Healthy Heart

Volume-9 | Issue-99 | February 5, 2018

Price : ₹ 5/-

Honorary Editor :
Dr. Urmil Shah

From the Desk of Hon. Editor:

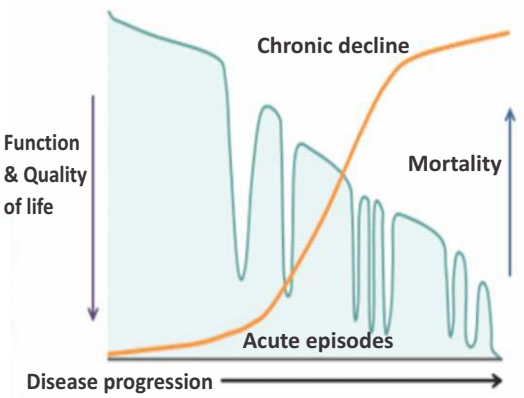
Heart failure is a life-threatening disease and should be considered a global health priority. Congestive Heart Failure (HF) is increasing worldwide due to the aging population and improvement in (acute) care for patients with cardiovascular diseases.

The prognosis for patients with HF is very poor without treatment. Furthermore, (repeated) hospitalizations for cardiac de-compensation cause an increasing economic burden. Modern drugs and the consequent implementation of therapeutic recommendations have substantially improved the morbidity and mortality of HF patients.

Two guidelines recently published focuses on diagnosis as well as management of Heart Failure. Two newer drugs have been approved by US FDA for management of heart failure. So it become relevant to know about this guideline as well as newer molecule

Chronic Heart Failure Management: New Drug/ New Guideline

Between 2002 and 2014, the number of new cases of heart failure in the UK increased by 12%. The number of new Chronic Heart Failure cases in 2014 was similar to the combined number of new cases of breast, prostate, lung and bowel cancer. Similar trend is also seen in country like India in recent years.



HF is a progressive condition with high mortality

- **1-year death rates for patients hospitalized with HF vary between 17-45%.**
- **For men, a patient hospitalized for HF will survive on an average for 2.3 years. Whereas in females, it could be 1.7 years.**

In 2016, the European Society of Cardiology (ESC) presented their new and updated guidelines on the diagnosis and therapy of HF. Simultaneously, a working group of representatives from the American Heart Association (AHA), the American College of Cardiology (ACC), and the Heart Failure Society of America (HFSA) published an update to the guidelines, which focused on the pharmacological management of HF. In this article, we will be mainly focusing on diagnosis and management of chronic Heart Failure with LV Dysfunction.

Signs and Symptoms of Heart Failure according to newer guidelines :

SYMPTOMS OF HF

TYPICAL

- Breathlessness
- Ankle swelling
- Orthopnea
- Fatigue, tiredness, increased time to recover after exercise
- Paroxysmal nocturnal dyspnea
- Reduced exercise tolerance

LESS TYPICAL

- Nocturnal cough
- Syncope
- Wheezing
- Palpitations
- Bloated feeling
- Confusion

SIGN OF HF

MORE SPECIFIC

- Laterally displaced apical impulse
- Elevated jugular venous pressure
- Third heart sound (gallop rhythm)
- Hepatojugular reflux

LESS SPECIFIC

- Weight gain
- Tissue wasting (cachexia)
- Peripheral edema (ankle, sacral, scrotal)
- Hepatomegaly
- Pulmonary crepitations
- Irregular pulse
- Reduced air entery and dullness to percussion at lung bases (plural effusion)

Elevated Natriuretic Peptides (NP) :

NP measurement (NT-proBNP or BNP) is a very useful bio marker in diagnosis of Heart Failure.

Natriuretic Peptides cut-offs for exclusion of Heart Failure according to new guideline

NT-proBNP ⩾125 pg/Ml

BNP ⩾35 pg/Ml

NP measurement is also very important for risk stratification as high levels are associated with recurrent hospitalization and risk of sudden death. High BNP levels are related to ventricular dysfunction severity and more advanced HF stages. So NP measurement according to guideline is **Class IA Indication** for both diagnosis and prognosis of Heart Failure. For pre discharge risk assessment and for prevent new heart failure onset NP measurement very useful and is recommended as **Class II A Indication.**

2017 ACC/AMA/HFSA HF Guidelines

2017 Heart Failure Clinical Practice Guideline

INDICATION	CLASS
NPs for diagnosis	Ia
NPs for prognosis	Ia
NPs for predischarge risk assessment	IIa
NPs to prevent HF onset	IIa
NPs to guide HF therapy	IIb

One must be aware of many condition other than HF for increasing BNP as shown below.

