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RESEARCH ARTICLE

SPERMATIC DNA FRAGMENTATION INDEX OF INFERTILE MEN: INTEREST IN THE CHOICE OF PMA TECHNIQUE PRELIMINARY STUDY

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Abstract

Introduction: Infertility constitutes a real public health problem. In men, the examinations involved in the choice of the PMA technique are sometimes insufficient in relation to the real procreation potential of the spermatozoa which could be detected by the sperm DNA fragmentation test. This preliminary study aimed to highlight the benefit of taking into account the sperm DNA fragmentation test in the choice of the proposed PMA technique.

Material and Methods: This was a preliminary descriptive cross-sectional study carried out in a private spermiology laboratory in Abidjan. It included 52 patients who came for consultation for infertility and who gave their written consent to participate in the study. Spermogram, spermocytogram, migration survival (TMS) test and DNA fragmentation index were studied. The DNA fragmentation index (DFI) was determined by the Sperm Chromatin Dispersion (SCD) technique.

Results: The majority of patients were aged between 35 and 45 years (47%) with an average age of 45 years (+/-8). The most common spermogram abnormalities were mobility abnormalities. 52% of patients had a high fragmentation index. A high fragmentation index was found in a patient with normal sperm standard parameters. Likewise, 8 patients for whom intrauterine insemination had been recommended according to the TMS result had a fragmentation index greater than 30%.

Conclusion: The first-line request for the fragmentation index in the exploration of male infertility must be studied since it could take into account the integrity of the genetic material, a limiting factor in the current tests used for the choice of the PMA technique.

Introduction:-

Infertility is a real public health problem. According to the World Health Organization (OMS, 2023), one person in six worldwide is affected by infertility, defined as the absence of pregnancy after more than 12 months of regular sexual intercourse without contraception. Globally, the cause of a couple's infertility is female in around 30% of cases, male in around 20% and of mixed origin in around 40%. It remains unexplained in just under 10% of

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cases(CNGOF, 2006). Various methods have been explored to provide solutions to this problem. In this context, Medically Assisted Reproduction (PMA) today gives satisfactory results and positions itself as the real beacon of hope. Unfortunately, although effective, ART methods often give rise to failures, linked to the complexity of the internal dialogue between the embryo and the uterine cavity (Ollivier, 2021). In men, spermograms, spermocytograms and the Survival Migration Test (TMS) are still the examinations involved in the choice of PMA technique, but are sometimes insufficient to assess the actual procreative potential of spermatozoa, particularly in the face of fertilization failure or lack of progressive pregnancy(Eecke, 2019; Muriel et al., 2006; Zhao et al., 2014).

For several years, teams have been focusing on sperm DNA quality as a diagnostic marker of infertility(Agarwal et al., 2017; Farkouh et al., 2023; Nielsen et al., 2023). A correlation between evolutionary pregnancy failure and increased sperm DNA fragmentation index has been described(Haddock et al., 2021; Henkel et al., 2022; Jin et al., 2015; Simon et al., 2014). Indeed, these studies have highlighted the deleterious effects of sperm DNA alteration on fertilization rates and early embryonic development(Esteves et al., 2021; Setti et al., 2011; Simon et al., 2010). Similarly, a significant increase in DNA damage can be found in spermatozoa from men with normal standard sperm parameters(Check et al., 2005; Evenson, 1999).

Thus, some authors advocate the search for the sperm DNA fragmentation index as an independent predictor of fertility in couples undergoing MPA (Check et al., 2005; Evenson, 1999).

Furthermore, for some authors, when faced with a high fragmentation index, intracytoplasmic insemination (ICSI) should be the recommended technique in order to obtain a better result (Esteves et al., 2021; Vončina et al., 2021).

In view of the high cost of medical assistance for procreation(Njagi et al., 2023), the management of infertile couples must be based on total and perfect mastery of the exploratory tests in order to make the right choice of PMA technique.

With a view to improving the management of infertile couples, the aim of this preliminary study was to highlight the value of taking sperm DNA fragmentation testing into account when choosing the proposed PMA technique.

