# The Impact of Bacteriospermia on Semen Parameters: A Meta-Analysis

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# Abstract

Objective: To evaluate the impact of bacteriospermia on semen parameters.

**Materials and methods:** We used the Medline (1966-2017), Scopus (2004-2017), Clinicaltrials.gov (2008-2017), EMBASE, (1980-2017), LILACS (1985-2017) and Cochrane Central Register of Controlled Trials *CENTRAL* (1999-2017) databases in our primary search along with the reference lists of electronically retrieved full-text papers. Meta-analysis was performed with the RevMan 5.3 software. **Results:** Eighteen studies were finally included. Men were stratified in two groups, healthy controls (5,797 men) and those suffering from bacteriospermia (3,986 men). Total sperm volume was not affected by the presence of bacteriospermia when all pathogens were analyzed together (MD 0.02 95%Cl -0.13,0.17). Both sperm concentration (MD -27.06, 95% Cl -36.03, -18.08) and total sperm count (MD -15.12, 95% Cl -21.08, -9.16) were significantly affected by bacteriospermia. Decreased rates of normal sperm morphology were also found (MD -5.43%, 95% Cl -6.42, -4.44). The percentage of alive sperm was significantly affected by bacteriospermia (MD - 3.64, 95% Cl -6.45, -0.84). In addition to this, progressive motility was also affected by bacteriospermia (MD - 12.81, 95% Cl -18.09, -7.53). Last but not least, pH was importantly affected (MD 0.03, 95% Cl 0.01, 0.04).

**Conclusion:** Bacteriospermia significantly affects semen parameters and should be taken in mind even when asymptomatic. Further studies should evaluate the impact of antibiotic treatment on semen parameters and provide evidence on fertility outcome.

Keywords: Sperm; Semen; Infection; Fertility; Bacteriospermia; Meta-Analysis

### Introduction

Bacteriospermia is diagnosed when bacteria in the ejaculate exceed 1000 cfu/ml (1). It is usually the result of acute or chronic bacterial infections and is regarded as a major health care problem which has a negative impact on male fertility (1-3). Specifically, it has been

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shown that approximately 15% of infertile men have significant number of bacterial pathogens in the sperm (1). Bacterial infections may affect various sites of the male genitourinary system, such as the prostate, the epididymis, the testis and the urethra (1, 3). The most common isolated pathogenic bacteria are Escherichia Coli, Chlamydia trachomatis, Ureaplasmaurealyticum, Mycoplasma, Staphylococci, Streptococci and Enterococcus faecalis (1, 4).On the other hand, the male urinary system is not completely sterile as it has been

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already shown that certain bacteria, such as Staphylococcus epidermidis, are identified in otherwise healthy reproductive men (4). The impact of different bacteria on sperm quality remains to date unknown (5).

The last decades, the constantly increasing population of infertile couples, has turned scientific interest towards the investigation of the impact of bacteriospermiaon male reproductive ability (6). Various pathophysiologic mechanisms have been investigated confirm correlation to the ofbacteriospermia with seminal parameters, including motility and vitality (7). It is speculated that both the direct bacterial interaction and the participation of the immune competent cells influence spermatogenesis, impair semen function and obstruct the urogenital tract (7, 8). However, the actual impact of each pathogen on seminal parameters remains unknown.

The purpose of our meta-analysis is to accumulate current knowledge in the field and to provide recommendations for clinical practice, as well as new scientific targets for the future.

# Materials and methods

Study design: We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to design this systematic review (9). Eligibility criteria were predetermined by the authors. Language and date restrictions were avoided during the literature search. All observational studies (both prospective and retrospective, randomized and non-randomized) that reported the impact of bacteriospermia (irrespective of the pathogen) on seminal parameters were held eligible for inclusion and tabulation. Case reports and review articles were excluded. Animal studies were also excluded.

The study selection took place in three consecutive stages. In the first stage, two researchers (VP, NK) independently reviewed the titles and/or abstracts of all electronic articles to assess their eligibility. Next, the articles that met or were presumed to meet the criteria for inclusion in the present meta-analysis were retrieved in full text. During the third stage, two authors (NK, PK) tabulated the selected indices in structured forms. Potential disagreements in the evaluation of the methodological quality, retrieval of articles, and statistical analysis were resolved after discussing with the remaining authors.

*Literature search and data collection:* We used the Medline (1966-2017), Scopus (2004-2017), Clinicaltrials.gov (2008-2017), EMBASE, (1980-2017), LILACS (1985-2017) and Cochrane Central Register of

Controlled Trials *CENTRAL* (1999-2017) databases in our primary search along with the reference lists of electronically retrieved full-text papers. The date of our last search was set at 31<sup>st</sup>December, 2017. Search strategies and results are shown in Figure 1.

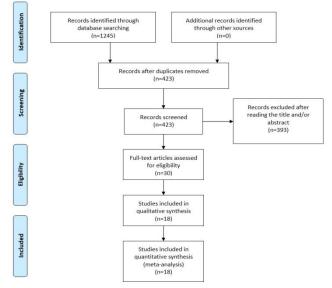


Figure 1: Search plot diagram

Our search strategy included the words semen; sperm; bacteria; bacteriospermia; infection; ureaplasma; mycoplasma; Neisseria; chlamydia; gardnerella; Escherichia coli; streptococcus. The PRISMA flow diagram schematically presents the stages of article selection (Figure 1).

