THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (March–April 2014) 64(2):134–142
DOI 10.1007/s13224-013-0484-1

ORIGINAL ARTICLE

Success in Pregnancy Through Intrauterine Insemination at First Cycle in 300 Infertile Couples: An Analysis

Panda Babita · Mohapatra Lita · Sahu Mahesh C. · Padhy Rabindra N.

Received: 2 August 2013 / Accepted: 14 October 2013 / Published online: 1 December 2013

Abstract
Objective The aim of this article was to determine digital levels of the association of factors of pregnancy success after the first cycle of intrauterine insemination (IUI) with 300 infertile couples.
Methods The IUI procedure was followed at 36 h after triggering the ovulation, if at least one follicle measured >15 mm. Endometrium thickness (ET) and serum luteinizing hormone (LH) levels were measured at day 10 for each patient. The post-wash total motile fraction (TMF) of semen of the partner of each patient was also evaluated. The principal component analysis (PCA) was done with the data to quantify the associations of related factors.
Results The clinical pregnancy rate of first cycle IUI attempts was 17.3 %, observed in females, aged 20–39 years and men with TMF >5 million spermatozoa. The ovarian stimulation enabled the development of follicles measuring >16 mm, with LH levels <10 mIU/L and ET >5 mm for success. The PCA revealed that with the female-age parameter, three factors, NF, ET, and LH were related in the component 1; similarly, NF, LH, and RFS were related in component 2; age, NF, ET, LH, LFS, and TMF were related in component 3; and NF, ET, LH, RFS, and LFS in component 4 were related, i.e., the best correlation.
Conclusions Associated principal determinative factors, LH, female-age, NF and LFS values were highly significant, but the factors, ET, RFS and TMF were statistically insignificant for success through IUI in pregnancy.

Keywords Intrauterine insemination · Endometrium thickness · Luteinizing hormone · Number of follicles · Fallopian tube · Total motile fraction of semen

Introduction

Infertility is the inability to contribute to conception within after 12 months of unprotected intercourse, and it is an important public health/social peril found approximately with one in every six couples. Its causes could be broadly divided into three groups: female, male, and unexplained factors. The female factor includes problems with the ovulation due to obesity or polycystic ovarian changes, or due to erratic levels of progesterone, particularly at levels greater than 1,800 ng/dL in the mid-luteal phase, or due to adhesion problems from pelvic inflammatory diseases,

Panda B. · Mohapatra L.
Infertility Unit, Department of Obstetrics and Gynaecology, Institute of Medical Sciences & Sum Hospital, Siksha 'O' Anusandhan University, Kalinga Nagar, Bhubaneswar 751003, Odisha, India
e-mail: drpandababita@rediffmail.com

Sahu M. C. · Padhy R. N. (✉)
Central Research Laboratory, Institute of Medical Sciences & Sum Hospital, Siksha 'O' Anusandhan University, K-8 Kalinga Nagar, Bhubaneswar 751003, Odisha, India
e-mail: rnpadhy54@yahoo.com

tubal obstruction, and endometriosis, or due to unidentified cervical factors [1]. Determinative causes of pelvic inflammatory diseases would be tubal damages from bacterial infections with *Neisseria gonorrhoeae* and/or *Chlamydia trachomatis,* or a previous episode of pelvic surgery, or prior miscarriages, or unsafe abortion or ectopic pregnancy [2].

As a solution to the infertility problem, the wielded intrauterine insemination (IUI) lands at the positive outcome compared with the conventional intravaginal/intracervical insemination [3], and its pregnancy success rate per cycle is about 8–22 % [4]. Moreover, the IUI method is less expensive and less complicated compared with the other assisted reproductive technology, the in vitro fertilization (IVF) protocol. Since six clinical factors—the female-age, endometrial thickness (ET), luteinizing hormone (LH), number and size (mm) of ovary follicles, and male factor, i.e., total motile fraction (million)—controlled the success rate of an IUI protocol, it was intuitive to study the role of individual factors in the success. Basically, a multivariate analysis of the associated factors could have helped in evaluating the role of individual factors, but a principal component analysis (PCA) was employed here in, as the individual factors are not independent of each other. For example, an optimum LH level can facilitate follicle growth and oocyte formation; also, LH levels should have indirect ameliorating effects on other factors, such as estradiol level. For a digital analysis of roles of cited individual factors during an astute planning for the popular solution for infertility—the IUI protocol, PCA which is suitable for this multifactor event is essential, compared with other multivariate analyses, as the fewer the encumbrances the better the solving of a health problem in a young patient.

