

## Cardiac Sarcoidosis Can Also Be Managed By Natural Approaches

Mishra Tejesvi<sup>1</sup>, Batra Unnati<sup>1</sup>, Choudhary Preeti<sup>1</sup>, Bansal Priya<sup>2\*</sup>, Kumar Abhishek<sup>2</sup>, Katiyar Deepti<sup>3</sup><sup>1</sup>UG Scholar, KIET School of Pharmacy, Ghaziabad, Uttar Pradesh, India<sup>2</sup>Department of Pharmacology, KIET School of Pharmacy, Ghaziabad, Uttar Pradesh, India<sup>3</sup>Department of Pharmacognosy, KIET School of Pharmacy, Ghaziabad, Uttar Pradesh, India

\*Corresponding author: Priya Bansal

| Received: 09.05.2019 | Accepted: 19.05.2019 | Published: 30.05.2019

DOI: [10.21276/sijtcn.2019.2.3.3](https://doi.org/10.21276/sijtcn.2019.2.3.3)

### Abstract

Sarcoidosis is a disease in which inflammatory granulomas cells are formed in the affected areas of body. Sarcoidosis, without a known aetiology commonly affects lymph nodes, lung tissues, skin, CNS, eyes, muscles, bone and heart. Cardiac sarcoidosis (CS) an infiltrative granulomatous disease of the myocardium that may present in about 2-7% of sarcoidosis patients and more than 20% cases are clinically silent. CS patients may suffer from asymptomatic left ventricular dysfunction, congestive heart failure, atrioventricular block, atrial or ventricular arrhythmia and sudden death. These symptoms are common in CS. The diagnosis could be done by using echocardiography, endocardiography, nuclear imaging like PET, CMR imaging and endomyocardial biopsy. Although randomized therapeutic trials have not been done but still corticosteroids (alone or combined with additional immunosuppressive medications) are usually used for the treatment. The natural approaches have also proved to be very beneficial for the management of the disease. These methods offer a cheaper, easily available and effective therapy devoid of side effects. The current manuscript mainly highlights the clinical manifestations, diagnosis, imaging techniques and therapies including the natural approaches to treat the disease.

**Keywords:** Cardiac sarcoidosis, ICD, PET, Echocardiography, Cardiac Transplantation, Natural approaches.

**Copyright @ 2019:** This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

### INTRODUCTION

Existence of non-caseating granulomas in the involved tissues characterizes chronic multisystem granulomatous disease, sarcoidosis (formerly called Mortimer's Malady) with undefined etiology. Being general in women, Sarcoidosis commonly affects lymph nodes, lungs tissues, skin, central nervous system, eyes, muscles, bone and heart [1, 2]. Dr James Hutchinson first gave the declaration of Sarcoidosis in 1869, after interpreting a patient with "colour on his extremities" and "an attack of gout" [3]. Only 2-7% patients afflicted with Sarcoidosis are exposed with cardiac sarcoidosis and remaining 20% cases of sarcoidosis remained clinically silent [1]. In 1952, Longcope & Freiman reviewed that the tumor necrosis occur in factor alpha and HLA II genes due to the phenomenon of polymorphism showed the development of cardiac sarcoidosis, & thus it reveals the first description of myocardial involvement in 20% of 92 necropsied case of sarcoidosis [4, 5].

About 58% of Japanese patients are entangled with cardiac sarcoidosis (that is highest percentage in the world), which makes 85% of deaths among Japanese patients with sarcoidosis [1]. Although in few

cases the symptoms of this condition are observed, whereas in many others it remains undiagnosed even in late staged disease. Arrhythmias, heart blocks, heart failure, pericarditis, heart valve problems, heart attack are usually associated with cardiac sarcoidosis. It tends to affect younger people broadly in between 25 to 45 years [6, 7]. Early diagnosis is the key to prevent the potentially devastating effect of cardiac sarcoidosis. Important diagnostic method for cardiac sarcoidosis mainly includes electrocardiography, electro physiologic studies, echocardiography, holter monitoring, nuclear imaging, cardiac magnetic resonance imaging, cardiac positron emission tomography (PET) and heart biopsy [1].

