International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 10, Issue 1, pp: (8-14), Month: April 2022 - September 2022, Available at: www.researchpublish.com

The Role of Sperm Chromatin Compactness and Sperm Maturity to Fertility and Embryo Development

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DOI: https://doi.org/10.5281/zenodo.6464545

Published date: 12-April-2022

Abstract: **The analysis of semen has been used to diagnose complications associated with reproductive health. It is also worth noting how the same diagnostic procedure is accurate in determining fertility as well as embryo development. The objective of this systematic review was to assess the role of sperm chromatin and sperm maturity to fertility and embryo development. The study included 28 articles from the PROQUEST online database. Several inclusion criteria were used in the selection of relevant articles. The criteria were: (1) the year of publishing, where studies published in 2000 or later were included, (2) studies that applied primary data, and (3) the relevance of the articles as per the independent and dependent variables. The results showed that sperm chromatin and sperm maturity play critical roles in male fertility and embryo development. Regarding the former, the researchers agreed that sperm chromatin plays a major role in the transmission of genetic information. Therefore, the resulting genetic makeup of the embryo depends on the normality or abnormalities of the sperm chromatin. Concerning the latter, this review confirmed a high level of agreement among scholars that a mature spermatozoa is more likely to fertilize than an immature one. The practical implication of this study is the justification of fertility diagnostic tests that examine the sperm chromatin structure and functionality.**

Keywords: **Reproductive health, Spermatozoa, Chromatin, Fertility, Embryo development.**

1. INTRODUCTION

Rationale

Fertility and embryo development are critical aspects of reproductive health, as scientists seek new ways to solve the problem of infertility. A study by Tandara et al. (1) revealed that infertility affects at least 15% of couples around the globe. The current body of literature shows that sperm chromatin and sperm maturity are linked to fertility and embryo development. However, it remains unclear whether the findings from various groups of scholars from different parts of the globe match or differ. This systematic review bridges the gap of knowledge by providing a platform for comparing the findings of studies on the role of sperm chromatin and sperm maturity to fertility and embryo development.

Objectives

1. To determine the role of sperm chromatin to fertility and embryo development.
2. To determine the role of sperm maturity to fertility and embryo development.
3. To assess the combined role of sperm chromatin and sperm maturity to fertility and embryo development.

2. METHODS

Protocol and Registration

This systematic review focused on peer-reviewed articles from PROQUEST, an online database dealing with various types of articles. Using the filter provided by the search engine, it was possible to select peer-reviewed articles only.

