ISSN No: -2456-2165

Life-Birth Rate After Classical Treatment of Severe Oligoteratoasthenozoospermia- an Open Clinical Study

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Abstract:- Severe oligoasthenoteratozoosperiam (OATS) is a kind of male factor that can cause male infertility where the sperm count, motility and normality should be very low. Traditional (non-assisted reproductive techniques or non-ART) treatment of OATS is still a matter of difficulties. The objective of this study was to evaluate the clinical outcomes of non-ART therapy for couples with severe OATS. One hundred twelve infertile men were diagnosed as OATS and all of them were included in this study. Their wives were reproductively fertile. Husband's FSH, LH, Testosterone were normal and prolactin level was mild elevated. Seminal fluid infection was noted in all cases. Couples were treated for 2 months (Doxycycline® 100mg tablet, Vita Zinc® Capsules, Speman®, Dostinex® (Cabergoline) 0.5 tablet, Human Chorionic Gonadotropin® 5000 IU / vial, Postmenopausal Gonadotropin injection®, Vials 150 IU/vial). During the course-treatment, 79/112 got a spontaneous pregnancy. A spontaneous pregnancy was confirmed by transabdominal pelvic ultrasonography where the gestational sac with viable fetus with a gestational age of 4-7 week was documented. The live-birth rate was succeeded in 42/79. In conclusion, male factor infertility due to sever OATS can get babies before we recommend them start the ARTs therapy.

Keywords:- *Oligoasthenoteratozoosperiam, Male Infertility, Spontaneous Pregnancy, Life-Birth Rate.*

I. INTRODUCTION

Infertility is a worldwide health problem and determines as a one of the most predominant health disorders among young adult couples (Allow Ahmed, Sadeeq Abdulmogni, 2016). According to our previous paper, male infertility factor is a responsible factor for 1/3 (29.90%) of cases (1281/2622) and the percentage of isolated oligoasthenoteratozoospermia (OATS) was around 7% out of 2622 infertile patients (Allow *et al.*, 2016). Jo and Ja Kang in 2016 reported that in 30–45% of cases, the cause of abnormal semen parameters is idiopathic; however, a standardized approach for the treatment of idiopathic male infertility remains elusive (Jo Junyoung, 2016). From another side, traditional (non-assisted reproductive techniques non-ART) treatment of OATS is still a matter of difficulties. Regarding the classical oral traditional therapy of male infertility due to OATS, a gap in the published review was noted in the last decade. Furthermore, the conventional ART therapy is still expensive and usually used as the last chance of infertility treatment. To date no studies have evaluated the clinical outcomes of non-ART therapy for couples with severe oligoasthenoteratozoospermia.

II. PATIENTS AND METHODS

One hundred and twelve infertile couples were involved in this descriptive study during their attendance to In-Vitro Fertilization Center on duration from January 2016 until February 2018. For husbands, no history of testicular injury, varicocele, torsion or hydrocele, previous operation in the genital organs and cancer chemotherapy were documented. Physical examination revealed normal for all couples, bilaterally vas deferens was palpable, and no abnormal gross anatomy was noted. Sex-hormonal profile and prolactin was evaluated. Their wives were performed complete reproductive evaluation and found their condition was normal. Oral and written ethical approval was taken from the couple prior to publication of this anonymous data.

- *Semen analysis*

The semen analysis was investigated at the first visit to the clinic with sexual abstinence period 3-5 days. Semen was collected in the outpatient semen-laboratory in a sterile plastic container where the name and date had mentioned. During the analysis, the volume was measured using a graded tube. Concentration was measured by slide method. Motility was scored manually, as percentages of (A) fast forward progressive, (B) slow forward progressive, (C) non-progressive and (D) immotile spermatozoa in 200 spermatozoa in at least five power fields per replicate. Percentage of sperm agglutination, and sperm-shaky head movement was evaluated. The sperm viability, which was extended to 24 hours, was done for all couples before and

ISSN No: -2456-2165

after getting a positive sign of ongoing pregnancy. All semen analysis was done according to the World Health Organization manual (WHO, 2010)(Ahmed Allow, Bracamonte and Belqees, 2018).

