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Review Article

# Ovarian Cancer in the Sudan - Identifying the Social and Clinical Factors that Prevent an Early Diagnosis

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**Abstract**

Ovarian cancer, because it often presents with vague symptoms, is a difficult disease to diagnose at the early stages, especially in developing countries. In Sudan, diagnosis is further complicated by additional factors and challenges. First, as in any developing country, access to treatment, facilities and medical staff is generally lacking. Secondly, Sudan is the second largest country in Africa: its very size presents difficulties for the implementation of a centralized health system. The two tertiary hospitals in or near the capital have long patient waiting lists.

The lack of female education in sub-Saharan Africa, together with social and economic issues affecting women, is a further obstacle to disease diagnosis and management. Misdiagnosis, leading to inappropriate treatment, may result from the presence of comorbid diseases such as Tuberculosis (TB), which can mimic ovarian cancer and obstruct early detection. Most patients are identified at the later stages when the complications associated with invasive procedures and conventional chemotherapy make treatment much less effective. The early detection of biomarkers may prove to be a vital tool to indicate targets for immunotherapy treatment.

Financial aid may help improve the outcomes for patients with ovarian cancer in the Sudan, assisting with diagnosing and management procedures including training medical staff. Research and development, documentation and updating the statistical register for the whole country are also important requirements for future improvements.

Finally, there is a need to promote interdisciplinary work between surgeons and clinical oncologists to optimize international guidelines and protocols in accordance with the facilities available.

**Keywords:** Biomarker; Ovarian cancer; Early detection; Diagnosis; Sub-Saharan Africa; Tuberculosis

## Abbreviations

CA125: Cancer Antigen 125; CT: Computer Tomography; EOC: Epithelial Ovarian Cancer; HE4: Human Epididymis Protein 4; OC: Ovarian Cancer; PPV: Positive Predictive Value; TB: Tuberculosis; TVS: Transvaginal Sonography; WHO: World Health Organization

## Introduction

Ovarian Cancer (OC) remains one of the most challenging diseases to diagnose as the menopause (Rossing et al. 2010) often hides its symptoms. The highest incidence rate of OC has been reported in Northern Europe (13.3 per 100,000 person-years), followed by Western Europe (11.3 per 100,000 person-years) and Northern America (10.7 per 100,000 person-years), while North Africa has the lowest incidence rate (2.6 per 100,000 person-years) [1]. Although the rates of OC are highest in developed countries, disease presentation is often at a later stage in sub- Saharan Africa due to issues around religion (leading to delayed visits for invasive tests), distance to medical facilities and travel costs. This has a greater impact on sub-Saharan households where families are larger (5.7 members versus 2.3 in Europe) and the population is younger [2].

Little is known about OC in Sudan. The incidence rate for the whole country is not well known and there is no complete national cancer register; published data depends entirely on retrospective hospital studies. Thus, most reports indicate either cancer frequency ratios or absolute numbers [3-5]. Hospital-based statistics from the National Registry for Khartoum State between 2009-2010, suggest the frequency is around 188 per 100,000 population [6]. Moreover, little is known about the mortality and survival rates, as most of the females are diagnosed at late stage, and there is a lack of documentation such as death certificates [6,7]. Hospital studies [4] suggest that OC frequency has increased steadily in recent years and mortality rates remain high due to late diagnoses.

OC is a highly treatable cancer when diagnosed at an early stage and this poses a global issue. In most countries, owing to the difficulty in identifying OC-specific and sensitive biomarkers, and an affordable non-invasive screening process, OC is often diagnosed in the later stages. However, this is exacerbated in Sudan as most women present when the cancer has already spread, treatment is least effective and the risk of relapse is high. A study by Abuidris et al. suggested that the administration of neoadjuvant chemotherapy prolonged the survival




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rate in stage III and IV patients (P=0.002 and P<0.001, respectively) but that this had no benefits for earlier diagnosed patients [3]. Moreover, this study and previous research showed that neoadjuvant therapy has no additional survival benefits compared with standard treatments of advanced OC [8,9].

