

Hysteroscopy: The uterine stethoscope- Decoding implantation failures

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Aim and Objectives

1. To study the rationale of hysteroscopic diagnosis and treatment of intrauterine pathologies in patients with previous ART Failures
2. To compare hysteroscopic diagnosis and treatment of intrauterine pathologies in patients with previous ART failures to No ART Failure.
3. To study the impact of hysteroscopic treatment in improving implantation rates in IVF cycle.

Introduction

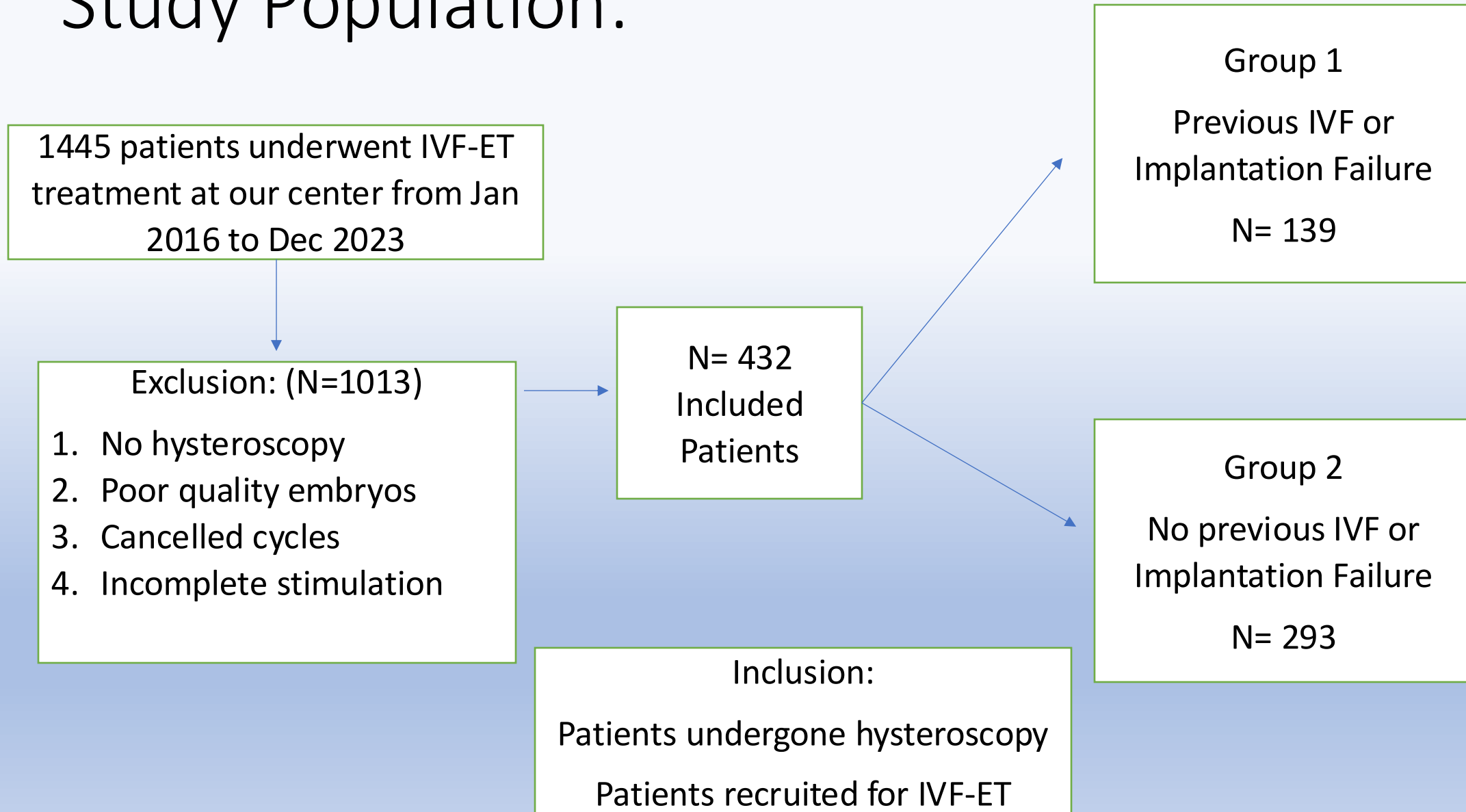
- Many studies support the notion that uterine cavity and endometrial integrity must be evaluated primarily by hysteroscopy in infertile population³⁻⁸.
- On the other hand, many authors consider hysteroscopy as a complementary procedure in case abnormal findings are detected by other modalities^{2,9-12}.