*Quality assessment:* We assessed the methodological quality of all included studies using the Oxford Level of Evidence criteria and the GRADE list (10).

Statistical analysis: Statistical meta-analysis was performed with the RevMan 5.3 software (Copenhagen: The Nordic *Cochrane Centre*, The Cochrane Collaboration, 2011). Confidence intervals were set at 95%. We calculated pooled odds ratios (OR), mean differences (MD) and 95% confidence intervals (CI) with the DerSimonian-Laird random effect model due to the significant heterogeneity of included studies (11). Similarly, publication bias was not tested due to the small number of studies and their gross heterogeneity (significant confounders that may influence the methodological integrity of these tests) (12).

Analyzed indices and subgroup analysis: The analyzed indices were tabulated in structured forms, which included significant sperm characteristics, such as sperm volume, Ph, total sperm count, concentration, normal morphology, total motile sperm count, progressive and total motility, sperm vitality and WBC. Subgroup analysis according to the type of pathogen was performed.

# Results

Table 1: Study characteristics

*Excluded studies:* Twelve studies were excluded from the present meta-analysis as they either did not include a control group of infertile men or did not investigate the outcomes of interest (13-24).

Included Studies: Eighteen studies were finally

included (25-42). Men were stratified in two groups, healthy controls (5,797 men) and those suffering from bacteriospermia (3,986 men). In the latter group, 858 patients suffered from mixed bacterial infection, 204 from Chlamydia trachomatis, 640 from Mycoplasma, 2,255 from Ureaplasma Urealyticum, 5 from Ureaplasma Parvum and 24 from Gardnerella vaginalis. The majority of available evidence was drawn from studies of low quality (Level of Evidence 2b and 3b – Table 1).

	Trmo of study	CDADE	Indución oritorio
Date; author	Type of study		Inclusion criteria
1985; Grizard	Prospective	2b	Men with significant bacteriospermia were included in the study. None of them had
G. et al	cohort		any clinical or gormonal abnormalities.
1997; Bussen	Prospective	2b	Men who consecutively entered the IVF program of the clinic during a seven-month
S.	cohort		period in 1995 were included in the study. None of these patients had symptoms of
			genital tract infection or were treated with antibiotics 4 weeks before the treatment cycle.
2003; L.Knox	Prospective	2b	Male partners from couples who participated in an assisted reproductive technology
C.	cohort		(ART) treatment cycle were included inb the study.
2003; Rodin	Prospective	2b	Asymptomatic men who were undergoing infertility evaluation were included in the
M.D.	cohort	20	study.
2004:	Prospective	2b	Men who attended the University Research Clinic (Jessop Hospital for Women,
		20	
Hosseinzadeh	cohort		Sheffield, United Kingdom) for diagnostic semen analysis. All men were undergoing
S.			semen analysis as a part of a work-up for infertility suggestions after failing to
2005 0 1	D (	01	conceive with their partner after one year of unprotected intercourse.
2005; Sanocka-	Prospective	2b	Men with or without genital tract infection were included in the study. Men had no
Maciejewska	cohort		ability to conceive for at least 2 years of sexual intercourse.
2005; Motrich	Prospective	2b	Men with Chronic Prostatitis Syndrome, whose age was 20-50 years, were included in
R.D.	cohort		the study.
2006; De	Prospective	2b	Men from couples who were undergoing an IVF program between January 1998 and
Barbeyrac B,	cohort		November 2001 were included in the study. Men were between 18 and 55 years old
			and they didn't have azoospermia.
2006; Wang Y.	Prospective	2b	Men aged 20-45 years who attended the andrology clinic in Shanghai Tonghi Hospital
et al	coĥort		and SanghaiRenji Hospital from March 1, 2001 to March 1, 2003 were included in the
			study. All men did not present any reproductive abnormalities and had not received any
			antibiotic treatment.
2008; Gdoura	Prospective	2b	Men who were attending obstetrics and gynecology clinics in Sfax for infertility were
R. et al	cohort		included in the study. All patients did not present any clinical symptoms of genital tract
			infections except for their infertility health problem.
2009; Andrade-	Prospective	2b	Men who had history of infertility for at least one year and had never received
Rocha	cohort		antibiotic treatment before semen analysis were considered as the patient group.
2009; Gallegos	Prospective	2b	Men from couples who were attending the andrology infertility clinic with diagnosed
– Avila G. et al	cohort		genitourinary infection from Chlamydia trachomatis and Mycoplasma were included in
			the study. The age of men ranged from 25-51 years.
2009; A El feky	Case control	3b	Men with leycocytospermia, who were attending the out- patient infertility clinic in the
2009, 11 Er leky	Cuse control	50	department of Dermatology, Venereology and Andrology, Assiut University Hospital
			during June 2007 to May 2008, were included in the study. Their age ranged from 24
			to 49 years old.
2010 Kokab A.	Prospective	2b	Consecutive men who were attending the Avesina Research Institute in Tehran, Iran
et al	cohort	20	for diagnostic semen analysis were included in the study. All men were undergoing
ct ai	conort		semen analysis as a part of a work-up for infertility investigations with their partner
			after failing to conceive after 1 year of unprotected intercourse. None of them reported
			any symptoms of genital tract infections.
2011; De	Retrospective	2b	Men who were referred to the Microbiology Laboratory Group of Brescia's main hospital
Francesco	cohort	20	for semen analysis, as a part of infertility work-up were included in the study. Patients
M.A.	conort		had visited the clinic between 1 January 2004 and 31 December 2008.
2012; Rybar R.	Drognostiva	2b	Men with no urogenital tract discomfort with a minimum sexual abstinence of 2 days
	Prospective	20	
et al	cohort	2b	were included in the study. Male pertners from infortile couples without female factor subfartility and without
2013; Lee J.S.	Prospective	20	Male partners from infertile couples without female factor subfertility and without
2015, Uuana C	study	25	reproductive or hormonal abnormalities were included in the study.
2015; Huang C.	Prospective	2b	Men of infertile couples who visited the Reproductive Center, the Reproductive and
et al	study		Genetic Hospital of CITIC, Xiangya, China, from January to December 2014 were
			included in the study. The men had failed to impregnate their wives after at least one
			year of unprotected intercourse.

