Practicing Behaviour of Indian Physicians for the Management of Dyslipidemia versus 2016 ESC/EAS Guidelines for the Management of Dyslipidemia: ACCORDANCE Study

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**ABSTRACT**

**Background:** In 2016, European Society of Cardiology (ESC)/ European Atherosclerosis Society (EAS) released guideline for the management of dyslipidemia. On this background, a survey was conducted to assess differential practicing behaviour of Indian physicians and to assess the level of their accordance with 2016 ESC/EAS guidelines. **Methods:** Survey questionnaire consisting of 10 questions pertaining to management of dyslipidaemia in real-world clinical settings was prepared and validated in a small group of physicians. This was then administered to physicians and cardiologists who attended 68th Annual Conference of Cardiological Society of India, Kochi 2016. **Results:** Responses of 437 physicians were received. For lipid analysis, most of the physicians (68.65%) preferred a fasting blood sample. For assessing the CV risk in an individual, 62.47% physicians preferred LDL cholesterol (LDL-C). Most of the physicians (75.74%) practice the recommended LDL-C goal of ≤70 mg/dL or reducing it to 50% if the baseline LDL-C is between 70-135 mg/dL in very high risk patients. In cases where lipid goals were not achieved, 39.59% physicians preferred to up-titrate the statin dose till the highest tolerable dose, while 32.27% physicians preferred combination of statin with ezetimibe. **Conclusion:** Our survey findings suggest that there appears to be consensus amongst Indian practitioners for following most of the recommendations of ESC for risk assessment, treatment goals, choice of therapy and treatment approaches. Assessment of lipids in fasting state and target LDL-C in high CV risk patients though differ slightly.

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INTRODUCTION:
Cardiovascular disease (CVD) is considered to be a leading cause of death globally. Even in India there is a drastic increase in the CVD prevalence in last 20 years. Almost 24.8% of all deaths in India are attributable to CVD.[1] It has been predicted that by the year 2020, there will be an increase in the prevalence of global CVD by almost 75% and almost all of this increase will occur in developing countries.[2] By 2030, it has been estimated that almost 23.6 million people will die from CVDs, mainly from heart disease and stroke. These will be the single leading causes of death.[3] CVD has attained epidemic proportions in India as well. According to the World Health Report 2002, CVDs will be the largest cause of death and disability in India by 2020. According to the World Health Report of 2002, deaths due to CHD in India rose from 1.17 million in 1991 to 1.59 million in 2000 and 2.03 million in 2010.[4] Atherosclerosis is the major cause of coronary artery disease and dyslipidemia is one of the most important risk factors for atherosclerosis.[5] One-third of ischemic heart diseases in the world are due to hypercholesterolemia and is responsible for 2.6 million (4.5%) deaths in the world.[6] There is a huge burden of atherosclerotic cardiovascular disease (ASCVD) in India which is a cause of concern. Indians usually suffer from ASCVD at an early age, have a more severe form of the disease and have poorer outcome as compared to the western populations.[7]

In 2016, European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) released guideline for the management of dyslipidemia. However, considering the obvious lifestyle, genetic, socioeconomic, and cultural differences along with differences in the characterization of dyslipidemia in Indians as compared to European population, the unmet need for developing India-specific dyslipidemia guidelines accommodating these differences was very much evident. Two such recent attempts were consensus statement on management of dyslipidemia in Indian subjects by Chandra KS et al published in 2014 and expert consensus statement by Lipid Association of India in 2016.[7,8] However, there is no uniformly accepted guidelines for managing dyslipidemia in Indian patients. Therefore, on the background of recently published 2016 ESC/EAS Guidelines for the Management of Dyslipidemias, this survey was done to assess differential practicing behaviour of Indian physicians and to assess their level of accordance with these guidelines. This article highlights the real-world clinical practice in India for the management of dyslipidemia in comparison to the 2016 ESC/EAS Guidelines.

MATERIALS AND METHODS:
This was a prospective, cross sectional, questionnaire-based survey of physicians and cardiologists managing the patients of dyslipidemia across different geographic areas in India. A survey questionnaire consisting of 10 questions related to the management of dyslipidemia in real-world clinical settings on the background of 2016 ESC/EAS dyslipidemia guidelines was prepared. The questionnaire comprised of 10 questions which focused on taking insights on the management of dyslipidemia by Indian physicians and to further compare the same with the 2016 ESC/EAS dyslipidemia guidelines. The questionnaire was later validated in a small group of physicians and then administered to the physicians and cardiologists who attended the 68th Annual Conference of Cardiological Society of India (CSICON), December 2016 at Kochi, Kerala. Delegates attending CSICON 2016 were approached for seeking their prescribing behaviors for managing dyslipidemia patients, explained the objective of doing this survey and those willing to provide their views were given the questionnaire. No remuneration was given to the participants for filling these survey questionnaire. Total 523 physicians and cardiologists completed the survey. The completed questionnaire were collected and analyzed. Physicians’ and cardiologists’ responses from the questionnaire were entered in a Microsoft excel sheet and descriptives were calculated as frequencies.

