Review Article

“Perspective of Ischemic Heart Disease (Iqfari Marad-i-Qalb) with reference to Unani Medicine”

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Abstract:

Background: Ischemic heart disease (IHD) also known as coronary artery disease (CAD) is the leading cause of death worldwide. IHD is caused by obstruction of one or more coronary arteries. Among the various causes of obstruction atherosclerosis is the leading cause. Physical inactivity, smoking, saturated fat rich diet, hypertension, diabetes mellitus, dyslipidaemia are modifiable risk factors for atherosclerosis which ultimately results in IHD. In this article we will discuss the disease in the light of Unani system of Medicine and how to manage it depending on the understood concepts. Methods: A number of classical Unani textbooks were referred for description of various heart diseases and various search engines such as PubMed, Google Scholar and Research Gate were cited for recent advancements using the key words IHD, atherosclerosis, cardio-protective herbal drugs, etc. Conclusion: Owing to the irreversible damage due to IHD it is better to prevent myocardium damage by minimising the risk factors at its earliest. In Unani system of medicine many cardio-protective drugs have been described which when combined with lifestyle modification can play vital role in keeping cardiac diseases at bay.

Keywords: Atherosclerosis; Cardio-protective; Ischemic Heart Disease; Unani medicine

Introduction:

IHD can be defined as a condition where there is an imbalance between myocardial oxygen supply and demand or insufficient blood supply or oxygen transport to a portion of heart muscle¹. It is the leading cause of death worldwide. IHD affects about 126 million people worldwide, 1.72% of the population². In the year 2017, 1.54 million deaths in India alone, were attributed to IHD³. The risk for various heart diseases has increased as a result of modern lifestyle factors and a number of illnesses, including diabetes mellitus, hypertension, and dyslipidaemia. By 2030, the prevalence rate of IHD, which is currently 1,655 per 100,000 people, is predicted to increase to 1,845 per 100,000 people². The most frequent cause of IHD is atherosclerotic plaque-induced obstruction, or stenosis of one or more epicardial coronary arteries. Stable angina develops when the obstruction is fixed and there is transient ischemia. Acute coronary syndrome manifests as the plaque erodes or ruptures, causing thrombus formation that obstructs the vessel. If there is no evidence of myocytic necrosis

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it is Unstable Angina. When myocytic necrosis is evident and occlusion is partial it is Non-ST segment elevation Myocardial Infarction (NSTEMI); whereas, ST-segment elevation myocardial infarction (STEMI) occurs when the occlusion is abrupt and complete. Other non-atherosclerotic causes include coronary spasm, arterial thrombi, emboli, arteritis, dissection, myocardial bridging, hypertrophic or dilated cardiomyopathy, tachycardia and also some non-cardiac causes such as anemia, sickle cell disease, hypoxemia, carbon monoxide poisoning, hyper viscosity, hyperthyroidism, pheochromocytoma1,4. IHD can be diagnosed on the basis of its clinical features and some invasive and non-invasive techniques. For confirmatory diagnosis exercise ECG is the first line investigation for stable angina, if it is normal or inconclusive stress echocardiography or myocardial perfusion scanning is indicated5. Sequential measurements of cardiac biomarkers are found to be normal in unstable angina and increased in MI. Echocardiography is performed to evaluate ventricular function and to find additional complications1,5. When bypass graft surgery or percutaneous coronary intervention is being considered for revascularization, coronary angiography is advised5. Among the various pharmacological and symptomatic treatment of ischemia and angina aspirin, ACE inhibitors, and lipid-lowering agents have been proven to lower morbidity and mortality in patients with stable coronary heart disease (CHD) and preserved LV function, whereas beta blockers have been found to reduce mortality in patients who have previously experienced a MI. Other therapies, such as nitrates, beta-blockers, calcium channel blockers, and ranolazine, are not found to reduce mortality in patients with stable IHD but can improve angina and exercise performance, as well as reduce ischemia6. A new bundle branch block or characteristic ST segment elevation in two adjacent leads on the ECG are indications for immediate PCI (percutaneous coronary intervention)5, and coronary artery bypass graft (CABG) is considered in more complicated conditions like left main or triple-vessel disease, diffuse coronary stenosis, completely obstructed vessels, abnormal left ventricular function, and diabetes1. In this article, IHD will be discussed in context of the Unani system of medicine, as well as how to manage it based on the concepts that have been understood.