The presence of cardiac disease is affiliated with eloquent morbidity and mortality; thus there is an important need to diagnose and treat cardiac involvement. This disease is incurable but its effects can be successfully managed. Treatment mainly includes therapy of corticosteroids with or without immunosuppressive drugs, anti-arrhythmic drugs, implantable cardioverter defibrillator (ICD) and heart implantation [1, 3]. The natural approaches have also proved to be very beneficial for the management of the disease. These methods offer a cheaper, easily available

and effective therapy devoid of side effects. This review mainly focus on etiology and pathophysiology of disease with a special focus on recent development in diagnostic procedures and treatment of cardiac sarcoidosis.

## EPIDEMIOLOGY

Being a multisystem chronic disorder sarcoidosis is characterized with noncaseating granulomas present in various tissues and organs. It majorly affects the organ system including lymph node, skin, eyes, heart and nervous system, musculoskeletal, renal and endocrine system [4]. Conceding a foregoing data the prevalence of sarcoidosis is of 10 to 40 out of 100,000 persons in the United States and Europe. Its higher prevalence is seen in African Americans when compared to Caucasians, with a ratio between 10 and 17 to 1 [1].

It is more common in females of Japan whether in case of USA; African Americans have 3-4 fold greater risk for the disease as compared with whites. In Europe there is an increment in rate of 50-60 cases per 100,000 populations suffered from cardiac sarcoidosis [4, 5]. Tendency of systemic sarcoidosis is prominent in women between the ages of 20 to 40, whereas gender has no influence in myocardial infection [1, 8]. The exceptional challenging case study showed that 40-50% of cardiac sarcoidosis patients are preferred for diagnosis of necrosis as myocardial evidence found to be life threatening [9].

It has been reported that left ventricular ejection fraction is the most important clinical predictor of mortality among patients with this disease [10]. 40% of CS patients had no signs of extra cardiac involvement in a retrospective study whereas, 66% of them had disease isolated to the heart. On the basis of literature it is clear that CS percentage vary in different countries based on their genetic structure.

## PATHOPHYSIOLOGY

Being a disease of unknown etiology, the principle causes of sarcoidosis leads to the formation of granuloma that progress to fibrosis. Infectious agents (Mycobacterium tuberculosis, Mycoplasma species, Corynebacteria species, Spirochetes) and environmental agents (aluminium, pollen grains, clay, and talc) have been implicated as potential antigens. These antigens primarily trigger the helper inducer T-cells that lead to granuloma abrasion. Earlier the sarcoid infiltrates consist of mononuclear phagocytes and CD4+ T-cells with T helper type 1 response secreting interleukin-2 and interferon  $\lambda$ . At later stage, there is a shift of cytokine profile to T- helper type 2 responses that has formed during fibroblastic phase of granulomas and is affirmed to have an anti-inflammatory effect that leads to tissue scarring. Moreover the high concentration of interleukin-6 are found in circulation at the onset and

before the inception of immunosuppressive therapy but not after that [1, 4].

Interleukin-6 was assured to be intricated in maintenance of inflammation by inducing the precreation of T-cells. The clinical demonstration of sarcoidosis is dependent on both, the amplexness and location of granulomas. The cardiac sarcoidosis leads to formation of lumps together with noncaseating granulomas that involve the left ventricle free wall, basal ventricular septum, right atrium and left atrium [2].

Genetic susceptibility of sarcoidosis is shown by variability of disease presentation among different races and in individuals with specific HLA sub-types and the presence of some familial clusters. The first generation of patients with sarcoidosis is found to be at higher risk. Mode of inheritance of the risk for sarcoidosis can be polygenic as shown by the HLA analysis of concerned families, primarily associated with class I HLA-A1 and B8 and class II HLADR3 genotype. Genetically predisposed individuals are credible to enroot granulomas after exposure to antigens that activate an exaggerated cellular immune response [4].