Early detection of OC is critical for curative disease management. Current methods are inadequate for early-stage diagnosis, and globally only 25% detection occur at this earliest stage [10]. Cancer Antigen 125 (CA125) is approved for clinical practice and elevated in 50% of patients with stage I OC. But, it has neither sufficient specificity nor sensitivity for early detection although its use as a biomarker for progression and regression of diagnosed OC (follow-up) is well established [11,12]. Recently, the Food and Drug Administration (FDA) approved the use of Human Epidermis protein 4 (HE4) to screen patients with OC for recurrence of disease. High HE4 has higher sensitivity than CA125 for OC detection especially in premenopausal women. However, HE4 lacks the specificity as it is also elevated in renal failure and lung cancer [13]. A combination of CA125 and HE4 is superior to any marker alone with sensitivity of 60% and specificity of 100% distinguishing OC from benign uterine tumours. This finding could have diagnostic and prognostic effect on overall survival and progression-free survival. However, these findings still lack validation [14].

## The Impact on the Fragile Economy

Because the median age of the Sudanese population is lower than that of Europeans, the women who are diagnosed with OC have a lower average age, although this diagnosis often happens at a later stage of the disease [2]. Families rely on women financially and emotionally, and women in sub-Saharan Africa often work extremely long hours in agriculture and vulnerable employment (unpaid work in the home). As Sudanese women often use more of their earnings to support their families [15], the economic burden is very high for patients and their families, given the high costs of diagnosis, treatment and accommodation in Khartoum while attending hospital appointments or staying to visit family members. This is exacerbated by the fact that most patients have to travel great distances from rural sites, often at the country's borders, to the only public hospital for cancer patients (Dafur Medical City Hospital) which in addition to having long waiting lists, has a shortage of medicines and limited expertise in OC. However, early detection of OC in Sudan improves the chance of survival for patients and decreases the prevalence of comorbid conditions, polypharmacy, functional dependence, cognitive impairment, depression, frailty, poor nutrition and limited social support [3].

## What contributes to the Later Diagnosis of Patients with OC in the Sudan?

The majority of the Sudanese population (>80%) resides in rural areas or is nomadic which presents a great challenge to any disease control initiative [16]. Most health providers reside and work in Khartoum State, limiting the Ministry of Health's capability to provide healthcare services to people living in rural areas [17]. Accurate screening tests can eliminate the delivery of unnecessary treatment, especially chemotherapy, which is often used before surgery due to misdiagnosis. Groups are working to develop sensitive and non-invasive tests to detect OC in its earliest stages (recently reviewed in [18]). Nevertheless, a suitable non-invasive test has yet to be validated as able to detect OC with sufficient specificity and sensitivity to be clinically viable.

Poor training of clinical gynecological staff, often dealing with out-of-date ultrasound and other equipment in the Sudan, commonly leads to misdiagnosis [19]. Gynecological oncologists are also in short supply, even though the number of women newly diagnosed with OC increases every year, and each case depends on a Computer Tomography (CT) scan and CA125 screening to confirm the diagnosis. As a result, there is a long list of patients waiting for primary surgery for OC and debulking after chemotherapy [3,17,20].

Awareness of OC and diagnostic tests are limited in the Sudan, additionally impacted by the reluctance of women to access facilities due to poverty and a lack of education [20]. These high mortality rates would be largely avoidable if appropriate screening, ideally brought into communities, were available to detect the disease early, when tests and treatment could be prioritized to those that need it and when treatment is most effective, easiest and cheapest to administer [21]. This would positively impact the health and wellbeing of women, who often support families emotionally and financially (https://www.aljazeera.com/indepth/features/2017/07/woman-burden-war-torn-south- sudan-170730132806188.html).

