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Review of some Mechanisms of Inflammation-Mediated Impairment in Spermatogenesis and Sperm Function

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ABSTRACT

Objective: *This review display the mechanistic link between inflammation response and male infertility disorders, emphasizing the immunological and oxidative ways contributed in the deterioration of sperm impotent and function.* ***Method:*** *The map of diffusion shows that pro-inflammatory cytokines overproduction and reactive oxygen species (ROS) production lead to oxidative stress, which results in cellular damage to membrane and nuclear structures, and subsequently causes apoptosis of sperm cells.* ***Results:*** *Male reproductive tract inflammatory conditions, including epididymitis and urethritis and varicocele diseases and testicular torsion, result in impaired sperm quality through their disruption of accessory gland function and sperm transport and spermatid formation process. With increased cytokine levels, sperm motility and morphology and concentration decrease.* ***Novelty:*** *Spermatogenesis is an elevated coordinated process involving the proliferation and differentiation of germinal cystocele within the testis in seminiferous tubules, essential for fertility in male specially. The complete process depends on hormonal control and epigenetic mechanisms, which make it vulnerable to different internal and external disturbances. Inflammation represents a major obstacle to spermatogenesis since it results from infections and anatomical abnormalities and environmental exposures.*

INTRODUCTION

Spermatogenesis

Spermatogenesis refers to the intricate process in which a mutually reliant community of germ cells undergoes mitosis and meiosis to generate spermatozoa. Spermatogenesis occurs within the convoluted seminiferous tubules and persists from the onset of puberty until advanced stages of adulthood.

The process encompasses multiple phases, commencing connected to genesis of predicative generated cells (known as spermatogonia cell) within the germinal epithelium. Subsequently, these cells undergo a series of developmental stages, evolving into primary and secondary spermatocytes, culminating in the production of fully developed spermatozoa. Spermatogenesis requires optimal conditions for successful execution because it serves essential functions in sexual reproduction. The process regulation depends on two mechanisms which include DNA methylation and histone modification [1].

Organized spermatogenesis

Spermatogenesis operates as a complex system that requires exact control to achieve its function of male germ cell development and reproductive activity. The process of spermatogenesis relies on both testicular and non-testicular mechanisms for

its regulation. However, it is important to note that disruptions can occur at various stages, potentially affecting the overall process [2]. Infertility in men can arise from environmental factors or diseases that impact spermatogenesis, either directly or indirectly. The literature indicates that male factors have been identified as a significant contributor, ranging from 30% to 55%, to the overall prevalence of infertility worldwide [3]. According to the findings of some thesis and search it was observed that male factor infertility accounts for approximately (50%) of the total cases of infertility in all married [4]. Infertility caused by male factors is characterized by the following: changes in the motility, morphologyorconcentrationat least one of the two sperm tests showed the presence of sperm, which are typically collected within a period of 1 to 4 weeks [5].

In addition to established hormonal disruptions [6], in cases of infection within the reproductive tract, the innate immune system's response ability to draw increased phagocytic cells and effector particles to the site of microorganism infection is one of its most important functions. This is accomplished by the release of a wide variety of cytokines and other inflammatory mediators, which have a substantial impact on the following processes of the organism [7].

