


# Endometrial Status and Embryonic Implantation about 150 Cases at the Medically Assisted Procreation Laboratory “Le Diafounou”

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## Abstract

**Background:** The endometrium is the tissue that lines the inside of the uterus. It undergoes multiple changes during the menstrual cycle and prepares to welcome the fertilized egg. Endovaginal ultrasound is a first-line examination in the assessment of female infertility. **Objective:** We aimed to determine the impact of endometrial status by endovaginal ultrasound on the outcome of embryo transfers. **Subjects and Methods:** This was a prospective cross-sectional study of 150 women collected between January and October 2020 at the “Le Diafounou” medically assisted procreation laboratory. Were included in the study, women presenting for desire of pregnancy and having continued the treatment until the transfer of fresh or frozen embryos. An uterine score was used. This score took into account the thickness of endometrium, its coffee bean aspect, the presence of the notch, the echogenicity of the endometrium, the pulsatility index, the presence of the flow at the end of diastole and sub-endometrial flow. Ultrasounds were performed using a General Electric logic 500, logic 9 and Voluson E8 device. The data was entered into Excel and then analyzed using SPSS version 21. **Results:** 150 women were selected for the study. 83 women or 55.3% were between 17 and 35 years old and 44.7% were over 35 years old with an upper limit of 50 years old. The number of women who became pregnant was 69% or 46%. The average thickness of the endometrium was 11.40 mm with extremes of 4.65 mm and 18.6 mm. There was a correlation between the thickness of the endometrium

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and obtaining a pregnancy ( $p < 0.005$ ). 133 women had a homogeneous endometrium, *i.e.* 88.7%. The pulsatility index was relatively low for those who started a pregnancy, *i.e.* 90%. The high pulsatility index is one of the reasons for the failure of embryo implantation. The correlation was significant ( $p = 0.009$ ). 141 women had no notch in the uterine arteries, *i.e.* 94%. 94 women or 62.7% had a triple line endometrium or typical coffee bean appearance. End-diastolic flow was observed in 127 women, *i.e.* 84.7%. The sub-endometrial flow was found in 128 women or 85.3%. **Conclusion:** The Knowledge of the status of the endometrium is essential and has an impact on the outcome of embryo transfers. The thinner (<7) or thicker the endometrium, the higher the failure rate. Optimal endometrial thickness is needed (>7 and <15). Doppler factors also play an important role.

### Keywords

Endometrial Status, Embryonic Implantation, Medically Assisted Procreation

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## 1. Introduction

Infertility has become a public health problem, especially in developing countries where resources are limited. *In Vitro* Fertilization (IVF) and Intra Cytoplasmic Sperm Injection (ICSI) are offered as alternative choices for infertile or subfertile couples. Endometrial receptivity is important for the outcome of transferred embryos. The endometrium is the tissue of embryo implantation. We know that the treatments administered during IVF can be responsible for a negative maturation asynchrony for the implantation of the embryo [1]. It is under the influence of ovarian hormones.

At the beginning of each menstrual cycle, it thickens and becomes richly vascularized to eventually be able to accommodate an embryo during implantation. It is then sometimes called uterine lace [2]. The search for improving the implantation rate of embryo transfer resulted in defining embryo quality standards, making it possible to select embryos with the best potential for implantation. A favorable uterine environment is the other primordial factor of successful embryo implantation.

In addition to the endometrial thickness, which is a traditional criterion, many sonographic parameters likely to reflect the uterine receptivity state must be studied. Lots of studies dealt with their predictive value and practical interest [3]. The thickness, the triple line aspect where we can see three leaflets, the homogeneity, the hemodynamic aspect with color Doppler, *i.e.* the pulsatility index of the uterine arteries, the end-diastolic flow, the blood flow under -endometrial and the presence or absence of notch are all factors taken into account and which can influence the result of the embryo transfer [3]. In the event of failure of the embryo implantation, many factors can be incriminated, such as hormonal and genetic assessments and endometrial biopsy. Endometrial failure factors are treated according to the causes [3].

