

ORIGINAL ARTICLE

Impact of Early Detection and Treatment on the Prognosis of Endometrial Cancer in High-Risk Populations

SAJIDA RAZZAQ¹, SOFIA MANZOOR², SADIA DILAWAR³, LUBNA MALIK⁴, MAHPARA SHAUKAT⁵, AROOJ MUSHTAQ⁶¹Postgraduate Resident Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore²Senior Woman Medical Officer Obstetrics and Gynaecology, Sir Ganga Ram Hospital, Lahore³Assistant Professor Obstetrics and Gynaecology, Abbottabad International Medical College Abbottabad⁴Assistant Professor Anatomy, Avicenna Medical College, Lahore⁵Assistant Professor Obstetrics and Gynaecology, Sahiwal Teaching Hospital, Sahiwal⁶Postgraduate Resident Obstetrics and Gynaecology, Pakistan Atomic Energy Commission/General Hospital, IslamabadCorrespondence to: Sajida Razzaq, Email: noorkhanniazi@hotmail.com, Cell: +92 335 1435361

ABSTRACT

Background: Endometrial cancer is a common gynecologic malignancy whose prognosis largely depends on the stage at diagnosis and the timeliness of treatment.

Objective: This study aimed to assess the effect of early detection and prompt treatment on the prognosis of endometrial cancer among high-risk patients.

Methodology: This retrospective observational study was conducted at Sir Ganga Ram Hospital, Lahore from November 2022 to May 2023. It included 165 female patients with histologically confirmed endometrial carcinoma. Patients were categorized into two groups: the early detection and treatment group (Stage I–II, treated within four weeks; n = 92) and the delayed detection and treatment group (Stage III–IV or treated after four weeks; n = 73).

Results: The mean age of the study population was 58.7 ± 9.8 years, with obesity (59.4%) and diabetes (46.1%) being the most prevalent comorbidities. Endometrioid adenocarcinoma was the most common histological subtype (76.4%). The three-year overall survival rate was 91.3% in the early group compared to 63.0% in the delayed group ($p < 0.001$). Disease-free survival was also significantly higher in the early group (87.0% vs. 55.0%, $p = 0.002$). Recurrence occurred in 11.9% of early cases and 32.9% of delayed cases. Treatment-related complications were more frequent in the delayed group (21.9% vs. 9.8%).

Conclusion: It is concluded that early detection and timely treatment significantly improve survival and reduce recurrence in endometrial cancer, particularly among high-risk women. Delayed diagnosis or initiation of therapy adversely affects prognosis and increases treatment-related morbidity.

Keywords: Endometrial cancer, early detection, prognosis, high-risk populations, survival, treatment delay

INTRODUCTION

Endometrial cancer is one of the most common gynecologic malignancies, ranking as a major cause of morbidity and mortality among women worldwide. Originating from the endometrial lining of the uterus, it is characteristically related to menopausal bleeding, a symptom which facilitates relatively early clinical recognition. This apparent diagnostic benefit, however, is not equally available to all women. High-risk populations, including women with obesity, diabetes mellitus, hypertension, excessive estrogen exposure, nulliparity, or genetic conditions such as Lynch syndrome, tend to present the condition at more advanced stages, which translates into more negative outcomes and increased mortality. The prognosis is substantially improved in cases of early disease, where the entire uterus can be resected with curative intent, leading to an excellent survival rate and minimal need for adjuvant therapy. In contrast, the prognosis is poor when substantial disease is present and is accompanied by lymphovascular invasion, distant metastasis, and resistant disease. The diagnosis timing influences the therapy type and the therapy level and a patient's quality of life. Early detection of endometrial cancer enables potentially curative rather than palliative interventions, highlighting the importance of action and surveillance in public health and clinical practice⁴. For high-risk patients, the challenge goes beyond the biological aggressiveness of some tumor subtypes to include systemic and behavioural factors that hinder recognition. For many patients, early warning signs, like irregular bleeding, are unreported as they are assumed benign or related to aging⁵. Gaps in health service availability, poorly designed awareness initiatives, and sociocultural barriers to openly addressing gynecological issues further fuel delays to diagnosis⁶. Unfortunately, this results in a malignancy that is preventable and easily treatable evolving to a life-threatening illness. With regard to endometrial cancer, the speed and appropriateness of therapy after diagnosis primarily influence recurrence, survival, and other critical outcomes, illustrating the

importance of treating the disease early⁷. The shift in more surgical staging to minimally invasive approaches to management has resulted in fewer complications and improved recovery times⁸. The adjuvant use of radiotherapy or chemotherapy can be avoided in early-stage cases. In stark contrast, a delay in treatment will most certainly result in worse outcomes and higher morbidity and psychological burden due to the requirement of extensive surgery followed by aggressive adjuvant therapy⁹⁻¹¹.

