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Effects of Zinc (Zn) on the Growth of the Progeny from the Formation of Foetal Sperm Through Parturition: A Review.

Anjali Goswami[1], Vivek Kumar[2], Gaurav Kumar3, Sonalika Singh[4]

[1,2]PhD Scholor, Nims University Jaipur, Rajasthan
[3]Assistant Professor, Nims University Jaipur, Rajasthan
[4]Associate Professor, Nims University Jaipur, Rajasthan

ABSTRACT:

The amount of zinc (Zn), another extremely important trace element, in human beings is substantial. Since the human body is unable to retain zinc, dietary intake of zinc is necessary for a number of bodily processes and metabolism. The testicles, epididymis, and prostate are the three main accessory sex glands, and normal development of these glands depends on the intake of Zn as it moves through the body. The early phases of the growth of germ cells and sperm development, the stages of sperm cell maturation and development, ejaculating the liquefaction the attachment of the male reproductive system and prostasomes, capacity, and fertilization are all important processes in which it participates. During ejaculation, the male reproductive system discharges higher zinc into the seminal fluid, which is important for the release and motility of sperm. The portion of Zn is essential during the gestational, labour, perinatal, and neonatal periods. During the maternity period, the average daily dietary intake of zinc in developing nations is 8–12 mg. Critical evidence has been used to discuss the lack of Zn and its effects. A thorough summary of the activities and roles played by Zn in effective fertilization has been provided. In the simplest terms, our current research highlights Zn's importance at every step of human reproduction, from spermatogenesis through birthing. Future research on reproductive biology now has a new avenue to explore thanks to the significance of zinc and its supplementation in in-vitro fertilization (IVF).

KEYWORDS: Cellular Metabolism, Human Reproduction, Male Infertility, Seminal Plasma, And Zinc.

INTRODUCTION:

A crucial trace element called zinc (Zn) is necessary for many healthy body processes. Variations in our bodies might result from any zinc dysfunction or deficit[1]. Humans commonly have Zn insufficiency, as do many different communities throughout the globe[2]. The development of humans is hampered by hormonal imbalances brought on by zinc deficiency throughout the growth period, and gonadal maturation is also impacted[3]. According to estimates from the World Health Organization (WHO), Zn deficiency contributes to a number of human ailments and affects one-third of the world's population[4]. Zn is necessary for healthy fertilization, making it important for both male and female ability to reproduce. The sperm cells are shielded from bacterial assault by the 85 to 90 times greater Zn level in semen than in blood, according to research. When sperm cells reach the female reproductive system, zinc acts as a barrier to protect them from genetic damage[5].

There is a lot of evidence that Zn is important for early spermatogenesis (the process by which germ cells become sperm cells), epididymal sperm cell maturation, seminal mobility of cells, and pre-fertilization processes in the female reproductive tract. It performs a variety of distinct pre-fertilization tasks, including sperm activation, sperm the zona pellucida (ZP) binding, the acrosome reaction, which is a complex procedure, penetration at the ZP site, participation in both the sperm and the oocyte binding process, activation of the egg or zygote, and the final stage of zona reaction[6]. In addition, Zn has significant effects from post-fertilization through delivery [7]. deficient sperm quality and idiopathic male infertility are both caused by a diet deficient in Zn. Both males and females have impaired reproductive function when Zn levels are reduced by less than 5-7 ppm [8].

According to several study findings, Zn has anti-inflammatory properties and may even be a key player in oxidation[9]. Zn's regulatory actions on spermatogonial multiplication and its requirement for the preservation of germ cells without damage during the meiosis phase demonstrate how the percentage of Zn in the testis rises throughout the early spermatogenesis period[10]. Thymidine kinase, a crucial enzyme for DNA synthesis, is transcriptionally regulated by zinc (Zn)[11]. Any modification in thymidine kinase brought on by Zn shortage will impair sperm generation and cause germ cell arrest. Zn has a significant role in an adult's testicular growth and development, enabling healthy reproductive functions[12]. Hypogonadism, inappropriate secondary sexual features, and other reproductive problems are all strongly linked with deficiencies in zinc in the testes[13]. During ejaculation, the prostate increases the amount of Zn released into the seminal plasma and has a major impact on sperm release and motility[14]. Semen's ability to clot will be impacted by decreased Zn levels in prostate secretions and seminal vesicles. Semen has a viscous consistency, and hyperviscosity is typically correlated with seminal vesicle secretion[15] . Major sex hormones, particularly testosterone, are produced, stored, and transported in large part by zinc (Zn)[16]. The Zn ions found in both prostasomes and intracellular Zn ions facilitate their transport and fusion. Apoptosis, a condition that occurs when cells and tissues naturally die, is exacerbated in Zn deficiency[17]. This has been shown to be a significant contributor to cell death brought on by zinc shortage. The antioxidant capability is restored by Zn supplementation. Ejaculation that occurs prematurely and erectile dysfunction have both been successfully treated with oral Zn supplementation[18].

