

Bacteriospermia – An Important Factor Which Needs More Attention in Infertility Care

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Infertility is one of the increasing problems in the global scenario that affects a large number of human couples. The fertilizing potential of semen or seminal parameters such as sperm concentration, motility, morphology, etc., is declining in healthy men which needs to be approached in a broad manner in terms of diagnosis and treatments. Genitourinary tract infection by microorganisms is one of the causes of male infertility and particularly bacteriospermia, the inflammation by bacterial pathogens play a major role that result in abnormal seminal parameters. Apart from their influence on seminal parameters, bacteriospermia is also associated with DNA fragmentation in sperms and production of reactive oxygen intermediates in semen. This review discusses on the influence of various bacteria that affect the seminal parameters and thereby cause male infertility. It has become a necessity to consider bacteriospermia as an influential factor affecting male fertility and hence, screening for bacterial infection should be essentially carried out before treatment to overcome infertility.

Keywords: Bacteriospermia; DNA Fragmentation; Infertility; IVF; ROI; Seminal Parameters.

Infertility affects relatively a large number of couples of about 186 million globally.¹ Many reports have indicated that the fertilizing potential of semen in healthy men is declining over a period.²⁻⁴ Epidemiological studies also show that the sperm concentration in United States declines by 1.5% per year and by 3% in Australia and Europe.⁵ Significant declines in sperm count, motility, and morphology have also been reported in Denmark,⁶ Sweden,⁷ France,⁸ Austria⁹ and Finland.¹⁰ Similarly, mean concentration of spermatozoa in Italy has also fallen down.¹¹

At present, semen analysis performed based on the WHO laboratory manual for the examination and processing of human semen is considered to be the standard method for semen examination, where the semen parameters such as semen volume, pH, sperm concentration, motility, morphology, etc. are evaluated.¹² Modern life-style changes, high stress levels, smoking, alcohol consumption, lack of exercise, exposure to radiations could be the possible causes of decline in the seminal parameters.¹³ Apart from all these factors, the genital tract infection plays

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a vital role in declining the seminal parameters and has a direct impact on male infertility.¹⁴ A number of studies report that 8-32% of male infertility cases are associated with infections and inflammation of the male genitourinary tract by microorganisms such as bacteria, virus, fungi, and protozoa.¹⁵⁻¹⁷ Infection with these microorganisms lead to infertility problems such as sperm damage, pyospermia, asthenospermia, teratospermia, etc by adversely affecting the spermatogenesis, causing inflammatory disorder, anatomical obstruction, scarring and initiating leukocyte response with its concomitant oxidative stress.¹⁸

Bacteriospermia, the infection with bacteria is one of the major and significant factors in male infertility that result in abnormal semen parameters and even lead to impairment of sperm functions and seminal tract obstruction.¹⁹ However, in most of the occasions, this bacteriospermic condition among men is not considered as one of the obstacles in fertility treatment when compared to all other investigative factors such as hormone levels and irregularities in menstruation cycles among women. Even though numerous studies independently report the effect of bacteriospermia on seminal parameters, only a few studies highlighted the importance in sperm DNA fragmentation and Reactive Oxygen Intermediates (ROI). This review discusses on various literature that describe about the different bacteria that involve in seminal tract infection, their influence on semen parameters such as count, motility, DNA fragmentation and the role of certain radicals (Reactive Oxygen Intermediates) that are produced as a result of bacterial infection.

Effects of Bacteriospermia

Acute and chronic genital tract infections are well known causes for male infertility.²¹ *Escherichia coli*, is one of the main bacteria isolated from human semen has the most negative influence on sperm morphology^{22, 23}. Semen infected with *E. coli* has also shown abnormal parameters such as low sperm concentration and reduced motility.^{24, 25}

Klebsiellae are opportunistic gram negative bacterial pathogens which cause seminal tract infections¹⁵. It has been reported that semen sample infected by *Klebsiella* appeared yellowish in colour with offensive odour with many pus cells. The presence of *Klebsiella* negatively influenced

the semen parameters and possibly could be a cause for death of all spermatozoa in semen leading to a condition called necrozoospermia.²⁶

Staphylococcus aureus is an ubiquitous gram positive bacteria found in semen samples of both fertile and infertile males. Studies reported that *S. aureus* was the most dominant microorganism in semen culture of infertile men with high prevalence rate than other bacteria.²⁷ Various reports signify that there is decrease in sperm motility and agglutination of sperms when spermatozoa were co-incubated with *S. aureus*.²⁹⁻³¹ It is evident that presence of *S. aureus* has negatively influenced the semen parameters causing spermatozoa immobilization, agglutination of spermatozoa and has had a main role in deterioration of spermatogenesis and disability of sperm function.^{32, 33} It is evident that *Staphylococcal* infection, can decrease the sperm count thereby leading to oligozoospermia^{34, 35} and in some cases azoospermia.³⁶

Pseudomonas aeruginosa, a gram-negative, opportunistic pathogenic bacterium is found to be associated with the seminal tract infection that produces a quorum signaling molecule, 3-oxododecanoyl-L-homoserine lactone which has detrimental effects on human spermatozoa. It affects the seminal parameters such as sperm cell death- necrosis and premature acrosomal loss.³⁷

Enterococci are gram-positive cocci and reported as the common organism isolated from semen that affect semen quality.³⁸

