

Scar endometriosis: Does the medical treatment with LHRH analogue have an effect on its symptomatology and lesions sizes?

Original
Article

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ABSTRACT

Background: Endometriosis defined as the presence of endometrial glands and stroma like tissues outside the uterine cavity. Scar endometriosis (SE) is a rare entity that is difficult to reach diagnosis due to the absence of a uniform clinical presentation with a variety in symptomatology and signs. It is usually a conflict for physicians of different specialists (surgeon, dermatologist, obstetrician, and gynecologist) that delay diagnosis.

Objective Studying the effect of medical treatment with luteinizing hormone-releasing hormone (LHRH) analogue on pain and mass size as a short-term therapy for cases with scar endometriosis that help postponing and reducing dissection size of the surgical intervention.

Patients and Methods: Our study included 14 patients, aged 18 to 40 y, having a previous gynecological or obstetric operation, a painful scar that may increase with menstruation, tender scar and mass palpable under scar diagnosed as scar endometriosis seen in our Mansoura University Hospital (MUH) and Private Clinic over 4.5 years. All patients underwent the following steps to reach a diagnosis ; history taking, examination and lab investigation, operative details and pain (visual analog scale). VAS scores pre-treatment were recorded then patients referred to ultrasound evaluation where any patients with suspicion of scar endometrioma underwent confirmation with FNAC (fine needle aspiration cytology). Patients diagnosed as scar endometriomas received LHRH analogue (Zoladex 3.6mg/month) for 6 months, then VAS score and ultrasound mass size were performed monthly and at the end of the medical treatment period. Patients who had no pain relief at the end of the treatment period were prepared for wide surgical excision with safety margins. Evaluation of the effect of short-term medical treatment as the post-treatment pain VAS score and mass size in comparison to their pretreatment findings were recorded in addition to its effect on surgical intervention postpone.

Results: The study of the 14 patients showed that mean±SD of age was 28.79±4.99, mean±SD of BMI was 26.4 ±1.7, previous operation scar (Umbilical laparoscopic port 2 [14.3%], episiotomy 3 [21.4%] and cesarean scar (CS) scar 9[64.3%]). Cystic mass was 8[57.1%], heterogeneous mass was 6 [42.9%] and mean±SD of US size/cm was 2.42±0.67 (1.6-4.1). Median of pain duration/months was 26.0 (5.0-60.0). Mean±SD of pain VAS score before treatment was 8.0 (6.0-10.0), while after was 2.0 (0-8.0). Median of pain VAS score in cases with cystic lesions before and after treatment was 7.5 (6.0-9.0) and 1.0(0.0-7.0), respectively, with a statistically significant difference. Also, median of pain VAS score in cases with heterogeneous lesions before and after treatment was 9.0 (7.0-10.0) and 7.0 (2.0-8.0), respectively, with a statistically significant difference with more pain relieve in cystic cases than heterogenous one. Patients needed for surgical intervention and not responding to medical treatment were 8 [57.1%]. The cut of the level of US size of cystic lesions was ≤2.65cm, while for heterogeneous lesions was ≤2.20cm with an accuracy of 87.5% and 83.3 %, respectively.

Conclusion: LHRH analogue short-term treatment for scar endometriosis is significantly effective in pain to relieve and decrease mass size in cystic lesions ≤2.65cm and heterogeneous lesions ≤2.05cm that allow surgical intervention postpone and minimize surgical dissection site.

Key Words: LHRH analogue, scar endometriosis, surgical intervention, VAS score

Received: 16th August 2019, **Accepted:** 14th September 2019

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ISSN: 2090-7625, November 2019, Vol.9, No. 4

INTRODUCTION

Extrapelvic endometriosis is a rare condition, which was defined as the presence of endometrial tissue outside

the pelvis^[1,2]. Scar endometriosis is an uncommon form of extrapelvic endometriosis that is usually misdiagnosed as a desmoid tumor, lipoma, sebaceous cyst, hematoma, abscess, suture granuloma, incisional hernia or tumors, causing