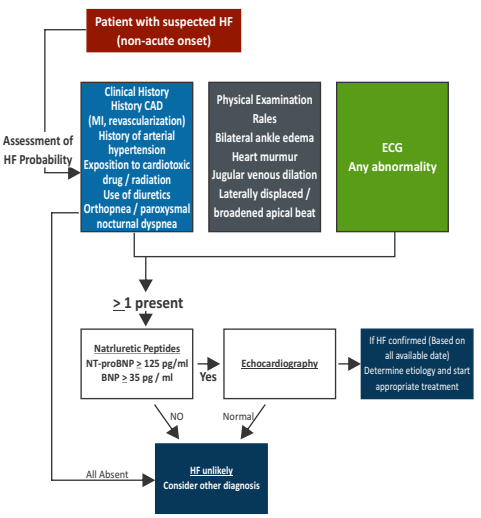
CARDIAC

- Heart Failure
- Acute coronary syndromes
- Pulmonary embolism
- Myocarditis
- Left ventricular hypertrophy
- Hypertrophic or restrictive cardiomyopathy
- Valvular heart disease
- Congenital heart disease
- Atrial and ventricular tachyar-rhythmias
- Heart contusion
- Cardioversion, ICD shock
- Surgical procedures involving the heart
- Pulmonary hypertension

NON-CARDIAC

- Advanced age
- Ischemic stroke
- Subarachnoid haemorrhage
- Renal dysfunction
- Liver dysfunction (mainly livercirrhosis with ascites)
- Paraneoplastic syndrome
- Chronic obstructive pulmonary disease
- Severe infection (including pneumonia and sepsis)
- Severe burns
- Anaemia
- Severe metabolic and hormone abnormalities (e.g. throtoxicosisi, diabetic ketosis)

