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Article

Prevalence and Impact of Biofilms on Bloodstream and Urinary Tract Infections: A Systematic Review and Meta-Analysis

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1.Search Terms and Search Strategies

2.Study Characteristics

1.Search Terms and Search Strategies

1.1. Bloodstream Infections Systematic Review

1.1.1. PubMed Database Search

"((((biofilm[MeSH Terms]) OR (biofilm[Title])) AND ((((((((((((mortality) OR (hospital stay)) OR (length of stay)) OR (virulence)) OR (persistence)) OR (recurrence)) OR (biofilm formation)) OR (biofilm presence)) OR (biofilm incidence)) OR (biofilm prevalence)) OR (outcome)) OR (impact)) OR (risk factor)) OR (antibiotic resistance))) AND ((((((((((((((((((bacteremia[MeSH Terms]) OR (candidemia[MeSH Terms])) OR (bacteraemia[MeSH Terms])) OR (candidaemia[MeSH Terms])) OR (bloodstream infections[MeSH Terms])) OR (catheter associated bacteremia[MeSH Terms])) OR (catheter related bacteremia[MeSH Terms])) OR (catheter associated bloodstream infections[MeSH Terms])) OR (cathether related bloodstream infections[MeSH Terms])) OR (catheter bloodstream infections[MeSH Terms])) OR (catheter bacteremia[MeSH Terms])) OR (bacteremia[Title])) OR (bacteraemia[Title])) OR (candidemia[Title])) OR (candidaemia[Title])) OR (bloodstream infection[Title])) OR (bloodstream infections[Title]))) NOT ((((((((((Review[Publication Type]) OR (Letter[Publication Type])) OR (Case reports[Publication Type])) OR (Meta-analysis[Publication Type])) OR (Editorial[Publication Type])) OR (Conference abstract[Publication Type])) OR (Correspondence[Publication Type])) OR (Comment[Publication Type])) OR (Systematic review[Publication Type] OR (Clinical trial[Publication Type] OR (randomized controlled trial[Publication Type])))))) AND (2005:2020[pdat]) AND (english[Filter] OR french[Filter] OR portuguese[Filter])".

1.1.2. Web of Science Database Search

"TOPIC: (biofilm) *AND* **TITLE:** (mortality OR virulence OR recurrence OR persistence OR morbidity OR hospital stay OR length of stay OR antibiotic resistance) *AND* **TOPIC:** (bloodstream infections OR bacteremia OR bacteraemia OR candidemia OR candidaemia OR catheter related bloodstream infections OR catheter associated bloodstream infections) *NOT* **DOCUMENT TYPES:** (Review)

Refined by: DOCUMENT TYPES: (ARTICLE)".

1.2. Urinary Tract Infections Systematic Review

1.2.1. PubMed Database Search

"((((urinary catheter associated infections[MeSH Terms]) OR (urinary tract infections[MeSH Terms]) AND (english[Filter])) AND ((((biofilm[MeSH Terms]) OR (biofilm[Title])) OR (biofilms[MeSH Terms])) OR (biofilms[MeSH Terms]) AND (english[Filter]))) AND ((((((((mortality) OR (persistence)) OR (hospital)) OR (outcome)) OR (clinical)) OR (recurrence)) OR (risk factor)) OR (resistance) OR (impact) OR (epidemiology) OR (production) AND (english[Filter]))))) NOT ((((((((((((((Review[Publication Type]) OR (Letter[Publication Type])) OR (Case reports[Publication Type])) OR (Meta-analysis[Publication Type])) OR (Editorial[Publication Type])) OR (Conference abstract[Publication Type])) OR (Correspondence[Publication Type])) OR (Comment[Publication Type])) OR (Systematic review[Publication Type] OR (Clinical trial[Publication Type] OR (randomized controlled trial[Publication Type])))))))) AND (english[Filter])) AND ((english[Filter]) AND (2005:2020[pdat])) AND (english[Filter]) AND (english[Filter]) Filters: English, French, Portuguese".

1.2.2. Web of Science Database Search

"TOPIC: (biofilm) *AND* **TITLE:** (mortality OR recurrence* OR persist* OR hospital* OR outcome OR clinical OR resist* OR impact* OR epidemiology OR risk factors OR production) *AND* **TOPIC:** (urinary tract infections OR urinary catheter associated infections) *NOT* **DOCUMENT TYPES:** (Review)".

2. Study Characteristics

Table S1. Studies Describing in vitro BFP prevalence in isolates from BSI patients.