## CLINICAL MANIFESTATIONS

The clinical manifestations of cardiac sarcoidosis can be identified by the location and conduction of abnormalities in ventricular arrhythmic region followed by granulomatous inflammation. In 20-30% of cases complete heart block has found to be the most common clinical evidence; while due to the basal system and nodal artery, ischemia becomes a major problem that can lead to the first degree heart blockage as well as bundle branch blockage. Ventricular Tachycardia (VT) act as the non frequent arrhythmia in around incidence of 23% while 67% of these cases suffered by arrhythmia causes sudden death also [4, 5].

The another manifestation can be congestive heart failure that attributed to the widespread infiltration of the myocardium, ventricular aneurysm, rhythm disturbances, corpulmonale, valvular regurgitation or a combination of these processes [4, 7]. Usually cardiac sarcoidosis rarely anticipates the involvement of other organs to be affected, while in preeminent scenario it may prior to become as SCD (sudden cardiac death) [9]. But the heart failure is not a specific sign of cardiac sarcoidosis although it may be considered as an indicator. According to Mehta et al, a significant prevalence of cardiac symptoms in systemic sarcoid patients compared with healthy controls was found to be 46% vs 5% respectively [11].

Meanwhile in more than 50% of cases the poor prognosis may cause clinical heart failure and withstand existence of cardiomyopathy of the left ventricular ejection fraction (LVEF) (9). The multifaceted clinical

manifestations of this disease is still challenging, therefore many cases of cardiac sarcoidosis remain clinically unrecognized [8, 9].

## DIAGNOSIS

Every disease must be diagnosed at earliest to prevent the potentially devastating effects of that disease. Sarcoidosis being a disease of unknown etiology in which more than 20% cases are clinically silent hence diagnosis of cardiac sarcoidosis is arduous as being a patient of cardiac sarcoidosis is very hard to notice [1]. The clinical implications in cardiac sarcoidosis are neither specific nor diagnostic. It is related to bad prognosis when in concern with sign and symptoms development [7].

The correct diagnosis was found in the person suffering from cardiac sarcoidosis when heart is the only organ affected in the case of sarcoidosis. Often cardiac sarcoidosis involves the procurement of different organs leading to undiagnosed conditions [11, 12]. These are not a single laboratory test that will categorize the presence of noncaseating granulomas which may give any official guidelines for the diagnosis to the doctors [2]. Sign & symptoms of asymptomatic left ventricular dysfunction, congestive heart failure, atrioventricular block or ventricular arrhythmias or sudden death may show up cardiac sarcoidosis [7].

The first diagnosis in a clinical manner may include medicational history, physical examination, ECG (Electrocardiograph), 24 hour Holter monitoring and echocardiography [1, 8]. A perfect diagnosis of cardiac sarcoidosis can be formed after the documentation of clinical aspects and biopsy giving the presence of noncaseating granulomas. The diagnosis of the cardiac sarcoidosis found to involve atrioventricular block in 26-62% of cases; ventricular tachycardia in 2-42% cases while 10-30% of cases of congestive heart failure with 12-65% cases of sudden death [13]. In 2006, the Japanese Society of Sarcoidosis and Other Granulomatous Disorders published the revised guidelines for the diagnosis of cardiac sarcoidosis [7]. These guidelines are useful, particularly in a patient with proven no cardiac sarcoidosis in whom a suspicion of cardiac involvement exists. These guidelines are as follows-

### Histological Diagnosis

Cardiac sarcoidosis is confirmed when cardiac biopsy specimens demonstrate noncaseating epithelioid cell granuloma with histologic or clinical diagnosis of extracardiac sarcoidosis.

### Clinical Diagnosis Group

Cardiac sarcoidosis is diagnosed in the absence of an endomyocardial biopsy specimen or in the absence of typical granulomas on cardiac biopsy when extracardiac sarcoidosis has been proven and a

combination of major or minor diagnostic criteria has been satisfied as follows.

- More than 2 of 4 major criteria are satisfied, OR
- 1 of the 4 major criteria and 2 or more of the minor criteria is satisfied.

