Prevalence, Incidence, and Definition of Severe Hypertriglyceridemia: A Comprehensive Review and Weighted Summary

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BACKGROUND

- Hypertriglyceridemia (HTG) is characterized by elevated plasma triglycerides (TGs)
- Elevated TGs are associated with health risks such as pancreatitis and atherosclerotic cardiovascular disease
- HTG may manifest as either primary HTG (with a substantial genetic component) or secondary/acquired (in which secondary factors increase risk)
  - Secondary factors include obesity, uncontrolled diabetes, alcohol abuse, physical inactivity, metabolic syndrome, hypothyroidism, and select medications
- Current clinical practice guidelines describing HTG vary in their categorization of TG levels, particularly in defining severe HTG (sHTG)

OBJECTIVE

- To summarize definitions of sHTG based on TG levels as outlined in clinical practice guidelines
- To synthesize published literature on prevalence and incidence of sHTG among adults in the general population of various countries/settings

STUDY DESIGN

- A comprehensive literature search was performed
  - Embase and MEDLINE® were searched up to September 27, 2023
  - Conference abstracts were identified via Embase, and bibliographies of pertinent literature reviews were searched
- Study eligibility criteria were pre-defined[1] (**Table 1**)
  - Clinical practice guidelines and consensus statements providing a definition of sHTG were included; epidemiological studies reporting prevalence or incidence of primary or unspecified/mixed* sHTG were also included
- Prevalence estimates were stratified by
  - sHTG type (primary vs. unspecified/mixed*)
  - sHTG thresholds: TG ≥500 mg/dL (≥5.6 mmol/L), ≥886 mg/dL (≥10 mmol/L), ≥1000 mg/dL (≥11.2 mmol/L), and other (i.e., less commonly reported)
- Pooled prevalence estimates were calculated after excluding studies with substantial bias[1] or methodological issues
  - Analysis using random-effects model via metafor package (v4.6-0) in R (v4.4.0)
  - Random-effects estimates were weighted by $1 / (SE^2 + \tau^2)$, where SE is the standard error for the study and τ^2 is the between-study variance

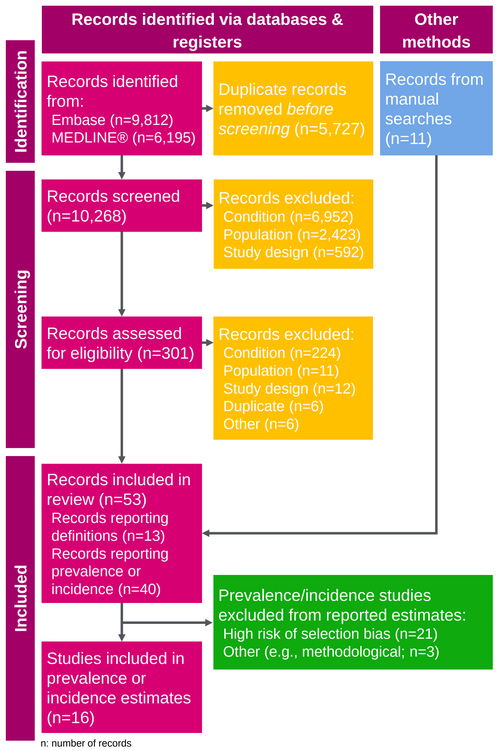
TABLE 1: Study eligibility criteria

Item	Inclusion Criteria	Exclusion Criteria
Condition	Primary or unspecified/mixed* sHTG, described by authors as sHTG or HTG with TG levels ≥5.6 mmol/L (≥500 mg/dL)	Strictly secondary or acquired sHTG
Context	Any country	
Population	Adults in the general population (typically aged ≥18 years)	Special populations (e.g., pediatric, elderly)
Additional Criteria	• Epidemiological studies reporting sHTG incidence/prevalence • Clinical practice guidelines for sHTG treatment/management • Reviews/commentaries on clinical practice guidelines	
Language	English (abstracts available in English were included)	

* Encompassing both primary and secondary/acquired cases

RESULTS

FIGURE 1: PRISMA flow diagram



n: number of records

- 13 guidelines/consensus documents[2-14] and 40 epidemiological studies were included (**Figure 1**)
  - 16 studies were included in prevalence/incidence estimates[15-30]
- In guidelines, the most used sHTG definition was ≥500 mg/dL (n=10); TG ≥886 mg/dL was used in Europe
- Terminology for labelling differed, with HTG referred to as "severe", "very high", or "distinct"
- Most epidemiological studies used medical records or lab data

PREVALENCE (n=15)

- Most included studies were from Europe (n=5) and the US (n=4), followed by China (n=3)
- Prevalence of unspecified/mixed* sHTG varied for different TG levels (**Figures 2-4**)
  - Pooled rates in China were high (1.56%; TG ≥500 mg/dL)
- Data on primary sHTG were limited
  - 0.80% for TG ≥500 mg/dL in a US study[28]
  - 0.15% for TG >500 mg/dL in a Spanish study[24]

