

## Editorial

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## Editorial

We thank the Editor in Chief of the Journal of Obstetrics and Gynaecology, Dr Ayman Ewies, for giving us the honour of commenting on some selected papers that have provided exciting insights for clinical practice and future research directions in gynaecology and obstetrics.

Kassa *et al.* (2023) published a systematic review and meta-analysis about associated factors to the survival rate in women with cervical cancer (CC) in East Africa. The paper showed a 5-year overall survival of 36%, which is much lower than in developed countries. This interesting review highlights the critical issues in the prevention of CC. It is the only gynecological cancer with primary prevention [Human Papilloma Virus (HPV) vaccine] and secondary prevention (CC screening through the HPV-DNA test and traditional or liquid phase cytology) (WHO 2018). Despite these tools, CC is one of the most widespread gynecological oncological diseases, with 80% of cases in developing countries (WHO 2018). In this regard, the World Health Organisation launched the initiative to achieve the following goals by 2030 for its elimination (WHO 2018): (i) 90% vaccination coverage in girls by the age of 15, (ii) CC screening coverage of 70%, and (iii) A possibility of appropriate treatment in 90% of pre-invasive and invasive cervical lesions. We are far below these numbers worldwide (Bogani *et al.* 2023). The strategy of the single dose of vaccine compared to 2 or 3 doses can help to obtain a wider vaccination diffusion at less cost (HPV Vaccines: WHO position paper 2022). Every country globally should achieve these goals through information and awareness campaigns for women of screening age and parents with daughters of vaccination age.

In a retrospective observational study, Zheng *et al.* (2023) analysed five years of follow-up regarding overall survival, progression-free survival, and local control in women with CC and locoregional recurrence subjected first and only to surgery and then to life-saving radiotherapy. We know that women with locoregional recurrence of cervical cancer (Central Pelvic Recurrence After Primary Surgery) should undergo definitive chemotherapy and image-guided adaptive brachytherapy. Image-guided brachytherapy can be used for small superficial vaginal lesions less than 5 mm thick (Cibula *et al.* 2023). The study by Zheng *et al.* measured the dose-dependent effect of radiotherapy on survival, a topic on which few studies in the literature have focused. Interestingly, a salvage dose greater than or equal to 72.6 Gy appears optimal for more extended local control of extravaginal recurrence (Zheng *et al.* 2023).

Unlike what has been said for CC, endometrial cancer (EC) is the most common gynaecological cancer in developed countries (Siegel *et al.* 2021). Consequently, it represents a public health problem. Although EC diagnosis usually occurs

in the early stages, there were approximately 13,000 EC deaths in the United States in 2021 (Siegel *et al.* 2021). Therefore, the study of new diagnostic and prognostic biomarkers is undoubtedly a topic of clinical relevance. In this regard, Li *et al.* (2023) studied circular RNA (circRNA) and micro-RNA (miRNA) expression profiles in EC. The authors found a downregulation of hsa\_circRNA\_079422 and an upregulation of miR-136-5p in tissues from women with EC (Li *et al.* 2023). Such data are of interest for clinical implications given that these biomarkers can predict the diagnosis and prognosis of the disease and identify targeted treatments for a more personalised medicine. Further interest in this area is given by the fact that circRNAs could also be detected on liquid biopsies through saliva, plasma, or urine samples (Kristensen *et al.* 2022). This aspect is very interesting for the early diagnosis of diseases in which there is a need for invasive methods for tissue sampling, such as in EC and ovarian cancer (OC).

As evidence of the interest in the study of new and promising biomarkers in the oncology field, there is another fascinating study by Cheng *et al.* (2023) about the expression of Kruppel-like factor 2 (KLF2) in EC. Several studies have demonstrated the role of KLF2 as a tumour suppressor in various oncological diseases (Taghehchian *et al.* 2023). On the contrary, very little data is available on the role of KLF2 in EC. Of interest, Cheng *et al.* (2023) showed that KLF2 provides anti-tumour action in EC by suppressing the expression of Nucleophosmin 1 (NPM1), which has pro-tumour activity. As reported by the authors, these data are relevant given that the induction of KLF2 overexpression could be the aim of future research to evaluate its impact as a treatment in EC.

Wang *et al.* (2023) focused on studying BAG3 mRNA in gynecological cancers. BAG3 is a member of the BAG family of co-chaperones whose expression can be induced by stress stimuli or malignancy (De Marco *et al.* 2021). Several studies have found BAG3 to increase cell survival and resistance to therapy in various malignancies (De Marco *et al.* 2021). The mechanisms of action of BAG3 in gynaecological cancers appear to increase cancer cell invasion, cell motility and invasiveness, cell survival and proliferation, HPV-mediated cell transformation, and chemoresistance (De Marco *et al.* 2021). In their paper, Wang *et al.* (2023) showed that BAG3 expression is closely associated with signalling pathways linked to tumour growth, invasion, and resistance to therapy in breast, CCs, ECs, and OCs. Blocking BAG3 expression through anti-BAG3 antibodies could be a successful strategy in combination with other anti-cancer therapies (De Marco *et al.* 2021). Furthermore, it could be an innovative diagnostic and prognostic marker in gynaecological cancers.

Finally, the role of new serum biomarkers is a topic of interest even in the obstetric field. Ji *et al.* (2023) studied serum proteomic profiles in patients with early-onset pre-eclampsia compared with healthy pregnant women. The authors showed significant differences between cases and controls in serum chorionic somatomammotropin hormone 1 (CSH1) and lysophosphatidic acid (LPA) values. Higher and lower serum levels of LPA and CSH1, respectively could be used as markers to predict the early onset of pre-eclampsia (Ji *et al.* 2023), facilitating earlier diagnosis and individualisation of care.

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