This review discusses Zn's crucial functions at various stages, including testicular development, spermatogenesis, the transformation of germ cells into sperm cells, activities in accessory sex glands, ejaculation, in the female reproductive tract, in the pre-fertilization process (including capacitation), and from post-fertilization until childbirth. It is also discusses the need of utilizing oral Zn supplements in conjunction with cutting- edge assisted reproductive technologies.

The transportation of Sperm with Zinc Trafficking:

In terms of reproductive biology, Zn has been very well explained, but in terms of a dynamic research at different phases of sperm generation, Zn's involvement has hardly been examined or reviewed[19]. Precise groups of transporters called ZnTs, particularly participate in effluent discharge, support Zn transportation through the membrane[20]. Numerous sperm activities entail zinc, which is anticipated to be absorbed at its highest rate during sperm transit in the post-epididymal phase[21] after they have passed through the epididymis. Male reproductive functions, including spermatogenesis and spermiation, undergo tracking and have been found to be carried out by ZnTs[22]. From this key vantage point, the aforementioned study supported the notion that large modifications (less content) happen in the ejaculating phase whereas the testicular and epididymal stages had high Zn concentration[23]. However, there isn't enough solid data to support the idea that the increase in hypermotility (detected by flow cytometry) is the main cause of the Zn content loss during ejaculation. Although additional research is required to establish the benefits of Zn dietary supplementation, this study offered a scientific idea that Zn supplementation may be employed as a treatment for infertility among men patients[24].

Zinc's Function in Regular Spermatogenesis:

Poor sperm production will result from the Zn concentration being affected by the changed Zn transporter expression[25]. Ellis revealed in 2014, the necessity of Zn and its existence in reproductive cell survival before maturation, as well as in protamine replacement during spermatogenesis[26]. Zn is important for spermatogenesis and the initial stages of seminal cell development because it accumulates in spermatocytes and is found in the nucleus and chromosomes of sperm cells [27]. As shown by its regulatory actions in spermatogonial multiplication and throughout the meiosis phase for the preservation of the germinal cells without damage, Zn concentration in the testes rises within the early sperm development period[28]. Zn decrease at this point in time will cause germ cellular death without the development of functional mature sperm cells, as well as unreliable spermatogonia growth[29]. This increases the likelihood that there will be less mature sperm cells accessible in the testis as a whole. As a result, there may be fewer spermatozoa present in the ejaculate, leading to the wrong identification of oligospermia[30]. A decreased sperm count and compromised spermatozoa during ejaculation are often symptoms of poor spermatogenesis.

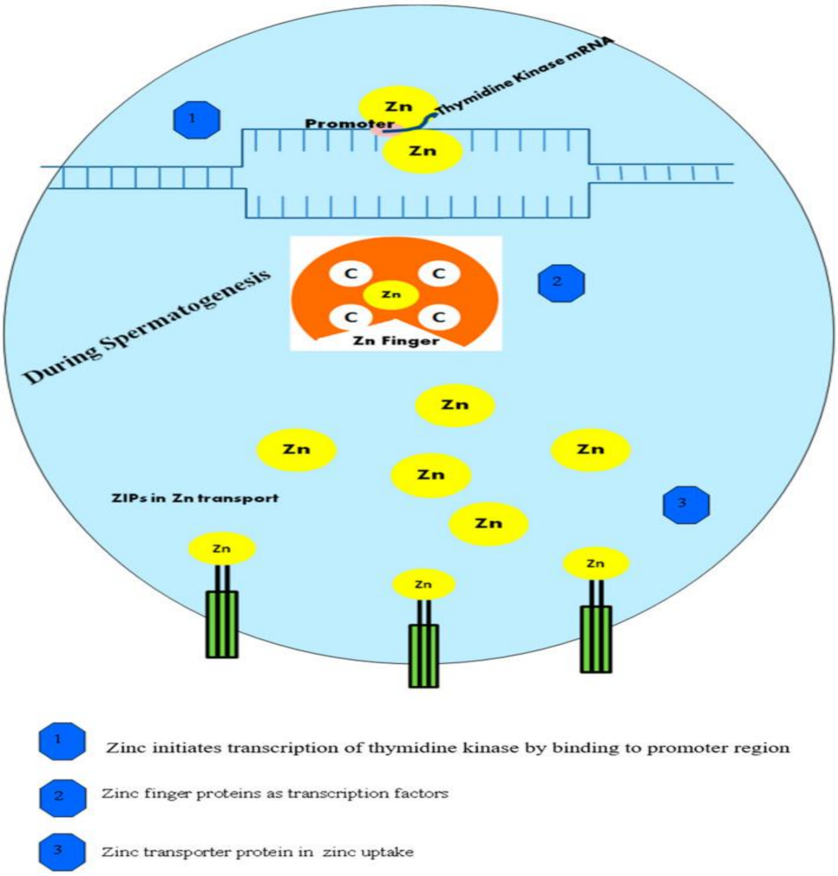


FIGURE - Iron-regulated transporter-like proteins, often known as IPs, are zinc-regulated transporters. the molecular function of zinc (Zn) in the development of sperm. The mechanism of Zn intake during spermatogenesis and how Zn finger proteins work as transcription factors are shown in the figure.