Eligibility Criteria and Information Sources

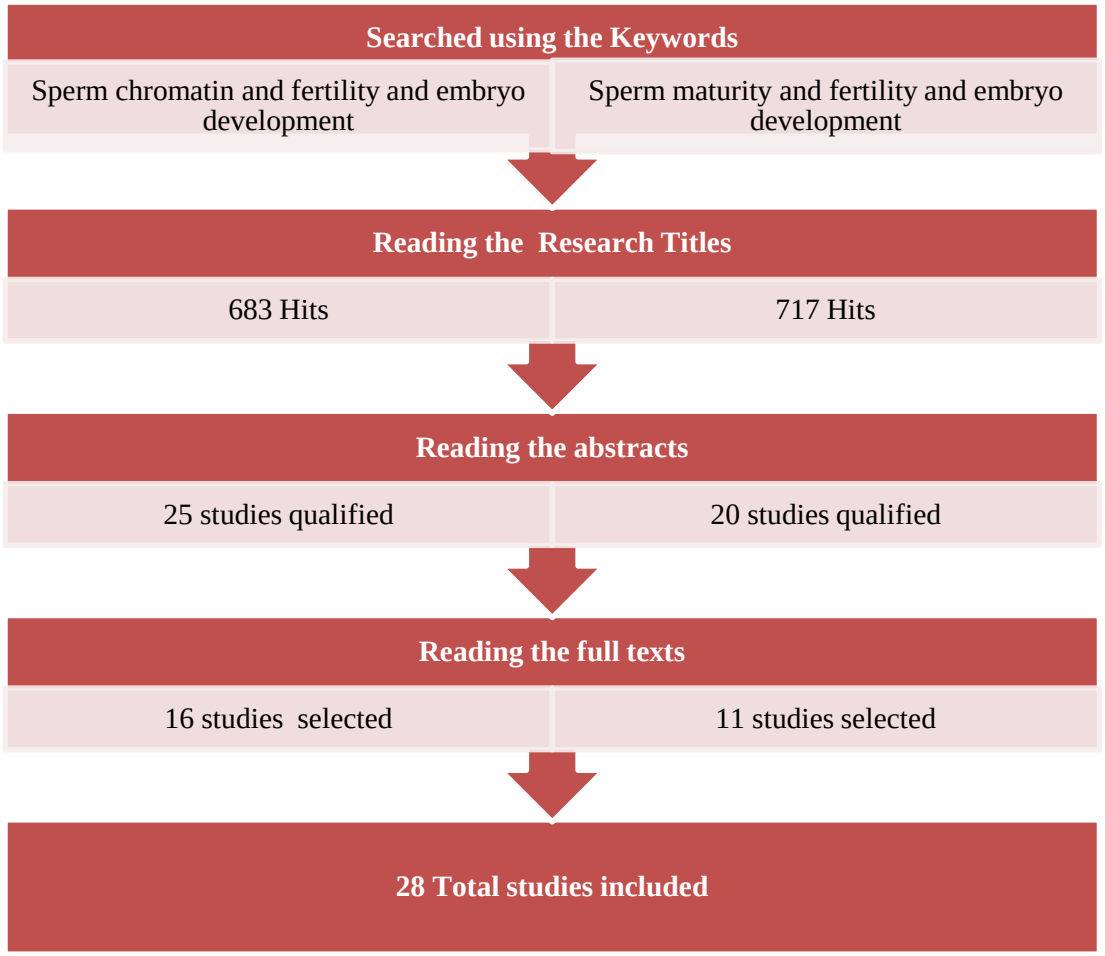
The review focused on findings regarding the role of sperm chromatin and sperm maturity on fertility and embryo development. Hence, studies that were published since the beginning of the 21st Century were included. As mentioned above, articles were selected from the PROQUEST database. Specifically, the articles were searched between 12th January 2022 and 14th January 2022.

Search

This study focused on determining the relationship between two independent variables (sperm chromatin and sperm maturity) and two dependent variables (fertility and embryo development). The information was searched using the variables as keywords. Therefore, two sets of keywords were used in line with the first two objectives. The keywords were: (a) "sperm chromatin" and "fertility and embryo development" and (b) "sperm maturity" and "fertility and embryo development".

Study Selection

Once the keywords were entered into the search engine and processed, three steps were used to select the relevant articles. Firstly, reading the title allowed the identification of the promising articles. Secondly, reading the abstract assisted in narrowing down the most relevant studies as far as the research objectives, variables, and findings were concerned. Finally, reading the full text of the selected articles allowed further elimination of the specific articles that qualified for all the inclusion criteria. The same procedure was repeated as per the two independent variables.



Data Collection Process

Since this is a systematic review, the collection of data focused on the interpretation of the findings in line with the variables. As part of the data collection, information regarding the research method used and the data collection applied, the findings, and the conclusions were put together. The idea was to compare the studies and determine the similarities and differences in their outcomes.

Data Items, Risk and Bias in Individual Studies

As indicated above, the independent variables were sperm chromatin and sperm maturity while the dependent variables were fertility and embryo development. These variables were used as the data items to determine how the independent variables lead to the dependent variables. Regarding the risk and bias, the study focused on the outcome and recommendations.

