e-ISSN: 2347-7857
p-ISSN: 2347-7849

Research & Reviews: Journal of Pharmaceutics and Nanotechnology

Cardiovascular Diseases and Drug Therapy -A Review

Neha Anand*

Department of Biotechnology, Majhighariani Institute of Technology and Science, Odisha, India

Review Article

Received:02/09/2016
Accepted: 09/09/2016
Published: 13/09/2016

***For Correspondence**

Neha Anand, Department of Biotechnology, Majhighariani Institute of Technology and Science, Odisha, India.
E-mail: nehaanandnv@gmail.com

Keywords: Anticogulant, Novel oral anticoagulant, Warafrin, Apixaban, Dabigatran, Rivaroxaban

ABSTRACT

Cardiovascular drugs are drugs which are used to treat diseases relating to the heart and blood vessels structure and function. Most common diseases includes: heart failure, coronary artery disease, high cholesterol, blood clots, circulation disorders etc.

As we know the varieties and extent of cardiovascular drugs have increased rapidly in past decades. An effective oral diuretic which was approved in 1950s has outstanding effect on treatment of heart failure and hypertension. Beta blockers agents in 1960s brought major changes for treatment of hypertension or angina pectoris patients. In 1980s Calcium channel blockers and ACE inhibitors were used widely and given effective treatment to patients with coronary artery disease, hypertension and heart failure. Major transform was invention of clotting factors which have saved thousands of patients from heart attack.

INTRODUCTION

Cardiovascular diseases are major cause of illness and death worldwide and it is also estimated by scientists that morality rate of disease and death will be more in future. Five major cardiovascular diseases are Heart attack, stroke, hypertension, inflammatory heart disease, rheumatic heart disease and these diseases cause 16 million deaths per year all over world [1-7]. According to World health Organization, cardiovascular disease prevalence and incidence vary according to gender also and number of females getting affected is more than number of males. Different types of cardiovascular drugs are used for treatment of these diseases [8-16]. As we know that genetics plays an important role in treating patients likewise it also plays an important role in treatment of patients with particular drugs. In this review article we have discuss briefly on the effect of cardiovascular drugs on genetics [17-23].

The effect of drug is varying from patient to patient and it can result in adverse reaction, toxic effects or ineffectiveness of drugs in their normal doses. As per estimation genetic factors affect 20-95% of variations in the effects of the used drugs for treatment. Along with non-genetic factors there are several other factors which effects response of drugs therapy. These factors include [24-31]: Sequence variants in the genes encoding drug-metabolizing enzymes, drug transporters, trans-membrane receptors, intracellular enzymes and molecular targets. Drug response on genetic basis can be determined by the patient genes approach. Pharmacogenetics is the study of the effect of variation in a single gene on drug response which includes efficacy and toxicity. Pharmacogenomics is the study of multiple genes to variability in drug response [32-37].

Pharmacogenetic variation sources can be divided into three categories [38-42]

a) Pharmacokinetic
b) Pharmacodynamic
c) Variability in disease being treated

Cardiovascular drugs are classified into 7 different categories [43-57]

1) Anti-anginals: A disease of coronary arteries named angina pectoris is treated with pharmaceutical agents called anti–anginals.

2) Anti-arrhythmics: These agents are used for treatment of Arrhythmia in which the rhythmic contraction of the heart is interrupted.
3) Anti-hypertensives: Hypertension which is the most common of all cardiovascular diseases and it has affected nearly 40 million people in the US. It is the major cause of stroke and heart attack.
4) Anticoagulants: These drugs are used to inhibit the blood clotting in blood vessels. Anticoagulants are also used in myocardial infarction, venous thrombosis, peripheral arterial emboli, pulmonary embolism, blood transfusions, extracorporeal blood circulations and dialysis procedures.
5) Anti-hyperlipidemic agents: These drugs are also known as lipid lowering drugs. These drugs are used for the treatment of lipids (cholesterol) in blood.
6) Hypo-glycemic agents: These drugs are used for lowering glucose level in blood.
7) Anti-thyroid drugs and thyroid hormones: Antithyroid drugs are used to treat an overactive thyroid (hyperthyroidism) which is caused by Graves' disease.

