Intrauterine insemination (IUI) has latterly become less important in reproductive medicine. The aim of this retrospective analysis was to identify and evaluate the success rates of repeated insemination cycles in women of different ages. All women who underwent intrauterine insemination in the Wiesbaden Fertility Clinic between 1998 and 2010 were included in the analysis. Additional inclusion criteria were: not more than 45 years old, previous FSH stimulation and slight to moderate subfertility of the male partner. A total of 4246 insemination cycles in 1612 patients were included in the analysis. The average number of IUI cycles per patient was 2.24 (1–14). Patient age ranged from 19 to 45 years (mean: 33.9 years). Logistic regression analysis showed a drop in pregnancy rates with increasing age (p = 0.000). However, for the first three cycles the pregnancy rates for women aged 40 and 41 did not differ from those of women aged between 35 and 39 years. Overall pregnancy rates were stable in women up to the age of 40, even after several insemination cycles (7.5 and 10%). Insemination is therefore still an effective procedure in selected patients. Stable pregnancy rates were recorded even after more than 3 cycles. After 3 cycles, the success rates for women aged 40 and 41 did not differ from those of women below the age of 40.
Introduction

The term “intrauterine insemination” (IUI) is used to describe the transfer of sperm into the uterus. It is one of the oldest techniques of reproductive medicine, first performed in 1790 by the English physician Dr. John Hunter and described by Home in 1799 [1]. The current practice of intrauterine insemination comprises sorting and washing the sperm, determining the optimal time of conception and introducing the sperm into the uterine cavity. In many cases, women additionally undergo controlled ovarian stimulation to trigger ovulation. The prerequisite for successful insemination is an intact tubular and uterine transport system, sufficient numbers of healthy sperm, and guaranteed ovulation. Intrauterine insemination should not lead to any delay in attempting more effective procedures. Intrauterine insemination is less widely used than other, more effective but much more invasive procedures in reproductive medicine such as in vitro fertilisation (IVF) and intracytoplasmic sperm injection (ICSI). In 2008, 21,000 IUI cycles were carried out in Germany in addition to 42,958 IVF and ICSI cycles [2]. Intrauterine insemination can be a successful procedure in selected patients. Acceptance of IUI by patients is high as it is similar to natural insemination and is perceived to be a less invasive intervention in the couple's reproductive life.

Since 2004, § 27a of the SGB V (German Code of Social Law) requires statutory health insurance companies in the Federal Republic of Germany to contribute to the costs of 3 insemination cycles for women in different age groups. Statistical analysis was done using the statistical software programme SPSS 18. Logistic regression analysis was used to calculate the impact of maternal age on becoming pregnant. The odds ratio was calculated. The level of significance α was set at 5%.

Method

Between 1998 and 2010, the Wiesbaden Fertility Clinic carried out a total of 6053 homologous intrauterine inseminations in 2262 patients. Insemination was only done after previous examination found no indications of tubular damage. All patients were ovulating, either as part of their natural cycle, or following low-dose FSH stimulation or stimulation with clomifene. Ovulation was triggered by the administration of human chorionic gonadotropin (hCG).

Inclusion criteria for this retrospective analysis were a maximum patient age of 45 years, limited sperm motility of the patient’s partner and stimulation with FSH. A total sperm count of at least 20 million/ml and a motility of at least 35% were required for insemination. A total of 4246 insemination cycles in 1612 women were included in the analysis. The average number of IUI cycles per patient was 2.24 (1–14). In this patient cohort, 158 patients became pregnant more than once through insemination. A second insemination after a previous pregnancy was classified as a first cycle, so that 1770 “treated cases” were evaluated overall. Previous treatments in other fertility clinics were not included in this analysis.

Preparation of the ejaculate consists of washing and the swim-up technique. Washing of the ejaculate is done to separate sperm cells from seminal plasma. Washing is done by mixing and centrifuging the ejaculate with a culture medium. After the heavier spermatozoa collect at the bottom, the remaining liquid are siphoned off and the spermatozoa are mixed and diluted with another culture medium for direct use. In a further preparation step termed “swim-up”, the washed semen is centrifuged again and the supernatant siphoned off. The remaining sperm are mixed with a culture medium. The motile sperm swim upwards and can be directly aspirated with a catheter [3]. The insemination cycles were analysed retrospectively. Patient age, number of insemination cycles carried out till pregnancy or until this form of treatment was abandoned and pregnancy rates were included in the analysis. The study was approved by the Ethics Commission of the Johannes-Gutenberg University. All patients gave their informed consent to the study.