Summary Measures, Synthesis of Results, Risk, and Bias across Studies

Since this is a systematic review, the summary measure for this study was the interpretation of the qualitative analysis. Therefore, the synthesis of results was done by interpreting the common keywords used to define the relationship between the independent and the dependent variables. In this study, the selection bias was the main possible factor that affected the cumulative evidence. For instance, it was necessary to identify enough articles for each independent variable to ensure a well-balanced systematic review. In doing so, some weaker articles were selected for the study on sperm maturity just to ensure that at least 12 studies are included. The additional analysis focused on assessing the practicality of the recommendations by other researchers based on the findings in this study.

3. RESULTS

Study Selection

In brief, a total of 45 studies were screened. However, only 28 articles passed all the eligibility criteria after reading the full text due to several reasons. In particular, 13 articles failed the relevance criterion since the purpose of the studies diverted from the variables targeted. The remaining four articles were excluded since they were reviewed literature and meta-analyses. The exclusion of studies with secondary data was necessary to achieve uniformity and relevance. The analysis of studies with primary data only ensured the much-needed data characteristics to facilitate comparison.

Results of Individual Studies

Sperm Chromatin in Fertility and Embryo Development

The researchers (1-15) agreed in unison that sperm chromatin integrity is a critical factor in male fertility. Specifically, many studies (6-9, 12, 16) showed that sperm chromatin played a critical role in transmitting paternal genetic information to the offspring. For instance, Sadeghi et al. (3) reported a higher fertilization rate for a group with less than 10% chromatin abnormality. Another study by Shamsi et al (8) noted that the abnormal organization of genome material in the sperm cells leads to 20% of cases of male infertility. As Table 1 shows, it is evident that most of the studies on the role of sperm chromatin to fertility and embryo development lead to similar or related outcomes.

Table 1: A Summary of individual Studies on Sperm Chromatin

Study	*Authors*	*Year*	*Findings*
1	Tandara et al.	2013	Higher sperm DNA damage adversely affects the embryo quality
2	Agarwal et al.	2003	Sperm chromatin abnormalities may lead to the accurate transmission of the genetic information
3	Sadeghi et al.	2009	Sperm chromatin integrity is critical in ensuring successful fertilization, embryo development, and normal pregnancy
4	Agarwal	2014	Sperm DNA damage is linked to reduced fertilization rates and embryo quality
5	Erenpreiss et al.	2006	Sperm chromatin abnormalities may result in male infertility
6	Cebesoy et al.	2006	defects in the chromatin structure led to infertility and poor embryo quality
7	Singh et al.	2001	Sperm chromatin integrity plays a critical role in ensuring male fertility
8	Shamsi et al.	2008	The sperm chromatin influences embryo development depending on the paternal genetic information transferred

9	Hammoud et al.	2009	Sperm chromatin played a critical role in transmitting paternal genetic information to the offspring which is linked to embryonic development
10	Khajavi et al.	2009	Sperm chromatin plays a critical role in transmitting paternal genetic information to the offspring
11	Revay et al.	2009	Sperm chromatin influences embryo development
12	Cocuzza et al.	2007	Sperm chromatin damage is associated with male infertility
13	Agarwal	2003	Oxidative stress and sperm chromatin damage are linked to male infertility
14	Oikos et al.	2015	The damage of sperm chromatin, which is linked to aging, leads to impaired fertility
15	Zini et al.	2014	Sperm chromatin defects and DNA damage leads to infertility
16	D'Occhi et al.	2007	The structure and quality of sperm chromatin influence male fertility and embryonic survival
17	Simon et al.	2014	The sperm DNA integrity plays a major role in early embryonic development

Sperm Maturity in Fertility and Embryo Development

The maturity of spermatozoa is yet another concept that has been linked to fertility and embryo development. In this study, one of the questions is how sperm maturity influences fertility. This question is critical in addressing the issue of infertility since it informs the sexual behaviors, especially frequencies that lead to increased fertility. For instance, a study (18) on assisted reproduction techniques revealed the problems associated with immature sperm cells, where the cells are unable to swim naturally to facilitate fertilization. Table 2 presents a summary of the findings for each of the studies on the role of sperm maturity on fertility and embryo development.