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		fected			Control		0.200	Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Mixed Infection									80
1985; Grizard	3.6	0.3	36	3.9	0.2	22	8.0%	-0.30 [-0.43, -0.17]	*
2005; Maciejewska	2	0.8	39	2.9	0.7	30	5.8%	-0.90 [-1.25, -0.55]	
2005; Motrich et al	2.96	0.56	11	2.57	0.28	15	5.7%	0.39 [0.03, 0.75]	
2011 ; De Francesco M.A.	2.9	1.5	156	3.32	1.6	36	3.8%	-0.42 [-0.99, 0.15]	
2015; Huang	2.95	1.17	343	3.17	1.67	3368	7.9%	-0.22 [-0.36, -0.08]	-
Subtotal (95% CI)			585			3471	31.2%	-0.28 [-0.55, -0.01]	•
Heterogeneity: Tau <sup>2</sup> = 0.07;	$Chi^2 = 2$	6.02, c	f = 4 (F	< 0.00	01); I <sup>2</sup> =	85%			
Test for overall effect: Z = 2.	03 (P = (	0.04)							
1.1.2 Mycoplasma Hominis									
2011; Rybar	4.7	2.1	26	3.5	1.7	173	2.3%	1.20 [0.35, 2.05]	
2013; Lee J.S. et al	3.2	1.4	10	2.8	1	88	2.2%	0.40 [-0.49, 1.29]	
2015; Huang		1.86	604		1.67	3368	7.7%	0.36 [0.20, 0.52]	-
Subtotal (95% CI)	0.00	1.00	640		1.010	3629	12.2%	0.54 [0.08, 1.00]	-
Heterogeneity: Tau <sup>2</sup> = 0.09;	$Chi^2 = 3$	66 df		= 0.16)	F = 459				
Test for overall effect: Z = 2.			20.	0.10),	+5	~~~			
1.1.3 Ureaplasma Urealytic	cum								
2006; Wang		0.14	136	3.42	0.15	210	8.4%	-0.25 [-0.28, -0.22]	
2007; Gdoura		0.33	18	3.41		102	7.8%	-0.39 [-0.55, -0.23]	-
2011; Rybar	4.1	1.4	41	3.5	1.7	173	4.4%	0.60 [0.10, 1.10]	
2013; Lee J.S. et al	3.1	1.4	36	3.4	1.4	62	3.8%	-0.30 [-0.87, 0.27]	
2015; Huang			1951		1.67	3368	8.2%	0.10 [0.00, 0.20]	-
Subtotal (95% CI)	0.21		2182	0.11	1.01	3915	32.6%	-0.09 [-0.33, 0.14]	•
Heterogeneity: Tau <sup>2</sup> = 0.05;	Chi <sup>2</sup> = 6	2.02.0		≪ 0.00	0011				-
Test for overall effect: Z = 0.		and the second	a – 4 (i	0.00	0017,1	- 54%			
1.1.4 Chlamydia trachoma	tis								
2004; Hosseinzadeh	3.45	1.52	31	2.93	1.38	611	4.0%	0.52 [-0.03, 1.07]	
2005; Motrich et al	3.58	1.39	4	2.57	0.28	15	1.1%	1.01 [-0.36, 2.38]	
2006; De Barbeyrac	3.5	1.4	40	3.8	1.8	191	4.4%	-0.30 [-0.80, 0.20]	
2009; Feky	2.85	1.67	75	2.54	0.68	25	4.7%	0.31 [-0.15, 0.77]	++
2010; Kokab	2.9	1.4	16	3.2	1.4	239	3.0%	-0.30 [-1.01, 0.41]	
2011; Rybar	3.8	1.9	38	3.5	1.7	173	3.3%	0.30 [-0.36, 0.96]	
Subtotal (95% CI)			204			1254	20.5%	0.17 [-0.17, 0.50]	*
Heterogeneity: Tau <sup>2</sup> = 0.07;			= 5 (P :	= 0.13);	I <sup>2</sup> = 429	%			
Test for overall effect: Z = 0.	98 (P = (	J.33)							
1.1.6 Ureaplasma parvum									
2007; Gdoura Subtotal (95% Cl)	4.38	0.73	5 5	3.31	0.15	115 115	3.4% 3.4%	1.07 [0.43, 1.71] 1.07 [0.43, 1.71]	•
Heterogeneity: Not applicab	le								
Test for overall effect: Z = 3.		0.001)							
Total (95% CI)			3616			12384	100.0%	0.02 [-0.13, 0.17]	•
Heterogeneity: Tau <sup>2</sup> = 0.07;	Chi <sup>2</sup> = 1	84.07.	df = 19	(P < 0.)	00001)	I <sup>2</sup> = 90	%	3	-2 -1 0 1 2
Test for overall effect: $Z = 0$ .				8		3			
Test for subgroup difference			6 df	4 (P = 0)	0002)	I <sup>2</sup> = 81 -	1%		Favours control Favours infected