difficulty in diagnosis. It mostly occurs in old surgical scars from obstetrical and gynecological procedures^[2]. Scar endometriosis is a rare entity but is becoming more frequent nowadays after increasing the rate of cesarean section (Pfannenstiel syndrome) as demonstrated in a systematic review by Horton *et al.*^[3] It was also reported in a trocar port following laparoscopic surgery with increasing in the number of laparoscopic procedures in gynecologic and general surgery procedures^[4,5]. The cause of scar endometriosis is unknown till now and many theories have been postulated. However, one of the most accepted theory is the iatrogenic transplantation of endometrial tissue or placental cells into the wound edge during abdominal or pelvic surgery^[6-9]. The presentation of scar endometriosis and surgical procedure interval vary from months to years (3 months-10 years) in many series^[10]. Scar endometriosis manifestations are nonspecific and may be associated with abdominal pain increasing at time of menstruation^[11], tender scar and/or a firm and palpable nodule^[12]. It should be suspected when there is pain and swelling at an incisional site after gynecologic or obstetric surgery in the reproductive age of the lady^[10]. Many non-invasive diagnostic imaging modalities like ultrasonography with color Doppler, CT scan and MRI that can give correct but nonspecific diagnosis^[6,13]. The accuracy of FNAC from the mass documented in many studies as an important confirmatory investigation^[14,15]. The definitive diagnosis is made through a biopsy or through a fine needle aspiration biopsy (FNA) showing the usual morphological features of endometriosis^[16,17]. Therapeutic management is essentially based on large surgical excision, with safety margins and damaged tissue fascial defect reconstruction that may need closure with synthetic mesh. Medical treatment including hormone suppression has been suggested to relieve clinical symptoms^[18].

PATIENTS AND METHODS

This is a prospective cohort study that was conducted in the antenatal clinic, Mansoura University Hospital Antenatal Department and Private Clinic over 4.5 years. The study was approved by the local Institutional Research Ethical Committee (institutional research board). Our study was carried out on 14 patients aged (18 to 40 y) having a previous gynecological or obstetric operation, painful scar that might increase with menstruation, tender scar, mass palpable under scar (Fig. 1) and did not complain of pelvic endometriosis symptomatology or history of pelvic endometriosis and

diagnosed as scar endometriosis. All patients underwent the following steps to reach diagnosis, history taking, examination and lab investigation, operative details and pain VAS scores pre-treatment were recorded then patients referred to ultrasonography with color Doppler evaluation where scar mass were evaluated (Figs. 2 and 3) and any patients with suspicion of scar endometrioma (nonhomogeneous hypoechoic texture with scattered internal hyperechoic echoes in addition to irregular spiculated margins, that infiltrating the adjacent tissues with a variable size hyperechoic ring and an avascular single pedicle entering the mass at the periphery with color Doppler)^[6,13] were undergone confirmation with FNAC (fine needle aspiration cytology) using 10ml syringe and a 25-gauge needle where air-dried direct smears were stained with Papanicolaou stained following alcohol fixation (endometriosis identification with FNA is based on the presence of at least two of three findings- endometrial glandular cells, spindle endometrial stromal cells, and hemosiderin-laden macrophages)^[19]. Patients diagnosed as scar endometriomas had received LHRH analogue (zoldex3.6mg) monthly for 6 months, then pain VAS score and ultrasound mass size were performed monthly and at the end of medical treatment period and patients who did have pain relief at the end of the treatment period were prepared for wide surgical resection with safety margin (Fig. 4) and the specimens were referred for histopathological confirmation. Evaluating the effect of short-term medical treatment as the post-treatment pain VAS score and mass size in comparison to their pretreatment findings were recorded in addition to its effect on surgical intervention postpone. Written consent was given for all participants before being included and after explaining the study with the patient's ability to be withdrawn at any time under her own will.

STATISTICAL ANALYSIS:

Data were fed to the computer and analyzed using IBM SPSS software package version 22.0. Qualitative data were described using number and percent. Quantitative data were described using range (minimum and maximum), mean, standard deviation and median. The significance of the obtained results was judged at the 5% level. Mann Whitney U test and Wilcoxon signed rank test for comparison of parametric continuous variables comparing between groups and between before and after treatment. Spearman correlation was used to correlate continuous non-parametric variables.

