Advance Research Journal of medical and clinical science
Received 2 May 2021 | Revised 29 May 2021 | Accepted 6 June 2021 | Published Online 9 June 2021

DOI: https://doi.org/10.15520/arjmcs.v7i06.324
ARJMCS 07 (06), 582–589 (2021)

ISSN (O) 2455-3549 IF:1.6

RESEARCH ARTICLE

Infiltration of leukocytes into the human ejaculate and its association with semen quality and oxidative stress with sperm function, and leukocytospermia management.

Noureddine Louanjli [1] | Aya Al-ibraheemi [2] | Mustafa Zakaria [3*] | Abdelhafid Natiq [4] | Romaissa Boutiche [5] | Modou M. Mbaye [6] | Mohamed Zarqaoui [7]

[1]Chairman of the LABOMAC Laboratory, and IRIFIV Fertility Center, AFC Fertility Center, Association for Scientific Research of the IRIFIV-AISRG Group Casablanca, Morocco

[2]Embryologist, UK. researcher in the Scientific Research Group -and Member of the Association for Scientific Research of the IRIFIV-AISRG Group – UK

[3]MD. Senior Clinical Embryology and Assisted Conception , Consultant in IRIFIV Fertility Center , IVF laboratoy, Casablanca ,Morocco

[4]Genopath, Faculty of Medicine and Pharmacy, Mohammed V University Rabat Morocco, Team of Genomics and Molecular Epidemiology of Genetic Diseases (G2MG), Genomic Center of Human Pathologies (GENOPATH). Faculty of Medicine and Pharmacy. Mohammed V University in Rabat, Researcher in the Association for Scientific Research of the IRIFIV-AISRG Group. Rabat, Morocco.

[5]Embryologist, Laboratory IVF Algeria, Rotary Fertility Center, Algiers, Algeria,Member in of the Association for Scientific Research of the IRIFIV-AISRG Group -Algeria.

[6]Laboratory of Physiopathology,Genetics Molecular and Biotechnology (PGMB), Faculty of Sciences Ain Chock, Research Center. Health and Biotechnology, University Hassan II - Research Associate at the fertility center Irifiv a rsearcher in the Scientifi Research Group – Casablanca, Morocco

[7]Chairman of the IRIFIV Center Fertilit y-Obstetrics and Gynecology and Association for Scientific Research of the IRIFIV-AISRG Group Casablanca, Morocco

Abstract
Leukocytes are white blood cells that are specialised in initiating an immune response against pathogens. There are several types of leukocytes in the human body with various functions; also, leukocytes can be found in different parts of the body, protecting against pathogens. In the male reproductive system, leukocytes can be detected through many methods, and it has been shown the effectiveness of those leukocytes in defending the reproductive system. Yet, the high level of leukocytes can generate reactive oxygen species that can harm the sperms. Moreover, a high level of leukocytes can lead to a condition called leukocytospermia, which can point to low fertilisation, pregnancy and embryo development rate. Accordingly, this article will discuss the potential harm of high leukocytes level, in addition to the management and treatment of leukocytospermia.
Keywords: Leukocytes function and location, Female reproductive tract, Male reproductive tract, Leucocytes and male fertility, Management of leucocytospermia .

