

Infertility Causing Microbial Flora

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Abstract

Infertility is a growing issue that is encountered today with couples today around the globe. Different microbial floras are active in promoting infertility causing infections. Usually bacteria affects only males, only females or both males and females. Their modes of actions are different in affecting the human ability to reproduce offspring. Disturbance in natural microbial flora may result in serious urogenital tract impairment. These infections may be acquired after sexual contact or due to unhygienic practice. Sometimes people often face infertility due to sudden exposure of exogenous microbial pathogens either of gram-positive or gram-negative origin. The infectious sites include different organs of genital tract irrespective of gender. Cases of infertility due to microbial exposure are mostly reported from Africa, Middle East, South Asia, Central Asia and Central Eastern Europe. Though different strategic measures are taken to deal with these infertility complications still more low cost remedies and programed general public awareness is required.

Keywords: Infertility, microbial flora, exogenous microorganisms, sexual contact urogenital tract impairment.

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INTRODUCTION

The ability to produce off springs, found naturally in humans, is called fertility [1]. Infertility is a worldwide circumstance from which about 186 million individuals are suffering [7]. "Human Genome Project" was the forum established in 2001 for the researches including reproduction. It was mean because without being expertise on "2nd genome" of microorganisms that makes humans host, we'll be thoroughly disable to understand the point [6]. An endeavor was set globally in 2007 to do the sequencing of human microbiome in order to make conclusions about the microbial circle. It was in the perspective of human's healthy lifestyle and disease [9]. The project was categorized as "Human Microbiome Project" in US by NIH (National Institutes of Health). The drive National Institutes of Health strategy for sake of biomedical research where the particular human microbiome from 4 body plots from the healthy participants, mainly vagina as a primary site of study was done [10].

Microbial Flora and Infertility

If a male or female is incompetent to produce the off springs due to any reason still after the twelve times of successive sexual mating, it is termed as infertility. Many couples are suffering from infertility.

Situation of not conceiving is a stress full for both male and female because it has involved the physique and intellect. Africa, Middle East, South Asia, Central Asia and Central Eastern Europe are the countries listed for the premium rate of infertility [1]. Aspects behind the disfigurement of both male and female reproductive functioning are in charged. These can be either man infertility factors or woman infertility factors [2].

Various microorganisms are known to cause the change in sperm form and its function during laboratory analysis in infertility health center. Bacteriospermia is found in men and women having infertility. *Chlamydial* and *gonorrheal* bacteria were pointed earlier [11]. While after many years, some more bacteria are known to occur in humans namely, *Staphylococcus*, *E. coli*, *Gardenella*, *Niesseria*, *Mycobacteria* etc., to cause the immobility and coagulation of sperms. *Anaerococcus prevotella* are known to lower the sperm quality [12] and defects in sperm [13].

Microbial Flora Irrespective of Gender

Escherichia coli

Very frequent uropathogen on sperm task. Cause agglutination of sperm very immediately and unalterable. It usually adheres with the spermatozoa and

brings ultrastructural damages. Spermatozoa are immobilized. These organisms cause the ejaculation of oligo-sperms. Proteins of *E. coli* ceases the activity of sperm [14-17, 19].

Staphylococcus aureus:

Generally located in the genital tract of women and also located in the semen of both normal and infected men. An unusual and the most victorious microbe of humans. This microbial flora reduces the motility of sperm and coagulates it [18, 20].

Pseudomonas aeruginosa

It is a gram negative bacterium. It belongs to transmitted infections and infections of urinary tract. Deleterious effects on spermatozoa. It causes to lose the early acrosome depending upon calcium. Apoptosis and/or necrosis of spermatozoa occurs [21].

Candida Albicans

Seize the sperm motility and coagulates the spermatozoa. Live span of spermatozoa is reduced after exposure to *C. albicans*. Cell free filtrates and being themselves, *C. albicans* affect the human spermatozoa by inhibiting them. It hinders the ultrastructure of spermatozoa. It is mainly concerned to the male infertility. Farnesol is produced by *Candida albicans*. Farnesol cause various injuries to the sperm. It leads the sperm to necrosis and apoptosis. Acrosome is lost. DNA of Spermatozoa is disintegrated. Potential of mitochondrial membrane is decreased [22, 23].