### Major Criteria

- Advanced AV block.
- Basal thinning of the ventricular septum.
- Positive cardiac gallium uptake.
- Left ventricular ejection fraction less than 50%.

### Minor Criteria

- Abnormal electrocardiogram findings including ventricular tachycardia, multifocal frequent premature ventricular contractions, complete right bundle branch block pathologic Q waves, or abnormal axis deviation.
- Abnormal echocardiogram demonstrating regional wall motion abnormalities, ventricular aneurysm, or unexplained increase in wall thickness
- Perfusion defects detected by myocardial scintigraphy
- Delayed gadolinium enhancement of the myocardium on cardiac MRI scanning
- Interstitial fibrosis or monocyte infiltration greater than moderate grade by endomyocardial biopsy [7].

### These Guidelines Were Believed To Be Useful but Were Not Universally Accepted

Clinicians are dependent on non-invasive imaging technique to diagnose cardiac sarcoidosis. A secure and perfect method for evaluation of myocardial diseased state is percutaneous endomyocardial biopsy. Now-a-days Gadolinium enhanced Cardiac Magnetic Resonance Imaging and Positron Emission Tomography / Computed Tomography are most efficient diagnostic basis in recent scenario [12, 14].

### Type of Diagnosis Echocardiography

This technology uses high-frequency sound waves (also called ultrasound) to produce two-dimensional images of the heart. The image can help doctors to identify problems with heart valves and heart chambers. Echocardiograms will be better at picking up signs of late-stage cardiac sarcoidosis than early heart complications [1, 2].

### Radionuclide Scan

Nuclear medicine imaging is an important tool in the diagnosis of cardiac sarcoidosis. The fibrogranulomatous lesions in the myocardium display segmental areas of decreased uptake in nuclear imaging. Most useful studies are performed with thallium 201 and technetium 99m sestamibi [15]. Radionuclide scan help doctors to detect heart blockages and heart injury, and it can be useful for

identifying difference between cardiac sarcoidosis and other heart problems, such as coronary artery disease [14].

### Cardiac Positron Emission Tomography (PET)

PET with 18F-fluorodeoxyglucose (FDG) is a form of functional imaging that indicates inflammation and that is useful in early diagnosis, monitoring of therapy, and image-guided biopsy. The PET scan may be useful in patients with a pacemaker or cardioverter-defibrillators implanted who are unable to undergo MRI because of the safety concerns related to potential adverse effects on the device arising from the strong magnetic and radiofrequency forces generated by MRI. The specificity of PET as a diagnostic tool relies on the suppression of normal myocyte uptake of glucose. For this reason, prolonged fasting (>12 hours), fatty acid loading, and heparin are commonly used before imaging to suppress myocardial glucose metabolism in favor of oxidation of free fatty acids. PET scans may show different patterns of diffuse and focal uptake. Patchy and focal uptake patterns are most specific for cardiac sarcoidosis [1, 2, 8, 16].

### Electrocardiography

A resting ECG is an appropriate screening test in all patients with sarcoidosis. Abnormalities on ECG (e.g., conduction disturbances, arrhythmias, or nonspecific ST and T-wave changes) have been noted in 20 to 31% of sarcoid patients. ECG can be useful in estimating the extent of disease or inflammatory activity but only persistent ventricular tachycardia can predict an adverse outcome. Although the role of signal-averaged ECG (SAECG) in diagnosing CS is unclear, a recent study reported that it had a sensitivity of 52% and specificity of 82% as a technique to screen for CS.

Twenty-four hours Holter monitoring and exercise ECGs can detect abnormalities (e.g., tachyarrhythmias or heart block) even when resting ECGs are normal. Any abnormality on ECG or Holter monitor should be further evaluated by echocardiography or other imaging techniques [1, 16].

