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Prevalence Of Anaerobic Bacterial Infections In Routine Clinical Specimens After Surgery: A Comprehensive Review And Meta-Analysis Procedure

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ABSTRACT

Surgical site infections (SSIs) are a significant public health concern. In surgical infections, anaerobic bacteria are known to be major pathogens. Aerobes predominated over anaerobes in previous studies of bacteria detected in postoperative wounds. However, the epidemiology of SSI and the microorganisms that cause it are poorly understood, especially in eastern Nepal. As a result, the goal of this systematic review and meta-analysis has to assess the prevalence of anaerobic bacteria and associated variables in persons with post-operative wound infections in eastern Nepal. Pub Med, Google Scholar, Web of Science, Nepal Journals Online and Allied Health Literature for studies that reported the prevalence of postoperative anaerobic bacterial infections in people with SSI worldwide from January 1, 2000 to March 31, 2020. The 2 test on Cochran's Q statistic are used to assess heterogeneity, and H and I 2 statistics are used to quantify it. A random effect meta-analysis methodology is used to pool the prevalence data. To identify sources of heterogeneity in prevalence estimates, subgroup and Meta regression analyses are conducted. These works are described using the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) as a guideline. Since this study is based on published data, it does not require ethical approval. This systematic review and meta-analysis is intended to serve as a basis for determining the burden of anaerobic bacteria in SSIs for identifying data gaps and for guiding future investigations in Nepal. PROSPERO acknowledgement of receipt number is [265198].

Keywords: Anaerobic infection, SSIs, Systematic review, Meta-analysis

INTRODUCTION

According to the CDC's healthcare-associated infection (HAI) prevalence survey, inpatient procedures resulted in an estimated 110,800 surgical site infections (SSIs) in 2015. [1] According to the results of the 2020 HAI data provided in the NHSN's HAI Progress Report, the SSI standardized infection ratio (SIR) connected to all NHSN operational procedure categories combined decreased by roughly 5% in 2020 compared to the previous year. [2] Infections affecting the incision or deep tissue at the operation site are known as Surgical Site Infections (SSIs). Within one year of a surgical treatment with an implant, and within 30 days without any left implant, these infections arise.[3] Anaerobic bacteria make up a large portion of our natural flora. Despite the fact that a vast number of anaerobic organisms are found throughout the gastrointestinal system, only a small number of organisms are responsible for clinical disease in postoperative infection patients. [4] Anaerobic infections are becoming more virulent, have a higher incidence, are resistant to metronidazole therapy, and have worse outcomes. Some of these illnesses are extremely dangerous and have a high probability of fatality. Anaerobic infections may no longer be ignored as they formerly were, and must be appropriately recognized. [5] Skin and soft tissue infections caused by anaerobic bacteria are common in parts of the body that have been damaged or wounded by foreign bodies, trauma, ischemia, malignancy, or surgery.[6] Anaerobes are more typically identified in endogenous polymicrobial aerobic and anaerobic illnesses. Infections by these bacteria result from the introduction of endogenous flora into typically sterile regions as a result of breaches in mucosal barriers caused by surgery, trauma, tumors, or ischemia. [5,7] Bacteroides fragilis, pigmented Prevotella spp. and Porphyromonas spp., Fusobacterium spp., Peptostreptococcus spp., Clostridium spp.and Actinomyces spp. are the most prevalent anaerobes found in clinical specimens.[6] Various frequencies of anaerobic bacteria isolation have been reported from various clinical illness sites around the world.[8, 9, 10] The microbiology lab is critical in providing information regarding surgical infections that are slowly worsening or failing to heal. Pigmented Gram-negative anaerobes (Prevotella and Porphyromonas spp.), non-pigmented Gram-negative anaerobes (primarily Bacteroides, Prevotella, and Fusobacterium spp.), Peptostreptococcus spp., and Clostridium spp. are the main pathogens or groups of microorganisms that a microbiology laboratory should routinely detect.[6,11] We offer a procedure for a global systematic review and meta-analysis of data on the prevalence of anaerobic bacteria in persons with postoperative infections. The goal is to offer accurate data to guide future research and to devise cost-effective therapies to reduce the global burden of postoperative anaerobic infections.

