

Review Article

Asian Pacific Journal of Reproduction

Journal homepage: <https://journals.lww.com/apjr/>

doi: 10.4103/apjr.apjr_175_24

Impact of antisperm antibodies on sperm functions and fertility in livestock: A narrative review

Channareddi Kuntareddi[#], Kamaraj Elango[#], Pradeep Nag, Arumugam Kumaresan[✉]*Theriogenology Laboratory, Southern Regional Station of ICAR–National Dairy Research Institute, Bengaluru–560030, Karnataka, India*

ABSTRACT

Spermatozoa are recognized as foreign cells by both male and female immune systems, leading to the production of antisperm antibodies (ASAs) when sperm are exposed to immune system due to a breach in the mucosal barrier. ASAs can be found in both sexes, though concentrations vary by individual and sex. This review examines ASAs production, their specific binding locations on sperm, and how ASAs may impair key sperm functions, including motility, viability, acrosome reaction, and capacitation. While ASAs are known to potentially interfere with sperm quality and sperm binding to zona pellucida in both humans and livestock, their impact on fertility remains debated, as ASAs are also detected in a significant number of fertile individuals. Furthermore, the practical relevance of ASAs screening in fertility assessment lacks consensus, with some findings suggesting that ASAs might even aid fertilization under certain conditions. By compiling the information on ASAs and their effects on semen quality and fertility, this review aims to provide a comprehensive understanding of the role of ASAs in infertility.

KEYWORDS: Subfertility; Antigen; Sperm quality; Male fertility; Immunological infertility; Fertilization

1. Introduction

Breeding soundness evaluation, currently used for bull selection, aims to assess the likelihood of mating ability, semen production and to some extent sperm quality but not the actual fertility of bulls. Subfertility or infertility in breeding bulls can have profound negative consequences in the dairy industry because semen from one bull is used to artificially bred several thousand cows. In our earlier study, we found that both semen quality and semen production ability showed a decreasing trend over a period of time in breeding bulls[1]. Sub-fertile/infertile bulls delay conception, prolong the calving season, reduce calf weaning weights, and increase the numbers of females culled, thereby resulting in economic losses[2]. Multiple etiologies are ascribed

to male infertility/sub-fertility including deviations in testicular cytological composition[3–5], single nucleotide polymorphisms[6], transcriptomic profile[7,8] and protein profile[9,10]. Similarly, several studies have reported altered functional attributes[11,12], transcript profile[13,14], protein profiles[15–17] and metabolomic profile[18–20] of spermatozoa as a reason for infertility/sub-fertility in breeding bulls. In a recent review, the importance of sperm DNA integrity and sperm molecular health on bull fertility has been discussed in detail[21]. In spite of all these advancements, prediction of bull fertility still remains as a challenge. A considerable proportion of breeding bulls selected after a rigorous breeding soundness evaluation yield poor conception rate[22]; the etiology for such sub-fertile conditions is not yet understood.

The possible causes of sub-fertility or infertility in bulls are poorly defined, but one important cause may be immunological conditions[23]. Immunological causes of infertility have been studied in detail in human beings[24–28]; however, such studies are limited in livestock[29,30]. Sperm of humans, non-human primates, and other mammalian subjects is considered to be allogeneic antigens by the female body[31]. Therefore, any disruption of the mucosal layer of the female reproductive tract allows exposure of sperm antigens to mucosal immune system leading to production of antisperm antibodies (ASAs). However, ASAs were believed to be present in both males and females in considerable amounts but higher concentrations of ASAs were observed among infertile patients[32]. On the other hand, ASAs are also present in fertile male and females for unknown reasons, or the function is still not explored

[#]Contributed equally to this manuscript.

[✉]To whom correspondence may be addressed. E-mail: ogkumaresan@gmail.com; A.Kumaresan@icar.gov.in

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

©2024 Asian Pacific Journal of Reproduction Produced by Wolters Kluwer- Medknow.

How to cite this article: Kuntareddi C, Elango K, Nag P, Kumaresan A. Impact of antisperm antibodies on sperm functions and fertility in livestock: A narrative review. *Asian Pac J Reprod* 2024; 13(6): 251-260.

Article history: Received: 7 October 2024; Revision: 29 October 2024; Accepted: 11 November 2024; Available online: 10 December 2024

properly[33]. Although the prevalence and impact of ASAs on fertility was fairly studied in females, such studies on males are very few. Earlier studies reported that the incidence of ASAs in bulls ranged from 7.8% to 58.1% with a clear difference in the concentrations between satisfactory and non-satisfactory breeders[34–36].

Although spermatid and spermatozoa are protected from the immune system within the seminiferous tubule by Sertoli cell tight junctions of blood-testis barrier, naturally occurring ASAs have been recognized in many species including human[37,38], bulls[29], stallion[39] and dogs[40]. Contradictory reports exist on the effect of ASAs on male fertility; several reports suggest that ASAs affect the bull fertility by reducing the number of motile and competent spermatozoa in an insemination dose. Also, ASAs have been shown to interfere with sperm capacitation and sperm oocyte interactions; on the other hand, few studies suggested no effect of ASAs on sperm parameters and that ASAs presence seems to be innocuous for fertility[25]. The presence of higher levels of ASAs in semen is reported to lower the chance of the sperm fertilizing an egg[41]. Recently, it was reported that the proportion of spermatozoa responding to ASAs was higher in low-fertile compared to high-fertile breeding bulls[42]. In addition to the economic loss, sub-fertile/infertile bulls may have adverse effects on animal welfare due to failure of conception and delayed calving. Therefore, a thorough understanding on the effect of ASAs on sperm function is required to appreciate the influence of ASAs on male fertility. Accordingly, in this review, the earlier findings on ASAs in relation to semen quality and male fertility are compiled and analyzed. Furthermore, the causes and consequences of ASAs are described, together with a review of advances in methods for detection of ASAs, and the prognostic value of ASAs on male fertility.

2. Immunological infertility

Fertility is one of the key factors for the lifetime production and reproduction of an animal; when normal functions of the reproductive system are impaired, it results in infertility. Infertility/subfertility in cow and bulls has significant negative consequences on the economics of dairying[43]. In female, infertility may be due to number of factors, like aberration of ovulation, obstruction of fallopian tubes, presence of pathological lesions in reproductive tract and poor quality of cervical mucus[44]. However, unexplained infertility, characterized by a lack of obvious symptoms, presents a significant challenge for veterinarians[45–47]. In both sexes, one of the causes of infertility is an immunological factor[36,48,49] associated with the presence of antibodies against spermatozoa as a result of autoimmunization in males and iso-immunization in females[50,51]. The immunological infertility due to the perturbed homeostatic machinery of immune system was earlier considered as an unexplained infertility[52]. This has been reported as a cause of infertility in several species including humans[53,54], cattle[47,51,55] and swine[56].

Table 1. Incidence of immunological infertility.

