Chinese Journal of Cancer Prevention and Treatment

eISSN: None / ISSN: 1673-5269 Open Access

Research Article

Evaluation of PD-L1 Expression in Endometrial Carcinoma and its Association with Clinicopathological Parameters: A Cross-sectional Analytical Study from a Tertiary Care Centre in South India

[1]Dr. Shivangi.J.Sindhe, [2]Dr. Natarajan Suresh, [3]Dr. Divya Lakshmi

Department of Pathology, Sree Balaji Medical College and Hospital, BIHER, Chennai

Corresponding Author
Dr. Shivangi.J.Sindhe
Email: shindhe.ashiv@gmail.com

Article History
Received: 22.07.2026
Revised: 02.08.2026
Accepted: 18.08.2026
Published: 03.09.2026

Citations:
Sindhe SJS, Suresh N, Lakshmi D. Evaluation of PD-L1 expression in endometrial carcinoma and its association with clinicopathological parameters: a cross-sectional analytical study from a tertiary care centre in South India. Chin. J. Cancer Prev. Treat, 33(8) 15-23, 2026.

Abstract: ***Introduction:*** Endometrial carcinoma (EC) is the most common malignancy of the female genital tract and demonstrates increasing global incidence due to obesity, metabolic syndrome, and ageing populations. Programmed death-ligand 1 (PD-L1) has emerged as an important immune checkpoint biomarker with therapeutic relevance in EC, particularly in mismatch repair-deficient and microsatellite instability-high tumours. However, the association between PD-L1 expression and clinicopathological parameters remains inconsistent across studies. Aim: To evaluate PD-L1 immunohistochemical expression in endometrial carcinoma and analyse its association with clinicopathological parameters. ***Materials and Methods:*** This cross-sectional prospective analytical study was conducted in the Department of Pathology, Sree Balaji Medical College and Hospital, Chennai, from January 2024 to April 2026. Thirty histopathologically confirmed cases of endometrial carcinoma were included. PD-L1 immunohistochemistry was performed using rabbit monoclonal antibody clone B7H1P on formalin-fixed paraffin-embedded tissue sections. Expression was assessed using Tumour Proportion Score (TPS) and Combined Positive Score (CPS). Associations with tumour grade, histological subtype, myometrial invasion, and lymphovascular space invasion (LVSI) were analysed using Chi-square/Fisher's exact test and Spearman correlation. ***Results:*** The mean age of patients was 58.6±8.9 years. Endometrioid carcinoma constituted 62.9% of cases. Grade 2 tumours were most common (40%), followed by Grade 3 tumours (34.3%). Mean TPS and CPS values were 21.8±17.6 and 32.4±25.8 respectively. Moderate TPS expression was observed in 51.4% cases, while high CPS was identified in 22.9%. A statistically significant association was observed between TPS and tumour grade ($p=0.048$) and between CPS and LVSI ($p=0.021$). CPS demonstrated stronger positive correlation with tumour grade ($\rho=+0.48$; $p=0.018$) compared to TPS. Higher CPS expression was also observed in deeply invasive tumours, although statistical significance was not reached ($p=0.062$). ***Conclusion:*** PD-L1 expression demonstrates substantial heterogeneity in endometrial carcinoma and correlates with markers of tumour aggressiveness, particularly tumour grade and lymphovascular invasion. CPS appears to better reflect tumour microenvironment interactions compared to TPS. PD-L1 may serve as a useful prognostic and predictive biomarker in EC, especially in resource-limited settings where molecular profiling is not routinely available.

Keywords: Endometrial carcinoma; PD-L1; Tumour proportion score; Combined positive score; Immunohistochemistry; Lymphovascular invasion

INTRODUCTION

Endometrial carcinoma (EC) is the most common malignancy of the female genital tract and represents a major public health concern worldwide due to its steadily increasing incidence and mortality [1,2]. Lifestyle transitions associated with obesity, diabetes mellitus, sedentary behaviour, and increasing life expectancy have significantly contributed to the rising burden of disease, particularly in developing and middle-income countries [3-5]. Although EC predominantly affects postmenopausal women, younger women with obesity, chronic anovulation, and polycystic ovarian syndrome constitute an increasingly recognised subgroup [4].

