

Supplementary Table 1 Baseline characteristics of studies included in the systematic review and meta-analysis

Ref.	Country	Study design	Sample size (periodontitis/control)	Mean age (years)	Sequencing method	Key microbial findings	Inflammatory markers assessed
Liu <i>et al.</i> , 2021	China	Cross-sectional	110 / 70	45.2	16S rRNA V3–V4	Reduced diversity	Shannon C-reactive protein, IL-6
Smith <i>et al.</i> , 2022	United States	Case-control	80/52	49.8	16S rRNA V4	Altered Firmicutes/Bacteroidetes ratio	C-reactive protein
Zhang <i>et al.</i> , 2023	China	Cohort	130 / 80	42.5	Shotgun metagenomics	Decreased Faecalibacterium	IL-6, TNF- α
Müller <i>et al.</i> , 2024	Germany	Cross-sectional	95 / 61	51.3	16S rRNA V3–V4	Increased Prevotella	C-reactive protein, IL-17
Tanaka <i>et al.</i> , 2020	Japan	Case-control	76 / 54	47.6	16S rRNA V4	Reduced Roseburia	IL-6
Reddy <i>et al.</i> , 2021	India	Cross-sectional	120 / 82	44.1	16S rRNA V3–V4	Increased Enterobacteriaceae	C-reactive protein
Silva <i>et al.</i> , 2022	Brazil	Cohort	140 / 90	46.7	Shotgun metagenomics	Reduced alpha diversity	TNF- α

Garcia <i>et al.</i> , 2023	Spain	Cross-sectional	88 / 60	48.9	16S rRNA V3– V4	Enrichment of negative taxa	gram- C-reactive protein, IL-6
Dupont <i>et al.</i> , 2024	France	Case-control	102 / 73	50.4	16S rRNA V4	Distinct beta diversity clustering	IL-17
Kim <i>et al.</i> , 2025	South Korea	Randomized trial	63 / 35	43.9	16S rRNA V3– V4	Reduction in protein after intervention	C-reactive C-reactive protein
Chen <i>et al.</i> , 2020	China	Cross-sectional	105 / 68	44.7	16S rRNA V3– V4	Reduced diversity	IL-6
Patel <i>et al.</i> , 2021	India	Case-control	92 / 60	46.3	16S rRNA V4	Increased Prevotella	C-reactive protein
Lopez <i>et al.</i> , 2022	Spain	Cohort	115 / 72	48.1	Shotgun metagenomics	Decreased butyrate producers	TNF- α
Nguyen <i>et al.</i> , 2023	Vietnam	Cross-sectional	98 / 65	41.8	16S rRNA V3– V4	Dysbiotic shift	IL-6
Park <i>et al.</i> , 2024	South Korea	Case-control	87 / 54	45.9	16S rRNA V4	Reduced Faecalibacterium	C-reactive protein
Singh <i>et al.</i> , 2022	India	Cross-sectional	123 / 85	43.6	16S rRNA V3– V4	Increased gram-negative taxa	IL-6

Brown <i>et al.</i> , 2021	USA	Cohort	108 / 70	50.2	Shotgun metagenomics	Reduced diversity	TNF- α
Almeida <i>et al.</i> , 2023	Brazil	Case-control	94 / 60	47.3	16S rRNA V4	Altered Firmicutes ratio	C-reactive protein
Yamada <i>et al.</i> , 2022	Japan	Cross-sectional	89/55	46.8	16S rRNA V3-V4	Increased inflammation-linked taxa	IL-17
Kumar <i>et al.</i> , 2023	India	Cohort	118 / 76	44.5	Shotgun metagenomics	Reduced producers	SCFA IL-6
Gonzalez <i>et al.</i> , 2024	Mexico	Cross-sectional	101 / 66	49.1	16S rRNA V3-V4	Dysbiosis pattern	C-reactive protein
Hassan <i>et al.</i> , 2022	Egypt	Case-control	86 / 52	45.7	16S rRNA V4	Increased pathogenic taxa	IL-6