Sl. No.	Species	Incidence of ASAs	References
1	Cows	Serum (34.5%) Cervical mucus (37.9%)	[65]
2	Cows	Serum (39.5%)	[67]
3	Cows	Serum (17.6%)	[68]
4	Cows	Serum (25.5%)	[46]
5	Mice	Serum (62.5%)	[69]
6	Zebu cattle	Serum (11.8%)	[47]
7	Cows	Serum (100.0%)	[55]
8	Cows	Serum (69.6%) Cervical mucus (45.0%)	[62]
9	Cows	Serum (61.0%)	[70]

Mucosal immunity in the female genital tract is influenced by the level of antibodies, cytokines and hormones; neutrophils and macrophages are first line of innate immune response recruited by cytokines to the site of inflammation[57]. Antibodies can develop against various antigens related to reproductive functions in males and females but ASAs present in seminal plasma, cervical mucus, uterine fluid, follicular fluid or sera[58] has been reported to delay conception by impairing fertilization leading to infertility[59–62]. During the early phase of the primary immune response after exposure to an antigenic agent, IgM antibodies are produced. When the immune system is exposed to the same antigen again, the antibodies switch into secondary immune response; therefore, IgG and IgA are produced in response to the secondary immune response or after repeated exposure to the same antigen[63]. Among the five immunoglobulins (IgM, IgG, IgA, IgD, and IgE) and three immunoglobulin (Ig) isotopes namely IgM, IgG and IgA are involved in immunologically mediated infertility. They are present in the blood serum as IgG and in genital tract secretion as IgA in both male and female bovine[51].

There are reports relating the presence of ASAs with infertility in several species, including human[45,64], cattle[46,47,49,51,55,62,65], swine[56] and in other farm animals[66]. The reported incidence of ASAs in serum and cervical mucus[46,47,55,62,65,67–70] are given in Table 1. Ulcova and Gallova suggested that ASAs present in cervical mucus is agglutinating in nature[71]. These locally produced anti-sperm antibodies do not differ from ASAs that are produced systematically; thus, they affect sperm capacitation, acrosome reaction, motility of spermatozoa and interfere with binding and penetration of zona pellucida by spermatozoa as well as embryo implantation in uterus[72]. The effect of ASAs on fertility is substantiated by the findings of several reports indicating higher concentrations of ASAs in blood and cervical mucus of infertile cows as compared to normal cows. Presence of ASAs in blood serum of dairy cattle was studied and found that about 60% of blood serum in repeat breeding cows were positive for ASAs against only 14% positivity in regular breeders[73]. Similarly, Vikrant *et al* also found higher titer and higher prevalence of ASAs in infertile cows as compared to normal cows[62].

3. Production of ASAs

ASAs are antibodies or immune reactive proteins that are produced against spermatozoa by lymphoid tissue or competent cells of immune system. Spermatozoa are foreign cells because they are not produced until the time of puberty. Spermatozoa-specific surface antigens first appear on pachytene stage of primary spermatocytes[74], but their progenitors, during spermatogenesis, are separated from coming into contact with the immune system by a blood-testis barrier and Sertoli cell junctions[75]. Blood-testis barrier plays an important role in maintaining immune privileged status of testis and removal of antigenic cells by phagocytosis. Sertoli cells release immunosuppressive factors and contribute to an immunologically protective status to the testis[76]. Disruption or breach in the blood-testis barrier induced by infectious, inflammatory or degenerative changes leads to exposure of sperm antigens to the immune system (Figure 1), activation of which leads to production of ASAs[76,77]. Epididymal abnormalities were also linked with the production of ASAs as assessed by mixed antiglobulin reaction (MAR) test[78]. Scrotal insulation also reportedly causes increase and long-term persistence of ASAs in bulls[79]. The effect of ASAs on fertility depends on their regional specificity, location, antibody class, isotype and antigen specificity[80,81]. The high percentage of ASAs bound spermatozoa, which are detected in ASAs-positive bulls[29,49], could significantly reduce the number of motile and competent spermatozoa in an insemination dose, thereby affecting the fertilization, conception rate and fertility of the bull.

Immunological incompatibility was observed between spermatozoa and oocyte due to ASAs in both male and female animals[51]. Spermatozoa are foreign to the female reproductive tract. For development of ASAs, spermatozoa have to come in contact with

blood; therefore, inflammation of genital organs, such as vaginitis, cervicitis and metritis or trauma and bleeding while mating or artificial insemination plays important role in development of ASAs[82,68]. Any mechanical or chemical disruption of the mucosal layer of the female reproductive tract allows exposure of these sperm antigens to mucosal immune system leading to ASAs formation by activation of mucosal immune system of the genital tract[83]. The regulation of local immunological mechanism is dependent on vaginal and cervical tissues with active and sensitive mucosal immune system. This explains the high percentage of infertile patient's association with local immune reactions leading to an inflammation as well as high levels of serum ASAs[84]. Serum ASAs are related to long-term exposure of female to spermatozoal antigens and seminal deficiency in immuno-suppressive factors[83,85]. Even the parenteral administration/immunization of whole sperm was also reported to induce ASAs production in genital secretion and serum[86]. Furthermore, the presence of ASAs is also influenced by number of factors like age, number of services, pregnancy status, lactation number, genital infections and immune status as well as hormonal status[87].

The immune response to spermatozoal antigens in natural mating usually does not occur due to the low immunogenicity of sperm and seminal plasma constituents[88]. Also, all body fluids which are important for sperm function and fertilization (seminal plasma, cervical mucus, follicular and uterine fluid) exert immunosuppressive effects to escape from mucosal immune system[89]. In artificial insemination, there are increased chances for immunization of females to sperm antigens because seminal plasma is diluted several times, thus reducing its strong immunosuppressive effects[90] and also because of new antigens emanating from semen extenders. It has been documented by sperm agglutination and

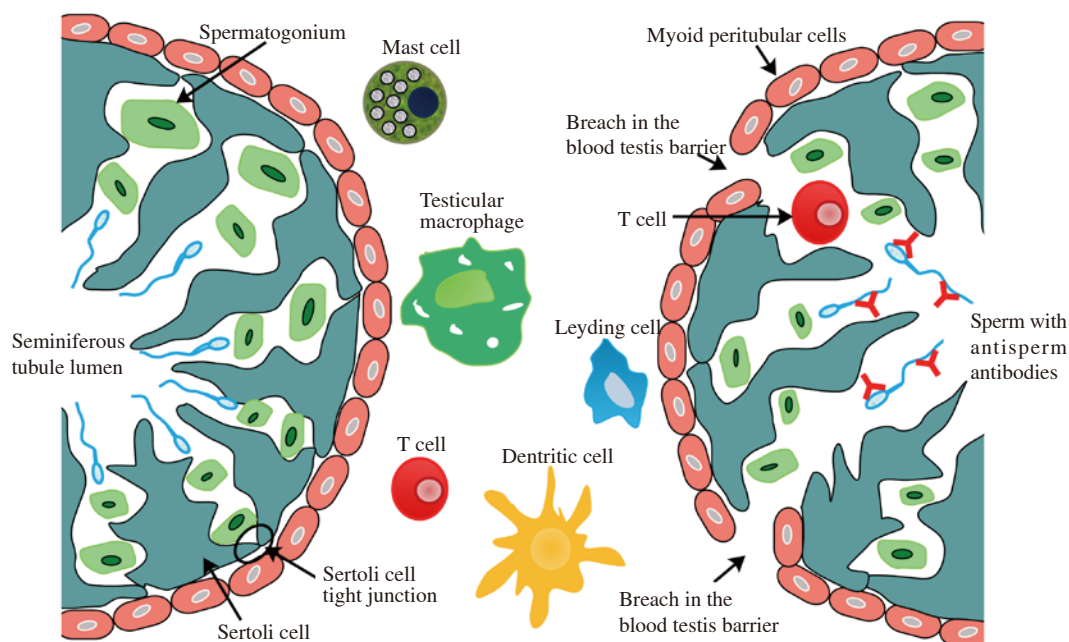


Figure 1. Production of antisperm antibodies. Left side-Seminiferous tubule with intact blood testis barrier; Right side-Breach in the blood testis barrier and the production of antisperm antibodies due to the exposure of sperm to the immune system.