Table 2: A Summary of individual Studies on Sperm Maturation

Study	*Authors*	*Year*	*Summary*
18	Machtinger et al.	2015	Post-testicular sperm maturation processes such as sperm motility acquisition and the reduction of the oxidative stress are critical in facilitating the movement and fertilization
19	Arenas-Ríos et al.	2005	Spermatozoa maturity increases fertility by facilitating the process of fertilization
20	Asmarinah et al.	2016	Low sperm chromatin maturity at the level of <87% correlated significantly with the cleavage rate of the zygote.
21	Sellami et al.	2013	There is a strong correlation between sperm immaturity and acrosome abnormalities
22	Moore et al.	2010	Sperm maturation in the epididymis gives the spermatozoa the motility ability required in fertilization
23	Gil-Guzman et al.	2001	The immaturity of spermatozoa leads to infertility
24	Durairajanayagam et al.	2015	Sperm maturity is a critical step in the fertilization process
25	Cayli et al.	2003	Male fertility is strongly related to the quality of spermatozoa.
26	Hallak et al.	2001	Sperm maturity is linked to embryonic quality and development.
27	García-Ferreyra	2015	The maturity of sperm determines sperm DNA fragmentation, which determines the fertility
28	Zini et al.	2005	The sperm DNA damage due to immaturity affects the quality of the embryo

4. DISCUSSION

Summary of Evidence

Sperm Chromatin in Fertility and Embryo Development

Most of the studies (5-17) revealed that current semen screening methods such as sperm concentration, motility, and morphology do not identify any defects in sperm chromatin structure. Specifically, the study by Shamsi et al. (8) revealed that the conventional parameters of semen analysis are insufficient for the evaluation of the reproductive potential. This limitation provides a clear picture of the role of sperm chromatin in embryo development. One common agreement in

most of the studies (2, 5-6, 9-15) was that sperm chromatin plays a major role in the transmission of genetic information. Therefore, the sperm chromatin influences embryo development depending on the paternal genetic information transferred.

Sperm Maturity in Fertility and Embryo Development

The second question is how the maturity of the spermatozoa influences the development of the embryo. The studies (17-28) revealed that poor quality and immature sperms are linked to the delayed pronuclear formation and sluggish embryonic development. This is informed by the revelation that the sperm is involved in embryonic quality and development. Some of the studies (20-21) also showed that poor maturity and integrity of the sperm chromatin adversely affect the development of the zygote.

Limitations

Several limitations associated with the systematic review study approach were evident. Firstly, the study focused on a shallow assessment and interpretation of the findings from each individual study rather than a detailed analysis of the study effects. Secondly, other factors and the study environment were ignored. For instance, the health condition of the subjects involved in each of the studies was not part of the assessment. Therefore, the conclusion below is limited to just the comparison of the findings regarding the relationship between the independent and dependent variables. Thirdly, the parameters used by the various researchers were not different. Therefore, it was impossible to use meta-analysis that could give a platform for statistical analysis of the data.

5. CONCLUSIONS

The systematic review provided crucial insights regarding the role of sperm chromatin and sperm maturity to fertility and embryo development. From the findings, sperm DNA integrity is critical in assessing the accurate transmission of genetic information. This revelation is critical today due to the nature of screening methods used in determining fertility and embryo development. For example, a comparison of the studies showed that semen screening methods such as sperm concentration, motility, and morphology do not identify any defects in sperm chromatin structure. Therefore, these approaches are lacking since they do not assess sperm chromatin. As indicated above, sperm chromatin plays a major role in the transmission of genetic information. Therefore, the sperm chromatin will always play a significant role in the development of the embryo. Therefore, the researchers recommended, that it is critical to apply diagnostic tools that examine the chromatin structure in spermatozoa. With such techniques, it will be possible to identify defects that might not only cause infertility but also affect the development of the embryo after fertilization.