While early diagnosis facilitates a range of treatment options and improves the individuals' outcomes, even in the Global North, the advanced stages of OC require a regime of platinum-based chemotherapies with severe side effects and residual disease (American Cancer Society Chemotherapy for Ovarian Cancer Centre). Late diagnosis is one of the contributors of the National Health Service (NHS) cancer costs and significant cost savings could be achieved with an early diagnosis even in the UK. In the UK, stage 1 cost of treatment is £5,328 while stage 4 costs on average £15,081 [22]. Individuals with OC usually have extra costs to meet, which is especially daunting for low-income earners or those who have to suspend their jobs (Health Talk.org), despite support from the UK government in the form of statutory sick pay, and the existence of critical illness and income protection insurance policies (often viewed as a luxury item by the poorest in the community). These policies are, however, unattainable for women in Sudan, who are often significant income contributors in the family and earn the equivalent of between £81-1,216.43 monthly (Salary Explorer Sudan, 2019). If 40% of the Sudanese counterparts in the UK have financial difficulties even with higher income and support, what would be the fate of the Sudanese women with much lower income, larger families and limited access to diagnostic centers?

## The Prioritization of Women's Health in the Sudan

On July 31 and August 1, 2017, the African Union Commission with World Health Organization (WHO) and partners launched Sudan's participation in the Campaign to Advance the Reduction of Maternal Mortality in Africa (CARMMA) (http://www.emro.who.int/sdn/sudan-events/all-eyes-on-maternal-health.html). CARMMA is a major initiative of the African Union Commission (AUC), aimed at improving maternal, newborn and child health in the African

Region. The main objective is to accelerate the availability and use of universally accessible quality health services. Though there was a Sudanese maternal health policy, affirmed by the then Prime Minister General Bakri Hassan Saleh, to decrease morbidity and mortality rates, a National Cancer Institute-University of Gezira study showed an increase in OC incidence between 2000 and 2009 [3] (http://www.emro.who.int/sdn/sudan-events/all-eyes- on-maternal-health.html).

## CT scanning and CA125 for OC Diagnosis

We recently examined a cohort of 90 OC patients from the Omdurman military hospital, one of the gynecological specialist hospitals established in 1957 to treat cancer patients. These patients were identified using the OC register. Participants' information was collected at baseline during the admission process and before diagnosis. The information was collated by experienced staff and the study approved by the Ethics Committee of the hospital. The subjects' ages ranged from 18 to 80 with many women of reproductive age and less than 45 years old. Participants with no history of chemotherapy for OC, who may have had a diagnosis of breast cancer, were eligible for the study. Exclusion criteria included other diagnoses apart from OC and breast cancer, and incomplete data. Patient histories were recorded which included signs and symptoms, CT scan (adnexal mass), biomarker (CA125) and histopathology report after the surgery. Participants were all from the same racial background (sub-Saharan Africa). The results revealed that 4% of patients had a family history of breast or OC. 95% of patients had identifiable either bilateral or unilateral adnexal masses. 5% of females appeared (through probable errors of detection) to have no mass at either the benign or advanced stage. CA125 levels were very high in patients with OC (mainly serous subtype; 67.8%) while the remaining individuals had normal levels of 35U/ml and included late stage, endometroid subtype and stage I serous OC patients. Histopathology reports revealed that 62 (68.8%) of participants had OC; 17 (19%) had TB; 11 (12.2%) had benign ovarian mass (mainly teratoma) and 62 patients were postmenopausal. The common subtype was serous adenocarcinoma in stage three and four. Less common type was endometroid OC and less than 3% were germ cell OC.

Our findings, as per previous results [23], were that the CT scan and blood tests of CA125 levels were not accurate measures that indicated an OC diagnosis. CA125 was not good marker for OC but still, nothing available is better. False positive results were common in CT scans, and with its low sensitivity, often time no mass was seen intraoperatively. CA125 is also elevated in other conditions such as abdominal TB and some benign ovarian tumours such as teratoma. In the literature, there is a discrepancy in the results due to thresholds difference in study settings including image techniques such as CT, CA125 and mathematical calculations are used for OC diagnosis with variables considering such as age and threshold of CA125. Consequently, the sensitivity and specificity of the results depend on an algorithm and the image techniques' efficiency [24].