- But what about those pathologies which are not detected on ultrasound?

Endometritis

- With this background, we recruited the patients for this study.

Study Population:



Treatment plan and diagnosis of Intrauterine pathologies:

- All of the included patients were in direct follow-up with one of the authors of this study.
- A standard protocol of transvaginal ultrasound (TVS) assessment of the uterus and adnexa was performed on every patient on day 2 of their menstrual cycle followed by standardized protocols for ovarian stimulation followed by, ovum-pick up during their treatment cycle.
- Freeze-all protocol for embryos was followed for all included patients.
- In the subsequent cycles before embryo transfer, TVS was performed again to document any pathology.
- Hysteroscopy was performed in the proliferative phase of menstrual cycle.
- After the procedure and relevant treatment FET was performed. Embryos of quality 3AA and above were transferred.

- Hysteroscopy was performed by either one of the authors.
- We used 2.9 mm telescope with 30-degree angle with operating sheath by Karl Storz, Germany for all procedures.
- Saline was used as the distension media.
- A 400-watt LED light source by Haeger Germany was used with 1188 High Definition Camera system by Stryker was used with Vision Pro 26 LED Display Screen.

The exploration of the uterine cavity started with the panoramic view of the cavity followed by both ostia, endometrium and cervix.

- Digital photograph at all check-points were taken.
- Abnormalities in the endometrium were noted as focal or diffuse hyperemia, micro-polyps, endometrial polyp, adhesions and stromal edema.
- These findings were classified as Chronic endometritis (tubercular/ non-tubercular) after histopathological confirmation from the endometrial sample.
- Other findings such as septum (partial/ complete), submucous myoma or other mullerian anomalies previously diagnosed were noted and surgically corrected.

Statistical Analysis:

We made contingency tables as to see the relationship between different parameters using frequency and percentage.

We used Chi square test of independence to check if the relationship found in the contingency table is significant or not as 5% level of significance.

Results- Baseline parameters:

| S. No | Parameter | Results |
|-------|----------------------------------|-----------------|
| 1. | Total number of studied patients | N= 432 |
| 2. | Median Age Both groups | 30 years |
| 3. | Primary infertility | 77.1% |
| 4. | Secondary Infertility | 22.9% |
| 5. | Overall Implantation rate | 47% (n= 203) |
| 6. | Overall Live birth rate | 27.3% (n= 118) |
| 7. | Mullerian Anomalies detected | 24.3% (n=105) |
| 8. | Chronic Endometritis detected | 59.25% (n= 256) |

| S. No | Group 1 | Group 2 | P value |
|---|---------------------|----------------------|---------|
| Intrauterine pathology detected | | | |
| 1. | 70.5% (n=98 of 139) | 79.9% (n=234 of 293) | <0.0031 |
| Endometritis detected | | | |
| 2. | 51.1% (n=71 of 139) | 63.1% (n=185 of 293) | <0.017 |
| Implantation Rates with Endometritis diagnosis | | | |
| 3. | 47.9% (n=34 of 71) | 46.5% (n=86 of 185) | - |
| Implantation Rates with Other Pathologies | | | |
| 4. | 45.9% (n=45) | 47.9% (n=112) | - |

1. Intrauterine pathology- polyp, intrauterine infections, sub endometrial collection, calcification, intrauterine adhesions, submucous myoma, endometritis or mullerian anomaly. Not all of these pathologies were detected on ultrasound prior to hysteroscopy. This may be due to the absence of 3D ultrasound or a lower resolution of ultrasound machine or operator bias.