REVIEW QUESTIONS

1. What is the prevalence and etiology of anaerobic bacterial infections among people with postoperative infections?

2. What are the sources of heterogeneity of the prevalence of anaerobic bacteria in people with postoperative wound infections?

METHODS AND ANALYSIS

Design and registration

The Centre for Reviews and Dissemination criteria had followed for this systematic review and meta-analysis approach. The Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols were used to report the current systematic review and meta-analysis protocol.[12, 13]

Criteria to consider studies for this review

Inclusion criteria

1. Types of studies: cross-sectional studies, case–control studies, baseline data of cohort studies, surveillance data.

2. Types of participants: Studies were conducted in people with clinically diagnosed post operative wound infections residing in other countries regardless of age group and settings. Post operative infections had to be diagnosed by a physician.

3. Types of outcomes: Studies reporting the prevalence of anaerobic bacterial infections regardless of laboratory diagnostic technique used. Prevalence was calculated as the number of anaerobic bacterial infections on the number of people with post operative wound infections among which anaerobic bacteria were searched.

4. Studies that have been published from 1 January 2000 until 31 March 2020.

Exclusion criteria

1. Studies conducted during or after outbreak period.
2. Case reports, letters, conference abstracts, comments, editorials and case series (<30 participants).
3. Studies with imported cases of anaerobic bacterial infections.

Search strategy for identifying relevant studies

In electronic databases, a search method that included the names of all distinct countries were used. By combining keywords in the field of post-operative infections, relevant publications were found. Medline through Pub Med, Google Scholar and Web of Science, Cumulative Index to Nursing and Allied Health Literature, and Global Index Medicus were the databases used.

Records identified through database searching (google scholar) (n = 130). Additional records identified through pubmed (n =10). Records after duplicates removed and screened (n =100).Records excluded based on titles and abstracts (n = 40).Full-text articles assessed for eligibility (n = 60).Full-text articles excluded (n=53),Book chapters=15,Reviews=24,Commentary=2 and RAPID identification not included=12.Studies included (n = 7).

Selection of studies for inclusion in the review

Four review authors were independently evaluate the full text of the selected records. Discrepancies were resolved by consensus. The agreement between the two first review authors were estimated by Cohen's kappa coefficient.[13]

