Role of CD147 in Sperm Motility and Fertilization Capacity in Infertile Males

Original Article

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ABSTRACT

Introduction: Infertility is defined as the failure to achieve pregnancy after 12 months of regular unprotected sexual intercourse. Male infertility is a complex, often multifactorial pathological condition. Sperms undergo a series of processes to acquire their fertilizing capacity. These processes include the initiation and maintenance of motility, the induction of hyperactivation and capacitation during transit in the uterus and oviduct, and the acrosome reaction. Defects in any of these processes lead to subfertility or infertility. CD147 is a member of the immunoglobulin (Ig) superfamily. CD147 is normally detected in the reproductive tract brain, eye, muscle, kidney, colon, and other glandular epithelial cells. CD147 plays central roles in sperm functions, such as sperm motility and acrosomal reaction.

Aim: The current study aimed to investigate whether CD147 expression could be used as a reliable marker for the evaluation of sperm quality and male fertility.

Patients and methods: This study was conducted as a case-control study on 90 male participants and involved three groups attending the outpatient clinic, andrology unit, dermatology, andrology & STDs department, Mansoura University Hospital for management of infertility. Assessments included detailed medical history, physical and genital examinations, semen analysis, level of CD147, acrosin activity index, malondialdehyde, total antioxidant capacity, and DNA fragmentation.

Results: CD147 expression was significantly higher in the control group compared to asthenozoospermia and astheno-teratozoospermia, highlighting its potential role in male fertility.

Conclusion: The findings of this study showed the essential role of CD147 in sperm motility, capacitation, and acrosin reaction. The significant correlations observed between CD147 levels and semen parameters suggested its potential as a biomarker for diagnosing male infertility. The antioxidant effect may be a possible mechanism influencing its action in sperm functions.

Key Words: CD147, infertility, motility, sperm function.

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INTRODUCTION

Male infertility is defined by the World Health Organization (WHO) as the inability of a male to make a fertile female pregnant after at least 1 year of regular unprotected intercourse. Infertility may be caused by a number of different factors in either the male reproductive systems, female reproductive system or both. However, it is sometimes not possible to explain the cause of infertility [1].

Sperms undergo series of complex processes to acquire their fertilizing capacity. These processes include the initiation and maintenance of motility, the induction of hyperactivation and capacitation during transit in the uterus and oviduct, and the acrosome reaction (AR) [2]. Defects in any of these processes lead to subfertility or infertility [3]. Ca^{2+} mobilization in sperm, which is mainly attributed to extracellular Ca^{2+} influx due to their lack of endoplasmic reticulum, plays central roles in sperm functions, such as sperm motility and acrosomal Reaction [4].

Sperm motility is a crucial aspect of male fertility, with spermatozoa being a highly specialized, motile cell with a condensed nucleus and scant cytoplasm. After maturation in the epididymis, sperm travels through the female reproductive tract to the ampullary site of the uterine tube. Spermatozoa can be classified as progressively motile, non-progressive, or immotile based on their movement and velocity. Asthenozoospermia, characterized by disorders in sperm motility, is a major contributing factor to male infertility [5]. Asthenozoospermia is defined as having

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a count of total motile sperm less than 42%, or that of progressive motile sperm less than 30% [1].

Capacitation is defined as the series of biochemical events of the sperms which is needed for competence to undergo the acrosome reaction and fertilization. Those events include both cytoplasmic events, such as an influx of calcium, and membrane events, such as the removal of sterols. In addition, capacitation is associated with the activation of hyperactive motility of the sperm in the reproductive tract of the female [6].

CD147, also known as Basigin or EMMPRIN (Extracellular Matrix Metalloproteinase Inducer), is a transmembrane glycoprotein involved in various physiological and pathological processes. CD147 is a member of the immunoglobulin superfamily that is commonly detected in the reproductive tract and other glandular epithelial cells of various organs [7]. CD147 maintains sperm motility before capacitation. Soluble CD147 from the female tract interacts with sperm-bound CD147 to induce an acrosome reaction in capacitated sperm. After treatment of capacitated sperm with a CD147-neutralizing antibody or rCD147 and examination of hyperactivated motility and AR, Results showed that rCD147 treatment induced a 3-fold increase in AR. The study also found that soluble CD147 is a potent AR inducer, but not hyperactivation.The results suggest a physiological role of soluble CD147 in inducing AR. CD147 promotes sperm motility and acrosome reaction (AR) by eliciting Ca^{2+} influx through soluble CD147 binding to sperm-bound CD147 [8].

