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Pregnancy Rate In Non-Azoospermia With Normal Or Suboptimal Semen Parameter Versus Azoospermic Male Treated By IVF-ICSI Cycle

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Abstract

Background: Intracytoplasmic sperm injection (ICSI) opens the gate for many cases of male factor infertility to be the biological fathers of their sibling since 1992. Most of cases were non-obstructive azoospermia and different levels of oligoastheno-teratozoospermia. Nowadays many cases of reduced semen parameter or female factor infertility are treated by IVF-ICSI Cycle for better pregnancy rate, biochemical and clinical, and live birth rate.

Aim of the study: The study aims to compare biochemical, clinical pregnancy rate and outcome of pregnancies in the group with ejaculated sperm with normal or suboptimal semen parameter and group with non-obstructive azoospermia in whom sperm retrieved by TESE, using ICSI.

Method: A retrospective cohort study was conducted between January, 2016 and February, 2023 in the fertility center of Al-Sader Medical City, a total of 372 couple, 90 of the males gave semen sample by masturbation and 282 of the males were non-obstructive azoospermia and their sperms were retrieved by TESE; all are treated by ICSI, all of their female partner were under age of 37 year, the maternal medical condition and obstetric history were not included in this study. Simple random sampling was depended, SPSS version 26 was used to perform the statistical analysis processes.

Results: There was a highly significant difference in pregnancy rate by β.HCG between ejaculate group (43.3 %) and azoospermia (26.6 %) with p. value =0.003. A significant difference in clinical pregnancy rate by ultrasound between the ejaculate group (31.1%) and azoospermia (20.9%) with p. value =0.047. There was no statistically significant difference in live birth rate between ejaculate group as (24.4 %) and azoospermia as (17.4 %) with p.value=0.137.

Conclusion: Freshly ejaculated sperm with normal or suboptimal semen parameter gave a better biochemical and clinical pregnancy rate than obtained from NOA by TESE, while live birth rate was not largely different in both groups

Keywords: ICSI, TESE, Ejaculate, Non-obstructive azoospermia

INTRODUCTION

Most literature supports the fact that male factor infertility can be responsible for about half of cases of infertility among couples and can even reaches 70% of all cases of infertility [(1)]. It is estimated that 1 out of 100 healthy men is azoospermic, the sole treatment till now is the testicular sperm retrieval and ICSI [(2)]. According to the way that testis produce sperm, azoospermic men are divided into obstructive azoospermia (OA) and non-obstructive azoospermia (NOA); the second type is more common and can be responsible for more than 60% of cases[(3)]. Testicular sperm extraction (TESE) and ICSI nowadays regards as the gold standard for most of non-obstructive azoospermia management; and enable them to have their biological children, despite retrieval rate nearly half of cases[(4)]. The new technique for sperm retrieval which is microscopic TESE (m.TESE) is regarded as the most effective technique for high sperm retrieval rate and minimal postoperative complication[(5)]. However, clinical pregnancy by using testicular sperm recorded by many research paper, some researchers like (Bernardini *et al.*,) [(6)] and (Rodrigo *et al.*,) [(7)] found an increment in chromosomal aberration in sperm retrieved from NOA patients. So, concerns about the risk of congenital anomaly in children born after ICSI with testicular spermatozoa are pertinent. Up to date, the neonatal health of children born after ICSI using testicular spermatozoa from patients with NOA is not well documented. Sperm donation for many years was the only hope for azoospermic men to have children, but ethical, legal, religious and psychological issues had limited the use of sperm donation in many countries, nowadays it becomes more acceptable for couples specially in the western countries[(8)]. Some men with varying degrees of oligozoospermia, asthenozoospermia, and teratozoospermia, who cannot conceive naturally are best treated by ICSI, which, since its invention at 1992, makes revolutionized management in male factor infertility; it involves insertion of single morphologically normal live spermatozoon into oocyte by fine glass micropipette and the resulting embryos are transferred to the uterine cavity or cryopreserved [(9)] [(10)].