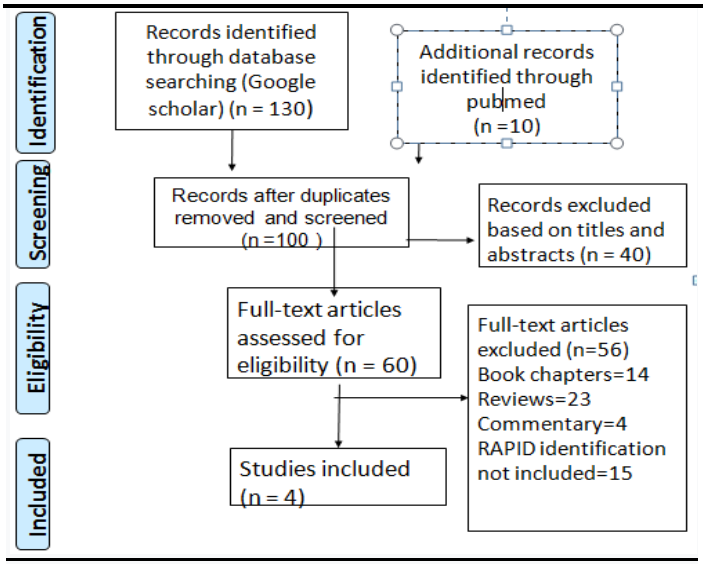


Fig 1. PRISMA model

Study ID	Study design	Sampling method	Sample size	Clinical presentation	Clinical isolate	Prevalence	AST S/R
Huang TT et al., 2006	Cross-Sectional	Sys temic random sampling	128	Deep neck infections	59.3%	NA	NA
Singhal R et al., 2006	Cross-Sectional	Sys temic random sampling	1743	Anaerobic bacteremia	1.14%	NA	NA
Citron DM et al., 2007	Cross-Sectional	Sys temic random sampling	454	Diabetic foot infections	45.2%	gram-positive cocci (45.2%),	NA
De A et al., 2001	Cross-Sectional	Sys temic random sampling	2591	Diverse clinical infections	80%	gram negative an aerobic bacilli (30.1%),	NA
De A et al.,2002	Cross-Sectional	Sys temic random sampling	100	Pleuropulmonary infections	72%	NA	NA
De A et al., 2003	Cross-Sectional	Sys temic random sampling	580	Gas gangrene	26.8%	39 (30.8%) Cl. perfringens	NA
Saini S et al., 2004	Cross-Sectional	Sys temic random sampling	117	Surgical infections	50.4%	Gram-negative anaerobes	NA
Tanaka K et al., 2005	Cross-Sectional	Sys temic random sampling	224	Bartholin's gland abscess	53.1%	NA	NA
Boyanova L et al., 2006	Cross-Sectional	Sys temic random sampling	118	Deep-space head and neck infections	74.6%	Gram-negative anaerobes	clindamycin a metronidazole 5?4 and 2?5 %
Gadepalli R et al., 2006	Cross-Sectional	Sys temic random sampling	80	Diabetic foot ulcer	35%	28 (15.3) Gram-negative anaerobes	NA
Huang TT et al., 2006	Cross-Sectional	Sys temic random sampling	128	Deep neck infections	59.3%	NA	NA
Singhal R et al., 2006	Cross-Sectional	Sys temic random sampling	1743	Anaerobic bacteremia	1.14%	NA	NA
Citron DM et al., 2007	Cross-Sectional	Sys temic random sampling	454	Diabetic foot infections	45.2%	gram-positive cocci (45.2%),	NA
Ng LS et al., 2008	Cross-Sectional	Sys temic random sampling	38	Diabetic foot infections	78.9%	Peptostreptococcus spp. (47%)	00
López VN et al., 23 2009	Cross-Sectional	Sys temic random sampling	124	Iliopsoas abscess	15.1%	NA	NA
Mathew A et al., 24 2010	Cross-Sectional	Sys temic random sampling	50	Necrotising fasciitis	18.5%	gram-positive cocci 7.4% ,	NA
Al-Benwan K et al., 25 2011	Cross-Sectional	Sys temic random sampling	114	Breast abscess	28%	Bacteroides spp. (16, 14%),	resistant to clindamycin3
Vishwanath S et al., 2012	Cross-Sectional	Simple Random sampling	94	Chronic suppurative otitis media	19.14%	gram positive cocci(38.9%)	NA
Urban E et al., 2012	Cross-Sectional	Simple Random sampling	43992	Anaerobic bacteremia	0.69%	Clostrid-ium spp. (12.8%)	NA

Vishwanath S et al., 2013	Cross-Sectional	Simple Random sampling	25	Clostridium difficile infection	16%	C. difficile and C. perfringens(25%)	NA
Kamble S et al., 2014	Cross-Sectional	Simple Random sampling	50	Cutaneous and subcutaneous wound infections	18%	Bacteroides fragilis(42.2%)	NA
Garg R et al.,2014	Cross-Sectional	Simple random sampling	100	Diverse clinical infections	19%	Peptostreptococcus 11%	Metronidazol resistance a4

Table 1. Study characteristics

Risk of bias assessment

An adapted version of the risk of bias instrument for prevalence studies was produced by modifying an existing measure and evidence of interpreter agreement was used to assess included research for risk bias. [14]

Data extraction and management

Study characteristics such as name of the first author, year of publication, study Gram-negative anaerobes population, number of bacteria searched, study design, setting, diagnostic criteria, outcomes measured, location and country in which the study was conducted, criteria for sample selection and sample size, city, clinical presentation, number of clinical isolates. Data extractions were done independently by four review authors.