Material and methods

For the search of the Unani literature, authentic books such as Paradise of Wisdom (Firdaws al-Hikmat fi’l-Tibb), The Complete Book of the Medical Art (Kamil al-Sana), Canon of medicine (Al-Qanun fi’l Tibb), Zakhirah Khaawarizm Shahi, Continens Liber (Kitab al-Hawi fi’l Tibb), Kitabul Mukhtarat Fi Tib, Kitab al-Mansuri, Iksir-i-A’zam, Tibb-i-Akbar, Ghina Muna, Risala-e-Adwia Qalbia etc were referred. Further, browsing of PubMed, Google Scholar, Research Gate, AYUSH Portal, Springer, Science Direct, Scopus and other websites was carried to collect the recent advancements related to the topic using the key words IHD, atherosclerosis, cardio-protective herbal drugs, etc.

Unani Perspective

According to the standard medical terminology of Unani medicine Ischemic Heart Disease is termed as Iqfari Marad-i-Qalb with code UMA- 0354. However, no direct description is found in the classical literatures for it, but can be well understood and managed on the basis of the studied pathology for the disease. According to classical texts available, a number of pathologies of heart have been considered to be responsible for all heart diseases, such as 1) Sue Mizaj mufrad or murakkab (alteration in the normal temperament of heart towards either heat or cold and moisture or dryness alone or in combination) which may be of sada or maddi i.e. it may or may not involve akhlat (humours) 2) Waram (Inflammation) 3) Tafarruq ittisal (discontinuity / anatomical disruption) 4) Sue mizaj shirki (alteration in temperament associated with involvement of nearby organs)5) Sudad (obstruction) in the heart vessels and also 6) Amraz-e-waza-e-Qalb (abnormal placement of heart)6. In Kitab Al-Hawi, Dard-e-Qalb (Chest Pain /Angina) is mentioned as pain in heart arises from left ventricle10 and it is multifactorial such as 1) Ghashi (Syncope), 2)the pain may be in association with diseased condition of various organs like Tah lil-e-quwwat meda (dissolution of faculty), Ikhtanaq-e-dimagh (cerebral hypoxia) and Qulanj (biliary colic), 3) Munqabiliz quwa haywaniyya (intense grief causes vital powers to gets buried inside the body), 4) Tehleel ruh (dissolution of pneuma due to extreme joy), 5)Sue Mizaj Qalb (alteration in the temperament of heart) 6)Marz murakkab/compound disease i.e. warm (inflammation), tafarruq ittisal (damage to heart structures).

10 Out of these etiopathologies waram and taffaruq ittisal are considered as highly fatal conditions and hardly give heart enough time to present with symptoms6 and thus can be understood as pathology behind sudden cardiac death. It is said
that heart cannot tolerate any of the mentioned pathological conditions except for sue mizaj. This sue mizaj can be sue mizaj sada (without humoral involvement) or sue mizaj maddi (with humoral involvement). According to the doctrine of Unani medicine the mizaj (temperament) of heart is haar (hot)\(^9\). In the state of sue mizaj har the mizaj of the heart gets inclined towards hararat (heat) beyond the normal limits and thus develops symptoms. If the alteration in temperament is ghair mustahkam (unstable) it presents with nabz azeem (high volume pulse), sari (rapid), and mutawatwar (frequent). Temperature of the chest rises locally with humma lazma (continuous fever) and intense thirst which is relieved with cool air. Patient is dominated by feeling of gham, bechaimi, iltihab and zuban (sadness, anxiety, agitation, washed out). When the sue mizaj har gets mustahkam (established), it presents with khatfqaan (Palpitation) and ghashi (Syncope). These symptoms are consistent with that of IHD. Sue mizaj barid (alteration of temperament of Heart towards cold) has contrasting features to that of sue mizaj har. Here pulse and respiration becomes saqheer (shallow), bati (slow), mutafawit (infrequent) while in saqooq quwwat (Shock) it is frequent (mutawatwar). Patient becomes lethargic, pale; body turns like that of elderly persons and symptoms get relieved on exposure to hot environment and fragrances. This presentation inclines more towards cardiogenic shock which is a sequel of IHD. Sue-mizaj yabis (alteration of temperament of Heart towards dryness) and sue-mizaj ratab (alteration of temperament of Heart towards moisture) have much deleterious effect and are extremely fatal\(^11\). The causative factors for sue mizaj har ghalb are psychological factors such as anger and anxiety, difficult breathing, obstruction of channels for movement of fresh air (Oxygenated blood/Oxygen), hammam garam (Hot Turkish bath) or exposure to hot air for prolonged period, consumption of garam ghizayen and mashroob (food and drinks having hot temperament), inhalation of hot fragrances\(^8\). Among all these causative factors obstruction of channels is also the leading cause of IHD according to modern concept. Obstruction of vessels may be due to either tangi-e-majari (constriction/stenosis of vessels) or sudad-e-majari (Blockage of vessels). Tangi-e-majari occurs due to increase in quwwat-e-masika (retentive faculty), decrease in quwwat-e-daafia (expulsive faculty), excessive burudat/qabz/yaboosat (coldness/astringency/Dryness), there may be compression from adjacent structures, disfigurement of normal vasculature, waram (inflammation), sticking of inner layer of vessels after wound healing (fibrosis)\(^11\). Sudad can be due to presence of shae ghareeb (foreign substance) within the vessel which may be in abnormal quantity or quality i.e., ghaleez and lazaj (thick and viscous)\(^9\). There may be various causes for development of sudad like suql ghaleez and kaseer (retention of thick and copious substance), Stone, qarah and jarah, (injury to vessel walls after erosion or lesion), new growth within the walls of the vessels (saleel, masse, laham sulooli), inflammation in adjacent structures, after using astringent medicines, increase in quwwate masika, extreme cold and thus high incidence during winter season\(^8\), coagulated blood as a result of turbulence to blood flow\(^9\).