Material and Methods:-

This was a preliminary descriptive cross-sectional study conducted in a private spermiology laboratory in Abidjan. It included 52 patients who came for an infertility check-up and gave their written consent to participate in the study. Each subject was subjected to a questionnaire based on a survey form. Sperm was collected in the laboratory by masturbation in a sterile wide-mouth bottle from subjects who had observed an abstinence of 3 to 5 days. The spermogram, spermocytogram, survival migration test and DNA fragmentation index measurement were performed on the same day as collection.

The spermogram was interpreted according to WHO (2010) criteria. The Krüger classification was used to interpret the spermocytogram.

The survival migration test was performed by upward migration (density gradient centrifugation) and interpreted according to capacitation (= number of selected spermatozoa) according to the following standards:
- Capacitation ≥ 1,000,000 sperm for intrauterine insemination (IUI)
- Capacitation between 500,000 and 1,000,000 spermatozoa for conventional in vitro fertilization (FIV).
- Capacitation < 500,000 spermatozoa: intracytoplasmic insemination (ICSI)

The DNA fragmentation index was determined using the Sperm Chromatin Dispersion (SCD) technique (Fernández et al., 2003).

This is the determination of sperm chromatin quality by DNA disruption with an alkylating agent and vital staining. As a general rule, an index > 20% could explain repeated failure in PMA , while a fragmentation rate > 30% is considered high and indicative of extremely altered chromatin.

Results:-

The majority of patients were between 35 and 45 years of age (47%), with an average age of 45 (+/-8). The minimum age was 31 and the maximum 60. The most common medical histories were urogenital infections, hydrocele and diabetes, respectively. 33% of patients consumed alcohol and 20% tobacco (Table 1).

Spermogram abnormalities were found in 73.1% of patients, the most common being motility abnormalities (Figure 1). According to the TMS result, intrauterine insemination (IUI) was recommended as the PMA technique in 56% (Figure 2). 52% had a high fragmentation index (Figure 3). The highest indices were found in patients with oligoasthenoteratozoospermia (OAT) (Figure 4).

On the other hand, among patients with no spermogram abnormalities (normal spermogram + spermocytogram), we found one with a high fragmentation index (Table 2).

In addition, we found 8 patients for whom intrauterine insemination had been recommended on the basis of the TMS result, but who had a fragmentation index greater than 30% (Table 3).

Figure 1:-Distribution of patients according to sperm abnormalities(Asthenozoospermia, oligozoospermia, asthenoteratozoospermia, oligoteratozoospermia, teratozoospermia, oligoasthenozoospermia, oligoastenoteratozoospermia).