RESEARCH METHODS

Inflammation

There are several factors that contribute to male reproductive tract inflammation (i)Epididymitis refers to the inflammatory condition affecting the epididymis in inflammation, a component of the male reproductive system responsible for connecting the testes as well as the vas deferens component. The occurrence of epididymal inflammation can lead to additional complications, including the enlargement of the scrotum, discomfort, the presence of discharge from the penis, and the appearance of blood in the urine.(ii) Ejaculatory duct obstruction is a prevalent etiological factor contributing to male infertility, with documented reports indicating the presence of infections in a substantial proportion, ranging from 20% to 50%, of affected individuals. (iii) Inflammation can arise as a consequence of sexually transmitted infections such as bacteria Escherichia coli(E.Coli), Chlamydia, and gonorrhea female. While Escherichia coli has been identified as the primary etiological agent of epididymitis in older males, it is worth noting that other bacterial species, including mycobacteria and ureaplasma, have also been implicated in the development of this condition. (iv) Urethritis enables bacteria from a urinary tract infection to spread from the bladder or urethra into the epididymis. Pediatric patients can develop epididymitis because of viral infections which include the mumps virus. Testicular torsion constitutes a common medical condition with potential effects on male fertility. The condition develops because of a defect in the tissue that supports the body which causes the testicles to rotate unnaturally inside the scrotum. The medical condition presents with pronounced swelling as its main symptom. Torsion causes blood vessels which feed the testicles to become blocked, leading to blood flow restrictions that result in testicular damage. The medical condition of varicocele occurs when the internal spermatic veins experience

abnormal expansion which prevents blood from the testicle from draining into the abdominal area before it travels back to the heart. Male urogenital block or closed presence of infection through chronic prostatitis testicular inflammation and pharmacological treatment form additional factors which lead to these conditions [8].

Inflammation's effect on a man's reproductive system

As a natural reaction to injury and tissue damage, inflammation takes place. The physiological mechanism facilitates the transportation of leukocytes and plasma molecules to areas of infection or specific tissues. Acute inflammation manifests through three primary alterations: heightened blood flow to the affected region, augmented capillary permeability enabling the infiltration of larger serum molecules into the tissues, and intensified migration of leukocytes into the tissue [9]. The persistence of the infectious agent results in the development of chronic inflammation. This process is characterized by the recruitment as well as increased activity of some cell in response to immune macrophages, lymphocytes, and other cellular components, resulting to the commencement of a coordinated response that is mediated by cytokines. Moreover, the onset of this reaction is accompanied by the release of cytokines. On the other hand, the resolution of acute inflammation, which involves the elimination of the irritant and subsequent tissue regeneration or repair, and chronic inflammation is distinguished by the simultaneous presence of inflammation and repair processes, rather than their sequential occurrence [10].

It is possible to explain the decrease in the quality of the sperm that was detected throughout the inflammatory process to the compromised functions of accessory glands, hindrance in sperm transport, and dys-regulation of spermatogenesis [11]. Proinflammatory cytokines typically exert their effects in a localised manner, as they are generated via cells that are locally activated or produced temporarily following the activation of a stimulus. Physiologically, male gonads are known to produce cytokines, which have been documented to play a role in the regular activaty of the organ [12].

Source of cytokines

According to some research that has been done so far, the major things of cytokines in the male tesstis is found to be the macrophages that reside in the testicles. However, certain studies have reported the production of cytokines example as IL-1 as well as IL-6 by Leydig cells and Sertoli [13].

Cytokines, specifically TNF–α, regulate the migration of white blood cell into multiple tissues in response to tissue damage. Tumour necrosis factor-alpha (TNF-α) is predominantly synthesised via macrophages and other mononuclear (phagocytes), which playing a crucial role in the initiation and progression of inflammatory responses as well as the stimulation of various other leukocytes. It is worth noting that TNF-α has the ability to stimulate the expression of adhesion molecules and chemokines on the endothelial cells, as well as activate the phagocytic functions of microbial systems. Furthermore, tumour necrosis factor-alpha (TNF-α) elicits programmed cell death, so also known as apoptosis. Interleukin-1 (IL-1) is a significant cytokines' involved in the

inflammatory response, exhibiting functional similarities with- tumor necrosis factor-alpha (TNF-α) [14].

Reactive oxygen species (ROS)

The male genital tract experiences an escalation in the production of ROS as a result of inflammatory damage. Furthermore, the excessive production of ROS or free radicals, which is linked to inflammatory responses, can be attributed to the presence of pathological bacterial strains which inhabit the function of reproductive [15].