**Unani Pathophysiology**

Madda (potential matter) when present in large quantity or have excessive cohesiveness, block the coronary arteries\(^9\). This sudad (obstruction to the coronary arteries) restricts the movement of fresh air to the heart while also preventing hot and harmful air from exiting the heart, resulting in sue-mizaj har. The Ruh (Pneuma) becomes trapped within the vessels and declines\[^8\] eradicating hararat-e-ghariziya (innate heat). As a result, heart is unable to perform its function of contraction and relaxation\(^10\).

**Ethical Clearance:** Not Applicable

**Treatment**

In Unani system of medicine IHD is managed according to the underlying pathophysiology. First, sudad is resolved followed by correction of temperament of heart. Sudad is difficult to treat when in blood vessels, especially arteries and arteries of Azae Raeesa (Vital organs of body i.e. Heart, Brain and Liver). If the cause is ghaleez khilt (thick matter), it is treated with mulattif and mullahil drugs and regimens (demulcents and resolvents). However, care should be taken while choosing adviya-e-mohali, as if it is less potent the madda will not get resolve completely, instead it will become active and may dislodge thereby increasing the size of sudad. This can be understood as thrombo-embolism. Moreover, if the mullahil is potent enough lateef ajza (light matters) get resolved but kaseef ajza (heavy matters) become stiff and it becomes necessary to add murrki (gile makhtoom/yellow chalk, ambar/ambergris, Pista/ Pistacia vera) and mulayyin drugs (halela kabuli/ Terminali chebula, ward/Rosa damascena)\[^12,13,14\] (relaxant and laxative). When the sudad is because of khilt lazij (sticky matter) in that case such medicines
are used which can penetrate in between the sticky matter and inner layer of the vessel wall and detach it from there and make it easy to remove such as sikanjabeen (a compound of honey and vinegar)\textsuperscript{11}. When the cause is khilt kaseer (excessive collection of matter) then istifragh (evacuation) is done by means of fasd and ishal (venesection and purgation)\textsuperscript{9}. The basic treatment for sudaad, which is when present in arteries of heart are drugs having properties of 1) Mufattih (Vasodilator) like Faranjmushk/Ocimum gratissimum, Bahman/Centaurea behen 12,13,14 2) Muhallil (Amla/Emblica officinalis, Zafran/Croccus sativus), 3) Muflattif (Abresham/Bombyx mori, Zarnab/Taxus baccata, Zaranbad/Curcuma Zedoaria), 4) Qabiz (Astringent) like Amla, Aas/Myrtus communis, Sumbul/Nardostachys jatamansi, Saad/Cyperus rotundus, Sazaj/Cinnamomum tamala, Badi elaichi/Amomum subulatum, 5) Khushbooedar (Fragrant) Badaranjboya/Melissa officinalis, Daarchini/Cinnamomum zeylanicum, Kafoor/Cinnamomum camphor, Kishnee/Coriandrum sativum and 6) Muhafiz-e-galb (Cardioprotective). For e.g. Arq Kasni is muflattih and qabiz\textsuperscript{21} as well some other cardioprotective and fragrant drugs are Mushk/Moschus moschiferus, Zafran, Zarnab, Darchini, Ood/Paeonia officinalis, Ambar, Abresham, Post turaan/Citrus medica outer coat, Badaranjboya, Sumbul, Sazaj, Faranjmushk, Gaozaban/ Borago officinalis, etc. Further correction of temperament of heart is done. Firstly madda-e-ghalib (dominant humour) is stabilized. If it is dam (Blood) fasd is done while safra (Yellow Bile) is stabilized by istifragh safra. Next temperature is brought down by various ways as follows: inhalation of cool fragrances like Bed mushk/Salix caprea, Gile Armani/Armenian Bole, Sandal/Santalum album, Kafoor, Arq-e-gulab/Rose water, Neelofar/Nymphaea alba, Sirka/Vinegar