CHARACTERISTICS OF LIPID PROFILES ANALYSIS IN A PUBLIC HOSPITAL PRACTICE IN NORTHEASTERN NIGERIA.

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Background: Northeastern Nigeria is peculiar concerning lipid metabolism due to sizeable multiethnic population, common practice of consanguineous marriages, and high intake of animal fats (mai shanu). Therefore, rational requests and interpretation of results in the diagnosis of dyslipidaemia is very important in this part of the country. In spite of these seemingly obvious predisposing factors of dyslipidaemia, little, if any, report at all on hyperlipidaemia in this region has been documented.

Objectives: This retrospective study intends to shed light on the characteristics of requests for lipid analysis, the subjects with hypercholesterolaemia and their lipid profile results when available.

Methods: The clinical records of 328 (29.5%) out of 1110 patient requests received in the University of Maiduguri Teaching Hospital Laboratory with hypercholesterolaemia over a period of three years (1998-2000) were retrieved and analyzed.

Results: There was a slight male preponderance 179(54.6%) over females 149(45.4%) with a ratio of 1.2:1. Hypercholesterolaemia in particular was poorly investigated as the primary cause was not sought in 40(12.2%) cases, 24(7.3%) discovered on routine checkup were not investigated further, and only 19(5.8%) of 176 cases with moderate to severe levels had lipid profile, of which 4(1.2%) alone had HDL-Cholesterol done together with total cholesterol at first request. Hypercholesterolaemia in this environment was most commonly associated with cardiovascular diseases and diabetes mellitus with or without hypertension. Factors such as alcohol intake, cigarette smoking and thiazide diuretic use were not significant causes of hypercholesterolaemia.

Conclusion: Documentation/requests for lipid investigations were incomplete. The need for estimating both total cholesterol and HDL-Cholesterol on first request and their ratio determined alongside Body Mass Index (BMI) is emphasized as a standard routine especially in hypertension with or without diabetes mellitus, cerebrovascular diseases/stroke and obesity.

Key wards: *Requests, Lipid analysis, Public Hospital practice, Northeastern Nigeria.*

Introduction

Disorders of lipoprotein metabolism can result in premature arteriosclerosis and other metabolic consequences[1-6]. Whereas evidence exists that death from coronary artery disease (CAD) is declining in the developed world[7], the epidemic is gaining momentum in the developing countries.[7-9]

In addition to promoting systemic atherosclerosis, dyslipidaemia may also contribute to the development of glomerulosclerosis and therefore chronic renal failure[4]. Furthermore, Islet B-cell dysfunction caused by lipotoxicity may result in perturbed insulin secretory capacity and result in hyperglycaemia, which also leads to hyperlipidaemia-vicious circle.[5,6]

As in most clinical settings, it is important to establish a diagnosis of hyperlipidaemia and judiciously institute treatment. It is of even greater importance to know whose lipid and lipoproteins should be measured since accurate management of disease usually involves the rational use of laboratory investigations[10]. It is not enough to order investigations simply because they are routine. Considerations of cost in human, material and technical terms must impose a moratorium on test requests. Rational test requests and interpretation of results in the diagnosis of dyslipidaemia is therefore very important[11], in the developing world. This becomes pertinent in this part of the country with a sizeable multiethnic population, as wide variations in plasma lipids are frequently encountered in different ethnic groups since genetic and environmental factors seem to modulate the levels of plasma lipids[12], intake of animal fats is high even among the poor communities and many tribes in the region practice consanguineous marriage.

In spite of these seemingly obvious predisposing factors, little, if any, report at all on hyperlipidaemia in northeastern Nigeria has been documented.

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This retrospective analysis therefore aimed at highlighting the characteristics of requests for lipid analysis, causes of hypercholesterolaemia, bringing to fore the significance of proper request, sample collection, result interpretations as well as awareness on this preventable cardiovascular risk factor.

Materials and Methods

Subjects.

This was a hospital based review where data was retrieved from Chemical Pathology Laboratory day sheets and Medical Records in University of Maiduguri Teaching Hospital of patients seen over a period of 3 years (January 1998-December 2000). The study only analysed results, which showed hypercholesterolaemia, a critical clinical decision point, to reflect on the general characteristics of not only requests but a decision of handling an abnormal lipid result as less attention might be given to normal ones.

During the study period, 1110 requests for lipid analysis were made however, only 328(29.5%) results showed hypercholesterolaemia (defined as serum total cholesterol greater than 5.5mmol/L according to the reference value of the study laboratory) results formed the result subjects analysed in this study.

Basic demographic data, weight and height for Body Mass Index (BMI) calculation, primary diagnosis and urea, creatinine and uric acid to rule out renal causes of hypercholesterolaemia were extracted from the case notes. The lipid profile (Total Cholesterol, Low-density lipoprotein cholesterol, High-density lipoprotein and Triglycerides) of each patient when available was recorded.