Study (Reference)	Country	Study type	Microorganism	BFP prevalence n/N (%)
[1]	Turkey	NS	*Candida* spp.	8/50 (16%)
[2]	France	Prospective cohort	*E. coli*	67/53 (43.8%)
[3]	Spain	NS	*E. faecalis*	18/22 (81.8%)
[4]	Greece	NS	CoNS	58/100 (58.0%)
[5]	Spain	Retrospective	*S. aureus*	162/323 (50.1%)
[6]	Spain	Retrospective	*Candida* spp.	45/54 (83.3%)
[7]	Egypt	NS	*Staphylococcus* spp.	37/58 (63.8%)
[8]	Brazil	NS	*S. aureus*	25/40 (62.5%)
[9]	Norway	NS	CoN *S. epidermidis*	79/130 (60.8%)
[10]	Israel	NS	*S. aureus*	14/33 (42.4%)
[11]	Spain	Prospective	*E. coli*	79/185 (42.7%)
[12]	Turkey	NS	*Candida* spp.	15/52 (28.8%)
[13]	South Africa	Prospective	MSSA	13/21 (61.9%)
[14]	France	Retrospective	*S. epidermidis*	59/98 (60.2%)
[15]	Greece	Retrospective	CoN *S. epidermidis*	14/19 (73.7%)

[16]	Brazil	NS	CoNS	59/59 (100%)
[17]	Brazil	NS	MR *S.haemolyticus*	23/24 (95.8%)
[18]	Brazil	NS	*S. haemolyticus*	39/48 (81,3%)
[19]	Hungary	Retrospective	*Candida* spp.	43/93 (46.2%)
[20]	Austria	NS	Viridians *Streptococci*	6/22 (27.3%)
[21]	Austria	Prospective	*S. epidermidis*	53/60 (88.3%)
[22]	Italy	NS	*C. parapsilosis*	31/31 (100%)
[23]	Japan	NS	MR *Corynebacterium* spp.	14/17 (82.4%)
[24]	Brazil	NS	CoNS	72/176 (40.9%)
[25]	Slovenia	NS	*E. coli*	55/105 (52.3%)
[26]	Brazil	NS	*S. epidermidis*	8/31 (25.8%)
[27]	Thailand	NS	*Candida* spp.	58/84 (69.0%)
[28]	China	Retrospective	*E. coli*	81/324 (25.0%)

Notes: NS: Not specified; E. coli: Escherichia coli; E. faecalis: Enterococcus faecalis; CoNS: Coagulase-negative Staphylococci; CoN: Coagulase-negative; S. aureus: Staphylococcus aureus; S. epidermidis: Staphylococcus epidermidis; MSSA: Methicillin-susceptible Staphylococcus aureus; MR: Methicillin-resistant; S. haemolyticus: Staphylococcus haemolyticus; C. parapsilosis: Candida parapsilosis.

Table S2. Studies describing in vitro BFP prevalence in resistant and susceptible strains of isolates from BSI patients.

Study (Reference)	**Country**	**Study type**	**Microorganism**	**BFP prevalence** n/N (%)	***p*-value**
[29]	South Korea	NS	MRSA	28/44 (63.6%)	0.040 *
			MSSA	5/16 (31.3%)	
[5]	Spain	Retrospective	MRSA	53/137 (38.7%) **	0.135 *
			MSSA	109/348 (31.3%) **	
[7]	Egypt	NS	MR *Staphylococcus* spp.	18/25 (72.0%)	0.285 *
			MS *Staphylococcus* spp.	19/33 (57.6%)	
[9]	Norway	NS	CoN MRSE	70/98 (71.4%)	<0.001
			CoN MSSE	9/32 (28.1%)	
[10]	Israel	NS	MRSA	9/16 (55.5%)	0.166 *
			MSSA	5/17 (29%)	
[28]	China	Retrospective	ESBL *E. coli*	57/160 (35.6%)	<0.001

			Non ESBL *E. coli*	24/164 (14.6%)	

Notes: *Missing *p*-value from data extraction were calculated; **only High BFP; NS: Not specified; MRSA: Methicillin-resistant *Staphylococcus aureus;* MSSA: Methicillin-susceptible *Staphylococcus aureus;* CoN: Coagulase-negative; MRSE: Methicillin-resistant *Staphylococcus epidermidis;* MSSE: Methicillin-susceptible *Staphylococcus epidermidis;* ESBL: Extended-spectrum beta-lactamase; *E. coli*: *Escherichia coli*.