**Figure 2:** Mean differences of total sperm volume according to presence of bacteriospermia. The overall effect was not statistically significant (p = 0.80). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% CI).

**Outcomes:** Total sperm volume was not affected by the presence of bacteriospermia when all pathogens were analyzed together (MD 0.0295%CI -0.13,0.17, Figure 2). However, mixed infection, Mycoplama hominis and Ureaplasmaparvum may be associated with decreased volume (evidence from eight studies). A significant increase of pH was observed (MD 0.03 95%CI 0.01, 0.04, Figure 3).

Both sperm concentration (MD -27.06, 95% CI -36.03, -18.08, Figure 4) and total sperm count (MD -15.12, 95% CI -21.08, -9.16, Figure 5) were significantly affected by bacteriospermia. Decreased rates of normal sperm morphology were also found (MD -5.43%, 95% CI -6.42, -4.44, Figure 6). The percentage of alive sperm was also affected by bacteriospermia (MD -4.39 %, 95% CI -8.25, -0.53,

### Figure 7).

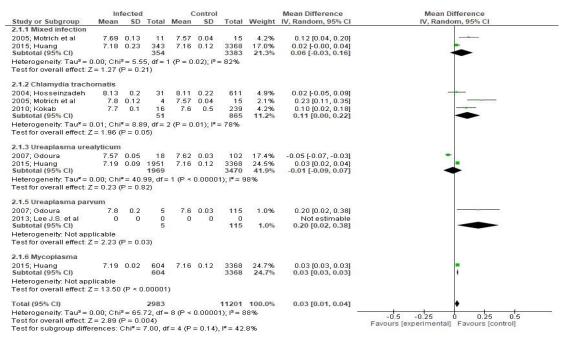
The assessment of motility parameters revealed that total motility was quite affected by bacteriospermia (MD -3.64, 95 CI -6.45, - 0.84 Figure 8). Moreover, progressive motility was alsoaffected significantly (MD -12.81, 95% CI -18.09, -7.53, p < 0.001 Figure 9) an effect that was not, however, evident in patients with Ureaplasma infection.

*Sensitivity analysis:* The findings of the sensitivity analysis did not significantly affect the aforementioned results.

### Discussion

Both acute and chronic infections of the genitourinary tract are considered significant causative factors in male infertility (4).

#### Bacteriospermia on Semen Parameters



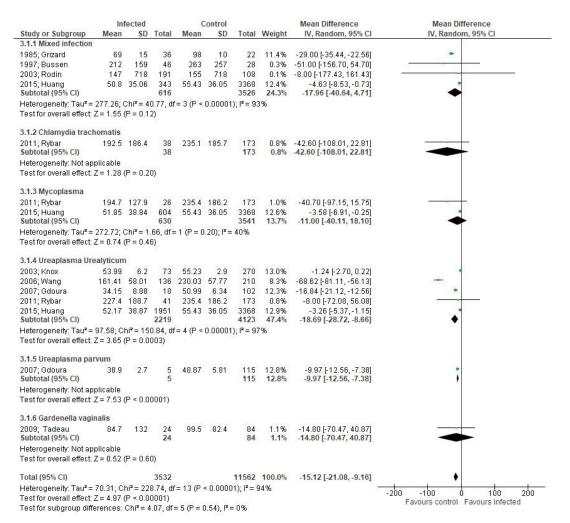
**Figure 3:** Mean differences in pH according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% Cl).

The effect of bacteriospermia in semen quality is not fully understood as the accurate pathophysiologic impact of the various bacteria in semen parameters remains vague (7).