In our facility, total cholesterol and triglycerides are analyzed by the enzymatic endpoint method[13,14] and the interday coefficients of variation are 5.1% and 7.2%, respectively. High-density lipoprotein (HDL)-cholesterol is determined by precipitation method using phosphatungestic acid in the presence of magnesium ions [15], with an interday coefficient of variation of 7.1% while Low-density lipoprotein (LDL)-cholesterol is calculated using the Friedewald equation[16].

All the coefficients of variation are within the acceptable limits of analytical variations of lipid and lipoprotein measurements [17].

No diagnosis was indicated where the diagnosis could not be found in both the day sheets and the casenote.

Results.

Majority of the study subjects were adults 76.5%(251) and only 4.3%(14) paediatric, however, the ages of 63(19.2%) were not indicated. There was male preponderance of 179(54.6%) compared to 149(45.4%) females, with male: female ratio of 1.2:1.

Out of the 328-hypercholesterolaemic subjects, 43.9% were between 30 and 50 years, 6.1% of subjects below 20 years, 7.9% above 61 years. Females were greater in number in third and fourth decades while males dominated the sixth and seventh.

Table 1 shows distribution of hypercholesterolaemia by degree of severity where 46.3% had mild, 36.3% moderate and 17.4% severe elevation. Clinically significant hypercholesterolaemia (moderate to severe) accounted for over half of subjects (53.7%). However, out of 328 patients with hypercholesterolaemia and the 53.7% that deserved lipid profile, only 19(5.8%) had complete lipid evaluation with a dismal 4 (1.2%) doing HDL-cholesterol together with total cholesterol on first request.

Table 3 shows the association of hypercholesterolaemia with diseases/diagnosis in this hospital. Ninety-eight (29.9%) of the hypercholesterolaemic results were associated with cardiovascular diseases, 60(18.3%) with diabetes mellitus with or without hypertension. Thus these two clinical conditions accounted for 158(48.2%) of the diagnosis/diseases associated with hypercholesterolaemia in this environment. Routine/medical checkup was the basis in 24 (7.3%), followed by chronic renal disease 16(4.9%), liver disease 11(3.4%), and obesity 11(3.4%) .A diagnosis was missing in 40 (12.2%) cases.

Only 92 (27.9%) of the patients were weighed and none had height measurement, therefore, the BMI could not be calculated to appropriately diagnose and classify obesity.

Alcohol consumption, cigarette and thiazide diuretic use were noted in only 8 (2.4%), 7(2.1%) and 15 (4.6%) of subjects, respectively.

Irrespective of cause, hyperuricaemia was seen in 68(20.7%) of cases, 5 of which were in hyperlipidaemias associated with renal diseases.

Table 1

Distribution of total cholesterol by degree of hypercholesterolaemia.

Degree,	mmol/L (mg/dl)	Frequency	%
Mild,	5.5-6.2 (215-239)	152	46.3
Moderate,	6.2-7.2 (240-270)	119	36.3
Severe,	>7.2 (270)	57	17.4
Total		328	100.0.

Discussions.

Overall, there was a male preponderance with a ratio of 1.2:1 however females were greater in number in the third and fourth decades. Males only dominated in the sixth and seventh decades. This might indicate an earlier presentation in females possibly due to pregnancy associated hypertension or deranged glucose metabolism. It may also be explained by high intake of animal fats especially that

from cows milk (mayin sanu) among females in this environment. Could it also be due to familial hyperalphalipoproteinaemia?

The younger age at presentation in both sexes[18, 19] where 43.9% occurred in 30-50 years of age may reflect the prevalence of hypertension and diabetes occurring at an earlier age in this environment as causes of hypercholesterolaemia. It also underscores the need to request lipid analysis earlier in this environment.

Children constituted only 4.3% of subjects indicating that lipid estimation was done less frequently in this group in our environment compared to the developed world[20]. Consanguineous marriages are common among the major tribes in this region raising the probability of familial hypercholesterolaemia, which manifests early in life. Lipid estimation in such children and adolescents as a method of detection and primary prevention as recommended by the National Cholesterol Education Program (NCEP) and American Academy of Paediatrics' [20] is preferred to the subsequent management of overt cardiovascular complications.

Hypercholesterolaemia when present was not properly investigated. This is evidenced by a diagnosis missing from the charts in 40(12.2%) cases, 24(7.3%) subjects for routine/medical checkup left without further investigations to determine the aetiology, out of the 328 cases only 19(5.8%) did lipid profile compared to the 53.7% who needed it, and only 4(1.2%) did HDL-cholesterol together with the total cholesterol. Also only 92(27.9%) of the patients were weighed and none had height measurement hence it was not possible to calculate the BMI for any patient despite obesity ranking fifth among the diagnoses associated with hypercholesterolaemia in the study. Obesity here was diagnosed based on weight alone. Ogunbiyi, *et al*, emphasized [21] that BMI is relatively a good predictor of body fat level by providing good within-population estimation of body fat as compared to weight alone. Not all these setbacks allowed us to properly classify the types of dyslipidaemia in this environment.

