naturally occurring CD4+CD25+ regulatory T cells (nTregs) which are the most important and they are derived as a functionally mature population from the thymus.

Other regulatory T cells are the type 1 regulatory (Tr1) cells and Th3 cells [4,5]. A better understanding of the mechanisms underlying the induction and functions of T regulatory cells in controlling the immune system is critical in view of a future cellular therapy to modulate immune-mediated pathologies. nTreg cells were first defined in 1995 by Sakaguchi and colleagues, who showed that the passive transfer of T cells lacking in the nTregs subset into a thymic nude mice resulted in the spontaneous development of various T cell-mediated autoimmune diseases. These cells appear to be capable of suppressing a wide variety of immune cells, consisting of those from both the innate and adaptive immune systems [6].

Rheumatic heart disease (RHD) is an autoimmune most severe sequel of group A streptococcal upper respiratory tract infection complicated by rheumatic fever (RF) [7]. It describes a group of acute (short-term) and chronic (long-term) heart disorders and many of its features in the chronic stage are a result of fibrosis occurring during the healing of the acute lesion [8]. Adaptive immune responses are characterized by the capacity to recognize and remember pathogen-specific antigens. When a cognate antigen is encountered, lymphocytes become activated, undergo clonal proliferation and acquire effector functions that enable the activated cells to eliminate the intruder. However, in the acute phase of streptococcal pharingitis, streptococcal antigens (especially M protein) act as the promoter of T cell activation. It is assumed that the streptococcal antigens are initially taken up and processed by antigen-presenting cells, predominantly macrophages, which present the antigens in the context of MHC II molecules to CD4-positive T cells [9]. CD4+ T cells are the major effectors of heart tissue lesions, and *Streptococcus*-primed T cells are able to recognize heart proteins by molecular mimicry. These T cells show a degenerate pattern of antigen recognition (streptococcal antigens and autoantigens) [10].

Naturally occurring CD4+CD25+ regulatory T cells, which comprise approximately 5-10% of peripheral CD4+ T cells, are a central component of active immune suppression [11] and populate the periphery as long-lived cells to control autoimmunity and regulate ongoing immune responses [12,13]. Here, in this study we try to determine the numbers of both nTregs and CD4+ T cells in the peripheral blood of chronic rheumatic heart disease patients to highlights the correlation between them.

Methods

This study was conducted from October 2006 to September 2007. Blood samples were taken from 48 patients with chronic rheumatic heart disease in Ibn Al-Bitar Hospital for Cardiac Surgery, Baghdad – Iraq. All patients were divided according to the positive or negative history of rheumatic fever (PHORF and NHORF), PHORF patients were subdivided according to the frequency of rheumatic fever, and according to the period of medication treatment into single attack under continuous medication (SA^{UCM}), single attack without continuous medication (SA^{WCM}), high risk under continuous medication (HR^{UCM}), and high risk without continuous medication (HR^{WCM}). Lymphocytes isolation was performed by using Ficoll method [14], nTregs and CD4+ T cells, also cell numbers were detected by using immunofluorescence staining technique [15] in the presence of Mouse anti- Human CD4 (FITC), CD25 (PE) Proteins, Dual Color (USBiological , USA)