1 | INTRODUCTION

1.1 | Leukocytes function and location

Leukocytes are white blood cells, which are part of the immune system. They participate in powring inflammatory responses to any pathogens. Leukocytes are produced in the bone marrow, which is the manufacture of thousands of immune cells. Leukocytes production starts with pluripotent stem cells differentiation into various immune cells (Raskin, Latimer and Tvedten, 2004). Leukocytes can be classified as granulocytes, including neutrophils, basophils, and eosinophils cells, agranulocytes that consist of lymphocytes and monocytes. Granulocytes leukocytes have granules (lysosomes) and special granules with unique substance to each cell's function. Therefore, granulocytes can be identified from each other by their nucleus morphology, their size, and their granules stain. On the other hand, agranulocytes don't have any granules and any specific substance (Tigner A, et, 2020). Leukocytes blood circulating time is almost hours, which is considerably shorter for erythrocytes, and consequently, their appearance in the peripheral blood indicates their transition from their site of production to function place. However total white blood cell count (WBC) is a regularly evaluated value on the routine complete blood count is useless if differential counts have not been performed to help recognise the specific altered cell types in number by processes such as exercise or disease. Moreover, leukocytes can be separated in the spleen; therefore, their appearance in the peripheral blood can be primarily influenced by exercising, thus changing the cortisol and catecholamine profile (McKenzie, 2014). Different types of Leukocytes have various functions in the body. For example, Neutrophils are responsible for pathogens defence, such as fungus and bacteria; they are released with early acute inflammation and makes up 60% of the leukocytes cells. While Eosinphile acts in allergic reaction and parasitic invasions. Other leukocytes such as Basophile are also involved in an allergic reaction, plus histamine release. Most importantly, macrophage cells are responsible for pathogens phagocytosis **(Figure 1)** (Al-Shura, 2014).

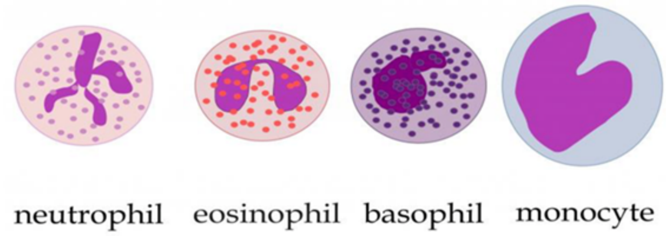

FIGURE 1: *Different types of Leukocytes in the human body (Bishop, 2021)*

2 | LEUKOCYTES IN THE REPRODUCTIVE TRACT

2.1 | Female reproductive tract

Leukocytes can be found in the reproductive tract to perform fundamental functions. Immune mechanisms play essential functions in the cervix, uterus, fallopian tubes and ovary; throughout the reproductive tract, several cells and mediators immune cells can be found. Reproduction disorder and infertility, such as pre-eclampsia, un-explained infertility, endometriosis, recurrent miscarriage, and disorganised fetal growth, can have a dysfunctional immune regulation. Through the female reproductive tract, the ovary also seems to be an essential immune-endocrine-reproductive interactions site. Moreover, leukocytes and their mediators, cytokines, are imperative components of normal physiological function, such as follicular development, ovulation and corpus luteum function (Norman, Bonello, Jasper and Van

Supplementary information The online version of this article (https://doi.org/10.15520/arjmcs.v7i06.324) contains supplementary material, which is available to authorized users.

Corresponding Author: *Mustafa Zakaria*
The Association for Scientific Research of the IRIFIV-AISRG Group
MD. Se-nior Clinical Embryology and Assisted Conception , Deputy Executive Director and Administrative Co-ordinator of the Association for Scientific Research of the IRIFIV-AISRG Group, Consultant in IRIFIV Fertility Center , IVF laboratoy, Casablanca ,Mo-rocco
Email: dr.zakaria@irifiv-aisrg.com

der Hoek, 1997). Neutrophils and macrophages are the primary immune cells observed in the ovary, although mast cells, eosinophils and lymphocytes can also be found. Most neutrophils or macrophages are ejected from the granulosa layer by the basement membrane within theca and granulosa layers. A massive increase of leukocyte numbers in the ovary is associated with LH surge, particularly neutrophils, macrophages and mast cells (Norman, Bonello, Jasper and Van der Hoek, 1997).