Transvaginal Sonography (TVS) provides a more precise image of the ovary and major studies in United Kingdom, United States and Japan encompassed the screening of 66,620 women with TVS [25,26]. In this study, TVS prompted 565 operations that led to the detection of 45 OCs, 34 of which were invasive. 82% of women who had OC detected by screening had stage I or stage II disease versus 34% of women in the unscreened historic control group (P <0.0001). In another study encompassing 107,276 screening years, 53 primary OCs were detected with 44 true-positive results and nine false-negative results with sensitivity of 85%, specificity of 98.7% and positive predictive value (PPV) of 14% [27]. Thus, TVS has moderate sensitivity and low PPV. Other studies were similar to the findings that TVS has less false positives when examining invasive epithelial ovarian/peritoneal cancers [28].

Unsurprisingly some Sudanese women have difficulties in meeting the cost of CT scan and screening for the detection of serum CA125 that costs patients around GBP £38/USD$53. Sudan has no health insurance for patients and the health system relies on assistance from the government or charities. However, most cancer patients refer either to Radiation and Isotope Centre in Khartoum (RICK) or to the National Cancer Institute of the University of Gezira (NCI-UG) in Wad Medani, both of which have partial funding from charities. The two centers are tertiary health care for supplementary diagnosis or treatment (chemotherapy or radiotherapy treatment) with long waiting lists and are each located in the densely populated and central areas of the Sudan [7].

Additionally, while women in the west undergo screening for six years on average, have seven to 11 screenings that include an annual CA125 serum test, and whose results are subjected to a calculation that includes the Risk of Ovarian Cancer Algorithm [29], most women in Sudan find it difficult to even meet the cost of the first diagnostic test. It is not surprising that, due to late diagnosis associated mainly with economic difficulties, of the 833 yearly cases of OC in the Sudan, 534 die [5] contributing disproportionately to the 152,000 women who die of OC worldwide annually [30]. As frequently suggested in the literature, a cheaper and non-invasive biomarker may assist in early diagnosis [31] and help save women's lives.

## Confounding Factors - Urogenital Tuberculosis

Many reports show Urogenital Tuberculosis (TB) resembles OC, either in the absence of symptoms accounting for 11% of cases, or the presence of symptoms including pelvic pain, ascites, abdomino-pelvic masses as well as menstrual problems such as amenorrhea and dysmenorrhea [32]. Urogenital TB remains a difficult disease to diagnose as it is often undetected by routine lab investigations including X-ray, Mantoux (tuberculin) test and acid-fast bacilli test, despite the presence of extensive disease. It can affect the ovary, endometrium and fallopian tube, and accounts for around 19% of gynecological admissions in some developing countries [33]. Polymerase Chain Reaction (PCR) for mycobacterium may be helpful in obtaining results, but this technique is not widely available due to the cost of reagents and PCR machines. Ascitic Fluid Adenosine Deaminase (ADA) activity has been proposed as a useful diagnostic test for abdominal TB. Therefore, these tests may not yield a definite diagnosis in countries with a high incidence of TB and in patients with high risk of OC [34,35]. Our study found a frequency slightly higher than in the literature, though this may be due to the small size of the group studied, poor instruments, poor procedure or the absence of detailed record keeping such as level of CA125 and a CT report. High serum CA125 levels are not helpful in the differential diagnosis of peritoneal TB and OC, though they may be a useful

marker for monitoring the efficacy of anti-TB treatment. It may not be possible to rule out ovarian malignancy or confirm abdominal TB without exploratory laparotomy. For example, laparoscopy may be a vital tool for differential diagnosis but it is expensive and requires trained staff [36].

Furthermore, OC is more common in post-menopausal women as reported worldwide. However, OC incidence is common at a median age of 61 in developed countries. The results in Sudan show many comparatively young females diagnosed with OC in the late 40s and 50s. This is similar to the situation in other sub-Saharan African and in other developing countries [37]. This may indicate that the incidence of OC in young African women, compared with other developed countries, is likely to be due to the difference in population age distribution between the two: Africa has, by far the youngest population of any of the continents. Given that age is the single substantive risk factor for most cancers, including OC, a younger population will have a lower overall incidence of OC and a lower median age of onset, based simply on the demographics of the population. It has been shown that the reports of residency and age from the cancer registries of African countries are often inaccurate [6,38,39]. Most cases present at a late stage and have high CA125 and adnexal mass. The most common subtype is serous OC. This is similar to previous studies by the Gurashi group reporting 43% of all OCs included in their study are diagnosed at an advanced stage (stage III and IV) and only 15% in early stage (stage II and I) [23].