AIM

The aim of the study was to investigate the role of seminal plasma CD147 in sperm motility, capacitation and infertility associated with asthenozoospermia and asthenoteratozoospermia and its correlation with other semen parameters.

PATIENTS AND METHODS

This present study included 90 participants who attended the andrology outpatient clinic at Mansoura university hospital seeking consultation for infertility and assisted reproduction. The study was conducted in the medical biochemistry department, faculty of medicine, Mansoura university, with a focus on assessing the biochemical and functional parameters of sperm in relation to fertility status.

Study design and participants: This was a case-control study in which the 90 participants were divided into three groups. The first group was the Control Group (*n*= 30), which included healthy volunteers who had achieved conception within one year of continuous unprotected sexual activity and had a normal semen analysis. The second group included infertile men with isolated asthenozoospermia (*n*= 30), defined by a total motile sperm count of less than 42% or progressive motile sperm less than 30%. The third group consisted of infertile men with asthenoteratozoospermia (*n*= 30), characterized by less than 42% motile sperm and less than 4% sperm with normal morphology.

Inclusion and exclusion criteria: Participants included were men aged 20 to 50 years, married for at least one year with a stable relationship and regular unprotected intercourse. Their female partners had regular ovulation and no systemic or gynecological issues affecting fertility. Exclusion criteria involved refusal to participate, presence of varicocele, azoospermia, hypogonadism, history of systemic diseases, and prior medical or surgical interventions that could negatively influence fertility.

Clinical evaluation: All participants underwent comprehensive assessments, including detailed history taking covering age, duration of infertility, prior evaluations or treatments, and sexual history. General physical examinations were conducted to evaluate systems relevant to fertility, including the endocrine, cardiovascular, respiratory, gastrointestinal, and neurological systems. Local genital examinations were performed to assess the penis, testes, epididymis, vas deferens, and inguinal region. Specific signs such as hypogonadism, gynecomastia, and galactorrhea were carefully examined and excluded. Additionally, color Doppler ultrasound was used for reflux grading, and semen analysis was carried out.

Laboratory techniques on spermatozoa: Semen samples were collected through masturbation after 2–5 days of abstinence and allowed to liquefy at 37˚C for 15–30 minutes. Computer-assisted semen analysis (CASA) was used to assess sperm count, total and progressive motility, and morphology according to WHO guidelines. CD147 levels in seminal plasma were measured using the enzyme-linked immunosorbent assay (ELISA) technique with anti-CD147 antibody kits. Acrosin activity was evaluated using gelatin-covered microslides and gelatinolysis techniques.

Biochemical analyses: Oxidative stress markers and antioxidant activities were also assessed. Malondialdehyde (MDA) levels were measured using the thiobarbituric acid (TBA) assay, where the MDA-TBA complex is read at 534nm. Additionally, superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities, as important antioxidant enzymes, were determined using commercial colorimetric diagnostic kits to assess the oxidative status of spermatozoa in the study groups.

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of the Faculty of Medicine, Mansoura University, and ensuring compliance with ethical standards in biomedical research involving human subjects. Written informed consent was obtained from all participants after a clear explanation of the study objectives, procedures, potential risks, and benefits, with assurance of confidentiality and the right to withdraw at any time without any consequences. Statistical analysis

was performed using the MedCalc® statistical software program. Continuous variables that did not follow a normal distribution were expressed as medians and ranges, while categorical variables were presented as frequencies and percentages. The Mann-Whitney *U* test was employed to compare differences between two independent groups for nonparametric data, and the Kruskal-Wallis test was used when comparing more than two groups. To assess the strength and direction of association between continuous or ordinal variables, the Spearman rank correlation coefficient was utilized. A *p*-value of less than 0.05 was considered statistically significant. These analytical approaches ensured robust interpretation of the results and minimized bias in data evaluation.

RESULTS

The study population consisted of 90 men aged 20–50 years, divided equally into three groups: fertile controls, infertile men with asthenozoospermia, and infertile men with asthenoteratozoospermia. All participants were married for over one year with regular unprotected intercourse. A comparative analysis of various semen parameters among the control, asthenozoospermia, and astheno-teratozoospermia groups revealed statistically significant differences across all measured variables. CD147 levels, halo diameter, halo percentage, acrosin activity index, and total antioxidant capacity were significantly lower in both patient groups compared to the control group, with the most pronounced reductions observed in the astheno-teratozoospermia group. In contrast, DNA fragmentation and malondialdehyde levels were markedly elevated in the patient groups, indicating increased oxidative stress and DNA damage. All differences between the control and patient groups, as well as between the asthenozoospermia and astheno-teratozoospermia groups, were highly significant ($P<0.001$ or $P<0.002$), underscoring the progressive impairment of sperm function and quality associated with these conditions (Table 1).