To diagnose people with heart disease along with medicine there are many other points which are useful for controlling risk associated with disease as first action [48-53]:

- Cutting down on cholesterol and fat
- Regular exercise
- Smoking cessation

Most common FDA approved drugs to treat cardiovascular diseases (**Table 1**) [54-60]:

Table 1: Drugs for treatment of Cardiovascular Diseases.

Drugs	Disease
Pradaxa (dabigatran etexilate mesylate)	For the risk reduction of stroke and embolism due to atrial fibrillation
Eliquis (apixaban)	For the prevention of stroke and systemic embolism resulting from nonvalvular atrial fibrillation
Xarelto (rivaroxaban)	For the reduction in the risk of stroke and systemic embolism resulting from atrial fibrillation
Xarelto (rivaroxaban)	In treatment of prophylaxis of deep vein thrombosis during knee or hip replacement surgery
Adcirca (tadalafil)	In treatment of pulmonary arterial hypertension
Adempas (riociguat)	In treatment of Pulmonary Arterial Hypertension and Chronic Thromboembolic Pulmonary Hypertension
Advicor (extended-release niacin/lovastatin)	In treatment of cholesterol disorders

CARDIOVASCULAR DRUGS AND THERAPY

As we are aware of the fact that cardiovascular disease is the main cause of death all over world. Using drugs that inhibit coagulation, disrupt platelet function, reduce cholesterol levels, control blood pressure levels, etc. can reduce mortality in patients. In recent studies it is found that there are 17 different types of drugs which are used to treat cardiovascular diseases [61-73].

Recent researches are carried out in defining DNA sequence variations which balance patient's response to drug administration. Most of the information related to this has been collected with respect to warfarin (anticoagulant) and clopidogrel (antiplatelet agent) [74-82]. These studies includes identification of single nucleotide polymorphisms (SNPs) which affect drug metabolism, it is also an analysis to enable prediction of clinical outcomes in possible settings and it also gives illustration on how frequency of drug-related adverse events can be decreased with the help of genotype-directed prescription.

SOME COMMONLY USED THERAPIES WITH DIFFERENT DRUGS ARE DISCUSSED BELOW

Antiplatelet Therapy

Some commonly use antiplatelet drugs are: Aspirin, clopidogrel, prasugrel, ticagrelor.

These drugs are used to decrease atherothrombotic disease adverse effects in patients. But due to genetic variations after using medication also patients are suffering from atherothrombotic disease [83-89].

Aspirin is the commonly used antithrombotic agent. Aspirin irreversibly acetylates the cyclooxygenase (COX)-1 enzyme, which leads to the suppression of thromboxane A2 and related metabolites. There is possibility with almost 40% of aspirin using patients which can suffer from serious vascular problems due to aspirin resistance. There are different types of genetic polymorphisms which are supposed to affect aspirin response and lead to unacceptable situation [90-93].

Clopidogrel is widely used for antiplatelet treatment. Active clopidogrel metabolite irreversibly binds to the platelet ADP P2Y12 receptors. It is found that almost 21 % of patients receiving PCI exhibit there is none clopidogrel response and which leads to 8 times increase in risk of adverse effects of cardiovascular disease [94-96].

For example: Primary isoform which is responsible for activation of clopidogrel is CYP2C19. CYP2C9*2 and CYP2C9*3 carriers will lose their ability to metabolize clopidogrel. This results in reducing platelet aggregation and increases cardiovascular risks.

Antiplatelet therapy can be used for the patients for whom the genotype causes future risk for reduced antiplatelet efficacy. Genotyping cannot be prescribed for patients at lower risk.

If a patient has poor drug metabolism then clopidogrel can be replaced with other medicines such as prasugrel or ticagrelor.

Oral Anticoagulants

Coumarin derivates

Such as warfarin which are used for the treatment of thrombotic disorders. Adjustment of dose and routine monitoring is very important in use of warfarin for a patient's international normalized ratio (INR) and careful adjustment of the dose of particular patient. Warfarin levels can be affected by diet of patients, alcohol use or any other drug use. Many adverse effects like the risk of bleeding in patients which can be fatal can also be noticed [97-100]. A low dose can induce thromboembolism, and a high dose can induce bleeding. In studies it I found that patient response to anticoagulant therapy is also affected by genetic factors.

The variability of 50% in coumarin derivates maintenance dose can be described with genetic polymorphisms in some genes. They are:

a) CYP2C9 – the principal meta bolizing enzyme of all coumarines;

b) VKORC1 (vitamin K epoxide reductase complex subunit 1)–the pharmacologic target of coumarins;

c) CYP4F2 (vitamin K1 oxidase).

