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# Predictors of Renal Involvement in Patients with Infective Endocarditis

*Thesis*

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بسم الله الرحمن الرحيم

وما توفيقي إلا بالله عليه توكلت واليه أنيب

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# List of Abbreviations

| | |
|---|---|
| **AIDS** | **Acquired immunodeficiency syndrome** |
| **AIN** | Acute interstial nephritis |
| **AKI** | Acute kidney injury |
| **ANCA** | Anticytoplasmic antibody |
| **ARF** | Acute renal failure |
| **ATN** | Acute tubular necrosis |
| **BAV** | Bicuspid aortic valve |
| **BD** | (BioMérieux, Inc., Durham, N.C.) |
| **BUN** | Blood urea nitrogen |
| **BUN/SCr** | Blood urea nitrogen/Serum creatinine |
| **CBC** | Complete blood count |
| **CHF** | Congestive heart failure |
| **CI** | Confidence interval |
| **CNS** | Central nervous system |
| **CrCl** | Creatinine clearance |
| **CRF** | Chronic renal failure |
| **CRP** | C- reactive protein |
| **CT** | Computerized tomography |
| **DCCT** | Diabetic control and complications trial |
| **DM** | Diabetes mellitus |
| **eGFR** | Estimated glomerular filtration rate |
| **ESR** | Erythrocyte sedimentation rate |
| **FENa** | Fractional excretion of sodium= [urine Na x plasma Cr /plasma Na x urine Cr] x100. |
| **FEurea** | Fractional excretion of urea= [urine urea x plasma Cr/plasma urea x urine Cr] x100. |
| **GFR** | Glomerular filtration rate |
| **GN** | Glomerulonephritis |
| **HACEK** | Hemophilus parainfluenzae, H. aphrophilus, H. paraphrophilus, H. influenzae, Actinobacillus actinomyctem comitans, Cardio bacterium hominis, Eikenella corrodens, Kingella kingae and K. denitrificans . |
| **HF** | Heart failure |
| **HB** | Haemoglobulin |
| **HCM** | Hypertrophic cardiomyopathy |
| **HIV** | Human immunodeficiency virus |
| **ICE** | International collaboration on endocrditis |

| | |
|---|---|
| **IDMS** | Isotope dilution mass spectrometry |

| | |
|---|---|
| **IE** | Infective endocarditis |
| **IVDU** | Intravenous drug use |
| **L-ASP** | L-asparaginase |
| **MVP** | Mitral valve prolapsed |
| **MRA** | Magnetic resonance angiography |
| **MDRD** | Modification of diet in renal disease |
| **MSSA** | Methicillin sensitive staphylococcus aureus |
| **NGAL** | Neutrophil gelainase associated lipocalin |
| **NSAIDS** | Non steroidal anti inflammatory drug |
| **NVE** | Native valve endocarditis |
| **PVE** | Prosthetic valve endocarditis |
| **rpm** | 3000 urine centrifuged |
| **S. aureus** | staphylococcus aureus |
| **SBE** | Staphylococcus aureus bacteremia |
| **S Cr** | Serum creatinine |
| **SD** | standard deviation |
| **SPSS** | Statistical package for social sciences |
| **SSA** | Sulfosalicylic acid |
| **TTE** | Transthoracic echocardiography |
| **TEs** | Thromboembolisms |
| **TEE** | Transoesophgeal echocardiography |
| **TLC** | Total leucocytic count |
| **VS** | Versus |

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# Abstract

**Background:** IE is not an easily treated disease. Renal involvement commonly occur in IE patients, and are usually multifactorial. Patients can develop different forms of renal involvement. A variety of organisms may be involved in those developing this involvement, with the most common being S. aureus. Renal involvement is associated with an increased risk of mortality.

**Objectives:** The aim of this study is to determine the prevalence and the predictors of renal involvement in IE patients treated in single tertiary care center in Egypt.

**Patients and methods:** The study involved 144 patients admitted at Cairo University Hospitals during the period from 2/2005 to 10/2008 with definite/possible IE according to the modified Duke criteria for the diagnosis of IE. The data of hospital admission were analyzed retrospectively.

**Results:** The prevalence of renal involvement in IE patients in our study was 71.6%. Males were more common than females (52.1% versus 47.9%). The most common organism was S. aureus (21.8%). Predictors of renal involvement were age (p= 0.003), diabetes mellitus (p=0.04), hospitalization within last 3 month (p= 0.01), heart failure (p= 0.01), leukocytosis (p= 0.02), anemia (p= 0.001) and vancomycin (p=0.04**)**. Renal failure occurred in 26.9% and dialysis was required in 5.2% of patients as a consequence of their renal impairment. Mortality rate of patients who developed renal involvement in IE was high, it represented 46.9%.

**Conclusion:** Heart failure, leukocytosis and anemia, the presence of S. aureus, and vancomycin used in IE treatment are all useful predictors of renal involvement.