Genital Mycoplasmas

Genital Mycoplasmas are located in genital organ and semen. Located in both men and women. It may cause NGU (non-gonococcal urethritis), orchitis and prostatitis in males and fertility disorders in females along with cervicitis and endometritis. It is associated with STIs (sexually transmitted infections) [24, 25].

Niesseria

Cause the infertility in humans. It is immotile diplococcus. It causes urethritis that is more complex than any other infections of reproductive system that diminish the male infertility. In females, the infection occurs in endocervix leading to infection of urethra. Pelvic Inflammatory disease may target 10 to 20 percent of women from infections that may include endometritis, salpingitis, tubo-ovarian abscess etc. These complexities advance towards infertility, ectopic pregnancy and long term pelvic pain. This microbe usually stops the advancement of healthy ova towards the uterus by harming the decontaminated cells having no cilia of tubal mucosa. That impact is obeyed by LPS (gonococcal lipopolysaccharide). The LPS thus make assurance of TNF α (tumor necrosis factor α) manufacturing [36, 37].

Gardnerella vaginalis

It is gram-negative in nature and located in the mucosal locus of vagina. It only causes the disease

when conditions are not suitable. In females, it is concerned to be present in the urogenital tract and mostly causes the bacterial vaginosis (BV). It shows its properties when the microbes of vagina are modified like *G. vaginalis*, *Atopobium vaginae*, *urogenital mycoplasmas*, *ureaplasmas* etc. Like a genus *Mobiluneus*, much of the microbes are characterized as they live without oxygen (anaerobic) and are not usually located in the mucosa of the vagina. *G. vaginalis* is present up to 44 percent mass in males. Physical appearance of that microbe is infrequent in males. It becomes massive in mucosa of genital tract in males and the sperm ejaculated are also tainted due to this contamination which in turn affects the female after sexual interchange [38, 39].

Mycobacterium tuberculosis

Mycobacterium tuberculosis is most popular microbe leading to lung diseases and has locus in urogenital tract. Infections caused by *Mycobacterium tuberculosis* may target different parts of reproductive tract. It mostly targets the fallopian tubes, ovaries, and uterine mucous membranes of female and sometimes cause scabies infection. While in males, it commonly targets testicles and/or prostate. Cluster of WBCs and other tissues known as granulomas may form in the reproductive tract accompanying the infection. These granulomas are hazardous to the reproductive tracts and affect the targeted person by reducing its capability to reproduce [40].

Chlamydia trachomatis

It is a microbe characterized as gram-negative and lives within the cells. It is well known to drive sexually transmitted infections after the microbial flora namely *Niesseria* and is known all over the world [44]. It targets both genders but females get five times more infectious as compared to the males. In 80 percent cases, symptoms of Chlamydial infection do not appear that causes the infection of urogenital tract. It targets females and youngsters that are more active sexually [45]. Disturbance or blockage of tube, ripping, adherence formation etc. takes place due to which the oocytes may be interrupted to move out through the tubes. Hence the genital tract of women is really interrupted due to microbial flora namely *chlamydia trachomatis*. Pelvic inflammatory diseases caused by this microbe makes female indefinitely infertile by ceasing the tract of fallopian tubes. Occurrence of *C. trachomatis* during pregnancy leads to the complexities like premature birth and underweight infants. Microbial infection may also transmit to the infant [45].

Staphylococcus

These are the microbes which are gram positive in nature [26, 27]. Their outcomes are very harsh on humans. They are having a diameter of 0.5-0.1 micrometer. They may enlarge in mass, pairs or in form of chains [26]. These microbes are of two types according to their capability of blood agglutination [28].

S. aureus are one of the most infectious species [29]. *S. aureus* are one of the most infectious microbes in humans among any other Staphylococci [30].

