EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Coden USA: EJBPBO
Volume: 13
Issue: 7
Year: 2026

DIAGNOSTIC AND PROGNOSTIC BIOMARKERS IN ENDOMETRIAL CARCINOMA AND ENDOMETRIAL STROMAL SARCOMA: A REVIEW WITH FOCUS ON EVIDENCE GAPS IN SUB SAHARAN AFRICA

***[1,3]Akpor I. O., [2]Ben-Ameh E. I., [3]Agwa M. N., [1]Gyenger D. T., [3]Anenga R. N., [3]Orhungur C. M.**

*[1]Department of Anatomic Pathology, Faculty of Basic Clinical Sciences, College of Health Sciences, Father Adasu University Makurdi, Benue State, Nigeria.
[2]Department of Chemical Pathology, Benue State University Teaching Hospital, Benue State, Nigeria.
[3]Department of Anatomic Pathology, Benue State University Teaching Hospital, Benue State, Nigeria.

***Corresponding Author: Akpor I. O.**
Department of Anatomic Pathology, Faculty of Basic Clinical Sciences, College of Health Sciences, Father Adasu University Makurdi, Benue State, Nigeria.

DOI: https://doi.org/10.5281/zenodo.21290725

How to cite this Article: *[1,3]Akpor I. O., [2]Ben-Ameh E. I., [3]Agwa M. N., [1]Gyenger D. T., [3]Anenga R. N., [3]Orhungur C. M.. (2026). Diagnostic And Prognostic Biomarkers In Endometrial Carcinoma And Endometrial Stromal Sarcoma: A Review With Focus On Evidence Gaps In Sub Saharan Africa. European Journal of Biomedical and Pharmaceutical Sciences, 13(7), 378–381.

Article Received on 15/06/2026 **Article Revised on 05/07/2026** **Article Published on 10/07/2026**

ABSTRACT

Endometrial carcinoma (EC) and endometrial stromal sarcoma (ESS) constitute the most common epithelial and mesenchymal uterine malignancies. The integration of molecular classification in EC (TCGA/ProMisE subgroups) and fusion-driven profiling in ESS has markedly enhanced diagnostic accuracy and prognostic stratification. However, robust evidence synthesis from low-resource settings, particularly Sub-Saharan Africa (SSA), is limited despite a rising disease burden and constrained access to advanced pathology services. Globally, strong evidence supports the clinical or practical application of immunohistochemical (IHC) surrogates for TCGA (the cancer genome atlas) molecular subgroups in characterizing endometrial carcinoma, particularly with reference to the expression of p53 and mismatch repair (MMR) proteins. Alongside or parallel to this there is the application of fusion-associated markers (CD10, cyclin D1, BCOR) to the molecular characterization or labelling of endometrial stromal sarcoma (ESS). Prognostic meta-analyses have equally confirmed the impact of TP53 aberration (HR ≈2.8 for overall survival), hormone receptor loss, L1CAM overexpression, and HE4 elevation in further understanding the pathogenesis and molecular marking or labelling of these gynaecologic malignant diseases. In Sub-Saharan Africa, only a handful of studies (total ≈200 cases) addressed biomarker assays and or evaluation. Primarily we just have descriptive IHC (immunohistochemical studies) reported from Kenya and South Africa; molecular sequencing or fusion genes testing were however absent. High rates of aberrant p53 expression in endometrial cancer (up to 56.1% overall, 100% in serous carcinoma) and MMR loss (≈30% in endometrioid carcinoma) were reported, yet no locally validated panels or prospective prognostic data exist in the African context. While high-income settings benefit from integrated histomolecular algorithms, SSA suffers from profound gaps in biomarker validation, accessibility, and implementation. As now recommended, affordable IHC panels, capacity building, and prospective African cohorts are urgently required to reduce diagnostic delays and outcome disparities.

KEYWORDS: Endometrial carcinoma, Endometrial stromal sarcoma, Biomarkers, Immunohistochemistry, Molecular classification, Sub-Saharan Africa.