The first studies which were interested in the thickness of the endometrium measured, either on the day of the onset of ovulation or that of the embryo transfer, were very enthusiastic about the predictive value of this criterion. They were followed by as many contradictory results [4], and today, the thickness of the endometrium is no longer considered a sufficient predictive criterion for embryo implantation. It should be remembered that the thickness of the endometrium does not reflect the quality of the endometrial tissue, it is ultrasound data and not histological.

This is why we initiated this study in order to bring the role of other parameters to give more clarification to the previous studies in order to allow an increase in the rate of pregnancy.

## 2. Materials and Methods

This was a prospective cross-sectional study involving 150 women collected between January and October 2020 at the “Le Diafounou” medically assisted procreation laboratory. Were included in the study were women presenting for desire of pregnancy and having continued the treatment until the transfer of fresh or frozen embryos. Were not included those who did not undergo IVF or whose treatment was interrupted or those who did not agree to participate in the study. To do this, a uterine score was used. This score takes into account the thickness of the endometrium, its coffee bean or triple line appearance, the notch of one or both uterine arteries, the echogenicity of the endometrium, the pulsatility index, the presence of end-diastolic flow and sub-endometrial flow. To this score, we added the age of the participants. These parameters were taken from the work of the Medically Assisted Procreation (PMA) team in Montpellier [2] and are measured by endo-vaginal ultrasound during the last ultrasound, *i.e.* the day ovulation is triggered. On behalf of *in Vitro* Fertilization (IVF) or Intra Cytoplasmic Sperm Injection (ICIS) for fresh embryos and the day before or the day of transfer for frozen embryos. The endometrium was measured at its thickest part and perpendicular to the midline. Informed consent of the participants was requested and obtained before any inclusion. The data was entered into Excel and then analyzed using SPSS version 21.

## 3. Results

### 3.1. Distribution of Patients According to Whether Pregnancy was Achieved

Of the 150 women, 69 had a pregnancy, a success rate of 46% (Table 1).

**Table 1.** Distribution of patients according to the occurrence or not of pregnancy.

PREGNANCY	NUMBER	POURCENTAGE %
YES	69	46%
NO	81	54%
<b>TOTAL</b>	<b>150</b>	<b>100%</b>

### 3.2. Distribution of Patients According to Age Group

150 women were selected for the study. 83 women or 55.3% were between 17 and 35 years old and 44.7% were over 35 years old with an upper limit of 50 years old. The average age was 33 years old (Table 2).

The age of the participants was decisive because the age group of 17-35 years having had a pregnancy was 59.42% against 40.58% for the age group over 35 years ( $p < 0.005$ ).

### 3.3. Distribution of Patients According to Endometrial Thickness

Our study shows that 50 women or 72.4% of those who obtained a pregnancy had an endometrium of thickness between 8 and 13 mm (Table 3). This shows that endometrial thickness is a very important factor in implantation after embryo transfer. The thinner the endometrium, the lower the chances of implantation. Thicker endometria are also less likely. There is therefore a correlation between the thickness of the endometrium and obtaining a pregnancy ( $p < 0.005$ ).

**Table 2.** Distribution of patients according to age group.

AGE	NUMBER	POURCENTAGE %
17 - 35 YEARS	83	55.30%
>35 YEARS	67	44.70%
<b>TOTAL</b>	<b>150</b>	<b>100%</b>

**Table 3.** Distribution of patients according to endometrial thickness and occurrence of pregnancy.

PREGNANCY	YES	NO	TOTAL
<b>ENDOMETRIAL THICKNESS</b>			
THIN (<8 mm)	07 (10.1%)	24 (29.6%)	31 (20.6%)
OPTIMAL (8 - 13 mm)	50 (72.4%)	46 (56.8%)	96 (64.0%)
THICK (>14 mm)	12 (17.4%)	11 (13.6%)	23 (15.3%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>