Male Infertility Factors

There can be number of factors responsible for the infertility like, congenital disorders, hormonal disturbances, lifestyle hustle, mental stress, environmental risks, etc. these aspects may have impact on the performance of the genital organs i.e. sperm cells production, standard of sperm and semen, convey of sperm to the oocyte, fertilization of both sperm and ova and their insertion [3, 4].

Crucial Factors

There are several scientific aspects including microbial infection can cause many serious issues including infertility/clinical consequences.

A good sperm has some known characteristics including motility, undamaged surface, firm DNA and normal structure and form. These are all some vital factors in aided reproduction [32, 33]. Different Microbial flora affects the male fertility and targets different location as shown in Table 2.

Bacterial Transmit

A human male sperm can transmit several microbes that eventually taint the oocyte estrogenically. Microbial effects of microbes on sperm can cause more degeneration of zygote, change in DNA, and decrease in fertilization, also affects the quality of embryo and maturation [34, 35].

Table 1: Microbial flora middle region and tail region of sperm [71]

Microbial Flora Infecting Middle Region of Sperm	Microbial Flora Infecting Tail of Sperm
<i>E. coli</i>	<i>U. urealyticum</i>
<i>U. urealyticum</i>	<i>M. hominis</i>
<i>M. genitalium</i>	<i>P. aeruginosa</i>
<i>M. hominis</i>	<i>C. trachomatis</i>
<i>E. faecalis</i>	<i>H. pylori</i>

Sperm Parts and Different Microbial Infections

Bacteria have been divided into three regions (Table 1). These three regions are head, mid piece and tail. Head region has nucleus, acrosome and neck.

Middle region has mitochondrial piece. Whereas tail has plasma membrane [31]. As it is shown in given below in Figure 1.

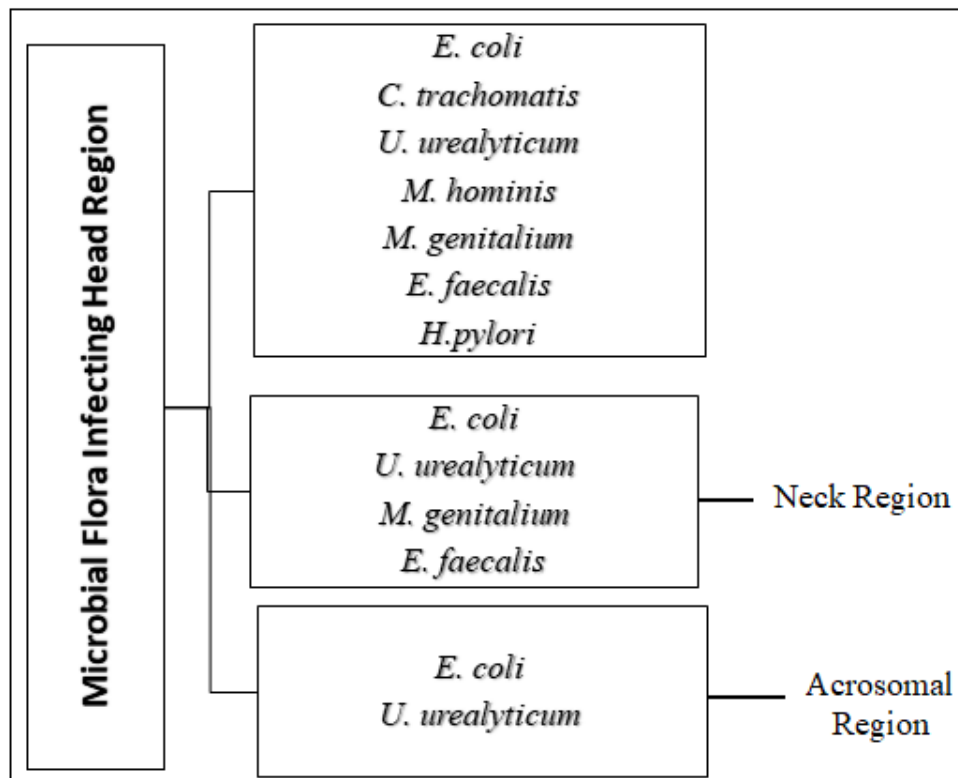


Figure 1: Microbial flora infecting head region, neck region and acrosomal region of male sperm [71]