	In	fected			Control			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.1.1 Mixed infection									
1997; Bussen	68.4	59.6	46	77.4	79	28	4.3%	-9.00 [-42.95, 24.95]	
2005; Maciejewska	8	2	39	63	50	30	7.6%	-55.00 [-72.90, -37.10]	
2005; Motrich et al	40.4	11.7	11	64	13.2	15	9.7%	-23.60 [-33.21, -13.99]	-
2008; Galleggos	44.06	24.33		74.71	33.63	50	9.6%	-30.65 [-40.79, -20.51]	and the second se
2011 ; De Francesco M.A. Subtotal (95% Cl)	55	66.1	156 395	116.5	68.3	36 159	6.0% 37.1%	-61.50 [-86.10, -36.90] -36.28 [-50.85, -21.71]	•
Heterogeneity: Tau <sup>2</sup> = 186.	74; Chi <sup>2</sup> =	= 16.62,	df = 4	(P = 0.0)	02); I <sup>2</sup> =	76%			
Fest for overall effect: Z = 4	.88 (P < 0	0.00001	)						
I.1.2 Chlamydia trachoma	itis								
2004; Hosseinzadeh		48.67	31		50.45	611	7.7%	-2.80 [-20.39, 14.79]	
2005; Motrich et al		14.56	4	64	0	15		Not estimable	
2006; De Barbeyrac	50.7	51.2	40	45.5	48.4	191	7.8%	5.20 [-12.09, 22.49]	-
2009; Feky		24.24	75		28.51	25	9.0%	-39.74 [-52.19, -27.29]	
2010; Kokab	110	68.8	16		102.7	239	3.9%	-10.00 [-46.14, 26.14]	
2011; Rybar	192.5	186.4	38	235.1	185.7	173	1.6%	-42.60 [-108.01, 22.81]	
Subtotal (95% CI)			204			1254	30.0%	-15.13 [-38.37, 8.10]	-
Heterogeneity: Tau² = 499. Test for overall effect: Z = 1			df = 4	(P = 0.0	002); I²:	= 82%			
4.1.3 Mycoplasma									
2011; Rybar	44.5	28.8	26	69.5	48.2	173	8.8%	-25.00 [-38.20, -11.80]	
2013; Lee J.S. et al Subtotal (95% CI)	115.7	97.9	10 36	229.5	101.6	88 261	1.7% 10.5%	-113.80 [-178.08, -49.52] + -63.60 [-149.87, 22.68]	
Heterogeneity: Tau <sup>2</sup> = 3382 Test for overall effect: Z = 1			df = 1	(P = 0.0	08); I² =	86%			
4.1.4 Ureaplasma Urealyti	cum								
2006; Wang		23.14		70.58		210	10.5%	-36.54 [-41.52, -31.56]	*******
2011; Rybar	55.1	37.9	41	69.5	48.2	173	8.7%	-14.40 [-28.04, -0.76]	
2013; Lee J.S. et al Subtotal (95% CI)	120.3	103.1	36 213	118.9	96.9	62 445	3.3% 22.5%	1.40 [-40.02, 42.82] -21.84 [-42.52, -1.17]	•
Heterogeneity: Tau² = 239.) Test for overall effect: Z = 2			df = 2	(P = 0.0	03); I²=	83%			
Total (95% CI)			848			2119	100.0%	-27.06 [-36.03, -18.08]	•
Heterogeneity: Tauª = 192. Test for overall effect: Z = 5 Test for subgroup differenc	.91 (P < 0	0.00001	)	1			%	100	-100 -50 0 50 100 Favours control Favours infected

**Figure 4:** Mean differences of sperm concentration according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% Cl).

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**Figure 5:** Mean differences of total sperm count according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% Cl).

To date, to our knowledge, no previous metaanalyses in the field have been undertaken. In our meta-analysis we sought to gather all available evidence from the international literature to evaluate the influence of bacteriospermia in semen quality and male infertility.

According, to our findings significantly decreased rates have been found in several parameters such as total sperm concentration, total sperm count, normal morphology and progressive motility.

During the last decades, several studies have investigated the contribution of male factor and especially the role of bacteriospermia in couples' infertility. Both symptomatic and asymptomatic bacteriospermia is associated with both acute and chronic inflammation of the genitourinary tract. Specifically, inflammatory mediators, such as cytokines and reactive oxygen species, restrain the normal function of Sertoli cells leading to restricted spermatogenesis and unsuccessful acrosome reaction. As a consequence, many couples due to various unsuccessful efforts of automatic pregnancy, are led to in vitro fertilization. However, because of reduced inducibility of acrosome reaction, in vitro fertilization efforts often fail (43). Thus, appropriate antibiotic treatment, according to Bieniek et al., is necessary to improve semen characteristics and reduce couple subfertility rates.

*Implications for current clinical practice and future research:* According to the findings of the present systematic review, bacteriospermia clearly affects several semen parameters.

