

## Clinical Outcomes of Intrauterine Insemination for Male Infertility in Brunei Darussalam

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### ABSTRACT

**Objectives:** This study aims to evaluate the factors influencing the success of Intrauterine insemination (IUI) in infertile patients due to male causes in Brunei Darussalam.

**Methodology:** Pre-diagnosed male infertility patients of all ages were included in this retrospective cohort analysis from the “Raja Isteri Pengiran Anak Saleha (RIPAS) Hospital's” Brunei Darussalam between January 2015 and December 2020. South Asian criteria were used for BMI categorization. Statistical evaluation of the data was conducted utilizing R-studio.

**Results:** Out of 240 research participants, 92.1% were Malay. IUI resulted as a successful pregnancy for 18 males (7.5%), while 222 subjects (92.5%) had unsuccessful conception. The semen parameters were correlated with age and BMI. Although the difference was statistically insignificant, the male subjects with successful outcomes after IUI were young, BMI was less, and the semen quality variables were better than the male subjects who had unsuccessful outcomes.

**Conclusion:** The male study subjects with the outcome of successful IUI resulting in pregnancy were younger, and had lower BMI and better semen parameters than the group in which IUI failed to result in pregnancy.

**KEYWORDS:** Age; Body mass index; Intrauterine Insemination; Male Infertility

### INTRODUCTION

Infertility is a condition that hampers an individual's ability to conceive, either independently or with a partner, or the incompetence of achieving a clinical pregnancy after twelve months of regular unprotected sexual contact. Male factor infertility is managed differently according to the underlying causes. Where certain treatments are inappropriate or unsuccessful, ‘assisted reproductive technology (ART) has become an adjunct treatment option for infertility secondary to the male factor.<sup>1</sup> Intrauterine insemination (IUI) is one example of ART for infertile couples due to both male and non-male

causes. Since IUI is relatively inexpensive and non-invasive as opposed to other interventions for infertility, it is considered a primary therapy option for some couples before consideration of other ART such as in-vitro fertilization (IVF).<sup>1</sup>

The success of conception following IUI varies from 2.7% to 70%, subject to other factors in the couple.<sup>2</sup> The prognostic reasons for a subsequent successful pregnancy are still under research.<sup>3</sup>

The first step in diagnosing male cause of infertility is typically semen analysis. Parameters such as semen volume, sperm concentration, motility, and morphology are commonly examined following standard values set by the World Health Organization (WHO).<sup>4</sup>

These parameters are crucial indicators of successful IUI, but a reliable predictor of a successful pregnancy is still yet to be defined. This may be because men with normal semen parameter values may be clinically infertile, and as such, these values may not be accurate predictors of male infertility.<sup>5</sup> Paternal age is also considered a factor influencing

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the success of IUI because the development of ARTs has allowed males experiencing reproductive challenges owing to advanced age to have children.<sup>6</sup> Male sexual organs are impacted by ageing in various ways, and studies show that semen parameters are negatively correlated with ageing. However, since the production of sperm continues until old age, we may then question the true association between the increased age of males and abnormalities associated with sperm.<sup>7</sup> The incidence of overweight and obese individuals has been increasing globally for decades, and global average data shows that in some countries, high BMI is significantly more prevalent in males than females.<sup>8</sup> Currently, no study evaluating the clinical results of infertile male patients receiving IUI in Brunei Darussalam has been conducted. Therefore, this research aims to ascertain how male factors in infertile patients may influence the success of IUI in Brunei Darussalam.

### METHODOLOGY

This retrospective study was conducted in the “Department of Obstetrics and Gynecology, Raja Isteri Pengiran Anak Saleha Hospital”, Brunei Darussalam during January 2022 to April 2022. Ethical approval for retrieving retrospective data of patient’s record from above mentioned department was taken from institute of Health Sciences Research Ethics committee (UBD/PAPRSBIHS REC/2021/107). Retrospective data from January 2015 to December 2020, where infertile patients of all ages with male factor infertility, scheduled for IUI were included in the data analysis. During the study period, desk records of 380 couples were retrieved, out of which 244 males, listed for IUI procedures due to male infertility were included. Four patients with missing data were excluded from the study.