Furthermore, there are no national cancer prevention programmes adopted in the Sudan to identify females at high risk in contrast to developed countries [19]. For example, recruiting women in the Sudan is one of greatest obstacles in cancer studies creating a social dilemma about cancer patients, owing to a general poor level of education among the fragile economy. However, recruitment strategies could be developed through knowledge of the factors that promote or hinder participation, seeking the views of non-participants in any given study is by definition a significant obstacle. Generally, there is a lack of data on prospective participants because they often cannot be easily reached, even in instances where they are known, due to their own reluctance. There are also difficulties in obtaining ethical approval to pursue their engagement in questionnaires and/or treatment beyond a certain point [40]. Moreover, this knowledge gap hinders the efficacy of the research in terms of identifying cancer aetiology in the earliest stages in Sudan. Domestic collaboration is limited between different institutes and hospitals. Data from PhD and master's students are not published due to a lack of funding, even in online University-held databases. Lack of financial support from the government and the private sector limits both the occurrence and dissemination of basic and clinical research [5].

Not only do cancer patients often have to travel a long distance to seek medical help, the primary investigation takes more than a year, as the waiting list is long, with poor protocols for investigations. When patients are finally booked in for surgery, their cancer occurs with complications, due to the delay in the treatment, which automatically discourages others from seeking interventions. Early screening for OC offers an opportunity to minimize the impact of ill health on women and their dependents. This is particularly significant in the Sudan as conflict disproportionately affects women, with serious implications for their safety and well-being, as well as affecting the health and economy of people in the region generally.

Financial aid is clearly an important factor in the earlier diagnosis of the disease. If females were able to access a diagnosis at an earlier stage, it would circumvent many of the issues arising from late-stage disease treatment and failure.

## Strengths and Weaknesses

As far as it is known, this is the first review that explores the unique economic and financial difficulties women are faced with regarding OC diagnosis and treatment in Sudan as well as the challenges common to developing countries. The qualitative nature of analysis and the limited number of participants mean that the findings cannot be generalized, however, because they are peculiar to this group of individuals. More research is needed to advance knowledge and understanding about the socio-economic factors that impact women ability to seek and find a diagnosis of OC when appropriate. We want to identify the tools to improve the earlier diagnosis and treatment of OC in sub-Saharan Africa through non-invasive tests.

## Conclusion

This review identifies some of the challenges to an early diagnosis of OC in the Sudan. Some Sudanese women with overwhelming economic difficulties need further specialist cancer treatment at the earliest stage of disease when treatment is most effective. One recommendation by these authors is that there is a concerted effort to educate females in the signs and symptoms of OC and an introduction of portable diagnostic measures for routine practice.

It is of course, critically important that we identify biomarkers that would enable the early detection of OC. A simple but robust urine test [18] would enable the travel of tests to women in areas otherwise poorly serviced by healthcare and professionals.

By enabling women an opportunity to determine in their hometown, whether further hospital tests are needed, we could priorities the referral of women with overwhelming financial and economic difficulties for further specialist cancer treatment at the earliest stage of disease when treatment is most effective.