The WHO recommended that there be approximately twenty billion sperm per milliliter. During spermatogenesis, a decrease in count caused by a Zn deficit[31] may aid in oligospermia diagnosis. The significance of Zn throughout spermatogenesis and its effects on diagnosis are supported by substantial data[32]. Zn plays a crucial role in epididymal transit, because it stabilises the sperm cells before to or during ejaculation, as shown by the high Zn level in the prostate[33]. A crucial role in spermatogenesis is played by zinc finger proteins (ZFPs)[34].

A broad family of transcription factors known as ZFPs mostly consists of zinc[35]. These transcription factors have a variety of roles throughout growth and development, including DNA binding, cell death, and the activation of transcription and translational processes[36]. They are also crucial for these processes to occur. Numerous academics have talked about how important ZFPs are for spermatogenesis, germ cell proliferation, and differentiation. The overexpression of ZFP185 in Leydig cells, which results in the generation of testosterone, is important for spermatogenesis[37]. Spermatogenesis is significantly influenced by zinc transport molecules (ZIPs), which help with Zn absorption into the cell's cytoplasm and function at the internal zinc level[38].At various phases of spermatogenesis, ZIPs' decreased expression throughout the transport and absorption of Zn into the internal lumen may cause problems[39]. The amount of Zn in the blood and the amount consumed throughout spermatogenesis is positively correlated[40]. Numerous studies have looked at how Zn and cadmium interact in the adult testes[41]. Positive correlations have been shown between hypogonadism and inappropriate development of additional sexual features and Zn insufficiency in the testes[42-43]. Due to commonalities in their ion pair compositions, Zn and Cd interact competitively[44].The activities of sperm formation in the testes are disrupted as a result of reduced Zn absorption by spermatogonia, competitive replacement by cadmium, and decreased Zn concentration[45].

The germ cell capacity may be significantly decreased due to the diminished testes size caused by Zn deficiency [46,] which will automatically result in impaired spermatogenesis and will inhibit spermatid differentiation [47]. The reduced level of Zn in the testes causes severe damage and reduced testes weight [40]. Testicular Zn shortage alters the shape of Leydig cells and interferes with their ability to proliferate and differentiate. Reduced levels of sex hormones, spermatogenesis impairment, and subpar fertilisation are caused by low Zn levels in the testes and issues with the Leydig cells[48]. Because of the low quality of fertilisation caused by reduced Zn in the testes, oxidative damage to lipids, altered transcription and translation, and damaged DNA and proteins in testicular cells also result [49]. Zn competitive binding has been linked to the toxicity and damage caused by cadmium to the testicles in a rat model[50.]

Importance of Zinc in the Prostate: The human body has Zn in every cell. Zn is crucial for the prostate, where it is found in high amounts as compared to different soft tissues [51,52].During ejaculation, the male reproductive system releases more zinc into the seminal plasma, where it is essential for the release and movement of sperm [53]. The amount of zinc in the tissues of the human prostate is 150 g/g, a number that is three times more than any other types of soft tissue. The Zn content of prostatic fluid is similar, coming up at around 500 g/mL [54]. Zn primarily serves to offer antibacterial action in the prostate, which lessens sperm cell assault during ejaculation. Numerous active bacteria may be found in a female's upper reproductive canal, and once the male reproductive organ enters, they have the potential to harm it [55]. Zn has antibacterial qualities that enable it to protect and safeguard the cells that make sperm from harm [56]. Zn is used to guarantee that the Krebs cycle produces the most citrate possible in the prostate tissue [57]. For spermatozoa to operate normally, this is necessary. In the prostate, Zn homeostasis is tightly controlled. Zn needs may change as a child develops sexually. ZNT1 is required for proliferation of cells, as shown by the fact that it expresses less after reaching maturity in sexuality [58] and that Zn accumulates in the prostate around this time [19].

The Zn-Induced Capacitation Mechanism: The process of sperm capacitation is crucial to successful fertilisation [59]. Zn spark is viewed as a unique indicator of embryonic mammalian quality and other developmental potential traits. There hasn't been much study on Zn ions and their effects on flow [60]. One important factor in capacitation is the proton extrusion process. Its significance in voltage-gated proton channels has been shown in several investigations [61]. For the entrance of Ca2+ ions across another channel termed CatSper, the control of this channel is more crucial. The stimulation of protein tyrosine phosphorylation during capacitation has been connected to this process [62]. In the presence of Zn flux or spark, pH maintenance and proteasomal activity take place [63].

ZINC in Human Seminal Vesicles: Mechanism: Human seminal vesicle secretion is important in the latter phases of ejaculation [64]. The five roles played by seminal vesicles in healthy fertilisation are: promoting sperm motility, preserving sperm stability, inhibiting sperm motility, and performing various antioxidant tasks [65]. Semen has a thick consistency. When ejaculation makes contact with the seminal vesicles, it quickly coagulates [66]. The coagulum is largely made up of semenogelin proteins, and Zn ions either mediate or stimulate coagulation [67]. These Zn ions play a crucial role in motility inhibition and coagulation. Zn deficiency can affect semen coagulation in seminal vesicles and prostate discharge [68]. Hyperviscosity is frequently associated with the consistency of the seminal vesicles and their secretions [69]. Seminal vesicles contain Zn, and when there is intense secretion, hyperviscosity develops. Semen hyperviscosity is frequently accompanied by poor semen volume, impaired normal morphology, and decreased motility [70]. When a Zn chelating agent is abundant, high or hyperviscous semen samples are thought to be responsible for increased chromatin stability [71]. Semen sample hyperviscosity may be caused by seminal vesicle hypofunction, and Zn is crucial in this regard [72]. Prolactin is secreted by the seminal vesicles and has been linked to Zn in studies. Prolactin is thought to be a motility enhancer and may have a function in sperm motility. One of the crucial pathways involved in normal sperm motility after ejaculation is this one [73].