3 | MALE REPRODUCTIVE TRACT

As for the male reproductive system, leukocytes can be found in the semen, whose physiologic function is to eliminate abnormal germline from the ejaculate. During the male lifetime, most fertile and infertile men will have significant leukocytes in their seminal fluid (Rossi and Aitken, 1997). Leukocytes normality in semen has been defined as I x 106 ml with values more; any higher number of leukocytes in the seminal fluid is considered leukocytospermic as identified by the World Health Organization. The exact origin of seminal leukocytes is still unknown; however, histological examinations have shown leukocyte populations in almost all male reproductive tract tissues (Rossi and Aitken, 1997). Leukocytes can be found in different parts of the male reproductive; in the testes, male germ cells grow while separated from the immune system by the blood-testis barrier. Therefore, the male gamete continues to grow for a period of time in an immunologically privileged place. Yet, in the rete testes and epididymis, no such wall exists. The immunological and inflammatory responses can directly contact the millions of spermatozoa stored in this organ. The epididymis is an immunologically competent tissue that can evoke inflammatory reactions such as epididymitis infection (Rossi and Aitken, 1997). Moreover, in normal fertile men, a vast amount of macrophages were identified within the seminiferous tubules in direct contact with the external layer of the tubule wall and surrounding the blood vessels in the interstitium (Barratt, Bolton and Cooke, 1990). Furthermore, in the rete testis of man, macrophages cells are mainly found in the connective tissue, where most of them expressed HLA DR antigens, showing their ability to start an immune response. However, it still not clear if these cells are phagocytic and antigen-presenting (Barratt, Bolton and Cooke, 1990). There is now solid experimental data which indicates that immunoregulation in the testicular and epididymal leukocytes perform a fundamental role, both systemically and locally, in the male tract. The immunoregulation mechanisms and the specific purpose of the leukocytes still need to be illustrated clearly. It is suggested that the macrophages of the testis and epididymis can limit antigen presentation by phagocytosis of spermatozoa with the consequent rapid loss of antigenicity; yet, macrophages primary function is antigen-presenting **(Figure 2)** (Barratt, Bolton and Cooke, 1990).

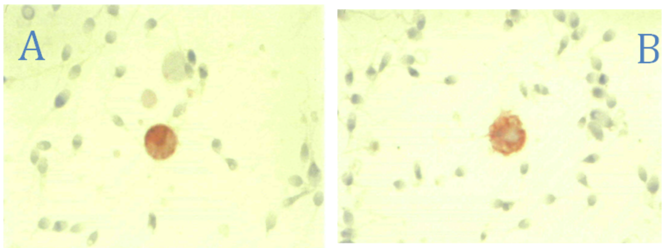

FIGURE 2: *Immunocytochemical staining of white blood in male semen. A) Macrophages in male seminal fluid. B) Neutrophil in male seminal fluid (Barrett, Bolton and Cooke, 1990).*

Some researchers have described a positive correlation between seminal leukocyte and semen quality as phagocytosis by leukocytes help to reduce abnormal spermatozoa from the semen. Furthermore, it has been shown that higher seminal leukocyte concentration can improve sperm motility (Ooi, et al., 2020). As in (Tomlinson et al., 1992) study, the results indicates high suggestive of a phagocytic mechanism for the elimination of morphologically abnormal spermatozoa in the ejaculate. However, in teratozoospermia patients, both the leukocyte total and the number of functional phagocytes were significantly lower, proposing that in teratozoospermia patients, the mechanism of abnormal spermatozoa elimination was inadequate. In addition, there was an influential association with the total of both macrophages and HLA-DR expression in head defects sperms. This indicates that abnormal sperms can be detected via antigenicdeterminants around the headregion of the spermatozoon (Tomlinson et al., 1992).

4 | LEUKOCYTES AND MALE FERTILITY

As mentioned earlier leucocytes is common to be found the human seminal fluid, yet several studies reported negative effect of leucocytes on sperms parameters, fertility and semen quality. Male infertility has been found to be link with an increase in the rate of leucocytes in semen beginning from subclinical infections of the epididymis, the prostate, or and the seminal vesicles, which also can influence fertilization, implementation and embryo development (GEYTER et al., 1994). Leukocytospermia-induced sperm defects is a possible outcome of the high levels of reactive oxygen species (ROS) derived by leukocyte and inflammatory mediators. High-level ROS production has generally been identified as the mechanism by which pathogens and leukocytes are producing harm to the sperms through triggering lipid peroxidation and damaging mitochondrial activity. Also, it is well known that spermatozoa are very sensitive to ROS and oxidative stress due to their unique plasma membrane and cytoplasm, which contains a high level of polyunsaturated fatty acids (Henkel, Offor and Fisher, 2020). ROS is recognised in the male genital tract to generate immature spermatozoa and leukocytes (chiefly neutrophils and macrophages). The invade of bacteria triggers tissue site defences of the host in unique or non-specific immunity way in all the tract including testis, epididymis, prostate gland and seminal vesicles. Spermatozoa in seminal plasma are in contact with leukocytes for a comparatively short period of time, particularly from the point of ejaculation till the male germ cells reach the cervix (Ooi, et al., 2020). The mechanism of ROS action starts with ROS production by the leukocytes to fight infections by attacking pathogens through stimulating G6PDH activity, allowing high NADPH levels production. NADPH oxidase then reduces NADPH electron to transform oxygen to superoxide anion **(Figure 3)** (Ooi, et al., 2020).