### References

1. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA: a cancer journal for clinicians. 2005; 55: 74-108.
2. Adam W, Gurashi RA, Humida MA, Abdelaziz F. Ovarian Cancer in Sudan. Journal of Medical and Biological Science Research. 2017; 3: 37-41.
3. Abuidris DO, Weng HY, Elhaj AM, Eltayeb EA, Elsanousi M, Ibnoof RS, et al. Incidence and survival rates of ovarian cancer in low-income women in Sudan. Molecular and clinical oncology. 2016; 5: 823-828.
4. Saeed ME, Cao J, Fadul B, Kadioglu O, Khalid HE, Yassin Z, et al. A five-year survey of cancer prevalence in Sudan. Anticancer research. 2016; 36: 279-286.
5. Elamin A, Ibrahim ME, Abuidris D, Mohamed KEH, Mohammed SI. Part I: cancer in Sudan-burden, distribution, and trends breast, gynecological, and prostate cancers. Cancer medicine. 2015; 4: 447-456.
6. Saeed IE, Weng HY, Mohamed KH, Mohammed SI. Cancer incidence in Khartoum, Sudan: first results from the Cancer Registry, 2009–2010. Cancer medicine. 2014; 3: 1075-1084.
7. Mohammed ME, Hassan AM, Elsadig MG, Adam DM, Abdelhadi HA, Elmamoun K, et al. Burden and pattern of cancer in the Sudan, 2000-2006. Journal of Advances in Medicine and Medical Research. 2013: 1231-1243.

8. Tangjitgamol S, Manusirivithaya S, Laopaiboon M, Lumbiganon P, Bryant A. Interval debulking surgery for advanced epithelial ovarian cancer. Cochrane Database of Systematic Reviews. 2013.

9. Bristow RE, Eisenhauer EL, Santillan A, Chi DS. Delaying the primary surgical effort for advanced ovarian cancer: a systematic review of neoadjuvant chemotherapy and interval cytoreduction. Gynecologic oncology. 2007; 104: 480-490.

10. Kamal R, Hamed S, Mansour S, Mounir Y, Abdel Sallam S. Ovarian cancer screening-ultrasound; impact on ovarian cancer mortality. Br J Radiol. 2018; 91: 20170571.

11. Bast RC, Badgwell D, Lu Z, Marquez R, Rosen D, Liu J, et al. New tumor markers: CA125 and beyond. International Journal of Gynecologic Cancer. 2005; 15: 274-281.

12. Bast RC. Early detection of ovarian cancer: new technologies in pursuit of a disease that is neither common nor rare. Transactions of the American Clinical and Climatological Association. 2004; 115: 233-248.

13. Escudero JM, Auge JM, Filella X, Torne A, Pahisa J, Molina R. Comparison of serum human epididymis protein 4 with cancer antigen 125 as a tumor marker in patients with malignant and nonmalignant diseases. Clin Chem. 2011; 57: 1534-1544.

14. Angioli R, Plotti F, Capriglione S, Montera R, Damiani P, Ricciardi R, et al. The role of novel biomarker HE4 in endometrial cancer: a case control prospective study. Tumour Biol. 2013; 34: 571-576.

15. Jiggins J. How poor women earn income in sub-Saharan Africa and what works against them. World development. 1989; 17: 953-963.

16. Hamad H. Cancer initiatives in Sudan. Annals of oncology. 2006; 17: viii32-viii6.

17. Abuidri D, Ahmed AO, Elmadani AE, Eltayeb EA, Elgaili EM, Elwali NA, et al. Cancer management in Sudan: current status and future perspectives. Sudan Journal of Medical Sciences. 2009; 4.

18. Grayson K, Gregory E, Khan G, Guinn B-A. Urine biomarkers for the early detection of ovarian cancer–are we there yet? Biomarkers in cancer. 2019; 11: 1-8.

19. Awadelkarim KD, Mariani-Costantini R, Elwali NE. Cancer in the Sudan: an overview of the current status of knowledge on tumor patterns and risk factors. Science of the Total Environment. 2012; 423: 214-228.

20. Abuidris DO, Hassan EM, Ibnoof R, Eltayeb E, Eljaili E, Elsanousi M. Clinical features of ovarian malignancies in Sudan. Sudanese Journal of Public Health. 2013; 8: 189-193.

21. Holschneider CH, Berek JS, editors. Ovarian cancer: epidemiology, biology, and prognostic factors. Seminars in surgical oncology. 2000; 19: 3-10.

22. Collaborative Group on Epidemiological Studies of Ovarian C. Menopausal hormone use and ovarian cancer risk: individual participant meta-analysis of 52 epidemiological studies. The Lancet. 2015; 385: 1835-1842.