and also keeping the surrounding cool, use of vegetables of cold temperament such as Khas/ Andropogon muricatus, Kasni/Cichorium intybus, Khurfa/Portulaca oleracea, Kadu/Cucurbita Pepo. Sharbat Sandal and Qurs Kafoor are recommended to be taken orally while Sandal, kafoor and Arq-e-gulab can be applied over the chest to bring down the temperature locally\textsuperscript{11}. According to Ibn-e-Sina in order to correct the hot temperament of heart apart from using cold items muqawwi rub (tonic for pneumonia) medications should also be used such as Gaozaban, Tabasheer (Bambusa arundinaceae) is described as muqawwi-e-galb (cardiogenic) specifically when there is Sue-Mizaj Har. Some other drugs are also suggested to be used in case of Sue-Mizaj Har Qalb such as Tukhm Kahu muqasshir/Lactuca sativa, Tukhm Kasni, Tabasheer, Gul-e Surkh, Sandal Safaid, Tukhm Khurfa Siyah, Gaozaban, Kishnee Khushk, Busd/Corallium rubrum, Marwareed/Mytilus margaritiferus\textsuperscript{13}.

The renowned Unani physician Ibn-e-Sina has mentioned 63 drugs of plant, mineral and animal origin as Adwia-e-galbia for their efficiency in cardiovascular diseases. Various preclinical and clinical studies have been conducted to explore the cardioprotective properties of some of these drugs. Abresham (Bombyx mori) and its formulations (Kamira Abresham Hakeem Arshadwala and Kamira Abresham sada) have antioxidant and free radical scavenging effects\textsuperscript{16,17}. Additionally, the amino acids histidine, tryptophan, and cysteine as well as the active ingredient sericin improve dyslipidaemia. It not only delays the onset of atherosclerosis but also aids in reducing the size of plaques\textsuperscript{18,19}. Badranjboya (Melissa officinalis) has been shown to have mild antiarrhythmic properties by slowing down atrioventricular conduction\textsuperscript{21}, altered ECG by prolonging QRS, QTc, TpTe and JT intervals\textsuperscript{22} and also acts as vasorelaxant\textsuperscript{21}. Alkaloids like saponins and glycosides decreases heart rate\textsuperscript{24}. Flavonoids, phenolic acids, terpenes, rosmarinic acid and caffeic acids impart antioxidant property to it. It brings about a sharp decline in MDA (malondialdehyde), lowers MAP (mean arterial blood pressure), and maintains cardiac contractility\textsuperscript{25}. It reduces the risk of development of heart diseases by improving lipid ratios HDL, TGs, hs-CRP. Gaozaban (Borago officinalis) have a vasodilatory effect on the aorta, suppresses atrial force and rate of contractions\textsuperscript{26}. It has also shown to have a positive ionotropic effect on the frog’s heart\textsuperscript{27}. Amla (Emblica officinalis) can reverse atheromatous plaque and improve dyslipidaemia by virtue of its antioxidant property and ability to lower LDL level and prevent LDL oxidation\textsuperscript{29}. Its ability to significantly increase the activities of myocardial SOD (Superoxide dismutase), CAT (Catalase), GPx (Glutathione peroxidase), and GSH (glutathione) along with GSH (glutathione) imparts it its primary cardioprotective effect\textsuperscript{29}. Clinical studies have shown a decrease in arteriosclerosis and an increase in subendocardial viability ratio (SEVR)\textsuperscript{30}. Additionally, It can also restore SAP (Systolic arterial pressure), DAP (Diastolic arterial blood pressure), MAP (Mean arterial blood pressure) and HR (Heart rate) which may drop during myocardial damage. Moreover, it has shown reduction in inflammation, myonecrosis, and also decreases connective tissue myocardial fibres\textsuperscript{29}. 

