Unanticipated Lipid Profiles in Victims of Sudden Unexpected Death: Low Low-density Lipoprotein Cholesterol and an Elevated Triglyceride to High-Density Lipoprotein Cholesterol Ratio

Nisha Hosadurg, MBBS[1]; Brittany Bogle PhD, MPH[2]; Golsa Joodi MD, MPH[1]; Murrium I. Sadaf, MD[1]; Philip M. Mendys, PharmD[3]; Ross J. Simpson, Jr. MD, PhD[1]

UNC SCHOOL OF MEDICINE

[1]Division of Cardiology, University of North Carolina (UNC) School of Medicine; [2]Department of Epidemiology, UNC Gillings School of Public Health; [3]UNC Eshelman School of Pharmacy University of North Carolina, Chapel Hill, NC

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Introduction

- Although low-density lipoprotein cholesterol (LDL-C) is a proven cardiovascular risk factor, substantive data on LDL-C levels in victims of sudden cardiac or sudden unexpected death is lacking.
- Several post-mortem studies have demonstrated higher concentrations of remnant-like lipoprotein particles (RLP) in sudden cardiac death victims.
- The triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL) is reflective of serum RLP levels, but has not been reported in victims of sudden death.

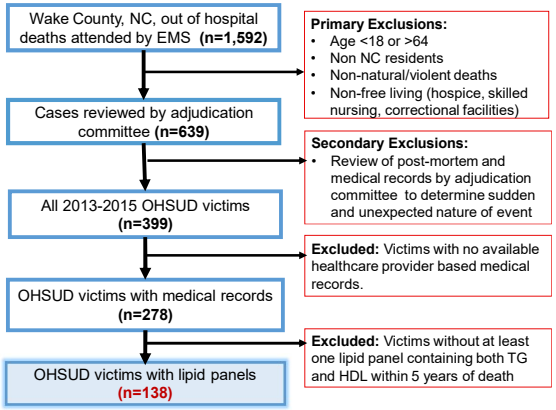
Hypothesis

- We hypothesized that out-of-hospital sudden unexpected death (OHSUD) victims would have similar or higher calculated LDL-C levels and higher TG/HDL ratios when compared with living National Health and Nutrition Examination Survey (NHANES) participants.

Methods

- From March 1, 2013 to February 28, 2015 all EMS (Emergency Medical Services) attended out-of-hospital deaths in Wake County, North Carolina, were screened to identify OHSUD cases among free living 18-64 year olds.
- All available data from death certificates, EMS narratives, medical examiner and/or autopsy reports and medical records was used to ascertain the group of sudden unexpected death victims pertinent to this study [Figure 1].

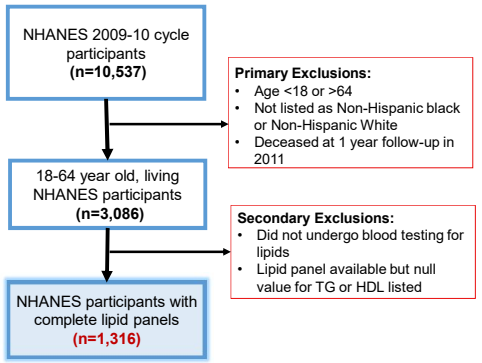
Figure 1. Ascertainment process for OHSUD Victims



Methods (contd.)

- The final 138 victims had an available lipid panel at an average of 1.2 years prior to death.
- Emulating a similar follow-up period, we constructed a control group of NHANES participants (2009-10 cycle) to serve as a comparison group [Figure 2].
- Only Non-Hispanic black and Non-Hispanic white races were included as adjudicated OHSUD victims were only black or white.

Figure 2. Ascertainment process for NHANES Participants comparison group.



Covariate Reporting [Table 1]
- OHSUD victims: Abstracted from medical records.
- NHANES participants: Self-reported via survey.

Statistical Analysis
- Multiple linear regression was used to assess the difference in lipid measures between OHSUD victims and NHANES participants.
- Adjusted for: Age, gender, race, triglycerides, prevalent dyslipidemia, diabetes, hypertension, body mass index (BMI), and coronary artery disease (CAD), use of lipid lowering medication (LL Meds) and clinic visits per year.
- For analysis pertaining to LDL-C, subjects with TG>400 mg/dL were excluded.