Their wives were treated by antibiotic (doxycycline) and vaginal wash for 2 weeks. At the same time, intercourse was recommended to avoid during the course of treatment and given them advice (to husband) to masturbate and ejaculate at least 1-2 times per week without direct vaginal intercourse, table 1.

Table 1: Treatment (similar results were published in our previous publication(Ahmed Allow, Bracamonte and Belqees, 2018). For those on-going pregnant women, an additional supportive therapy by progesterone and low-dose aspirin supplementation was recommended.

	Husband	Wife	Note
Doxycycline® 100mg tablet	1x2 for 2 weeks	1x2 for 2 weeks	
Vita Zinc® Capsules	1x1 for 45 days	Nil	
Speman®	1x2 for 2 months	Nil	
Dostinex®(Cabergoline) 0.5 tablet	1/5 tablet per week for two months	Nil	
Human Chorionic Gonadotropin® 5000 IU / vial	Intramuscular injection once per week for 2 months	Nil	
Postmenopausal Gonadotropin injection®, Vials 150 IU/vial	Intramuscular injection once per week for 2 months	Nil	
Vaginal wash	Nil	Daily for 10 days during the antibiotic treatment and starting from day 7 of menstrual period	
Intercourse and intravaginal ejaculation	Was avoid for 1 month starting from day one of treatment		For husband: outside ejaculation was recommended ,2-3 times per week during the first month of treatment

Table 1:- Treatment of husbands with severe OATS and their wives.

III. RESULTS

Primary infertility was diagnosed in 89/112 of cases. Duration of infertility was between 3 and 12 years. After classical treatment of these cases, an improvement in the sperm volume, count, motility, and presence of excellent grade 1 motile sperms was harvested, table 2.

Male Fertility Parameters	Reference Range (WHO, 2010)	Upon Presentation	Post-Treatment	Notes
Sperm volume (ml)	2-5	2.35±0.75	3.05±0.92	Improved
Sperm count (10^6/ml)	> 20	0.1±0.02	10.7±2.74	Increased
Sperm motility (%)	>50%	Zero	41.3±8.51	Increased markedly
Sperm abnormal morphology (%)	>40%	78.5%±13.59	45.2±10.37	Decreased
Grade-A of activity (%)	15%	Zero	3.18±0.32	Increased markedly
Grade-B of activity (%)	25%	Zero	9.4±2.64	Increased
Grade-C of activity (%)	35%	Zero	25.2±3.78	Increased
Grade-D of activity (%)	25%	100%	62.22±13.41	Decreased
FSH mIU/mL	1.24-15.6	6.19±1.46	9.4±2.10	Normal
LH mIU/mL	1.42-7.8	4.38±2.19	5.2±0.72	Normal
Testosterone ng/mL	3-11	4.01±0.36	9.3±1.12	Normal (but shifting to the upper limit)
Prolactin ng/mL	2-17	25.47±3.94	10.8±2.15	Normal

Table 2:- Fertility investigations before and after treatment.

