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New Developments in our Understanding of the Pathology of Inherited Cardiomyopathy

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ABSTRACT:-

The term "cardiomyopathy" refers to a group of disorders that affect the myocardium and can result in cardiac dysfunction, including heart failure, arrhythmia, and even unexpected death. In both children and adults, cardiomyopathies are a leading cause of morbidity and mortality, and they are also a common reason for heart transplantation. Specific cardiomyopathies and primary cardiomyopathies were identified as the two fundamental categories in which cardiomyopathies should be categorised by a joint task force of the World Health Organization (WHO) and the International Society and Federation of Cardiology (ISFC) in the year 1995. 1 Certain heart muscle diseases, such as those related with myocarditis, specific cardiac diseases, or broad systemic diseases, fall under the category of specific cardiomyopathies. On the other hand, primary cardiomyopathies are diseases that are inherent to the myocardium itself, and they are categorised according to their pathophysiological processes. This category encompasses unclassified cardiomyopathy, dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), restricted cardiomyopathy (RCM), and arrhythmogenic right ventricular cardiomyopathy (ARVC).

Keywords: pleomorphism, nutritional deficiency, intertrabecular, tafazzin, Endomyocardial biopsy.

INTRODUCTION: -

There is an estimated prevalence of at least 36.5 cases of idiopathic dilated cardiomyopathy (DCM) for every 100 000 people in the United States. This makes it the leading cause of congestive heart failure in young people [1]. An increase in myocardial mass and a decrease in the thickness of the ventricular wall are two of the hallmarks of DCM. The heart takes on the appearance of a sphere, and there is significant dilatation of the ventricular chambers, extensive endocardial thickening, and atrial enlargement, frequently accompanied with thrombi in the appendages. The histological changes that are related with DCM are typically non-specific, and it is possible that not all characteristics will be present. Myocyte attenuation, interstitial fibrosis, myocyte nuclear hypertrophy, and pleomorphism are all components of this constellation. When individual myocytes die, there is frequently an increase in the number of interstitial T lymphocytes as well as focal accumulations of macrophages that occur simultaneously. In many cases, there is a widespread loss of myofibrils, which gives the myocytes the appearance of being hollow or vacuolated.

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Even though the cause of most of these cases is unknown, studies have shown that up to 35 percent of those who have idiopathic DCM also have the condition in their families [2]. This has been demonstrated by in-depth pedigree examinations of relatives of index patients who were diagnosed with DCM, in conjunction with the detection of single gene mutations in structural proteins of the myocyte cytoskeleton or sarcolemma [3]. As a consequence of this, the hypothesis that familial DCM is a kind of cytoskeletalopathy has been put up. A coronary artery disease, myocarditis, nutritional deficiencies, systemic disease, cardiotoxins (such as anthracycline), puerpurium, alcohol, and skeletal muscle wasting diseases (that is, the muscular dystrophies) are three of the secondary causes of DCM.

There are a few different ways that familial DCM (FDCM) can be passed down across generations; these ways include autosomal dominant inheritance, X-linked inheritance, autosomal recessive inheritance, and mitochondrial heredity [4]. The autosomal types of FDCM are the most common, and they can be further subdivided into a pure DCM phenotype or a DCM that is associated with a disorder of the cardiac conduction system. Significant headway has been achieved in the research aimed at locating possible disease loci and the genes that are involved for FDCM. A number of mutations can be found in the genes that code for cardiac actin, desmin, d-sarcoglycan, b-sarcoglycan, cardiac troponin T, and a-tropomyosin, among others [2]. However, to this day, only one gene, known as the lamin A/C gene, has been identified as being responsible for DCM associated with cardiac conduction system dysfunction despite the fact that four putative genetic loci have been discovered for the condition [4]. In addition to being the cause of autosomal dominant FDCM with minor skeletal myopathy, mutations in the lamin A/C gene are also responsible for the development of autosomal dominant Emery-Dreifuss muscular dystrophy.

DISCUSSION:-

Restrictive Cardiomyopathy: RCM is the kind of cardiomyopathy that occurs the least frequently and is characterised by restrictive filling and reduced diastolic volume of either or both ventricles with normal or near normal systolic function and wall thickness. RCM is the least common type of cardiomyopathy. Clinically and hemodynamically, RCM mimics the symptoms of constrictive pericarditis, which might result in diagnostic ambiguity [5, 6]. RCM is typically the outcome of myocardial or endomyocardial illness, which can have a variety of causes. These diseases "stiffen" the heart through infiltration or fibrosis, which can lead to RCM [7]. There is the possibility of classifying RCM as either primary or secondary. Endomyocardial fibrosis (EMF), Loeffler's endocarditis, and idiopathic restrictive cardiomyopathy are the three principal forms of restrictive cardiomyopathies. The latter type is non-infiltrative, and interstitial fibrosis of the myocardium is the only evident pathological abnormality [6, 7]. Idiopathic RCM is frequently characterised by skeletal myopathy and is transmitted in an autosomal dominant manner.

