Microbiome Patterns Differ Between Simple and Complicated Pediatric Appendicitis: A Systematic Review

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BACKGROUND

The Problem → Acute appendicitis represents a leading cause of pediatric surgical emergencies, especially in middle to high income countries.
Knowledge Gap → Research exploring gut microbiome differences between complicated and uncomplicated pediatric appendicitis remains sparse.
Why This Matters:
- Geographic variations in microbiome patterns are poorly understood
- Identifying bacterial biomarkers could enable personalized treatment approaches

STUDY HYPOTHESIS

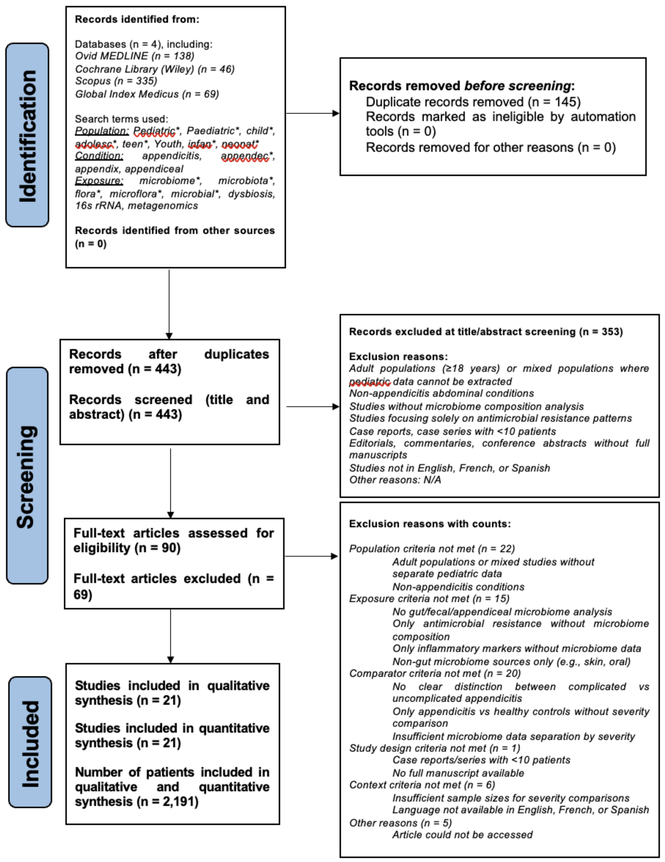
Gut microbiome composition influences the severity of appendicitis and differs systematically between complicated and uncomplicated cases, with potential geographic variation.

OBJECTIVES

- To systematically review and synthesize evidence on gut microbiome compositional differences between complicated and uncomplicated acute appendicitis in pediatric patients.
- Identify specific bacterial taxa and microbial biomarkers associated with appendicitis severity
- Evaluate clinical utility of gut microbiome profiles for treatment decisions
- Assess geographic and demographic factors correlating with microbiome differences
- Evaluate methodological approaches in pediatric appendicitis microbiome research

METHODS

Study Design
Registration: PROSPERO (CRD420251076665)
Search Date: July 9, 2025
Databases: Ovid MEDLINE, Cochrane Library, Global Index Medicus, *Scopus*
Guidelines: PRISMA
Study Selection: ***PRISMA DIAGRAM***



**Two independent reviewers screened all 443 abstracts; 32 disagreements resolved by third reviewer; 21 ultimately selected inclusion post full text review*

RESULTS

General Characteristics & Demographics

2,191
Total Pediatric Patients

1,375
Simple Appendicitis

816
Complicated Appendicitis

Characteristic	Value
Age range	1 month - 18 years
Mean age ± SD	9.8 ± 2.9 years
Gender (studies reporting)	~55% male, 45% female

Study Design & Geographic Distribution

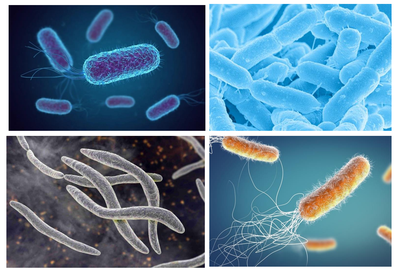
Study Type	Count (%)
Prospective studies	17 (81%)
High-income countries	18 (86%)
Middle-income countries	3 (14%)