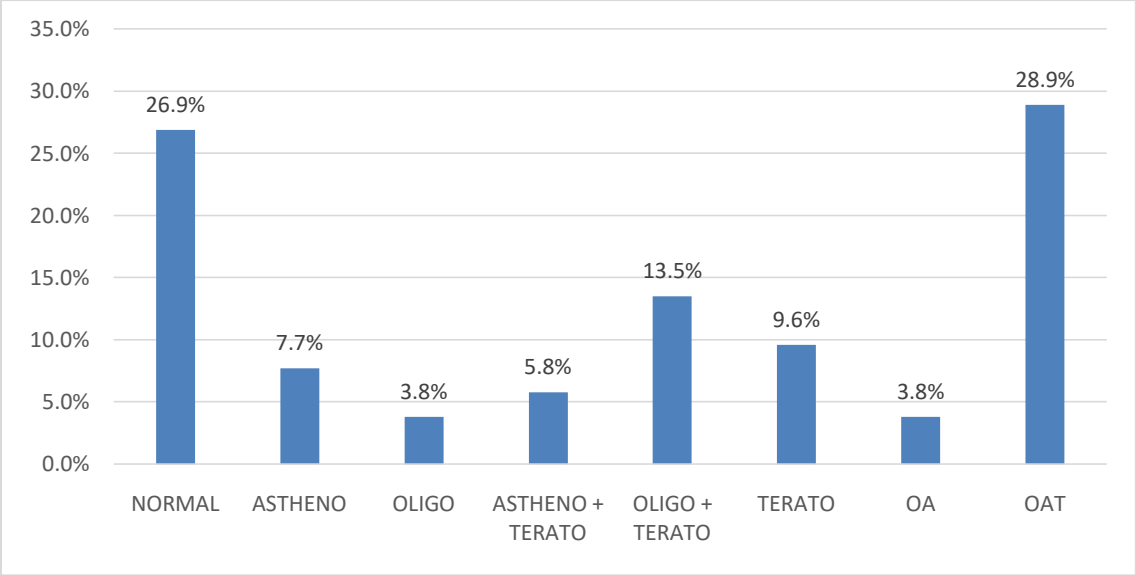

Table 1:- General characteristics of the study population.

	Mean +/- Standard deviation	Minimum	maximum
Age (year)	45 +/- 8	31	60
Mean duration of infertility (year)	6 +/- 4	1	25
		Number	Percentage
Age range	< 35 years	7	13%
	[35 – 45[years	24	47%
	≥ 45 years	21	40%
Medicalhistory	Urogenital infection	17	33%
	Diabetes	17	33%
	Hydrocele	10	20%

Lifestyle	Alcohol	17	33%
	Tobacco	10	20%

Figure 2:- Patient distribution by TMS result.

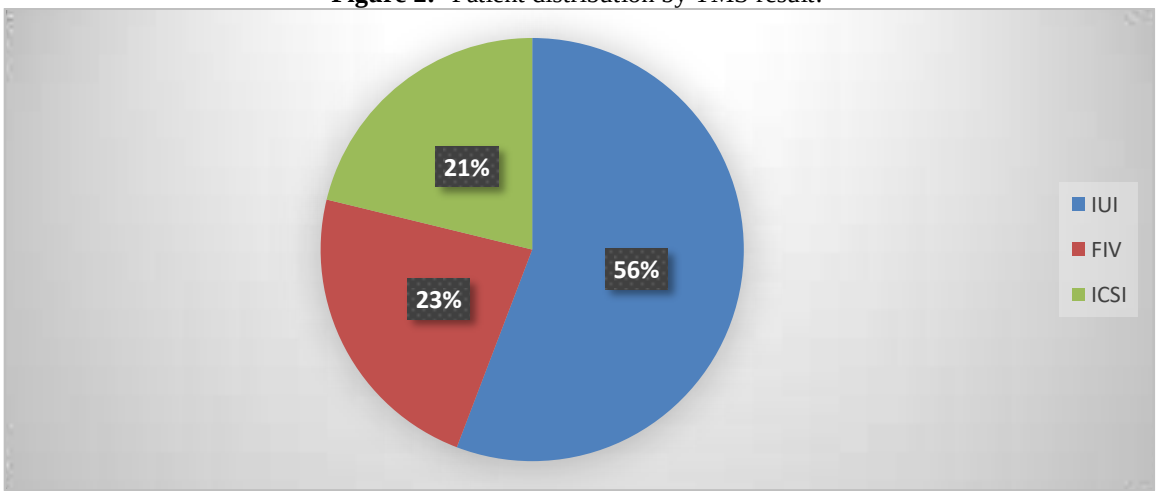

Figure 3:- Proportion of fragmentedsperm.