Table S3. Studies describing in vitro BFP prevalence in isolates from persistent and non-persistent BSI.

Study (Reference)	**Country**	**Study type**	**Microorganism**	**BFP outcome description**	**BFP prevalence** n/N (%)		***p*-value**
					Persistent BSI	Non-persistent BSI	
[30]	Spain	Retrospective cohort	*Candida* spp.	Moderate/high metabolic activity	27/30 (90.0%)	131/177 (74.0%)	0.064
[31]	Greece	Prospective	CoN *Staphylococci*	BF positive	54/97 (55.7%)	26/73 (35.6%)	0.013
[5]	Spain	Retrospective	*S. aureus*	Only High BFP	16/48 (33.3%)	146/437 (33.4%)	1.000 *
[32]	Taiwan	Retrospective	*Candida* spp.	Only High BFP	41/68 (60.3%)	15/68 (22.1%)	<0.010
[33]	Brazil	Multicenter cohort	*Candida* spp.	Only High BFP	12/37 (32.4%)	1/18 (5.5%)	0.041 *

Notes: *Missing *p*-value from data extraction were calculated; CoN: Coagulase-negative; *S. aureus: Staphylococcus aureus* .

Table S4. Studies describing in vitro BFP prevalence in isolates of BSI survivors and non-survivors.

Study (Reference)	**Country**	**Study type**	**Microorganism**	**Mortality description**	**BFP outcome description**	**BFP prevalence** n/N (%)		***p*-value**
						BSI non-survivors	BSI survivors	
[5]	Spain	Retrospective	*S. aureus*	30-day mortality	Only High BFP	18/55 (32.7%)	144/430 (33.5%)	1.000 *
[34]	Taiwan	Retrospective	*C. meningosepticum*	14-day mortality	BF-positive	13/22 (59.1%)	4/18 (22.2%)	0.019
[11]	Spain	Prospective	*E. coli*	In-hospital	BF-positive	8/20 (40.0%)	71/165 (43.0%)	0.800
[35]	Spain	Retrospective cohort	*Candida* spp.	30-day mortality	Only high BFP	34/95 (35.8%)	56/185 (30.3%)	0.418
[19]	Hungary	Retrospective	*Candida* spp.	30-day mortality	BF-positive	23/43 (53.5%)	20/50 (40%)	0.216 *
[36]	Italy	Retrospective	*C. parapsilosis*	30-day mortality	High and moderate BFP	61/89 (68.5%)	45/101 (44.6%)	0.010

[37]	Italy	Retrospective	*Candida* spp.	In-hospital	BF-positive	39/61 (63.9%)	34/85 (40.0%)	0,010
[38]	Italy	Retrospective cohort	*Candida* spp.	30-day mortality	BF-positive	56/154 (36.3%)	24/140 (17.1%)	<0.001
[39]	Hungary	Retrospective	*Candida* spp.	30-day mortality	High and moderate BFP	59/70 (84.3%)	38/57 (66.7%)	0.023
[28]	China	Retrospective	*E. coli*	30-day mortality	High and moderate BFP	30/71 (42.2%)	51/253 (20.2%)	0.002

Notes: *Missing p-value from data extraction were calculated; C. meningosepticum: Corynebacterium meningosepticum; E. coli: Escherichia coli; C. parapsilosis: Candida parapsilosis.

Table S5. Studies describing in vitro BFP prevalence in isolates from UTI patients.

Study (Reference)	**Country**	**Study type**	**Microorganism**	**BFP prevalence** n/N (%)
[40]	Bangladesh	NS	*Enterococcus* spp.	76/118 (64.4%)
[41]	Iran	NS	*E. coli*	33/35 (94.3%)
[42]	Iran	Cross Sectional	*E. coli*	98/130 (75.4%)
[43]	Iran	Cross Sectional	*E. coli*	74/79 (93.7%)
[44]	Brazil	NS	*E. coli*	80/100 (80.0%)
[45]	Poland	NS	*Enterococci*	81/100 (81%)
[46]	Egypt	NS	*Klebsiella* spp.	54/64 (84.4%)
[47]	India	Prospective	*Enterococcus* spp.	21/50 (42.0%)
[48]	Egypt	NS	*E. coli*	134/175 (76.6%)
[49]	Iran	NS	*E. coli*	200/250 (80.0%)
[50]	Egypt	NS	*E. coli*	89/112 (79.5%)
[51]	Australia	Prospective	*E. coli*	404/623 (64.8%)
[52]	India	NS	*E. coli*	138/150 (92.0%)
[53]	Iran	NS	MR *Staphylococcus* spp.	94/108 (59.3%)
[54]	Iran	Retrospective	*Proteus* spp.	82/88 (93.2%)
[55]	Europe *	NS	*Acinetobacter baumannii*	104/128 (81.3%)

Notes: *5 countries; NS: Not specified; *E. coli*: *Escherichia coli*; MR: Methicillin-resistant.