Furthermore, ROS can harm the sperm plasma membrane through lipid peroxidation, which has a re-

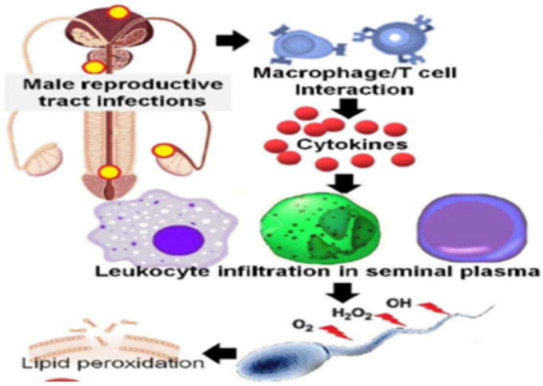

FIGURE 3: *Mechanisms male reproductive tract infection. The above diagram illustrates how the leukocyte's cell invade and fight the pathogens in the male reproductive tract (Ooi, et al., 2020).*

markably high quantity of polyunsaturated fatty acids; consequently, it is prone to oxidative damage. Moreover, ROS has been correlated to an increase in sperm DNA fragmentation (SDF). Thus, DNA-damaged spermatozoa can be found in all-male reproductive tract sites, reflecting that the oxoxidative damage can happen in testis and epididymis, and the ejaculate (Henkel, Offor and Fisher, 2020). Even if the male accessory sex glands are infected, sperm function, including the DNA, can be influenced through the influence of ROS generated by stimulated leukocytes as they stimulate apoptosis in mature human spermatozoa Bacteria can too cause spermatozoa apoptosis. Sperm DNA injury can influence early post-implantation embryo development and therefore reduce the fertility and pregnancy rate (Henkel, Offor and Fisher, 2020). Free radicals can immediately harm sperm DNA by attacking the purine and pyrimidine bases. Most sperm genome is connected to central nucleoproteins that defend them from free radical attack; therefore, ROS produce injury to single and double-strand DNA breaks, cross-links, and chromosomal rearrangements (Wagner, Cheng and Ko, 2018) an infertile male usually has insufficient protamination, allowing their sperm DNA more exposed to ROS damage. Also, another spermatic DNA damage mechanism is free radical-initiated apoptosis, pointing to DNA destruction. Sperm repair mechanisms in haploid spermatozoa are required to provide chromatin rearrangement; however, spermatozoa have an insufficient capacity to repair DNA and can barely be performed through specific stages of spermatogenesis. Interactions of sperm with an locate can permit some DNA repair, affecting fertilisation and possible pregnancy **(Figure 4)** (Wagner, Cheng and Ko, 2018).

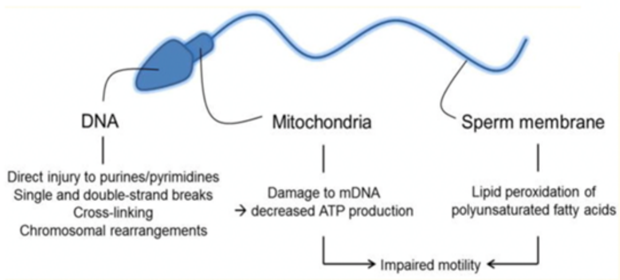

FIGURE 4: *Pathological effects of ROS onspermatogenesis and function (Wagner, Cheng and Ko, 2018)*