Data synthesis

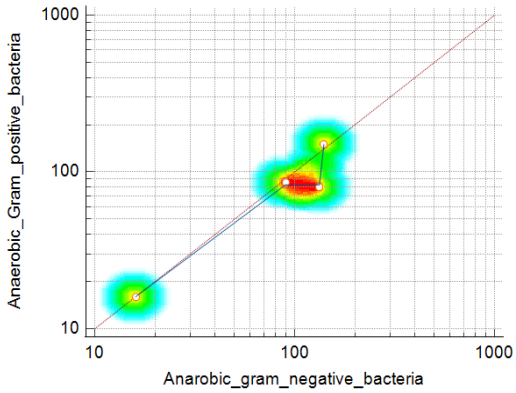
The R statistical software's'meta' and 'metaphor' packages were used to analyze the data (V.3.4.4, R Foundation for Statistical Computing, Vienna, Austria). The prevalence was presented along with its 95% confidence level and projection. Before pooling the data with the random-effects meta-analysis model, the variances of the study-specific prevalence were stabilized via the Freeman-Tukey double arcsine transformation.[15] Only studies that were conducted in populations with similar clinical presentations/underlying conditions and used the same laboratory diagnostic technique will be combined. The presence of publication bias was detected using Egger's tests.[16]On Egger's test, a p value of less than 0.10 was considered statistically significant publication bias. The 2 test on Cochran's Q statistic was used to assess heterogeneity, which was measured by H and I^2 values. [17] The I^2 statistic calculates the percentage of total variation between research that may be attributed to actual differences across trials rather than chance. In general, I^2 values of more than 60%–70% suggest the presence of significant heterogeneity. Subgroup and meta-regression analyses were employed to identify sources of heterogeneity where there was a lot of it. A manual forward selection technique was used to find characteristics that were independently linked with the variation in overall prevalence. The model with the lowest Bayesian Information Criterion was chosen as the final candidate. Statistical significance is defined as a p value of less than 0.05.[18]

RESULTS

Table-2. Data extraction and analysis

Study	Sample size	Monomicrobial	Polymicrobial	Anaerobic_Gram_positive_bacteria	Anarobic_gram_negative_bacteria
Al-Benwan K et al. 2011	115	65	18	16	16
Garg R et al.2014	393	115	226	80	133
Boyanova L et al. 2016	118	93	23	86	90
Antony B et al.2016	2227	118	28	150	140

	Group A	Group B	Group C	Group D	Group E	Group F
Col. title	**Study**	**sample_size**	**monomicrobial**	**polymicrobial**	**Anaerobic_Gram**	**Anarobic_gram_**
Mean	2.5	713.25	97.75	73.75	83	94.75
Standard deviation (SD)	1.291	1017.6	24.514	101.58	54.760	56.964
Sample size (N)	4	4	4	4	4	4
Std. error of mean(SEM)	0.6455	508.78	12.257	50.791	27.380	28.482
Lower 95% conf. limit	0.4460	-905.67	58.749	-87.867	-4.123	4.120
Upper 95% conf. limit	4.554	2332.2	136.75	235.37	170.12	185.38
Minimum	1.000	115.00	65.000	18.000	16.000	16.000
Median (50th percentile)	2.500	255.50	104.00	25.500	83.000	111.50
Maximum	4.000	2227.0	118.00	226.00	150.00	140.00



Sample size	4
Correlation coefficient r	0.8740
Significance level	P=0.1260
95% Confidence interval for r	-0.5443 to 0.9973

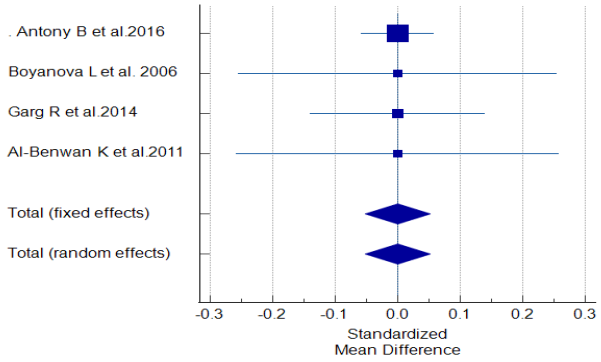
Fig 2. Correlation coefficient

The results of the individual studies included in the meta-analysis: number of cases, the correlation coefficient with 95% CI.