The aim of this study was to analyze the account of a retrospective study on the clinical pregnancy rate after first cycle IUI attempts with infertile couples visiting the infertility unit at a teaching hospital. As several factors influence the conduction of a series of treatment options along with monitoring body functions, in preparing an infertile couple for an IUI that could prevent the inveterate psychosocial abomination of a section of young people, a digital evaluation of the associated factors is required. This analysis could help clinicians assessing each reproductive factor digitally in resource-limited settings. A vivid analysis of factors of infertility, being unavailable in the literature for an effective application of the IUI method, the PCA of a dataset is done herewith, which should help in accurate decisions being taken by obstetricians. This lamplit analysis using the wonted PCA provides digital values on roles of several inherently linked infertility factors governing the IUI protocol.

Literature Review

The treatment with follicle-inducing clomiphene citrate (CC) and the hormonal treatment with human menopausal gonadotropin (hMG) for the induction of ovulation followed by the IUI as the assisted method in the therapeutic module are known for ratcheting up the pregnancy rate per cycle. Nevertheless, the CC treatment before an IUI protocol is known even to trigger multiple pregnancies, leading to associated complications [5, 6]. Anyway, the hMG treatment combined with an IUI method often lands at the cumulative pregnancy in three cycles with a blithesome success rate, comparable with a single IVF treatment [7]; the latter has always been the tedious method, following the failure from intravaginal/intracervical insemination or IUI attempts.

Implicitly, a poorly developed endometrium before the implantation period is considered as one of the vital causes of infertility; on the other hand, on the day of treatment with the human chorionic gonadotropin (hCG), a triple-lined endometrium is induced for the eventual success of the IUI protocol [8]. Furthermore, greater number of follicles with sizes ≥16 mm along with a good estradiol level at the time of hCG injection had registered comparatively a higher rate of pregnancy outcome in IUI cycles [9]. In addition, the luteinizing hormone (LH) level from pituitary gland plays a stonking role in controlling the menstrual cycle—facilitates ovulation, prepares uterus for implantation and assists in secretions of estrogen and progesterone by ovaries [10]. Moreover, ideal LH values have determinative roles in the series of events, follicle growth, oocyte formation, and continuation of pregnancy; as reported, LH values between 0.5 and 1.0 IU/mL had a better result compared with higher values >1.5 IU/L [10]. In addition, along with an optimal LH level, the use of a follicle-stimulating hormone (FSH) too is essential for both follicular growth and oocyte formation [10]. In the case of a 42-year-old woman, the sub-septate uterus with a bilateral free-spillage was corrected by hysteroscopy followed by the transcervical septal resection for a successful outcome [11]. Thus, several female factors are determinative for the success in pregnancy.

The male factor (semen of the husband) accentuates the infertility problem. If the concentration of spermatozoa remains ≥20 million/mL, then a total amount of semen with a total count of ≥40 million in 2 mL with progressive motility of ≥50 % with normal forms of ≥30 % is required for the success (Dickey et al. [1]). Indeed, morphologically normal sperms, with the ability of capacitating and undertaking the acrosome reaction for the penetration into an oocyte's cumulus oophorus and the zona pellucida for the fertilization, are required for the success in an IUI attempt [12]. Twenty to 25 % cases of male infertility are due to the smattering of normal motile sperms [13] Apart from chronic infections affecting semen quality from fibrosis of the vas deferens, testicular torsion and varicocele too nudge to male infertility [14]. Not surprisingly, environmental and lifestyle factors (smoking, drugs, pollution, and radiation hazards) and diseases (diabetes, cancer, and infections) contribute to male infertility [15]. At the same time, therapeutic benefit of an inveterate combination of CC with an antioxidant to enhance semen parameters is consensus [16]. In the limit of course, defects in any of these necessary events may lead to subfertility or infertility. As is well known, chromatin integrity of sperm was related to IUI pregnancy rates. At length taken in balance, the situation of unexplained infertility is the normality in the linked parameters obtained with standard investigations for both partners without any conception spontaneously; incidences of this group remained maximally up to a 25 % of infertility cases, as recorded elsewhere [17].

Undoubtedly, IUI is less complicated and much less expensive than IVF and can be a cost-effective solution for infertile couples, and it is reasonable that the IUI procedure may be considered and selected as a first-line treatment for infertility problems, before undertaking more aggressive, assisted, reproductive treatments (ARTs), in cases in which, the pregnancy rate is low. Alternately, there are several cases, patients with blocked fallopian tubes, advanced endometriosis, very poor sperm parameters/severe male factor infertility, or vasectomy in which, other ART (such as IVF) would be the most cost-effective and the sought after therapy. Hence, some couples would benefit from undergoing IVF sooner rather than having more tests, more surgery, and more IUI cycles; in other words, IUI may be helpful to a couple having the trouble in conceiving. It is a possible solution, but not the only solution.

Methods

This is a retrospective study on clinical pregnancy rate after the first cycle IUI on a self-selected group of 300 infertile couples visiting Infertility Center, Institute of Medical Sciences and Sum Hospital, between 2009 and 2011. Participants consisted of women aged 20–44 years and their male partners aged 21–55 years. The institutional “Review board and Ethics committee” had approved this study. The evaluation protocol consisted of husband-semen analysis, the assessment of the luteal phase, and the confirmation of tubal patency with hysterosalpingogram (HSG) and/or laparoscopy of the female partner.