Role of Zn in Major Sex Hormones: Major sex hormones, particularly testosterone, which is thought to be a key regulator of spermatogenesis, are produced, stored, and transported in large part by zinc (Zn) [74, 75]. To ascertain the synthesis of testosterone, dietary Zn monitoring is crucial [76]. Therefore, specialists keep an eye on Zn consumption during in vitro fertilisation (IVF). Low quantities of testosterone are present in the seminal plasma and serum, but a diet lacking in Zn causes an increase in the amount of circulating luteinizing hormone [77]. This shows that dietary Zn has significant effects. Leydig cell population reduction or damage, alterations in proliferating and differentiating themselves, Leydig cell apoptosis, and testis damage are all positively linked with Zn deficiency [78]. Testicular inflammation and Leydig cell oxidative damage are caused by Zn deficiency [79]. Lower or inadequate Zn levels are frequently indicated by impaired spermatogenesis, reduced testosterone levels, damaged luteinizing hormone, also known as (LH) receptors in the body damaged Leydig cells, and changes in the morphology of the Leydig cells [80].

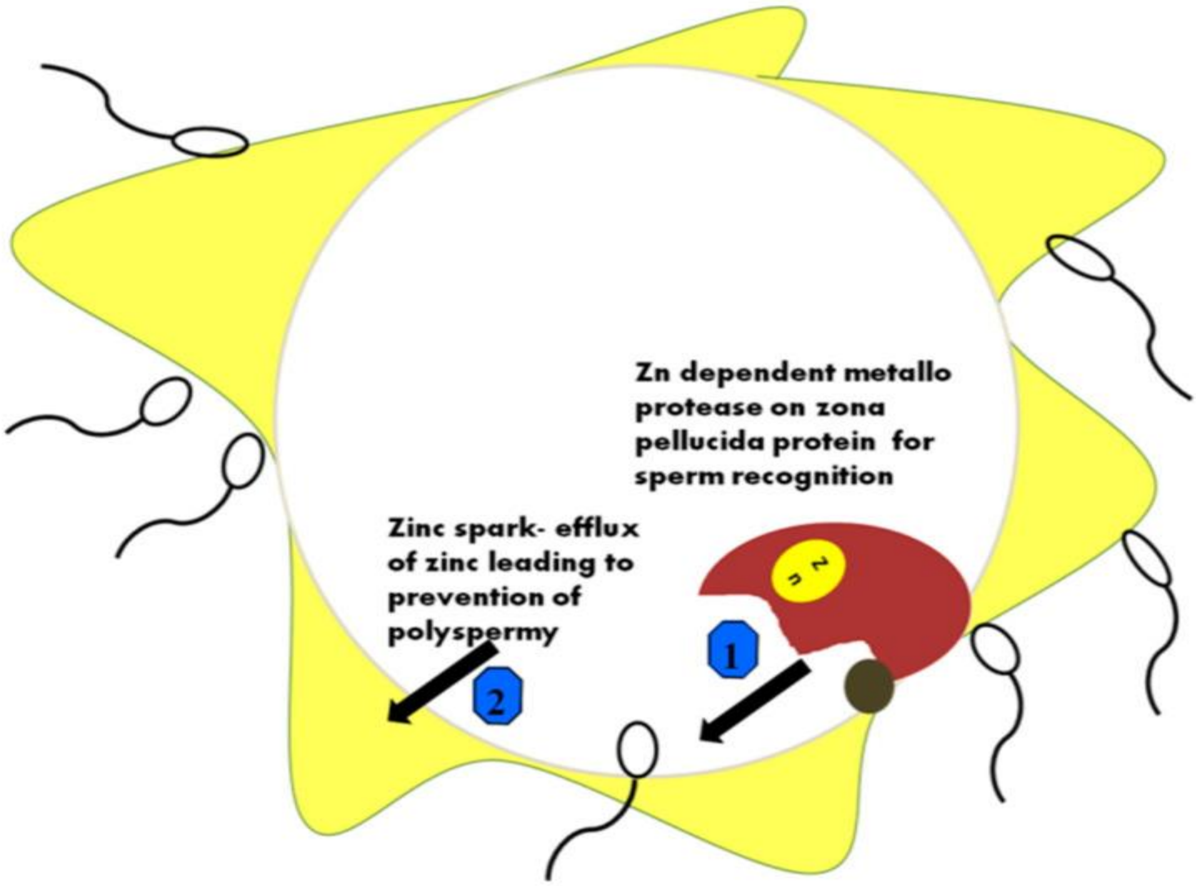
Role of Zn in Prostasomes and Sperm-Binding Activity: The prostate gland secretes prostasomes, which are membrane extracellular vesicles that are present in semen. Prostasomes contain large amounts of phospholipid proteins and lipids [81,82]. The fusing of spermatozoa and protosomes, which is mediated by pH and protein, aids in proper fertilisation. For the spermatozoa to move properly, the amino peptidase found in prostasomes must be transported [83]. Zn ions found in prostasomes and intracellular Zn ions both play a role in the transfer and fusion processes. Sperm must acquire proteins that are tied to membranes, and Zn ion-mediated transfer makes this happen [84].