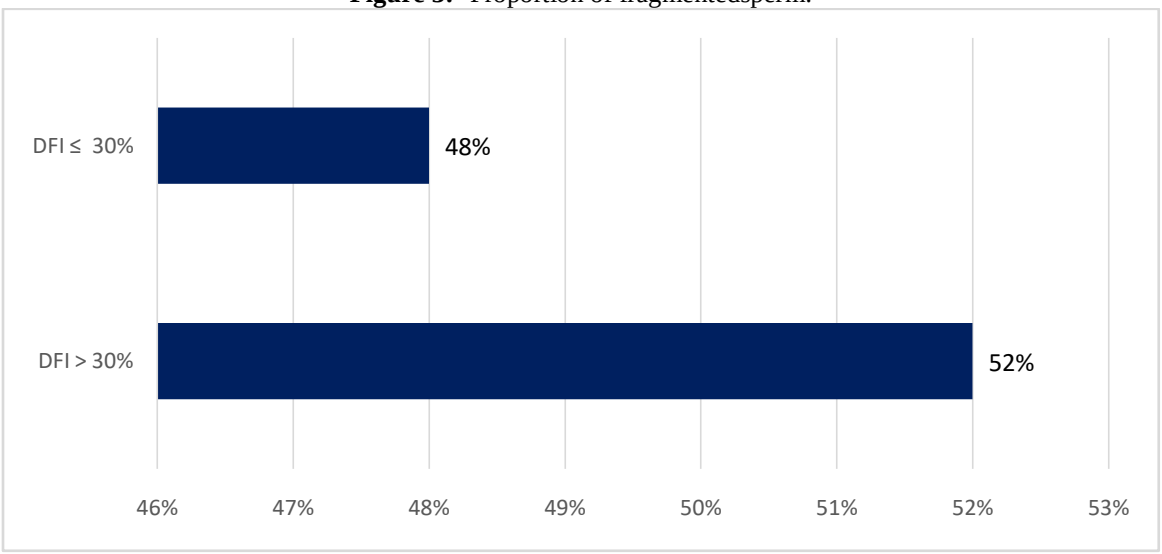

Table 2:- Fragmentation index in patients with normal standard sperm parameters.

Variables		**Normal spermogram**	**Abnormal spermogram**	**Normal spermogram Spermocytogram**
DFI (%)	**=<20 (n)**	8	8	5
	20-30 (n)	3	7	3
	>30 (n)	2	24	**1**

Figure 4:- DNA fragmentation index as a function of sperm abnormalities.