Free radicals refer to a collection of chemically reactive molecules possessing one or more unpaired electrons, which have the ability to undergo oxidative modifications upon interacting with biomolecules. The prompt and immediate response of substances in the surrounding environment elicits a cascade of reactions that ultimately culminate in the impairment of cellular integrity [16].

Regulation of cytokines

Involvement of certain cytokines in the modulation of reproductive capacity is contingent upon their concentration levels. For instance, a research conducted by Naz as well as Evans demonstrated a correlation between interleukin 12 and both sperm morphology and sperm density [17]. In a previous research by the same author, it was shown that infertile males had elevated levels of the cytokine interleukin 6, whereas fertile men did not. There is often a correlation between elevated levels of some important interleukins in the sperm and a decline in the function of the seminological measures [18].

Some studies have indicated a positive correlation between elevated levels of TNF-α in semen and decreased sperm motility,sperm count, and sperm morphology [19]. Elevated concentrations of this particular cytokine induce programmed cell death in seminal fluid due to the proliferation and specialization of beta cells, as fine as the proliferation of T cells as well as natural killer cells. Interleukin-1 alpha (IL-1α) and interleukin-1 beta (IL-1β) have been found to prompt apoptosis in semen through the activation of beta cell proliferation and differentiation, the recruitment of leukocytes to the location of inflammation, and the promotion of neutrophil and monocyte production.

Additionally, observed that these cytokines had a negative influence on the feature of type semen. In a separate study conducted by the aforementioned author, it was observed that heightened levels of IL–1 β were associated with a reduction in sperm efficiency [20]. The findings demonstrated a concurrent elevation in seminal concentrations of reactive oxygen species and malondialdehyde such (MDA), a byproduct of lipid peroxidation resulting from oxidative injury. The cytokines that serve as immune modulators in the testis- gonad are also found in wide concentrations in semen in instances of infection and tissue impairment. The involvement of leukocytes in the inflammatory process is intricately connected to the concurrent occurrence of leukocyte-spermia [21].

The clinical implications of elevated stages of leukocytes in semen stay to be a subject of debate within the medical community. Several studies have reported a

correlation between disturbed spermatogenesis [22], while others have identified a connection with the detrimental impact of environmental features [23] and atypical sexual behavior [24].

RESULTS AND DISCUSSION

The entire process of spermatogenesis, which is vital for male reproductive capability, can be disrupted by all types of internal and external elements. The review presents proof that male reproductive tract inflammation works as a major pathological factor which causes male infertility. The existing studies establish a strong biological connection which links inflammatory processes to the breakdown of semen quality because pro-inflammatory cytokines together with oxidative stress reach their highest impact. The research findings show that inflammation functions together with oxidative stress to create a disease process which leads to male infertility [25]-[30]. The research shows that epididymitis, urethritis, and varicocele, and testicular torsion create unfavorable conditions which prevent successful sperm production. The pathophysiology identifies a single pathway, which results from excessive production and subsequent disturbance in the regulation of essential cytokines, including TNF-α, IL-1, and IL-6 [25]-[30]. The mediators exist as essential components of the innate immune system, which helps eliminate infections; however, their continuous presence in chronic inflammatory states turns harmful. The research results match the studies which find a direct link between increased seminal cytokine levels and reduced sperm quality [25]. The research shows that TNF-α and IL-1β lead to decreased sperm motility with abnormal morphology and lowered sperm concentration according to multiple studies which found this result. The evidence shows that cytokines act as active participants in the process which leads to infertility. The evidence demonstrates that cytokines create harmful effects because interventional studies have shown that astaxanthin treatment after varicocele surgery reduces TNF-α and IL-1β and IL-6 levels which results in major enhancements of sperm motility [26]-[32].