Role of Zn in Anti-Cell Death and Anti-Apoptosis: In the past three decades of study, evidence supporting the Zn's mode of action in apoptosis has been discovered [85]. Apoptosis, a process that results in the death of cells and tissues, is linked to Zn deficiency [17]. The development of sperm cells, the male gonads necessary for successful fertilisation, requires a number of steps for the germ cells [86]. Zn shortage in Leydig cells is linked to increased apoptosis and a decrease in testis volume, which lowers the proportion of germ cells that differentiate into sperm cells [87]. Important genes and proteins including Caspase 3 and Bcl-2 are involved in how apoptosis is brought on by a Zn shortage [88]. Numerous pathways are linked to the way that zinc protects cells against apoptosis. The process by which Zn is delivered to important targets, the labile Zn that shields cells from harm, requires further study. [89]. Cellular defence is significantly aided by Zn's control of apoptosis via Bcl 2 and caspase 3 [90]. The anti-apoptotic characteristics of zinc have been discovered by several studies, however the way by which zinc defends against apoptosis is unclear and varies depending on the amount of protection. Leydig cells may undergo apoptosis as a result of DNA fragmentation due to an endonuclease reaction that is Ca2+- and Mg2+-dependent [91]. These ions can be inhibited by Zn, which will stop fragmentation of DNA and apoptosis. Another element that impacts the entire process is oxidative stress, which results in apoptosis and elevated levels of the reactive oxygen species (ROS) in sera and seminal plasma [92]. Zn promotes antioxidant activity and functions as a mediator to entrap ROS [93]. Zn deficiency mediates a rise in ROS and, as a result, causes oxidative stress-driven apoptosis [94]. Through protein-mediated SH (Sulfhydryl) group binding, zinc (Zn) preserves sperm cell membranes by acting as a coating layer [95]. Sperm membrane fluidity rises, which mediates the correct spermatozoa fertilising potential. Malondialdehyde levels in serum and seminal plasma are higher in Zn deficient patients, although antioxidant levels such SoD (superoxide dismutase) are lower [96].

Zn and Its Significance in Estrogen: In the physiology of female reproduction, Zn is a crucial trace element. In a research employing rats as a model [97], rodents were fed a diet lacking in zinc, which decreased or suppressed the amounts of hormones that stimulate follicles and LH (luteinizing hormone) [98]. The significance of Zn in the physiology of female reproduction is shown by this result. The menstrual cycle is disrupted and aberrant ovarian functions are more common as a result of Zn deficiency, giving rise to erroneous hopes of typical fertilisation [99]. Zn interactions with hormone receptors serve as the foundation for the mechanism or basis of Zn in both male and female reproduction [100]. Sex hormones in both the male and female reproductive systems cannot be triggered in the absence of the Zn metalloenzyme [101]. In the presence of RNA polymerase, Zn metalloenzymes produce a complex structure that binds to sex hormone receptors. Fetuin-A and B are crucial for sustaining female fertility [102]. Fetuin-A is crucial for bone mineralization, according to research using gene knockout mice. Additionally, the animal model study supports the importance of Fetuin B in determining female fertility [102]. Due to the zona pellucida's stiffening, this protein's absence or deficiency may result in female infertility. Oocytes that have not been fertilised contain the metalloproteinase ovastacin, which is the source of this [103]. The hormone-receptor complex and DNA binding may both be prevented by any Zn dysfunction or deficit. As a result, oestrogen cannot perform its usual actions [104]. Additionally, several genes mentioned here lose their ability to operate as activators and regulators, impairing the monitoring and synthesis of oestrogen [105].