Study	N1	N2	Total	SMD	SE	95% CI	t	P	Weight (%) Fixed	Weight (%) Random
. Antony B et al. 2016	2227	2227	4454	0.000	0.0300	-0.0587 to 0.0587			78.00	78.00
Boyanova L et al. 2006	118	118	236	0.000	0.130	-0.256 to 0.256			4.16	4.16
Garg R et al.2014	393	393	786	0.000	0.0713	-0.140 to 0.140			13.79	13.79
Al-Benwan K et al. 2011	115	115	230	0.000	0.131	-0.259 to 0.259			4.05	4.05
Total (fixed effects)	2853	2853	5706	0.000	0.0265	-0.0519 to 0.0519	0.000	1.000	100.00	100.00
Total (random effects)	2853	2853	5706	0.000	0.0265	-0.0519 to 0.0519	0.000	1.000	100.00	100.00

Test for heterogeneity

Q	0.0000
DF	3
Significance level	P = 1.0000



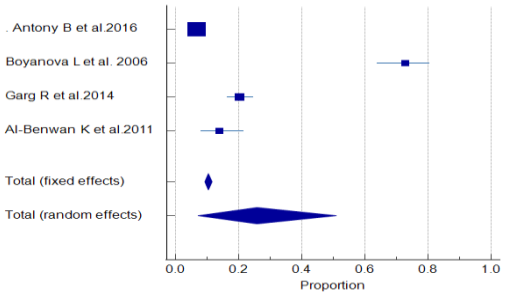
Table/Fig-6. Continuous measures

The total Standardized Mean Difference with 95% CI is given both for the Fixed effects model and the Random effects model. If the value 0 is not within the 95% CI, then the SMD is statistically significant at the 5% level (P<0.05).Cohen's rule of thumb for interpretation of the SMD statistic is: a value of 0.2 indicates a small effect, a value of 0.5 indicates a medium effect and a value of 0.8 or larger indicates a large effect.

Study	Sample size	Proportion (%)	95% CI	Weight (%) Fixed	Weight (%) Random
. Antony B et al. 2016	2227	6.736	5.730 to 7.857	77.98	25.40
Boyanova L et al. 2006	118	72.881	63.925 to 80.654	4.17	24.70
Garg R et al.2014	393	20.356	16.484 to 24.681	13.79	25.21
Al-Benwan K et al. 2011	115	13.913	8.167 to 21.609	4.06	24.68
Total (fixed effects)	2853	10.374	9.280 to 11.551	100.00	100.00
Total (random effects)	2853	25.790	7.156 to 50.914	100.00	100.00

Test for heterogeneity

Q	299.2228
DF	3
Significance level	P < 0.0001
I^2 (inconsistency)	99.00%
95% CI for I^2	98.50 to 99.33



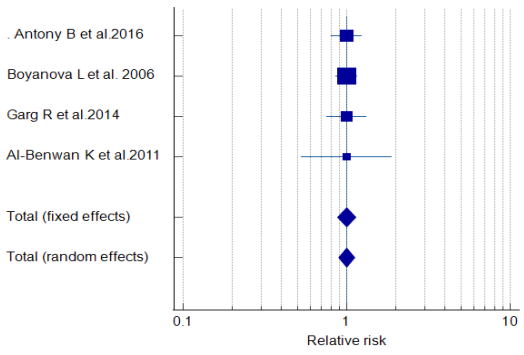
Table/Fig 7. Proportion meta analysis

The proportions (expressed as a percentage), with their 95% CI, found in the individual studies included in the meta-analysis.

Study	Intervention	Controls	Relative risk	95% CI	z	P	Weight (%) Fixed	Weight (%) Random
. Antony B et al. 2016	150/2227	150/2227	1.000	0.804 to 1.244			26.94	26.94
Boyanova L et al. 2006	86/118	86/118	1.000	0.856 to 1.168			53.12	53.12
Garg R et al.2014	80/393	80/393	1.000	0.758 to 1.319			16.83	16.83
Al-Benwan K et al. 2011	16/115	16/115	1.000	0.526 to 1.902			3.11	3.11
Total (fixed effects)	332/2853	332/2853	1.000	0.879 to 1.138	0.000	1.000	100.00	100.00
Total (random effects)	332/2853	332/2853	1.000	0.893 to 1.120	0.000	1.000	100.00	100.00

Test for heterogeneity

Q	0.0000
DF	3
Significance level	P = 1.0000



Table/Fig 8. Relative risk meta-analysis

The pooled relative risk with 95% CI is given both for the Fixed effects model and the Random effects model. If the value 1 is not within the 95% CI, then the relative risk is statistically significant at the 5% level (P<0.05).