Region	Studies
High-income countries	18 (86%)
Middle-income countries	3 (14%)

→ ***Countries represented:*** USA, Japan, France, Austria, Netherlands, Sweden, Latvia, Slovakia, Turkey, China, Colombia, Ukraine, Papua New Guinea (14 total)

Most Common Organisms Identified

Organism	Association
Escherichia coli	Most common (60-85% of cases)
Fusobacterium spp.	Higher in complicated (53.1% vs 32.3%)
Bacteroides spp.	Common in both types
Pseudomonas aeruginosa	Elevated in complicated cases
Enterococcus spp.	Higher in perforated appendicitis



KEY FINDINGS

Fusobacterium as a Significant Biomarker Associated with Complicated Appendicitis

53.1% vs 32.3%
Complication Rate: With vs Without Fusobacterium

→ ***Critical finding:*** Patients *with* Fusobacterium had 53.1% complication rate compared to 32.3% in patients *without* Fusobacterium (RR=1.64, 95% CI: 1.48-1.83)
→ ***Relative Risk*****:** 1.64 (95% CI: 1.48-1.83)
→ ***Key species*****:** *F. nucleatum*, *F. necrophorum*

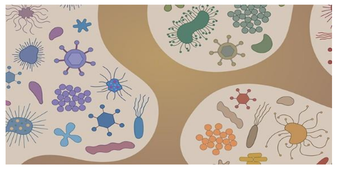
Geographic Variation in Fusobacterium

Region	Fusobacterium Association
High-income countries	11 of 18 studies (61%)
Middle-income countries	0 of 3 studies (0%)

→ ***Critical finding:*** high income countries have a higher fusobacterium association than middle income countries, suggesting significant geographic/socioeconomic variation in microbiome patterns

Pathogenic Organisms Associated with Complicated Appendicitis
- *Pseudomonas aeruginosa* (more prevalent in complicated cases)
- *Enterococcus* species (higher in gangrenous/perforated cases)
- *Bacteroides fragilis*

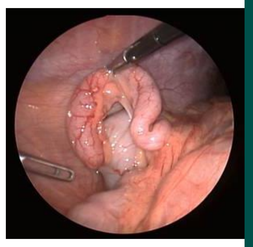
Microbiome Characteristics by Severity
- Increased bacterial diversity (higher alpha diversity)
- Higher prevalence of anaerobic bacteria
- Greater antibiotic resistance patterns
- Polymicrobial infections more common



DISCUSSION

Clinical Implications →
- **Risk Stratification:** Specific bacterial taxa (Fusobacterium, P. aeruginosa, Enterococcus) can inform risk assessment for perforation and complications
- **Personalized Management:** Microbiome patterns may contribute to tailored pediatric appendicitis treatment strategies
- **Geographic Considerations:** Loco-regional differences in microbiome composition should inform clinical decision-making and antibiotic selection
- **Improved Outcomes:** Enhanced risk stratification may lead to better patient outcomes

Future Directions →
- Prospective validation studies of identified microbial biomarkers
- Development of clinical prediction tools incorporating microbiome data
- Investigation of mechanisms underlying geographic variations
- Multi-center studies across diverse populations and income levels
- Assessment of microbiome-targeted therapeutic interventions



Limitations →
- Heterogeneity in microbiome analysis methods across studies
- Limited representation from low- and middle-income countries
- Variability in appendicitis severity classification systems
- Predominantly retrospective and observational study designs

CONCLUSIONS

This systematic review provides the first comprehensive synthesis of gut microbiome differences between complicated and uncomplicated pediatric appendicitis. Fusobacterium species emerged as the most significant biomarker, but only in high-income countries, revealing important geographic variation. All in all, complicated appendicitis is characterized by increased bacterial diversity and higher prevalence of specific pathogenic organisms.

REFERENCES

Scan QR Code for Complete Reference List :

Full systematic review protocol registered in PROSPERO (CRD420251076665) and available at www.crd.york.ac.uk/PROSPERO.

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