**Figure 1.** (a) Thin endometrium (< 8 mm); (b) Optimal endometrium (8 mm); (c) Thick endometrium (>14 mm).

### 3.4. Distribution of Patients According to the Appearance of the Endometrium and the Occurrence of Pregnancy

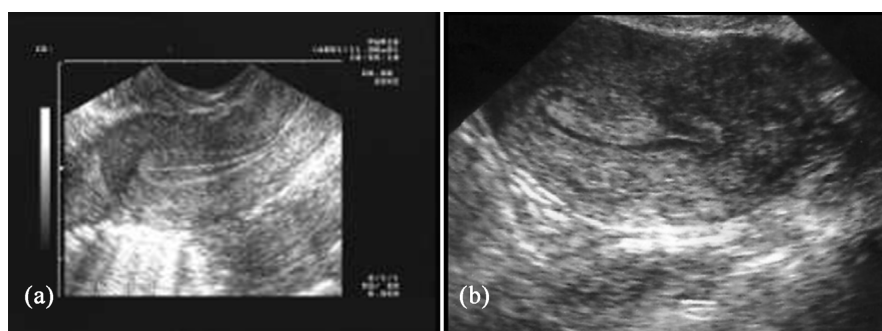
Of the 150 participants, 94% or 62.7% had a triple line or “coffee bean” aspect of the endometrium and 68.1% of them became pregnant (**Table 4**). Those that had another appearance included polyps, adenomyosis, myomas, etc. and had lost this triple line appearance, the difference was not significant ( $p > 1$ ).

### 3.5. Distribution of Patients According to the Presence of Notch of One or Both Uterine Arteries

Notch is a drop in blood supply to one or both uterine arteries. It is a pro-diastolic notch on the Doppler spectrum. In our study, 141 women or 94% had no notch and only 9% or 6% had a notch (**Table 5**). 94% of those who had the pregnancy had no notch (**Table 5**). The presence of the notch is a poor prognosis for the implantation of the embryo because its existence is evidence of high resistance at the level of the distal part of the spiral arteries. In our study, no

**Table 4.** Distribution of patients according to the appearance of the endometrium and the occurrence of a pregnancy.

PREGNANCY	YES	NO	TOTAL
<b>ENDOMETRIAL APPEARANCE</b>			
TRIPLE LINE- COFFEE BEAN	47 (68.1%)	47 (58%)	94 (62.7%)
OTHER ASPECT	22 (31.9%)	34 (42%)	56 (37.3.0%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>



**Figure 2.** (a) Triple line endometrium; (b) Endometrium with polyp

**Table 5.** Distribution of patients according to the presence or no notch and the occurrence of pregnancy.

PREGNANCY	YES	NO	TOTAL
<b>NOTCH</b>			
PRESENT	04 (6%)	05 (06%)	9 (06%)
ABSENT	65 (94%)	76 (94%)	141 (94%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>

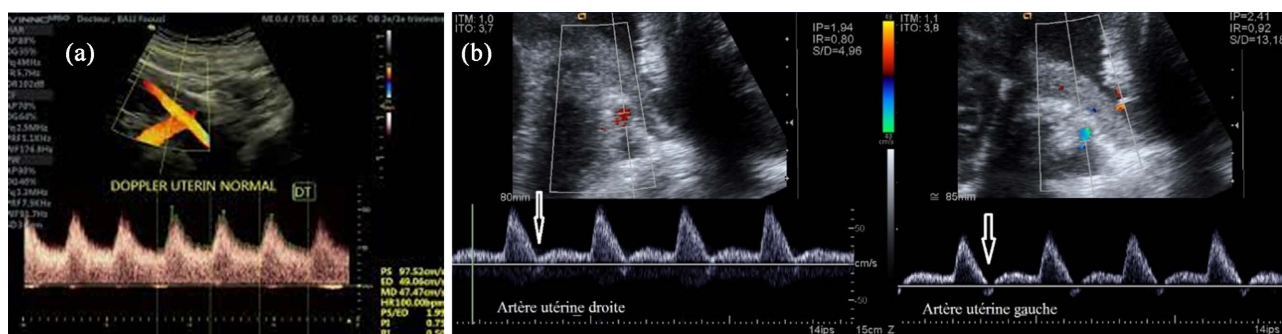
link was found between the presence of the notch and implantation failure ( $p = 1.00$ ).