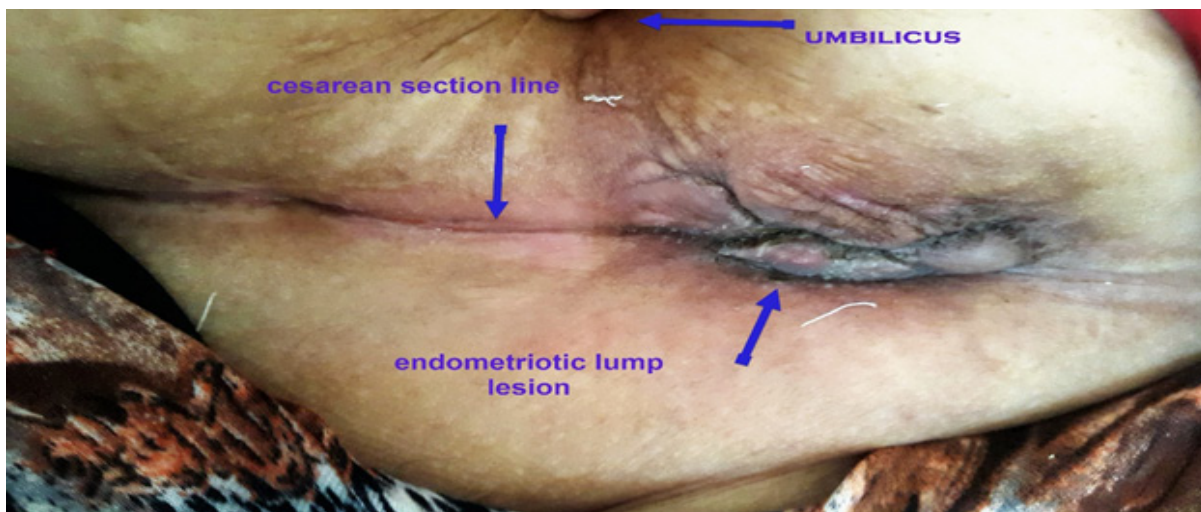


Fig. 1: Dark bluish mass involving the left side of the cesarean incision

fairly defined oval shaped hypo-echoic lesion measures about 4 x 2 cm is noticed involving the subcutaneous layer of the suprapubic region (involving the site of previous cesarean scar) with no surrounding edema or signs of increased vascularity seen inside (suspicious endometrioma)

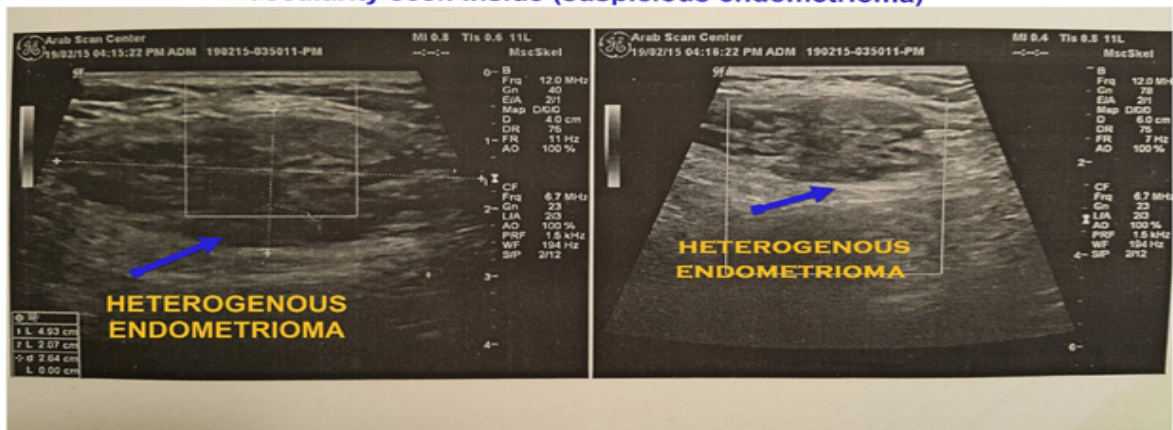


Fig. 2: Oval shaped heterogenous mass 4 x 2 cm in subcutaneous layer at cesarean scar incision