Table 1: Comparison of the study parameters between studied groups:

	Control	Asthenozoospermia	Astheno-teratozoospermia	*P* value
CD147	75.3(42.19-93.15)	40.87(22.5-60.1)	26.61(12.11-38.44)	*P1*=0.001* *P2*=0.001* *P3*=0.001*
Halo diameter	17.4(12.8-23.7)	15.33(12.4-18.4)	13.5(9.4-16.8)	*P1*=0.001* *P2*=0.001* *P3*=0.001*
Halo percent	74(63-90)	63.5(44-80)	38(8-59)	*P1*=0.001* *P2*=0.001* *P3*=0.001*
DNA fragmentation	19(13-28)	28(18-40)	39(25-55)	*P1*=0.001* *P2*=0.001* *P3*=0.001*
Acrosin activity index	12.87(8.98-19.49)	10.15(5.5-13.98)	5.08(0.94-9.74)	*P1*=0.001* *P2*=0.001* *P3*=0.001*
Malondialdehyde	1.77(1.13-3.44)	3.42(1.96-4.23)	4.98(2.1-9.74)	*P1*=0.002* *P2*=0.001* *P3*=0.001*
Total antioxidant capacity	2.16(1.24-3.75)	1.72(1.19-2.5)	1.17(0.6-1.7)	*P1*=0.001* *P2*=0.001* *P3*=0.001*

P1: Control Versus Asthenozoospermia group; *P2*: Control Versus Astheno-teratozoospermia group; *P3*: Asthenozoospermia group Versus Astheno-teratozoospermia group.

A statistically significant correlation was observed between CD147 levels and various semen quality parameters across the studied groups. CD147 exhibited strong positive correlations with halo diameter ($r= 0.521$), halo percentage ($r=0.725$), acrosin activity index ($r=0.711$), total antioxidant capacity ($r= 0.615$), sperm morphology ($r= 0.620$), grade A motility ($r= 0.709$), combined grade A+B motility ($r=0.672$), velocity ($r=0.626$), linear velocity ($r= 0.689$), and linearity index ($r= 0.709$), all with *p*-values <0.001. These associations suggest that elevated CD147 levels are linked to improved sperm function, motility, morphology, and antioxidant status. Conversely, CD147 levels showed significant negative correlations with DNA fragmentation ($r= –0.630$) and malondialdehyde levels ($r= –0.535$), also with *p*-values <0.001, indicating that lower CD147 expression is associated with increased oxidative stress and sperm DNA damage. Collectively, these findings highlight the potential of CD147 as a

biomarker of sperm quality, reflecting multiple aspects of sperm function, structural integrity, and oxidative balance (Table 2).

Table 2: Correlation between CD147 and the study parameters among studied groups.

	CD147	
	r	*P*
Halo	0.521	0.001*
Halo percent	0.725	0.001*
DNA fragmentation (%)	-0.630	0.001*
Acrosin index	0.711	0.001*
Malondialdehyde	-0.535	0.001*
Total antioxidant capacity	0.615	0.001*
Morphology	0.620	0.001*
Grade A motility	0.709	0.001*
Grade A+B motility	0.672	0.001*
Velocity	0.626	0.001*
Linear velocity	0.689	0.001*
Linearity index	0.709	0.001*

DISCUSSION

This study found that there is a significant difference in CD147 levels among the studied groups. The study found higher CD147 in the control group compared to both asthenozoospermia and astheno-teratozoospermia groups highlighting its potential role in the diagnosis and treatment of male fertility.

In line with current results, Chen *et al.,* (2021) [8] showed that CD147 can be used as a marker for evaluation of sperm function and male fertility. Its deficiency correlates with impaired motility and acrosome reaction, suggesting its potential as a therapeutic target in asthenozoospermia. The level of soluble CD147 in seminal plasma was positively correlated with the fertilization rate and pregnancy outcome in infertile couples undergoing assisted reproductive techniques.

The current study observed that grade A motility, velocity and linear velocity showed significant positive correlation with CD147 levels .These findings support the potential role of CD147 in induction and activation of sperm motility.

Similarly, Fok (2023) [9] found that recombinant CD147 (rCD147) restored sperm functions, including motility and acrosome reaction, by promoting calcium influx, supporting its clinical relevance in treating asthenozoospermia. Asgari *et al*., (2023) [7] studied the role of CD147 in sperm function by blocking sperm-bound CD147 with a neutralizing antibody and the results of the study showed that the anti-CD147 antibody treatment significantly reduced sperm motility compared to normal IgG treatment.