Traditionally, endometrial carcinoma has been classified according to Bokhman's dualistic model into Type I and Type II tumours [6]. However, advances in molecular pathology have demonstrated that EC comprises a biologically heterogeneous group of neoplasms with distinct genomic, immunological, and prognostic profiles [7]. The Cancer Genome Atlas (TCGA) identified four molecular subgroups: POLE-ultramutated, microsatellite instability-high (MSI-H), copy-number low, and copy-number high tumours, each associated with different immune microenvironments and therapeutic implications [8,9].

The tumour microenvironment plays a pivotal role in carcinogenesis and tumour progression. Among immune regulatory pathways, the programmed death-1/programmed death-ligand 1 (PD-1/PD-L1) axis has gained substantial clinical importance [13,14]. PD-L1 is a transmembrane protein expressed on tumour cells and immune cells that suppresses T-cell-mediated immune responses by interacting with PD-1 receptors on activated lymphocytes [13]. Tumours exploit this mechanism to evade immune surveillance and establish an immunosuppressive microenvironment [14].

Immune checkpoint inhibitors targeting PD-1/PD-L1 pathways, including pembrolizumab and dostarlimab, have transformed the management of advanced and recurrent EC, especially in mismatch repair-deficient and MSI-H tumours [15,38]. Consequently, PD-L1 expression has emerged as both a predictive and prognostic biomarker in EC. However, published studies report highly variable PD-L1 positivity rates ranging from 20% to 70%, largely due to methodological differences involving antibody clones, scoring systems, and tumour heterogeneity [21-24].

Several studies have demonstrated significant associations between PD-L1 expression and adverse pathological parameters such as higher tumour grade, deep myometrial invasion, and lymphovascular space invasion [23,26,27]. Conversely, other studies suggest that increased PD-L1 expression may reflect an active antitumour immune response and improved outcomes [28,32]. These inconsistencies highlight the need for further evaluation of PD-L1 expression patterns and clinicopathological correlations in different populations.

In resource-limited settings where comprehensive molecular testing is not universally available, immunohistochemical assessment of PD-L1 may provide an accessible surrogate biomarker for identifying patients likely to benefit from immunotherapy. Therefore, the present study was undertaken to evaluate PD-L1 expression in endometrial carcinoma and analyse its association with clinicopathological parameters including tumour grade, histological subtype, depth of myometrial invasion, and lymphovascular space invasion.

MATERIALS AND METHODS

This cross-sectional prospective analytical study was conducted in the Department of Pathology, Central Laboratory, Sree Balaji Medical College and Hospital, Chennai, from January 2024 to April 2026 after obtaining approval from the Institutional Ethics Committee.

A total of 30 histopathologically confirmed cases of endometrial carcinoma were included. The study population consisted of hysterectomy specimens and endometrial biopsy samples diagnosed as endometrial carcinoma during the study period. Cases of endometrial hyperplasia without invasion, atypical hyperplasia, non-epithelial uterine malignancies, and poorly preserved tissue unsuitable for immunohistochemistry were excluded.

Clinical details including age, presenting symptoms, menopausal status, and imaging findings were obtained from pathology requisition forms and hospital records. Gross examination of hysterectomy specimens included assessment of tumour size, tumour location, myometrial invasion, cervical involvement, adnexal involvement, and serosal extension.

Tissues were fixed in 10% neutral buffered formalin and routinely processed. Sections measuring 4–5 µm were stained with Hematoxylin and Eosin (H&E). Histopathological diagnosis, tumour grade, and subtype were determined according to WHO Classification of Female Genital Tumours, 2020 [24].

Immunohistochemistry

PD-L1 immunohistochemistry was performed on representative formalin-fixed paraffin-embedded tumour blocks using rabbit monoclonal antibody clone B7H1P. Fresh sections measuring 3–4 µm were mounted on

positively charged slides. Deparaffinisation was carried out using xylene followed by rehydration through graded alcohol.

Heat-induced antigen retrieval was performed using TRIS-EDTA buffer (pH 9). Endogenous peroxidase activity was blocked using hydrogen peroxide. Slides were incubated with primary PD-L1 antibody followed by application of secondary antibody detection system. Diaminobenzidine (DAB) was used as chromogen, and Harris hematoxylin was used for counterstaining.

Normal placental tissue served as positive control. Only membranous staining in viable tumour cells was considered positive.

PD-L1 Scoring

PD-L1 expression was assessed using:

1. Tumour Proportion Score (TPS)
2. Combined Positive Score (CPS)

TPS represented the percentage of viable tumour cells demonstrating membranous positivity.

