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The Impact of Advanced Paternal Age on Sperm DNA Fragmentation: Implications for Fertility

Eva Kadoch BSc[1], Artak Tadevosyan PhD[1,2], Simon Phillips PhD[1], François Bissonnette MD[1,3], Armand Zini MD[1,4], Isaac-Jacques Kadoch MD[1,3]

[1]Clinique ovo, Montreal, QC, Canada. [2]Department of Pharmacology and Physiology, Faculty of Medicine, University of Montreal, Montreal, QC, Canada. [3]Department of Obstetrics and Gynecology, University of Montreal, Montreal, QC, Canada. [4]Division of Urology, Department of Surgery, McGill University, Montreal, QC, Canada.

INTRODUCTION

- Postponing fatherhood has become more prevalent in recent years, leading to an increase in average paternal age.[1]
- High sperm DNA fragmentation levels are associated with adverse reproductive outcomes.[2]
- Factors that can harm sperm DNA include environmental toxins, lifestyle choices, genetic mutations, and oxidative stress.[3,4]
- Advanced paternal age may lead to DNA damage in sperm, but the age at which this risk becomes significant is not clearly defined.

STUDY QUESTION

- What is the impact of advanced paternal age (APA) on sperm DNA fragmentation (SDF) levels ?

OBJECTIVES

- To evaluate the impact of APA on SDF levels.
- To define the cut-off age beyond which SDF levels rise significantly.
- To emphasize the importance of male age when evaluating male fertility.

METHODS

- **Study Design.** Retrospective cohort study of 4,612 consecutive semen samples from men undergoing fertility evaluation at the OVO clinic in Montreal between April 2016 and May 2023. Participants were stratified into seven age groups.

- **Methods.** Semen samples were collected after 2-3 days of abstinence. For patients who underwent more than one SDF testing, only the first sample was included, and any duplicates were excluded. SDF was evaluated by flow-cytometry based TUNEL assay.

- **Main Outcome Measures:** Comparing SDF levels across the age groups and assessing the prevalence of normal, intermediate, and high SDF.

- **Statistical Analysis.** One-way ANOVA was used followed by T3 Dunnett post-hoc multiple comparison test and Pearson's correlation coefficient.

RESULTS

Basic Patient Demographics:

- Mean overall age: 37.4 ± 6.4 years (range: 18-71 years).
- Mean overall SDF: 20.3 ± 13.5 % (range: 0.3-118.4 %).

Distribution of SDF:

- A positive correlation was observed between paternal age and SDF (r=0.183, p<0.001) (Figure 1).
- SDF remained relatively constant until the age of 35 but increased significantly beyond age 35 (p<0.001) (Figure 1).

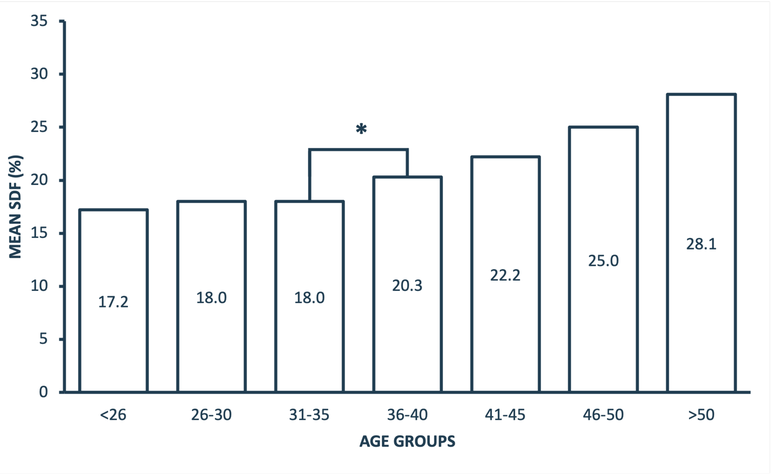

Figure 1. Impact of paternal age on sperm DNA fragmentation.

SDF Prevalence:

- The prevalence of normal SDF (<17%) was highest among the younger age groups (Figure 2).
- The prevalence of high SDF (>30%) was highest among the older age groups (Figure 2).
- The prevalence of intermediate SDF remained relatively constant throughout the age groups (ranging between 29.0% to 36.0%) (Figure 2).

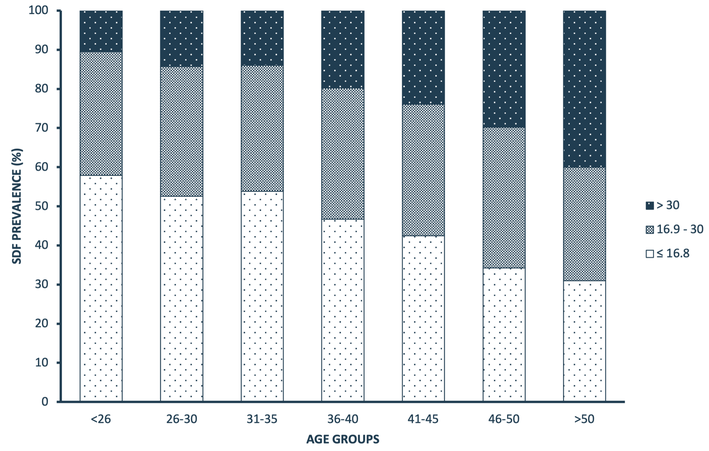

Figure 2. Prevalence of SDF levels across age groups.

CONCLUSION

- The increase in SDF after the age of 35 highlights the importance of considering male age in infertility evaluations, similar to the concept of the "biological clock" in women.
- Assessing sperm DNA fragmentation in men over the age of 35 is crucial in couples seeking to conceive.
- Educating society about the advantages of early parenthood and raising awareness about the impact of aging on fertility can help address the issue.

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