ROS level can be measured through direct or indirect assays. Direct assays measure the oxidation levels of the sperm cell membrane. Indirect assays measure the damaging impacts of oxidative stress, like sperm DNA damage levels. The chemiluminescence technique is a direct assay that is usually applied to measure seminal ROS (Takeshima, Kuroda and Yumura, 2018). Several pieces of research look into the effects of abnormal leucocytes on sperm parameters and fertility outcomes. Effects on semen parameters In YILMAZ et al., study, they tried to determine the impacts of leucocytospermia on semen parameters and ICSI result in infertile patients. The median leucocyte concentration was 2.68 million/mL in the leucocytospermic group. Semen forward progressive motility rates were (1.5% vs 3%), and sperm concentrations (12 vs 29 million/mL). Sperm concentrations were significantly lower in the leucocytospermic patients. The total motility rates were similar between the groups (56% vs 58%). However, after semen preparation, there was no difference between progressive forwarding motility (16% vs 19%) and total motility rates (85% vs 79%) within the groups (YILMAZ et al., 2005). In addition, the effects of leucocytes on ICSI was determined by fertilization rate and embryo development. The detection of leucocytes reduced fertilization and embryo development rates. Fertilization rates (82% vs 87%) and embryo development rates (79% vs 86%) in the leucocytospermic group were significantly lower than those of the non-leucocytospermic group. Still no significant difference in embryo quality between the leucocytospermic group and the non-leucocytospermic group (88% and 92% for good quality embryos and 11% and 3% for deficient embryos respectively) (YILMAZ et al., 2005). They also reported that low fertilization rates seem to be reasonable as leucocytospermic samples produced oxidative stress enough to damage DNA in sperms, and the rate of spermatozoa with fragmented DNA is proposed to have a negative association with fertilization rates in IVF (YILMAZ et al., 2005). Moreover, the presence of leucocytes cells negatively influenced both the fertilization and the pregnancy rate in IVF and embryo transfer. Both the number of fertilized oocytes and the pregnancies rate were decreased in the presence of more than 4 x 10' of leucocytes cells/ml in semen samples. However, the differences were not statistically significant. Also, the fertilization rate was decreased significantly (p<O.O5) in the presence of >8% of leucocytes cells. Besides, it was reported that that the detection of any seminal leukocytes was related to oxidative stress; thus, it not possible to establish the minimum level of WBCs correlated with oxidative stress. In addition, there was a significant negative correlation between oxidative stress and sperm concentration, motility, and sperm morphology, indicating the influential association of ROS with poor semen quality (SHARMA et al., 2001). Also, in SHARMA et al., 2001 study, ROS was detected in artificial conditions while the seminal plasma washed away. This method, consequently, indicates the generation of ROS by granulocytes and macrophages only in the absence of seminal plasma. Such leukocyte-derived ROS can be free to harm and attack spermatozoa while they are washed free of seminal plasma through the swim-up method (SHARMA et al., 2001). Moreover, to assess the outcome of assisted reproductive treatment, it has been reported that fertile male had a higher mean number of round cells in their semen than infertility patients; also, pregnancy percentage increased from 12.4% with no round cells sperms to 18.0% and 16.8% with rising concentrations of round cells. In addition, there was a significant rise in the percentage of pregnancyloss, from 13.2% for the group with no leukocytopenia to 36.4% when leukocytes were higher than 106/mL, and followed by a reduction in the delivery rate from 83.7% to 63.6% (Barraud-Lange et al., 2011). Accordingly, a better pregnancy rate was obtained, with significantly better motility, vitality, and sperm morphology. The study was concluded by that, leukospermia does not impact the pregnancy rate, yet, it is linked with increased pregnancy loss, as in infertility patients (Barraud-Lange et al., 2011). Furthermore, a significant number of asymptomatic infertile men were diagnosed with leukocytospermia; in addition, leukocytospermia was negatively associated with sperm morphology. Therefore, solvent leukocyte cells can influence fertility through reducing sperm motility and fertilizing ability (G. Arata De Bellabarba, I. Tortoler, 2000). G. Arata De Bellabarba, I. Tortoler, 2000 results show that leukocytes in the semen of infertile men are correlated with a significant decrease in sperm concentrations, percent motile sperm, sperm membrane integrity, and sperm morphology, implying that leukocyte cells can impair male fertility. On the other hand, several researchers have been performed to assess the impact of leucocytes on the sperm parameters, which include motility, morphology and numbers of sperms. One study illustrates an increase in normal morphology and progressive motility in semen samples with leukocyte concentrations ranging from 0-1.0 × 106/mL. However, there was a reduction in each parameter at a leukocyte threshold >1 × 106/mL. Moreover, all sperms types had damages rose progressively with rising leukocyte counts (Lackner et al., 2010). Moreover, in RJ, K and D, study they examined the semen profile, as they found that the presence of various leukocyte types in the human ejaculate was significantly linked with exfoliated germ cells. There were few exfoliated germ cells detected; however, there was a significant correlation with the size of the different leukocyte subpopulations in the human ejaculate. The presence of several leukocyte species was also correlated with sperms concentration, especially with type B cells or monocytes/macrophages. Additionally, sperm function was also observed, where a significant impact of leukocyte contamination on the capacity of the washed sperm preparations for sperm-oocyte fusion was detected. Accordingly, when those leukocytes were recognised in these washed sperm preparations, sperm-oocyte fusion did not happen due to the high rate of ROS activation.