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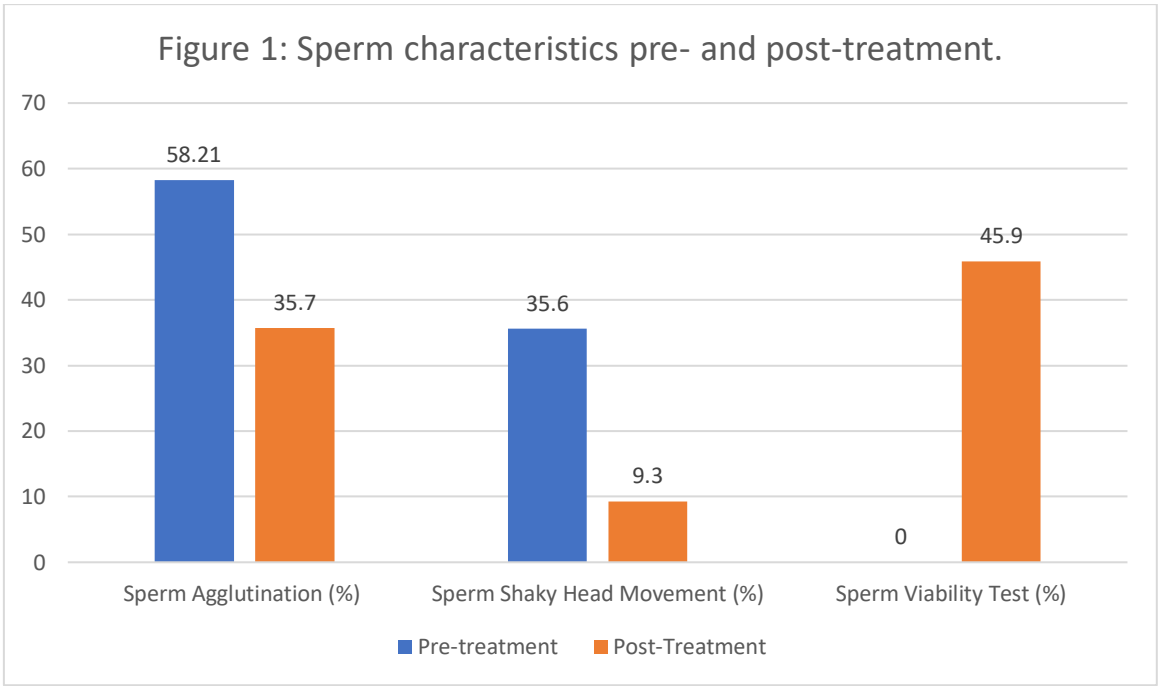
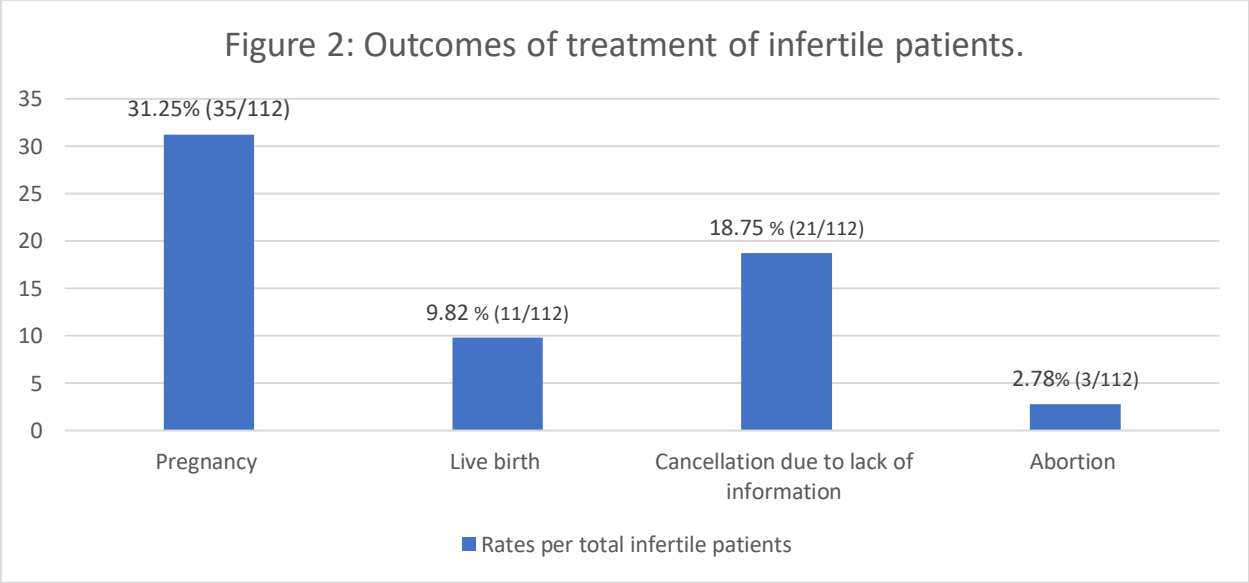


Results shows that percentage of sperm agglutination, sperm shaky head movement were markedly decreased after treatment whereas the viability test was improved, figure 1.