#### Bacteriospermia on Semen Parameters

		fected			Control	-		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
5.1.1 Mixed	1222	192	6000	12983	12	5533/cr	10000-007		
1985; Grizard	48	2	36	64	2	22		-16.00 [-17.06, -14.94]	· · · · · · · · · · · · · · · · · · ·
1997; Bussen	42.1	17.6	46	41.5	14.5	28	1.4%	0.60 [-6.80, 8.00]	
2003; Rodin	128	539	191	130	539	108	0.0%	-2.00 [-129.19, 125.19]	•
2005; Maciejewska	11	3	39	39	7	30	4.5%	-28.00 [-30.68, -25.32]	
2005; Motrich et al	21	4.9	11	37.5	1.8	15	4.1%	-16.50 [-19.54, -13.46]	
2008; Galleggos	18.15	5.38	143	32.11	3.68	50	6.0%	-13.96 [-15.31, -12.61]	
2011 ; De Francesco M.A.	35.9	18.8	156	55.8	7.5	36	3.3%	-19.90 [-23.73, -16.07]	
2015; Huang	4.79	1.72	343	6.79	1.72	3368	6.7%	-2.00 [-2.19, -1.81]	
Subtotal (95% CI)	4.10	1.72	965	0.75	1.7.4	3657	32.2%	-13.80 [-21.61, -6.00]	
Heterogeneity: Tau <sup>2</sup> = 108.2 Test for overall effect: Z = 3.4			38, df =	7 (P < (	0.00001)	; I² = 10			
5.1.2 Chlamydia trachomat	tie								
Company of Charles and the Cha		10.10	24	47.04	10.10	044	0.50	4 05 / 4 70 5 000	
2004; Hosseinzadeh		10.18	31		10.42	611	3.5%	1.95 [-1.73, 5.63]	State State State
2005; Motrich et al	28.6	8.9	4	37.5	1.8	15	1.1%	-8.90 [-17.67, -0.13]	
2006; De Barbeyrac	42.9	14.7	40	38	19.8	191	2.3%	4.90 [-0.45, 10.25]	
2009; Feky	53		75	48.75	15.71	25	1.6%	4.25 [-2.51, 11.01]	A01. 00 00
2010; Kokab	32.6	9.3	16	28	11.9	239	2.6%	4.60 [-0.20, 9.40]	
2011; Rybar	23.3	10.9	38	22.4	13.7	173	3.2%	0.90 [-3.12, 4.92]	
Subtotal (95% CI)			204			1254	14.2%	2.08 [-0.72, 4.88]	◆
Heterogeneity: Tau <sup>2</sup> = 5.12; Fest for overall effect: Z = 1.4			= 5 (P =	0.11); P	<sup>2</sup> = 44%				
5.1.3 Mycoplasma									
2011; Rybar	16.8	11.7	26	22.4	13.7	173	2.5%	-5.60 [-10.54, -0.66]	
2013; Lee J.S. et al	6.7	4	10	8.1	6.7	88	4.3%	-1.40 [-4.25, 1.45]	
2015, Lee 5.5. et al 2015: Huang	6.45	1.41	607	6.79	1.72	3368	6.7%	-0.34 [-0.47, -0.21]	
Subtotal (95% CI)	0.40	1.41	643	0.79	1.72	3629	13.5%	-1.43 [-3.65, 0.79]	•
Heterogeneity: Tau <sup>2</sup> = 2.29; Test for overall effect: Z = 1.:			2 (P =	0.09); P	<b>*</b> = 59%				
5.1.4 Ureaplasma Urealytic	um								
2003; Knox	12.84	0.7	73	13.33	0.6	270	6.7%	-0.49 [-0.67, -0.31]	-
2006; Wang	53.46	3.21	136	55.45	2.21	210	6.5%	-1.99 [-2.61, -1.37]	-
2007; Gdoura	10.07	1.69	18	14.05	1.22	102	6.4%	-3.98 [-4.80, -3.16]	+
2011: Rybar	20.4	13.8	41	22.4	13.7	173	2.7%	-2.00 [-6.69, 2.69]	
2013; Lee J.S. et al	6.8	4.4	36	6.7	3.9	62	5.6%	0.10 [-1.63, 1.83]	-
2015; Huang Subtotal (95% Cl)	4.38	1.52	1951 2255	6.79	1.72	3368 4185	6.7% 34.5%	-2.41 [-2.50, -2.32] -1.84 [-3.02, -0.67]	
Heterogeneity: Tau <sup>2</sup> = 1.71; Test for overall effect: Z = 3.1				P < 0.00	001); l² =		54.57	-1.04 [-3.02, -0.07]	•
5.1.5 Ureaplasma parvum									
2007; Gdoura Subtotal (95% CI)	12.5	6.91	5	13.54	1.1	115 115	1.9% 1.9%	-1.04 [-7.10, 5.02] -1.04 [-7.10, 5.02]	-
Heterogeneity: Not applicab Test for overall effect: Z = 0.3		0.74)							
5.1.6 Gardenella Vaginalis									
2009; Tadeau Subtotal (95% CI)	7.6	7.4	24 24	16	8.7	84 84	3.6% 3.6%	-8.40 [-11.90, -4.90] -8.40 [-11.90, -4.90]	<b></b>
Heterogeneity: Not applicab Fest for overall effect: Z = 4.7		0.00001	)						
Fotal (95% CI)			4096			12024	100.0%	-5.43 [-6.42, -4.44]	•
				(D	00004			-3.43 [-0.42, -4.44]	<b>X</b>
Heterogeneity: Tau <sup>2</sup> = 3.81; Test for overall effect: Z = 10 Test for subgroup difference	).75 (P <	0.0000	1)	No. waxa	1.1				-20 -10 0 10 20 Favours [experimental] Favours [control]

**Figure 6:** Mean differences in normal sperm morphology according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% CI).

However, the impact of the various bacteria seems to differ. The clinical symptomatology does not necessarily correlate with the severity of these symptoms, as mild pathogens such as mycoplasma spp. may lead to significant alterations. Given these, clinicians should perform routine semen cultures when evaluating infertile couples and treat potential infections, despite the lack of substantial evidence for the effect of antibiotics on semen parameters.

Taking in mind the gaps in current literature, we strongly believe that future studies are needed to determine clearly the accurate impact of symptomatic or asymptomatic bacteriospermia in semen characteristics and to evaluate the effect of the various bacteria. Furthermore, given the lack of clinical data in the field of antibiotic treatment and fertility outcomes, future randomized trials will help us to evaluate the impact of the various antibiotics and compare them to placebo.