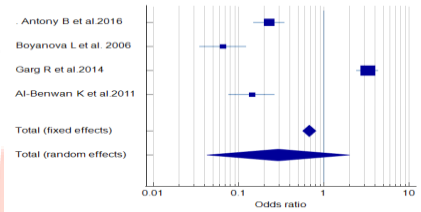
Publication bias

Egger's test	
Intercept	-21.2762
95% CI	-49.5124 to 6.9600
Significance level	P = 0.0834
Begg's test	
Kendall's Tau	-0.6667
Significance level	P = 0.1742

Study	Intervention	Controls	Odds ratio	95% CI	z	P	Weight (%)	
							Fixed	Random
Antony B et al. 2016	28/2227	118/2227	0.228	0.150 to 0.345			25.88	25.15
Boyanova L et al. 2006	23/118	93/118	0.0651	0.0345 to 0.123			11.15	24.77
Garg R et al.2014	226/393	115/393	3.271	2.435 to 4.395			51.43	25.30
Al-Benwan K et al. 2011	18/115	65/115	0.143	0.0765 to 0.266			11.53	24.79
Total (fixed effects)	295/2853	391/2853	0.675	0.564 to 0.807	-4.292	<0.001	100.00	100.00
Total (random effects)	295/2853	391/2853	0.292	0.0425 to 2.004	-1.253	0.210	100.00	100.00

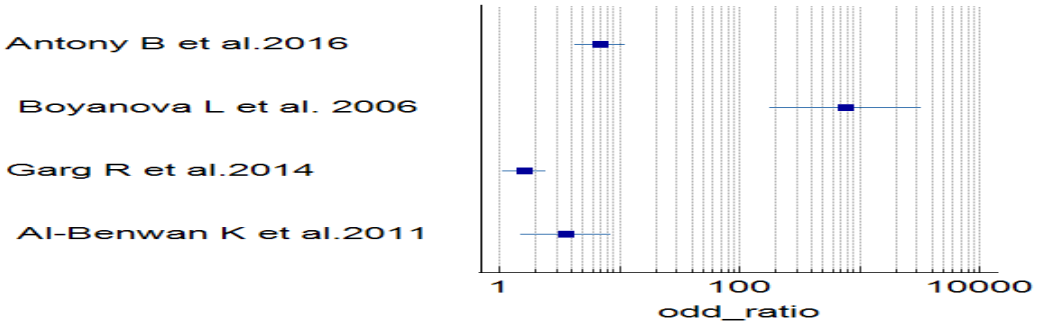
Test for heterogeneity

Q	211.9817
DF	3
Significance level	P < 0.0001
I^2 (inconsistency)	98.58%
95% CI for I^2	97.77 to 99.10



Table/Fig 9. Odds ratio meta analysis

The pooled odds ratio with 95% CI is given both for the Fixed effects model and the Random effects model. If the value 1 is not within the 95% CI, then the Odds ratio is statistically significant at the 5% level (P<0.05).



Table/Fig 10. Forest plot

A forest plot presents a series of central values and their confidence intervals in a graphic manner, so that they can easily be compared. The central values are represented by markers and the confidence intervals by horizontal lines.