RESULTS:
Out of 523 questionnaire, 437 questionnaire were completely filled and were eligible for further analysis. Out of 437 responders, majority of the
physicians (68.65%) preferred a fasting blood sample over non-fasting sample for lipid analysis in their clinical practice. Only 7.8% of physicians preferred non-fasting sample for lipid analysis, whereas 14.9% physicians were of the opinion that lipid analysis is done in their clinical practice irrespective of fasting or non-fasting states of patients.

For analyzing the CV risk in an individual, majority of the physicians (62.47%) preferred LDL-C values over non-HDL-C values (27.92%). LDL-C was also preferred as the primary treatment target by 71.85% physicians in their clinical practice, whereas, 19.68% physicians opted for non-HDL-C as the primary treatment target.

In very high CV risk patients (post cardiovascular event/ type 2 diabetes mellitus with end organ damage), most of the physicians (75.74%) practice the recommended LDL-C goal of <70 mg/dL or reducing it to 50% if the baseline LDL-C is between 70-135 mg/dL (Figure 1).

**Figure 1: Treatment goals for LDL-C followed in clinical practice in patients at very high CV risk**

In patients at high CV risk (TC > 310 mg/dL, BP ≥ 180/100 mmHg, T2DM), most of the physicians (51%) preferred reducing LDL-C to <70 mg/dL, whereas, only 19.4% physicians preferred reducing LDL-C to <100 mg/dL (figure 2).

LDL-C – low density lipoprotein cholesterol; the term “baseline LDL-C” refers to the level in a subject not taking any lipid lowering medication.

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**Figure 2: Treatment goals for LDL-C followed in clinical practice in patients at high CV risk**

Majority of the physicians (78.72%) agreed upon non-HDL-C to be the secondary treatment target in prevention of CVDs, whereas TG, TC and HDL-C were considered as the secondary treatment targets by 6.18%, 3.89 % and 3.43% physicians respectively in their clinical practice. In cases where lipid goals were not achieved with statin, 39.59% physicians preferred to up-titrate the statin dose till the highest tolerable dose rather than replacing the statin with another statin. Whereas, 32.27% physicians preferred to start combination of statin with ezetimibe (Figure 3).

**Figure 3: Physicians’ preferred treatment choices when recommended lipid goals not achieved with statin**

Majority of the physicians (65.22%) recommended a lipid analysis to be done after 3 months of initiating the treatment. However 19% physicians suggested a lipid analysis to be done after 1 month itself. In patients with hypertriglyceridemia [Triglycerides (TG) > 200 mg/dl], 36.16% preferred a combination of statin and fibrate along with lifestyle modifications in their patients, while 27.69% physicians preferred...
only statin therapy with lifestyle modifications. Treatment with fibrate with lifestyle modifications was preferred by only 12.59% physicians in these patients. As shown in figure 4, in patients on statin therapy who complains of myalgia and has a creatine kinase (CK) < 4 times upper limit of normal (4X ULN), most of the physicians (56.29%) preferred to discontinue statin for 6 weeks and then re-challenge with the same statin at low dose rather than re-challenging with the same dose or replacing the statin. Only 3.66% physicians were of the opinion of discontinuing statin completely.

**DISCUSSION:**
In this survey, majority of the physicians preferred a fasting blood sample over non-fasting sample for lipid analysis in their clinical practice and have recommended lipid analysis to be done after 3 months of initiating the treatment. LDL-C was also preferred as the primary treatment target by most of the (71.85%) physicians in their clinical practice and majority of them practice the recommended LDL-C goal of <70 mg/dL in both very high and high CV risk patient groups. In patients who were not able to achieve the recommended LDL-C goal while on statin, majority of physicians (39.59%) preferred to increase the dose of statin to highest tolerable dose rather than substituting ongoing statin with another statin or adding additional hypolipidemic agents to statin therapy. Initiating treatment with combination of statin and fibrate along with lifestyle modification formed the best treatment strategy adopted by most of the physicians for treating hypertriglyceridemia. Dyslipidemia is a known modifiable risk factor for CVD and in India its burden is substantial. Evidence-based guidelines are published internationally from time to time to provide new evidence-based recommendations in dyslipidemia management. The Task Force for the Management of Dyslipidemias of the ESC/EAS have drafted the guidelines for management of dyslipidemias in 2016. However, there are various lifestyle, genetic, socioeconomic and cultural differences between Indians and their European counterparts. There are unique challenges in managing dyslipidemia in Indian patients not only because of high burden of dyslipidemia but also the pattern of dyslipidemia is different from the western
Therefore, different treatment approaches for optimal management of dyslipidemia are required. Though some consensus statements on management of dyslipidemia in Indians were published in year 2014 and 2016 to address the lipid management issues in Indian patients, there are no uniformly accepted Indian guidelines for managing dyslipidemia. Therefore, following the recommendations of recently published 2016 ESC/EAS guidelines by Indian practitioner appears to be justifiable. With this survey, we tried to find out extent of inclination of Indian practitioners towards 2016 ESC/EAS guidelines in managing their patients and areas of adaptation to meet needs of Indian patients. This survey is expected to give an insight on prescribing behaviors of Indian physicians in managing patients of dyslipidemia vis-a-vis 2016 ESC/EAS guidelines.