Details including the date when infertility was diagnosed, age, race, smoking status, weight, height, BMI, type of infertility, semen analysis parameters, and pregnancy outcome of the patient were documented. Numerical variables such as age

were denoted in years, weight in kilogram, height in meters and BMI in kg/m<sup>2</sup>. As for categorical variables, smoking status was grouped into smoker or non-smoker, race was either Malay or others, type of infertility was either primary or secondary, and pregnancy outcome was successful or unsuccessful. Subjects were divided based on: “normal BMI (18–22.9 kg/m<sup>2</sup>), overweight (23–24.9 kg/m<sup>2</sup>), and obese (>25 kg/m<sup>2</sup>)” as per the ‘South Asian criteria’.<sup>9</sup> The semen variables were classified according to the “World Health Organization's (2010)” standard values for standard semen analysis: volume: > 1.5 millilitres (mL), sperm count:  $3.9 \times 10^7$  sperm per ejaculate or more and sperm motility: > 32% actively moving. The cohort was dichotomized based on pregnancy outcome positive or negative outcome).

### STATISTICAL ANALYSIS

Data was statistically analyzed utilizing R-studio1.3.1093. Fisher’s exact test was employed where > 20% of expected cell counts were <5, whereas the Chi-square test was used if less than or equal to 20% of expected cell counts were less than.<sup>5</sup> The quantitative data was analyzed using the independent t-test and Mann-Whitney test based on normal/abnormal distribution of the data. Quantitative data was compared by One-way ANOVA. The correlation between numerical variables was achieved by Spearman’s correlation. A p-value < 0.05 reflected significance.

### RESULTS

There were 240 identified infertile male IUI patients. Patients’ average ages ranged from  $35.5 \pm 6.1$  years with BMI of  $26.4 \pm 3.5$  kg/m<sup>2</sup>. Two hundred and twenty-one were Malay (92.1%), and 19 were non-Malays (7.0%). Of these, 185 patients (77.1%) were primary infertile, 55 patients (22.9%) were secondary infertile, 171 participants (71.3%) were non-smokers and 69 (28.8%) were current cigarette smokers. Semen analysis showed that the mean semen volume was  $3.0 \pm 1.3$  ml, total sperm count was  $122.6 \pm 118.5$  ( $\times 10^6$ /ejaculate), sperm

concentration was  $43.0 \pm 37.6$  ( $\times 10^6/\text{ml}$ ), sperm vitality was  $74.9 \pm 16.5$  %, total motile spermatozoa was  $63.0 \pm 12.6$  % and normal morphology was  $9.8 \pm 4.8$  %.

Eighteen (7.5%) of the 240 male patients had successful IUI resulting in pregnancy, while 222 (92.5%) had unsuccessful pregnancies. The comparative demographics of the two groups, stratified on fertility results, showed the group with successful pregnancy following IUI was younger, and had lesser BMI, and higher semen parameters than the group that had unsuccessful pregnancy (Table 1).

Table 1: Demographic findings of male subjects who underwent Intrauterine Insemination stratified on pregnancy outcomes.			
Intrauterine Insemination Outcomes			
Variable	Successful Pregnancy (n=18)	Unsuccessful Pregnancy (n=222)	P value
Age at diagnosis (years)	35.2 $\pm$ 4.2	36.6 $\pm$ 4.1	0.33
Body Mass Index (kg/m <sup>2</sup> )	24.6 $\pm$ 3.5	25.9 $\pm$ 3.4	0.62
Abstinence (days)	3.7 $\pm$ 2.1	4.3 $\pm$ 3.5	0.52
Types of infertility			
Primary	14 (7.6%)	171 (92.4%)	1
Secondary	4 (7.3%)	51 (92.7%)	
Semen parameters			
Volume (milliliters)	3.2 $\pm$ 0.4	3.1 $\pm$ 0.2	0.53
Total count (10 <sup>6</sup> /ejaculate)	155.0 $\pm$ 113.1	117.8 $\pm$ 113.0	0.08*
Concentration (10 <sup>6</sup> /ml)	58.4 $\pm$ 43.7	40.8 $\pm$ 35.7	0.14
Viability (% alive)	80 $\pm$ 10.4	74.6 $\pm$ 15.7	0.15
Total motile spermatozoa (%)	65.3 $\pm$ 6.9	61.9 $\pm$ 12.3	0.21
Normal forms (%)	11.4 $\pm$ 6.2	9.4 $\pm$ 4.6	0.32

P value  $\leq$  0.05 taking significant

There were 33 patients classified as having a normal BMI, 37 as overweight, and 170 as obese according to BMI categories. Normal BMI group showed all semen parameters lower than the obese group (Table 2). A trend of decreasing semen parameters has been noted with increased BMI.