### 3.6. Distribution of Patients According to the Pulsatility Index of the Uterine Arteries

The pulsatility index was relatively low (between 1.5 and 2) for those who started a pregnancy, *i.e.* 90% (Table 6). The high pulsatility index is one of the reasons for the failure of embryo implantation. The correlation is significant ( $p = 0.009$ ).

### 3.7. Distribution of Patients According to the Presence of End-Diastolic Flow

End-diastolic flow was recorded in 127 women, *i.e.* 85%. This flow indicates good endometrial perfusion and indicates the absence of vascular occlusion (Table 7). A normal uterine spectrum is characterized by a high diastolic residual flow. All participants who became pregnant had good end-diastolic flow. There is a relationship between the presence of end-diastolic flow and embryo



**Figure 3.** (a) Normal Doppler spectrum of the uterine artery; (b) Protodiastolic notch of the uterine artery.

**Table 6.** Distribution of patients according to the pulsatility index (PI) of the uterine arteries and the occurrence of pregnancy.

PREGNANCY	YES	NO	TOTAL
<b>PULSATILITY INDEX (PI)</b>			
PI BETWEEN 1.5 AND 2	62 (90%)	59 (73%)	121 (80.7%)
PI > 3	7 (10%)	22 (27%)	29 (19.3%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>

**Table 7.** Distribution of patients according to the presence of end-diastole flow and the occurrence of a pregnancy.

PREGNANCY	YES	NO	TOTAL
<b>END-DIASTOLE FLOW</b>			
PRESENT	60 (87%)	67 (82.7%)	127 (85%)
ABSENT	9 (13%)	14 (17.3%)	23 (15%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>



implantation ( $p < 0.005$ ).

### 3.8. Distribution of Patients According to the Presence of Subendometrial Flow

Color Doppler ultrasound allows an assessment of endometrial receptivity in ART and in particular in *in vitro* fertilization, by visualizing the sub-endometrial flow (during the cycle, an invasion of the endometrium by small vessels from the myometrium is observed). The better the sub-endometrial flow, the better the endometrial receptivity.

This phenomenon was observed in 87% of our participants who became pregnant (Table 8). In our case, no link was found between the presence of sub-endometrial flow and the occurrence of pregnancy ( $p = 1$ ). (Figure 4)