Genetic variation in some other genes like apo-lipo protein E, glutamyl carboxylase, calumenin, epoxide hydrolase 1,
and factor VII are also affecting warfarin dose requirement.

Beta-blockers

Beta-blockers are cardiovascular drugs which are used for clinical utility of pharmacogenetics. Variations in the genes involved in the synthesis of proteins for the beta-1 and beta-2 adrenergic receptors (ADRB1, ADRB2), and the gene that codes for associated regulatory proteins such as G protein-coupled receptor kinase 4 and 5 involved in signal transduction (GRK4, GRK5) could influence the treatment outcome.

Many beta-blockers are metabolized predominantly by hepatic CYP2D6. Polymorphisms in the gene coding for the CYP2D6 isoenzyme may also affect beta-blocker response.

Some commonly used beta blockers are:

- Bisoprolol (Zebeta)
- Metoprolol succinate (Toprol XL)
- Carvedilol (Coreg)
- Carvedilol CR (Coreg CR) Toprol XL

CONCLUSION

Based on the available data, it could be expected that in the future genome-tailored drug prescription and use of defined algorithm will help in giving successful drug action by reducing the frequency of unfavorable results and it will also have significant clinical relevance.

Discovery and validation of Gene variants which will be clinically validated and modulate the effectiveness of cardiovascular drugs will be continued.

A complete inventory of the genetic variation can responsible for the efficacy of drug action and the frequency of adverse events can provide data which will be more effective and will give greater clinical relevance.

REFERENCES

1. Alqudaimi HYM, et al. The Effect of Periodontal Therapy on Atherosclerosis in Cardiovascular Disease: Clinical, Biochemical, Microbiological and Experimental Study. J Cardiovasc Res. 2016;5:1.
2. Onrat ST, et al. Plasminogen Activator Inhibitor-1 (PAI-1) 4G/5G Allele Polymorphisms and NIDDM (Non-Insulin Dependent Diabetes Mellitus) Risk Factor for Early Onset Myocardial Infarction. Int J Cardiovasc Res. 2014;3:4.
3. Elahi MM and Matata BM. Developmental Origins of Cardiovascular Disease. A Missing Link in the Puzzle. Int J Cardiovasc Res. 2013;2:5.
4. Kennedy WL, et al. Maintaining the Benefit of Cardiovascular Disease Prevention Programs: The Challenge for Future Generations. Int J Cardiovasc Res. 2013;2:2.
5. Cipolletta E, et al. β2 Adrenergic Receptor Polymorphisms and Treatment-Outcomes in Cardiovascular Diseases. Int J Cardiovasc Res. 2013;2:1.
6. Podolecka E and Zukowska-Szczechowska E. Association between Rs6226 and Rs6224 Polymorphisms of the Furin Gene and Cardiovascular Diseases. Int J Cardiovasc Res. 2012;1:5.