Strengths and limitations of the study: Our study is based in a meticulous review of the current literature as we investigated thoroughly the majority of electronic databases and the grey literature. However, selection bias partially limits interpretation of our findings as the majority of included studies did not use data from the general population, but rather couples attending IVF centers; hence, it remains unclear whether the actual differences reflect the truth in the general population.

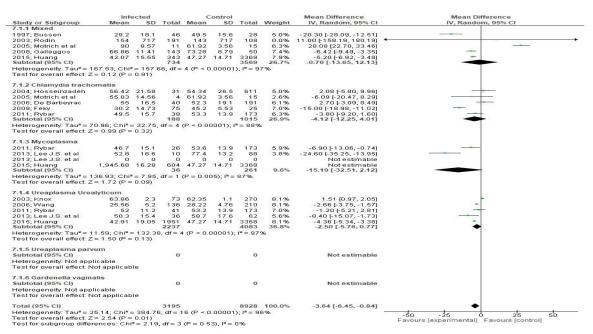
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	le.	fected			Control			Mean Difference	Mean Difference
Study or Subgroup	Mean		Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
5.1.1 Mixed									
1985; Grizard	48	2	36	64	2	22	6.2%	-16.00 [-17.06, -14.94]	+
1997: Bussen	42.1	17.6	46	41.5	14.5	28	1.4%	0.60 [-6.80, 8.00]	100 100 100 100 100 100 100 100 100 100
2003; Rodin	128	539	191	130	539	108	0.0%	-2.00 [-129.19, 125.19]	• •
2005; Maciejewska	11	з	39	39	7	30	4.5%		
2005; Motrich et al	21	4.9	11	37.5	1.8	15	4.1%		
2008; Galleggos	18.15	5.38	143	32.11	3.68	50	6.0%	-13.96 [-15.31, -12.61]	
2011 ; De Francesco M.A.	35.9	18.8	156	55.8	7.5	36	3.3%	-19.90 [-23.73, -16.07]	
2015; Huang Subtotal (95% CI)	4.79	1.72	343	6.79	1.72	3368 3657	6.7% 32.2%	-2.00 [-2.19, -1.81] -13.80 [-21.61, -6.00]	· ·
Heterogeneity: Tau <sup>#</sup> = 108.: Test for overall effect: Z = 3.			88, df=	7 (P < 0	1.00001)	; I≊ = 101	0%		
5.1.2 Chlamydia trachoma	tis								
2004; Hosseinzadeh		10.18	31	17.21	10.42	611	3.5%	1,95 [-1,73, 5,63]	
2005: Motrich et al	28.6	8.9	4	37.5	1.8	15	1.1%	-8.90 [-17.67, -0.13]	
2006; De Barbeyrac	42.9	14.7	40	38	19.8	191	2.3%	4.90 [-0.45, 10.25]	
2009; Feky	53	12.35	75	48.75	15.71	25	1.6%	4.25 [-2.51, 11.01]	200 - CO - CO
2010; Kokab	32.6	9.3	16	28	11.9	239	2.6%	4.60 [-0.20, 9.40]	
2011; Rybar	23.3	10.9	38	22.4	13.7	173	3.2%	0.90 [-3.12, 4.92]	
Subtotal (95% CI)			204			1254	14.2%	2.08 [-0.72, 4.88]	
Heterogeneity: $Tau^{z} = 5.12$ ; Test for overall effect: $Z = 1$ .			5 (P =	0.11); P	= 44%				
5.1.3 Mycoplasma									
2011; Rybar	16.8	11.7	26	22.4	13.7	173	2.5%	-5.60 [-10.54, -0.66]	
2013; Lee J.S. et al	6.7	4	10	8.1	6.7	88	4.3%	-1.40 [-4.25, 1.45]	and the second sec
2015; Huang	6.45	1.41	607	6.79	1.72	3368	6.7%	-0.34 [-0.47, -0.21]	
Subtotal (95% CI)			643			3629	13.5%	-1.43 [-3.65, 0.79]	
Heterogeneity: Tau <sup>a</sup> = 2.29; Test for overall effect: Z = 1.			2 (P =	0.09); 1	'= 59%				
5.1.4 Ureaplasma Urealyti	cum								
2003; Knox	12.84	0.7		13.33	0.6	270	6.7%	-0.49 [-0.67, -0.31]	-
2006; Wang	53.46	3.21	136	55.45	2.21	210	6.5%	-1.99 [-2.61, -1.37]	*
2007; Gdoura	10.07	1.69		14.05	1.22	102	6.4%	-3.98 [-4.80, -3.16]	+
2011; Rybar	20.4	13.8	41	22.4	13.7	173	2.7%	-2.00 [-6.69, 2.69]	Concerning of the second se
2013; Lee J.S. et al	6.8	4.4	36	6.7	3.9	62	5.6%	0.10 [-1.63, 1.83]	+
2015; Huang	4.38	1.52	1951	6.79	1.72	3368	6.7%	-2.41 [-2.50, -2.32]	
Subtotal (95% CI)			2255			4185	34.5%	-1.84 [-3.02, -0.67]	•
Heterogeneity: Tau <sup>2</sup> = 1.71; Test for overall effect: Z = 3.			11 = 5 (H	< 0.00	001); 1-=	99%			
5.1.5 Ureaplasma parvum									
2007; Odoura Subtotal (95% CI)	12.5	6.91	5	13.54	1.1	115	1.9%	-1.04 [-7.10, 5.02] -1.04 [-7.10, 5.02]	-
Heterogeneity: Not applical Test for overall effect: Z = 0.		0.74)							
5.1.6 Gardenella Vaginalis									
2009; Tadeau Subtotal (95% CI)	7.6	7.4	24	16	8.7	84	3.6%	-8.40 [-11.90, -4.90] -8.40 [-11.90, -4.90]	<b></b>
Heterogeneity: Not applicat Test for overall effect: Z = 4		0.00001	)						
Total (95% CI)			4096			12924	100.0%	-5.43 [-6.42, -4.44]	•
Heterogeneity: Tau <sup>2</sup> = 3.81;	$Chi^2 = 2$	521.00,	df = 24	(P < 0.1	00001);	= 99%			-20 -10 0 10 20
Test for overall effect: Z = 1 Test for subgroup differenc	0.75 (P <	0.0000	1)						Favours [experimental] Favours [control]