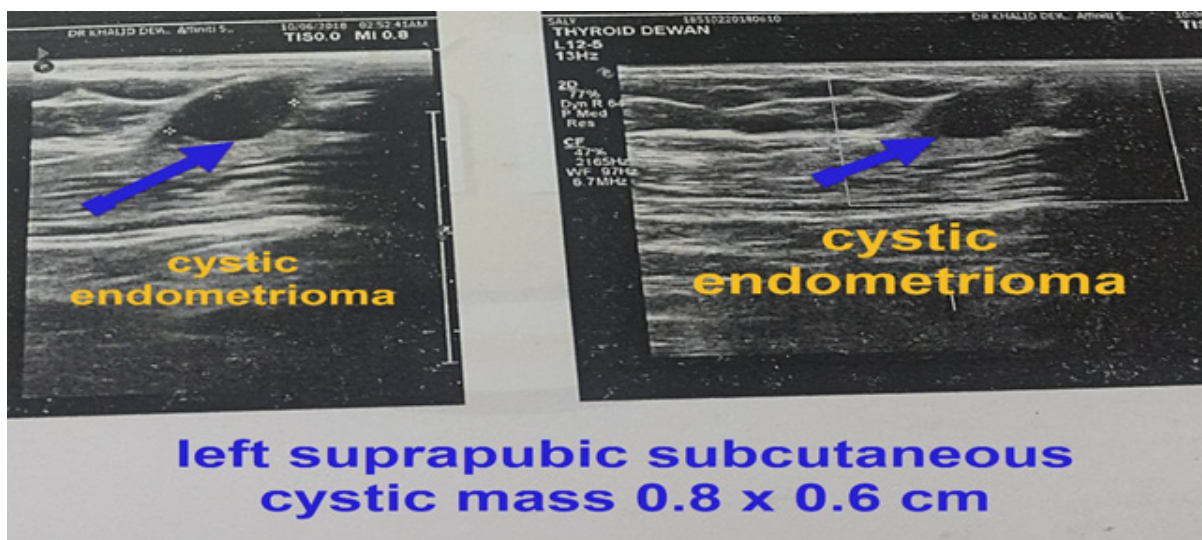


Fig. 3: Left cystic lump under cesarean scar incision about 0.8 x 0.6 cm

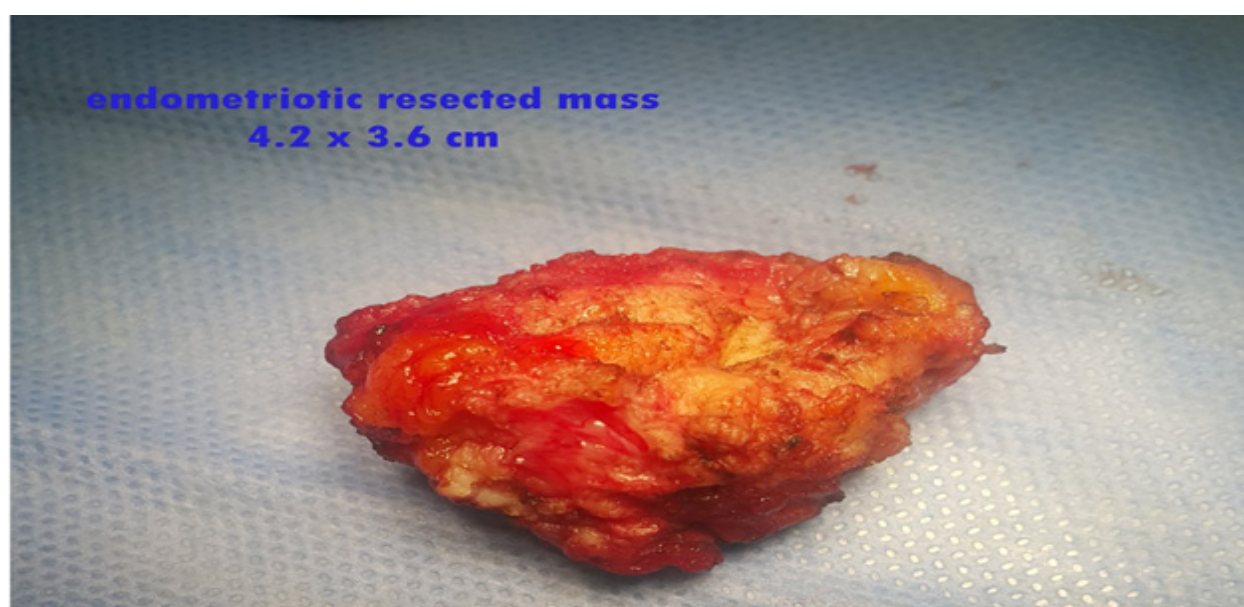


Fig. 4: Excised endometrioma from the subcutaneous tissue under cesarean section scar

RESULTS

The study was carried out on 14 patients diagnosed as scar endometriosis which revealed that patient's age mean was 28.79 (21-37), BMI mean was 26.4 (22.6-29.3), patients mostly multigravida and multipara with median was 2 (0-4) and 2 (0-3), respectively, previous operation scar (mostly had previous cesarean section (CS) scar 9[64.3%], then episiotomy 3 [21.4%] and lastly umbilical laparoscopic port 2 [14.3%]), US mass consistency criteria revealed that 8 cystic mass [57.1%] and 6 heterogenous mass [42.9%] as shown in diagram 1, the mean of US size/cm was 2.42 (1.6-4.1), the mean of pain VAS score before medical treatment was 8.0 (6.0-10.0) while after was 2.0 (0-8.0) with a highly significant statistical difference between them, the pain duration median/months was 26.0 (5.0-60.0) and patients needed for surgical intervention (wide local excision with safety margins) and not responding to medical treatment were 8 [57.1%] while those respond to treatment (pain relief and decrease mass size) were 42.9% as shown in table 1 and diagram 2. Most of the patients referred to our department after confusion in their assessment by different consultant specialties (surgeon, internal medicine specialist and dermatologist). Comparison of the pain VAS score change after treatment among studied cases showed that the pain VAS score pretreatment between cystic and heterogeneous mass was 7.5 (6.0-9.0) and 9.0 (7.0-10.0),