Zn as a Regulator in the Female Reproductive Tract: Once the sperm enter the female reproductive tract, numerous immune responses against sperm cell entry are activated [106]. The presence of Zn helps to reduce these responses and sends a signal that this is for reproductive action and that the process should not be disturbed [107]. This is because Zn acts as a cofactor for many proteins in the female reproductive tract and activates them, allowing complete fertilization competency [108]. Zn ions play a key parameter in sperm capacitation in the female reproductive tract and act as a regulating authority for other important events, ensuring effective fertilization [109]. Zn efflux is important for Ca^{2+} influx, and this process is mandatory for capacitation to occur. Any malfunction or deficiency in the process of zinc ion efflux will reduce capacitation [110]. Effective sperm-oocyte interactions are necessary for embryo development, which is anti-polyspermy. This inhibits several sperm cells from entering an oocyte's cytoplasm during fertilisation [111]. Due to the complexity of the anti-polyspermy defence system, a deep knowledge of the underlying process is necessary. Polyspermy during fertilisation is caused by embryo polyploidy lethality. There are two main processes that prevent polyspermy from occurring [112]. Cortical exocytosis and membrane depolarization are the first and second, respectively. These two processes by which the polyspermy process is stopped are seen with the aid of Zn2+ ions released from the cortical area of oocytes [113]. Numerous investigators have demonstrated the significance of this release, known as Zn Sparks, in the female reproductive system [114]. Using its anti-polyspermy properties, Zn controls the sperm that enters the oocytes during this time for freshly fertilised eggs. Other sperm cells that are present close to the fertilised egg may also be decapitated by Zn [115]. For the purpose of preventing pregnancy caused by polyspermy, this procedure is known as the zinc shield [116]. According to additional research, Zn2+ ions can prevent fertilisation when they are introduced to IVF medium components. Zn in the ZP mechanism is complex, and the underlying mechanism has not yet been fully understood [117]. A crucial component in increasing male fertility is the presence of Zn2+ ions in the seminal fluid [118]. Low sperm counts and poor sperm quality are the outcomes of any deficit in or reduction in Zn2+ content in seminal plasma [119]. The concentration of Zn ions and sperm, as well as the typical shape of sperm cells, have been found to positively correlate by several researches. An improvement in sexual function and a decrease in sexual dysfunction are shown in rats and uremic males who receive Zn supplements [120]. A rise in the number of sperm was seen in oligospermic individuals after Zn and folate treatment [121]. Zn supplementation can rebuild Zn's antioxidant capability by removing ROS from the semen and serum [122]. A Zn-mediated mechanism is responsible for monitoring the blood flow to the penile veins during an erection [123]. The treatment of premature ejaculation and erectile dysfunction with oral Zn.

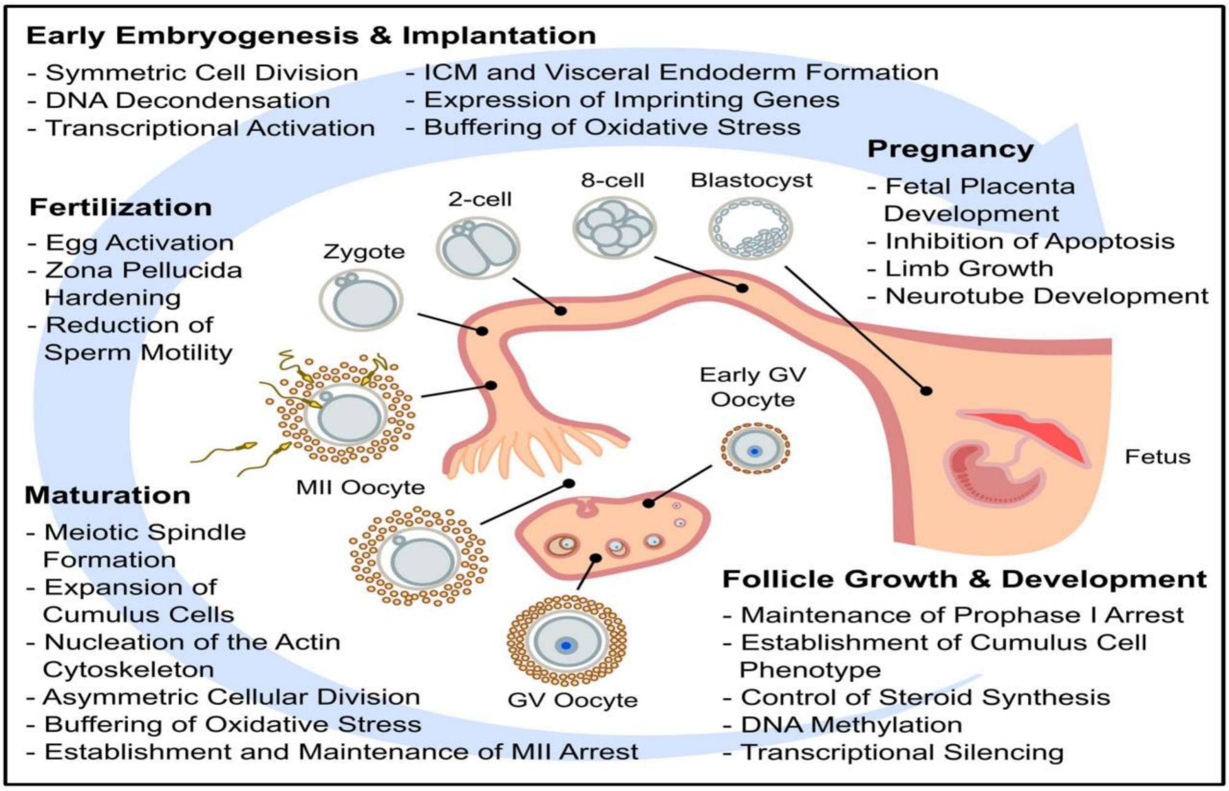
FIGURE-



When sperm and ova interact, Zn ions play several roles. When the ZP protein utilises the Zn-binding protease, the Zona pellucida (ZP) hardens through changes in membrane proteins. The image illustrates zinc's main roles in preventing polyspermy. To recognise sperm, zona pellucida needs the Zn-dependent metalloprotease. Polyspermy is caused by Zn efflux.