Targeted Location of Male Genital Tract:**Table 2: Male fertility affected by microbial flora at different locus in genital tract [71]**

Microbial Flora	Disorders of Male Fertility	Infection Site
<i>E. coli</i>	Mitochondrial membrane malfunctioning, destruction of acrosomal reaction, disablement of sperm movement and morphology, massive decrease of sperm and also DNA damage.	Prostate, Epididymis, Testes, Seminal vesicles, Urethra
<i>C. trachomatis</i>	Disablement of acrosomal reaction, massive decrease in sperm amount, sperm mobility, capability and ultrastructure, DNA damage.	Prostate, Epididymis, Testes, Seminal vesicles, Urethra
<i>U. urealyticum</i>	Disablement of acrosome reaction, sperm mobility, ultrastructure damage, massive decrease in sperm amount, life span decreased also damage to DNA.	Prostate, Epididymis, Urethra
<i>M. hominis</i>	Sperm and its mobility is disabled, ultrastructure disrupted, less no. of sperms are produced and capability affected, DNA affected.	Urethra, Prostate
<i>M. genitalium</i>	Disablement of sperm mobility, less sperms produced, life span and DNA affected.	Urethra, Prostate
<i>N. gonorrhoeae</i>	Disablement of sperm wholeness and give harm to DNA.	Prostate, Epididymis, Testes, Seminal vesicles, Urethra

Female Infertility Factors

Infertility aspects in women are categorized into following; vaginal, cervical, endocrine, uterine, tubal and pelvic peritoneal. Several factors may have role that lead towards infertility issue [6]. Trichonomal vaginitis, bacterial vaginosis (BV), vulvovaginal candidiasis may cause by microbial infections [60]. Further research is contemplated about the micro-flora role on genital tract. Characteristic micro-flora of the vagina and the genital tract are considered as the major factor of conceiving [1, 2]. Some Microbial flora are native and some are exogenous that may target different parts of female genital tract as shown in Table 3.

Bacterial Vaginosis

Bacterial vaginosis is usually symptomless. It is commonly indicated by the vaginal discharged which

is whitish or greyish in color, fish like odor after mating, during monthly menses and acceleration in pH of vagina higher than 4.5 [62-65]. Universality of BV depends on earthly locus and origin and have range from 8% – 51% [66].

Vulvovaginal Candidiasis

It commonly occurs due to yeast mostly *candida albicans*, growth in abundance, that are the important portion of vaginal microbe [67]. It is characterized by vaginal excretion, inflammation, itch and ache. In this case, vaginal excretion is characterized as pot cheese [65]. 75.0% females face this microbial infection in life [68].

Targeted Location of Female Genital Tract and their Complexities:**Table 3: Female Genial Complexities caused by microbial flora [61]**

Native Locus	Fallopian Tube, Vagina, Cervix
Exogenously Acquired Locus	Cervix, Fallopian Tube
Infertility Causing Complexities	Vaginosis, Cervicitis, Endometritis, Salpingitis, Ectopic pregnancy, Sterility, Tubal Abscess

Diagnosis

PCR machine is used for diagnostic purpose of infections caused by *Gardnerella vaginalis* such as bacterial vaginosis, metronidazole and clindamycin [40]. Infections associated with *Mycobacterium tuberculosis* are diagnosed by using PCR along with gold standard Ziehl–Nielson staining. Radiography is also used [41-43].

Strategies to Combat Infertility**IVF Treatment**

Micro biome is of prime importance in the therapy of infertility and plays a lead role to advancement in the victory rate of reproductive

medication like IVF [8]. It is used to combat the infertility among males and females. But most of the measures of IVF can alter the microbial environment of vagina [69]. However, infixing of embryo may get failure due to change in vaginal microbial environment [70].

