






LDL AND FRIEDEWALD EQUATION

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PATIENT HISTORY

- 55 years old male
 - History of Dyslipidemia
 - Routine lipid panel done at our lab
 - And the result showed...
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Component Ref Range & Units	1 mo ago (8/31/22)	1 yr ago (5/7/21)	1 yr ago (3/8/21)	6 yr ago (2/23/16)
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Cholesterol <200 mg/dL	<50	108 ^{CK}		111 ^A
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Comment: Desirable Total Cholesterol: Less than 200 mg/dL
 Borderline High Total Cholesterol: 200-239 mg/dL
 High Total Cholesterol: 240 mg/dL or greater

Triglycerides <150 mg/dL	272 ^A	55 ^{CK}	64 ^A	86 ^A
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Comment: Borderline High : 150-199 mg/dL
 High: 200-499 mg/dL
 Very High: >500 mg/dL

High Density Lipoprotein Cholesterol 26 - 74 mg/dL	11 ^V	52	53 ^A	37 ^A
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Low Density Lipoprotein, Calculated <100 mg/dL	-15 ^V	45 ^{CK}	49 ^A	
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Comment: Optimal LDL Result : <100 mg/dL
 Near Optimal Result : <130 mg/dL
 Borderline High: 130-159 mg/dL
 High: 160-189 mg/dL
 Very High: > 190 mg/dL

Cholesterol/High Density Lipoprotein Ratio	4.55	2.08 ^{CK}		
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Comment: Atherosclerosis Risk Ratios for LDL,HDL,and Cholesterol:

	Risk	LDL/HDL	CHOL/HDL
Men:	1/2 Avg	1.00	3.43
	Average	3.55	4.97
	2x Avg	6.25	9.55
	3x Avg	7.99	23.3
Women:	1/2 Avg	1.47	3.27
	Average	3.22	4.44
	2x Avg	5.03	7.05
	3x Avg	6.14	11.04

After Castelli: Average Risk Implies a 20-25%
 Chance of Developing CHD by Age 60

Low Density Lipoprotein/High Density Lipoprotein Ratio	-1.36	0.87		
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WHAT CAN CAUSE THE LDL TO BE A NEGATIVE
VALUE IN THE LAB REPORT ?

“FRIEDEWALD EQUATION”



FRIEDEWALD EQUATION

- First described in 1972 by Friedewald et al
- Most common and important method of LDL-C determination
- Total cholesterol, triglycerides, and HDL cholesterol measured directly by routine methods

FRIEDEWALD EQUATION

- Measured values **total cholesterol, triglycerides, and HDL** cholesterol are used to calculate LDL-C (mg/dL) by Friedewald Equation
- **Friedewald Equation:**
 - $LDL-C = \text{Total cholesterol} - \text{HDL cholesterol} - [\text{Triglyceride} \div 5]$

LIMITATIONS OF FRIEDEWALD EQUATION

- Friedewald equation inaccurate in certain samples
 - Triglyceride concentration ≥ 400 mg/dL or very low total cholesterol
 - Calculated LDL-C falsely depressed
 - High chylomicrons
 - Nonfasting
 - Type III dyslipidemia (dysbetalipoproteinemia)

HOW OUR PATIENT VALUE WAS IN THE NEGATIVE ?

- According to his lab values

- Total cholesterol: 50 mg/dL
- HDL : 11 mg/dL
- Triglycerides: 272 mg/dL

- Putting these values in Friedewald Equation

- $LDL-C = \text{Total cholesterol} - \text{HDL cholesterol} - [\text{Triglyceride} \div 5]$

- $LDL-C = 50 - 11 - [272 \div 5]$

- $LDL-C = 39 - [54.4]$

- $LDL-C = -15.4 \text{ mg/dL}$

DISORDERS THAT CAUSE HYPOCHOLESTEREMIA

- **Genetic Causes:**

- Familial Hypobetalipoproteinemia
- Abetalipoproteinemia
- Chylomicron Retention Syndrome
- Familial Hypoalphalipoproteinemia
- Apolipoprotein A1 Mutations

- **Secondary Causes:**

- Malabsorption
- Sepsis
- Liver failure
- Cachexia syndromes
- Malnutrition

SO WHAT ARE THE OPTIONS TO MEASURE ACCURATE LDL OF SUCH PATIENTS ?

- Ultracentrifugation and Beta quantification method:
 - Gold standard to measure LDL
 - Expensive and inconvenient for the routine laboratory
 - Limited to specialized lipid laboratories
- Using other equations:
 - About 15 calculations developed since Friedewald, all trying to tackle challenges presented by Friedewald – not all have been validated in large cohorts

- **Martin-Hopkins equation**

- It outperformed the Friedewald equation
- Validated in patients on lipid lowering therapy
- But it underestimated VLDL-C in hypertriglyceridemic samples (>400mg/dL)

- **A new promising equation...**

- **Sampson Low-Density lipoprotein Equation**

Sampson Low-Density lipoprotein Equation

- **$LDL-C = TC/0.948 - HDL-C/0.971 - (TG/8.56 + TG \times non-HDL-C/2140 - TG^2/16100) - 9.44$** ²⁵⁾
- Similar performance like Martin-Hopkins equation in patients on Lipid lowering therapy
- Allows accurate determination of LDL-C with triglycerides up to 800 mg/dL
- Although more complex than Friedewald equation, it is compatible with modern laboratory informatics systems.

TAKE AWAY HOME POINTS

- Communicate and educate the laboratory technicians about the potential of errors in reporting low level of LDL
- Communicate with laboratory technician to report such kind of errors to the lab director so that it can be thoroughly investigated

PATIENT SAFETY ASPECTS

- When building chemistry tests involving formulae important to check the calculations to identify typographical errors
- Before going live with any test important to check:
 - Results are crossing over from instrument-to-EMR interface correctly
 - Different sample concentration scenarios are tested to check integrity of the formulae
 - Scenario's where formulae produces negative results appropriate comments are added with test result



THANK YOU!