Supplementation has been proven to be successful. Although the effectiveness of dietary Zn consumption in enhancing fertility has not been demonstrated experimentally, after ejaculation, a rise in the proportion of uncapacitated sperm cells was seen [124]. No scientifically sound explanation for the mechanism behind this procedure has been found. Although many researchers have noted the effects of oral Zn dietary supplementation. on both male and female reproductive processes and used Zn therapy as a measure to improve sexual performance, there is also evidence to suggest that Zn intake greater than 100 mg/day has been linked with prostate cancer [125]. The assumption that zinc causes cancer is not supported by any data [126], although experts have claimed that there should be a limit on the quantity that may be ingested since a fast increase in intake may result in prostate cancer [54]. Consuming less than 100 mg of zinc per day does not raise the chance of developing prostate cancer, however taking more than 100 mg of zinc per day as a supplement may.

Role of zinc in female reproduction:



Zn's Functions in Pregnancy, Birth, and Postpartum Care: The major challenge for academics and doctors worldwide is lowering the death rates of perinatal, neonatal, and young babies [127]. The mortality rate for women can be decreased with proper macro- and micronutrient intake monitoring and supplementation [128]. Developing nations use this approach more frequently than industrialised nations do. Zn has a significant impact on newborn, baby, and mother survival [129]. Uncertainty exists regarding the significance of Zn during pregnancy and childbirth [130]. In poor nations, during the maternity period, the average dietary Zn consumption ranges from 8 to 12 mg Zn/day. The average daily dietary Zn consumption for expectant and nursing moms is between 9.6 and 11.2 mg worldwide [131]. Although drinking water marginally enhances Zn consumption, the intake should still be at least 4 L/day [132]. Low Zn levels during pregnancy are linked to reduced birthweight, whereas excessive Zn levels can cause spontaneous miscarriage and a variety of defects, including congenital ones [133]. Pregnant women with mild Zn insufficiency may experience a variety of difficulties during stages 1 and 2 of labour, including early membrane rupture and the need for operational interventions in certain cases [134]. Zn serves as a cofactor during this period and can be used to monitor oxytocin secretion [135]. newborn infection, newborn hypoxia, and respiratory distress are further effects of these problems [136]. The child may inherit the mother's Zn deficit. These newborns may exhibit signs including dermatitis, baldness, appetite loss, diarrhoea, and immune system impairment [137]. This kind of zinc deficiency illness, which affects newborns and preterm babies, is brought on by a shortage of zinc in breast milk. Pedigree study has demonstrated that zinc deficiency is inherited from mothers to their unborn children through their breast milk. Additionally, it was discovered that maternal zinc supplementation had no impact on the Zn content of breast milk [137]. Recent significant research on Zn and reproduction are included here.

Important investigations into the roles of Zn in human reproduction and human male infertility and its implications.

S.N.	Author And Year	Zn Role In Human Reproduction And Infertility	Study Conclusion
1	Qu et al., 2007 [138]	Zn-2-glycoprotein, often known as ZAG, has a significant impact on sperm motility.	Human semen may include ZAG, which may support both normal motility and the PKA (Protein Kinase A) signalling pathway.
2	Saleh, 2008 [139]	Semen has the highest levels of copper and zinc of any bodily fluid. This keeps the quality of sperm high.	Zn and Cu estimate are crucial for accurate male infertility diagnosis.
3	Colagar et al., 2009 [140]	Low sperm quality may arise from increased reactive oxygen species (ROS) and oxidative damage caused by the absence or mild shortage of Zn in the seminal plasma.	It was discovered that sperm count and typical sperm morphology were strongly positively linked with seminal Zn content. Low semen quality and idiopathic male infertility are caused by low or nonexistent Zn consumption.
4	Dissanayake et al., 2010 [141]	Zn is a key factor in influencing other factors, such as sperm count and proper morphology.	In this study, it was determined the Zn content and the overall quantity of Zn per volume of ejaculate. The amount of total zinc, or Zn (T), was strongly linked with both sperm count and typical morphology.
5	Khan et al., 2011 [142]	Zn deficiency is a major factor in male infertility in humans. Hypogonadism and inadequate growth of secondary sex traits are linked to zinc deficiency.	The normal functioning of the sperm is aided by sufficient Zn in the seminal plasma. A higher Zn concentration reduces sperm motility, although a lower Zn concentration in the seminal plasma was linked to a higher sperm count. Monitoring the Zn level in seminal plasma is essential.
6	Hadwan et al., 2012 [143]	There are three different kinds of ligands for human seminal Zn: high, middle, and low molecular mass ligands. Sperm motility in asthenospermic patients increases with an increase in oral Zn intake.	According to the study's findings, high and low molecular Zn ligand levels are often increased in asthenospermic individuals who received zinc supplements due to an increase in motility.
7	Sundaram et al., 2013 [144]	For Zn fingers and DNA-binding proteins, zinc serves as a cofactor.	Zn could be the greatest biochemical marker for severe semen abnormalities and for correctly identifying male infertility in humans.
8	Foresta, 2014	After the peak of the post-	Zn is trafficked throughout the lifespan of