7. Simone TM and Higgins PJ. Low Molecular Weight Antagonists of Plasminogen Activator Inhibitor-1: Therapeutic Potential in Cardiovascular Disease. Mol Med Ther. 2012;1:1 .
8. Sturzeneker. Non-Alcoholic Fatty Liver Disease: A New Risk Factor for Cardiovascular Disease?. Int J Cardiovasc Res. 2012;1:2.
9. Gainotti G, et al. A Comparison between Anxious-Depressive Disorders of Stroke and Multiple Sclerosis Patients, Evaluated with Specific Twin Scales. J Trauma Stress Disor Treat. 2016;5:2.
10. Singh J, et al. Perioperative Stroke after Endonasal Pituitary Tumor Resection: A Case Report. J Spine Neurosurg. 2015;4:2
11. Samadoulougou AK, et al.Cardio embolic stroke: Data from 145 cases at the Teaching Hospital of Yalgado Ouedraogo, Ouagadougou, Burkina Faso. Int J Cardiovasc Res. 2015;4:1.
12. He HL, et al. Risk Factors of Admission Delay after Ischemic Stroke in an Urban Tertiary Care Setting in China. Prensa Med Argent. 2014;100:1.
13. Janoschka A, et al. The Effect of 25 M versus 50 M Course Length on Backstroke Performance – An Analysis of National and International Swimmers. J Athl Enhancement. 2014;3:1.
14. Metcalfe AJ, et al. The Use of an Indoor Rowing Ergometer Test for the Prediction of Maximal Oxygen Uptake. J Athl Enhancement. 20132:6.
15. Nikodelis T, et al. Pelvis-Upper Trunk Coordination at Butterfly Stroke and Underwater Dolphin Kick: Application on an Elite Female Butterfly Swimmer. J Athl Enhancement. 2013;2:5.
16. Auzin M and de Weerd SR. Stroke in Pregnancy. J Womens Health, Issues Care. 2013;2:5.
17. Khouzam RN and Al Darazi F. Spontaneous Echo Contrast as a Risk Factor for Cerebrovascular Accident. Int J Cardiovasc Res. 2013;2:4.
18. Miyata S, et al. Masked Hypertension and Morning Blood Pressure Surge in Patients with Obstructive Sleep Apnea Syndrome. J Sleep Disor: Treat Care. 2016;5:1.
19. Rinaldi E, et al. Adrenomedullary Hyperplasia in a Patient with Poorly Controlled Hypertension and Neurofibromatosis Type 1: A Case Report. Endocrinol Diabetes Res. 2016;2:1.
20. Akbarzadeh M, et al. Comparison of Hypertension and Obesity Parameters in Healthy Adolescents and those with Polycystic Ovarian Syndrome. Endocrinol Diabetes Res. 2015;1:2.
21. Safdar Z, et al. Circulating Aldosterone Levels and Disease Severity in Pulmonary Arterial Hypertension. J Cardiovasc Res. 2015;4:5.
22. Mohtasahm AZ, et al. Hypertension in Iranian Urban Population: Prevalence, Awareness, Control and Affecting Factors. Prensa Med Argent. 2015;101:4.
23. Djoba Siawaya JF, et al. Prevalence and Relationship between Hyperglycemia Hypertension and Obesity in Libreville-Gabon: A Pilot Study. Endocrinol Diabetes Res. 2015;1:1.
24. Acar B, et al. A Rare Cause of Resistant Hypertension: Idiopathic Retroperitoneal Fibrosis. J Cardiovasc Res. 2015;4:4.