indirect immunofluorescence assay that antigenic activity of bull spermatozoa differs due to the addition of different extenders, cryopreservation and thawing procedures and reduction of seminal plasma volume during semen preparation in artificial insemination technology[61]. Insemination of the semen to infected and inflamed genital tract triggers the immune response for ASAs production. Infectious agents bind to sperm membrane and may serve as an antigen or hapten, eliciting an immune response[83]. Subsequently ASAs are formed from mucosal immune system of cervix and endometrium, and consequently they enter the blood circulation and transudate back into genital tract secretions. ASAs production rate was higher in cows which were inseminated three or more times[91].

4. Target location of ASAs on sperm

Immunolocalization of antigens on the surface of spermatozoa helps to locate prone areas for attack of immune system and subsequently to know where exactly ASAs will bind (for instance acrosome, acrosomal cap, apical part, post acrosomal region, midpiece and tail piece of sperm) and alter the fertility of spermatozoa (Table 2)[92–101]. Few studies reported multiple ASAs in infertile subjects[102] but not all these ASAs cause infertility. Understanding the ASAs formation and its mechanism of action or effects on sperm functions could improve the treatment and managerial interventions. Immunofluorescence detection of ASAs binding to spermatozoa showed different localization patterns. A very strong signal was observed on acrosome surface, post acrosome region and principal piece of spermatozoa[92] indicating the presence of ASAs against acrosome surface, post acrosome and principal piece surface proteins in the blood serum/cervical mucus of artificially inseminated animals. Milovanovic *et al* also observed localization of ASAs on the head, tail or neck of the sperm cell when blood serum or cervical mucus of artificially inseminated Holstein Friesian cows was incubated with spermatozoa[103]. ASAs bind frequently to spermatozoa head and cytoplasmic droplets than midpieces and principal pieces as was confirmed by confocal microscopy[48]. Immunolocalization of sperm antigens using ASAs by Kuntareddi *et al* revealed three patterns of ASAs in sperm namely AR (acrosomal pattern-bright green fluorescence over the entire acrosome area), AP (apical pattern- bright green fluorescence only in apical region) and AT (fluorescence over acrosome and tail). The AR and AT pattern had a significant negative correlation with conception rate[42].

The binding pattern of ASAs to sperm depends upon the sperm protein against which antibody was developed. Different sperm molecules (heparin, heparin-binding proteins, and sulfated glycosaminoglycan) play crucial role in fertilization. Heparin-binding proteins induce capacitation and acrosome reaction in mammalian sperm[104]. The FA-1 antigen is a glycoprotein that has a ligand activity for oocyte's zona pellucida glycoprotein (ZP3) receptor[94]

Table 2. Location of antisperm antibodies on spermatozoa.

Sl.No.	Antigens on bull spermatozoa	Location on spermatozoa	References
1	HBP (heparin binding proteins)	Posterior head region of ram and bull sperm and acrosome of stallion sperm. Intense signal on acrosomal cap. Strong signal on post acrosomal cap.	[92,93]
2	FA-1 (fertilization antigen)	Post acrosome, midpiece and tail region of human spermatozoa. Post acrosomal, midpiece and tail region. Post acrosomal cap. On acrosomal cap. Post acrosomal region of rhesus monkey sperm.	[92,94,95,96]
3	SP-10 (seminal plasma protein-10)	Intra acrosomal protein.	[97]
4	BS-17 (calpastatin)	Over the acrosomal region and to a low extent in tail.	[98]
5	TIMP-2 (tissue inhibitor of metalloproteinases type-2)	Posterior head of bull and ram sperm, but exclusively found on acrosomal cap of stallion sperm. More concentrated on acrosomal cap than acrosome and post acrosomal cap.	[92,93]
6	IZUMO 1 protein	Integral membrane protein	[99,100]
7	ACTL7a (actin like protein 7a)	Acrosome and tail of mature spermatozoa.	[101]

and it also has effects on bovine *in vitro* fertilization[95]. The presence and abundance of tissue inhibitor of metalloproteinases-2 (TIMP2) in bovine semen and its ability to bind heparin[105] suggests that it has an important relationship with reproduction and fertility of bulls. The intra-acrosomal localization of bovine SP-10 antigen states that antibodies against SP-10 exerted their anti-fertilization effect by reducing sperm-zona secondary binding[97]. The sperm-specific protein actin-like protein 7A (ACTL7a), located in the acrosome and tail of mature spermatozoa, serves as a tyrosine phosphorylation substrate in capacitated buffalo spermatozoa[106] and is also essential for sperm capacitation in mice[107]. Antibodies against the ACTL7a protein inhibit its function mentioned above and also block its function during spermiogenesis[108]. It was reported that 56% of immune infertile women sera reacted positively with IZUMO 1, a spermatozoa specific protein, while none of the fertile women sera reacted with this protein[99].

5. Effects of ASAs on sperm functions

It has been reported that ASAs cause infertility by either affecting

sperm functions or by preventing sperm-oocyte interaction[109] or by limiting embryo development and implantation leading to early embryonic mortality[33,38,41]. ASAs adversely affect sperm motility, viability, capacitation, and acrosome reaction (Figure 2) which is detailed below.

5.1. Effect of ASAs on sperm motility

ASAs targeting the head and principal piece of spermatozoa significantly reduce the sperm's ability to penetrate cervical mucus[110,111]. It was reported that the IgG and IgA isotypes of ASAs in cervical mucus cause immobilization of spermatozoa by shaking phenomenon (when spermatozoa come in to contact with cervical mucus, the progressive propulsion of the spermatozoa changes to a stationary state)[112]. It was suggested that ASAs reacting with the sperm head or tail main piece, but not those reacting with the tail tip, prevented cervical mucus penetration[113]. Immobilization of spermatozoa caused clumping and limited the motility through cervical mucus[61]. Sperm immobilizing antibodies were significantly higher ($P<0.05$) in sera of repeat breeders compared to other groups of cows and these antibodies adhere on the surface of spermatozoa adversely affecting their movement[70]. It was shown that higher percentage of IgG and IgA ASAs in cervical mucus of crossbred cows binds to the antigens on the spermatozoa surface and because of antigen-antibody reaction there is head-to-head, head to tail or tail to tail agglutination[61,62]. Recent study by Archana *et al* revealed that percentage of sperm that can penetrate mucus, mitochondrial membrane potential and the sperm kinematic parameters such as straightness, linearity, curvilinear velocity, straight-line velocity, and average path velocity were significantly higher in samples with lower levels of ASAs[114]. The human papilloma virus (HPV) patients had a higher level of ASAs than non-HPV group. The HPV and ASAs affected infertility through impacting sperm count and motility[73].