Diagnostic Algorithm for a Diagnosis of HF of Non-Acute Onset

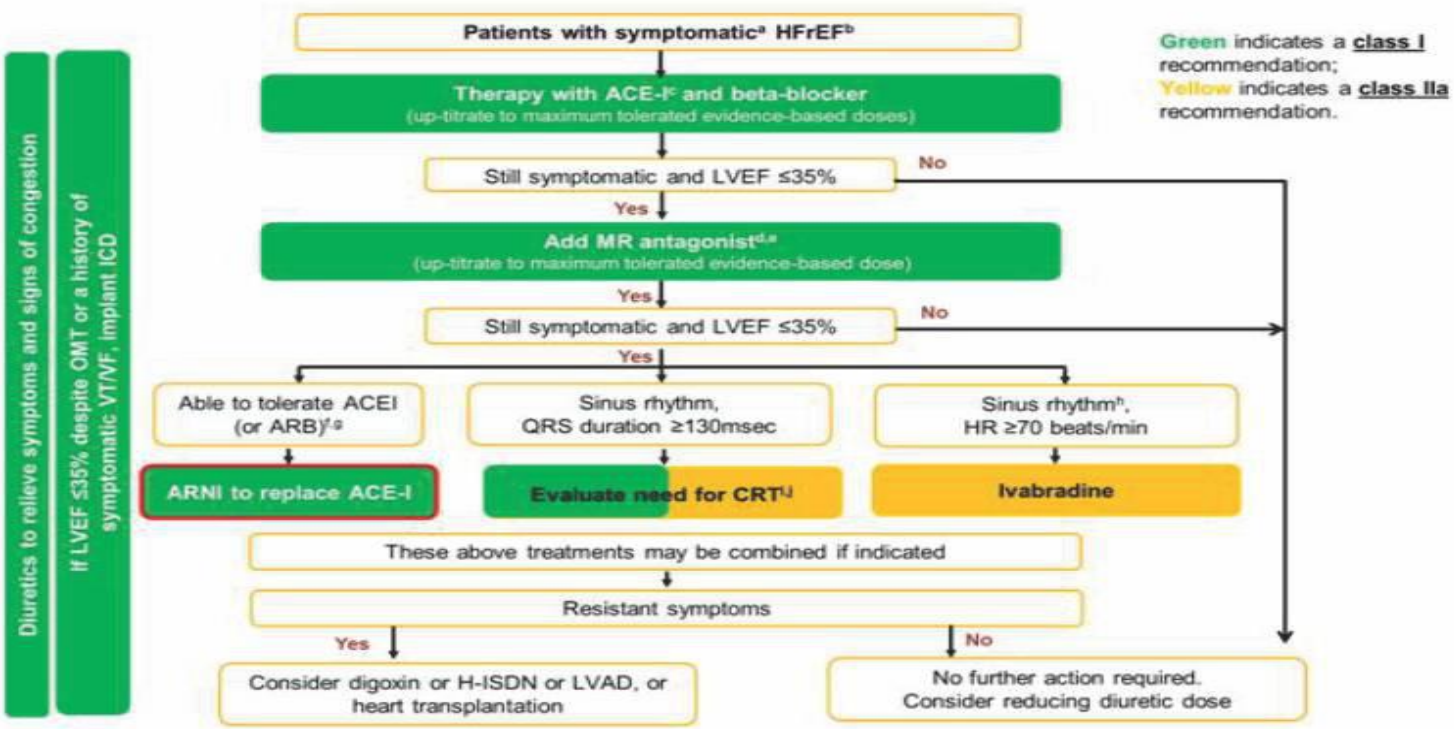


NP measurement is so important in diagnosis of patient suspected of Heart Failure, that it is recommended even before echo-cardiography in the flow chart. Echo is done not for diagnosis of Heart Failure but to find out whether HF is associated with normal EF or reduced EF.

Therapeutic approaches for HF differ in two well-established types are HF with reduced ejection fraction (HFrEF; LVEF <40%) and HF with preserved ejection fraction (HFpEF; LVEF ⩾50% and signs of diastolic dysfunction).

The New European Guideline introduced another form of HF, called HF with mid-range ejection fraction

Treatment strategy for the use of drugs (and devices) in patients with HF



(HFmrEF; LVEF 40%–49% and signs of diastolic dysfunction). Though there is no clear recommendation for the treatment of HFmrEF patients (EF between 40-50%) there is evidence that patients with HFmrEF might more likely benefit from drug therapy established for HFrEF compared to patients with HFpEF . So HF with EF 40-49 % should be managed similar to HF with reduce EF.

The fundamental objectives for HF therapy are as follow:

- Symptom Improvement
- Functional Capacity Improvement
- Enhancing Quality of life
- Reducing the frequency of hospitalizations
- Decreasing associated mortality

New Guideline recommendation and new molecule for management of Chronic Heart Failure with reduced Ejection Fraction.

Mineralocorticoid Receptor Antagonists (MRA) for Treatment of Heart Failure according to new guideline

Spironolactone and Eplerenone are MRAs recommended to patient of HF with reduced EF, who remain symptomatic in spite of standard treatment like beta blocker, ACE Inhibitor / ARB, Diuretics. RALES, Emphesus and EMPHASIS Study showed significant mortality benefit compare to placebo. MRA not only gives systematic benefit but also modify the disease and improve mortality so it's is class I recommended according to new guideline

MRAs are commonly used as add-on diuretic that provides incremental benefit for salt-and-water excretion above and beyond what may be seen with a loop diuretic and/or a thiazide-type diuretic. The adverse electrolyte and renal function side effects with MRAs are not uncommon in at-risk patients, such as those with CKD or HF; therefore, dosing should take into account the propensity for these drugs to cause clinically relevant benefits.

NEWER MOLECULE

The introduction of an angiotensin receptor–neprilysin inhibitor (ARNI) (valsartan/sacubitril) and a sinoatrial node modulator (ivabradine), both recently approved by US FDA has made their way into new treatment guidelines. These guidelines recommend sacubitril/valsartan as standard of care for HFrEF for replacement of ACEi/ARBs in HF patients tolerating ACEi/ARBs who remain symptomatic (mild to moderate

symptoms NYHA Class II-III). Ivabradine is recommended in patient with sinus rhythm and heart rate more than 70 after uptitrating maximum beta blocker.