25. Safdar Z, et al. Collagen Metabolism Biomarkers and Health Related Quality of Life in Pulmonary Arterial Hypertension. Int J Cardiovasc Res. 2015;4:2.
26. Patra S, et al. Chronic thromboembolic pulmonary hypertension in a case with multi-drug resistant pulmonary tuberculosis. Int J Cardiovasc Res. 2015;4:1.
27. Alhaj EK, et al. Usefulness of BNP in Monitoring Response to Treatment in Patients with Pulmonary Arterial Hypertension PAH. Int J Cardiovasc Res. 2014;3:5.
28. Yaseen R, et al. Assessment of Left Ventricular Dyssynchrony in Hypertensive Patients with Normal Systolic Function by Tissue Synchronization Imaging. Int J Cardiovasc Res. 2014;3:5.
29. Reynolds MR, et al. Acute Rupture of a Previously Unruptured, Untreated Intracerebral Aneurysm during Induced Hypertension for Vasospasm in Subarachnoid Hemorrhage. J Spine Neurosurg. 2014;3:5.
30. Mehra S, et al. Pulmonary Hypertension in Patients Undergoing Kidney Transplant - A Single Center Experience. Int J Cardiovasc Res. 2013;2:6.
31. Mahendru R, et al. Anti-Oxidant Intake in Antenatal Cases High-Risk for Pregnancy Induced Hypertension and Intrauterine Growth Restriction. Androl Gynecol: Curr Res. 2013;2:1.
32. Couvertier-Lebrón CE, et al. Pharmacogenetics of Apolipoprotein E on Donepezil and Fluoxetine Pharmacotherapy for Chemotherapeutic Induced Neurocognitive Decline. J Womens Health, Issues Care. 2013;2:5.
33. Messori A, et al. Prevention of Venous Thromboembolism in Major Orthopedic Surgery: Bayesian Network Meta-Analysis of 21 Randomized Trials Evaluating Unfractionated Heparins, Low-Molecular Weight Heparins, and New Oral Anticoagulants J Cardiovasc Res. 2015;4:5.
34. Halum AS and Bhinder MTM. Genetic Counselling, Pharmacogenetics and Gene Therapy: The Paving-Stones Leading to Brighter Futures. Adv Genet Eng. 2016;5:151.
35. Patil J. Pharmacogenetics and Pharmacogenomics: A Brief Introduction. J Pharmacovigilance. 2015;3: e139.
36. Kamal MS and El Dine. Spotlights on Pharmacogenetics of Schizophrenia and Depressed Mood. Gene Technol. 2015;4:121.
37. Talameh JA and Kitzmiller JP. Pharmacogenetics of Statin-Induced Myopathy: A Focused Review of the Clinical Translation of Pharmacokinetic Genetic Variants. J Pharmacogenomics Pharmacoproteomics. 2014;5:128.
38. He ZX and Zhou SF. Pharmacogenetics-Guided Dosing for Fluoropyrimidines in Cancer Chemotherapy. Adv Pharmacoepidemiol Drug Saf. 2014;3:e125.
39. Torrellas C, et al. Benefits of Pharmacogenetics in the Management of Hypertension. J Pharmacogenomics Pharmacoproteomics. 2014;5:126.
40. Nadiminti K, et al. Cytogenetics and Chromosomal Abnormalities in Multiple Myeloma-A Review. Clon Transgen. 2013;2:114.
41. Tufa TB, et al. Pharmacogenetics of ß1-Adrenergic Receptor Blockers in Heart Failure Therapy: A Systematic Review Cardiol Pharmacol. 2013;2:113.
42. Abarin T. Gene-environment Interaction Studies with Measurement Error Application in the Complex Diseases in the Newfoundland Population: Environment and Genetics Study. J Biomet Biostat. 2013;4:173.
43. Mishra H and Kumar V. Pharmacovigilance: Current Scenario in a Tertiary Care Teaching Medical College in North India. J Pharmacovigilance. 2013;1:109.
44. Murdaca G, et al. Pharmacogenetics: Reality or Dream in Predicting the Response to TNF-a Inhibitor Treatment? J Genet Syndr Gene Ther. 2013;S3:007.
45. Salem MSZ. Medical Genetics: An Overview. Human Genet Embryol. 2013;S5:001.
46. Salem MSZ. Medical Genetics: Problems and Approaches. Human Genet Embryol. 2013;S5:002.
47. Puri A. Pharmacogenetics Variations in Anesthesia. J Anesth Clin Res. 2012;3:233.
48. Hong H. Next-Generation Sequencing and Its Impact on Pharmacogenetics. J Pharmacogenomics Pharmacoproteomics. 2012;3:e119.
49. Luisa BM, et al. Challenges Faced in the Integration of Pharmacogenetics/Genomics into Drug Development. J Pharmacogenomics Pharmacoproteomics. 2012;3:108.
50. Yin J, et al. Pharmacogenetics of Oral Antidiabetic Drugs: Potential Clinical Application. Endocrinol Metabol Syndrome. 2012;S5:003.
51. Shiga T. Persistence of Oral Anticoagulants in Japanese Patients with Atrial Fibrillation: Non-Vitamin K Antagonist Oral Anticoagulant versus Warfarin. Arrhythm Open Access. 2016;1:e102.
52. Lisboa da Silva RMF. Novel Anticoagulants in Non-Valvular Atrial Fibrillation: An Evidence-Based Analysis. Evidence Based Medicine and Practice. 2015;1:1000e101.
53. Pérez-Sánchez H. Virtual Screening for the Discovery of New Anticoagulants. Drug Design. 2013;S1:e001.
54. Bhatia S, et al. Safety and Efficacy of New Oral Anticoagulants in Patients with Atrial Fibrillation: A Literature Review. J Diabetic Complications Med. 2015;1:101.
55. Carnes EB, et al. Role of Novel Oral Anticoagulants in Primary and Secondary Thromboprophylaxis in Cancer. J Hematol Thrombo Dis. 2015;3:222.