**Figure 7:** Mean differences in percentage of alive cells according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% CI).

# Conclusion

Bacteriospermia seems to deteriorate semen parameters from normal values. However, current data are very limited as well as our understanding on the impact of antibiotic therapy on semen values. Future studies should focus on the impact of the various bacteria to corroborate our findings and enhance our knowledge in the pathophysiology and treatment of male infertility.



**Figure 8:** Mean differences in sperm motility according to presence of bacteriospermia. The overall effect was statistically significant (p < 0.01). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% Cl).

#### Bacteriospermia on Semen Parameters

Chudu an Culantaun		fected	Tetal		Control		Mainhe	Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Contractor Contractor Contractor		12	20	74	40	20	0.00	63.001.67.03 50.401	2010 C
2005; Maciejewska 2011 ; De Francesco M.A.	8	4	39 156	71	13 12.7	30 36	9.3%	-63.00 [-67.82, -58.18]	-
2015: Huang	34.7	18.9 12.65		52.6 28.77		3368	9.2% 10.0%	-17.90 [-23.00, -12.80] -6.95 [-8.36, -5.54]	
ubtotal (95% CI)			538			3434	28.4%	-29.24 [-62.53, 4.05]	
Heterogeneity: Tau² = 860.8 Fest for overall effect: Z = 1.3			8, df = 2	? (P < 0.	00001)	; I² = 10	0%		
3.1.2 Gardenella vaginalis									
2009; Feky Subtotal (95% CI)	24	15.9	75 75	46.5	12.3	25 25		-22.50 [-28.52, -16.48] -22.50 [-28.52, -16.48]	•
Heterogeneity: Not applicab Fest for overall effect: Z = 7.3		0.00001	)						
3.1.3 Chlamydia trachomat	is								
2010; Kokab Subtotal (95% CI)	32.7	20	16 16	43.4	18	239 239	7.3% 7.3%	-10.70 [-20.76, -0.64] -10.70 [-20.76, -0.64]	•
Heterogeneity: Not applicab Fest for overall effect: Z = 2.0		0.04)							
3.1.4 Ureaplasma Urealytic	um								
007; Gdoura	31.43	3.12	18	30.16	1.34	102	9.9%	1.27 [-0.19, 2.73]	+
013; Lee J.S. et al	45.8	15.5	36	53.3	16.7	62	8.7%	-7.50 [-14.05, -0.95]	
:015; Huang Subtotal (95% CI)	24.55	13.91	1951 2005	28.77	13.5	3368 3532	10.0% 28.6%	-4.22 [-4.99, -3.45] -2.85 [-7.52, 1.82]	•
Heterogeneity: Tau² = 14.24 Fest for overall effect: Z = 1.3			lf = 2 (F	P ≤ 0.00	001); P	95%			
3.1.5 Ureaplasma parvum									
2007; Gdoura Subtotal (95% CI)	29	4.3	5	30.4	1.27	115 115	9.5% 9.5%	-1.40 [-5.18, 2.38] -1.40 [-5.18, 2.38]	*
Heterogeneity: Not applicab Fest for overall effect: Z = 0.7		0.47)							
3.1.6 Mycoplasma									
2013; Lee J.S. et al	48.5	16.6	10	58.2	4.2	88	7.2%	-9.70 [-20.03, 0.63]	
2015; Huang Subtotal (95% CI)	27.98	12.23	604 614	28.77	13.5	3368 3456	10.0% 17.2%	-0.79 [-1.87, 0.29] -3.70 [-11.90, 4.49]	<b>.</b>
Heterogeneity: Tau² = 25.66 Test for overall effect: Z = 0.8			= 1 (P	= 0.09);	I <sup>2</sup> = 65	%			
otal (95% CI)			3253			10801	100.0%	-12.81 [-18.09, -7.53]	•
Heterogeneity: Tau <sup>2</sup> = 72.34 Fest for overall effect: Z = 4.7 Fest for subgroup difference	76 (P < 0	0.00001	)	Al nen reses					-100 -50 0 50 10 Favours [experimental] Favours [control]

**Figure 9:** Mean differences in progressive cell motility according to presence of bacteriospermia. The overall effect was statistically significant (p<.001). (Vertical line = "no difference" point between two groups. Squares = mean differences; Diamonds = pooled mean differences for all studies. Horizontal lines = 95% CI).

# **Conflict of Interests**

Authors have no conflict of interests.

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