respectively, without a significant difference, while was 1.0 (0.0-7.0) and 7.0 (2.0-8.0) posttreatment, respectively, with a significant statistically differences in pain relieve between cystic and heterogenous scar mass as shown in tables 2 and 3. The pain VAS score in cases with cystic lesions before and after treatment was 7.5 (6.0-9.0) and 1.0 (0.0-7.0), respectively, with a statistically significant difference, also VAS score in cases with heterogeneous lesions before and after treatment was 9.0 (7.0-10.0) and 7.0 (2.0-8.0), respectively, with a statistically significant difference with more pain relieve in response to medical treatment in cystic cases than heterogenous one as shown in table 4. The comparison of lesion US size in cm before and after treatment as shown in table 5 revealed that, the mean was 2.42 ± 0.67 before treatment and 1.75 ± 0.65 after treatment with a highly significant difference between them but without a significant difference either it was cystic or solid. The correlation between Lesion size by US, pain duration and pain VAS score showed that US lesion size had a positive correlation to pain VAS score before and after medical treatment with no relation to pain duration/months, in addition, there was no correlation between pain VAS score before and after treatment and pain duration/months as shown in table 6. The cut of the level of US size of cystic lesions that respond to medical treatment was ≤ 2.65 cm while for heterogenous lesions was ≤ 2.20 cm with accuracy reaching to 87.5% for cystic lesions and up to 83.3 % for heterogenous lesions as shown in diagrams 3 and 4.