Conventionally, lipid analysis is done in fasting state in most parts of the world. However available data suggest that fasting and non-fasting sampling give similar results for TC, LDL-C and HDL-C. For risk estimation, non-fasting has a prediction strength similar to fasting, and non-fasting lipid levels can be used in screening and in general risk estimation. TG is the only exception for this; TGs are affected by food, resulting in approximately 27 mg/dL higher plasma level, depending on the composition and the time frame of the last meal and therefore for follow-up of patients with hypertriglyceridemia, fasting samples are recommended. Present survey findings are in contrast to ESC recommendation; most of the survey physicians preferred a fasting blood sample over non-fasting sample for lipid analysis in their clinical practice, thereby emphasizing the the conventional way of lipid analysis. ESC has also recommended that lipid analysis should be repeated after 1-3 months of starting treatment and then annually once the patient has reached the target or optimum lipid levels. Survey findings are in accordance with ESC recommendations for repeat post-treatment lipid analysis.

Assessment of total CAD or CV risk has been unanimously recommended by all current guidelines on the prevention of CVD in clinical practice. Measures for prevention of CVD should be adopted to individual patient’s total CV risk. Out of various risk assessment systems, 2016 ESC/EAS guidelines have recommended use of Systemic Coronary Risk Estimation (SCORE) to estimate total CV risk. The SCORE system estimates the 10-year cumulative risk of a first fatal atherosclerotic event. The intervention strategies recommended by ESC are based on total CV risk (SCORE) and LDL-C levels. Different intervention strategies are recommended for various levels of LDL-C. LDL-C is recommended to be used as the primary lipid analysis for screening, risk estimation, diagnosis and management (Class IC recommendations). Furthermore, LDL-C is recommended as the primary target for treatment (Class IA recommendation), whereas non-HDL-C should be considered as a secondary treatment target and TC should be considered as a treatment target if other analyses are not available.

Present survey findings suggest that majority of physicians considered LDL-C as the primary treatment target (71.85%) and non-HDL-C as a secondary treatment target (78.72%) in their patients which is in accordance with 2016 ESC/EAS guidelines. However, small proportion of survey physicians (19.68%) preferred non-HDL-C as as the primary treatment target which is in contrast to the ESC recommendations. Both ESC/EAS guidelines for the management of dyslipidemias and the American Heart Association/American College of Cardiology (AHA/ACC) guidelines on the treatment of blood cholesterol to reduce atherosclerotic CV risk in adults strongly emphasized on reducing LDL-C to prevent CVD. Thus, survey findings are well supported by various dyslipidemia guidelines including AHA/ACC. Based on total CV risk, patients can be grouped as at very high, high, moderate or low CV risk. Very high CV risk category includes patients with documented CVD. Such as previous myocardial infarction (MI), acute coronary syndrome (ACS), coronary revascularisation (percutaneous coronary intervention (PCI), coronary artery bypass graft surgery (CABG)) and other arterial revascularization procedures, stroke, transient ischaemic attack (TIA), and peripheral arterial disease (PAD); DM with target organ damage such as proteinuria or with a major risk factor such as smoking, hypertension or dyslipidaemia; severe CKD.
(GFR <30 mL/min/1.73 m²); a calculated SCORE ≥10% for 10-year risk of fatal CVD. The high risk cases include TC >310 mg/dL or blood pressure ≥ 180/110 mmHg, diabetes mellitus, moderate CKD (GFR 30-59 mL/min/1.73m²) and a calculated SCORE ≥5% and <10% for 10-year risk of fatal CVD.[9]