5.2. Effect of ASAs on sperm viability

ASAs modify sperm plasma membrane permeability or fluidity, leading to reduced viability. In humans, Rossato *et al* reported that the mean percentage of membrane intact spermatozoa in ASAs positive semen samples was $(58.7\pm12.1)\%$, which was significantly

lower than that observed in ASAs negative semen samples $(77.5\pm5.9)\%$ [115]. The proportion of membrane intact spermatozoa differed significantly between bulls with low ASAs titers (45.4%) and high ASAs titers (39.6%)[29]. When blood serum of different groups (the control group, calf group, heifer group and cow group) was incubated with bull spermatozoa, it was observed that the number of viable spermatozoa in the control group (85.78 ± 1.01) and calf group (68.60 ± 1.88) was significantly more when compared to the cow group (55.73 ± 1.04) [116].

5.3. Effect of ASAs on sperm capacitation

Capacitation of spermatozoa is a crucial component of fertilizing ability of spermatozoa which includes multiple physiological and biochemical process and is essential to facilitate the acrosome reaction. The effect of ASAs on the capacitation process, such as calcium uptake or hyper activated motility after stimulation with follicular fluid was also studied with conclusive results[117]. Sperm bound ASAs significantly reduced the ability of bovine spermatozoa to undergo changes in membrane fluidity under capacitating conditions, therefore interfering in sperm oocyte interaction and inhibiting penetration of spermatozoa into the zona-pellucida leading to failure of fertilization[49]. The proportion of capacitated or acrosome reacted spermatozoa was significantly higher in semen of bulls with high ASAs titer in blood serum compared to bulls with low ASAs titer[29]. Further, it was reported that ASAs from infertile women reduced sperm capacitation by inhibiting tyrosine phosphorylation of sperm proteins[118].

5.4. Effect of ASAs on sperm acrosome reaction

Acrosome reaction is calcium dependent event, during which the plasma membrane of spermatozoa fuses with the outer acrosomal membrane, allowing the release and exposure of the acrosomal contents such as hyaluronidase and acrosin enzymes that are essential to allow spermatozoa to penetrate the oocyte membranes[119]. ASAs have been shown to enhance the rate of *in vitro* acrosome reaction of bull spermatozoa and ASAs in the cow uterine fluid have been shown to induce premature acrosome reaction[116]. Binding of ASAs to spermatozoa membrane during incubation in tyrode's albumin

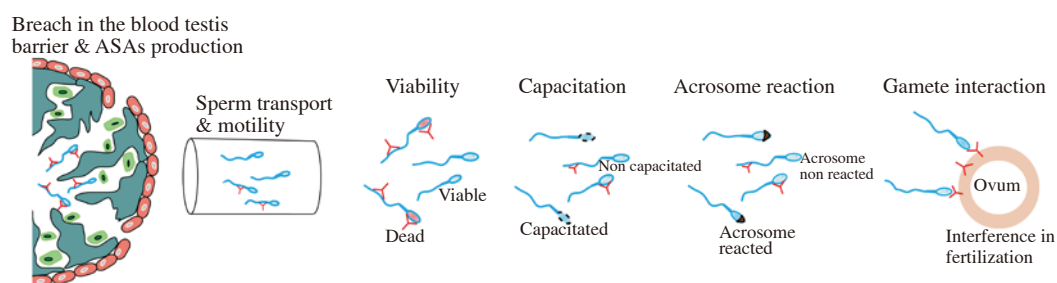


Figure 2. Impact of antisperm antibodies (ASAs) on spermatogenesis, sperm function and fertilization. Breach in blood testis barrier leads to production of ASAs that impairs sperm motility, viability, capacitation, acrosome reaction and gamete interaction.

lactate pyruvate (TALP) medium supplemented with serum showed an enhanced acrosome reaction and generation of reactive oxygen species. In an *in vitro* experiment, it was shown that antibodies that are directed against the proteins in periacrosomal membrane reduced the ability of spermatozoa to bind oviductal epithelial cells[120]. The proportion of acrosome-reacted sperm was significantly higher in the antibody-exposed sperm than in the controls [(47.0±13.2)% vs. (39.3±12.1)%][121]. Recently, Kuntareddi *et al* also reported the negative correlation between the reactivity of sperm with ASAs and the sperm membrane and acrosomal integrity[42]. On the other hand, spermatozoa incubated with serum containing immobilizing ASAs showed reduced rates of both spontaneous and induced acrosome reactions compared to sperm that were not incubated with the serum[122]. Further, it was found that 7 out of 12 ASAs-containing sera inhibited the zona pellucida-induced acrosome reaction[123]. Sperm coated with IgG and IgA antibodies exhibited high levels of spontaneous acrosome reaction[124]. Taken together, it may be informed that ASAs have a variable effect on the acrosome reaction and capacitation; while some ASAs can adversely alter the ability of spermatozoa to undergo capacitation or acrosome reaction, other ASAs do not.

6. Conclusions

Based on available literature, the ASAs production mechanism and the impact of ASAs on sperm functions and fertilization process are still poorly understood. The ASAs in semen were found not only in infertile males but also in fertile males. Therefore, the exact cutoff values of ASAs, above which it causes male infertility, need to be established. Furthermore, studies need to be undertaken to assess the prevalence and magnitude of infertility due to ASAs. This will help us to decide the level of importance of ASAs assessment in routine male fertility testing as well as in assisted reproductive technologies.

Conflict of interest statement

Authors declare no conflicts of interest in this study.

Funding

The study received no extramural funding.

Authors' contributions

Channareddi Kuntareddi and Elango Kamaraj conducted the literature search and were primarily responsible for drafting the initial manuscript. Pradeep Nag reviewed the study's concept and

design. Arumugam Kumaresan conceived the study, reviewed and edited its concept and design. All authors have read and approved the final version of the manuscript.