In a manner similar to this, a subset of individuals who have familial HCM caused by troponin I mutations might likewise present largely with restrictive physiology and may be

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similar to RCM [8]. The specific heart muscle illnesses that are included in the secondary types of RCM are more common, and they include the instances in which the heart is afflicted as part of a multisystem ailment. These conditions can be further categorised as non-infiltrative (for instance, carcinoid heart disease and anthracycline toxicity), infiltrative (for instance, amyloidosis and sarcoidosis), or storage (for instance, haemochromatosis, glycogen storage disease, and Fabry's disease). The infiltrates that are present in interstitial disease are found between the myocytes, whereas the deposits that are present in storage disorders are found inside the cells [7].

The diagnosis of cardiac amyloidosis, a condition in which amyloid protein deposits surround individual myocytes and form a characteristic "honeycomb" pattern, can be made more accurately with the help of endomyocardial biopsy. The identification of a subset of patients who have particular kinds of RCM can therefore be facilitated through the use of endomyocardial biopsy. This prevents some patients with constrictive or restrictive physiology from undergoing unneeded thoracotomy, which is necessary in cases where distinguishing restrictive cardiomyopathy from constrictive pericarditis might be challenging. In addition, it is possible to determine the kind of amyloid fibril by conducting immunohistochemistry investigations on endomyocardial biopsy specimens. These studies can be performed on the tissue obtained from the biopsy. The National Amyloidosis Centre, which has its headquarters at the Royal Free Hospital in London, is in charge of providing this service in the United Kingdom [9, 10]. Typing is important because it is necessary to categorise the subtype of amyloidosis in order to be able to provide suitable treatment for those who have the condition. For instance, RCM brought on by light chain deposition might be reversible after the patient has responded well to treatment and the underlying plasma cell dyscrasia has gone into remission [11]. In a similar manner, people who have FAP caused by mutant TTR and who receive an early diagnosis may benefit from liver donation.

Arrhythmogenic Right Ventricular Cardiomyopathy: Arrhythmogenic right ventricular cardiomyopathy, also known as arrhythmogenic right ventricular cardiomyopathy (ARVC), is a condition that affects the right ventricular myocardium the most and is characterised by the gradual death of myocytes. This is due to the advancement of fatty or fibro-fatty tissue from the epicardium to the endocardium, sparing the trabeculae as it moves from the epicardium to the endocardium. This can either be a large or partial replacement of the myocardium. A substrate for electrical instability is provided by the presence of residual islands or strands of myocytes that are surrounded by fatty or fibrous tissue. This instability can lead to prolonged ventricular arrhythmias and abrupt death [12]. Exertion is one of the risk factors that can bring in sudden death, which is more common in teenagers and young adults. A primarily "fatty" variant and a "fibrofatty" variant have both been described as problematic variants in the research that has been done so far. Both of these variants can be found in the literature [13]. The "fatty" form is characterised by transmural infiltration of adipose tissue without wall weakening and sparing of the septum and left ventricle. Additionally, the "fatty" variant is referred to as adipose infiltration [14, 15]. The "fibrofatty" or "cardiomyopathic" variation,

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on the other hand, is distinguished by substantial replacement-type fibrosis. Islands or strands of surviving myocytes show a mix of degenerative change and myocyte vacuolisation, and they are commonly linked with focal mononuclear inflammatory cell infiltrates. This is because surviving myocytes have undergone vacuolisation and degeneration simultaneously.

Hypertrophic Cardiomyopathy: The autosomal dominant form of hypertrophic cardiomyopathy, also known as HCM, is a prevalent genetic condition that affects 1:500 people in the community [16]. Donald Teare, a pathologist, was the first person to report this ailment in 1958. He defined the distinctive asymmetrical thickening of the left ventricular wall in a series of young adults as a benign muscular hamartoma of the heart. This condition was first seen in young adults.

CONCLUSION:-

Recent developments in molecular genetics have paved the way for the identification of single gene abnormalities as well as candidate disease loci that are responsible for DCM, HCM, RCM, and ARVC, in addition to cardiomyopathies of unknown aetiology such as isolated LVNC. These advancements, in conjunction with assessments of the link between phenotype and genotype, have indicated that the pathophysiology of multiple different kinds of cardiomyopathy includes a significantly wider morphological range than was previously understood. The recognition of isolated LVNC as a separate cardiomyopathy with distinctive morphological and histological characteristics has been assisted by pathological research. The utility of an endomyocardial biopsy in the diagnostic process for certain forms of cardiomyopathy is still a matter of some debate. However, endomyocardial biopsy combined with routine electron microscopy has emerged as a useful tool in the diagnostic arsenal for distinguishing a subset of individuals with cardiac Fabry's disease, which clinically simulates hypertrophic cardiomyopathy (HCM). The significant impact that scientific advancement will have in the future on the process of elucidating the genetic basis and aetiology of primary myocardial illness will, without a doubt, have the effect of broadening present conceptions surrounding the pathology of primary cardiomyopathies.

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