### Heart Biopsy

In some cases, a doctor might recommend a heart muscle biopsy to look for cardiac sarcoidosis and to exclude other diseases. However, heart biopsies are invasive, and they are rarely used today to diagnose cardiac sarcoidosis. While a positive biopsy would provide strong evidence of the disease, a negative biopsy – which is likely – doesn't prove anything. Many people with cardiac sarcoidosis have negative biopsies because the granulomas show up only in patches [1, 3].

## TREATMENT

Cardiac sarcoidosis is an indication for treatment because of increased risk of sudden death.

Treatment is given to reduce inflammation. Unveiling of cardiac sarcoidosis after the diagnostic method; the management starts with the drug therapy mainly corticosteroids [2, 8].

### Drug Therapy

#### Corticosteroids and Immunosuppressive Drugs

On various imaging result corticosteroids must be initialized as the therapy for cardiac sarcoidosis. Most doctors initially treat cardiac sarcoidosis with corticosteroids medications which are also called glucocorticoids or steroids. A patient of cardiac sarcoidosis when managed with steroid, congestive heart failure is most important prognostic factor. Corticosteroids can be taken alone or in combination of other drugs also [1, 2]. There is a tipping point of steroid efficacy where responsive active granulomatous inflammation / infiltration transform towards non-responsive fibrosis. Prolonged steroid therapy is not without risk, but an ominous mortality curve and resistant to treatment of advanced disease compel early action [8].

Initial dose of steroids must be 60-80 mg per day and minimum maintenance dose is 10 mg per day during the period of 6 month. If the disease appears to be improved and dormant, then the steroids can be slowly tapered further. At any sign of recurrence, steroids should be started at the dose of 60 mg/day or higher. Long-term corticosteroid therapy is often required [11].

Long- term steroid use in patients with a left ventricular ejection fraction (LVEF) > 55% may prevent LV remodeling and altered cardiac function. Steroids most benefited those patients with a LVEF < 54% who showed significant reduction in LV volumes and LVEF improvement. In patients with a LVEF < 30%, steroid therapy did not improve the LV volume or function [13]. The starting of this therapy at the earliest stage accelerates the later stage outcome by reducing chances of heart and LV systolic function preservation [16].

Treatment with other immunosuppressive drugs like methotrexate, azathioprine, anti-TNF  $\alpha$  antibodies, hydroxychloroquine and Mycophenylate mofetil can be preferable in cases where corticosteroids are contraindicated or the patient is resistant to steroid therapy. There are no studies revealing the overall effect of other immunosuppressive drugs [1, 2]. Recently, the pathophysiological importance of TNF-  $\alpha$  in the formation of granulomata has become evident, prompting trials of infliximab (a TNF-  $\alpha$  antagonist) in CS. Infliximab is showing promising results in reducing myocardial inflammation as well as improved clinical outcomes [9].



## Heart Transplantation

Doctors recommend heart transplantation only in severe cases of cardiac sarcoidosis, Cardiac transplantation is reserved for end-stage disease unresponsive to medical therapy. Major indications for cardiac transplantation are resistant ventricular tachyarrhythmias and severe intractable heart failure, especially in younger patients. Heart transplantation is actually recommended for younger patients because the procedure is very risky and body might reject the transplant. With early diagnosis of the disease and corticosteroid treatment, transplantation can be avoided.

Younger patients not responsive towards the immunosuppressive therapy should undergo evaluation for cardiac implantation. A review of 65 patients documented systemic sarcoid who underwent orthotopic heart transplant and found better 1- year survivability than non sarcoid patients [11].

## Medications and Devices

Corticosteroids will reduce the inflammation associated with granulomas, but they might not correct ventricular tachycardia. For people with lethal ventricular arrhythmia or heart blockage, pacemaker or implantable cardioverter defibrillator (ICD) may be recommended. Antiarrhythmic drug therapy for ventricular tachycardia in patients with cardiac sarcoidosis is associated with a high rate of recurrence or sudden death. Amiodarone use in this group of patients may be limited by the occurrence of pneumonitis and/or pulmonary fibrosis [2, 14].

In the nutshell early diagnosis and treatment of cardiac sarcoidosis is essential and a cost-effective algorithmic approach can be successfully used in treatment of cardiac sarcoid patients [9].