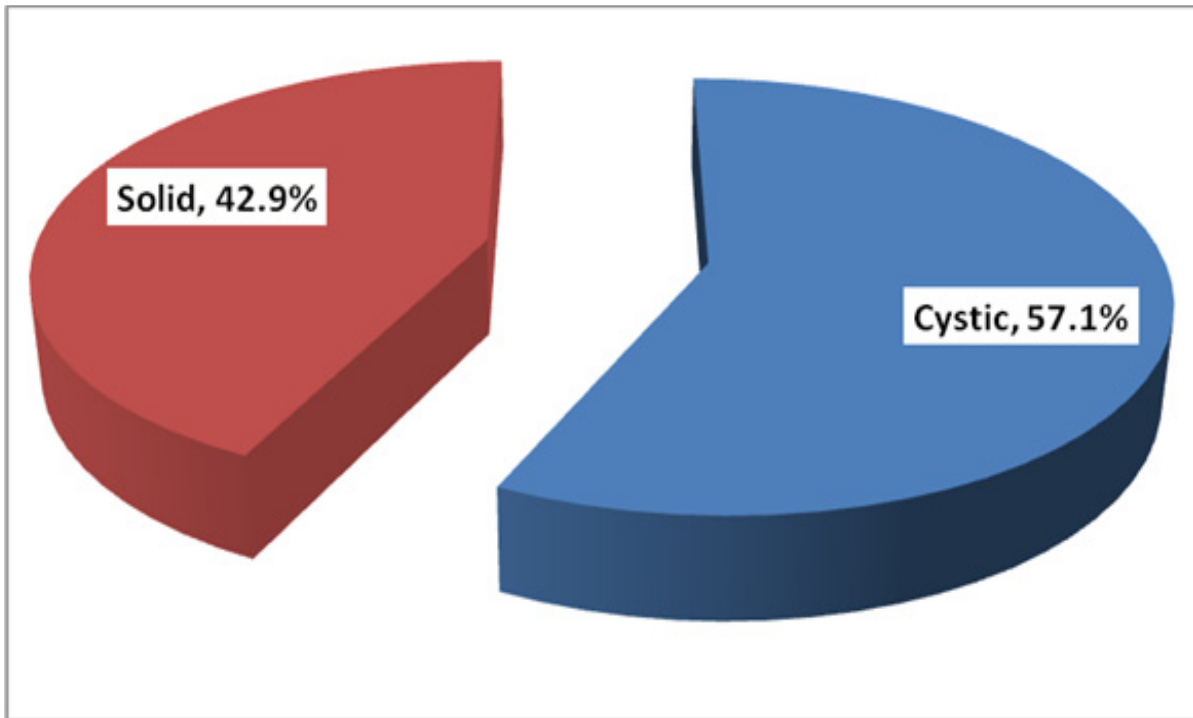


Diagram 1: It shows the consistency percentage of endometriomas masses

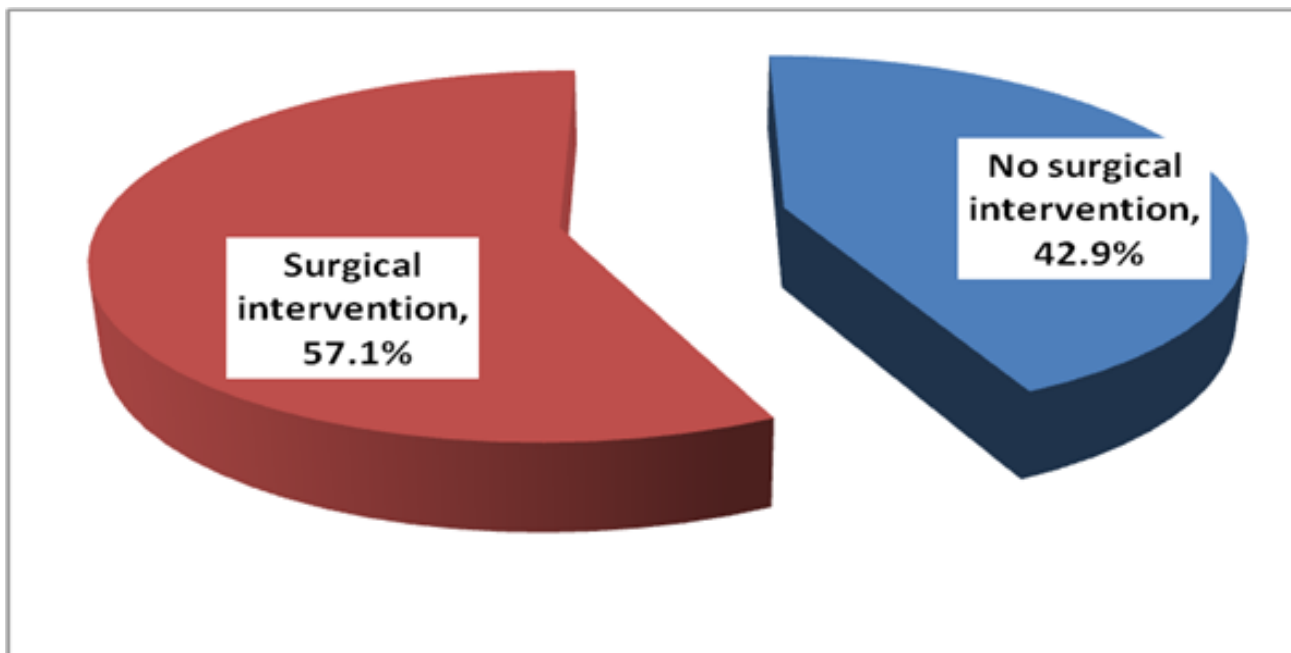


Diagram 2: It show the percentage of patients undergone surgical intervention

Table 1: Demographic characteristics of the studied cases

| | n=14 | % |
|--------------------------------------|----------------|------|
| Age/years | | |
| Mean±SD | 28.79±4.99 | |
| (Min-Max) | (21.0-37.0) | |
| BMI kg/m ² | | |
| Mean±SD | 26.4±1.7 | |
| (Min-Max) | (22.6-29.3) | |
| Gravidity median(min-max) | 2.0(0-4.0) | |
| 0 | 1 | 7.1 |
| 1 | 3 | 21.4 |
| 2 | 4 | 28.6 |
| 3 | 3 | 21.4 |
| 4 | 3 | 21.4 |
| parity median(min-max) | 2.0(0-3) | |
| 0 | 1 | 7.1 |
| 1 | 3 | 21.4 |
| 2 | 5 | 35.7 |
| 3 | 5 | 35.7 |
| Previous operation scar | n | % |
| Umbilical lap port | 2 | 14.3 |
| Episiotomy | 3 | 21.4 |
| Cs | 9 | 64.3 |
| Pain VAS score before Mean±SD | 8.0 | |
| (Min-Max) | (6.0-10.0) | |
| Pain VAS score after Mean±SD | 2.0 | |
| (Min-Max) | (0-8.0) | |
| Surgical intervention | N | % |
| 0 | 6 | 42.9 |
| 1 | 8 | 57.1 |
| Pain duration/months median(min-max) | 26.0(5.0-60.0) | |
| | n | % |
| Cystic | 8 | 57.1 |
| Solid | 6 | 42.9 |
| US size/cm before treatment | | |
| Mean±SD | 2.42±0.67 | |
| (Min-Max) | (1.6-4.1) | |
| US size/cm after treatment | | |
| Mean±SD | 1.75±0.65 | |
| (Min-Max) | (0.9-3.2) | |

Table (2): Comparison of VAS score change after treatment among studied cases

| VAS score | Before treatment | After treatment | test of significance |
|---------------------|------------------|-----------------|----------------------|
| Median (Min-Max) | 8.0(6.0-10.0) | 2.0(0-8.0) | Z=3.34 p=0.001* |

Z: Wilcoxon Signed rank test p: probability *Statistically significant ($p < 0.05$)

Table (3): Comparison of VAS score change after treatment among studied cases

| VAS score | Solid n=6 | Cystic n=8 | test of significance |
|--------------------------------------|---------------|---------------|----------------------|
| Before treatment median (min-max) | 9.0(7.0-10.0) | 7.5(6.0-9.0) | z=1.73 p=0.08 |
| After treatment median (min-max) | 7.0(2.0-8.0) | 1.0(0.0-7.0) | z=2.32 p=0.02* |

Z: Mann Whitney U test p: probability *Statistically significant ($p < 0.05$)