Objective: This study aimed to assess the effect of early detection and prompt treatment on the prognosis of endometrial cancer among high-risk patients.

METHODOLOGY

This was a retrospective observational study conducted at Sir Ganga Ram Hospital, Lahore from November 2022 to May 2023. A total of 165 patients diagnosed with histopathologically confirmed endometrial carcinoma were included in the study. Non-probability consecutive sampling was used to select eligible patients who fulfilled the inclusion and exclusion criteria.

Inclusion Criteria:

1. Female patients aged 35 years and above.
2. Histologically confirmed diagnosis of endometrial carcinoma.
3. Belonging to high-risk groups such as obesity, diabetes mellitus, prolonged unopposed estrogen therapy, polycystic ovarian syndrome, or a positive family history of endometrial or colorectal cancer.
4. Patients who underwent surgical or combined modality treatment with available follow-up data.

Exclusion Criteria:

1. Patients with incomplete medical records or lost to follow-up.
2. Secondary malignancies involving the endometrium.
3. Patients previously treated for other gynecologic cancers.

Data Collection: Data were retrieved from hospital records, pathology reports, and follow-up charts. Information collected included demographic details, risk factors, presenting symptoms, diagnostic methods, stage at diagnosis, treatment modalities, and follow-up outcomes. Patients were categorized into early detection (Stage I–II) and late detection (Stage III–IV) groups. Treatment

Received on 25-06-2023

Accepted on 02-11-2023

timeliness was classified based on the interval between diagnosis and initiation of definitive therapy. The primary outcomes evaluated were overall survival, disease-free survival, and recurrence rate. Secondary outcomes included the relationship between detection timing, treatment delay, and stage at diagnosis among high-risk patients.

Data Analysis: All data were entered and analyzed using SPSS version 26.0. Quantitative variables such as age and BMI were presented as mean \pm standard deviation, while categorical variables such as stage of disease, detection status, and treatment timing were expressed as frequencies and percentages. The chi-square test was used to assess associations between categorical variables, while independent-sample t-tests compared means where applicable. A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1 shows that the mean age of the 165 patients was 58.7 ± 9.8 years, and the mean BMI was 31.6 ± 5.4 kg/m², indicating that most patients were overweight or obese. Obesity was present in 59.4%, diabetes in 46.1%, and hypertension in 38.2% of cases. Both groups had similar comorbidity profiles; however, the mean time to treatment was significantly shorter in the early group (22.4 ± 6.1 days) compared to the delayed group (49.2 ± 8.7 days, $p < 0.001$).

Table 2 shows the stage and histopathological distribution. In the early group, 68 patients (73.9%) were diagnosed at Stage I and 24 (26.1%) at Stage II, while none had advanced disease. In contrast, the delayed group had 46 (63.0%) Stage III and 18 (24.7%) Stage II cases. Endometrioid adenocarcinoma was the most frequent histologic subtype, accounting for 126 cases (76.4%), followed by serous carcinoma in 22 (13.3%) and clear-cell carcinoma in 17 (10.3%). Aggressive histologic variants were more common among the delayed group.

Table 1: Baseline Demographic and Clinical Characteristics (n = 165)

Variable	Total (n = 165)	Early Detection/Treatment (n = 92)	Delayed Detection/Treatment (n = 73)
Mean Age (years)	58.7 ± 9.8	57.9 ± 9.2	59.8 ± 10.3
BMI (kg/m ²)	31.6 ± 5.4	30.9 ± 5.1	32.5 ± 5.6
Obesity (%)	98 (59.4%)	52 (56.5%)	46 (63.0%)
Diabetes Mellitus (%)	76 (46.1%)	40 (43.5%)	36 (49.3%)
Hypertension (%)	63 (38.2%)	33 (35.9%)	30 (41.1%)
Family History of Cancer (%)	18 (10.9%)	8 (8.7%)	10 (13.7%)
Mean Time to Treatment (days)	35.1 ± 13.4	22.4 ± 6.1	49.2 ± 8.7

*Significant at $p < 0.05$

Table 2: Histopathological and Stage Distribution

Parameter	Early Group (n = 92)	Delayed Group (n = 73)	Total (n = 165)
Stage I	68 (73.9%)	9 (12.3%)	77 (46.7%)
Stage II	24 (26.1%)	18 (24.7%)	42 (25.4%)
Stage III	0 (0%)	46 (63.0%)	46 (27.9%)
Histologic Type			
– Endometrioid	78 (84.8%)	48 (65.8%)	126 (76.4%)
– Serous	9 (9.8%)	13 (17.8%)	22 (13.3%)
– Clear Cell	5 (5.4%)	12 (16.4%)	17 (10.3%)