Table S6. Studies describing in vitro BFP prevalence in resistant and susceptible strains of isolates from UTI patients.

Study (Reference)	Country	Study type	Microorganism	BFP prevalence n/N (%)	*p*-value
[56]	Portugal	Retrospective	MDR *E. coli*	6/21 (28.6%)	0.393 *
			Non MDR *E. coli*	16/79 (20.2%)	
[47]	India	Prospective	VRE	7/17 (41.2%)	1.000 *
			VSE	14/33 (42.4%)	
[48]	Egypt	NS	MDR *E. coli*	129/159 (81.1%)	<0.001
			Non MDR *E. coli*	5/16 (31.3%)	
[50]	Egypt	NS	MDR *E. coli*	56/73 (76.7%)	0.462 *
			Non MDR *E. coli*	33/39 (84.6%)	
[57]	India	NS	MDR *E. coli*	65/88 (73.9%)	0.001
			Non MDR *E. coli*	4/12 (33.3%)	
[58]	Iran	Cross Sectional	MBL *K. pneumoniae*	17/17 (100%) **	0.003
			N-MBL *K. pneumoniae*	61/92 (66.3%) **	
[51]	Australia	Prospective	st131 *E. coli*	125/131 (95.4%)	<0.001
			Non st131 *E. coli*	279/492 (56.7%)	
[59]	Nepal	Cross Sectional	ESBL *E. coli*	53/69 (76.8%)	0.050
			Non ESBL *E. coli*	55/139 (39.6%)	
[53]	Iran	NS	MDR MRSA	60/73 (82.2%)	0.086 *
			Non MDR MRSA	23/35 (65.7%)	
[60]	Nepal	Cross Sectional	MDR *E. coli*	58/120 (48.3%)	0.015
			Non MDR *E. coli*	15/53 (28.3%)	
[61]	Iran	NS	ESBL *E. coli*	68/81 (83.9%)	0.010 *
			Non ESBL *E. coli*	31/48 (64.6%)	
[62]	Nepal	Prospective	MDR *E. coli*	17/23 (73.9%)	0.006 *
			Non MDR *E. coli*	6/21 (28.6%)	
[63]	Nepal	Cross Sectional	ESBL *E. coli*	48/81 (59.3%)	0.205 *
			Non ESBL *E. coli*	38/78 (48.7%)	

Notes: *Missing *p*-value from data extraction were calculated; **only High/moderate BFP; NS: Not specified; MRSA: Methicillin-resistant *Staphylococcus aureus;* ESBL: Extended-spectrum beta-lactamase; *E. coli*: *Escherichia coli*; MDR: Multi-drug resistant; VRE: *Vancomycin-Resistant Enterococci; VSE: Vancomycin-Susceptible Enterococci; MBL: Metallo-Beta-Lactamase; K. pneumoniae: Klebsiella pneumoniae.*

Table S7. Studies describing in vitro BFP prevalence in isolates from CAUTI and UTI non-CAUTI.

Study (Reference)	Country	Study type	Microorganism	BFP prevalence n/N (%)		*p*-value
				CAUTI	UTI non-CA	
[64]	India	Prospective	*E. coli*	34/46 (73.9%)	40/44 (90.9%)	0.052 *
[47]	India	Prospective	*Enterococcus* spp.	9/23 (39.1%)	12/27 (44.4%)	0.779 *
[57]	India	NS	*E. coli*	44/49 (89.7%)	25/51 (49.0%)	<0.001 *
[52]	India	NS	*E. coli*	21/21 (100%)	30/55 (54.5%)	<0.001*
[65]	Nepal	Prospective	Gram (-) bacilli & Gram (+) cocci	53/70 (75.7%)	89/401 (22.2%)	<0.001 *
[66]	Australia	NS	*E. coli*	42/88 (47.7%)	52/88 (59.1%)	0.174

Notes: Only BF-positive; *Missing *p*-value from data extraction were calculated; *E. coli*: *Escherichia coli;* Gram (-): Gram-negative; Gram (+): Gram-positive.

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