As a female factor, ovulatory dysfunction was monitored by conducting a transvaginal sonography (TVS) on the 13th/14th day of the menstrual cycle; tubal malfunction was diagnosed by HSG or laparoscopy. Laparoscopy was performed on patients presenting with history of excessive pain during sexual intercourse, menstruation, and either restricted or no spillage on HSG. However, the presence of pelvic pathological conditions, such as adhesions or endometriosis or tubal blockage being nonconducive for the IUI, were ruled out by laparoscopy with each patient. During laparoscopy patients with endometriosis were diagnosed, and its severity was assessed/classified. Further, for cases with the blockage in the proximal part of the fallopian tube, a hysteroscopic cannulation was done.

Semen analyses were conducted with samples that were collected 3–7 days following abstinence from sexual activity. Several disturbing lifestyle habits, such as smoking and a few more, were abetted for preventing adverse comeuppance with male partners, mainly during the said abstinence, as the Hawthorne effect. With the results of at least two semen analyses, conducted at an interval of 3 months, patients were diagnosed as having the male-factor with the following abnormalities: sperm concentration below 20×10^6/mL, progressive motility less than 50 %, or without normal morphology less than 30 % [18].

The IUI was conducted for a patient who fulfilled the following criteria: first, patients with infertility since $\geq$2 years and did not conceive after even a controlled ovarian stimulation followed by the timed intercourse for at least 4–5 cycles; second, on the day 3 of menstrual cycle, serum FSH would be at <10 IU/mL; third, at least one healthy fallopian tube was evident; and finally, the sperm count was more than 10 million [19]. In this study, male-partners with mild-to-moderate variations in motility, count, and morphology of sperms were administered a course of antioxidant supplements and CC (a dose of 25 mg) for 3 months [20]. In addition, the exclusion criteria included those patients with bilateral tubal blockage, moderate-to-severe endometriosis and severe deficiency in the male factor.

Female patients were given CC (100 mg) from day 2/3 for 5 days of their menstrual cycle, following which they were given gonadotropin injections, hMG (FSH/LH) (75/150 IU) on day 5 or 7 of the cycle, for a controlled ovarian stimulation. A TVS was conducted on the day 10 of the cycle for assessing the following parameters, endometrium thickness (ET), as well as follicle size and number in both right and left ovaries. Once the dominant follicular size reaches >15 mm, the patient was advised for a serum LH evaluation. If the LH value was <15 mIU/L, then hCG (5,000 IU) was injected to the patient, and an IUI procedure was planned at 36 h after the hCG treatment. If the LH value was >15 mIU/L, then the hCG injection was withheld, and the IUI was planned for the next day, as previously described [4]. In addition, folic acid and other antioxidant administrations were prescribed during the course, as often followed [19, 21].

Sperm Preparation and IUI Procedure

On the day of the IUI, the collected semen sample was liquefied by incubating at 37 °C for 20–25 min. For the sperm-processing, the "Puresperm Grade 2 sperm-processing kit" with three solutions (puresperm A—1 mL 80 % density gradient, puresperm B—1 mL 40 % density gradient, and puresperm C—4 mL wash solution) was used for further processing. A washing of the liquefied sample was done using the density gradient method with a centrifugation. During the preparation of the semen sample for IUI, the components in the kit and the semen sample were raised to the temperature of 37 °C. However, a pre-wash analysis of sperm motility and the count of the total motile fraction (TMF) value were done using the Makler's chamber. An aliquot of 1 mL puresperm A (PA) solution was transferred to the bottom of a conical tube, and an aliquot of 1 mL puresperm B (PB) solution was layered on the top of the PA solution. Under sterile conditions, an aliquot of 2 mL of liquefied semen sample was transferred to the top of the PA-PB mixture. The whole sample-mixture was centrifuged at 2,000 rpm for 15 min. After centrifugation, the supernatant was discarded. An aliquot of 3 mL of puresperm-C was added to the sperm-pellet, gently stirred, and re-centrifuged at 1,000 rpm for 5 min. The supernatant was again discarded, and an additional aliquot of 0.4 mL of puresperm C was added to the sperm pellet. The processed semen sample was drawn into the insemination catheter; a vaginal speculum was used to assist in the passage of the catheter to deliver the semen sample into the uterine cavity.

For a luteal phase support till conception, progesterone supplements were administered vaginally to the patient following the IUI procedure [20]. After confirmation of the pregnancy, at 3–4 weeks after the gestation, a TVS was performed to visualize the gestational sac, foetal pole and cardiac activity [20]. These patients were followed on the monthly basis during the antenatal period. The outcome of pregnancy was monitored, and the number of miscarriages and live births were recorded.

