Introduction
Cardiovascular disease (CVD) includes all diseases of the heart and circulation including coronary heart disease, heart failure, congenital heart disease and stroke [Maton, 1993]. Such CVD is a leading cause of death for a large segment of the population historically. It is found with its footprints since 4000 years of human history [Thompson et al., 2013] to Egyptian mummies [Allam et al., 2011] and till now which is likely increasing influenced by modern phenomenon [Hopkins, 2013].

CVD begins with damage to the circulatory system like inner layers of coronary arteries followed by formation of plaque and finally hardening, which narrows the coronary arteries and reduces the flow of oxygen-rich blood to the heart. CVD is also influenced by infection, which was first suggested over one hundred years ago with the finding of embolism from vegetations in 1852.

CVDs are the number one cause of death globally, more people die annually from CVDs than from any other cause. An estimated 17.3 million people died from CVDs in 2008, representing 30% of all global deaths. Over 80% of CVD deaths take place in low and middle-income countries and occur almost equally in men and women [WHO, 2011].

Infective endocarditis (IE) is a kind of CVD. Osler first described the bacterial endocarditis as a mushroom-shaped in a patient aneurysm in 1885. The manifestations of IE have been documented by clinicians over the last several centuries. The normal heart is relatively resistant to infection. Bacteria and fungi do not easily adhere to the endocardial surface, and constant blood flow helps prevent them from settling on endocardial structures. Thus, the IE usually occurs by either a predisposing abnormality of the endocardium or entering of
microorganisms in the bloodstream (bacteremia) [Infective Endocarditis, Merck Manual, 2014].

Periodontal disease turns to be systemic which are silent but deadly. Improper periodontal care relates to cardiovascular disease like IE. The accumulation of epidemiologic, in vitro, clinical and animal evidence suggests that periodontal infection is a contributing risk factor for heart disease. Periodontal pathogens could enter the bloodstream, invade the blood vessel walls and ultimately cause atherosclerosis [Genco et al., 2002; Persson and Persson, 2008].

The symptoms of IE includes: fever, chills, sweating, lack of energy, aching joints and muscles. It also changes to the skin, such as red or purple spots or bumps on the hands, feet, face, chest, mouth, or eyes. Patients suffering from this have trouble in breathing, lose weight for no known reason also have swelling of the feet, legs, or abdomen [Von Reyn et al., 1981; Beynon et al., 2006].

IE has not changed substantially over the past 30 years. Without treatment, IE is usually lethal [Murdoch et al., 2009]. IE is a disease that is continually changing, with new high risk patients, new diagnostic procedures, the involvement of new microorganisms, and new therapeutic methods [Mylonakis and Calderwood, 2001; Beynon et al., 2006]. It is among the most severe infectious diseases, the prevention of which has not decreased its incidence [Thuny et al., 2014]. The rise of multidrug resistant bacteria challenges conventional treatment regimens such as penicillin individually or in combination with gentamicin or aminoglycosides (which includes high risks) [Elliott et al., 2004; Beynon et al., 2006; Werdan et al., 2014]. VGS have emerged resistance to antibiotics, which is a cause of persistence of infective endocarditis [Pancharoen et al., 1999; Knoll et al., 2007]. Because of the paucity of novel drug targets for IE, it has been difficult to define optimal treatment. Thus,
recommendations for therapy have largely been made on the basis of consensus opinion.

Reliable technologies for addressing target identification are the foundation of successful drug development. There exists various traditional in vitro, in situ or in vivo approaches to identify new drug targets which are based upon technologies like microarrays (nucleic acid and protein), antisense technology (antisense oligonucleotides and RNA interference), haplotype analysis, chemical-driven random mutagenesis, chemical genomics and proteomics, activity-based protein profiling, etc. [Wang et al., 2004; Sakamoto et al., 2012]. With the real threat of emerging drug resistance and continued dependence on the limited availability of drug targets, there is a need for identification of new targets, normally proteins (or DNA/RNA), whose modulation might inhibit or reverse disease progression. Though new drug targets are essential, their identification is hampered due to requirement of huge laboratory investments, time consuming, laborious and painstaking.

On the contrary, in silico based methodologies provide alternative approaches and have the potential to cut costs and time in identifying candidate drug targets and drugs. Bioinformatics has been used for understanding microbes in many ways: computationally analyzing the wet-lab data, genome sequencing, identification of protein coding segments [Azad et al., 2004], and genome comparison to identify the gene function [Altschul et al., 1990; Mount, 2004], the development of genomic and proteomics databases [Bairoch, 1991; Bateman et al., 2004]. Later, this field has also been used to understand higher level functions such as, automated reconstruction and comparison of metabolic pathways [Ogata et al., 1998; Bansal and Woolverton, 2003], study of protein-protein and protein-DNA interactions to understand regulatory pathways [Aloy and Russell, 2004; Gelfand et al., 2000], modeling 2D and 3D structure of proteins [Baker and Sali, 2001; Pawlowski et al., 2001], and simulating the docking of 3D models of proteins with drugs [Halperin et al., 2002].
Such bioinformatic approaches are primarily based on the use of genome, metabolome and structure data from various databases that are publically available. There are several recent developments with a combined bioinformatic approach for discovering new candidate drug targets. Bioinformatic approach can develop appropriate subtractive filters that can be used to identify potentially essential genes of infective agents and generate a pool of pre-validated candidate targets. The contribution of bioinformatics made possible the mapping of the entire human genome [Venter et al., 2001; Lander et al., 2001] and genomes of many other pathogens in just over a decade. Comparative sequence analysis can be used to eliminate genes with possible human orthologs. Combined with other measures of ‘druggability’, prioritization steps and algorithms can be used to produce targets for experimental validation. These predictions along with current efforts to determine gene and protein functions, have improved our ability to understand the root causes of human diseases.

Among the genus Streptococcus, VGS are predominantly isolated for causing IE [Elshibly et al., 2014]. Streptococcus mitis group organisms are resistant to more antimicrobial agents than the other VGS species [Doern and Burnham; 2010]. Availability of complete genome of S. gordonii [Vickerman et al., 2007], which also belongs to VGS and is a primary colonizer [Xu et al., 2014], provides an opportunity to identify novel drug targets.

It is very interesting to note that the bioinformatic study on IE around the globe is very recent and no much information is available on S. gordonii. Based on these observations the present study was planned by drawing the following objectives.

1. To carryout Synteny based classification of homologues and non-homologues protein coding genes among S. gordonii and other strains of VGS causing IE
2. To annotate all the non-homologues protein coding genes and identify non-host proteins of *S. gordonii*.
3. To conduct pathway annotation and re-annotation of all non-homologues and non-host proteins of *S. gordonii*.
4. To perform Druggability analysis of non-host protein coding genes of *S. gordonii*.
5. To identify the unique hub protein and it's *in silico* molecular virtual screening.

The approach was planned and implemented, leading to reduction of biological information from genome scale to identification of a specific drug target. Several subtractive filters were applied starting with the use of *S. gordonii* as reference genome compared with the strains causing IE. Then continuing with annotation of unique essential genes to identify proteins exclusively present in the pathogen by deducing the homology with human host. Followed by which subtraction was performed at metabolome level. Protein-protein interaction analysis within the subject strain and leading to an identification of specific drug target. Thus, ultimately leading to the identification of a virtual candidate drug molecule against IE causing pathogen.