References

- [1] Thippeswamy VB, Layek SS, Kumaresan A, Mohanty TK, Gupta AK, Chakravarty AK, et al. Effects of pedigree and exotic genetic inheritance on semen production traits of dairy bulls. *Asian Pac J Reprod* 2014; **3**(1): 13-17.
- [2] Kastelic JP. Male involvement in fertility and factors affecting semen quality in bulls. *Animal Front* 2013; **3**(4): 20-25.
- [3] Rajak SK, Kumaresan A, Gaurav MK, Layek SS, Mohanty TK, Aslam MM, et al. Testicular cell indices and peripheral blood testosterone concentrations in relation to age and semen quality in crossbred (Holstein Friesian Tharparkar) bulls. *Asian-Australas J Anim Sci* 2014; **27**(11): 1554.
- [4] Rajak SK, Thippeswamy VB, Kumaresan A, Layek SS, Mohanty TK, Gaurav MK, et al. Testicular cytology indicates differences in Sertoli cell counts between “good freezer” and “poor freezer” bulls. *Indian J Exp Biol* 2016; **54**(1): 17-25.
- [5] Tripathi UK, Chhillar S, Kumaresan A, Aslam MM, Rajak SK, Nayak S, et al. Morphometric evaluation of seminiferous tubule and proportionate numerical analysis of Sertoli and spermatogenic cells indicate differences between crossbred and purebred bulls. *Vet World* 2015; **8**(5): 645.
- [6] Sinha MK, Kumaresan A, Rao Talluri T, Ebenezer Samuel King JP, Prakash MA, Nag P, et al. Single nucleotide polymorphisms cumulating to genetic variation for fertility in crossbred (*Bos taurus*×*Bos indicus*) bull spermatozoa. *Anim Biotechnol* 2023; **34**(7): 2875-2886.
- [7] Elango K, Kumaresan A, Sharma A, Nag P, Prakash MA, Sinha MK, et al. Sub-fertility in crossbred bulls: Deciphering testicular level transcriptomic alterations between zebu (*Bos indicus*) and crossbred (*Bos taurus*×*Bos indicus*) bulls. *BMC Genom* 2020; **21**(1): 502.
- [8] Paul N, Kumaresan A, Das Gupta M, Nag P, Guvvala PR, Kuntareddi C, et al. Transcriptomic profiling of buffalo spermatozoa reveals dysregulation of functionally relevant mRNAs in low-fertile bulls. *Front Vet Sci* 2021; **7**: 609518.
- [9] Tripathi UK, Aslam MK, Pandey S, Nayak S, Chhillar S, Srinivasan A, et al. Differential proteomic profile of spermatogenic and Sertoli cells from peri-pubertal testes of three different bovine breeds. *Front Cell Dev Biol* 2014; **2**: 24.
- [10] Aslam MKM, Kumaresan A, Rajak SK, Tajmul M, Datta TK, Mohanty TK, et al. Comparative proteomic analysis of high- and low-fertile buffalo bull spermatozoa for identification of fertility-associated proteins. *Reprod Domest Anim* 2019; **54**(5): 786-794.
- [11] Singh RK, Kumaresan A, Chhillar S, Rajak SK, Tripathi UK, Nayak S, et al. Identification of suitable combinations of *in vitro* sperm-function test for the prediction of fertility in buffalo bull. *Theriogenology* 2016; **86**(9): 2263-2271. e1.

- [12] Kumaresan A, Johannisson A, Al-Essawe EM, Morrell JM. Sperm viability, reactive oxygen species, and DNA fragmentation index combined can discriminate between above-and below-average fertility bulls. *J Dairy Sci* 2017; **100**(7): 5824-5836.
- [13] Saraf KK, Kumaresan A, Sinha MK, Datta TK. Spermatozoal transcripts associated with oxidative stress and mitochondrial membrane potential differ between high-and low-fertile crossbred bulls. *Andrologia* 2021; **53**(5): e14029.
- [14] Prakash MA, Kumaresan A, Ebenezer Samuel King JP, Nag P, Sharma A, Sinha MK, et al. Comparative transcriptomic analysis of spermatozoa from high-and low-fertile crossbred bulls: Implications for fertility prediction. *Front Cell Dev Biol* 2021; **9**: 647717.
- [15] Aslam MM, Kumaresan A, Sharma VK, Tajmul M, Chhillar S, Chakravarty AK, et al. Identification of putative fertility markers in seminal plasma of crossbred bulls through differential proteomics. *Theriogenology* 2014; **82**(9): 1254-1262. e1.
- [16] Aslam MK, Kumaresan A, Rajak SK, Tajmul M, Datta TK, Mohanty TK, et al. Comparative proteomic analysis of taurine, indicine, and crossbred (*Bos taurus*×*Bos indicus*) bull spermatozoa for identification of proteins related to sperm malfunctions and subfertility in crossbred bulls. *Theriogenology* 2015; **84**(4): 624-633.
- [17] Kumaresan A, Sinha MK, Paul N, Nag P, Ebenezer Samuel King JP, Kumar R, et al. Establishment of a repertoire of fertility associated sperm proteins and their differential abundance in buffalo bulls (*Bubalus bubalis*) with contrasting fertility. *Sci Rep* 2023; **13**(1): 2272.
- [18] Saraf KK, Kumaresan A, Dasgupta M, Karthikkeyan G, Prasad TSK, Modi PK, et al. Metabolomic fingerprinting of bull spermatozoa for identification of fertility signature metabolites. *Mol Reprod Dev* 2020; **87**(6): 692-703.
- [19] DasGupta M, Kumaresan A, Saraf KK, Karthikkeyan G, Prasad TK, Modi PK, et al. Preliminary comparative deep metabolomic analysis of spermatozoa from zebu and crossbred cattle suggests associations between metabolites, sperm quality and fertility. *Reprod Fertil Dev* 2021; **33**(6): 427-436.
- [20] Talluri TR, Kumaresan A, Sinha MK, Paul N, Ebenezer Samuel King JP, Datta TK. Integrated multi-omics analyses reveals molecules governing sperm metabolism potentially influence bull fertility. *Sci Rep* 2022; **12**(1): 10692.
- [21] Kumaresan A, Das Gupta M, Datta TK, Morrell JM. Sperm DNA integrity and male fertility in farm animals: A review. *Front Vet Sci* 2020; **7**: 321.
- [22] Kumaresan A, Elango K, Datta TK, Morrell JM. Cellular and molecular insights into the etiology of subfertility/infertility in crossbred bulls (*Bos taurus*×*Bos indicus*): A review. *Front Cell Dev Biol* 2021; **9**: 696637.
- [23] Hunter AG. Immunology and fertility in the bovine. *J Dairy Sci* 1989; **72**(12): 3353-3362.
- [24] Zandieh Z, Ashrafi M, Aflatoonian K, Aflatoonian R. Human sperm DNA damage has an effect on immunological interaction between spermatozoa and fallopian tube. *Andrology* 2019; **7**(2): 228-234.
- [25] Vickram AS, Dhama K, Chakraborty S, Abdul Samad H, Latheef S, Sharun K, et al. Role of antisperm antibodies in infertility, pregnancy, and potential for contraceptive and antifertility vaccine designs: Research progress and pioneering vision. *Vaccines* 2019; **7**(3): 116.
- [26] Wasilewski T, Łukaszewicz-Zajac M, Wasilewska J, Mroczko B. Biochemistry of infertility. *Clin Chim Acta* 2020; **508**: 185-190.
- [27] Malíčková K, Ambrusová Z, Belvončíková S, Bergendiová K, Krátká Z, Lešťan M, et al. Current possibilities of diagnostics and treatment of immunological causes of female infertility. *Cas Lek Cesk* 2021; **160**(1): 5-13.
- [28] Shibahara H. Production of anti-sperm antibody (ASA) in men. In: Shibahara H, Hasegawa A. (eds.) *Gamete immunology*. Singapore: Springer; 2022, p. 127-142.
- [29] Zodinanga V, Cheema RS, Mavi PS. Relationship of naturally occurring antisperm antibodies in blood serum and seminal plasma of cattle bulls with sperm function and fertility tests. *Open J Anim Sci* 2015; **5**(02): 114.
- [30] Hernández JLG, Resendiz EGP, Aparicio ED, Sánchez VMD, Dibarrat JPA, Gutiérrez VRT, et al. Detection of antisperm antibodies in blood sera of rams naturally infected with *Brucella ovis*. *Small Rumin Res* 2022; **216**: 106807.
- [31] Nagaria T, Patra PK, Sahu JP. Evaluation of serum antisperm antibodies in infertility. *J Obstet Gynaecol India* 2011; **61**: 307-316.
- [32] Bozhedomov VA, Nikolaeva MA, Ushakova IV, Lipatova NA, Bozhedomova GE, Sukhikh GT. Functional deficit of sperm and fertility impairment in men with antisperm antibodies. *J Reprod Immunol* 2015; **112**: 95-101.
- [33] Cui D, Han G, Shang Y, Liu C, Xia L, Li L, et al. Antisperm antibodies in infertile men and their effect on semen parameters: A systematic review and meta-analysis. *Clin Chim Acta* 2015; **444**: 29-36.
- [34] Zralý Z, Bendova J, Šišák M, Diblíková I, Švecová D, Zajícová A, et al. Occurrence of antibodies to the sperms in blood sera of bulls and boars. *Vet Med-Czech* 1998; **43**(5): 137-144.
- [35] Zralý Z, Bendova J, Diblíková I, Švecová D, Kummer V, Mašková J, et al. Antisperm antibodies in blood sera of bulls and correlations with age, breed and ejaculate quality. *Acta Vet Brno* 2002; **71**(3): 303-308.
- [36] Ferrer MS, Laflin S, Anderson DE, Miesner MD, Wilkerson MJ, George A, et al. Prevalence of bovine sperm-bound antisperm antibodies and their association with semen quality. *Theriogenology* 2015; **84**(1): 94-100.
- [37] Chamley LW, Clarke GN. Antisperm antibodies and conception. *Semin Immunopathol* 2007; **29**: 169-184.
- [38] Francavilla F, Santucci R, Barbonetti A, Francavilla S. Naturally-occurring antisperm antibodies in men: Interference with fertility and clinical implications. An update. *Front Biosci* 2007; **12**(8): 2890-2911.
- [39] Ferrer MS, Miller LMJ. Equine sperm-bound antisperm antibodies are associated with poor semen quality. *Theriogenology* 2018; **118**: 212-218.
- [40] Attia KA, Zaki AA, Eilts BE, Paccamonti DL, Hosgood G, Dietrich MA, et al. Anti-sperm antibodies and seminal characteristics after testicular biopsy or epididymal aspiration in dogs. *Theriogenology* 2000; **53**(6): 1355-1363.
- [41] Chiu WWC, Chamley LW. Clinical associations and mechanisms of action of antisperm antibodies. *Fertil Steril* 2004; **82**(3): 529-535.