Statistical Analysis

The statistical analysis was performed using the Statistical Package for Medical Science version 17.0 (SPSS Inc., IL, USA). Principal component analysis, and analysis of variance (ANOVA) of the dataset of factors; female-age, ET, LH, number of follicles (NF), left follicular size (LFS), right follicular size (RFS), and TMF were performed.

Table 1 Effect of age, endometrial thickness, and luteinizing hormone levels as female factors in pregnancy success

	Age (years)					Endometrial thickness (mm)						Luteinising hormone (IU/mL)				
	20–24	25–29	30–34	35–39	40–44	5.1–6.0	6.1–7.0	7.1–8.0	8.1–9.0	9.1–10.0	10.1–12.0	0.1–2.0	2.1–4.0	4.1–6.0	6.1–8.0	8.1–10.0
Positive	6	27	15	4	0	4	12	15	6	5	10	0	6	31	12	3
N	20	137	101	35	7	51	63	64	20	30	55	9	38	73	51	30
% age	30	19.71	14.85	11.43	0	7.84	19.05	23.43	30.0	16.6	18.18	0	15.79	42.47	23.53	10.0

N number of positive outcomes

Table 2 Effects of number and size of follicles as female factors, and total motility fraction as the male factors, in pregnancy success

	Number of follicle		Follicle size (mm)				Male factor: total motile fraction (million)			
	One	Two	14.1–16.0	16.1–18.0	18.1–20.0	20.1–22.0	5–8	8–11	11–14	14–17
Positive	16	36	8	30	12	2	3	26	18	5
N	140	160	40	76	42	8	17	45	59	50
% age	11.43	22.5	80	65.21	28.5	75	17.65	57.8	30.51	10.0

N number of positive outcomes

Table 3 Correlation Matrix between the factors effecting the positive outcome in IUI

	Age	NF	ET	LH	RFS	LFS	TMF
Age	1.000						
NF	0.018	1.000					
ET	−0.049	−0.190	1.000				
LH	−0.063	−0.059	0.180	1.000			
RFS	−0.131	0.591	−0.250	0.019	1.000		
LFS	0.194	0.589	0.095	−0.114	−0.181	1.000	
TMF	0.015	0.004	−0.192	0.202	0.129	−0.109	1.000

Only cases for which outcome positives are used in the analysis phase. *NF* number of follicle, *ET* endometrium thickness, *LH* luteinizing hormone, *RFS* right follicle size, *LFS* left follicle size, *TMF* total motile fraction

Results

Three hundred infertile couples were studied for the fertility determinants: female-age, thickness of endometrium, LH concentration, size and number of follicles, and TMF as the male factor, too. Following the usual protocol of the IUI, 52 successful pregnancy outcomes were recorded, of which eight cases were with twin gestations, while seven cases were miscarriages at around 6–8 weeks. Further, ET, serum LH value, follicular size and number, and NF were measured at day 10 of the menstrual cycle. For the chance of positive fertility, several factors (female-age, ET, LH, NF, LFS, RFS, and TMF) were analyzed individually (Tables 1, 2), and their correlations (Table 3 and 4) were interpreted.

With the age as a factor, it was seen that females presenting their fertility status were of age 20–44 years, patients beyond the age of 40 years had no positive outcome. Not surprisingly, in the age group 20–24 years, the pregnancy rate after an IUI protocol was higher than those of other age groups. The positive outcome was evident in the range of 5–12 mm ET; specifically, 17 patients with ET <5 were not included in the group analysis. In addition, in the positive range of 5–12 mm ET, the highest pregnancy rate was recorded with 8–9 mm ET. The positive outcome was observed with a LH concentration at 2–10 IU/mL, while the LH value >10 IU/mL had negative outcome. The maximum pregnancy rate, 42.5 % was observed in women with LH concentration between 4.1 and 6.0 IU/mL. It was seen that participants with one and two dominant follicle(s) in an ovary had the positive outcome at 11.4 and 22.5 %, respectively. Patients with follicular size between 14 and 22 mm had the positive outcome. However, the maximum pregnancy rate, 62.5 % was observed in the group with follicular size, 14.1–16.0 mm (Table 1). The positive outcome was observed with TMF values, 5.1–20.0 million. TMF values less than 5 and greater than 20 million had the negative outcome. However, on evaluating the TMF, the highest pregnancy rate was observed with a range of 8–11 million sperm count (Table 2).