INCIDENCE (n=3)

- Incidence of unspecified/mixed* sHTG
  - 1:400 adults in Canada (TG 886–1771 mg/dL; 2010–2015)[16]
  - 39 per 100,000 person-years in Denmark (TG ≥886 mg/dL; 2008–2019)[23]
- Incidence of primary sHTG
  - 24 per 100,000 person-years in US (TG ≥500 mg/dL; 1998–2015)[28]

FIGURE 2: Forest plot of prevalence rates of unspecified/mixed* sHTG (TG ≥500 mg/dL; n=10)

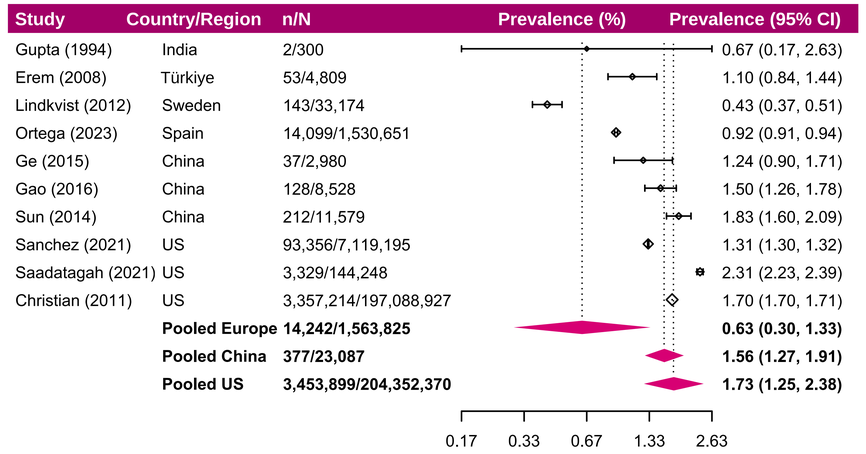


FIGURE 3: Forest plot of prevalence rates of unspecified/mixed* sHTG (TG ≥886 mg/dL; n=6)

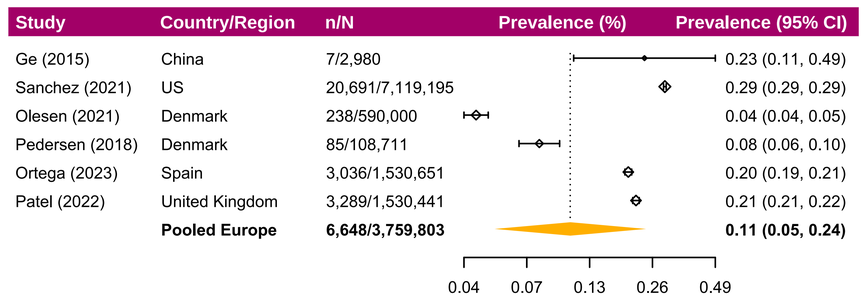
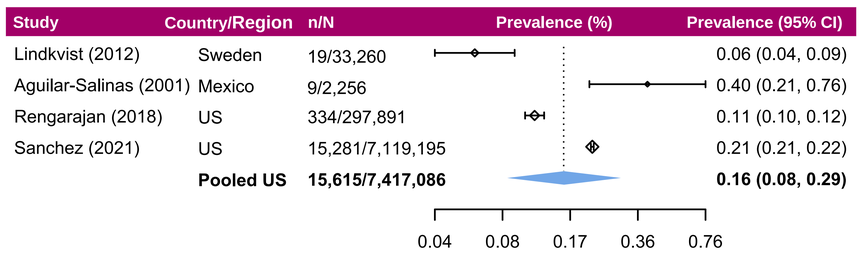


FIGURE 4: Forest plot of prevalence rates of unspecified/mixed* sHTG (TG ≥1000 mg/dL; n=4)



* Encompassing both primary and secondary/acquired cases; CI, confidence interval; n, number of cases; N, sample size; sHTG, severe hypertriglyceridemia; TG, triglycerides; US, United States

CONCLUSIONS

- This first review and analysis of prevalence data for sHTG highlights a lack of consensus and uniformity in the terminology used to describe sHTG in guidelines and epidemiological studies
  - Variability in thresholds used leads to inconsistent prevalence and incidence rates reported for sHTG
- Prevalence estimates ranged from 0.43–2.31% for sHTG defined as TG ≥500 mg/dL, 0.04–0.29% for ≥886 mg/dL, and 0.06–0.40% for ≥1000 mg/dL
- Studies used electronic health records or lab data, limiting generalizability of estimates
- Prevalence rates vary by region, suggesting geographical or population differences
- Distinction between primary and unspecified/mixed sHTG added complexity to prevalence and incidence estimates; variations in rates were observed based on classification
- All studies used a single TG value to determine prevalence; longitudinal studies are needed for more accurate estimates of prevalence
- Further standardization of the nomenclature, definition, and threshold used for sHTG should be advocated to facilitate comparisons of sHTG prevalence and incidence across studies

DISCLOSURES

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