If – Channel Inhibitor

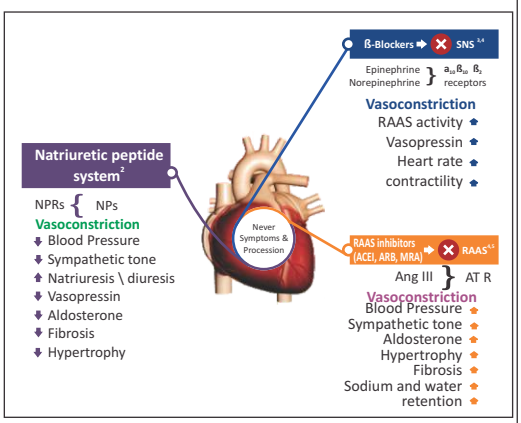
Ivabradine targets the sinu-atrial node and slows the sinus rhythm through If-channel inhibition. In SHIFT Study the administration of Ivabradine in addition to an optimized HF medication (including beta-blocker) resulted in a significant decrease in HF hospitalizations and cardiovascular mortality (primary endpoint, relative risk reduction 18%). Furthermore, left ventricular function was enhanced and quality of life improved. So Ivabradine was approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic HF.

Ivabradine is indicated to reduce the risk of hospitalization for worsening Heart Failure in patients with stable, symptomatic chronic heart failure with an LVrEF of 35% or lower, who are in sinus rhythm with a resting heart rate of 70 bpm or higher, and who are either on maximally tolerated doses of beta-blockers or have a contraindication to beta-blocker use.

Anginotensin Receptor-Neprilysin Inhibitor (ARNI) : Novel strategies targeting the neuro-humoral system.

Over activation of the RAAS and SNS underpins HF therapy. The renin-angiotensin-aldosterone system (RAAS) plays a critical role in the pathophysiology of heart failure with reduced ejection fraction (HFrEF). Targeting components of the RAAS has produced significant improvements in morbidity and mortality. Angiotensin-converting enzyme (ACE) inhibitors remain first-line therapy for all patients with a reduced ejection fraction. Angiotensin-receptor blockers may be used instead of ACE inhibitors in patients with intolerance, or in conjunction with ACE inhibitors to further reduce symptoms. Recent data support broader indications for aldosterone antagonists in heart failure, and the combination of an ACE-inhibitor and aldosterone antagonist has become the preferred strategy for dual blockade of the RAAS.

A new drug class has recently emerged in HF therapy. ARNI is a novel treatment concept in HF. The first and to this date only substance in this class is "LCZ696," which is comprised of an ARB (valsartan) and sacubitril, a neutral endopeptidase



(NEP, neprilysin) inhibitor. Neprilysin plays a crucial role in the degradation of natriuretic peptides. The therapeutic concept of the ARNI is based on the established inhibition of the renin-angiotensin-aldosterone system (RAAS) and an increase in endogenous natriuretic peptides by blocking their degradation. Inhibition of neprilysin counteracts the neurohumoral activation, which leads to vasoconstriction, sodium retention, and cardiac remodeling, increasing the RAAS-blocking effects.

The ARNI (RAAS and neprilysin inhibitor) LCZ696 simultaneously inhibits neprilysin and blocks AT1 receptors. In addition to the three cornerstone therapies of Heart Failure, replacing ACE inhibition by an ARNI has now been shown to further improve morbidity and mortality in HFrEF.

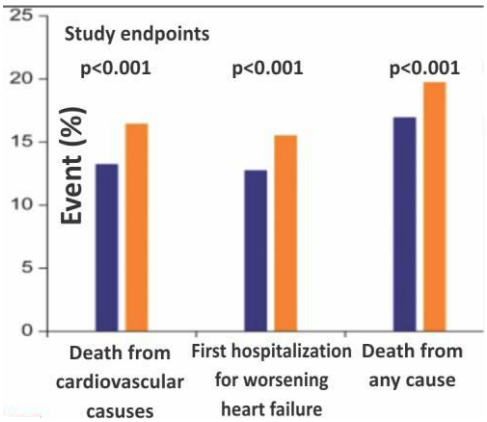
The Prospective Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) trial was a large randomized Phase III study to investigate the beneficial effects of this new therapeutic concept. The results of the PARADIGM-HF trial have been so pronounced that they have led to a class IB recommendation by the ESC for symptomatic patients despite the 'classic' HF medication.