Evidently, the evaluation of sperm head maturity, as part of routine semen analysis, is critical in assessing fertility in men. Sperm selection is critical in reducing immature sperm. From some of the studies (24-28), sperm abnormality is caused by the disruption of spermatogenesis. Therefore, creating an enabling environment for the maturation of spermatozoa can significantly increase fertility. On the same note, the maturation of sperm chromatin is critical for ensuring normal growth and embryo since the maternal genetic information transferred to the embryo becomes part of the embryo.

REFERENCES

[1] Tandara M, Bajic A, Tandara L, Sunj M, Jurisic Z, Jukic M. Correlation between proportions of sperm with DNA fragmentation assessed by Halosperm test and values of standard quality parameters of semen and possible impact on embryo quality. Zdravniski Vestnik. 2013 May 1;82(5).

[2] Agarwal A, Said TM. Role of sperm chromatin abnormalities and DNA damage in male infertility. Human Reproduction Update. 2003 Jul 1; 9(4):331-45.

[3] Sadeghi MR, Hodjat M, Lakpour N, Arefi S, Amirjannati N, Modarresi T, Jadda HH, Akhondi MM. Effects of sperm chromatin integrity on fertilization rate and embryo quality following intracytoplasmic sperm injection. Avicenna Journal of Medical Biotechnology. 2009 Oct;1(3):173.

[4] Agarwal A. Impact of sperm chromatin damage on natural fertility and ART success: evidence-based medicine. BMC Genomics. 2014 Apr 1;15(S2): O24.

[5] Erenpreiss J, Spano M, Erenpreisa J, Bungum M, Giwercman A. Sperm chromatin structure and male fertility: biological and clinical aspects. Asian Journal of Andrology. 2006 Jan 1;8(1):11-29.

[6] Cebesoy FB, Aydos K, Unlu C. Effect of sperm chromatin damage on fertilization ratio and embryo quality post-ICSI. Archives of Andrology. 2006 Jan 1;52(5):397-402.

[7] Singh A, Agarwal A. The role of sperm chromatin integrity and DNA damage on male infertility. Open Reprod Sci J. 2011; 3:65-71.

[8] Shamsi MB, Kumar R, Dada R. Evaluation of nuclear DNA damage in human spermatozoa in men opting for assisted reproduction. Indian Journal of Medical Research. 2008 Feb 1;127(2):115.

[9] Hammoud SS, Nix DA, Zhang H, Purwar J, Carrell DT, Cairns BR. Distinctive chromatin in human sperm packages genes for embryo development. Nature. 2009 Jul 23;460(7254):473-8.

[10] Khajavi NA, Razavi S, Mardani M, Tavalaee M, Deemeh MR, Nasr-Esfahani MH. Can the Zeta sperm selection method, recover sperm with higher DNA integrity compared to density gradient centrifugation? International Journal of Reproductive BioMedicine. 2009;7(2):73-7.

[11] Revay T, Nagy S, Kopp C, Flyckt A, Rens W, Rath D, Hidas A, Kovacs A, Johannisson A, Rodriguez-Martinez H, Andersson M. Macrocephaly in bull spermatozoa is associated with nuclear vacuoles, diploidy, and alteration of chromatin condensation. Cytogenetic and genome research. 2009; 126(1-2):202-9.

[12] Cocuzza M, Sikka SC, Athayde KS, Agarwal A. Clinical relevance of oxidative stress and sperm chromatin damage in male infertility: an evidence-based analysis. International Brazilian Journal of Urology. 2007 Oct; 33(5):603-21.

[13] Agarwal A. Significance of oxidative stress and sperm chromatin damage in male infertility. Male fertility and lipid metabolism. 2003 May 30; 13:157-83.