Table 3: Prognostic Outcomes by Detection and Treatment Timing

Outcome	Early Group (n = 92)	Delayed Group (n = 73)	p-value
3-Year Overall Survival (%)	91.3	63.0	$< 0.001^*$
3-Year Disease-Free Survival (%)	87.0	55.0	0.002*
Recurrence Rate (%)	11.9	32.9	0.001*
Mean Recurrence-Free Interval (months)	31.4 ± 4.2	24.1 ± 5.6	0.001*
Treatment-Related Complications (%)	9.8	21.9	0.03*

*Statistically significant at $p < 0.05$

Table 4: Treatment Modalities and Postoperative Course

Treatment Type	Early Group (n = 92)	Delayed Group (n = 73)	p-value
Surgery Only	79 (85.9%)	25 (34.2%)	$< 0.001^*$
Surgery + Radiotherapy	13 (14.1%)	42 (57.5%)	$< 0.001^*$
Chemoradiotherapy	0	6 (8.2%)	0.002*
Median Hospital Stay (days)	5 ± 1.3	8 ± 2.5	$< 0.001^*$
Post-Op Wound Infection	3 (3.3%)	7 (9.6%)	0.08
Re-admission within 30 Days	2 (2.2%)	5 (6.8%)	0.12

*Significant at $p < 0.05$

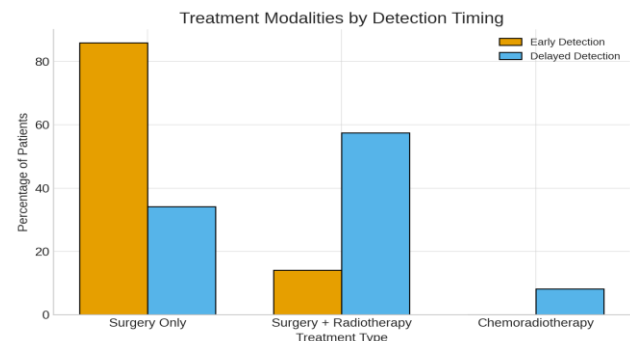
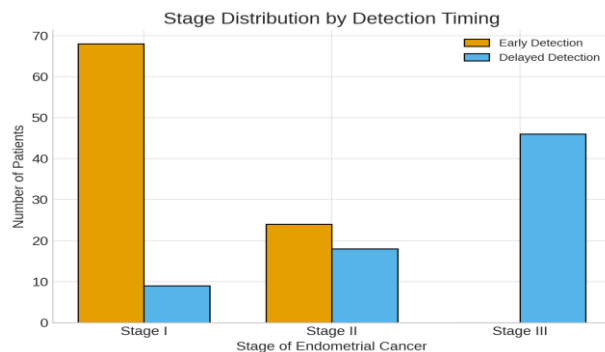


Table 3 indicates that survival outcomes were significantly better in early-detected cases. The three-year overall survival was 91.3% in the early group compared to 63.0% in the delayed group ($p < 0.001$). Disease-free survival was 87.0% versus 55.0% ($p = 0.002$). Recurrence occurred in 11.9% of early and 32.9% of delayed cases, and the mean recurrence-free interval was longer in early cases (31.4 ± 4.2 months) compared to delayed ones (24.1 ± 5.6 months).

Table 4 shows that 79 patients (85.9%) in the early group were treated with surgery alone, whereas only 25 (34.2%) in the delayed group underwent surgery without adjuvant therapy ($p < 0.001$). Combined surgery and radiotherapy were required in 42 delayed cases (57.5%), and 6 patients (8.2%) received chemoradiotherapy. The median hospital stay was shorter for early cases (5 ± 1.3 days) compared to delayed ones (8 ± 2.5 days, $p < 0.001$).