During the course of treatment, which was extended 2 months, thirty-five couples/112 (31.25%) were diagnosed as spontaneous on-going pregnancy. The live birth rate was reported in 11 cases (9.82%) and abortion rate was registered in 3 cases (2.78%). Due to unstable political issues in the country, we lost a direct or indirect communication with 21 pregnant women (18.75%), figure 2. Pregnancy was diagnosed by positive presence of gestational sac in the uteri of mothers. Further serum beta human chorionic gonadotropin was reported (serum beta hCG 427.13-3,183.2 IU/ml). No multiple-gestational sacs were recorded in all pregnancies.

IV. DISCUSSION

Multifactorial male infertility is still the dominant factor of infertility(Allow Ahmed, Sadeeq Abdulmogni, 2016). The reason behind that is not only sperm count but also it includes sperm motility, agglutination, viability and abnormalities. We had usually thought that the male infertility factor is a direct indicator for recommendation of assisted reproductive techniques (ART). In case of enrolling male infertility patients to ART, the policy of our IVF-center is to give opportunity for classical treatment for patients with male infertility. This kind of treatment is called non-ART treatment. Moreover, severe OATS is the most

ISSN No: -2456-2165

difficult cause on male infertility(Allow Ahmed, Sadeeq Abdulmogni, 2016). It can associated with 7% of total causes of infertility (Allow ahmed, Sadeek Abdulmugni, Bracamonte maryam, 2017). This is the first descriptive study, which is looking to report the non-ART treatment for male infertility factor with severe OATS.

We were used in this study a medication which is consisted of zinc (50 mg / 1 tablet) plus multivitamins (Vito-Zinc supplementation). In 2017, Alsalman and his co-workers reported that zinc supplementation caused a reduction in the levels of thiol oxido-reductive index, oxidized thiol, thiol and thiol-related enzymes activities in sub-fertile patients(Alsalman, Almashhedy and Hadwan, 2017). That means Zinc as a daily required supplementation plus multivitamins were caused an improvement in the sperm motility and sperm-viability tests, which are very important in the determination of male factor infertility. In our fertility center, sperm viability can be determined as an essential test for determination of male factor infertility than the sperm quality parameters.

Another non-hormonal natural herbal formulation is Speman had been used for those patients. This formulation is produced by Himalaya Drug Company. It consisting of many non-herbal products like Orchis mascula, Asteracantha longifolia, Lactuca scariola, Mucuna pruriens, Argyreia speciosa, Tribulus terrestris, Leptadenia reticulata and Parmelia perlata. The majority of these herbs are used in the traditional alternative medicine for many years. It is used as aphrodisiacs. Orchis mascula is used as a restorative and a tonic aphrodisiac in conditions associated with weakness or reduced sexual activity. All these herbs were used to enhance the sexual activity and improve its quality. With its combination of naturally occurring herbs, Speman can enhance testicular, seminal vesicle epididymal functions which will in turn result to a healthier sperm production. Agwawal and Kulkarni in 2003 reported their outcome after treatment of oligspermic patients for 6 months using Speman capsules, which produced by the Himalaya Drug Company(Agrawal and Kulkarni, 2003). They appointed that sperm count was improved from 27.64 ± 3.31 to 41.43 ± 5.96 and the percentage of abnormalities was decreased by 6 times (from 19.01 % to near to 3%) without any changes in the testosterone level. They concluded that Speman is effective in oligospermia, as it increases the sperm count and improves morphology (Agrawal and Kulkarni, 2003).