Table (4): Comparison of VAS score change after treatment among cystic and solid lesions

| | VAS score | | test of significance |
|--------|--------------------------------------|-------------------------------------|----------------------|
| | Before treatment median (min-max) | After treatment median (min-max) | |
| Cystic | 7.5(6.0-9.0) | 1.0(0.0-7.0) | Z=2.6 p=0.01* |
| Solid | 9.0(7.0-10.0) | 7.0(2.0-8.0) | Z=2.3 p=0.02* |

Z: Wilcoxon Signed-rank test p: probability *Statistically significant ($p < 0.05$)

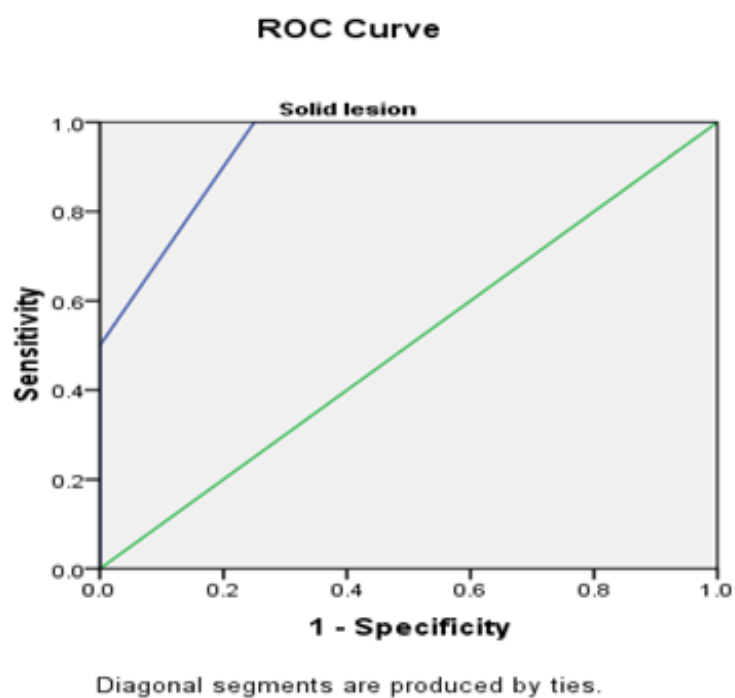
Table (5): Comparison of lesion size before and after treatment

| | before treatment | after treatment | paired t-test |
|---|------------------|-----------------|---------------------|
| US size/cm Mean±SD (Min-Max) | 2.42±0.67 | 1.75±0.65 | t=22.06 p<0.001* |
| US size in solid lesions Mean±SD (Min-Max) | 2.17±0.48 | 1.48±0.47 | t=22.2 p<0.001* |
| US size in cystic lesions Mean±SD (Min-Max) | 2.61±0.76 | 1.95±0.72 | t=13.31 p<0.001* |

Table 6: Correlation between Lesion size by US, pain duration and score

| | | Pain duration/months | Pain VAS score before | Pain relief VAS after |
|-----------------------|---|----------------------|-----------------------|-----------------------|
| US size/cm | r | -.194 | .773** | .687** |
| | p | .507 | .001 | .007 |
| | | | pain duration/ months | |
| Pain VAS score before | R | | -.309 | |
| | P | | .283 | |
| Pain relief VAS after | R | | -.291 | |
| | P | | .312 | |

r: Spearman correlation coefficient **statistically significant ($p < 0.05$)

**Diagram 3:** Show the validity of the solid lesion size in detection of pain improvement after treatment

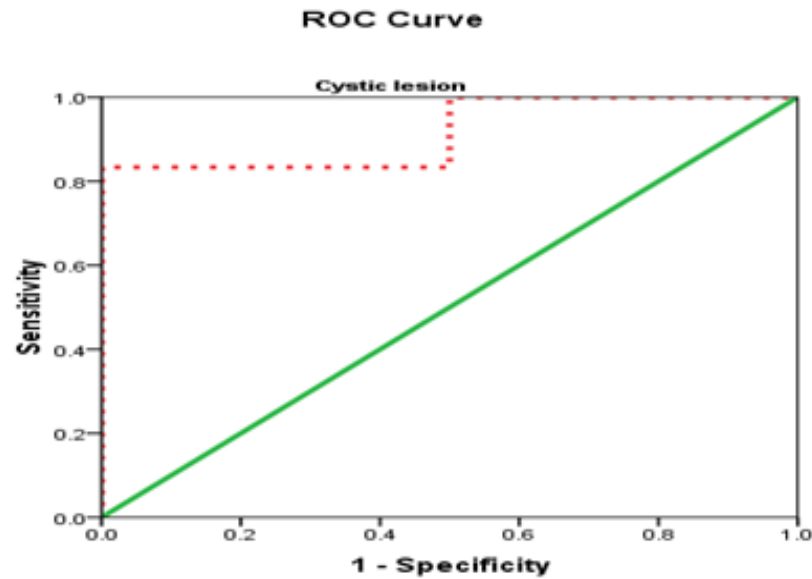


Diagram 4: Show the validity of the cystic lesion size in the detection of pain improvement after treatment