5 | MANAGEMENT OF LEUCOCYTOSPERMIA

There has been a considerable debate regarding the threshold point of the leukocytes percentage in the seminal fluid; some have found this value too low, others too high depending on their methods applying. The WHO Laboratory guidelines suggest that a single peroxidase test be performed in 1 + 9-diluted should be applied for semen to assess leukocytes to examine human semen (Cooper and Hellenkemper, 2010). The appearance of one activated leukocyte per 20000 sperm can result in a considerable number of ROS; therefore, even a deficient amount of leukocytes in the sperm suspension can impact the integrity of sperm and, accordingly, the result of assisted reproduction treatment. Thus having a precise and very sensitive technique to detect seminal leukocyte is of paramount importance (Ricci et al., 2009). In addition to the Peroxidase rest, swim-up and density gradient centrifugation are still the most well-known techniques for separating functionally healthy spermatozoa. Swim-up can give a sperm suspension with a lower level of leukocyte contamination than that obtained after density-gradient centrifugation (Ricci et al., 2009). *The most common management protocol for leuctocytospermia is the elimination of infection and protection against ROS generated within cellular mitochondria due to inflammation. Below is a flow chart that illustrates the clinical management of leuctocytospermia **(Figure 5)** (Khodamoradi et al., 2020).*

Several meta-analyses confirmed that applying broad-spectrum antibiotics to treat patients with leukocytospermia may enhance sperm concentration, motility, and morphology. Yet, these researches did not report any influence on pregnancy or adverse effects (Jung et al., 2016). Jung et al., 2016, reported a noticeable decrease in leukocytospermia percentage in the treated group than the untreated group, in addition to a significant reduction in

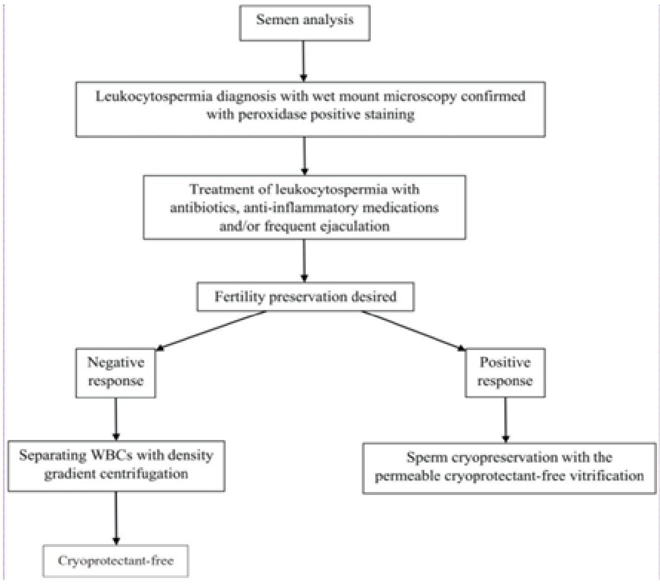

FIGURE 5: *Managementof semen samples obtained from leukocytospermic infertile males (Khodamoradi etal., 2020).*