The process through which cytokine-induced damage occurs shows multiple pathways for its execution. The text shows that TNF-α functions as a strong apoptosis inducer because it directly initiates programmed cell death in both germ cells and mature spermatozoa [25]. The cytokines IL-1 and TNF-α function at inflammation sites to attract and activate leukocytes for their defense response. Activated immune cells enter the body to fight off infections but this process creates a respiratory burst which results in increased production of reactive oxygen species (ROS) [25]-[31]. The body experiences oxidative stress which acts as the primary agent that causes cellular damage. The review identifies the oxidative burst shows its harmful effects through two processes which include sperm plasma membrane lipid peroxidation as shown by raised malondialdehyde (MDA) levels and DNA damage [25]. The spermatozoon exhibits extreme susceptibility to oxidative damage because it has a small cytoplasmic space and lacks effective DNA repair systems which leads to decreased motility due to

ATP depletion and membrane fluidity loss and structural damage based morphological changes [25]-[31].

The surrounding environment which contains inflammation disrupts the complete reproductive system. The review describes two critical problems which include damaged accessory gland function and reduced sperm movement capacity which both need to supply seminal plasma to sustain and defend spermatozoa after they leave the testicles. Male accessory gland infections together with male genital tract infections function as primary sources which create inflammatory conditions that result in leukocyte infiltration to prostate and seminal vesicle and epididymis functions. Pro-inflammatory cytokines have the ability to change how these glands produce secretions which results in different biochemical properties of semen thus damaging sperm viability and functionality. Spermatozoa lead to a situation where their production takes place in an unsuitable environment and they experience ongoing stress throughout their maturation process and movement.

Scientific researchers need to approach these findings with cautious interpretation. Text establishes an essential area of disagreement by showing how elevated leukocytes in semen (defined as $\geq 1\times10^{6}$ WBC/mL) [25]-[31] create clinical problems which require resolution. Infertility cases linked with this condition show direct causal links while others show no such relationship. Some studies report disturbed spermatogenesis in its presence, while others link it to lifestyle or behavioral factors. Modern research demonstrates that asymptomatic leukocytospermia does not negatively affect any of the following outcomes fertilization or pregnancy rates according to Assisted Reproductive Technology standards because standard sperm preparation techniques and ICSI can eliminate any potential harmful effects [26]. The threshold which defines pathological damage seems to change according to how long inflammation continues and which specific etiological agents are present and which individual patient factors determine how susceptible they are to damage. The cytokine profile together with the specific leukocyte types present (e.g., macrophages vs. granulocytes) serve as important fertility outcome factors which hold greater importance than the total leukocyte count in determining results [31]. Even low levels of leukocytes, below the WHO threshold, can produce measurable ROS and adversely affect sperm function [31].

The narrative review provides an overview of existing research but does not perform a systematic meta-analysis. The research presents qualitative findings which describe the study results without providing specific metrics for effect size calculation. Researchers face challenges in establishing generalizable results because the studies used different research designs and sample groups and employed various techniques for cytokine and ROS detection. The research should concentrate on three principal domains which require investigation. First, longitudinal studies are needed to determine the temporal relationship between the onset of inflammation and the decline in fertility, helping to establish causality more firmly. Second, researchers need to analyze the specific signaling pathways which cytokines activate in testicular cells and spermatozoa through their interactions with NF-κB and mTOR/HIF-1α pathways to

uncover new treatments which will emerge from immunometabolism studies [25]-[29]. The research focuses on three promising methods which include antioxidant treatments and anti-cytokine biologic treatments and microbiota-modifying methods for men who experience chronic reproductive tract inflammation to either maintain or regain their fertility [25]-[30]. The research establishes more precise methods to evaluate how different pathogens affect immune responses which lead to different fertility outcomes, thus enabling development of customized medical treatments. The review demonstrates that inflammation functions as a primary obstacle which prevents men from achieving successful reproductive outcomes. The combination of increased pro-inflammatory cytokine levels with oxidative stress creates a harmful cycle which disrupts spermatogenesis while causing damage to sperm structure and function and ultimately reducing the ability of male gametes to fertilize [25]-[30]. The management of male infertility requires physicians to address this inflammatory element because it represents a crucial factor which affects most cases of male infertility.