DISCUSSION

The findings of this study demonstrate that early detection and timely treatment significantly improve the prognosis of endometrial cancer, particularly in high-risk populations. Of the 165 patients evaluated, the outcomes in patients diagnosed and treated in the first month at Stage I–II were attributable to the increased overall survival, extended disease-free periods, and decreased disease recurrence. These findings strengthen the conviction in the clinical community that the optimal curative potential and enduring survivability for patients with endometrial cancer is most favorable when cancer is detected in the early stages. The findings in this study underscore the established link between the stage of disease at presentation and survival outcomes. This is consistent with the positioning of endometrial cancer within the wider context of global practice in gynecologic oncology. The majority of early endometrial carcinomas are confined to the uterine corpus, and surgical resection is curative. As our findings indicate, 85% of early diagnosed cases were able to undergo surgery, with more than 90% surviving the three-year mark. In contrast, more advanced cases with Stage III or IV disease are still inferior, even when response to systemic chemoradiation is achieved. The explanation is likely to be the aggressive nature of the disease with respect to the extent of local invasion and metastasis which is known to limit the impact of treatment, regardless of the extent of multimodal therapy employed¹². High-risk populations face unique challenges that can drive the onset or worsen the course of Disease X. Obesity, diabetes mellitus, and hypertension are also other conditions that can promote the hormonal and inflammatory environment that supports endometrial growth and malignancy and are present in the studied cohort, indicating the increasing burden of metabolic syndrome in developing nations¹³. In addition, System-level and behavioral barriers lead to delayed presentation in the individuals studied, particularly in individuals with metabolic comorbidities, as symptoms overlap, and reduced health literacy or sociocultural factors restrict access to health care. Data showed that women with metabolic comorbidities were overrepresented in the delayed group, illustrating how systemic and behavioral factors converge to worsen advanced disease stage at the time of diagnosis. The time to treatment became an independent predictor of outcome. Patients whose treatment was initiated within four weeks had better survival rates, less recurrence, and lower treatment delays compared to patients whose treatment was initiated later^{14–16}. The treatment initiation gap of nearly 27 days, recorded in this study between the two groups, is enough to significantly affect prognoses. This indicates that care in endometrial cancer has a critical window of opportunity where rapid surgical and adjunctive treatment can be therapeutic and halt the advancement of disease¹⁷. Transforming what should be a curable malignancy into a malignancy with a poor prognosis can be accomplished through delays resulting from administrative inefficiencies, delays in referrals, and patient hesitancy. The histopathological analysis in this instance further reinforces the value of early detection¹⁸. Considering cases diagnosed at early

stages, Endometrioid adenocarcinoma, the most common subtype, was the most dominant and is usually associated with a good prognosis^{19–21}. Conversely, the more aggressive non-endometrioid types like serous and clear-cell carcinoma were more prevalent in the group where diagnosis was delayed, reinforcing and accentuating the tendency of these tumors to present at more advanced stages. Histologic variation and the resulting aggressive course of the disease illustrate the compounded negative effect of poorly timed detection and the need for aggressive surveillance in high-risk patients. These findings become most important from a public health perspective. Women at high-cancer risk do not usually have access to organized screening and routine gynecological examinations, resulting in diagnosis well after the ideal early stages. Though there are no recommendations for uncontrolled population screening for endometrial cancer, there is a strong case for risk-based screening to reduce the incidence of late-stage disease. Raising awareness of early warning signs is particularly important in cases of post-menopausal bleeding and can be accompanied by the establishment of quick referral pathways in poorly resourced environments as a cost-effective means of early diagnosis.

CONCLUSION

It is concluded that early detection and timely treatment significantly improve the prognosis of endometrial cancer, especially among high-risk populations. Patients diagnosed at an early stage and treated promptly demonstrated markedly higher overall and disease-free survival, fewer recurrences, and lower treatment-related complications. Conversely, diagnostic or therapeutic delays were associated with advanced disease at presentation, poorer survival outcomes, and increased morbidity.