the amount of seminal bacteria in the treatment group (Jung et al., 2016). Usually, there is no clear protocol for the treatment of leukocytospermia; however, antibiotics can advance the overall quality of spermatozoa, but there is no evidence of increased pregnancy rates after antibiotic treatment of the male partner. The various medication has been used in the treatment for leukocytospermia (Khodamoradi et al., 2020). For instance, ketotifen, an antihistamine-like drug, enhanced sperm motility and morphology in patients with leukocytospermia. Antioxidants have been applied to decrease the generation of ROS by seminal leukocytes. Nonsteroidal anti-inflammatory drugs (NSAIDs) were observed to improve sperm count, motility, and morphology in asthenoteratozoospermia men with leukocytospermia. In conclusion, these researches show the conflict in the debate about the management and treatment of leukocytospermia (Khodamoradi et al., 2020).

6 | CONCLUSION

In conclusion, leukocytes infiltration into the human ejaculate is normal and can be detected in the healthy fertile male semen sample; however, if a high level of leukocytes is found in the seminal fluid, it can indicate a male reproductive tract infection that can potentially influence male fertility. Although leukocytes role is debatable, some researchers have suggested that seminal leukocytes can't be just a response to infection; however, it works to attack abnormal germ cells and can perform some positive role in surveilling and phagocytosing of abnormal and dead spermatozoa. Yet, it has been shown in this research paper that a high number of leukocytes in the seminal fluid can lead to leukocytospermia, which can impact male fertility, embryo development and pregnancy rate. Suppose proper sperm separation methods have been used to separate leukocytes from health sperms before assisted reproduction. In that case, the generated spermatozoa will be completely functional and able to fertilize the oocyte and develop an embryo.

7 | ACKNOWLEDGMENTS

Objective of the Association for Scientific Research of the IRIFIV-AISRG Group (IRIFIV-AISRG),Research foundation in Casablanca, Maintaining consistent and reliably high success rates is a monthly challenge for in IVF labs, the IRIFIV Fertility Center in Casablanca – Morocco Department of Reproductive Medicine and Reproductive Biology and Embryology , advocacy of interdisciplinary Department of Reproductive Medicine and Reproductive Biology and Embryology study, encompassing the areas of research, collections and publishing Articles.

Abbreviations

In-vitro fertilization **(IVF),** white blood cell count **(WBC)** , reactive oxygen species **(ROS)** ,sperm DNA fragmentation **(SDF).** , Nonsteroidal anti-inflammatory drugs **(NSAIDs)** ,

8 | REFERENCES

1. Al-Shura, A., 2014. Immune System 1. Hematology in Traditional Chinese Medicine Cardiology

2. Barratt, C., Bolton, A. and Cooke, I.,Functional significance of white blood cells in the male and female reproductive tract. Human Reproduction 5(6), pp.639-648.

3. Barraud-Lange, V., Pont, J., Pocate, K., Kunstmann, J., Chalas-Boissonas, C., Ducot, B. and Wolf, J., 2011. Seminal leukocytes and clinical outcomes with donor sperm insemination. Fertility and Sterility 96(6), pp.1320-1324.e1.

4. Bishop, D., 2021. What Are the Different Types of Human Blood Cells? [online] Wisegeek. Available at: <https://www.wise-geek.com/what-are-the-different-types-of-human-blood-cells.htm>.

5. Cooper, T. and Hellenkemper, B., 2010. Improving precision in the assessment of round cell numbers in human semen. Asian Journal of Andrology, 12(1), pp.111-114.

6. G. Arata De Bellabarba, I. Tortoler, 2000. NONSPERM CELLS IN HUMAN SEMEN AND THEIR RELATIONSHIP WITH SEMEN PARAMETERS. Archives of Andrology 45(3), pp.131-136.