This study found significant correlations between CD147 levels and acrosin activity index; aligned with published evidence on CD147's role in acrosomal function. The mechanism was also highlighted in the study by Chen *et al.,* (2021) [8] which demonstrated that soluble CD147 significantly enhances AR capability by promoting calcium signaling pathways essential for fertilization.

In agreement with the present study results, Fok (2023) [9] proposed that extracellular CD147 can be used as a reliable biomarker for assessing AR defects in male infertility. The ability to predict assisted reproductive techniques (ART) outcomes based on CD147 levels could help clinical practices by allowing more treatment regimens and better outcomes.

The current study showed that the control group exhibited higher values for halo diameter and halo percent, and lower values of DNA fragmentation, compared to both asthenozoospermia and astheno-teratozoospermia groups. Abd Elrahman *et al.,* (2021) [10] reported similar findings among asthenozoospermic patients compared to normozoospermic controls regarding the same parameters in the current study.

The current findings provide novel quantitative associations between CD147 and laboratory measures of sperm competence, particularly acrosin activity and halo formation. These results reinforce CD147's dual role as a functional regulator and diagnostic biomarker for male fertility.

In the current study CD147 expression showed variable correlation with oxidative stress and total antioxidant capacity.CD147 showed a negative correlation with malondialdehyde, an oxidative stress marker, and positive correlation with total antioxidant capacity. Kanyenda *et al.,* (2014) [11] found that Upregulation of CD147 expression was probably mediated by oxidative stress, as H2O2 in neuronal cultures potentially acting as a compensatory mechanism or a cell death signal. BU *et al.,* (2021) [12] showed CD147 overexpression was linked to oxidative stress resistant and increased cell survival. These findings suggest the possible antioxidant mechanism of CD147 affecting various sperm functions especially motility and acrosomal reaction. This study showed the potential role of CD147 as a diagnostic marker for male infertility

CONCLUSION

This study demonstrates the essential role of CD147 in sperm motility, capacitation and acrosin reaction, supporting its potential as a biomarker in diagnosing male infertility. The antioxidant effect may be a possible mechanism influencing its action in sperm functions.

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCES

1. World Health Organization. WHO laboratory manual for the examination and processing of human semen: World Health Organization; 2021.
2. Okabe M. (2013). The cell biology of mammalian fertilization. Development; 140(22):4471- 4479.
3. Wassarman PM., Jovine L., Litscher ES. (2001). A profile of fertilization in mammals. Nat Cell Biol; 3(2):E59-E64.
4. Correia J., Michelangeli F., Publicover S. (2015). Regulation and roles of Ca^{2+} stores in human sperm. Reproduction; 150(2):R65-R76.
5. Dcunha R., Hussein RS., Ananda H., *et al*. (2022). Current Insights and Latest Updates in Sperm Motility and Associated Applications in Assisted Reproduction. Reprod Sci; 29(1):7–25.
6. Breitbart H. (2003). Signaling pathways in sperm capacitation and acrosome reaction. Cell Mol Biol (Noisy-le-grand); 49(3):321–327.
7. Asgari R., Vaisi-Raygani A., Aleagha MSE., Mohammadi P., Bakhtiari M., Arghiani N. (2023). CD147 and MMPs as key factors in physiological and pathological processes. Biomed Pharmacother; 157:113983.
8. Chen H., Shi X., Li X., *et al*. (2021). CD147 deficiency is associated with impairedsperm motility/acrosome reaction and offersa therapeutic target for asthenozoospermia. Mol Ther Nucleic Acids; 26:1374–1386.
9. Fok E. (2023). Extracellular CD147 as a diagnostic marker for defective acrosome reaction in asthenozoospermia and idiopathic infertility: abridged secondary publication. Hong Kong Med J; 29(Suppl 4):31–35.
10. Abd Elrahman MM., El Makawy AI., Hassanane MS., Alam SS., Hassan NHA., Amer MK. (2021). Assessment of correlation between asthenozoospermia and mitochondrial DNA mutations in Egyptian infertile men. J Genet Eng Biotechnol; 19(1):11.
11. Kanyenda LJ., Verdile G., Martins R., *et al.* (2014). Is cholesterol and amyloid-β stress induced CD147 expression a protective response? Evidence that extracellular cyclophilin a mediated neuroprotection is reliant on CD147. J Alzheimers Dis; 39(3):545–556.
12. Bu X., Qu X., Guo K., *et al.* (2021). CD147 confers temozolomide resistance of glioma cells via the regulation of β-TrCP/Nrf2 pathway. Int J Biol Sci; 17(12):3013–3023.