- [42]Kuntareddi C, Kumaresan A, Saraf KK, Nag P, Paul N, Kurati SP, et al. Characterization of antisperm antibody binding patterns in relation to sperm phenotypic attributes and field fertility in dairy bulls. *Theriogenology* 2020; **141**: 161-167.
- [43]Siddiqui MAR, Das ZC, Bhattacharjee J, Rahman MM, Islam MM, Haque MA, et al. Factors affecting the first service conception rate of cows in smallholder dairy farms in Bangladesh. *Reprod Domest Anim* 2013; **48**(3): 500-505.
- [44]Hanson B, Johnstone E, Dorais J, Silver B, Peterson CM, Hotaling J. Female infertility, infertility-associated diagnoses, and comorbidities: A review. *J Assist Reprod Genet* 2017; **34**: 167-177.
- [45]Mahdi BM, Salih WH, Caitano AE, Kadhum BM, Ibrahim DS. Frequency of antisperm antibodies in infertile women. *J Reprod Infertil* 2011; **12**(4): 261.
- [46]Zralý Z, Čanderle J, Diblíková I, Švecová D, Mašková J, Kummer V. Antisperm antibodies in cows as related to their reproductive health. *Acta Vet Brno* 2003; **72**(1): 27-32.
- [47]Fayemi O. Sperm antibodies and reproductive efficiency in the zebu cattle in South-Western Nigeria. *Pak Vet J* 2005; **25**(3): 111.
- [48]Sardoy MC, Anderson DE, George A, Wilkerson MJ, Skinner S, Ferrer MS. Standardization of a method to detect bovine sperm-bound antisperm antibodies by flow cytometry. *Theriogenology* 2012; **78**(7): 1570-1577.
- [49]Ferrer MS, Klabnik-Bradford J, Anderson DE, Bullington AC, Palomares RA, Miller LMJ, et al. Sperm-bound antisperm antibodies prevent capacitation of bovine spermatozoa. *Theriogenology* 2017; **89**: 58-67.
- [50]Wright PJ. Serum spermagglutinins and semen quality in the bull. *Aust Vet J* 1980; **56**(1): 10-13.
- [51]Kim CA, Parrish JJ, Momont HW, Lunn DP. Effects of experimentally generated bull antisperm antibodies on *in vitro* fertilization. *Biol Reprod* 1999; **60**(6): 1285-1291.
- [52]Aitken RJ. The male is significantly implicated as the cause of unexplained infertility. In: *Seminars in reproductive medicine*. New York: Thieme Medical Publishers, Inc.; 2020, p. 3-20.
- [53]Bronson R, Cooper G, Rosenfeld D, Witkin SS. Detection of spontaneously occurring sperm-directed antibodies in infertile couples by immunobead binding and enzyme-linked immunosorbent assay. *Ann N Y Acad Sci* 1984; **438**(1): 504-507.
- [54]Shibahara H, Wakimoto Y, Fukui A, Hasegawa A. Anti-sperm antibodies and reproductive failures. *Am J Reprod Immunol* 2021; **85**(4): e13337.
- [55]Sarma DK, Baishya N, Sharma DK, Deka BC, Bhuyan D. Antisperm antibodies in serum and cervical mucus of normal and repeat breeding cows. *Indian J Anim Reprod* 2009; **30**(1): 54-56.
- [56]Fayemi OE, Morrison RB, Joo HS. Seroprevalence of sperm antibody in selected Minnesota swine breeding herds. *Anim Reprod Sci* 1992; **27**(4): 341-345.
- [57]Dadarwal D, Palmer C, Griebel P. Mucosal immunity of the postpartum bovine genital tract. *Theriogenology* 2017; **104**: 62-71.
- [58]Stern JE, Dixon PM, Manganiello PD, Brinck-Johnsen T. Antisperm antibodies in women: Variability in antibody levels in serum, mucus, and peritoneal fluid. *Fertil Steril* 1992; **58**(5): 950-958.
- [59]Shibahara H, Shigeta M, Inoue M, Hasegawa A, Koyama K, Alexander NJ, et al. Immunology: Diversity of the blocking effects of antisperm antibodies on fertilization in human and mouse. *Hum Reprod* 1996; **11**(12): 2595-2599.
- [60]Tian X, Zhang L, Wu Y, Yang C, Liu P. Relationship between serum antisperm antibodies and anticardiolipin antibodies and clinical pregnancy outcome in an *in vitro* fertilization and embryo transfer program. *Chin Med J* 1999; **112**(01): 34-36.
- [61]Lazarević M, Suljkanović A, Mickov L, Šabanović M, Paprikić N, Mlinar S. The influence of antisperm Ig G and Ig A antibodies from cows sera and cervical mucus on bull sperm motility. *Acta Vet* 2013; **63**(5-6): 499-511.
- [62]Vikrant J, Ranjna C, Amrit B, Vinod G, Shahbaz D. Status of antisperm antibodies in blood serum and cervical mucus of artificially inseminated crossbred cows in relation to infertility. *Anim Sci Rep* 2016; **10**(1): 34-40.
- [63]Batard T, Basuyaux B, Lambin P, Brémard-Oury C, Hamilton RG, David B, et al. Isotypic analysis of grass pollen-specific immunoglobulins in human plasma: 1. Specialization of certain classes and subclasses in the immune response. *Int Arch Allergy Immunol* 1993; **100**(1): 68-78.
- [64]Kremer J, Jager S. OPINION: The significance of antisperm antibodies for sperm-cervical mucus interaction. *Hum Reprod* 1992; **7**(6): 781-784.
- [65]Wang G. Antisperm antibodies in fertile and non fertile cows. *Anim Husb Vet Med Chin* 1989; **30**: 867-870.
- [66]Waziri MA, Fayemi OE. Seroprevalence of sperm antibodies in goats. *Vet Arh* 2000; **70**(2): 95-102.
- [67]Wang GL, Xie CX. The relationship between antisperm antibodies and progesterone in the serum of infertile dairy cows. *Acta Vet Zootech Sin* 1990; **21**(1): 26-30.
- [68]Risvanli A, Aydin M, Kaygusuzoglu E, Bulut H, Apaydin AM, Bolat Y. The prevalence of anti-sperm antibodies in cattle in the Eastern Anatolian region of Turkey. *Ir Vet J* 2003; **56**: 560-562.
- [69]Taneichi A, Shibahara H, Takahashi K, Sasaki S, Kikuchi K, Sato I, et al. Effects of sera from infertile women with sperm immobilizing antibodies on fertilization and embryo development *in vitro* in mice. *Am J Reprod Immunol* 2003; **50**(2): 146-151.
- [70]Srivastava SK, Shinde S, Singh SK, Mehrotra S, Verma MR, Singh AK, et al. Antisperm antibodies in repeat-breeding cows: Frequency, detection and validation of threshold levels employing sperm immobilization, sperm agglutination and immunoperoxidase assay. *Reprod Domest Anim* 2017; **52**(2): 195-202.
- [71]Ulcova-Gallova Z. Immunological and physicochemical properties of cervical ovulatory mucus. *J Reprod Immunol* 2010; **86**(2): 115-121.
- [72]Livi C, Barciulli F, Scarselli G. Antispermatozoon antibodies and cervical factor of sterility. *Acta Eur Fertil* 1991; **22**(1): 23-25.
- [73]Seshagiri VN, Pattabiraman SR, Krishnan AR. Incidence of sperm agglutinating antibody in regular and repeat breeding crossbred cows. *Cheiron* 1987; **6**: 152-154.
- [74]Romrell LJ, Michael GO. Capping and ultrastructural localization of sperm surface isoantigens during spermatogenesis. *Dev Biol* 1978; **63**(1):