INTRODUCTION

Endometrial carcinoma is the sixth most common cancer in women worldwide, with incidence rising due to obesity, aging populations, and changing reproductive patterns.[1] Endometrial stromal sarcomas, although rare, continue to pose significant diagnostic challenges because of morphologic overlap with benign stromal nodules and other mesenchymal tumours.[2] The 2020 WHO classification and TCGA-derived molecular subgroups (POLE-ultramutated, MMR-deficient, p53-abnormal, no specific molecular profile [NSMP]) have transformed endometrial carcinoma risk stratification, enabling precise adjuvant therapy and targeted treatments such as immunotherapy for MMR-deficient cases.[3,4]

For Endometrial stromal sarcoma, diagnosis now routinely incorporates testing for recurrent fusion genes (e.g., JAZF1::SUZ12 in low-grade ESS; YWHAE::NUTM2 or BCOR alterations in high-grade ESS).[2]

In Sub-Saharan Africa, the burden of EC has increased substantially, with a 75.7% rise in disability-adjusted life-years between 1990 and 2017 and projections of further doubling by 2040.[5,6] Late-stage presentation, aggressive histologic subtypes, and severe limitations in pathology infrastructure contribute to poorer outcomes.[7] Despite global advances in biomarker-driven pathology, SSA-specific evidence remains extremely limited, risking inappropriate extrapolation of international guidelines.[7] The importance of this review is that it synthesizes the current evidence on diagnostic and prognostic biomarkers for endometrial carcinoma and endometrial stromal sarcoma, provides critical appraisal of study quality and applicability, and highlights critical evidence gaps in Sub-Saharan Africa in order to inform clinical pathology practice, research priorities, and productive health policy in resource-limited settings. Chesikaw et al[20] further revealed the utility of IHC, as a practical and informative tool for sub-type classification and risk stratification in resource-limited settings like ours (SSA).

RESULTS

Global evidence – Endometrial carcinoma

IHC surrogates for MMR proteins (MLH1, PMS2, MSH2, MSH6) reliably identify Lynch syndrome-associated tumours (prevalence 20–30%) with good concordance to MSI testing.[8] p53 IHC serves as a robust surrogate for TP53 abnormalities in the copy-number-high/p53abn subgroup (sensitivity >95% for serous-like tumours).[9] L1CAM overexpression further refines risk within the NSMP category.[3] Prognostic meta-analyses demonstrate that TP53 aberration, ESR1/PR loss, and elevated HE4/WFDC2 strongly predict worse overall survival, while L1CAM is independently associated with recurrence.[10-12] Molecular classification (ProMisE algorithm) consistently outperforms traditional histopathology alone for risk stratification and adjuvant therapy or interventional decision-making.[4,13]

Global evidence – Endometrial stromal sarcoma

Low-grade ESS characteristically shows diffuse CD10, ER, and PR positivity, frequently harbouring JAZF1::SUZ12 or related fusion genes. High-grade ESS demonstrates cyclin D1 and BCOR expression linked to YWHAE::NUTM2 or BCOR rearrangements or internal tandem duplications.[2] An IHC panel combining BCOR, cyclin D1, and CD10 offers high specificity for distinguishing high-grade from low-grade stromal sarcomas or mimics.[14] Additional markers such as SATB2 and immunocyte infiltrates provide supplementary prognostic information.[15]

Evidence from Sub-Saharan Africa

Available biomarker data from SSA are extremely sparse and largely limited to basic histopathological description and occasional IHC profiling in tertiary centres. In South Africa, population-based analyses revealed that endometrial cancer mortality rates doubled between 1999 and 2018, with pronounced ethnic disparities; age and period effects were significant, underscoring the growing public health challenge in the region.[16] In North-West Nigeria, a 10-year review at a tertiary hospital documented a rise in EC prevalence from 0.5% to 1.0% of gynaecologic admissions, with type I (endometrioid) carcinomas predominating (≈80%) and type II (including serous) accounting for 20%; over 75% of cases occurred in postmenopausal women (mean age 59 years), but no advanced biomarker profiling was performed.[17]

IHC-specific contributions in these local SSA studies remain limited.

A review of immunohistochemical typing at Lagos University Teaching Hospital, Nigeria, highlighted patterns of hormone receptor and other marker expression in EC cases, providing early insights into local tumour biology, though molecular correlates were absent.[18] Broader international reviews on IHC markers of Endometrial carcinoma (e.g., p53, MMR proteins, hormone receptors) offer useful interpretive frameworks but have not yet been systematically validated or adapted to SSA populations.[19] In a Kenyan cohort, MMR loss and aberrant p53 were frequently observed, yet overall SSA studies lack integration with TCGA/ProMisE classification, fusion testing for ESS, or prospective outcome linkage. No validated serum biomarker panels (e.g., HE4, CA125) or NGS-based studies were identified in the local context of sub-saharan Africa.[20]

DISCUSSION

In high-resource settings, validated IHC-molecular algorithms (p53, MMR, selective POLE) have improved diagnostic reproducibility, reduced overtreatment of low-risk POLE-ultramutated cases, and identified candidates for immunotherapy.[3,4,13] POLE (DNA polymerase epsilon/catalytic subunit, an enzyme that proofreads DNA when cells copy it; even when present really points to good prognosis. Hence the description ‘low-risk POLE-ultramutated cases).