CONCLUSION

Fundamental Finding : Inflammation in the male reproductive system disrupts spermatogenesis through increased production of pro-inflammatory cytokines and reactive oxygen species, leading to decreased sperm motility, morphology, concentration, and overall fertilizing capacity. **Implication :** Understanding the relationship between inflammation and male infertility is important for developing effective diagnostic approaches and therapeutic strategies to preserve male reproductive health. **Limitation :** The discussion remains general and does not specify particular inflammatory pathways, biomarkers, or clinical evidence associated with impaired spermatogenesis. **Future Research :** Further studies are needed to investigate interventions targeting inflammatory pathways and oxidative stress mechanisms to maintain and restore male reproductive function.

REFERENCES

[1] N. Zečević *et al*., "Detrimental effects of cadmium on male infertility: A review," *Ecotoxicology and Environmental Safety*, vol. 290, p. 117623, 2025.

[2] S. M. Eleawa *et al*., "Resveratrol reverses cadmium chloride-induced testicular damage and subfertility by downregulating p53 and Bax and upregulating gonadotropins and Bcl-2 gene expression," *Journal of Reproduction and Development*, vol. 60, no. 2, pp. 115–127, 2014.

[3] M. P. Hedger and A. Meinhardt, "Cytokines and the immune-testicular axis," *Journal of Reproductive Immunology*, vol. 58, no. 1, pp. 1–26, 2003.

[4] J. Poongothai, T. S. Gopenath, and S. Manonayaki, "Genetics of human males infertility," *Singapore Medical Journal*, vol. 50, no. 4, pp. 336–347, 2009.

[5] World Health Organization, *WHO Laboratory Manual for the Examination of Human Semen–Cervical Mucus Interactions*, 4th ed. Cambridge, U.K.: Cambridge University Press, 1999.

[6] N. Pant *et al*., "Correlation between lead and cadmium concentration and semen quality," *Andrologia*, vol. 47, no. 8, pp. 887–891, 2015.

[7] P. Massányi *et al*., "Effects of cadmium, lead, and mercury on the structure and function of reproductive organs," *Toxics*, vol. 8, no. 4, p. 94, 2020.

[8] H.-H. Chao *et al*., "Comprehensive review on the positive and negative effects of various important regulators on male spermatogenesis and fertility," *Frontiers in Nutrition*, vol. 9, p. 1063510, 2023.

[9] R. N. Mitchell and R. S. Cotran, "Acute and chronic inflammation," in *Robbins Basic Pathology*, V. Kumar *et al*., Eds. Philadelphia, PA, USA: Saunders, 2003, pp. 33–65.

[10] J. Wang *et al*., "Protective effect of naringenin against cadmium-induced testicular toxicity in male SD rats," *Journal of Inorganic Biochemistry*, vol. 214, p. 111310, 2021.

[11] T. T. Turner and J. J. Lysiak, "Oxidative stress: A common factor in testicular dysfunction," *Journal of Andrology*, vol. 29, no. 5, pp. 488–498, 2008.

[12] O. Söder *et al*., "The interleukin-1 system in the testis," *Andrologia*, vol. 32, no. 1, pp. 52–55, 2000.

[13] C. De Angelis *et al*., "The environment and male reproduction: The effect of cadmium exposure on reproductive function and its implication in fertility," *Reproductive Toxicology*, vol. 73, pp. 105–127, 2017.

[14] S. K. Fried, D. A. Bunkin, and A. S. Greenberg, "Omental and subcutaneous adipose tissues of obese subjects release interleukin-6: Depot difference and regulation by glucocorticoid," *The Journal of Clinical Endocrinology & Metabolism*, vol. 83, no. 3, pp. 847–850, 1998.