23. Gurashi RA, Hummeida ME, Abdelaziz F. Diagnostic Value of Serum Cancer Antigen 125 in Ovarian Cancer Patients. International Journal of Development Research. 2018; 8: 18644-18650.

24. Menon U, Skates SJ, Lewis S, Rosenthal AN, Rufford B, Sibley K, et al. Prospective study using the risk of ovarian cancer algorithm to screen for ovarian cancer. Journal of Clinical Oncology. 2005; 23: 7919-7926.

25. Bast RC, Urban N, Shridhar V, Smith D, Zhang Z, Skates S, et al. Early detection of ovarian cancer: promise and reality. Ovarian Cancer. 2002; 107: 61-97.

26. Sato S, Yokoyama Y, Sakamoto T, Futagami M, Saito Y. Usefulness of mass screening for ovarian carcinoma using transvaginal ultrasonography. Cancer. 2000; 89: 582-588.

27. van Nagell Jr JR, DePriest PD, Ueland FR, DeSimone CP, Cooper AL, McDonald JM, et al. Ovarian cancer screening with annual transvaginal sonography: findings of 25,000 women screened. Cancer. 2007; 109: 1887-1896.

28. Jacobs IJ, Menon U, Ryan A, Gentry-Maharaj A, Burnell M, Kalsi JK, et al. Ovarian cancer screening and mortality in the UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS): a randomised controlled trial. The Lancet. 2016; 387: 945-956.

29. Henderson JT, Webber EM, Sawaya GF. Screening for ovarian cancer: updated evidence report and systematic review for the US preventive services task force. JAMA. 2018; 319: 595-606.

30. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: a review. Cancer biology & medicine. 2017; 14: 9-32.

31. Sarojini S, Tamir A, Lim H, Li S, Zhang S, Goy A, et al. Early detection biomarkers for ovarian cancer. J Oncol. 2012; 2012: 709049.

32. Nebhani M, Boumzgou K, Brams S, Laghzaoui M, El Attar H, Bouhya S, et al. Tuberculose pelvienne simulant une tumeur ovarienne bilatérale: À propos d'un cas. Journal de gynécologie obstétrique et biologie de la reproduction. 2004; 33: 145-147.

33. Sfar E. La tuberculose genitale feminine en Tunisie. A propos de 118 cas au Centre de Maternite et de Neonatalogie de la Rabta de Tunis (Janvier 1984-Decembre 1988). Rev Fr Gynecol Obstet. 1990; 85: 359-363.

34. Patel SM, Lahamge KK, Desai AD, Dave KS. Ovarian carcinoma or abdominal tuberculosis?-a diagnostic dilemma: study of fifteen cases. The Journal of Obstetrics and Gynecology of India. 2012; 62: 176-178.

35. Koc S, Beydilli G, Tulunay G, Ocalan R, Boran N, Ozgul N, et al. Peritoneal tuberculosis mimicking advanced ovarian cancer: a retrospective review of 22 cases. Gynecologic oncology. 2006; 103: 565-569.

36. Wu C-H, Changchien C-C, Tseng C-W, Chang H-Y, Ou Y-C, Lin H. Disseminated peritoneal tuberculosis simulating advanced ovarian cancer: a retrospective study of 17 cases. Taiwanese Journal of Obstetrics and Gynecology. 2011; 50: 292-296.

37. Vanderpuye V, Yarney J. Ovarian cancer: an analysis of forty-four patients at the National Radiotherapy Centre, Accra--Ghana. West African journal of medicine. 2007; 26: 93-96.

38. Harford JB. Breast-cancer early detection in low-income and middle-income countries: do what you can versus one-size fits all. The lancet oncology. 2011; 12: 306-312.

39. Jedy-Agba E, Curado MP, Ogunbiyi O, Oga E, Fabowale T, Igbinoba F, et al. Cancer incidence in Nigeria: a report from population-based cancer registries. Cancer epidemiology. 2012; 36: e271-e278.

40. Sun Z, Gilbert L, Ciampi A, Basso O. Recruitment challenges in clinical research: Survey of potential participants in a diagnostic study of ovarian cancer. Gynecologic oncology. 2017; 146: 470-476.