infectieuse sur valve native dans un hôpital en Tunisie au cours des 10 dernières années et de déterminer les facteurs prédictifs de complications.

Méthodes : Nous avons colligé prospectivement les données de 110 patients qui répondent aux critères modifiés de Duke de l'EI au cours des 10 dernières années. Le modèle de régression logistique a été utilisé pour identifier les facteurs prédictifs de mortalité.

Résultats : L'âge moyen des patients était de $39,2 \pm 14$ ans. Une prédominance masculine a été notée avec un sex-ratio de 1,34. Le délai médian entre l'admission et le diagnostic était de 15 jours. La cardiopathie rhumatismale (CR) était la principale pathologie sous-jacente (92%). L'agent infectieux a été identifié dans 40,9 % des cas, et les agents causaux les plus fréquents étaient les streptocoques (46,6 %), suivis des staphylocoques (42,2 %). L'échocardiographie a mis en évidence des végétations dans 90 % des cas, des abcès dans 12,7 % et une mutilation valvulaire dans 21 %. Les complications ont été dominées par l'insuffisance cardiaque chez 36% des patients. La chirurgie a été pratiquée pendant la phase aiguë de l'EI dans 29% des cas. La mortalité globale à l'hôpital était de 21,8 %. En analyse multivariée, l'infection à staphylocoques, l'insuffisance cardiaque, les complications neurologiques et les abcès étaient des facteurs prédictifs de la mortalité hospitalière.

Conclusion : L'EI native reste une maladie sévère affectant la population jeune en Tunisie. La CR reste la pathologie cardiaque sous-jacente la plus fréquente et les streptocoques ont été les principaux agents causaux. Son pronostic est encore sombre avec un taux de mortalité élevé.

MOTS-CLÉS

endocardite, cardiopathie rhumatismale, valvulopathie, échocardiographie

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INTRODUCTION

Despite recent advances in diagnosis and treatment, infective endocarditis (IE) remains a serious disease with high morbidity and mortality. Its profile has evolved continuously in developed countries [1,2]. However, few data were available concerning this profile in developing countries the last years.

Although several studies [1, 2] have evaluated possible predictors of mortality in patients with IE, recent reports from Tunisia are scarce.

The aim of the work is to describe the clinical manifestations, echocardiographic and laboratory findings, microbiological profile, management strategies and in-hospital outcome of patients with native infective endocarditis (NIE) who were admitted to a tertiary care hospital in Tunisia over a last 10 years and to determine predictors of in-hospital mortality.

METHODS

From December 2000 to December 2019, 110 patients with definite NIE according to the modified Duke's criteria, who were admitted to the cardiology department of Rabta Hospital, were included in the study.

We excluded right-sided valve endocarditis, prosthetic endocarditis, congenital disease and the case of probable or uncertain endocarditis in order to emphasize on NIE characteristics.

Clinical presentation, laboratory tests, and echocardiography were performed at admission to hospital.

Data recorded were concerning epidemiological characteristics, predisposing condition, clinical presentation, bacterial profile, echocardiographic finding (Transthoracic (TTE) and/or transesophageal TEE echocardiography), treatment approach and outcomes.

These data were gathered prospectively at diagnosis and during hospitalization.

Early surgery was defined as valve replacement or

repair performed during the course of the antibiotic therapy. The primary endpoint was the global in-hospital mortality.

STATISTICS ANALYSIS

Quantitative variables are expressed as means \pm standard deviations, and qualitative variables are expressed as percentages. Comparison between groups was carried out using Student's t-test or the Chi² test depending on the nature of quantitative or qualitative variables. Univariate then multivariate analyses were realized in order to determine predictor's factors of mortality using a logistic regression model. A $p < 0.05$ was considered significant.

RESULTS

General characteristics of population

The average age of our patients was 39.2 ± 14 years (range 30–78 years). More than 50% of patients were aged less than 40 years. The median time between onset of symptoms and diagnosis of IE was 15 days (6–55 days). A male predominance was noted with a sex ratio of 1.34.

Clinical and laboratory findings on admission were represented in **Table 1**.

Table 1. Clinical and laboratory findings on admission for IE.

| Predictor factors of mortality | Death (n : 24) | Survival (n : 86) | P Value |
|--------------------------------|----------------|-------------------|---------|
| Age | 42 \pm 2 | 39 \pm 6 | 0.6 |
| Positive Blood culture | 33% | 44% | 0.1 |
| Streptococcus | 28.4% | 12% | NS |
| Staphylococcus | 35% | 13.75% | <0.005 |
| Valvular Mutilation | 50% | 13% | p<0.001 |
| Abscess | 30% | 6% | P<0.001 |
| Heart failure | 60% | 26.25% | p<0.005 |
| Neurological complication | 35% | 11.25% | p=0.04 |
| Early surgery | 20% | 23% | 0.0 |

The most common underlying disease was rheumatic valvular disease, which was responsible for 92% of the cases of NIE (n=101), followed by degenerative valvopathies' in 8% (n=9).