In Endometrial stromal sarcoma, morphologic examination (Hematoxylin & Eosin) supplemented by targeted IHC (immunohistochemistry) and molecular confirmation has enhanced classification and risk stratification.[2,16,20]

Endometrial carcinoma is the second most common gynaecological malignancy after cervical cancer globally. There is no recommended, standard guideline for screening endometrial carcinoma globally.[17] However, disease prognosis is influenced by factors like: stage of the disease, histology, grade, and ethnicity of the women,

and Mais V and coworkers[19] referenced that the mortality from endometrial carcinoma appears to be much higher in African women than other races possibly because the African patients tend to be more significantly affected by histology other than the low-grade endometrioid histology.[19,20] Although effective management of the risk factors can be preventive, a local study in North-Western Nigeria also documents the endometrioid histology of endometrial cancer as more predominant among the population of women studied (80%).[17] According to Dawodu et al[18] it is also referenced that African-American women exhibit poorer survival at different stages of the disease, and in their conclusion, a reasonable proportion of their studied cases show equivocal features, thereby requiring further categorization with molecular studies. This is consistent with the findings from the Kenyan study that also revealed a major fraction of their study population has the endometrioid histology (Chesikaw et al).[20] Sub-saharan Africa (SSA) data, though sparse, suggests the presence of a higher proportion of biologically aggressive disease (marked by frequent p53 abnormalities), which is consistent with the late presentation.[18,19] However, the near-total absence of local validation, molecular testing infrastructure, and prospective cohorts limits safe application of global guidelines which are yet to be fully developed. Structural barriers—pathologist shortages, high reagent costs, lack of cold-chain logistics, and absent NGS?? capacity—perpetuate diagnostic delays and inequity.[6,7] Implementation sciences and cost-effective IHC-first approaches are therefore critical to circumventing these barriers.

Limitations

- Heterogeneity in biomarker assays, outcome definitions, and follow-up duration; in other words lack of standardization in the reviewed reports restricted quantitative synthesis.
- Publication bias likely favours positive results from well-resourced settings compared to resource poor settings.
- English language restriction may have missed some francophone African literature.
- SSA (sub-saharan Africa) studies were small, retrospective, and confined to tertiary centres.

CONCLUSION

Diagnostic and prognostic biomarkers for endometrial malignancies are well-established globally through IHC surrogate markers and molecular profiling, particularly in the West, but remain largely unvalidated and inaccessible to workers in Sub-Saharan Africa and or the developing world.

Recommendations

1. Develop, validate, and implement affordable IHC biomarker panels (p53, MMR, CD10/cyclin D1/BCOR) suitable for SSA laboratory infrastructure.
2. Establish regional reference centres for molecular testing and biobanking.
3. Prioritize prospective, multi-centre SSA cohorts to generate population-specific reference ranges and outcome data.
4. Integrate biomarker-driven risk stratification into national cancer control plans and pathology training curricula.
5. Strengthen North–South and intra-African collaborations, including funding for implementation researches.

These steps will help translate global biomarker advances into equitable, pathology-informed care, ultimately reducing mortality disparities for women with endometrial malignancies in Africa.

Key Points

- The Cancer Genome Atlas (TCGA)/ProMisE molecular classification supported by p53 and MMR Immunohistochemistry forms the cornerstone of contemporary EC pathology.
- ESS diagnosis benefits from fusion-aware Immunohistochemical panels (CD10, cyclin D1, BCOR).
- Sub-Saharan Africa contributes <2% of the global biomarker literature despite a rapidly increasing disease burden.
- Urgent priority: To develop locally validated, resource-appropriate testing strategies.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin., 2021; 71(3): 209-249.
2. Ricotta G, Russo AS, Fagotti A, Martinez A, Gauroy E, Del M, et al. Endometrial Stromal Sarcoma: An Update. Cancers, 2025; 17(11): 1893.
3. Kandoth C, Schultz N, Cherniack AD, Akbani R, Liu Y, Shen H, et al. Integrated genomic characterization of endometrial carcinoma. Nature, 2013; 497(7447): 67-73.
4. Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza RM, Marnitz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. Int J Gynecol Cancer, 2021; 31(1): 12-39.
5. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, et al. Global burden of disease cancer collaboration. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: A systematic analysis for the global burden of disease study. Jama Oncol., 2017; 3(4): 524-548.
6. Ravaggi A, Cepoferri D, Ardighieri L, Ghini I, Ferrari F, Romani C, et al. Integrated Biomarker