DISCUSSION

Scar endometriosis is uncommon diagnosis for gynecologist and obstetrician as it is a rare disease with confused presentation and lack of physician awareness and experience about it. Our study showed increasing in the patients presented with scar endometriosis diagnosis nowadays as there is an increase in CS frequency, in addition to increasing in laparoscopic uterine intervention which was reported by Horton *et al.* 2008.^[3] In our study, most of the cases presented with CS scar endometriosis then episiotomy scar as proved by the study of Medeiros FD, *et al.* 2011^[20] which revealed that the majority of cases have been noted in and adjacent to cesarean section (57%) or hysterectomy scars (11%). In the lower genital tract, the most common was episiotomy scars.^[21] A study by Blanco RG, *et al.* 2003^[2] has reported that scar endometriosis is the most common site after cesarean section followed by episiotomy, hysterotomy, hysterectomy and laparotomy scar. The symptoms are non-specific, typically involving abdominal wall pain at the time of menstruation. Clinical examination and other investigations also gave non-specific results.^[22] The most common presentation in our study was pain at the site of the scar with a firm lump or nodule that increased in intensity or size at time of menstruation, which was proved by Poonam Goel, *et al.* 2011^[10] as they stated that scar endometriosis is a rare condition and should be suspected when a lady in the reproductive age presents with pain and

swelling at scar site after obstetric surgery. Cyclicity, although not always present, is pathognomic for scar endometriosis^[23]. The SE diagnosis usually depends on biopsy, in this study based on data of clinical features, US and Doppler examination characteristic features for mass and FNAC characteristics findings. The US diagnostic features of SE reported by Francica *et al.*^[6] in their series were : a nonhomogeneous hypoechoic texture with scattered internal hyperechoic echoes, margins usually are spiculated with infiltration to the tissues surrounding and a variable width hyperechoic ring surround it^[6]. The presence of a single avascular pedicle attached to the mass at the periphery with color Doppler examination^[13]. FNAC is a simple and non-invasive technique which is the investigation of choice in SE cases for accurate and timely preoperative diagnosis^[2]. SE therapeutic management of choice is essentially based on wide surgical excision with safety margins at least 1cm and reconstruction of damaged tissue^[18]. Hormonal suppression with the use of progestogens, oral contraceptive pills and danazol is not effective and gives only partial relieve in SE symptoms. Recently, there has been a report of the use of LHRH analogue that has the prompt improvement in SE symptoms without a change in the lesion size^[24]. Hormonal therapy can be initiated as a treatment for SE disorders, so we can avoid unnecessary surgery in selected cases^[25]. Our study revealed that the treatment of SE with LHRH analogue for 6 months showed significant relieve of pain symptoms with more pain relieve in response to medical treatment in cystic cases than heterogenous one, in addition to significant

decrease in lesions sizes without a significant difference either it was cystic or solid lesions that allow the ability to postpone surgical intervention and decrease surgical dissection size or need for closure with synthetic mesh, as approved by Oh EM *et al.* 2014^[26], as their study reported that medical treatment with hormone suppression has been suggested to relieve SE symptoms, in addition to Purvis RS and Tying SK 1994^[27], studies which revealed that preoperative hormonal therapy can be used in SE cases with large endometriotic masses for reducing the size of the surgical defect. This study approved that the size of the US size of cystic lesions at which it responds to medical treatment was ≤ 2.65 cm, while for heterogenous lesions was ≤ 2.20 cm with accuracy reaching to 87.5% for cystic lesions and up to 83.3 % for heterogeneous lesions. On the other hand, F. M. González Valverde FM *et al.*^[28] reported that medical treatment with LHRH analogue, danazol or gestagens are ineffective in incisional endometriomas which are bigger than 2 cm. Scar endometriosis prevention through abdominal wall wound cleaning and irrigate it vigorously with high jet saline before closure^[29].

CONCLUSION

Medical treatment with LHRH analogue is effective in pain to relieve and minimizing lesions sizes which are 2.65 cm or less for cystic lesions and 2.20 cm or less for heterogenous lesions that provide treatment options to postpone surgical intervention desire, surgical contraindication, patient refusal and decrease surgical excision size that may minimize repair with synthetic mesh.

RECOMMENDATIONS:

We need for increasing awareness of extra-pelvic endometriosis disorder and more expanded studies to study the effect of LHRH analogue treatment on the need for synthetic mesh reconstructions during surgical excision of scar endometriomas.

CONFLICT OF INTEREST

There are no conflicts of interest.

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