The PCA of the dataset revealed that all the factors: female-age, LH, NF, LFS, RFS, ET, and TMF were found to have determinative roles, and their co-relation patterns for the positive outcome were elucidated (Table 3). Only four components could be extracted from the analysis, with eigen values, 1.712, 1.412, 1.235, and 1.235, which were more than 1.0; in other words, components with eigen values less than 1.0 were ignored. Among them, the component 1 was of the highest eigen value, 1.712, and the highest percent variance, 24.452; but the highest cumulative variance, 79.912 was found in the component 4 (Table 4). Positive values in the correlation matrix signify association of the factors, while negative values do not; for example, with the age factor—factors NF, LFS and TMF are correlated, but ET, LH and RFS are not correlated (Table 3). It was evident that with the age parameter, three factors: NF, LFS, and RFS were related as the component 1. Similarly, in the component 2, ET, LH, and LFS were

Table 4 Varimax-rotated component matrix of the PCA

	Component			
	1	2	3	4
Age	0.094	−0.133	0.821	0.049
NF	0.952	−0.214	−0.130	0.010
ET	−0.022	0.852	−0.068	0.040
LH	−0.008	0.369	−0.147	0.798
RFS	0.447	−0.512	−0.563	0.174
LFS	0.769	0.280	0.421	−0.157
TMF	−0.065	−0.382	0.152	0.734
Eigenvalue	1.712	1.412	1.235	1.235
Percent variance	24.452	20.173	17.649	17.638
Cumulative variance	24.452	44.625	62.273	79.912

Only cases for which outcome positives are used in the analysis phase. Note: Only cases for which outcome positives are used in the analysis phase. *NF* number of follicle, *ET* endometrium thickness, *LH* luteinizing hormone, *RFS* right follicle size, *LFS* left follicle size, *TMF* total motile fraction

related; in the component 3, age, LFS, and TMF were related; in the component 4, age NF, ET, LH, RFS, and TMF were related. The component 1 with the highest eigen value signifies that the associated factors were highly related to themselves than those of the component 2 with a lower eigen value. Similarly, the associated factors of the component 2 were highly related to themselves than with those of the component 3, and so on for the other components 3 and 4 with the progressively lower eigen value of 1.235. Not surprisingly perhaps, the age factor was related by 1.8 % to NF; among them, LFS was highly related, i.e., 19.4 % to the age factor, whereas TMF was the least related with 1.5 % only. Further, NF was related with three factors: RFS by 59.1, LFS by 58.9, and TMF by 0.4 %. Moreover, ET was related with LFS by 9.5 %, with TMF by 19.2 %, and with LH by 18.2 %. In a unifying narrative, it could be recorded that LH was related with RFS by 1.9 % and to TMF by 20.2 %. RFS was related with TMF by 12.9 % only; all factors were related to age (Table 3).

All the cited threadbare infertility factors could be analyzed with digital values of co-relation for the positive outcome. From PCA-associated ANOVA results, it was ascertained that the age factor had a *p*-value, 0.012 (highly significant). Similarly, NF had $p = 0.005$ (more highly significant), ET had $p = 0.137$ (highly insignificant), RFS had $p = 0.239$ (highly insignificant), LFS had $p = 0.041$ (significant), and TMF had $p = 0.61$ (highly insignificant), as significant values for the positive outcome (Table 5). From the Table 5, it is discernible that RFS and TMF had highly insignificant values, while age, NF, and ET were moderately significant; clearly, LH value with the *p*-value of 0.0001 was signifying an absolute dependency for success. Moreover, a pregnancy rate per cycle of 17.33 % (52/300) was obtained in which, 15.38 % (8/52) were twins. No major congenital anomaly was recorded, or were there any multiple pregnancies.

With the three scatter diagrams of the second, the third, and the fourth components versus component 1 after the Varimax rotation, it was clear that the component 1 and the component 2 were related with factors, age, NF, and LFS (Fig. 1). Similarly factors, NF, LFS, RFS, and TMF of components 1 and component 3 were highly significant; all correlated factors are in the double positive quarters of scatter diagrams as points (Fig. 2). Further, between the component 1 and the component 4, it was found that factors, TMF, NF, and age had significant values in the positive outcome (Fig. 3). Factors were strongly related in component 4. Percent variance value is the total variance values of factors of the column. A cumulative variance value at each column indicates the total variance of factors in each component, i.e., variability of the individual values in the data-set, along with those all previous column(s) (Table 4).

Discussion

In this study, the female age was found to be the most significant prognostic factor for conception, as per the expectation; additionally, other pertinent factors were quantified by the analysis. This could be corroborated by the fact that this center typically preferred treating women below 40 years of age; indeed, there were only 7 women aged over 40 years in this study. However, the exact age at which the positive result was adversely affected was from age 35 to 44 years. As described elsewhere, reduced fertility typically occurred among women in their late 30 to early 40 years of age, when there is a sharp decrease in the