- 76-93.
- [75]Furuya S, Kumamoto Y, Sugiyama S. Fine structure and development of Sertoli junctions in human testis. *Arch Androl* 1978; **1**(3): 211-219.
- [76]Comhaire FH, Mahmoud AMA, Depuydt CE, Zalata AA, Christophe AB. Mechanisms and effects of male genital tract infection on sperm quality and fertilizing potential: The andrologist's viewpoint. *Hum Reprod Update* 1999; **5**(5): 393-398.
- [77]Piroozmand A, Nasab SDM, Erami M, Hashemi SMA, Khodabakhsh E, Ahmadi N, et al. Distribution of human papillomavirus and antisperm antibody in semen and its association with semen parameters among infertile men. *J Reprod Infertil* 2020; **21**(3): 183.
- [78]Lotti F, Baldi E, Corona G, Lombardo F, Maseroli E, Degl'Innocenti S, et al. Epididymal more than testicular abnormalities are associated with the occurrence of antisperm antibodies as evaluated by the MAR test. *Hum Reprod* 2018; **33**(8): 1417-1429.
- [79]Ferrer MS, Palomares R, Hurley D, Bullington AC, Hoyos-Jaramillo A, Bittar JH. Antisperm antibodies and sperm function in bulls undergoing scrotal insulation. *Reprod* 2020; **160**(5): 783-792.
- [80]Yeh WR, Acosta AA, Seltman HJ, Doncel G. Impact of immunoglobulin isotype and sperm surface location of antisperm antibodies on fertilization *in vitro* in the human. *Fertil Steril* 1995; **63**(6): 1287-1292.
- [81]Krause WKH. Sperm functions influenced by immune reactions. In: Krause W, Naz R. (eds.) *Immune infertility*. Berlin, Heidelberg: Springer; 2009, p. 49-65.
- [82]Panchal MT, Dholakia PM, Derashri HJ, Kodagali SB. Investigation on immunoinfertility in repeat-breeding buffaloes. *Indian J Anim Sci* 1990; **60**(10): 1211-1212.
- [83]Mazumdar S, Levine AS. Antisperm antibodies: Etiology, pathogenesis, diagnosis, and treatment. *Fertil Steril* 1998; **70**(5): 799-810.
- [84]Lazarević M, Milanović S, Kirovski D, Milovanović A. Antisperm antibodies of the Ig A class in the cervical mucus and sera of artificially inseminated cows. *Acta Vet* 2003; **53**(5-6): 311-320.
- [85]Bohring C, Klepper L, Krause W. Localization of binding sites of naturally occurring antisperm antibodies on human spermatozoa by immunofluorescence. *Andrologia* 2004; **36**(5): 286-290.
- [86]Esmailnejad A, Nikahval B, Mogheiseh A, Karampour R, Karami S. The detection of canine anti-sperm antibody following parenteral immunization of bitches against homogenized whole sperm. *Basic Clin Androl* 2020; **30**: 1-7.
- [87]Tennakoon V, Yasawardene SG, Weerasekera DS. Possible risk factors for the formation of antisperm antibodies in a subfertile population. *Sri Lanka J Obstet Gyn* 2011; **33**(1): 12-19.
- [88]Hogarth PJ. *Immunological aspects of mammalian reproduction*. New York: Springer Dordrecht; 1982, p. 50-83.
- [89]Landers DV, Bronson RA, Pavia CS, Stites DP. Reproductive immunology. In: Stites DP, Terr AI. (eds.) *Basic and clinical immunology*. 7th ed. New Jersey: Prentice Hall; 1991, p. 200-215.
- [90]Lazarević M, Ejduš L, Rosić G. The influence of bovine seminal plasma, egg-yolk extender and their mixture on bovine lymphocyte blastogenesis. *Acta Vet Beograd* 1992; **42**(4): 227-236.
- [91]Risvanli A, Aydin M, Kaygusuzoglu E, Bulut H, Apaydin AM, Timurkan H. Use of cauda epididymis extract as immunocontraceptive. *Contraception* 2002; **66**(6): 459-462.
- [92]Cheema RS, Zodinanga V, Bansal AK. Characterization and immunolocalization of HBP, FA-1 and TIMP-2 like proteins in cattle bull semen: HBP modification in *in vitro* capacitated spermatozoa. *Theriogenol Insight-An Int J Reprod Anim* 2015; **5**(1): 53-67.
- [93]Dawson GR. *Localization on sperm, quantification and molecular features of two seminal proteins*. Doctoral dissertation. Tucson: the University of Arizona, 2005.
- [94]Naz RK, Wolf DP. Antibodies to sperm-specific human FA-1 inhibit *in vitro* fertilization in rhesus monkeys: Development of a simian model for testing of anti-FA-1 contraceptive vaccine. *J Reprod Immunol* 1994; **27**(2): 111-121.
- [95]Coonrod SA, Westhusin ME, Naz RK. Monoclonal antibody to human fertilization antigen-1 (FA-1) inhibits bovine fertilization *in vitro*: Application in immunocontraception. *Biol Reprod* 1994; **51**(1): 14-23.
- [96]Naz RK, Alexander NJ, Isahakia M, Hamilton MS. Monoclonal antibody to a human germ cell membrane glycoprotein that inhibits fertilization. *Science* 1984; **225**(4659): 342-344.
- [97]Coonrod SA, Herr JC, Westhusin ME. Inhibition of bovine fertilization *in vitro* by antibodies to SP-10. *Reproduction* 1996; **107**(2): 287-297.
- [98]Yudin AI, Goldberg E, Robertson KR, Overstreet JW. Calpain and calpastatin are located between the plasma membrane and outer acrosomal membrane of cynomolgus macaque spermatozoa. *J Androl* 2000; **21**(5): 721-729.
- [99]Clark S, Naz RK. Presence and incidence of izumo antibodies in sera of immunoinfertile women and men. *Am J Reprod Immunol* 2013; **69**(3): 256-263.
- [100]Sutovsky P. Sperm-egg adhesion and fusion in mammals. *Expert Rev Mol Med* 2009; **11**: e11.
- [101]Fu J, Yao R, Luo Y, Yang D, Cao Y, Qiu Y, et al. Immune infertility should be positively diagnosed using an accurate method by monitoring the level of anti-ACTL7a antibody. *Sci Rep* 2016; **6**(1): 22844.
- [102]Bohring C, Krause W. The role of antisperm antibodies during fertilization and for immunological infertility. *Immunol Gametes Embryo Implant* 2005; **88**: 15-26.
- [103]Milovanović A, Lazarević M, Milanović S, Kirovski D, Jovičin M. Open days period and antispermatozoal antibodies in artificially inseminated cows. *Acta Vet* 2005; **55**(5-6): 449-460.
- [104]Therien I, Bleau G, Manjunath P. Phosphatidylcholine-binding proteins of bovine seminal plasma modulate capacitation of spermatozoa by heparin. *Biol Reprod* 1995; **52**(6): 1372-1379.
- [105]McCauley TC, Zhang HM, Bellin ME, Ax RL. Identification of a heparin-binding protein in bovine seminal fluid as tissue inhibitor of metalloproteinases-2. *Mol Reprod Dev* 2001; **58**(3): 336-341.
- [106]Mohanarao GJ, Atreja SK. Identification of capacitation associated tyrosine phosphoproteins in buffalo (*Bubalus bubalis*) and cattle spermatozoa. *Anim Reprod Sci* 2011; **123**(1-2): 40-47.
- [107]Fu J, Song W, Zong S, Koide SS, Miao S, Wang L. Dynamic alterations in the expression and localization of ACTL7a during capacitation in mouse spermatozoa. *Fertil Steril* 2013; **99**(3): 882-888.