Probiotics Treatment

The most known probiotic microbe to treat the infertility is *Lactobacillus*. It protects the vagina in several ways from foreign agents or harmful microbes [46]. It constructs the lactic acid. Lactic acid makes the pH 3.5 to 4.7 and excludes the microbes. It also produces cervico-vaginal human mucus that discourage

the microbes indirectly [47, 48]. Bacteriocins are produced which are AMP (anti-microbial peptides) and proteins. Bacteriocins emerge due to dysbiosis of vaginal microbial flora and give the host a defending shield against the invading microbes [49, 50].

Phytotherapy

Moringa oleifera, *Adiantum concinnum*, *Petroselinum crispum*, *Musa sapientium*, *Scabiosa atropurpurea*, *Cassia alata*, *Ximenia Americana*, *Eremomastax speciose*, *Justicia insularis*, *Crinum distichum*, *Ageratum conyzoides*, *Senecio biafrae*, *Emilia coccinia*, *Zehneria scabra*, *Aloe buettneri*, *Paulinia pinnata*, *Solanum torvum*, *Ampelocissus Pentaphylla*, *Krameria lappacea* etc. are the different plants used to cure the infertility issues in females [51].

Antibiotics Treatment

Antibiotic namely doxycycline [52] and azithromycin [53] are used in different cases of infertility. Antibiotics can be used for the therapy of infertility both in men and women and can make the succession in conceiving rates and rate of births in patients. Several antibiotics are here to cure the microbial infertility causing infections like chronic endometritis. Antibiotics along with hysteroscopy and endometrial biopsy can be prescribed to treat the CE [54].

Allopathic Therapy

N. sativa are specifically used to make the alcoholic extracts that are responsible for the production of mobile sperms, increases the restoration of sperms in epididymis, responsible for increment in the weight of genital organs, increases the level of testosterone hormone in blood, increases the level of gonadotropin hormones and fertility rates are also increased. Another reported investigation highlight that sperm producing cells are enhanced by the effect of *N. sativa* on pituitary hormones that produce the sperms and recovers female reproductive issues too [72].

Pigmentation Therapy

Lycopene is a naturally occurring pigment that could be extracted from fruits, vegetable, algae, bacteria or other microorganisms [57] giving red color due to multiple double bonds. It is naturally occurring anti-oxidant. Gathering of these double bonds make a chromophore that absorbs maximum light because of greater wavelength value [59]. Lycopene is a fat soluble dietary compound. Ingestion of lycopene results in the defense of male sperms opposed to oxidative stress and any harm. Quality of sperm is improved due to ingestion of this carotenoid like morphology, quantity and mobility [56]. Lycopene is ingested orally and moves through gastrointestinal tract [58] and spread to the body organs and plasma through blood circulatory system [56].

Ayurvedic Treatment

Ayurveda is also recommended for the prevention of various infections caused by several different microbes. Various treatment related to Ayurveda are following; "Panchakarma" related to the therapy of corrupted three physical energies named as vata, kapha, and pitta in genital tract of women. Snehapana includes the consumption of oil that is suggested for medication. This processed along with Virechana therapy for sake of better status of egg or ovum. Various other treatments such as Phalaghrita, Ashokarishta, Kanchanara guggulu etc. are used to make the endometrium of female receptive to conceive. By tallying the fallopian tubes with Artavavaha Srotas (pathway/channel of menstrual blood flow), it's congest compared with the Sanga Srotodushti of this passage [55].

CONCLUSION

Reproductive tract of both men and women are exposed to any bacterial infections respectively. There are mostly endogenous microbes while mostly are exogenous. Different microbes affect males and females at different parameters. Sometimes, a little change in microbial environment of genital tract may cause severe infections that may lead to infertility. All the microbes have different mode of action on sperms and urogenital tract of men and women. Microbial flora targets different parts of genital tract. In some cases any alteration in the microbial environment of vagina may issue the prevalence of serious infections or complexities regarding to fertility issues. Different strategic measures are available which can help to prevent the infertility issues.

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