CPS was calculated using the formula:

(Number of PD-L1-positive tumour cells, lymphocytes, and macrophages / Total viable tumour cells) × 100

TPS was categorised as:

- Low (<10%)
- Moderate (10–49%)
- High (≥50%)

CPS was categorised as:

- Low (<10)
- Intermediate (10–49)
- High (≥50)

Statistical Analysis

Data were entered into Microsoft Excel and analysed using SPSS software. Continuous variables were expressed as mean±standard deviation. Categorical variables were expressed as frequencies and percentages. Associations between PD-L1 expression and clinicopathological variables were analysed using Chi-square test or Fisher's exact test. Spearman rank correlation coefficient was used to evaluate correlations between PD-L1 scores and tumour grade. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 30 histopathologically confirmed cases of endometrial carcinoma were included in the present study. Clinicopathological parameters including age, histological subtype, tumour grade, depth of myometrial invasion, and lymphovascular space invasion (LVSI) were analysed. Immunohistochemical evaluation of PD-L1 expression was performed in all cases using Tumour Proportion Score (TPS) and Combined Positive Score (CPS).

The mean age of the study population was 58.6±8.9 years, with age ranging from 45 to 74 years. The majority of cases belonged to the 50–69 year age group, collectively accounting for nearly 60% of the cohort. Endometrioid carcinoma constituted the predominant histological subtype. Intermediate and high-grade tumours collectively accounted for the majority of cases. Deep myometrial invasion was identified in nearly half of the tumours, while lymphovascular space invasion was present in approximately one-third of cases.

Table 1: Clinicopathological Profile of Endometrial Carcinoma Cases

Parameter	Category	Number (%)
Age	<50 years	6 (22.9)
	50–59 years	10 (31.4)
	60–69 years	10 (28.6)
	≥70 years	4 (17.1)
Histological subtype	Endometrioid carcinoma	20 (62.9)
	Serous carcinoma	3 (8.6)
	Papillary adenocarcinoma	1 (5.7)
	Poorly differentiated carcinoma	2 (5.7)
	Carcinosarcoma / High-grade	2 (8.6)
	Others	2 (8.6)
FIGO grade	Grade 1	7 (25.7)
	Grade 2	12 (40.0)
	Grade 3	11 (34.3)
Myometrial invasion	<50%	16 (51.4)
	≥50%	14 (48.6)

LVSI	Present	10 (34.3)
	Absent	20 (65.7)

Histopathological examination demonstrated characteristic malignant glandular architecture with nuclear pleomorphism and hyperchromasia in endometrioid carcinoma.

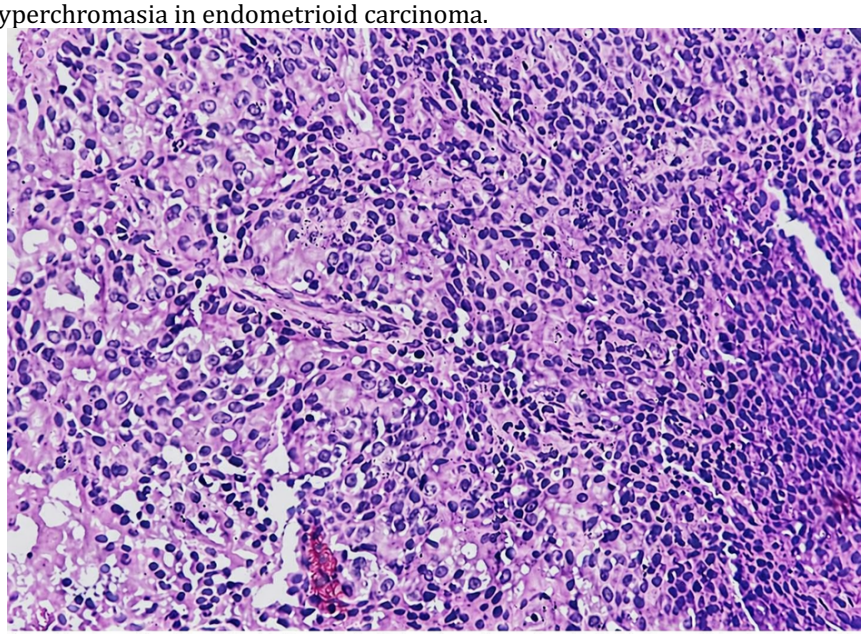


Figure 1: Endometrioid carcinoma showing malignant glandular architecture with nuclear pleomorphism and hyperchromasia (H&E, ×40)

Tumours demonstrating stromal infiltration showed irregular infiltrative malignant glands extending into surrounding stroma.