- [108]Fu J, Wang Y, Fok KL, Yang D, Qiu Y, Chan HC, et al. Anti-ACTL7a antibodies: A cause of infertility. *Fertil Steril* 2012; **97**(5): 1226-1233.
- [109]Bronson RA, Cooper GW, Rosenfeld DL. Correlation between regional specificity of antisperm antibodies to the spermatozoan surface and complement-mediated sperm immobilization. *Am J Reprod Immunol* 1982; **2**(4): 222-224.
- [110]Coddington CC, Demochowski R, Oehninger S, Auman JR, Hodgen GD. Hemizona assay: Evaluation of fertility potential in patients with vasectomy reversal. *Arch Androl* 1997; **38**(2): 143-150.
- [111]Witkin SS, Viti D, David SS, Stangel J, Rosenwaks Z. Relation between antisperm antibodies and the rate of fertilization of human oocytes *in vitro*. *J Assist Reprod Genet* 1992; **9**: 9-13.
- [112]Kremer J, Jager S. Characteristics of anti-spermatozoal antibodies responsible for the shaking phenomenon with special regard to immunoglobulin class and antigen-reactive sites. *Int J Androl* 1980; **3**(1-6): 143-152.
- [113]Wang C, Baker HG, Jennings MG, Burger HG, Lutjen P. Interaction between human cervical mucus and sperm surface antibodies. *Fertil Steril* 1985; **44**(4): 484-488.
- [114]Archana SS, Selvaraju S, Arangasamy A, Binsila B, Swathi D, Ramya L, et al. Seminal antigenicity affects mitochondrial membrane potential and acrosome reaction ability of the spermatozoa during cryopreservation. *Theriogenology* 2021; **159**: 132-139.
- [115]Rossato M, Galeazzi C, Ferigo M, Foresta C. Antisperm antibodies modify plasma membrane functional integrity and inhibit osmosensitive calcium influx in human sperm. *Hum Reprod* 2004; **19**(8): 1816-1820.
- [116]Ahuja AK, Cheema RS, Kumar A. Status of naturally developing antisperm antibodies in serum of calves, heifers, cows and their effect on *in vitro* capacitation and acrosome reaction. *J Bio Innov* 2016; **5**(6): 874-889.
- [117]Zouari R, De Almeida M, Feneux D. Effect of sperm-associated antibodies on the dynamics of sperm movement and on the acrosome reaction of human spermatozoa. *J Reprod Immunol* 1992; **22**(1): 59-72.
- [118]Pujianto DA, Hajizah H, Mansur IG, Amarudin A. Antisperm antibodies disrupt plasma membrane integrity and inhibit tyrosine phosphorylation in human spermatozoa. *Med J Indones* 2018; **27**(1): 3-11.
- [119]Jin M, Fujiwara E, Kakiuchi Y, Okabe M, Satouh Y, Baba SA, et al. Most fertilizing mouse spermatozoa begin their acrosome reaction before contact with the zona pellucida during *in vitro* fertilization. *Proc Natl Acad Sci* 2011; **108**(12): 4892-4896.
- [120]Thomas PGA, Ball BA, Ignatz GG, Dobrinski I, Parks JE, Currie WB. Antibody directed against plasma membrane components of equine spermatozoa inhibits adhesion of spermatozoa to oviduct epithelial cells *in vitro*. *Biol Reprod* 1997; **56**(3): 720-730.
- [121]Romano R, Santucci R, Marrone V, Francavilla F. Effect of ionophore challenge on hamster egg penetration and acrosome reaction of antibody-coated human sperm. *Am J Reprod Immunol* 1993; **29**(1): 56-61.
- [122]Myogo K, Yamano S, Nakagawa K, Kamada M, Maegawa M, Irahara M, et al. Sperm-immobilizing antibodies block capacitation in human spermatozoa. *Arch Androl* 2001; **47**(2): 135-142.
- [123]Francavilla F, Romano R, Santucci R, Marrone V, Properzi G, Ruvolo G. Interference of antisperm antibodies with the induction of the acrosome reaction by zona pellucida (ZP) and its relationship with the inhibition of ZP binding. *Fertil Steril* 1997; **67**(6): 1128-1133.
- [124]Lansford B, Haas Jr GG, Debault LE, Wolf DP. Effect of sperm-associated antibodies on the acrosomal status of human sperm. *J Androl* 1990; **11**(6): 532-538.

Publisher's Note

The Publisher of the *Journal* remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Edited by Lin LY, Lei Y