CLINICAL GUIDELINE

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This document was developed and shared by SASREG and is endorsed by SASOG as part of the BetterGYN® programme

SOUTH AFRICAN GUIDELINE FOR TREATMENT OF ENDOMETRIOSIS

Recommended treatment protocols for the South African patient population based on the European Society of Human Reproduction and Endocrinology (ESHRE) guidelines.

These Guidelines are based on the ***ESHRE Guideline: Management of women with endometriosis*** as published in Human Reproduction, Vol.29, No. 3 pp.400-412,2014.

Development of the South African Guidelines:

This document has been prepared by the SASREG Committee and assisted by:

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The SASREG Committee:

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- Dr C Venter

The abovementioned group of clinicians with a special interest in endometriosis from both the public and private sector attended a meeting in July 2016 to discuss the management of patients with endometriosis in the South African context. An attempt was made to set guidelines for the early diagnosis and effective treatment of patients with endometriosis presenting with pain and/or infertility.

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Funding for the meeting was sponsored by Bayer pharmaceuticals.

During this meeting, the ESHRE Guidelines were discussed in detail and where necessary, changes have been made to better serve our specific patient population.

Purpose of the Guideline:

1. To promote early diagnosis and initiation of medical therapy through education of health care workers and the public;
1. To prevent unnecessary or repeated and inappropriate surgery;
2. To set criteria where referral to centres of excellence needs to be considered;
3. To optimize patients' quality of life and improve their fertility potential;
4. To implement strategies to offer these services to all patients;
5. To offer these services in a cost effective way for public and private funders.

Current obstacles to effective care:

1. Poor knowledge of the disease amongst health care workers contributing to late diagnosis;
2. No guidelines available regarding medical treatment in primary health care facilities;
3. No referral system in place for patients failing to respond to first line therapy;
4. Poor education of young adolescent women in educational institutions and clinics regarding pelvic pain;
5. Lack of dedicated outpatient clinics for adolescent women and women of reproductive age for management of pelvic pain and /or infertility at secondary and tertiary level;
6. Lack of surgeons trained in advanced laparoscopic surgery for management of endometriosis in both public and private sector;
7. Repeated surgeries with poor documentation of surgical findings;
8. Poor communication between health care practitioners and patients regarding severity of disease and future follow up;
9. Severe shortages of dedicated centers in management of endometriosis especially in rural areas where multidisciplinary treatment can be offered;
10. Cost of ART and other barriers to undergo treatment including travelling long distances for patients in both the private and public sectors.

Suggested Guideline for effective care of women with endometriosis:

The Guideline addresses the following topics regarding management:

1. Accurate diagnosis of the disease
2. Management of the patient presenting with pain
   - 2.1. Medical management
   - 2.2. Surgical management

3. Management of endometriosis related infertility
   3.1. Medical management
   3.2. Surgical management
4. The role of ART in patients with Infertility
5. The adolescent patient

INTERPRETATION ON THE GRADES OF RECOMMENDATIONS

For each recommendation, a grade (A-D) were assigned based on the strength of the supporting evidence (scored from 1++ to 4). In case of absence of evidence, the GDG could decide on writing good practice points (GPP), based on clinical expertise.

Grades of recommendations	Supporting evidence
A	Meta-analysis, systematic review or multiple RCTs (high quality)
B	Meta-analysis, systematic review or multiple RCTs (moderate quality) Single RCT, large non-randomised trial, case-control or cohort studies (high quality)
C	Single RCT, large non-randomised trial, case-control or cohort studies (moderate quality)
D	Non-analytic studies, case reports or case series (high or moderate quality)
GPP	Expert opinion

Where additions or changes to the **ESHRE** guideline was made by the **SASREG** committee and advisors, **REC** is used to indicate level of evidence.

1. Accurate diagnosis of endometriosis:

Early detection of disease

- Clinicians should consider the diagnosis of endometriosis in all women of reproductive age with symptoms of pelvic pain, dysmenorrhoea, dyspareunia, infertility, fatigue and non gynaecological cyclical symptoms.

[GPP]

- Clinical examination should be performed in all women where endometriosis is suspected based on history and should include vaginal/ rectal examination where possible after full consent.

[GPP]

- Where the diagnosis is likely based on symptoms, further investigations should be performed even when the clinical examination is normal.

[C]

- If there is failure of medical therapy after 6 months, the patient should be referred to a clinician experienced in managing endometriosis for further assessment. Laparoscopy may be suggested in selected cases for the diagnosis. Should operative laparoscopy be needed, this should be performed by an experienced surgeon.

[REC]

- Transvaginal ultrasound must be part of the investigation to diagnose or exclude ovarian endometriomas in patients where it is possible.

[A]

- Currently there is not enough evidence to support the use of 3-D ultrasound and Magnetic Resonance Investigation (MRI) to diagnose peritoneal endometriosis.

[D]

- Specific investigations to exclude or confirm the presence of DIE, including MRI and Virtual Colonoscopy may be performed prior to surgery.

[REC]

- Histological and bodily fluid biomarkers or immunological biomarkers including CA-125 should not be used to screen for endometriosis or to confirm diagnosis as evidence is lacking regarding non-invasive screening tools.

[A]

2. Management of the patient presenting with pain:

2.1. Medical management

- Adequate counseling of women diagnosed with endometriosis should be accompanied by empirical treatment with adequate analgesia, including NSAID's and hormonal treatment.

[GPP]

- If there is failure of medical therapy after 6 months, the patient should be referred to a clinician experienced in managing endometriosis for further assessment.