7. GEYTER, C., GEYTER, M., BEHRE, H., SCHNEIDER, H. and NIESCHLAG, E., 1994. Peroxidase-positive round cells and microorganisms in human semen together with antibiotic treatment adversely influence the outcome of in-vitro fertilization and embryo transfer. International Journal of Andrology 17(3), pp.127-134.

8. Henkel, R., Offor, U. and Fisher, D., 2020. The role of infections and leukocytes in male infertility. Andrology , 53(1).

9. Jung, J., Kim, M., Kim, J., Baik, S., Koh, S., Park, H. and Seo, J., 2016. Treatment of Leukocytospermia in Male Infertility: A Systematic Review. The World Journal of Men's Health, 34(3), p.165.

10. Khodamoradi, K., Kuchakulla, M., Narasimman, M., Khosravizadeh, Z., Ali, A., Brackett, N., Ibrahim, E. and Ramasamy, R., 2020. Laboratory and clinical management of leukocytospermia and hematospermia: a review. Therapeutic Advances in Reproductive Health 14, p.263349412092251.

11. Lackner, J., Agarwal, A., Mahfouz, R., du Plessis, S. and Schatzl, G., 2010. The association between leukocytes and sperm quality is concentration dependent. Reproductive Biology and Endocrinology, 8(1).

12. LACKNER, J., MARK, I., SATOR, K., HUBER, J. and SATOR, M., 2008. Effect of leukocytospermia on fertilization and pregnancy rates of artificial reproductive technologies. Fertility and Sterility, 90(3), pp.869-871.

13. McKenzie, E., 2014. Hematology and serum biochemistry of the equine athlete. Equine Sports Medicine and Surgery, pp.921-929.

14. Norman, R., Bonello, N., Jasper, M. and Van der Hoek, K., 1997. Leukocytes: essential cells in ovarian function and ovulation. Reproductive Medicine Review, 6(2), pp.97-111.

15. Ooi, Chai & Dutta, Sulagna & Sengupta, Pallav. (2020). Role of leucocytes in reproductive tract infections and male infertility. Chemical Biology Letters. 7. 124-130.

16. Raskin, R., Latimer, K. and Tvedten, H., 2004. Leukocyte Disorders. Small Animal Clinical Diagnosis by Laboratory Methods, pp.63-91.

17. RJ, A., K, W. and D, B., 1994. Leukocytic infiltration into the human ejaculate and its association with semen quality, oxidative stress and sperm function. Journal of Andrology, 15(4).

18. Rossi, A. and Aitken, R., 1997. Interactions between Leukocytes and the Male

19. SHARMA, R., PASQUALOTTO, F., NELSON, D., THOMAS JR, A. and AGARWAL, A., 2001. Relationship Between Seminal White Blood Cell Counts and Oxidative Stress in Men Treated at an Infertility Clinic. American Society of Andrology, 22(4).

20. Takeshima, T., Kuroda, S. and Yumura, Y., 2018. Reactive Oxygen Species and Sperm Cells. Reactive Oxygen Species (ROS) in Living Cells.

21. Tigner A, Ibrahim SA, Murray I. Histology, White Blood Cell. [Updated 2020 Sep 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing

22. Tomlinson, M., White, A., Barratt, C., Bolton, A. and Cooke, I., 1992. The removal of morphologically abnormal sperm forms by phagocytes: a positive role for seminal leukocytes? Human Reproduction, 7(4), pp.517-522.

23. Wagner, H., Cheng, J. and Ko, E., 2018. Role of reactive oxygen species in male infertility: An updated review of literature. Arab Journal of Urology, 16(1), pp.35-43.

24. YILMAZ, S., KOYUTURK, M., KILIC, G., ALPAK, O. and AYTOZ, A., 2005. Effects of leucocytospermia on semen parameters and outcomes of intracytoplasmic sperm injection. International Journal of Andrology, 28(6), pp.337-342.

How to cite this article: N.L., A.A., M.Z., A.N., R.B., M.M.M., M.Z. **Infiltration of leukocytes into the human ejaculate and its association with semen quality and oxidative stress with sperm function, and leukocytospermia management.**. Advance Research Journal of medical and clinical science. 2021;582−589. https://doi.org/10.15520/arjmcs.v7i06.324