	[20]	epididymal period, Zn has a role in a variety of sperm activities.	sperm.
9	Altaher and Abdrabo, 2015 [145]	In patients with oligospermia and asthenospermia, Zn and Cu play important roles.	A substantial decrease in Zn concentration was seen in azoospermia and oligospermia cases.
10	Zhao et al., 2016 [146]	Thorough data analysis indicates that Zn concentration is much smaller than in other fertile groups, demonstrating the importance of Zn in semen parameters.	Major semen metrics like volume, forward motility, and typical shape are all increased by zinc intake.
11	Nenkova et al., 2017 [137]	Zn has a significant role in spermatozoa's defense against oxidative damage.	There is proof that during ejaculation, trace elements have an antioxidative effect.
12	Fallah et al., 2018 [1]	In the female vaginal tract, zinc functions as an antimicrobial substance and even aids in immune shock defense.	Zn may serve as a nutritional indicator of male reproductive capacity.
13	Mirnamniha et al., 2019 [6]	Zn is essential for the activation of capacitation.	It is crucial to determine the level of Zn in the seminal plasma in cases of idiopathic male infertility.
14	Vickram et al., 2020 [84]	Zn has a key role in facilitating the attachment of prostasomes on sperm cells to transmit crucial substances, which opens the door for fertilization.	Male infertility and the detection of prostate cancer are both indicators for prostatesomes.

Discussion: The studies by Vickram et al. (2020), Mirnamniha et al. (2019), and Fallah et al. (2018) collectively highlight the multifaceted role of zinc (Zn) in male and female reproductive health. Vickram et al. (2020) underscore the importance of Zn in facilitating the attachment of prostasomes on sperm cells, a process crucial for the transmission of essential substances and, consequently, successful fertilization. This suggests a pivotal role for Zn in male fertility, with potential implications for cases of male infertility.

Mirnamniha et al. (2019) contribute to this narrative by emphasizing Zn's essential role in the activation of capacitation, a key process in sperm maturation. This further underscores the significance of Zn in male reproductive function, particularly in the context of fertilization.

In parallel, Fallah et al. (2018) shed light on the antimicrobial properties of Zn in the female vaginal tract, where it serves as a defensive mechanism against infections and aids in immune shock defense. Additionally, the indication that Zn may serve as a nutritional indicator of male reproductive capacity adds a layer of complexity to its role in assessing male fertility.

Collectively, these findings suggest that Zn plays a crucial and multifunctional role in reproductive processes, spanning from male fertility to female reproductive health. The determination of Zn levels in seminal plasma emerges as a critical aspect in diagnosing idiopathic male infertility, offering insights into potential treatments and interventions. Moreover, understanding the diverse functions of Zn contributes to the broader comprehension of reproductive biology and may have implications for the detection and management of conditions such as prostate cancer and female reproductive tract infections.

Conclusions: The ability of both men and females to reproduce is significantly influenced by the dietary intake of Zn. Zn cannot be stored by the human body, thus it must be obtained from nutrition in order to keep the body's metabolism functioning, especially for men and women who are of reproductive age. The WHO has published a study on worldwide illnesses or syndromes linked to zinc deficiency. At reproductive age and throughout pregnancy, women need more dietary zinc than men do. Zinc is taken up throughout the development of sperm, from germ cells to mature sperm cells, since zinc transporters are widely distributed throughout the genital canal. A modest amount of zinc is needed during spermatogenesis, but when maturity is attained, or during epididymal transit, a larger amount of zinc is required. Following this procedure, spermatozoa will be defeated by prostate Zn secretions, which will then function as a defence during ejaculation. In order to provide a clear path to fertilisation once the female reproductive tract is reached, seminal Zn and female Zn concentrations in the tract work together. The semenogelin protein utilises seminal Zn as a cofactor, which aids in the gel's production or liquefaction. Through the fusing of prostasomes into spermatozoa membranes and the transfer of all necessary components, zinc aids in motility, especially forward-directional motility. Zn promotes ZP binding and capacitation through a variety of methods. Zn mediates the pre-fertilization process in the secretions of the upper reproductive tract, however it is still unclear how this happens. Zn is crucial for both the maturation of the zygote after fertilisation and the sperm's entry into the oocyte. Zn supplementation has been extensively addressed during pregnancy, the perinatal period, and the neonatal period. Over 50% of instances of infertility benefit from Zn supplementation, on average. For both males and females receiving infertility therapy, zinc supplementation is crucial. For ART (assisted reproduction technology) procedures that use Zn supplementation as part of the treatment, pregnancy results are positively correlated. Many ART facilities choose to employ Zn supplementation, despite the fact that the mechanism underlying this is still not fully understood. From spermatogenesis through postnatal care, we have outlined the main Zn roles, mechanisms, and requirements in this study.

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