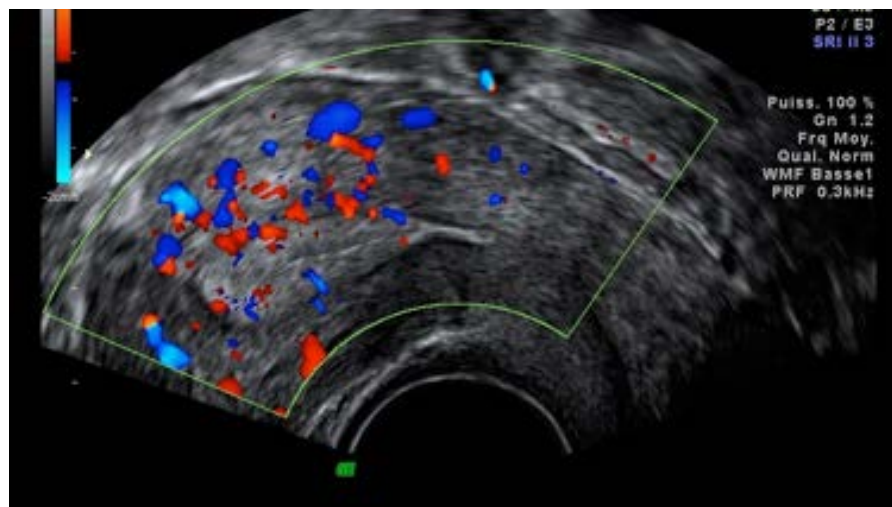
## 4. Discussion

In our context, few studies have been carried out on the endometrium. This is due to the scarcity of assisted reproduction centers in Mali and also the lack of knowledge on the impact of follicle-stimulating hormones on the thickness of the endometrium.

Our study involved 150 women, 69 of whom had a pregnancy, a success rate of 46%. This rate is comparable to that of Hans Arce [4] *et al.* in 2015 who found

**Table 8.** Distribution of the patients according to the presence of sub-endometrial flow and the occurrence of pregnancy.

PREGNANCY	OUI	NON	TOTAL
<b>SUBENDOMETRIAL FLOW</b>			
PRESENT	60 (87%)	68 (84%)	128 (85%)
ABSENT	09 (13%)	13 (16%)	22 (15%)
<b>TOTAL</b>	<b>69 (100%)</b>	<b>81 (100%)</b>	<b>150 (100%)</b>



**Figure 4.** Pre-ovulatory sub-endometrial flow (D12).

48.6% success rate and K.E. LIU *et al.* [5] who found 43.2% in their series in 2018.

Of the 150 women in our study, 83 women or 55.3% were between 17 and 35 years old and 44.7% were over 35 years old with an upper limit of 50 years old. The average age was 33 years old. This rate is lower than that of Haouzi D. and Hamamah S. who found 62% of patients under 35 years old. Age is a determining factor in endometrial receptivity because in our study 59.42% of patients had a pregnancy and the relationship was significant ( $p < 0.005$ ).

Our study shows that 50 women or 72.4% of those who obtained a pregnancy had an endometrium of thickness between 8 and 13 mm. Staessen C *et al.* [6] found in 2004, 70.25% pregnancy rate with an endometrial thickness between 07.50 mm and 12 mm and Weissman *et al.* [7] found a low pregnancy rate with an endometrium of more than 14 mm. This shows that endometrial thickness is a very important factor in implantation after embryo transfer. The thinner the endometrium, the lower the chances of implantation. Thicker endometriums are also less likely. There is therefore a correlation between the thickness of the endometrium and obtaining a pregnancy ( $p < 0.005$ ).

68.1% of those who started a pregnancy had a trifoliate aspect of the endometrium (triple line or type I). Fanchin *et al.* [8] found a 59% pregnancy rate with a trifoliate endometrium in their series in 2000. This aspect is the optimal aspect sought because the chances of pregnancy are relatively high. The difference was not significant ( $p > 1$ ).

Our study showed that 94% of women who started a pregnancy had no notch. Ardaens Y. *et al.* [9] reported 83% pregnancy rate without notch, just as Maurice N. Cauchi *et al.* [10] found a low pregnancy rate with the presence of notch. In our study, no link was found between the presence of the notch and implantation failure ( $p = 1.00$ ).

90% of our respondents who became pregnant had a relatively low pulsatility index (between 1.5 and 2). Steer *et al.* [11] and Zaidi J. [12] had only low pregnancy rates in their study with pulsatility indexes above 3 and above. The high pulsatility index is one of the causes of embryo implantation failure ( $p = 0.009$ ). The same authors had similar results for the presence of sub-endometrial flow and end-diastolic flow. These last elements sign a good blood circulation in the utero-ovarian vessels.

## 5. Conclusion

Endometrial receptivity is the key factor in the success or failure of embryo implantation. The endometrium changes during the cycle under hormonal influence. Its different aspects and its vascularization must be studied for a favorable outcome of medically assisted procreation.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.



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