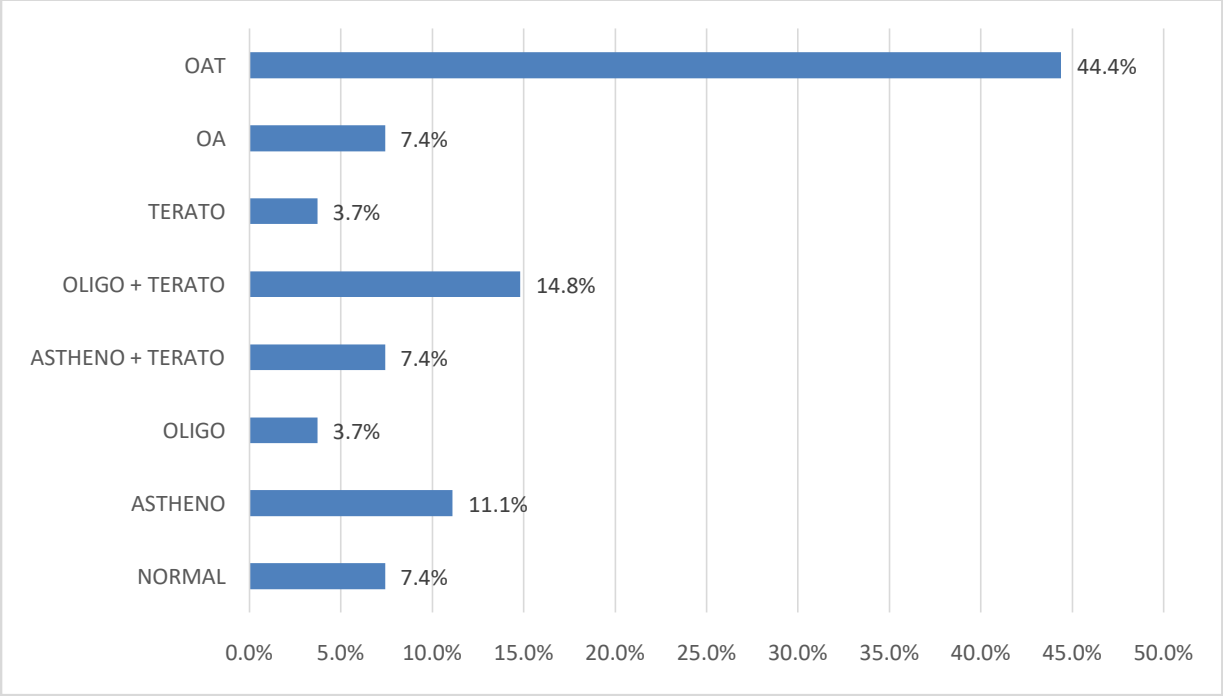

Table 3:- Fragmentation index as a function of TMS result.

	DFI ≤ 30%	**DFI > 30%**
IUI (n= 30)	22	8
FIV (n = 10)	3	7
ICSI (n = 12)	1	11

Discussion:-

This preliminary study was carried out on patients consulting for infertility in the Reproductive Biology laboratory of a private clinic in Abidjan. A total of 52 patients were included in the study. Epidemiological and clinical parameters were studied, as well as biological parameters (spermogram, spermocytogram, survival migration test and fragmentation index).

The majority of men in the study were between 35 and 45 years of age, with an average age of 45 (+/-8). This high age of infertile men has also been noted in other studies in Africa (Sakande et al., 2012; Traore et al., 2008). This could be explained by the fact that, in Africa, this age bracket corresponds to the period when men place much greater emphasis on reproduction in their conjugal lives. The most common sperm abnormalities were motility abnormalities, as described in other studies(Sakande et al., 2012; Traore et al., 2008; Yao-Yapo, 2018).

52% of patients had a high fragmentation index. Although fragmentation rates were predominantly high in pathological spermograms, we found a fragmentation index above 30% in one patient with no spermogram abnormalities (normal spermogram + spermocytogram). Indeed, one of the drawbacks of the spermogram and spermocytogram, the main tests used to diagnose male infertility, is its limitation in taking into account the integrity of the genetic material. Thus, a high fragmentation index can be found in patients with normal standard sperm parameters(Aitken et al., 2012; Check et al., 2005; Evenson, 1999).

The key test for choosing the right MPA technique for the patient remains the Migration Survival Test (TMS). In our study, based on the results of the TMS, intrauterine insemination was recommended in 56% of patients. As a reminder, this choice is based on capacitation, which corresponds to the number of progressively mobile spermatozoa after selection. Thus, for a capacitation greater than or equal to 1,000,000 spermatozoa, intrauterine insemination (IUI) is recommended. However, according to some authors, the recommended test for a high DNA

fragmentation index is intracytoplasmic insemination (ICSI) (Esteves et al., 2021; Vončina et al., 2021)in order to reduce the impact of fragmentation on fertilization, blastocyst formation, implantation, clinical pregnancy and IVF live birth rate (Henkel et al., 2022). However, in our study, we found 8 patients for whom intrauterine insemination had been recommended on the basis of the TMS result, but who had a fragmentation index greater than 30%. This suggests that the TMS may be inadequate for the choice of PMA technique. It might be appropriate to include the sperm DNA fragmentation index in the choice of PMA technique. Indeed, given the inaccessibility of the costs of medically assisted reproduction, which forces many couples to use almost all their savings, it is vital to take all aspects into account in order to make the right choice of PMA technique and thus reduce pregnancy failures, which are often difficult for infertile couples to accept.

Conclusion:-

This preliminary study of 52 patients who came to the Reproductive Biology Laboratory in a private clinic in Abidjan for infertility consultations showed that the sperm DNA fragmentation index is an important parameter in the management of infertile men. It is directly correlated with the chance of pregnancy. However, should this parameter be part of the 1st-line assessment in the management of infertile couples, or should it remain a 2nd-line examination, given the limitations of current tests used to select the PMA technique, and the moral and financial damage caused by a failed PMA attempt in infertile couples? On the other hand, a more in-depth study involving a larger number of patients and a comparison with the results of beta HCG tests and eventual pregnancies could help us to make better decisions.

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