[REC]

- Hormonal treatments that can be offered include:

Combined Oral Contraceptives	(Level B)
Progestogens	(Level A)
Anti-progestogens	(Level A)
GnRH agonists	(Level A)
Vaginal Contraceptive Ring	
Transdermal estrogen/progestogen patch	(Level C)
LNG IUS (Mirena)	(Level B)

When GnRH agonists are used, hormonal add-back should be considered from start of therapy.

[Level A]

- GnRH agonists should be used with caution in adolescent patients due to the possible effect on growing bone.

[GPP]

- In patients with pain from DIE refractory to surgical/medical therapy, aromatase inhibitors can be used in combination with other hormonal treatments.

[Level B]

2.2. Surgical management

2.2.1 Peritoneal disease

- When surgery is performed for the diagnosis and treatment of endometriosis, laparoscopy rather than laparotomy should be the preferred surgical approach.

[REC]

- Both ablation and excision of endometriosis is effective in reducing endometriosis associated pain.

[Level C]

- LUNA should not be performed as an additional procedure to reduce pain.

[Level C]

- Presacral neurectomy (PSN) is effective but is potentially a hazardous procedure.

[Level A]

2.2.2 Ovarian disease

- If current or future fertility is desired, patients with ovarian endometriomas should preferably be managed by Reproductive Medicine Sub Specialists.

[REC]

- In patients where their families have been completed, cystectomy leads to lower recurrence and better pain relief over time compared to drainage and coagulation.

[Level A/B]

2.2.3 DIE

- Clinicians should exclude DIE (bladder/ ureteric/rectovaginal space/ bowel /extrapelvic disease) by clinical examination and the use of special investigations. When DIE is suspected, these patients should be referred to a center of excellence that offer all available treatments in a multidisciplinary context.

[GPP]

- Hysterectomy may not always cure endometriosis pain and should only be offered when women have completed their families and failed to respond to more conservative measures. Before performing an hysterectomy, investigations for DIE should be performed.

[GPP]

- Patients should be informed pre-operatively that hysterectomy will unlikely cure their pain.
[GPP]
- Adhesive barriers should be used only in specific situations with products which has been shown to reduce adhesion formation specifically in endometriosis.
[B]

3. Management of the patient presenting with infertility:

3.1 Medical treatment

- Clinicians should not prescribe hormonal treatment for suppression of ovarian function to improve fertility.
[A]
- Adjunctive hormonal treatment before surgery as well as treatment following surgery to improve spontaneous pregnancy rates should not be prescribed as suitable evidence is lacking.
[GPP]
- GnRH agonist suppression for a period of 3-6 months prior to treatment with IVF does improve clinical pregnancy rates in infertile women with endometriosis.
[B]

3.2 Surgical management

- Laparoscopic surgical treatment of AFS Stage I/II endometriosis should be performed with adhesiolysis in order to increase ongoing pregnancy rates.
[A]
- Repeated surgical procedures should not be performed for infertility. When spontaneous pregnancy fails to occur following 6 months after the surgery, patients should be referred for ART rather than repeat laparoscopy.
[REC]
- Where the surgery has been performed as a diagnostic procedure and full excision /ablation/ adhesiolysis has not been performed, patients should be referred to Reproductive specialists trained in endoscopy to maximise the patient's chance to conceive without ART.
[REC]
- In infertile women with AFS stage III/IV endometriosis, operative laparoscopy to increase spontaneous pregnancy rates can be offered.
[B]
- Before endometriosis surgery is offered to patients to enhance fertility, the presence of other fertility factors that may necessitate ART should be excluded.
[REC]

- In patients with ovarian endometrioma undergoing surgery, adequate counselling regarding the risk of reduced ovarian function after surgery and possible loss of the ovary should be given.

  [GPP]
- In patients undergoing IVF who presents with endometrioma, surgical treatment should not be performed pre-IVF since it will not improve IVF outcome.

  [REC]
- In patients with repeated IVF failures, surgery may improve future IVF outcome when performed by surgeons experienced in treating endometriosis.

  [B]

4. Assisted Reproductive Techniques and Endometriosis associated Infertility:

- In the absence of a significant male factor and in patients < 35 years with intact tubal function, COS followed with IUI may be considered based on prediction models (EFI Score)

  [REC]
- In patients with the following factors, early referral for IVF should be done:
  - Associated male factor (Double/Triple factor/Azoospermia)
  - Tubal factor
  - Low ovarian reserve (AMH/AFC)
  - Maternal age >35 years
  - Longstanding infertility despite previous surgical management (>6/12)

  [REC]

5. Adolescent patient and Endometriosis:

- Adequate counselling and information should be given regarding the disease and future follow up.

  [REC]
- If a trial of medical therapy is not effective after 6 months, these patients should be referred to a center with a special interest in management of patients with endometriosis Operative laparoscopy can be considered in selected cases.

  [REC]
- Psychological support should be offered to patients with endometriosis, as well as contact details of patient support groups.

  [REC]

Implementation of Guidelines in Public and Private settings:

Patient Awareness Groups, the media and Department of Health: Development of strategies to educate patients at school level and clinics regarding endometriosis.

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Department of Health: Education of Primary care givers regarding the management of adolescent and young reproductive age women presenting with pain and/or infertility.

College of Medicine, Universities, WINNERS Program and DOH: Training of Gynaecologists in endoscopy as well as correct management of endometriosis and creating an effective referral system for each health District / City.

SASREG, Funders, DOH: Establishment of Centers with a specific interest in management of advanced endometriosis through a multidisciplinary team with Radiologists/ Reproductive specialists / Urologists and Colorectal surgeons.