Table 5 ANOVA of factors of IUI data

	Sum of squares	*df*	Mean square	*F* value	*p*-value
Age					
Between groups	92.801	1	92.801	6.348	.012
Within groups	4356.279	298	14.618		
Total	4449.080	299			
NF					
Between groups	1.998	1	1.998	8.192	.005
Within groups	72.669	298	.244		
Total	74.667	299			
ET					
Between groups	8.970	1	8.970	2.218	.137
Within groups	1204.907	298	4.043		
Total	1213.877	299			
LH					
Between groups	782.409	1	782.409	18.453	.000
Within groups	12635.264	298	42.400		
Total	13417.674	299			
RFS					
Between groups	74.051	1	74.051	1.390	.239
Within groups	15873.611	298	53.267		
Total	15947.662	299			
LFS					
Between groups	245.661	1	245.661	4.192	.041
Within groups	17464.824	298	58.607		
Total	17710.485	299			
TMF					
Between groups	9.258	1	9.258	0.260	.610
Within groups	10600.373	298	35.572		
Total	10609.630	299			

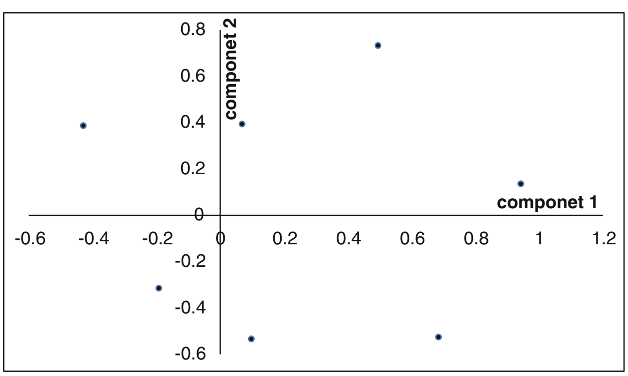

Fig. 1 Scatter of all samples on the planes of the first two principal components after the Varimax rotation

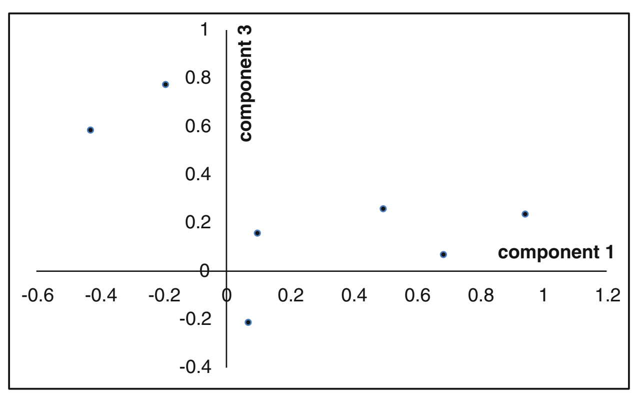

Fig. 2 Scatter of all samples on the planes of the first and third principal components after the Varimax rotation

production of oocytes [4]. Even more-effective treatment options, the IVF protocol, cannot completely overcome the negative impact of age [22]. In this study, a trend toward reduction in success rate with IUI was noted in women with age over 35 years. Many studies also have documented a significant drop in the success rate beyond the age 40 years, with the reported live births being as low as 1.4 % [23]. Summarizing, for women aged over 35, IUI as a treatment option needs to be conducted with adeptness

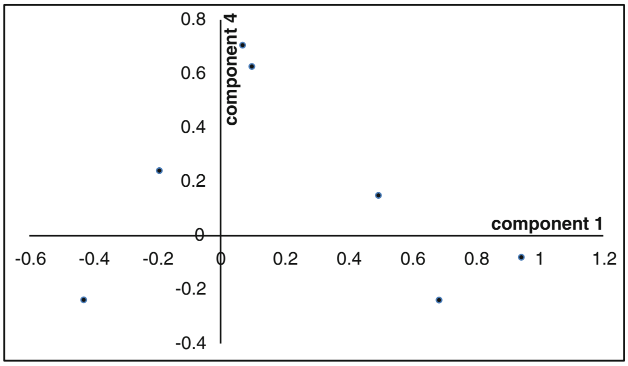

Fig. 3 Scatter of all samples on the planes of the first and fourth principal components after the Varimax rotation

and for women over 40, IUI is not a suitable treatment option, as discussed elsewhere [4].

Exquisite ovulation induction using the sequential treatment of CC and hMG, before the IUI protocol, as a treatment option for a variety of infertility diagnoses, significantly enhances the probability of pregnancy per cycle, compared with the use of IUI alone, or CC intake only and IUI excluding hMG. Although the pregnancy rate per cycle is increased with the use of CC-hMG and IUI, the risk for multiple pregnancies remains low, comparable to the risk seen with the use of CC and IUI only. Likewise, the use of CC-hMG before an IUI protocol was reported to be associated with a decreased rate of clinically significant ovarian hyper-stimulation syndrome (OHSS), compared with the hMG treatment before the IUI protocol [6].