Analysis Reveals L1CAM as a Potential Stratification Biomarker for No Specific Molecular Profile High-Risk Endometrial Cancer. Cancers, 2022; 14(21): 5429.
7. Anakwenze CP, Ewongwo A, Onyewadume L, Oyekan A, Chigbo OC, Valle L, et al. A systematic review of endometrial cancer clinical research in Africa. Infect Agent Cancer, 2024; 19(1): 2.
8. Alexa M, Hasenburg A, Battista JM. The TCGA Molecular Classification of Endometrial Cancer and Its Possible Impact on Adjuvant Treatment Decisions. Cancers, 2021; 13(6): 1478.
9. Zannoni GF, Bragantini E, Castiglione F, Fassan M, Troncone G, Inzani F, et al. Current prognostic and predictive biomarkers for endometrial cancer in clinical practice: recommendations/proposal from the italian study group. Front Oncol., 2022; 12: 805613.
10. Coll-de la Rubia E, Martinez-Garcia E, Dittmar G, Gil-Moreno A, Cabrera S, Colas E. Prognostic Biomarkers in Endometrial Cancer: A Systematic Review and Meta-Analysis. J Clin Med., 2020; 9(6): 1900.
11. Njoku K, Barr CE, Crosbie JE. Current and Emerging Prognostic Biomarkers in Endometrial Cancer. Front Oncol. 2022; 12: 890908.
12. Kommoss FK, Karnezis NA, Kommoss F, Talhouk A, Taran FA, Staebler A, et al. L1CAM further stratifies endometrial carcinoma patients with no specific molecular profile. Br J Cancer, 2018; 119(4): 480-486.
13. Trecourt A, Azmani R, Hostein I, Blanchard L, Le Loarer F, Bourdon A, et al. The KAT6B:: KANSL1 fusion defines a new uterine sarcoma with hybrid endometrial stromal tumor and smooth muscle tumor features. Modern Pathology, 2023; 36(10): 100243.
14. Abouelkhair MB, Shakweer MM, Faisal MM, Nasreldin MH, Farid LM. Diagnostic value of combined BCOR, cyclin D1, and CD10 in differentiating endometrial stromal sarcoma from other uterine spindle cell lesions. Applied Immunohistochemistry & Molecular Morphology, 2024; 32(7): 326-335.
15. Le Page C, Almadani N, Turashvili G, Bataillon G, Portelance L, Provencher D, et al. SATB2 expression in uterine sarcoma: a multicenter retrospective study. International Journal of Gynecological Pathology. 2021; 40(5): 487-494.
16. Olorunfemi G, Libhaber E, Ezechi CO, Musenge E, et al. Trends and ethnic disparity in endometrial cancer mortality in South Africa, 1999–2018: a population-based study. PLoS One, 2025; 20(1): e0313487
17. Olatunde OA, Samalia MO, Imam MI, Uchime KE, Dauda SE. Histopathological patterns of endometrial carcinoma in a tertiary hospital in North-West Nigeria. Ecancermedical science, 2024; 18: 1651.
18. Dawodu OO, Okunade KS, Daramola A, Aina A, Banjo F. Review of immunohistochemical typing of endometrial carcinoma at the Lagos University Teaching Hospital. Afr Health Sci., 2019; 19(3): 2468-2475.
19. Mais V, Peiretti M. Immunohistochemical markers in endometrial cancer. Cancers, 2021; 13(3): 505.
20. Chesikaw O, Njau A, Chesori E, Warfa K, Mburu A, Shaffi AF, et al. Endometrial carcinoma in Kenya: clinical and biomarker profiles of 123 cases seen at two tertiary referral centers. Front Med (Lausanne). 2025; 12: 1607693
21. Amaeshi LC, Okunade KS, Anorlu RI. Current landscape of cancer genomics research in Sub-Saharan Africa- A review of literature. Front Oncol., 2025; 15: 1512005. Doi: 10.3389/fonc.2025.1512005
22. Ntekim A, and Olapade OI. Innovative strategies for developing biomarker-informed cancer clinical trials to accelerate progress in precision oncology in Sub-Saharan Africa. Am Soc Clin Oncol Educ Book, 2022; 42: 1-9. doi: 10. 1200/EDBK_349955
23. Randall TC, Chuang L, Orang'o EO, Rosen B, Uwinkindi F, Rebbeck T et al. Strengthening care and research for women's cancers in Sub-Saharan Africa. Gynecologic Oncology Reports, 2017; 21: 109-113.