## NATURAL APPROACH TO TREAT CARDIAC SARCOIDOSIS

There are numerous natural ways to treat cardiac sarcoidosis which include:

- Intake of antioxidants which may include fruits such as cherries, tomatoes, blueberries and vegetables like bell peppers and squash [17].
- Foods rich in magnesium and low in calcium such as corn, soy, bran, barley, banana, avocado and potato should be included in diet.
- Refined foods such as pastas, sugar and white bread should be avoided.
- For protein source - lean meat, beans, tofu and cold water fish should be preferred.
- Olive oil or vegetable oils should be used.
- Intake of trans-fatty acids should be minimized by avoiding the usage of commercially available baked foods such as cookies, cakes and french fries [18].

- Usage of caffeine, alcohol and tobacco should be completely avoided.
- One should drink at least 6 -8 glasses of filtered water daily.
- 30 minutes of exercise daily, 5 days a week is essential.
- Usage of antioxidant vitamins A, C, E, B-complex and minerals such as calcium, magnesium, selenium and zinc may be beneficial [19].
- Omega-3-fatty acids such as fish oils in form of capsules should be taken daily.
- Bromelain – a mixture of enzymes from pineapple, 500 mg per day may be very beneficial. But doctor must be consulted before its usage as it may interact with other medications and enhance the risk of bleeding.
- Probiotic supplements containing *Lactobacillus acidophilus* shall be taken.
- Few of the herbs such as *Curcuma longa* (300 mg, thrice daily) commonly known as turmeric [20] and *Uncaria tomentosa* (20 mg, thrice daily) also known as Cat's claw [21] may help to strengthen and tone the body's system. But the doctor must be consulted before starting their usage.
- Homeopathic remedies may help in improving the general well-being of individuals with this disease. Some of the homeopathic medicines which have been used for improving the symptoms of sarcoidosis include *Tuberculinum bovinum*, *Beryllium*, *Euphrasia*, *Bacillinum*, *Carcinosin*, *Phosphorus*, *Arsenicum album*, *Graphite* and *Sepia*.

## CONCLUSION

Cardiac sarcoid is a relatively uncommon disease, but the risk of SCD, malignant arrhythmias and progressive heart failure are often the first signs of cardiac involvement in the heart, at which point mortality increases dramatically while intervention efficacy diminishes. That's why; clinicians must go for low-cost, easily accessible technology to screen for CS in all patients with extra cardiac sarcoid. In addition, patients with unexplained VT, type II second-degree or complete AV block, or cardiomyopathy should undergo an algorithm-based evaluation for this rare but insidious condition. Early diagnosis and treatment of CS is essential and a cost-effective algorithmic approach can be successfully used in diagnosis and treatment of CS patients.

## ACKNOWLEDGEMENT

The authors would like to acknowledge KIET School of Pharmacy for providing facility. We are also thankful to our Director, Col (Dr.) Amik K. Garg and CAO, Dr. Manoj Goel for providing all the facilities.