MATERIAL AND METHOD

The Study Design

This study is a retrospective cohort type which was held in the fertility center of Al-Sader Medical City between January, 2016 and February, 2023. It included a total number of three hundred seventy-two (372) couples with random sampling method; all reside at middle Euphrates region in Iraq. 90 male partners were non-azoospermia with normal or mild suboptimal semen parameter, isolated oligozoospermia, isolated asthenozoospermia or isolated terarozoospermia, who gave the semen sample by masturbation and 282 were azoospermia (non-obstructive type) whom diagnosed by urologist according to history, clinical examination, testicular size by ultrasound and hormonal levels (FSH, LH, testosterone and prolactin) in which the sperm retrieved from testis by TESE. A simple random sampling was depended in which each couple came to the center were assigned a unique number and “computer-generated lists used for random selection”. All the couples were residing at middle Euphrates region in Iraq. The range of age of all male partner was (21-58) year and the median of age of all male partner was 34 year irrespective to groups. The range of age of female partner was (16-38) year and the median age was 29 year. All the data were collected from patient's files and records. The maternal medical condition, obstetric history and type of stimulation protocol were not included in this study. All the results of biochemical pregnancy (by β.HCG), clinical pregnancy (by ultrasound) and live birth were taken. Biochemical pregnancy test (β-hCG) was performed 10-14 days after embryo

transfer. Clinical pregnancy was regarded by visualization of one or more gestational sacs by U\S during 4th to 5th week, the ectopic pregnancy also included, live birth was regarded as clinically viable newborn according to Zegers-Hochschild *et al.'s* [11] definitions.

Ethical approval

This study obtained the ethical approval from the internal ethical committee of the Urology Department/Faculty of Medicine, University of Kufa and the health directorate in Najaf Province.

Statistical Analysis

A statistical analysis was carried out by using SPSS version 26 (Inc. Chicago, IL, USA). Categorical variables were presented as frequencies and percentages. Chi square, Mann–Whitney and Pearson correlation were applied. A P-value < 0.05 is considered as significant and P-value< 0.01 is considered as highly significant.

RESULTS

The total number of the 372 couples were divided according to male partner, either ejaculate or azoospermia. The ejaculate group were 90 (24.2%) of the cases and the azoospermia group were 282 (75.8%). Median ± IQR for the age of ejaculate group was 34±10 years, while Median ± IQR for the age in the azoospermia group was 34± 8 years. Median ± IQR for the age of female partner in both groups was 29±8 years. Median ± IQR for retrieved oocyte in ejaculate group was 8.5 ± 8 oocytes, while Median ± IQR for retrieved oocyte in azoospermia group was 10 ± 6 oocytes. Median ± IQR for injected oocyte in ejaculate group was 7 ± 7 oocytes, while Median ± IQR for injected oocyte in azoospermia group was 8 ± 5 oocytes as shown in Table.1 There was a highly significant difference in the pregnancy rate by β.HCG between ejaculate group (43.3 %) and azoospermia (26.6 %) with P-value=0.003. A significant difference in clinical pregnancy rate by ultrasound between the ejaculate group (31.1 %) and azoospermia (20.9 %) with P-value=0.047. There was no statistically significant difference in live birth rate between ejaculate group (24.4 %) and azoospermia (17.4 %) with P-value=0.137 as shown in tab.2.

Table NO.1: A Comparison of variable characteristics between the two study groups.

	Ejaculate	Azoospermia
Number (Percentage)	90 (24.2%)	282 (75.8%)
Age (years) Median ± IQR for male partner	34 ± 10	34 ± 8
Age (years) Median ± IQR for female partner	29 ± 8	29 ± 8
Median ± IQR for retrieved oocyte	8.5 ± 8	10 ± 6
Median ± IQR for injected oocyte	7 ± 7	8 ± 5

Table NO.2: Comparison between the studied groups regarding biochemical pregnancy, clinical pregnancy and live birth rate.

	Ejaculate	Azoospermia	P. value
Pregnancy rate by β.HCG	43.3 %	26.6 %	**0.003 Group 1>group 2
Pregnancy rate by ultrasound	31.1 %	20.9 %	*0.047 Group 1>group 2
Live birth rate	24.4 %	17.4 %	0.137

P value< 0.05: significant* P value< 0.01: highly significant**

More details about the positive and negative pregnancy by β-HCG, clinical pregnancy and live birth are summarized in figures 2,3 and 4 respectively.