The mitral valve was the most frequently involved, affecting 88% of cases (n= 97)

A pathogenic microorganism was isolated from blood cultures in 45 cases (40.9%). The frequencies of the causative agents are represented in **Figure 1**.

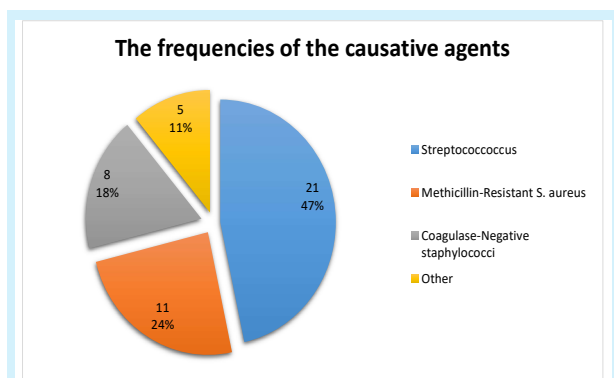


Figure 1. The frequencies of the causative agents of IE.

Streptococcus was the most common causative organism isolated in 21 patients (46.66%). Community-acquired methicillin-resistant staphylococcus aureus was found in 11 patients (24.44%) and coagulase-negative staphylococcus in 8 patients (17.77%). Culture negative endocarditis occurred in 55 patients (59.1%) and was commonly in 22 patients who received antibiotics prior to the diagnosis of NIE.

TTE was performed in all cases and TEE in 80% (n=72). Vegetation was evident in 90% of the cases (n=99) with a mean size of 11 ± 3 mm, and the majority of these were attached to a cardiac valve (89%). Abscesses were observed in 12.7% (n=14), valve mutilation in 21% (n=21).

The antibacterial treatment of NIE was started empirically and then adjusted according to the antibiotic susceptibility result. The mean duration of antibiotic was 35 days [10 -60]. The mean hospital duration was 39 (24–53) days, with a total range of 1–163 days. During this period,

complications were occurred in 80% of cases (n=88) and were dominated by heart failure in 40 patients, embolic complications were present in 14 patients, the major embolization sites were the brain (n=9), the spleen (n=3), peripheral arteries (n=1) and renal (n=1). Early surgery was performed in 32 cases (29%) with a mean time from admission to operation of 17 days with extreme of [1 - 30]. The indications for surgical treatment were congestive heart failure (20 patients (62.5%)), persistent signs of septicemia despite antibiotic treatment (10 patients (31.5%)) and recurrent embolization (two patients (6. %)).

24 patients died corresponding to an overall mortality of 21.8%. The principal causes of death were severe heart failure and septic shock.

Factors affecting in-hospital mortality in the univariate analysis were mentioned in **table 2** staphylococci infection, abscesses, neurological complications, heart failure, and valve mutilation. On multivariate analysis (**table 3**), staphylococcus infection (OR:2.95, p0.005), abscesses (OR :4.25, p 0.004), heart failure (OR:7.54, p 0.001) and neurological complications (OR 3; p 0.02) were predictors of in hospital mortality.

Table 2. Factors affecting in-hospital mortality in the univariate analysis

| | OR | IC | P |
|-----------------------------------|-------------|--------------------|--------------|
| Staphylococcus | 2.95 | [1,51-5,78] | 0.005 |
| Abscess | 4.25 | [1.42-4.58] | 0.004 |
| Heart failure | 7.54 | [1.86-30.6] | 0.001 |
| Neurological complications | 3 | [1.05 ; 11] | 0.02 |

Table 3. Variable analysis independent factors of hospital mortality

| Predictor factors of mortality | Death (n :24) | Survival (n : 86) | P Value |
|--------------------------------|---------------|-------------------|---------|
| Age | 42+2 | 39+6 | 0.6 |
| Positive Blood culture | 33% | 44% | 0.1 |
| Streptococcus | 28.4% | 12% | NS |
| Staphylococcus | 35% | 13.75% | <0.005 |
| Valvular Mutilation | 50% | 13% | p<0.001 |
| Abscess | 30% | 6% | P<0.001 |
| Heart failure | 60% | 26.25% | p<0.005 |
| Neurological complication | 35% | 11.25% | p=0.04 |
| Early surgery | 20% | 23% | 0.0 |

DISCUSSION

The major findings of our study are as follows:

1) NIE affects young in Tunisian population, 2) Rheumatic valve disease was the most common underlying heart disease, 3) High rate of negative blood cultures remains worrying, 4) Streptococcus remains the major pathogen agent, 5) Prognosis of NIE is still dark with high mortality 6) Independent factors of in-hospital mortality were staphylococcus infection, abscesses, heart failure and neurological complications.