Aim of the study was to identify the benefit of repeated insemination cycles for women in different age groups. Statistical analysis was done using the statistical software programme SPSS 18. Logistic regression analysis was used to calculate the impact of maternal age on becoming pregnant. The odds ratio was calculated. The level of significance α was set at 5%.

Results

Average patient age was 33.9 years at the start of therapy. Age range of patients was from 19 to 45 years. Patients were grouped into age groups to show age distribution. Both the pregnancy rates per cycle and the pregnancy rates per patient decreased significantly with increased age (Table 1).

Patient age had a statistically measurable impact on pregnancy rates. Logistic regression analysis showed a drop in pregnancy rates with increasing age (p < 0.000, CI: 0.905–0.962). The likelihood of becoming pregnant after insemination dropped by 6.7% in the analysed age groups, with an odds ratio of 0.933 per additional year of life.

Younger women had fewer insemination cycles than older women. Patients below the age of 25 years underwent an average of 1.91 cycles while women aged more than 43 years had an average of 2.42 cycles (Table 1). Pregnancy rates remained stable even after several insemination cycles. Up until cycle 7, pregnancy rates were between 7.5 and 10%. The number of patients...
who underwent more than 3 cycles had already dropped significantly by the 4th cycle (Table 2).

Table 3 shows the pregnancy rates per insemination cycle depending on maternal age. It is notable that the pregnancy rates of patients aged 40 and 41 did not differ from those of patients aged between 35 and 39. The success rates were similar for both groups up until the 3rd cycle. This is also shown in Fig. 1 which depicts the cumulative pregnancy rates for each age group.

### Discussion

Age has an important impact on the success rates after insemination. The pregnancy rate per patient was significantly higher for women below the age of 25 compared to women aged 35 to 39. Pregnancy rates gradually decrease over the course of a patient’s life. The difference between the youngest group of patients aged less than 25 years and the next group aged between 25 and 29 was very noticeable. There was a similar drop in pregnancy rates in the group aged more than 41 years compared to the group of patients aged 40 or 41. In the group of patients aged 40 and 41 there was still a concrete likelihood of becoming pregnant comparable to that for the group aged 35 to 39. Up until the 3rd cycle, the pregnancy rates of patients aged 40 or 41 did not differ from those of patients between 35 and 39 years of age. These data show that insemination therapy is still justified in patients aged 40 and 41. The data presented here confirm the results of many other studies [4–7], which have all described the impact of increasing age on the success of insemination.

Among the group of patients below the age of 25, no further pregnancies occurred after 2 insemination cycles. This could be an indication that their unfulfilled wish to have a child could have another cause, for example, that male subfertility was more pronounced than originally supposed. Our data suggest that it may not be useful to carry out more than 2 insemination cycles in these young patients. In all other patient groups below the age of 40, pregnancy rates per cycle averaged between 5 and 15% up until the 6th insemination. In women aged more than 40, only a few pregnancies were achieved after the 3rd attempt. Other working groups have recommended between 3–9 insemination cycles per couple [8–10].

The interpretation of the data in this study is complicated by the fact that out of a total of 1770 patients, only 218 underwent more than three attempts at insemination. This is most probably due to the fact that since 2004 statutory health insurance companies in Germany are not obliged to fund more than 3 cycles. The 4th to 6th insemination cycles continued to result in good pregnancy rates in women below the age of 40; however, the patient cohort...
undergoing these insemination cycles was significantly smaller than that in the first 3 cycles. Currently, statutory health insurance companies in Germany contribute to the costs of 3 insemination cycles after stimulation with FSH in women up to the age of 40. Our data shows that pregnancies in these patients can still result after additional insemination cycles. The chances of success for these later cycles correspond to those for the first 3 insemination cycles. In patients aged 40 and 41, a successful pregnancy is most likely with 3 insemination cycles. After more than 3 insemination cycles, pregnancies only occurred in isolated cases.

**Conclusion**

Intrauterine insemination can be a promising therapy in selected patients. Pregnancy rates for patients aged 40 years remained stable even after more than 3 cycles, up until 6 cycles. For the first 3 insemination cycles, the success rates for women aged 40 and 41 did not differ from those of women under 40. However, no more than 3 insemination cycles should be attempted in these women. The overall pregnancy rates after insemination were 5–15% and thus clearly lower than those obtained with more invasive reproductive methods such as IVF or ICSI, as demonstrated by data from the German IVF Registry [2]. Patients seeking to become pregnant should be given detailed information about this point. It could play an important role in the choice of method by older couples.

**Conflict of Interest**

None.

**References**


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