REFERENCES

- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. 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. doi:10.3322/caac.21660
- Cancer Research UK. Uterine cancer statistics [Internet]. 2023 [cited 2023 Jun 17]. Available from: <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/uterine-cancer#heading-Six>
- Gu B, Shang X, Yan M, Li X, Wang W, Wang Q, Zhang C. Variations in incidence and mortality rates of endometrial cancer at the global, regional, and national levels, 1990–2019. *Gynecol Oncol*. 2021;161(3):573–580. doi:10.1016/j.ygyno.2021.01.036
- Moss EL, Teece L, Darko N. Uterine cancer mortality and Black women: Time to act. *Lancet Oncol*. 2023;24(5):586–588. doi:10.1016/S1470-2045(23)00113-4
- Clarke MA, Devesa SS, Hammer A, Wentzensen N. Racial and ethnic differences in hysterectomy-corrected uterine corpus cancer mortality by stage and histologic subtype. *JAMA Oncol*. 2022;8(6):895–903. doi:10.1001/jamaoncol.2022.0009
- Ryan NAJ, Glair MA, Blake D, Cabrera-Dandy M, Evans DG, Crosbie EJ. The proportion of endometrial cancers associated with Lynch syndrome: A systematic review and meta-analysis. *Genet Med*. 2019;21(9):2167–2180. doi:10.1038/s41436-019-0536-8
- Brown KF, Rumgay H, Dunlop C, Ryan M, Quartly F, Cox A, et al. The fraction of cancer attributable to modifiable risk factors in the United Kingdom in 2015. *Br J Cancer*. 2018;118(8):1130–1141. doi:10.1038/s41416-018-0029-6
- Fortner RT, Hüsing A, Dossus L, Tjønneland A, Overvad K, Dahm CC, et al. Theoretical potential for endometrial cancer prevention through primary risk factor modification: Estimates from the EPIC cohort. *Int J Cancer*. 2020;147(5):1325–1333. doi:10.1002/ijc.32901
- Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: A systematic review. *Cancer Epidemiol Biomarkers Prev*. 2016;25(7):1018–1028. doi:10.1158/1055-9965.EPI-16-0121
- Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME, Singh N. Endometrial cancer. *Lancet*. 2022;399(10333):1412–1428. doi:10.1016/S0140-6736(22)00323-3
- Kitson SJ, Evans DG, Crosbie EJ. Identifying high-risk women for endometrial cancer prevention strategies: Proposal of an endometrial

- cancer risk prediction model. *Cancer Prev Res.* 2017;10(1):1-13. doi:10.1158/1940-6207.CAPR-16-0224
12. Luo J, Chlebowski RT, Hendryx M, Rohan T, Wactawski-Wende J, Thomson CA, et al. Intentional weight loss and endometrial cancer risk. *J Clin Oncol.* 2017;35(11):1189-1193. doi:10.1200/JCO.2016.70.5822
 13. Zhang X, Rhoades J, Caan BJ, Cohn DE, Salani R, Noria S, et al. Intentional weight loss, weight cycling, and endometrial cancer risk: A systematic review and meta-analysis. *Int J Gynecol Cancer.* 2019;29(9):1361-1371. doi:10.1136/ijgc-2019-000728
 14. Kitson SJ, Aurangzeb O, Parvaiz J, Lophatananon A, Muir KR, Crosbie EJ. Quantifying the effect of physical activity on endometrial cancer risk. *Cancer Prev Res.* 2022;15(11):605-621. doi:10.1158/1940-6207.CAPR-22-0129
 15. Rubino D, Abrahamsson N, Davies M, Hesse D, Greenway FL, Jensen C, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: The STEP 4 randomized clinical trial. *JAMA.* 2021;325(14):1414-1425. doi:10.1001/jama.2021.3224
 16. Valladales-Restrepo LF, Sánchez-Ramírez N, Usma-Valencia AF, Gaviria-Mendoza A, Machado-Duque ME, Machado-Alba JE. Effectiveness, persistence of use, and safety of orlistat and liraglutide in patients with obesity. *Expert Opin Pharmacother.* 2023;24(5):535-543. doi:10.1080/14656566.2023.2178900
 17. Melson E, Ashraf U, Papamargaritis D, Davies MJ. What is the pipeline for future medications for obesity? *Int J Obes.* 2024;48(1):1-4. doi:10.1038/s41366-024-01473-y
 18. Garvey WT, Batterham RL, Bhatta M, Buscemi S, Christensen LN, Frias JP, et al. Two-year effects of semaglutide in adults with overweight or obesity: The STEP 5 trial. *Nat Med.* 2022;28(10):2083-2091. doi:10.1038/s41591-022-02026-4
 19. Wadden TA, Tronieri JS, Sugimoto D, Lund MT, Auerbach P, Jensen C, et al. Liraglutide 3.0 mg and intensive behavioral therapy for obesity in primary care: The SCALE IBT randomized controlled trial. *Obesity.* 2020;28(3):529-536. doi:10.1002/oby.22726
 20. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: Similar, yet different. *J Endocrinol Invest.* 2019;42(2):117-128. doi:10.1007/s40618-018-0892-2
 21. Haghighat N, Kazemi A, Asbaghi O, Jafarian F, Moeinvaziri N, Hosseini B, et al. Long-term effect of bariatric surgery on body composition in patients with morbid obesity: A systematic review and meta-analysis. *Clin Nutr.* 2021;40(3):1755-1766. doi:10.1016/j.clnu.2020.10.001

This article may be cited as: Razzaq S, Manzoor S, Dilawar S, Malik L, Shaikat M, Mushtaq A: Impact of Early Detection and Treatment on the Prognosis of Endometrial Cancer in High-Risk Populations. *Pak J Med Health Sci.* 2023;17(12):690-693.