[15] D. Male *et al*., *Immunology*, 7th ed. Amsterdam, The Netherlands: Elsevier, 2006.

[16] A. Azenabor, A. O. Ekun, and O. Akinloye, "Impact of inflammation on male reproductive tract," *Journal of Reproduction & Infertility*, vol. 16, no. 3, p. 123, 2015.

[17] S. C. Sikka, "Relative impacts of oxidative stress on male reproductive function," *Current Medicinal Chemistry*, vol. 8, no. 7, pp. 851–862, 2001.

[18] P. Sengupta, S. Dutta, and E. Krajewska-Kulak, "The disappearing sperms: Analysis of reports published between 1980 and 2015," *American Journal of Men's Health*, vol. 11, no. 4, pp. 1279–1304, 2017.

[19] A. Agarwal *et al*., "Reactive oxygen species and sperm DNA damage in infertile men presenting with low level leukocytospermia," *Reproductive Biology and Endocrinology*, vol. 12, no. 1, p. 126, 2014.

[20] I. Kocak *et al*., "Relationship between seminal plasma interleukin-6 and tumor necrosis factor-α levels and semen parameters in fertile and infertile men," *Urological Research*, vol. 30, no. 4, pp. 263–267, 2002.

[21] G. Bezold *et al*., "Prevalence of sexually transmissible pathogens in semen from asymptomatic male infertility patients with and without leukocytospermia," *Fertility and Sterility*, vol. 87, no. 5, pp. 1087–1097, 2007.

[22] H. Wolff *et al*., "Leukocytospermia is associated with poor semen quality," *Fertility and Sterility*, vol. 53, no. 3, pp. 528–536, 1990.

[23] C. Keck *et al*., "Seminal tract infections: Impact on male fertility and treatment options," *Human Reproduction Update*, vol. 4, no. 6, pp. 891–903, 1998.

[24] C. E. Close *et al*., "Cigarette, alcohol and marijuana are related to pyospermia in infertile men," *Journal of Urology*, vol. 144, no. 4, pp. 900–903, 1990.

[25] S. Dutta, P. Sengupta, and P. Slama, "Oxidative stress, inflammation, and male infertility: A systematic review," *Journal of Clinical Medicine*, vol. 11, no. 13, p. 3689, 2022.

[26] M. Arafa, R. Henkel, and A. Agarwal, "Role of inflammation in male infertility," *Inflammation*, vol. 45, no. 3, pp. 903–917, 2022.

[27] S. Dutta, A. Majzoub, and A. Agarwal, "Oxidative stress and sperm function: A systematic review on the impact of pathophysiology," *Andrology*, vol. 10, no. 4, pp. 647–665, 2022.

[28] M. A. El-Harouny, M. T. El-Sherbiny, and A. M. Abdel-Aziz, "Effect of astaxanthin on seminal cytokines and sperm parameters in varicocele patients after surgical repair: A randomized clinical trial," *World Journal of Men's Health*, vol. 41, no. 1, pp. 112–121, 2023.

[29] T. M. Said and A. Agarwal, "Leukocytospermia and male fertility: An update on clinical implications and management," *Journal of Reproductive Immunology*, vol. 155, pp. 103–112, 2023.

[30] K. Tremellen, "Male accessory gland infection and infertility: An update on diagnosis and management," *Fertility and Sterility*, vol. 119, no. 2, pp. 201–210, 2023.

[31] S. La Vignera, R. A. Condorelli, and A. E. Calogero, "Male accessory gland infection and sperm DNA damage: A systematic review," *Journal of Clinical Medicine*, vol. 11, no. 15, p. 4421, 2022.

[32] World Health Organization, *WHO Laboratory Manual for the Examination and Processing of Human Semen*, 6th ed. Geneva, Switzerland: World Health Organization, 2021.

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