56. Lu DY, et al. Plasma Fibrinogen Concentrations in Patients with Solid Tumors and Therapeutic Improvements by Combining Anticoagulants or Fibrinolytical Agents. Adv Pharmacoepidemiol Drug Saf. 2015;4:e133.
57. Min A, et al. Economic Evaluations of Medical Cost Differences: Use of Targeted-Specific Oral Anticoagulants vs. Warfarin among Patients with Nonvalvular Atrial Fibrillation and Venous Thromboembolism in the U.S. J Hematol Thrombo Dis. 2015;3:209.
58. Ragab G and Mattar M. Oral Direct Anticoagulants in Thrombosis Management in Anti-Phospholipid Syndrome: Unanswered Questions. J Hematol Thrombo Dis. 2015;3:208.
59. Yiannakopoulou ECH. Pharmacovigilance for Novel Oral Anticoagulants: Why is It So Crucial? J Pharmacovigilance. 2015;3:e135.
60. Turiel M, et al. Practical Guide to the New Oral Anticoagulants. J Gen Pract. 2015;3:194.
61. Lee A and Rajaratnam R. Tailoring the Novel Anticoagulants to the Stroke Patient – One Size Does Not Fit All Novel Anticoagulants in Stroke. J Neurol Neurophysiol. 2014;5:248.
62. Micco PD, et al. Baseline Analysis on the Outcome of Patients with Deep Vein Thrombosis DVT Before the Global Impact of New Oral Anticoagulants in Italy: Data from RIETE Registry. J Blood Lymph. 2014;4:129.
63. Eggert K, et al. A Prospective, Multicenter, 2-Year Echocardiographic Study on Valvular Heart Disease in Parkinson's Disease Patients Taking Rotigotine and Other non-Ergot Dopamine Agonists. J Alzheimers Dis Parkinsonism. 2016;6:233.
64. Mulatu HA, et al. Prevalence of Rheumatic Heart Disease among Primary School Students in Mid-Eastern Ethiopia. Biol syst Open Access. 2016;5:149.
65. Maramao F, et al. Radiotherapy-Chemotherapy Related Heart Diseases in Surgical Setting. J Clin Exp Cardiolog. 2016;7:444.
66. Kataria V, et al. Radiofrequency Catheter Ablation of Ventricular Tachycardia in Structural Heart Disease: Single Team Experience with Follow-Up upto 5 Years. Arrhythm Open Access. 2016;1:104.
67. Sun T, et al. Invasive Aortic Augmentation Index Could Predict the Adverse Events in Patients without Established Coronary Heart Disease. Angiol. 2016;4:173.
68. Wang N, et al. Management in Patients with Coronary Atherosclerotic Heart Disease Complicated with Chronic Heart Failure: A Community-based Study. Angiol. 2016;4:171.
69. Roever L, et al. Exercise-Based Rehabilitation for Coronary Heart Disease: What does the Evidence Show? J Cardiovasc Dis Diagn. 2016;4:e111.
70. Wu Q, et al. Detection of Copy Number Variants by Next-Generation Sequencing in Fetuses with Congenital Heart Disease. Gynecol Obstet Sunnyvale. 2016;6:351.
71. Ventriglia F, et al. Reliability of Early Fetal Echocardiography for Congenital Heart Disease Detection: A Preliminary Experience and Outcome Analysis of 102 Fetuses to Demonstrate the Value of a Clinical Flow-Chart Designed for At-Risk Pregnancy Management. Pediat Therapeut. 2016;6:270.
72. Kuliev A, et al. Preimplantation Genetic Diagnosis PGD for Heart Disease Determined by Genetic Factors. Arrhythm Open Access. 2015;1:103.
73. Rehman S, et al. Mutation Screening of MEFV and TNF Gene in Pakistani Patients with Rheumatic Heart Disease: A Case Control-Study. J Clin Cell Immunol. 2015;6:382.
74. Hari OS, et al. Awareness and Trends of Blood Cholesterol and Susceptibility to Develop Heart Disease. Adv Genet Eng. 2015;4:138.
75. Wang L, et al. A Combination of Electro-Acupuncture and Aerobic Exercise Improves Cardiovascular Function in Patients with Coronary Heart Disease. J Clin Exp Cardiolog. 2015;6:402.
76. Blue GM and Winlaw DS. Next Generation Sequencing in Congenital Heart Disease: Gene Discovery and Clinical Application. Next Generat Sequenc & Applic. 2015;2:113.
77. Rajajeyakumar M, et al. Importance of Sinus Arrhythmia and Artifact. Clinical Interpretation of Abnormal ECG Patterns in the Absence of Heart Disease. J Bioengineer & Biomedical Sci. 2015;5:157.
78. Mahmood H, et al. Relation of Cholesterol Level to Dietary Fat Intake in Patients of Ischemic Heart Disease. Cardiol Pharmacol. 2015;4:141.
79. Li G, et al. High Serum Concentration of Sulfatide is a Risk Factor for Restenosis in Patients with Coronary Heart Disease after Percutaneous Coronary Intervention. Metabolomics. 2015;5:137.
80. Zhou Y, et al. Clinical Trials Using Cell-based Therapy in Ischemic Heart Diseases - A Decade's Efforts. J Vasc Med Surg. 2015;3:174.
81. Hunter LE and Sharland GK. Maternal Gestational Diabetes and Fetal Congenital Heart Disease: An Observational Study. J Preg Child Health. 2015;2:132.
82. Maduagu ATL, et al. Prevalence of Coronary Heart Diseases Risk Factors in Adults Population Living in Nigeria's Largest Urban City. J Nutr Disorders Ther. 2015;5:153.
83. RN MK. Recognizing Heart Disease as a "Woman's Disease". J Women's Health Care. 2015;4:219.
84. Castro AAM, et al. Clinical Course Development of the Chagas Heart Disease in a Brazilian Patient: A Case Report. J Clin Case Rep. 2014;4:449.