During recent years, there have been changes in the diagnosis and treatment of the infective endocarditis, and its epidemiological features have changed significantly over the past decades in developed countries [3,4]. However, information on the profile of NIE in developing countries is relatively scarce, but differences have been reported [5].

When comparing our results with other reports [5, 6], the male to female ratio was in agreement with most case series.

According to our study, rheumatic valvular disease remains the most common underlying heart disease. As a result, our patients were younger, which is consistent with previously published studies from developing countries [7]. But, this contrasts with recent reports showing a steady increase in the median age [8, 9] and especially this trend in the developed countries is likely due to 2 factors: the increasing proportion of elderly people in the general population and the decline in the incidence of rheumatic heart disease.

As in other series [8, 10], the diagnosis of infective endocarditis in our present experience was made relatively late in the course of the disease, and this feature has not been changed by the introduction of new diagnostic tools.

Similar to other reports [11], the classic signs and symptoms of IE described in the late William Osler were

only present in a minority of patients (5%). This might be due to the more acute presentation of the disease.

Rheumatic Heart Disease (RHD) was the most common underlying cardiac condition found in our study. This is commensurate with other reports from neighboring developing countries where the proportion of RHD reaching 53% in a Yemeni cohort [12] and 39% in Turkish case series [13] whereas many studies report very low proportion [14] especially in developed countries. This can be explained by the broad use of antibiotics, resulting in a decrease in the incidence of rheumatic fever during the last few decades.

The proportion of negative blood cultures was high in our series and was similar to what reported in developing countries [15,16]. This was probably explained by the frequency of antibiotic use by patients prior to hospitalization and by a non-compliance with the rules of practice for sampling according to the recommendations of the learned societies of cardiology and bacteriology [17,18].

Our data indicate that 80% of patients had complications. All complications described in our study have been previously reported in the literature [1,2,13]. In our study, heart failure is the most common complication in patients with IE which is in agreement with many previous reports [19].

The most common paravalvular complication observed in our patients' cohort was abscesses formation in 14 cases. This finding was comparable to contemporary reports [1]. The role of early surgical intervention in cases of NIE complications is now accepted widely [18]. However, randomized studies rather than case series are needed to confirm these conclusions. Many reports corroborate our results when the rate of early surgery ranged from 25% to 45% [1,2], but when comparing our results with a previous Tunisian reports, we found a trend to a decrease in early surgery frequencies (32% in our

report versus 56.4% and 50.7% in respectively Abdelatif [20] and Trabelsi studies [21]).

Despite advances in diagnostic imaging methods, blood culture techniques, antibiotic therapy, the surgical approach and the concept of «endocarditis team», NIE is still associated with a severe outcome. The overall in-hospital mortality rates remain high 21% and comparable to previous Tunisian studies rate [20,21] respectively 20% and 19%, higher than the rates 16% reported in CADRE-IE[22] and was in agreement with the available literature in which mortality ranges between 10% and 30% in developing countries [23-24].

Staphylococci infection, abscesses, congestive heart failure, embolic events were the independent risks factor of in-hospital mortality. Several reports corroborated our results [1,20,25] and especially staphylococcus infection which was a strong risk factor associated to mortality [26].

Limitations of study

Our study group was relatively small and included patients from a single large tertiary care center and explained by our select inclusion criteria. These facts may have caused selection bias resulting in limitations to the generalization of the results.

Therefore, a multi-centric study is needed to corroborate our conclusions

For the epidemiological study, IE should have been studied in all its aspects. But we are limited to left valve native IE because few studies have been interested in this type of IE.

The small sample size could have exerted some influence on the results of the multivariate analysis. Thus, studies including a larger number of events are necessary to confirm (or not) our findings regarding the independent predictors of in-hospital death.

CONCLUSION

NIE remains a severe disease affecting the young population in Tunisia, rheumatic heart disease continues to be the most common underlying heart condition and streptococci were the major causative agents, negatives blood cultures are worrying many factors influence in hospital mortality. Recognition of these factors could improve risk stratification and, therefore, the selection of patients for more intensive treatment.

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