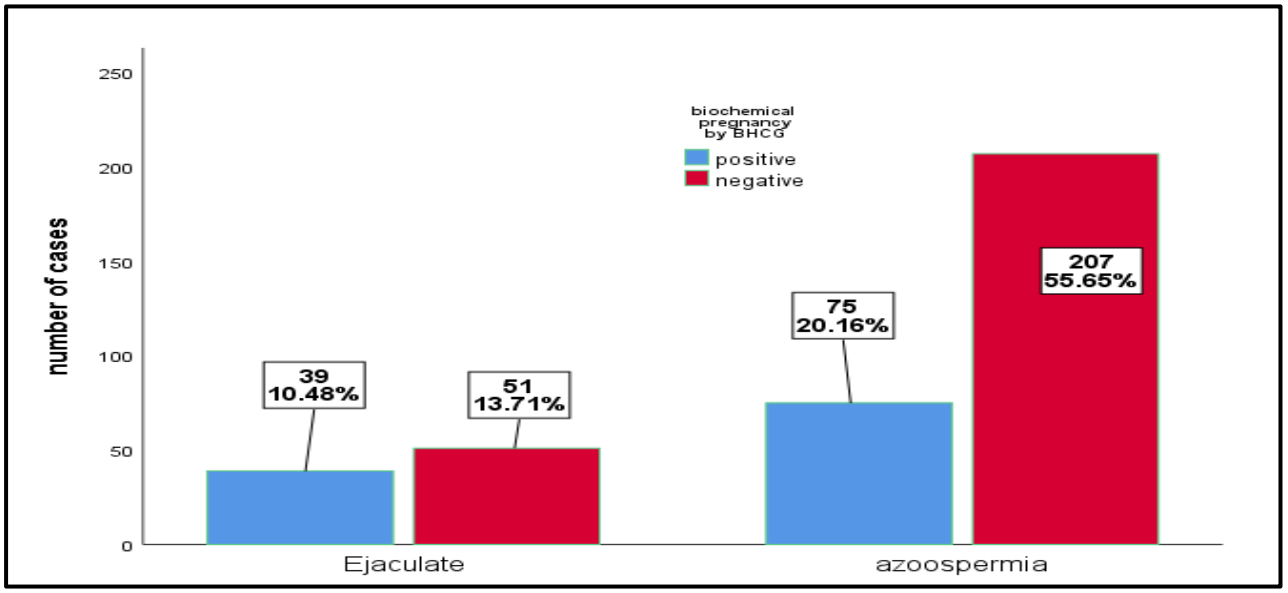

Figure NO.1: The distribution of cases according to β-HCG test result between the two studied groups.

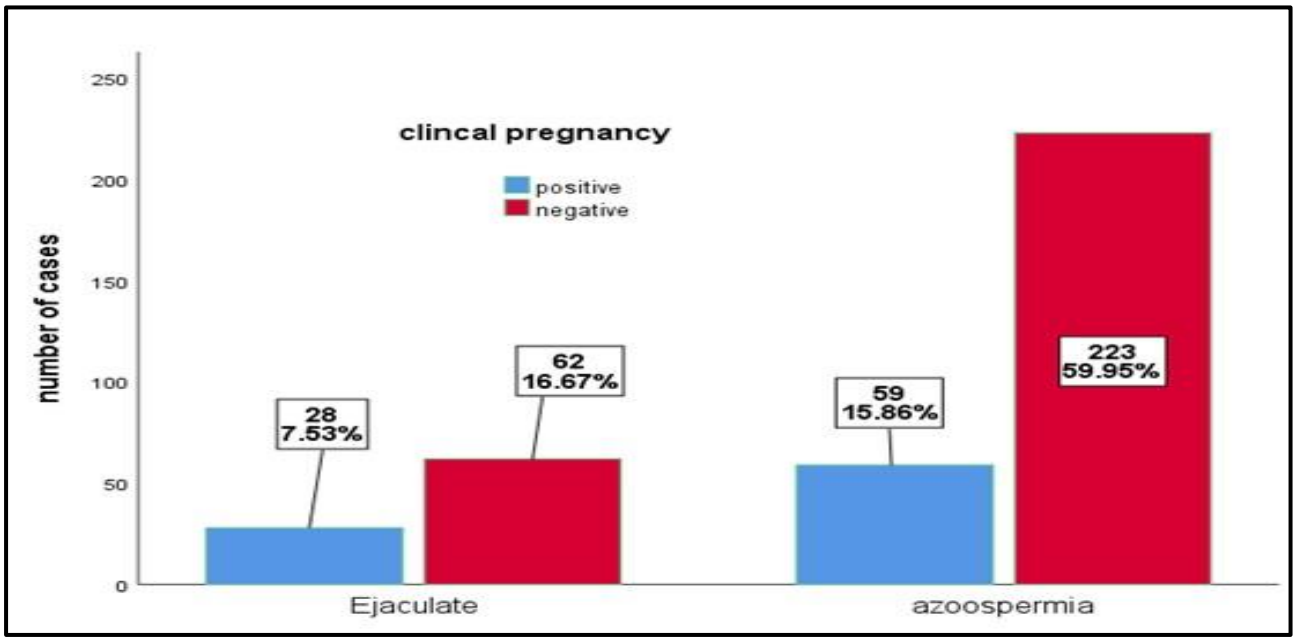

Figure NO.2: The distribution of cases according to clinical pregnancy result between the two studied groups.