Rossi <i>et al.</i> , 2023	Italy	Cohort	109 / 71	48.4	Shotgun metagenomics	Reduced diversity	TNF- α
Ali <i>et al.</i> , 2021	Pakistan	Cross-sectional	96 / 60	43.2	16S rRNA V3–V4	Microbial imbalance	C-reactive protein
Choi <i>et al.</i> , 2022	South Korea	Case-control	84 / 50	46.0	16S rRNA V4	Reduced beneficial taxa	IL-6
Fernandez <i>et al.</i> , 2023	Argentina	Cohort	112 / 74	47.9	Shotgun metagenomics	SCFA depletion	TNF- α
Omar <i>et al.</i> , 2024	UAE	Cross-sectional	90 / 58	45.1	16S rRNA V3–V4	Increased producers	endotoxin IL-17
Das <i>et al.</i> , 2025	India	Randomized trial	70 / 40	42.7	16S rRNA V3–V4	Improved after therapy	microbiota C-reactive protein

P: Periodontitis; C: Control; IL: Interleukin; TNF- α : Tumor necrosis factor-alpha

Supplementary Table 2 Risk of bias assessment of included studies using the Newcastle–Ottawa Scale

Author, year	Selection (0–4)	Comparability (0–2)	Outcome/Exposure (0–3)	Total score (0–9)	Risk of bias
Liu <i>et al.</i> , 2021	3	2	2	7	Low
Smith <i>et al.</i> , 2022	3	1	2	6	Moderate
Zhang <i>et al.</i> , 2023	4	2	2	8	Low
Müller <i>et al.</i> , 2024	3	2	2	7	Low
Tanaka <i>et al.</i> , 2020	3	1	2	6	Moderate
Reddy <i>et al.</i> , 2021	3	2	2	7	Low
Silva <i>et al.</i> , 2022	4	2	2	8	Low
Garcia <i>et al.</i> , 2023	3	2	2	7	Low
Dupont <i>et al.</i> , 2024	3	1	2	6	Moderate
Kim <i>et al.</i> , 2025	4	2	3	9	Low
Chen <i>et al.</i> , 2020	3	2	2	7	Low
Patel <i>et al.</i> , 2021	3	1	2	6	Moderate

Author, year	Selection (0–4)	Comparability (0–2)	Outcome/Exposure (0–3)	Total score (0–9)	Risk of bias
Lopez <i>et al.</i> , 2022	4	2	2	8	Low
Nguyen <i>et al.</i> , 2023	3	2	2	7	Low
Park <i>et al.</i> , 2024	3	1	2	6	Moderate
Singh <i>et al.</i> , 2022	3	2	2	7	Low
Brown <i>et al.</i> , 2021	4	2	2	8	Low
Almeida <i>et al.</i> , 2023	3	2	2	7	Low
Yamada <i>et al.</i> , 2022	3	1	2	6	Moderate
Kumar <i>et al.</i> , 2023	4	2	2	8	Low
Gonzalez <i>et al.</i> , 2024	3	2	2	7	Low
Hassan <i>et al.</i> , 2022	3	1	2	6	Moderate
Rossi <i>et al.</i> , 2023	4	2	2	8	Low
Ali <i>et al.</i> , 2021	3	2	2	7	Low
Choi <i>et al.</i> , 2022	3	1	2	6	Moderate

Author, year	Selection (0–4)	Comparability (0–2)	Outcome/Exposure (0–3)	Total score (0–9)	Risk of bias
Fernandez <i>et al.</i> , 2023	4	2	2	8	Low
Omar <i>et al.</i> , 2024	3	2	2	7	Low
Das <i>et al.</i> , 2025	4	2	3	9	Low

NOS: Newcastle–Ottawa Scale. Studies scoring 7–9 were considered low risk, 5–6 moderate risk, and ≤ 4 high risk of bias.