In our study, the selected patients were diagnosed with mild to moderate hyperprolactinemia. To solve this medical situation, we were used Dostinex-Cabergoline 0.5 mg tablets which is a dopamine receptor agonist. The chemical name for cabergoline is 1-[(6-allylergolin-8β-yl)- carbonyl]-1-[3-(dimethylamino) propyl]-3-ethylurea. Its empirical formula is $C_{26}H_{37}N_5O_2$ and its molecular weight is 451.62. Cabergoline is given, in this study, as a permanent (non-increasing dose) 0.25 mg a week for 2 months. The initial dose is 0.25 mg once weekly, at bed time. The weekly dose was not increased and continued for 2 months. No clearly side effects were noted and reported except mild nausea and postural hypotension. Many authors reported that treatment of hyperprolactinemia is significantly improved sperm parameters and sex-hormone levels, which improved fertility outcomes (Hyperprolactinaemia in male infertility: Clinical case scenarios, 2018).

The purpose of antibiotic use in these patients was lined to treat white blood cells in the semen analysis which was available with negative bacterial growth in the semen culture. Allow and his co-workers (2016) was reported that male infertility still the common male factor of infertility whereas the seminal fluid infection and sperm agglutination are the highest sub-division of male infertility factor (17.73% out of 29.90% of male infertility factor)(Allow Ahmed, Sadeeq Abdulmogni, 2016).

The role of antioxidant, in the course of treatment, was important to improve sperm parameter tests. In a study published by Ashok in 2017, it was reported that antioxidants such as glutathione, vitamins E and C, carnitines, coenzyme-Q10, N-acetylcysteine, selenium, zinc, folic acid, and lycopene have shown to reduce OS-induced sperm damage (Ashok, 2017). In our case the sperm parameters were improved.

The role of gonadotropins in these cases was markedly cleared in the improvement of sperm count, percentage of motility and increases its viability. In the observational study (166 infertile male partners of couples undergoing in-vitro fertilization) was showed that FSH treatment improves sperm DNA fragmentation, which in turn leads to increased pregnancy rates in infertile males undergoing in-vitro fertilization (Marco *et al.*, 2017).

The present study showed a 9.82% (11/112) life birth rate whereas the cancellation rate (due to lack of communication or patients had changes their phone numbers or addresses due to war) was 18.75% and abortion rate was documented in 3 cases only (2.78%). Actually, no similar data had been found in the media so this achievement (life birth rate = 10%) we could not compare with a possible data in the media. We have to assume that the life birth rate was zero for all cases and our project achieved near to 10% of live birth rate so it is really an achievement. Cancelation rate (due to lack of communication) was quite high (19%). The civil war was the main cause of lack of communication between our center and patients.

For all discussed events above, the husband became a father after a mild improvement in his sperm quality tests. We recommend in the end of this work to extend the study to cover more cases and make it as a last procedure for male infertile-patients with severe oligoasthenospermia before ART-therapy.

- *Clinical Implication*

Usually, the infertile patients with OATS or severe OAST are required any kind of ARTs. In our observation, we found that clinical therapy of those patients with classical method of treatment realized a life birth. Life-birth

for them is an achievement for them. So, we can use it for treatment of infertile cases with OATS before to involve them in the ARTs.

➢ *Authors' Contributions*

Belqees Allaw was involved in the data collection, manuscript drafting, and final approval of the manuscript. Bracamonte Maryam was involved in treatment of infertile couples as a gynecologist and fertility specialist, critical discussion and final approval of the manuscript. Ahmed Kaid was involved in design of project and treatment of couples as a fertility consultant, critical discussion and final approval of the manuscript. Saeed M. Saeed was contributed in the data collection, manuscript drafting, and final approval of the manuscript.

➢ *Ethics Approval and Consent to Participate*

This study was analyzed and exempt from ethical approval from Alaw IVF Center and Sana'a University Colleague of Medicine.

➢ *Consent for Publication*

Not applicable.

➢ *Competing Interests:*

The authors declare that they have no competing interests.

➢ *Funding:*

Local private research support by Alaw Medical and IVF center, Sana'a Yemen and Medical Colleague Sana'a University.

➢ *Acknowledgments*

The work was supported by grants from the Alaw IVF Center, Yemen (Grant No. S1-18-2019). Author and deeply appreciate the workers in the Alaw IVF Center for their help and ITD of Center. As well as the Colleague of Medicine Sana'a University.

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