Study	Estimate	Standard Error	95% CI	z	P	Weight (%)	
						Fixed	Random
Antony B et al.2016	6.940	11.358	-15.322 to 29.202			4.28	4.28
Boyanova L et al. 2006	768.910	3321.900	-5742.014 to 7279.834			0.000050	0.000050
Garg R et al.2014	1.651	2.502	-3.253 to 6.555			88.25	88.25
Al-Benwan K et al.2011	3.611	8.600	-13.245 to 20.467			7.47	7.47
Total (fixed effects)	2.024	2.350	-2.582 to 6.631	0.861	0.389	100.00	100.00
Total (random effects)	2.024	2.350	-2.582 to 6.631	0.861	0.389	100.00	100.00

Test for heterogeneity

Q	0.2969
DF	3
Significance level	P = 0.9606
I^2 (inconsistency)	0.00%
95% CI for I^2	0.00 to 0.00

Publication bias

Egger's test	
Intercept	0.3526
95% CI	-0.1330 to 0.8381
Significance level	P = 0.0890
Begg's test	
Kendall's Tau	0.6667
Significance level	P = 0.1742

Table/Fig 11. Standard error

Test for heterogeneity

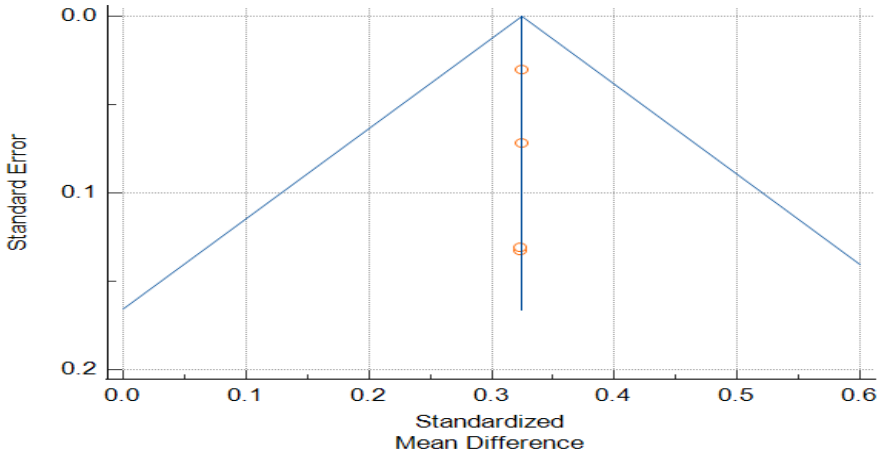
Q	0.0001093
DF	3
Significance level	P = 1.0000
I^2 (inconsistency)	0.00%
95% CI for I^2	0.00 to 0.00

Publication bias

Egger's test	
Intercept	-0.009219
95% CI	-0.01430 to -0.004141
Significance level	P = 0.0160
Begg's test	
Kendall's Tau	-1.0000
Significance level	P = 0.0415

Study	N1	N2	Total	SMD	SE	95% CI	t	P	Weight (%)	
									Fixed	Random
Al-Benwan K et al. 2011	115	115	230	0.324	0.132	0.0630 to 0.584			4.05	4.05
Garg R et al.2014	393	393	786	0.324	0.0717	0.184 to 0.465			13.79	13.79
Boyanova L et al. 2016	118	118	236	0.324	0.131	0.0664 to 0.581			4.16	4.16
. Antony B et al.2016	2227	2227	4454	0.325	0.0302	0.266 to 0.384			78.00	78.00
Total (fixed effects)	2853	2853	5706	0.325	0.0266	0.272 to 0.377	12.188	<0.001	100.00	100.00
Total (random effects)	2853	2853	5706	0.325	0.0266	0.272 to 0.377	12.188	<0.001	100.00	100.00

Table/Fig 11. Standard mean difference



Table/Fig 12. Funnel plot

Funnel plot is for publication bias. In this case there is symmetrical scatter of points both sides of the weighted average mean difference. Equal numbers are above or below.

Potential amendments

We did not plan to make any changes to this protocol. However, if substantial changes occur during the review, they were reported in the published results**.**

Patient and public involvement

Patients and the public were not involved in the conception and design of this protocol.

Ethics and dissemination

This work relies on published data and therefore does not require an ethical approval. The findings were published in a scientific peer-reviewed journal.

Conclusion

The findings from this systematic review and meta-analysis, which took into account the burden of anaerobic infections, were valuable for health stakeholders and provided information that can lead to efficient methods for controlling the burden of anaerobic bacterial infections. During a meta-analysis, different definitions of anaerobic bacterial infections and inclusion criteria might result in significant heterogeneity.

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