## REFERENCES

1. Ipek, E., Demirelli, S., Ermis, E., & Inci, S. (2015). Sarcoidosis and the heart: a review of the literature. *Intractable & rare diseases research*, 4(4), 170-180.
2. Sekhri, V., Sanal, S., DeLorenzo, L. J., Aronow, W. S., & Maguire, G. P. (2011). Cardiac sarcoidosis: a comprehensive review. *Archives of medical science: AMS*, 7(4), 546-554.
3. Birnie, D., Andrew, C. T., Gaula, J. L., Chakrabarti, S., & Beanlands, S. B. R. (2015). Cardiac Sarcoidosis. *Clinics in Chest medicine*, 67-75.
4. Doughan, R. A., & Williams R. B. (2006). Cardiac Sarcoidosis. *Heart*, 92, 282-288.
5. Lagana, S. M., Parwani, A. V., & Nichols, L. C. (2010). Cardiac sarcoidosis: a pathology-focused review. *Archives of pathology & laboratory medicine*, 134(7), 1039-1046.
6. Sun, B. J., Lee, P. H., Choi, H. O., Ahn, J. M., Seo, J. S., Kim, D. H., ... & Song, J. K. (2011). Prevalence of echocardiographic features suggesting cardiac sarcoidosis in patients with pacemaker or implantable cardiac defibrillator. *Korean circulation journal*, 41(6), 313-320.
7. Dubrey, S. W., & Falk, R. H. (2010). Diagnosis and management of cardiac sarcoidosis. *Progress in cardiovascular diseases*, 52(4), 336-346.
8. Skali, H., Schulman, A. R., & Dorbala, S. (2013). 18 F-FDG PET/CT for the assessment of myocardial sarcoidosis. *Current cardiology reports*, 15(4), 370.
9. Houston, B. A., & Mukherjee, M. (2014). Cardiac sarcoidosis: clinical manifestations, imaging characteristics, and therapeutic approach. *Clinical Medicine Insights: Cardiology*, 8, CMC-S15713.
10. Hulten, E., Aslam, S., Osborne, M., Abbasi, S., Bittencourt, M. S., & Blankstein, R. (2016). Cardiac sarcoidosis—state of the art review. *Cardiovascular diagnosis and therapy*, 6(1), 50-63.
11. Mantini, N., Williams Jr, B., Stewart, J., Rubinsztain, L., & Kacharava, A. (2012). Cardiac sarcoid: a clinician's review on how to approach the patient with cardiac sarcoid. *Clinical cardiology*, 35(7), 410-415.
12. Lorell, B., Alderman, E. L., & Mason, J. W. (1978). Cardiac sarcoidosis: Diagnosis with endomyocardial biopsy and treatment with corticosteroids. *The American journal of cardiology*, 42(1), 143-146.
13. Yang, J., Sin, D. D., Leipsic, J., McManus, B., & Ignaszewski, A. (2013). Cardiac Sarcoidosis. *British Columbia Medical Journal*, 55, 196-200.
14. Lynch III, J. P., Hwang, J., Bradfield, J., Fishbein, M., Shivkumar, K., & Tung, R. (2014, June). Cardiac involvement in sarcoidosis: evolving concepts in diagnosis and treatment. In *Seminars in respiratory and critical care medicine*, 35(3), 372-390.
15. Fluschnik, N., Lund, G., Becher, P. M., Blankenberg, S., & Muellerleile, K. (2016). Fulminant isolated cardiac sarcoidosis with pericardial effusion and acute heart failure: Challenging aspects of diagnosis and treatment. *World journal of clinical cases*, 4(3), 76-80.
16. Nagai, T., Nagano, N., Sugano, Y., Asaumi, Y., Aiba, T., Kanzaki, H., ... & Anzai, T. (2015). Effect of corticosteroid therapy on long-term clinical outcome and left ventricular function in patients with cardiac sarcoidosis. *Circulation Journal*, CJ-14.
17. Dryden, G. W., Deaciuc, I., Arteel, G., & McClain, C. J. (2005). Clinical implications of oxidative stress and antioxidant therapy. *Current gastroenterology reports*, 7(4), 308-316.
18. Krieg, C. (2005). The role of diet in the prevention of common kidney stones. *Urologic nursing*, 25(6), 451-457.
19. Massey, L. (2005). Magnesium therapy for nephrolithiasis. *Magnesium research*, 18(2), 123-126.
20. Funk, J. L., Oyarzo, J. N., Frye, J. B., Chen, G., Lantz, R. C., Jolad, S. D., ... & Timmermann, B. N. (2006). Turmeric extracts containing curcuminoids prevent experimental rheumatoid arthritis. *Journal of natural products*, 69(3), 351-355.
21. Gonçalves, C., Dinis, T., & Batista, M. T. (2005). Antioxidant properties of proanthocyanidins of *Uncaria tomentosa* bark decoction: a mechanism for anti-inflammatory activity. *Phytochemistry*, 66(1), 89-98.