The degree of hypercholesterolaemia indicated in Table 1 shows that more than half (53.7%) of subjects with moderate to severe hypercholesterolaemia needed lipid profiles[17-19] however, only 19(5.8%) had the investigation as against 176(53.7%) that needed it [18,19,22]. Only 4(1.2%) of the patients did HDL-cholesterol at the initial requests of serum cholesterol estimations. This grossly falls short of the recent NCEP (ATP11) guidelines which recommend the measurement of HDL-cholesterol as well as total cholesterol at the initial screening stage [17,22]. Total Cholesterol to HDL-cholesterol ratio is more informative than total cholesterol alone, and this will also help in deciding who should do lipid profile[17,22]. The ratio which also helps in ruling-out the fortunate hyperlipidaemia (hyperalphalipoproteinaemia), where HDL-cholesterol levels may be as high as or greater than 1.8mmol/L is very pertinent in middle aged females with hypercholesterolaemia where their LDL-cholesterol is usually normal. In our subjects male to female ratio is a unit in patients under 50 years contrary to expectations when it is expected to occur in those over 50 when the prospective effects of oestrogen would have been removed in the females. Further studies are recommended to find out the effect of hyperalphacholesterolaemia on causes of hypercholesterolaemia due to the practice of consanguineous marriages in this environment.

Cardiovascular diseases (29.9%), diabetes mellitus with or without (18.2%) hypertension constituted about half (48.2%) of the diseases associated with hypercholesterolaemia, indicating a rather narrow spectrum of diseases associated with hypercholesterolaemia in this study excluding conditions such as familial and metabolic causes[17,23]. There probably needs to be increased awareness on the part of requesting physicians in this phenomenon.

The contributions by confounding factors for dyslipidaemia were not significant in our subjects as only 8(2.4%) out of the 328 patients took alcohol, 7(2.1%) smoked cigarettes and 15(4.6%) were on thiazide diuretics (bendrofluorothiazide) which formed only 12.4% of those who had hypertension as their primary diagnosis and/or had hypertension in addition to their primary disease.

There was associated hyperuricaemia in 68(20.7%) cases, which was not limited to subjects with renal diseases. This is not surprising since the first 5 diseases associated with hypercholesterolaemia in this study are frequently associated with hyperuricaemia. However, a study is recommended to determine the effect of hyperchlolesterolaemia on uric acid metabolism in this environment.

The accurate diagnosis and management of diseases usually involves the judicious use of laboratory investigations. It is not enough to order for an investigation and call it routine without considering the cost especially in a resource-limited setting like ours. Out of the 1110 requests for total cholesterol less than one third (29.5%) revealed hypercholesterolaemia. In choosing types of laboratory investigations in patient's management, many factors come into play. In this case, if other cardiovascular risk factors [19,20] were considered before requesting for cholesterol estimation, the percentage of requests in those with normal serum cholesterol would have been reduced and the costs saved. Similarly laboratory investigations are usually requested to rule in/out a disease condition. In case of lipid and lipoprotein profile, dyslipidaemia is a critical clinical decision point than a normal result. The decision of the study to analysed the results that were hypercholesterolaemic did not only reflect the characteristics of lipid requests but also the critical clinical decision limit by the requesting physician in managing such

types of requests. Requesting for total cholesterol alone limited the requesting physician the benefit of interpreting the results since usually the predominant small, dense LDL particles, which are more susceptible to oxidation, and the decreased HDL-C found in diabetes mellitus patients are not typically associated with marked increased in plasma total cholesterol and LDL concentrations [24,25].

For accurate results patient preparation is essential before sampling for lipid analysis [19,20]. Fasting for 8-12 hrs, avoidance of alcohol on the evening before sampling, need to be on habitual weight-maintaining diet for at least 2-3 weeks, and discontinuation of drugs that affect lipid metabolism for at least 3 weeks. There is need also to defer analysis for 2-3 weeks after minor and 3 months after a major illness, surgery or trauma, and the patient resting for at least 5 minutes before sampling are prerequisites. Ideally, a sample is collected in EDTA bottles on ice [26]. However, this may not be practicable in the developing countries and hence samples should either be analysed the same day or be frozen immediately.

In conclusion, test strategies and interpretation of results play an important role in management of dyslipidaemias. Consideration in costs in human, materials and technical terms must impose a moratorium on test requests.

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