Further progress is announced with the premature termination for excess of benefit of the prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in Heart Failure (PARADIGM–HF) trial, with the dual angiotensin receptor and neprilysin inhibition as an alternative to angiotensin-converting enzyme inhibition in patients with chronic systolic HF.

The primary endpoint, composed of cardiovascular mortality and HF hospitalizations, was significantly reduced in the sacubitril/valsartan group (20%). Furthermore, significant reduction was shown for cardiovascular mortality (20%), all-cause mortality

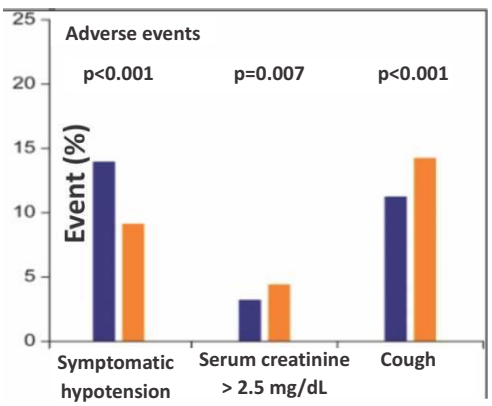
(16%), and HF hospitalization (21%). Endpoint data and adverse events are depicted in Figure.

Figure - Main results including study endpoints of the PARADIGM-HF trial comparing the ARNI sacubitril



/valsartan to the ACEI enalapril

Figure - Adverse event found PARADISM-HF trial comparing the ARNI sacubitril/valsartan to the ACEI



enalaprill

Side effects found was similar to ACE inhibitor with less chance of hyper kalemia/cough/impaired renal function and slightly more chance of hypo tension compare to ACE inhibitor.

Angioedema occur rarely with ARNI having similar incidence compare to ACE Inhibitor. ARNI Contraindicated in patient with history of angioedema.

Starting dose of ARNI is 100 mg two times a day in patient who is tolerating ACE Inhibitor. Dose should be uptitrated to 200 mg BD after three weeks.

For patient with relatively low blood pressure, 50 mg BD should be started and gradually after checking blood pressure and renal function.

- **ARNI is at present being evaluated in patient with HF and preserved ejection faction in PARAGON Study.**
- **PARADISE - MI Study will evaluated ARNI in Post Myocardial Injection Patient Reduce Ejection Faction.**

Hydralazine and nitrated combination is class II A Indication as specially in black population, with renal dis-fucntion, not tolerating ACE Inhibitor. Digoxin is class II B indication according to newer guideline.

Co-morbidities in Treatment of Chronic Heart Failure

Diabetes, Anemia, Chronic Obstructive Pulmonary Disease, Sleep Apnea, Stroke, Renal Dysfunction, Arrhythmia, and Depression are diagnosis that often coexist with HF. Early detection of concomitant diseases in patients with HF is important and should be considered carefully when initiating therapy. Medications commonly used to treat these co-morbidities may induce or worsen HF symptoms, so determining appropriate drug therapy is important.

- Diabetes: Metformin should be considered as a first line treatment of glycemic control in patients with diabetes and chronic heart failure, unless contraindicated for New York Heart Association (NYHA) Class IIa. SGLT Inhibitor like Empagliflozin and other molecule same group have been found to improve mortality and HF re-admission so it should be preferred over other anti diabatic.
- Iron Deficency: Ferric carboxy maltose may potentially lead to sustainable improvements in function, symptoms, and quality of life. IV Iron therapy is Class IIb recommendation for patients with NYHA Class II and III heart failure and iron deficiency (ferritin <100 ng/mL or 100-300 ng/mL if transferrin saturation <20%).
- Sleep Apnea: Patient having sleep apnea with HF have high rate of hospital re-admission. Continues Positive Air Pressure (CPAP) ventilation is found to have reduce re-hospitalization rate.