2. Endometritis- These patients did not have any ultrasound abnormality detected beforehand. This result shows that there is a significant role of performing hysteroscopy even without an obvious indication of intrauterine pathology diagnosed on ultrasound

3. With this result, we can conclude that 100% patients in group 1 had experienced failure in their past cycles. Out of which, 47.9% patients in the current cycle became pregnant. This shows that offering hysteroscopy and diagnosing endometritis has a positive impact on implantation rate.

Discussion

The accuracy of diagnosing intrauterine pathologies through 2D and 3D Ultrasound has been revolutionary. However, even today, pathologies are missed and some can simply not be identified on ultrasound (endometritis).

This is where hysteroscopy comes to play.

If we compare the cost effectivity of performing hysteroscopy versus experiencing IVF Failure, there will be no doubt that performing hysteroscopy is the cost-effective choice.

In our study, we found that 51.1% (n= 71 of 139) of the patients who had experienced IVF Failure in previous cycles were diagnosed with chronic endometritis and treated before the next transfer.

Of these 47.9% (n= 34 of 71) patients had a positive implantation rate in their subsequent cycle.

This data shows that nearly half of the patient with previous IVF failure had endometritis, not diagnosed otherwise, were treated and got a positive result!

Our results were comparable with the results found in the study by Cicinelli et al in 2015¹³ where 56.8% women with infertility presented with chronic endometritis. In women with Recurrent Implantation Failure (RIF) this prevalence is as high as 67.5%¹⁴

63.1% (n=185 of 293) of patients without previous IVF failure, in our study were detected and treated for chronic endometritis.

Of these 46.5% (n=86 of 185) patients had positive implantation in their first IVF cycle attempt!

These were the patients in whom ultrasound revealed no intrauterine pathology when performed prior to procedure.

To the best of our knowledge impact of chronic endometritis without the history of RIF has not been well documented in the literature.

- In our study, 70.5% of the participants in previous IVF Failure group and 79.9% patients in no previous failure group were detected with some intrauterine pathology.
- After detection and correction of these pathologies, 45.9% and 47.9% patients respectively in both groups had positive implantation rates.
- This data again suggests that in spite of all confounding biases for causing implantation failure in previous or ongoing IVF cycles, there is an approximately 50% chance of getting a positive result after performing hysteroscopy and treating the pathology.
- However, it also stands true that there is another half of the 50% participants who did not benefit from hysteroscopy at all. Neither was the pathology detected nor did they conceive. However, the overall implantation rate in our study was 47%. This data suggests that hysteroscopy has played a crucial role in patients with previous implantation failures by detecting chronic endometritis.
- There is enough data in the literature to support the surgeries for intrauterine pathologies such as submucous myomectomy¹⁵, metroplasty for mullerian abnormalities^{16,17}, polypectomy¹⁸ play an important role in improving implantation rates in subsequent IVF cycles.

Strength and Limitations:

- The study has been conducted in a **single center** thereby **operator bias for performing ultrasound, hysteroscopy** and necessary medical treatment was at its minimum. All patients were under follow-up to either one of the authors only. Therefore, there is **consistency** in our data. We considered single point procedure, Hysteroscopy. Thereby highlighting the **importance of one procedure**.
- Our study does have its own set of limitations. We did not filter-out the other possible factors that may impact the implantation rate such as **ovarian reserve, male factor, embryo number, embryo quality** etc. We did not highlight the **basis on which hysteroscopy** was offered to patients without previous failures. The reasons usually were longer married life, advanced maternal age, additional factors affecting fertility, financial restrictions. We did not highlight **the actual number of overall pathologies** detected on ultrasound prior to performing hysteroscopy. We **did not compare fertility outcomes** with the patients who **did not** undergo hysteroscopic procedure.

Conclusion

Although Cochrane review suggests low level of evidence to support screening hysteroscopy prior to IVF, the results of our study direct us to offer hysteroscopy preferably to all women planned for IVF-ET Cycle irrespective of the ultrasound findings and specially to the patients who have experienced IVF Failure in previous cycles.

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