**Table 2: Semen analysis of males who underwent Intrauterine Insemination stratified on BMI**

Semen parameters	Normal Weight (18 – 22.9 kg/m <sup>2</sup> ) (n=33) Mean $\pm$ SD	Overweight (23 – 24.9 kg/m <sup>2</sup> ) (n=37) Mean $\pm$ SD	Obese (>25 kg/m <sup>2</sup> ) (n=170) Mean $\pm$ SD	P value
Volume (milliliters)	3.4 $\pm$ 1.4	3.1 $\pm$ 1.2	2.8 $\pm$ 1.1	0.07
Total count (10 <sup>6</sup> /ejaculate)	131.5 $\pm$ 96.1	126.1 $\pm$ 80.4	121.0 $\pm$ 84.5	0.85
Concentration (10 <sup>6</sup> /ml)	46.5 $\pm$ 38.2	44.2 $\pm$ 34.8	40.7 $\pm$ 36.7	0.66
Viability (% alive)	75.4 $\pm$ 7.9	75.1 $\pm$ 13.6	74.9 $\pm$ 17.1	0.81
Total motile spermatozoa (%)	66.7 $\pm$ 8.2	64 $\pm$ 8.3	62.2 $\pm$ 13.0	0.18
Normal forms (%)	10.8 $\pm$ 5.6	10.6 $\pm$ 4.5	9.3 $\pm$ 4.6	0.17

P value  $\leq$  0.05 taking significant

Spearman's correlation showed that semen volume and BMI were significantly inversely correlated ( $r = -0.14$ ,  $p = 0.03$ ). Our findings indicate that when BMI increased, the overall number of motile spermatozoa and their normal forms also reduced. Furthermore, age showed an inverse relationship with semen volume ( $r = -0.19$ ,  $p < 0.05$ ), vitality ( $r = -0.31$ ,  $p < 0.05$ ), and total motile spermatozoa ( $r = -0.24$ ,  $p < 0.05$ ).

## DISCUSSION

There was no evidence of a significant impact of the infertile male's age, BMI, or semen characteristics on the success of IUI. Pregnancy was accomplished with young age, low BMI, and high-quality semen parameters.

Our study is contradicted by Tatsumi et al.<sup>7</sup>, where male age alone did not affect pregnancy outcomes in couples having IUI after confounding variables have been considered. Further, no significant correlation between any of the semen parameters and pregnancy after IUI supports our study.<sup>10</sup> There is a lack of literature analyzing the relationship between paternal BMI and pregnancy outcome of IUI. Nevertheless, when the female's BMI is within the normal range, a couple's risk of

infertility increases with the high BMI of infertile males.<sup>11</sup>

Volume and concentration of semen along with the total count, vitality, motility and normal morphology were less in the obese and overweight category however, results were insignificant. Similar findings were reported in a paper by Puri et al.<sup>12</sup>

In our study, an inverse relationship between semen volume and BMI has been established. A negative correlation of semen volume, concentration and motility with BMI was demonstrated.<sup>13</sup> Nevertheless, an association of BMI with sperm concentration, motility, or normal forms was not found to be significant by Sekhvat & Moein.<sup>14</sup> Results of another study also showed an association between BMI and semen volume, contradicting our findings.<sup>13</sup>

The relationship of age with semen parameters has been the subject of disagreement across several studies. According to the current analysis, there is a statistically significant inverse relationship between age and semen volume, vitality, and total motile spermatozoa. Our results are consistent with Verón et al., which demonstrated an inverse relationship between male age and the above-mentioned variables.<sup>15</sup>

Our study had several strengths that are important to note. All patients underwent identical IUI procedures which were carried out in a single institution setting, reflecting standardized results. The IUI success rates also largely match the literature, so this is good evidence that it is consistent and not an outlier. The substantial and thorough records maintained in “Bruneian healthcare data”, (Bru-HIMS), allow the acquisition of more complete data sets. This is the first study highlighting such findings from the Bruneian population.

Nevertheless, the study is limited to a single institution, thus the small sample size may not accurately depict the true correlations of the various male variables in infertility on the success of IUI.

## CONCLUSION

Young and normal-weight infertile male subjects had a greater chance of a successful IUI as depicted by a positive pregnancy outcome. To validate these results, larger studies are warranted however, awareness to plan for infertility treatments at a younger age with lifestyle modification is the key message from our study.

**Acknowledgements:** All authors would like to acknowledge the PAPRSB Institute of Health Sciences Dean for his support and Dr Mitra Dhanaraj for her intellectual input

**Declarations:** This article is a part of the Special Study module report.

**Conflict of interest:** none to declare.

**Funding Source:** None

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#### ***Author Contributions:***

**Aeryza Sufiri:** conceived the study designed, carried out the data collection and statistical analysis and drafted the manuscripts.

**Rehana Rehman:** Participated in its design and coordination. drafted, read and approved the final manuscript.

**Faiza Alam:** Participated in its design and coordination. Statistical analysis, drafted, read and approved the final manuscript.

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Date of Submission: 06-02-2024

Revised Date: 18-03-2024

Accepted Date: 20-05-2024