Based on these CV risk groups, treatment strategies vary. The lipid goals are part of a comprehensive CV risk reduction strategy. In very high CV risk patients, ESC/EAS 2016 recommends LDL-C goal of <70 mg/dL or a reduction of at least 50% if the baseline LDL-C is between 70 to 135 mg/dL.[9] The survey findings suggest that most of the survey physicians follow this recommended LDL-C goals in very high risk patients. In patients at high CV risk, ESC recommends LDL-C goal of <100 mg/dL or a reduction of at least 50% if the baseline LDL-C is between 100 to 200 mg/dL.[9] However, this survey suggests that in patients at high CV risk, most of the physicians adopt much lower LDL-C target than the recommended goal in their practice. Nearly half of the survey physicians preferred reducing LDL-C to <70 mg/dL, whereas, only 19.4% physicians preferred reducing LDL-C to <100 mg/dL. This suggests that Indian practitioners follow the same LDL-C goals in both very high and high CV risk patients.

ESC/EAS 2016 mentions statins to be the mainstay in the management of dyslipidemia. Statins are recommended at highest recommended or highest tolerated dose to achieve the lipid targets (Class IA). If the goal is not achieved then a cholesterol absorption inhibitor (Class IIA) or a bile acid sequestrant (Class IIB) should be added to statin therapy.[9] As per our survey, the Indian physicians preferred to up titrate the statin dose and/or would prefer a statin plus an ezetimibe combination therapy. Though there are some conflicts on the role of TG as a risk factor for CVD, recent collaborative analysis of 101 studies by Triglyceride Coronary Disease Genetics Consortium and Emerging Risk Factors Collaboration favors the role of TG in causation of CVD.[15] 2016 ESC/EAS guidelines recommended that in patient at high CV risk with hypertriglyceridemia, statin treatment may be considered as first drug of choice for reducing CVD risk (Class IIbB) and if TG remains >200 mg/dL despite statin therapy, fenofibrate may be considered in combination with statin (Class IIb C).[9] Survey findings suggest that for management of hypertriglyceridemia (TG > 200 mg/dL), majority of Indian physicians (36.16%) preferred to start statin plus fibrate combination along with lifestyle modifications, while 27.69% physicians preferred only statin along with lifestyle modifications. To a large extent, our survey findings seems to be in accordance with the current European guidelines. ESC recommends CK measurement at the start of statin therapy to identify the limited number of patients where treatment is contraindicated and thereafter only if patients develop myalgia. Post treatment with statin if patient complains of myalgia and if CK is elevated but less than 4 times the ULN, then most of the Indian physicians (56.29%) preferred to discontinue statin for 6 weeks and rechallenge with the same statin at a lower dose rather than replacing or discontinuing the statin completely. 2016 ESC/EAS guidelines, however recommends systematic approach; if patient is symptomatic but muscle symptoms improve after 2-4 weeks of washout of statin, consider second statin at usual or starting dose and is to be continued till maximum tolerable dose if there are no symptoms with second statin and if symptoms re-occur consider third potent low dose statin; if symptoms persists after 2-4 weeks of statin discontinuation, statin rechallenge to be done.[9] The survey findings are in accordance with ESC recommendations for elevated CK on statin.

LIMITATIONS OF STUDY:
Our survey has certain limitations. Firstly, as it is a questionnaire-based survey of physicians for seeking their views and experiences in managing dyslipidemia in real-world clinical settings, actual prescriptions were not traced to analyze the prescribing patterns. Secondly, responses were collected from physicians and cardiologists attending CSI 2016, which is a representation of a group of physicians and not a survey across the country. Lastly, this survey covered only some of the important aspects of management of dyslipidemia and the questions addressed were not exclusive; management of dyslipidemia in different clinical settings such as in special population and in
the presence of co-morbidities and other aspects of 2016 ESC/EAS guidelines were not explored. The study also did not include the impact of lipid triad classical of Indian dyslipidemia viz. low HDL-C, high TG and high or normal LDL-C.

CONCLUSION:
Significant lifestyle, genetic, socioeconomic, and cultural differences in Indians versus European population demand different treatment approaches for optimal management of dyslipidemia and CVD. Contrary to this thought, our survey findings suggest that there appears to be consensus to a great extent amongst Indian practitioners for following most of the recommendations of 2016 ESC/EAS for risk assessment, treatment goals, choice of therapy and treatment approaches in dyslipidemia. Assessment of lipids in fasting state and target LDL-C in high CV risk patients though differ slightly. Further elaborative study covering practicing physicians and cardiologists across whole country is warranted to have more data and knowledge on the behavioural pattern.

REFERENCES
15. Triglyceride Coronary Disease Genetics, Consortium and Emerging Risk Factors Collaboration, Sarwar N, Sandhu MS, Ricketts SL, Butterworth AS, Di Angelantonio E,

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