Recommendations for Cardiac Resynchronisation Therapy (CRT) in patients with Heart Failure according to new guideline, despite Optimum Medical Treatment to improve symptoms and reduce morbidity and mortality

- Patient with QRS duration ⩾150 ms , LBBB QRS morphology and with LVEF ⩽ 35% for New York Heart Association (NYHA) Class I level A.
- Patient with QRS duration ⩾150 ms , NON LBBB QRS morphology and with LVEF ⩽ 35% for New York Heart Association (NYHA) Class IIa level B.
- Patient with QRS duration 130-149 ms,LBBB QRS morphology and with LVEF ⩽ 35% for New York Heart Association (NYHA) Class I level B.

Cardiopulmonary Exercise Testing to guide Transplant Listing: As Heart Transplant is now possible in Ahmedabad it becomes relevant to know who are the group of patient who should under go Heart Transplant. 2016 guideline recommend a cut off for peak oxygen consumption (VO2) of ≤ 12 ml/kg/min, with presence of a β-blocker

and cut off for peak oxygen consumption (VO2) of ⩽ 14 ml/kg/min - in patient intolerant of a β-blocker is **Class I** Indication for re-commending heart transplant.

Which therapies should be avoided in acute heart failure?

- NSAIDs or COX-2 inhibitors are not recommended in patients with HF. Nonsteroidal anti-inflammatory drug (NSAID) use (nonselective or cyclooxygenase [COX]-2 selective [coxibs]) is associated with increased risk of first occurrence or exacerbation of HF. NSAID use is also associated with increased risk of renal dysfunction and hyperkalemia and impairment of responses to angiotensin converting enzyme (ACE) inhibitors and diuretics. Observational data in patients with HF indicated an association between NSAID (non selective or coxibs) use and increased mortality for New York Heart Association (NYHA) Class IIIb.
- Thiazolidinediones may cause fluid retention and heart failure by increasing renal sodium reabsorption for New York Heart Association (NYHA) Class IIIa.
- Do not use calcium channel blockers in acute heart failure; specifically, diltiazem and verapamil are to be avoided in acute heart failure with systolic dysfunction for New York Heart Association (NYHA) Class IIIc.
- ARB and ACE Inhibitor in combination is Class III Indication and should not be use an specially when patient is on MRA.

Conclusion :

Management of HF requires a multi disciplinary approach. Counselling by dietician, physiotherapist, psychiatrist is essential for this group of patient. HF clinic properly design have been found to be very effective in improving mortality and morbidity, fulfill the need of regular monitoring, improve the adherence to diet and medicine. We can also properly guide a patient regarding need of CRT and Heart Transplant at proper time.

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Dr. Chirayu Vyas (Visiting)

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Healthy Heart Registered under RNI No. GUJENG/2008/28043
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Postal Registration No. GAMC-1725/2018-2020 issued by SSP Ahmedabad valid upto 31st December, 2020
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Advanced Hemodynamic Monitoring

Course Directors	:	Dr. Niren Bhavsar / Dr. Chintan Sheth
Date	:	March 11, 2018 (Sunday)
Duration	:	1 day
Number of Seats	:	50
Venue	:	CIMS Auditorium

Programme Overview:

In intensive care and perioperative care, hemodynamic parameters are very dynamic and fluctuating. In-depth understanding of hemodynamic monitoring helps in early identification and prompt treatment of major alteration in it and will help assess the effect of your measures. Technology is rapidly changing and new gadgets are being added daily on a continual basis which directly and indirectly help achieve hemodynamic goals. One needs to be updated with the pace of technology. The course take one through the journey from basic fundamentals to the latest and advanced hemodynamic gadgetry and practical applications by experts.

Programme Highlights:

- Basic Hemodynamic monitoring- fundamentals
- Advanced cardiac output monitoring devices and their applications
- Echocardiography as hemodynamic monitoring tool
- Functional hemodynamic monitoring - changing paradigm
- Hemodynamics in operating room, ICU and emergency
- Simulation and hands-on workshop

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Printed, Published and Edited by Dr. Keyur Parikh on behalf of the CIMS Hospital
Printed at Hari Om Printery, 15/1, Nagori Estate, Opp. E.S.I. Dispensary, Dudheshwar Road, Ahmedabad-380004.
Published from CIMS Hospital, Nr. Shukan Mall, Off Science City Road, Sola, Ahmedabad-380060.