Results

Table 1. Unadjusted Population Characteristics of OHSUD Victims with Lipid Panels and NHANES Participants

	OHSUD Victims (n=138)	NHANES Participants (n=1316)	p-value
Age	54.6(7.9)	41(13.6)	<0.0001
Females, n (%)	44 (31.9)	690 (52.4)	<0.01
Blacks, n (%)	53 (38.4)	392 (29.8)	<0.05
Mean BMI	31.4(9.7)	28.9(7.9)	0.0007
Dyslipidemia, n (%)	104 (75.4)	324 (24.6)	<0.01
Use of LL medication, n (%)	61 (44.2)	153 (11.6)	<0.01
Diabetes, n (%)	62 (44.9)	82 (6.2)	<0.01
Hypertension, n (%)	112 (81.2)	281 (21.4)	<0.01
Coronary Artery Disease, n (%)	43 (31.2)	24 (1.8)	<0.01
Annual Clinic Visits	4.7(4.6)	3.9(3.9)	0.0383

All continuous variables reported as mean(SD). p-values reported for univariate case vs. control comparisons.

Figure 3. Unadjusted mean lipid profile components in OHSUD Victims and NHANES Participants

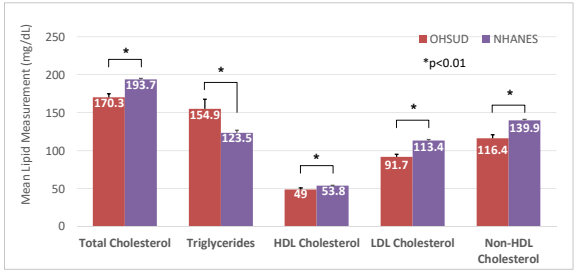
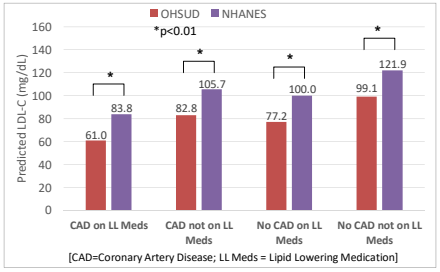
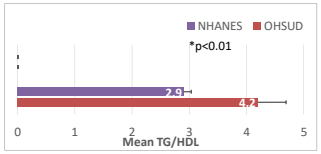


Figure 4. Predicted LDL-C after multivariate adjustment in a 50 year old white male with a diagnosis of diabetic, hypertension and dyslipidemic, TG of 140 mg/dL and BMI 30 kg/m².



Results (contd.)

Figure 5. Unadjusted mean TG/HDL Ratio in OHSUD Victims and NHANES Participants.



- OHSUD victims consisted of a higher proportion of males and blacks, had a higher BMI, and had more prevalent dyslipidemia, diabetes, hypertension and coronary artery disease than NHANES participants [Table 1].
- OHSUD victims had a lower unadjusted mean LDL than NHANES participants [Figure 3].
- **After multivariate adjustment, mean LDL of OHSUD victims was still 22.3 mg/dL lower than NHANES participants** (p<0.001) [Figure 4].
- **OHSUD victims had a higher unadjusted mean TG/HDL ratio than NHANES participants** [Figure 5]; this difference was mildly attenuated on adjustment for age, gender and race (p=0.05).

Conclusions

- Contrary to expectations, OHSUD victims had a more favorable LDL cholesterol profile, unexplained by differences in demographics, comorbid conditions or use of lipid lowering medication.
- The elevated TG/HDL ratio in victims corroborates an evolving hypothesis on the contributory nature of vasoactive, prothrombotic remnant-like lipoprotein particles to sudden unexpected death.

Limitations

- Inclusion of only OHSUD victims with lipid panels available in medical records. These results may be selectively biased towards sicker victims who had greater access to medical care and not reflective of all OHSUD victims.
- The use of NHANES participants for comparison as opposed to an appropriately matched control group from the same population.

References, Acknowledgements and Disclosures

References:

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Disclosures: Ross J. Simpson, MD, PhD consults with Merck, Pfizer, and Amgen. Philip M. Mendys, PharmD is an employee of Pfizer.