**Keywords:** Infective endocarditis, renal failure and mortality rate.

# Introduction

Infective Endocarditis (IE) is an inflammatory disease affecting the native endocardium, heart valves, or related structures. It can involve the prosthetic valves, aortopulmonary shunts, surgical patches, or indwelling central venous catheters. The infecting organism can be bacterial, fungal, viral, chlamydia, or rickettsial. It is a diagnostic and therapeutic challenge to clinicians. Today, the Duke Criteria presented in 1994 and subsequent modification are considered to be the most accurate [1-2]. The epidemiology, clinical, and microbiologic spectrum of IE is significantly different in the developing countries compared to the western world [3-4]. In addition, developing countries may have a higher incidence of 'culture negative endocarditis' than in the west, largely secondary to prior doctor-prescribed or self administered antibiotic use [5-6]. The incidence of IE is rising [9-10]. The mortality rate in recent decades has held steady at 15% to 50% [8].

The clinical outcome of IE is determined by the degree of damage to the heart, the location of infection (right side versus left side, aortic versus mitral valve) and type of organisms. IE is associated with a myriad of complications, one or more of which occur in the majority of patients. The frequency and type of complications due to IE have changed with advances in diagnosis and therapy. The life threatening complications from IE are still common despite echocardiographic diagnosis and use of effective antibiotics [7, 13-15]. Complications and outcomes are related in part to underlying co morbidities [11]. Complications of IE may involve cardiac structures when the infection spreads within the heart or extra cardiac ones when the cause is usually from embolic origin, they may also be due to medical treatment or to the septic condition itself.

Renal involvement defined as protein in urine greater than 150 mg per 24 h [105] with haematuria or impaired glomerular filtration rate. Renal involvement reflects a systemic manifestation of IE. The underlying etiology leading to a rapidly progressive renal impairment, might be due to haemodynamic impairment in cases with heart failure, sepsis, after cardiac surgery, antibiotic toxicity, nephrotoxicity of contrast agents used for imaging purposes and renal embolization [16, 20]. Renal involvement in patients with IE indicates a poor prognosis, [18] mostly for non-staphylococcal infection. A mildly abnormal creatinine concentration on admission carries a poor prognosis [17-18, 240]. Early prediction of renal involvement is valuable to allows identification of high risk patients who an aggressive strategy will be potentially useful.

Renal complications may occur in any form of endocarditis but are particularly frequent in patients with IE due to S. aureus in up to 40-50% of cases [17-20]. Localized infarction present in 31% and acute glomerulonephritis in 26% [18]. Acute interstitial nephritis found in 10%. Renal cortical necrosis present in 10%. Acute renal failure present in 30 % of patients and predicts poor prognosis. A rapid progression of glomerulonephritis due to immune complex associated with poor prognosis [20]. Membranoproliferative glomerulonephritis is the lesion most frequently seen in shunt nephritis, but in some patients in whom untreated, mild renal involvement may progress to the development of severe impairment such as crescents and sclerotic glomeruli, possibly through the prolonged immune mediated pathogenesis [21-23].

To prevent these complications, antibiotic doses should be adjusted for creatinine clearance with careful monitoring of its serum levels and imaging with nephrotoxic contrast agents should be avoided in those with haemodynamic

impairment or previous renal insufficiency. The initiation of effective antibiotic therapy for bacterial endocarditis is associated with a reduction in the incidence of emboli in the first one to two weeks of therapy [27]. Although effective strategies to treat rapidly progressive glomerulonephritis have not been established, steroid therapy, immunosuppressive therapy, and plasmapheresis in addition to antibiotic therapy has been shown to be beneficial [24-28].

# Aim of this study

- To detect the prevalence of renal involvement in patients with IE.
- To detect the predictors of renal involvement in patients with IE.

# Incidence and epidemiology

IE is a microbial infection of the endothelial surface of the heart. The characteristic lesion, the vegetation, is a variably sized amorphous mass of platelets and fibrin in which abundant microorganisms and scant inflammatory cells are enmeshed. Heart valves are most commonly involved; however, infection may occur at the site of a septal defect, on chordae tendineae, mural endocardium arteriovenous shunts, arterioarterial shunts (patent ductus arteriosus), or coarctation of the aorta [160].

Over the past 100 years the incidence of IE has not changed significantly. This may seem surprising as the detection of bacteremia has improved significantly during this time period, and the introduction of two dimensional echocardiography has revolutionized the diagnosis of bacterial endocarditis. Epidemiological studies demonstrate that IE accounts for about 1 case per 1,000 hospital admissions (range 0.16 to 5.4 cases per 1,000 admissions) [29]. The incidence of IE ranges from one country to another within 3–10 episodes/100,000 persons per year [35]. A recent systematic review of 15 population-based investigations accounting for 2371 IE cases from seven developed countries (Denmark, France, Italy, The Netherlands, Sweden, the UK, and the USA) showed an increasing incidence of IE associated with a prosthetic valve, an increase in cases with underlying MVP, and a decrease in those with underlying rheumatic heart disease [39].

The epidemiology, clinical and microbiologic spectra of IE is significantly different in the developing countries compared to the western world. These differences can be attributable to multiple factors present in poorer countries including: significantly higher incidences of rheumatic heart disease and uncorrected congenital heart disease, excessive and improper use of antibiotics,