[14] Ozkosem B, Feinstein SI, Fisher AB, O'Flaherty C. Advancing age increases sperm chromatin damage and impairs fertility in peroxiredoxin 6 null mice. Redox biology. 2015 Aug 31; 5:15-23.

[15] Zini A, Albert O, Robaire B. Assessing sperm chromatin and DNA damage: clinical importance and development of standards. Andrology. 2014 May 1;2(3):322-5.

[16] D'Occhio MJ, Hengstberger KJ, Johnston SD. Biology of sperm chromatin structure and relationship to male fertility and embryonic survival. Animal Reproduction Science. 2007 Sep 30; 101(1):1-7.

[17] Simon L, Murphy K, Shamsi MB, Liu L, Emery B, Aston KI, Hotaling J, Carrell DT. Paternal influence of sperm DNA integrity on early embryonic development. Human Reproduction. 2014 Sep 8; 29(11):2402-12.

[18] Machtinger R, Laurent LC, Baccarelli AA. Extracellular vesicles: roles in gamete maturation, fertilization, and embryo implantation. Human Reproduction Update. 2015 Dec 9; 22(2):182-93.

[19] Arenas-Ríos E, León-Galván MA, Mercado PE, Rosado A. Superoxide dismutase, catalase, and glutathione peroxidase during epididymal maturation and prolonged storage of spermatozoa in the Mexican big-eared bat (Corynorhinus mexicanus). Canadian Journal of Zoology. 2005 Dec 1;83(12):1556-65.

[20] Asmarinah, Syauqy A, Umar LA, Lestari SW, Mansyur E, Hestiantoro A, Paradowszka-Dogan A. Sperm chromatin maturity and integrity correlated to zygote development in ICSI program. Systems Biology in Reproductive Medicine. 2016 Sep 2; 62(5):309-16.

[21] Sellami A, Chakroun N, Ben Zarrouk S, Sellami H, Kebaili S, Rebai T, Keskes L. Assessment of chromatin maturity in human spermatozoa: useful aniline blue assay for routine diagnosis of male infertility. Advances in Urology. 2013 Oct 3;2013.

[22] Moore K, Lovercamp K, Feng D, Antelman J, Sutovsky M, Manandhar G, van Leyen K, Safranski T, Sutovsky P. Altered epididymal sperm maturation and cytoplasmic droplet migration in subfertile male Alox15 mice. Cell and Tissue Research. 2010 Jun 1; 340(3):569-81.

[23] Gil-Guzman E, Ollero M, Lopez MC, Sharma RK, Alvarez JG, Thomas Jr AJ, Agarwal A. Differential production of reactive oxygen species by subsets of human spermatozoa at different stages of maturation. Human Reproduction. 2001 Sep 1; 16(9):1922-30.

[24] Durairajanayagam D, Rengan AK, Sharma RK, Agarwal A. Sperm Biology from Production to Ejaculation. In Unexplained Infertility 2015 (pp. 29-42). Springer New York.

[25] Cayli S, Jakab A, Ovari L, Delpiano E, Celik-Ozenci C, Sakkas D, Ward D, Huszar G. Biochemical markers of sperm function: male fertility and sperm selection for ICSI. Reproductive Biomedicine Online. 2003 Jan 1; 7(4):462-8.

[26] Hallak J, Sharma RK, Pasqualotto FF, Ranganathan P, Thomas AJ, Agarwal A. Creatine kinase as an indicator of sperm quality and maturity in men with oligospermia. Urology. 2001 Sep 30; 58(3):446-51.

[27] García-Ferreyra J. Sperm DNA fragmentation and its relationship with fertility. In New Discoveries in Embryology 2015. InTech.

[28] Zini A, Meriano J, Kader K, Jarvi K, Laskin CA, Cadesky K. Potential adverse effect of sperm DNA damage on embryo quality after ICSI. Human Reproduction. 2005 Aug 25; 20(12):3476-80.