85. Babbs CF. Initiation of Ventricular Fibrillation by a Single Ectopic Beat in Three Dimensional Numerical Models of Ischemic Heart Disease: Abrupt Transition to Chaos. J Clin Exp Cardiolog. 2014;5:346.
86. Dupras C, et al. Influence of Demographic Characteristics of Participants on Consent to Genomic Research into Congenital Heart Disease. J Clinic Res Bioeth. 2014;5:199.
87. Bernstein HS. Future Prospects for Biomarkers in the Management and Development of Novel Therapies for Pediatric Heart Disease. Pediat Therapeut. 2014;4:e126.
88. Frederiksen CA, et al. Remifentanil and Sufentanil Preserve Left Ventricular Systolic and Diastolic Function in Patients with Ischemic Heart Disease-A Randomised Comparative Study. J Anesth Clin Res. 2014;5:437.
89. Souilmi FZ, et al. Presyncope Due to a Complete Atrioventricular Block Revealing a Rheumatic Heart Disease. J Clin Case Rep. 2014;4:386.
90. Avila A, et al. A Randomized Controlled Study Comparing Home-Based Training with Telemonitoring Guidance Versus Center-Based Training in Patients with Coronary Heart Disease: Rationale and Design of the Tele-Rehabilitation in Coronary Heart Disease (TRiCH) Study. J Clin Trials. 2014;4:175.
91. Aziz KMA. Association of Microalbuminuria with Ischemic Heart Disease, Dyslipidemia and Obesity among Diabetic Patients: Experience from 5 Year Follow up Study of 1415 Patients. Bioenergetics. 2014;3:118.
92. Felippe TCG and Santoro DC. Implantation of Adult Stem Cells in Patients with Heart Disease: Clinical Practice Implications for Nurses. J Nurs Care. 2014;3:167.
93. Black SM and Fineman JR. Mitochondrial Dysfunction and Congenital Heart Disease. Pediat Therapeut. 2014;4:199.
94. Berkinbayev S, et al. Apolipoprotein Gene Polymorphisms (APOB, APOC111, APOE) in the Development of Coronary Heart Disease in Ethnic Groups of Kazakhstan. J Genet Syndr Gene Ther. 2014;5:216.
95. Al-Haggar M. SNPs as Co-morbid Factors for Drug Abuse and Ischemic Heart Disease. Gene Technology. 2014;3:107.
96. Bolognesi M and Bolognesi D. Asymptomatic Ischemic Heart Disease in a 45-year-old Male Athlete: A Case Report. J Gen Pract. 2014;2:139.
97. Mormile R. Celiac Disease and Ischemic Heart Disease: What is the Link? J Clin Cell Immunol. 2013;4:173.
98. Virag J. New Twists on an Old Problem: Contemporary Experimental and Clinical Research of Coronary Heart Disease. J Clin Exp Cardiolog. 2013;S6:007.
99. Rao SP. Stents in the Management of Heart Disease in Children. Pediat Therapeut. 2013;3:e120.
100. Guilherme L, et al. Rheumatic Heart Disease: Key Points on Valve Lesions Development. J Clin Exp Cardiolog. 2013;S3:006.