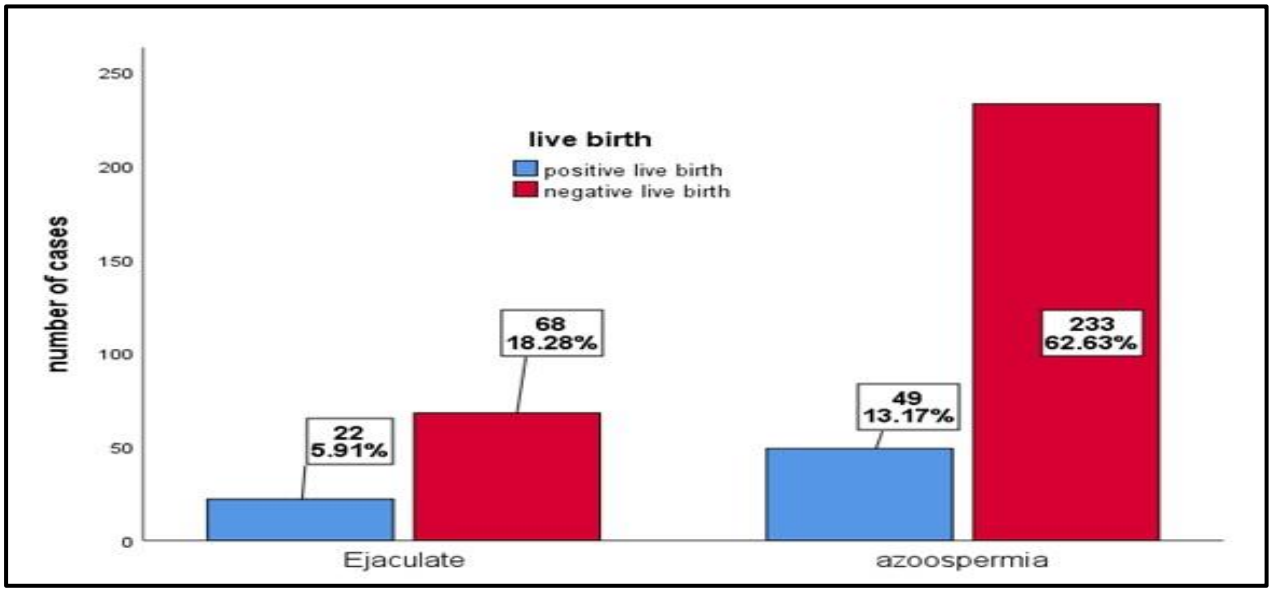

Figure NO.3: The distribution of cases according to live birth result between the two studied groups.

DISCUSSION:

Since the invention of ICSI, a dramatic improvement in cases of sever male factor infertility happened; nowadays, it became clear that ICSI could be used for male infertility with reduced semen parameter in which sperm had limited number or poor motility or poor morphology[12] [13]. The present study shows significantly a higher pregnancy rate, biochemical and clinical, in the ejaculate group rather than azoospermia group, while no significant difference regarding live birth rate between the two groups. This is supported by Göker et al.[14] who found similar results. Magli et al. [15] agreed with the study and found mosaicism and chromosomal aneuploidy in NOA patients that make embryos genetically abnormal and lead to decrement in clinical pregnancy when comparing them to normozoospermia. Bernardini *et al.* [6] reported that testicular germ cells had higher rates of sperm aneuploidy and diploidy than ejaculated sperm. It is important to note that neither sperm morphology nor chromatin condensation of testicular sperm from NOA patient can predict pregnancy outcome [16].

A study done by Yu et al., [17] in China used sperm from NOA patients by TESE and ejaculated sperm from donors and concluded that testicular sperm from NOA patients negatively affect clinical pregnancy while donor sperms were not, it also found no significant difference regarding live birth rate in both groups. In contrast, Ghazzawi et al.[18] found no significant difference regarding pregnancy rate and live birth rate between ejaculated sperm and testicular sperm of NOA patients. It is well known that in addition to surgical complications of TESE, the retrieval rate did not exceed 60% in best situation [19] [20].

CONCLUSION:

Freshly ejaculated sperms with normal or suboptimal semen parameter gave better biochemical and clinical pregnancy rate than obtained from NOA by TESE, while live birth rate was not largely different in both groups.

RECOMMENDATION: it is recommended that paternal genetic testing before ICSI cycle in NOA patients or use of pre-implantation genetic diagnosis (PGD) in the embryos.

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