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Arjun (Terminalia Arjuna) contains flavonoids which have antioxidant, anti-inflammatory, lipid lowering effect by reducing LDL levels\textsuperscript{31}, while glycosides have a cardiotonic effect. Significant inotropic\textsuperscript{32} and hypotensive effects can be seen in its bark. It also increases coronary artery blood flow and protects myocardium against ischemic damage. It also has a mild diuretic and antithrombotic effect. It increases prostaglandin E\textsmaller{2}, reduce left ventricular mass, and increase left ventricular ejection fraction\textsuperscript{31,33}. It may also prevent myocardial alterations brought on by chronic beta-adrenoceptor stimulation\textsuperscript{31}. By reducing the levels of free radicals it shows its anti-apoptotic properties such as ROS (Reactive Oxygen Species), hydroperoxide, and nitrite, as well as the rate of lipid peroxidation. It also increased antioxidant enzymes (superoxide dismutase, glutathione reductase, catalase, and glutathione peroxidase) and total glutathione levels\textsuperscript{34}. It exhibits its anti-atherogenic properties by increasing adiponectin while lowering pro-inflammatory adipokines and leptin levels\textsuperscript{35}. The cardioprotective effect of Zafran (Croccus sativus) is achieved through its antioxidant\textsuperscript{36}, anti-inflammatory, and anti-apoptotic mechanisms\textsuperscript{37}. One of its active constituents crocin, decreases Ventricular ectopic beats (VEBs), Ventricular tachycardia (VT) episodes and Ventricular Fibrillation (VF)\textsuperscript{38}. Safranal, another active constituent has the ability to normalise the activities of enzymes LDH and CK-MB, reduce lipid peroxidation and MDA levels of heart tissue\textsuperscript{39}. It can also significantly reduce peak MAP, SBP, and HR\textsuperscript{37}. Honey promotes cardio-protection by scavenging radical species, reducing lipid peroxidation, fortifying enzymatic and non-enzymatic antioxidant systems and stimulating/inhibiting pro-inflammatory markers by virtue of its various constituents\textsuperscript{40,41}. Apart from improving lipid profile by lowering total cholesterol, triglycerides, LDL, lipid peroxidation (LPO) and increasing HDL level, honey has also shown to reduce cardiac troponin I level as well as the activities of CK-MB, LDH, AST, ALT. It also reduces the inflammatory cells infiltration, protects cardiac muscle fibre and also enhances the structural and functional integrity of contractile apparatus\textsuperscript{42}.

Sumbul teeb (Nardostachys jatamansi) demonstrates its cardio-protective activity by its antioxidant and hypolipidemic activity. It also decreases the release of CK into the plasma\textsuperscript{43}. It is also found to decrease LDH, CPK, AST, ALT and MDA levels\textsuperscript{44}.

**Conclusion:**

As per the popular phrase “Time is Muscle” it can be understood how important it is to timely identify the risk for cardiac muscles. Once cardiac muscles start getting compromised and if not managed at right time it may lead to irreversible damage. Looking back into the history, people benefited with the use of herbal medicines for various diseases including cardiac ailments. Nowadays, medical field is again paying attention towards herbal treatment for effective management of diseases and also to avoid various untoward effects of long term use of synthetic products. One can explore the potential herbs used in Unani Medicine for cardiac disease such as Abresham, Gaozaban, Badranjboya, Amla, Arjun etc as several pre-clinical and clinical trials endorsed their effectiveness, further, trials are undergoing to understand the mechanism of action on their effectiveness.

**Conflict of Interest:** Declared none

**Funding Source:**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

This work has not been published previously and is not under consideration for publication elsewhere.

**Author’s Contribution:**

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All the authors read and approved the final version of this manuscript
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