In increasing the size of follicles above 15 mm in anovulatory women, the possibility of multiple deliveries was checked. It was demonstrated that as the size of follicles increased from 15 to 16 or 17 mm, there was a parallel increase in live birth rate (LBR). This relationship was also apparent in relation to the ovulatory status. By inducing an increase in the number of follicles in an anovulatory woman, there was a significant increase in clinical pregnancy rate and LBR compared to those in ovulatory women, without any increased risk in the number of multiple pregnancies [24]. Among the recorded clinical pregnancies following IUI protocols in this center, 44 cases were singletons and eight cases were twin pregnancies, and no case of a hyperstimulation was documented during the study period. However, a monofollicular response was observed in 71.87 % cycles. Indeed, with an increase in the number of preovulatory follicles, a corresponding increase was reported in the pregnancy rates, previously [4].

ET was a significant factor in predicting the success of IUI treatments in this study, and similar findings were demonstrated, elsewhere [25]. In a study, the success in pregnancy occurred, when ET on the day of hCG administration was <6 mm [26]. Further, when a LH surge occurs, spontaneous ovulation takes place within 24 h. However, the unawareness of LH surge might produce the negative outcome in IUI protocols that would not match to the ovulation. This study clearly demonstrated a high prevalence of LH surges of 36 % in the stimulated IUI cycles, but in another study, LH levels in blood had been recorded varying from 24 to 49 % for the pregnancy success [27]; on the contrary, a premature LH surge (6.57 %) caused a lower value of success. It had been known that the incidence of premature LH surge, in an IUI study, was around 24 %, which negatively influenced the outcome [28].

The TMF is an important prognostic factor for an IUI success. A significantly higher pregnancy rate (18.29 %) was recorded, when the TMF was in the range of 10–20 million. The pregnancy rate was lower, when the TMF value was in the range of 5–10 million (5.63 %). Moreover, a disappointing success rate was recorded, when the TMF was <5 million; unexpectedly, the pregnancy rates were also lower with a high TMF value (>20 million) [29]. When the TMF was <5 million, sperm morphology appeared to play an important role. With levels of TMF exceeding 10 millions for an IUI, no further improvement in conception rates was noted [30]. An approximation of the time of ovulation to that of the IUI protocol was determinative in the success. Thus, when several factors are in ideal levels, the positive outcome is attended with the IUI protocol. A post hoc analysis of results too prompts a prior imagination that right fallopian tube would have impairing tube-related function; thus, RFS could be regarded as a derisive factor in this analysis. The LBR was 15.0 % in this study, a lower value than that reported previously [31].

Conclusions

From this fixated analysis of the unfettered conundrum, all the well-known infertility factors could be analyzed with digital values of co-relation for the positive outcome of IUI. It could be inferred that the age as a stonking factor was highly significant at the *p*-value, 0.012; other factors were significant at *p*-value, NF 0.005 and LFS 0.041; but factors with *p*-values, ET 0.137, RFS 0.239, TMF 0.61 were not significant. In addition, the LH value was extremely significant for the positive outcome (pregnancy) with the *p*-value, less than 0.0001. With the analysis, it was ascertained that with the age parameter, three more factors, NF, LFS, and TMF were related in the component 1, with the highest eigen value of 1.712, as principal prognostics in the fruition. It is conjectured here that when this consortium of factors are not at suitable levels, chances of IUI success should plummet and would be curtailed to a hit-and-miss affair.

Acknowledgments The authors are grateful to Prof. SK Mohapatra, Head, Department of O & G, Prof. DK Roy, Medical Director, IMS & Sum Hospital for encouragements, and Shri G. Kar, Managing Member, IMS & Sum Hospital for facilities and to Prof. Dr. MR Nayak, Honourable President, S'O'A University, Bhubaneswar for support. MC Sahu is the Research Associate of the hospital.

Conflict of interest We declare that we do not have any conflict of interest.