Chlamydia trachomatis, an obligate intracellular gram negative bacterium and the most prevalent cause of sexually transmitted bacterial infections^{21, 39} has been reported that infection with this bacterium can alter the pH of semen and reduced ejaculate volume and when *C. trachomatis* and human spermatozoa were co-incubated in vitro, the motility of the spermatozoa has been affected thereby leading to premature death.⁴⁰

Ureaplasma urealyticum is considered to be a potentially pathogenic species that causes both genital infections and infertility in men.⁴¹ This *U. urealyticum*, was divided into two biotypes; biovar 1 and biovar 2.⁴² Infection with biovar 2 can cause increased seminal viscosity with decreased pH and also affect most of the important parameters such as sperm concentration, motility and

morphology of spermatozoa.⁴³ Interestingly, this *U. urealyticum* causes damage to the development and vitality of human embryos generated by in vitro fertilization (IVF) and less pregnancy rate after embryo transfer procedures.^{44, 45}

Mycoplasma genitalium and *M. hominis* are also found to be associated with decrease in sperm concentration and abnormality in sperm morphology respectively.⁴¹

Bacteriospermia and Sperm DNA fragmentation

DNA fragmentation in sperms may affect fertility by hindering fertilization, early embryo development, implantation, and pregnancy.⁴⁶ This could be possibly because of defects in the sperm chromatin structure that can be associated with abnormal nucleoprotein content and DNA strand breaks.⁴⁷ It was reported that increased sperm DNA fragmentation was a reason for recurrent pregnancy loss and also had negative influence on sperm morphology.⁴⁸ It was also reported that DNA fragmentation in sperms has declined the fertilization rate and pregnancy rate in IVF procedures.⁴⁹ Various factors influence fragmentation of DNA in sperms such as errors in spermiogenesis, oxidative stress, chemotherapeutic agents, radiations, poor chromatin compaction, endogenous caspases, endonucleases and infection.⁵⁰⁻⁵² It was suggested that the semen samples infected with *S. aureus*, *S. epidermis*, *S. haemolyticus*, *E. coli*, *Enterococcus faecalis* and *agalactiae* had shown high sperm DNA fragmentation and also poor sperm concentration, motility and chromatin condensation⁵³. There is another report that emphasizes the increase in DNA fragmentation index in semen samples infected with *U. urealyticum* and *M. genitalium*⁵⁴ which in turn affected the embryonic development.^{45, 55}

Bacteriospermia and Reactive Oxygen Intermediates

Apart from directly affecting the seminal parameters such as sperm motility and morphology bacteriospermia also affects indirectly by producing oxidative stress through the release of Reactive Oxygen Intermediates.⁵⁶⁻⁵⁸ These Reactive Oxygen intermediates include superoxide anion radical, hydrogen peroxide and hydroxyl radicals.⁵⁹ The presence of bacteria leads to the recruitment of white blood cells to the inflammatory site as a result of host defense and later the activated macrophages and neutrophils

produce reactive oxygen intermediates which affect the spermatozoa.^{60, 61} It was reported that bacteria themselves or the bacterial products stimulate ROI production in leukocytes.⁶² Studies carried out to reveal the significance of ROI in human semen reveal that there was higher ROI generation in bacterial infected semen samples than the uninfected semen samples.^{63, 64} Studies show that the attack of free radicals on the sperm membrane causes reducing the potency of spermatozoa in fertilization process.⁶⁵⁻⁶⁹ An invitro study reported that there was an increase in the ROI generated by leukocytes incubated with *E. coli* and *S. haemolyticus*. In addition, this increase in hydrogen peroxide in the presence of *B. ureolyticus* is believed to be associated with the superoxide dismutase (SOD) produced by the bacteria. This Hydrogen peroxide is highly toxic to the sperms. Moreover, the insufficiency in the levels of catalase and glutathione peroxidase leads to the increase in intensity of the oxidative stress.⁷⁰ Another study also suggests that the hydrogen peroxide and hydroxide ion produced by *U. urealyticum* are highly toxic to the sperms.⁷¹ Similarly the presence of *U. urealyticum* in semen has caused sperm DNA damage as well as elevated seminal reactive oxygen species.⁷²

CONCLUSION

The infertility rates in developing countries like India is in an increasing rate as the number of IVF procedures have increased at a rate of 18% and is expected to increase upto 20% by this year 2020.⁷³ This increase in infertility can be clinically correlated with the bacteriospermic condition which is common among couples undergoing IVF treatment.⁷⁴ The problem here is, these infections are asymptomatic in most of the cases that lead to a dilemma in treatment procedures.²⁶

Bacteriological investigations for semen are generally carried out only when microscopic observation reveals significant pus cells. But it is suggested to investigate for bacterial infection regardless the number of pus cells being observed.⁷⁵ Performing microbiological testing especially for the presence of bacterial infection before any assisted reproductive procedure has a high significance as these genital bacteria can attach

to the spermatozoa which can't be expelled even by sperm washing techniques for intra uterine insemination and in vitro fertilization procedures. Hence there is a high possibility of microbial contamination of IVF medium which can result in fertilization failure and or poor embryonic development.⁷⁶

The present review highlights the correlation of Bacteriospermia on vital sperm parameters through various published literature and suggests to include screening for the presence of bacterial infection even if they are asymptomatic to get better fertility rate in ART procedures to overcome infertility.

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