References

1. Dickey RP, Taylor SN, Lu PY, et al. Effect of diagnosis, age, sperm quality, and number of preovulatory follicles on the outcome of multiple cycles of clomiphene citrate–intrauterine insemination. Fertil Steril. 2002;78:1088–95.
2. Seshagiri PB. Molecular insights into the causes of male infertility. J Biosci. 2001;26:429–35.
3. Keck C, Gerber-Schafer C, Wilhelm C, et al. Intrauterine insemination for treatment of male infertility. Int J Androl. 1997;20:55–64.
4. Kamath MS, Bhave P, Aleyamma TK, et al. Predictive factors for pregnancy after intrauterine insemination: a prospective study of factors affecting outcome. J Hum Reprod Sci. 2010;3:129–34.
5. Garceau L, Henderson J, Davis LJ, et al. Economic implications of assisted reproductive techniques: a systematic review. Hum Reprod. 2002;12:3090–109.
6. Gelety TJ, Klassener FA, Silva MA, et al. Improved pregnancy outcomes with sequential clomiphene citrate (CC)/human menopausal gonadotropin (HMG) and intrauterine insemination. Fertil Steril. 2000;73:S1.
7. Matorras R, Diaz T, Corcostegui B, et al. Ovarian stimulation in intrauterine insemination with donor sperm: a randomized study comparing clomiphene citrate in fixed protocol versus highly purified urinary FSH. Hum Reprod. 2002;8:2107–11.
8. Malhotra N, Karmakar D, Kumar S, et al. Endometrial thickness and pattern, uterine and sub-endometrial blood flow in women with unexplained infertility undergoing COH and IUI. Fertil Steril. 2008;90:S157.
9. Sulit MT, Ezcurra D, Rosenwaks Z. 1353 Controlled ovarian stimulation (COH)/intrauterine insemination (IUI) cycles: is there any correlation between the number of follicles >16 mm and the serum estradiol level at the time of triggering in predicting pregnancy outcomes? Fertil Steril. 2006;86:S413.
10. Kumar P, Sait SF. Luteinizing hormone and its dilemma in ovulation induction. J Hum Reprod Sci. 2011;4:2–7.
11. Panda B, Das S, Mohapatra L, et al. Successful outcome from empirical use of heparin and aspirin in unexplained pregnancy loss. Asian Pacif J Reprod. 2012;1:323–5.
12. Makker K, Mahfouz R, Gupta S, et al. A evaluation of pre and post-wash sperm parameters on intrauterine insemination outcome. Fertil Steril. 2007;88:S382.
13. Egozcue S, Blanco J, Vendrell JM, et al. Human male infertility: chromosome anomalies meiotic disorders, abnormal spermatozoa and recurrent abortion. Hum Reprod. 2000;6:93–105.
14. Hargreave TB. Genetic basis of male fertility. Br Med Bull. 2000;56:650–71.
15. Agarwal A, Sekhon LH. The role of antioxidant therapy in the treatment of male infertility. Human Fertil. 2010;13:217–25.
16. Ghanem H, Shaeer O, El-Segini A. Combination clomiphene citrate and antioxidant therapy for idiopathic male infertility: a randomized controlled trial. Fertil Steril. 2010;93:2232–5.
17. DH. UK Health, Science and Bioethics Division, London. www.dh.gov.uk/publications (2009). Reference guide to consent for examination or treatment. Second edition. Gateway reference, 11911. First published July 2009. Assessed in August 2011.
18. Esteves SC, Agarwal A. Impact of the new WHO guidelines on diagnosis and practice of male infertility. Open Reprod Sci J. 2011;3:7–15.
19. Ebisch IMW, Thomas CMG, Peters WHM, et al. The importance of folate, zinc and antioxidants in the pathogenesis and prevention of subfertility. Hum Reprod Update. 2007;13:163–74.
20. Kim CH, Cho YK, Mok JE. Simplified ultralong protocol of gonadotrophin-releasing hormone against for ovulation induction with intrauterine insemination in patients with endometriosis. Hum Reprod. 1996;11:398–402.
21. Sekhon LH, Gupta S, Kim Y, et al. Female infertility and antioxidants. Curr Women Health Rev. 2010;6:84–95.
22. Leridon H. Can assisted reproduction technology compensate for the natural decline in fertility with age? A model assessment. Hum Reprod. 2004;19:1548–53.
23. Frederick J, Denker M, Rojas A, et al. Infertility: is there a role for ovarian stimulation and intra-uterine insemination after age 40? Hum Reprod. 1994;9:2284–6.
24. Park SJ, Alvarez JR, Weiss G, et al. Ovulatory status and follicular response predict success of clomiphene citrate-intrauterine insemination. Fertil Steril. 2007;87:1102–7.
25. Kolibianakis EM, Zikopoulos KA, Fatemi HM, et al. Endometrial thickness cannot predict ongoing pregnancy achievement in cycles stimulated with CC for intrauterine insemination. Reprod Biomed Online. 2004;8:115–8.
26. Dickey RP, Olar TT, Taylor SN, et al. Relationship of endometrial thickness and pattern to fecundity in ovulation induction cycles: effect of CC alone and with human menopausal hMG. Fertil Steril. 1993;59:756–60.
27. Cantineau AEP, Cohlen BJ. The prevalence and influence of luteinizing hormone surges in stimulated cycles combined with intrauterine insemination during a prospective cohort study. Fertil Steril. 2007;88:107–12.
28. Allegra A, Marino A, Coffaro F, et al. GnRH antagonist-induced inhibition of the premature LH surge increases pregnancy rates in IUI-stimulated cycles. A prospective randomized trial. Hum Reprod. 2007;22:101–8.
29. Wainer R, Albert M, Dorion A, et al. Influence of the number of motile spermatozoa inseminated and of their morphology on the success of intrauterine insemination. Hum Reprod. 2004;19:2060–5.
30. Van BJ, Barnett M, Sparks AE, et al. Effect of the total motile sperm count on the efficacy and cost-effectiveness of intrauterine insemination and in vitro fertilization. Fertil Steril. 2001;75:661–8.
31. Ibérico G, Vioque J, Ariza N, et al. Analysis of factors influencing pregnancy rates in homologous intrauterine insemination. Fertil Steril. 2004;81:1308–13.