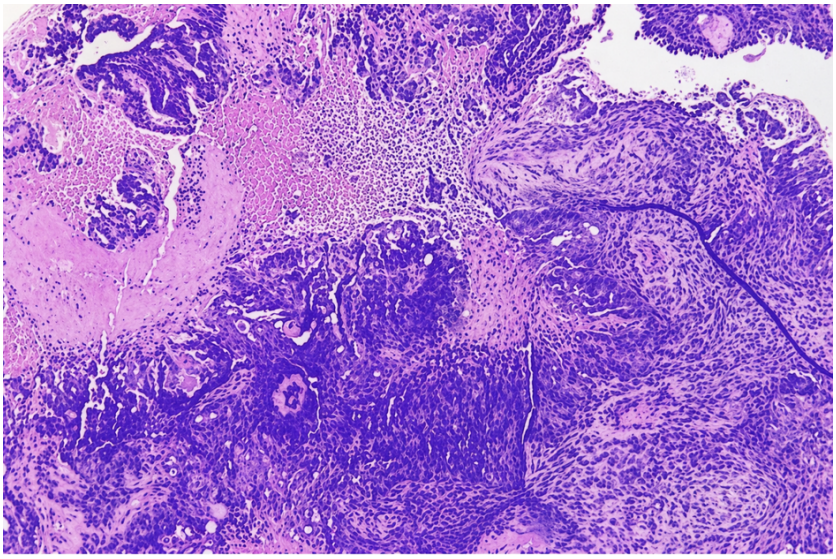
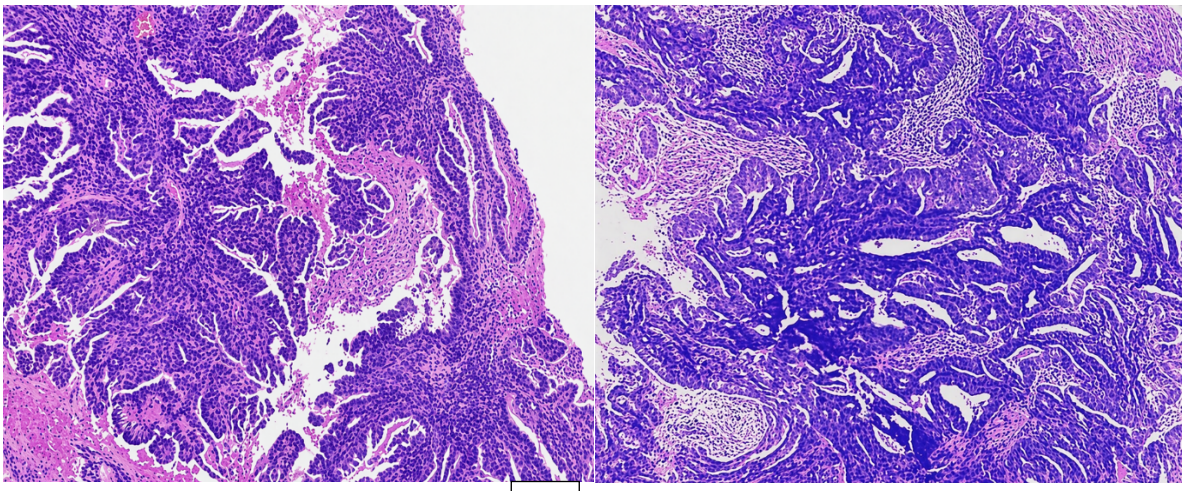


Figure 2: Endometrial carcinoma demonstrating irregular infiltrative glands with stromal invasion (H&E, ×10)

High-grade tumours demonstrated complex papillary and back-to-back glandular architecture with marked cytological atypia.



A B

Figure 3: High-grade endometrial carcinoma showing complex papillary and back-to-back glandular architecture (H&E, ×10)

Immunohistochemical analysis demonstrated universal PD-L1 positivity across all tumours, although expression levels showed marked heterogeneity. TPS values ranged from 1% to 80%, with a mean of 21.8±17.6. CPS values ranged from 2 to 100, with a mean of 32.4±25.8.

Table 2: PD-L1 Expression Profile using TPS and CPS

Parameter	Minimum	Maximum	Mean ± SD
TPS (%)	1	80	21.8 ± 17.6
CPS	2	100	32.4 ± 25.8

Categorical analysis demonstrated that moderate TPS expression was the most common category. CPS showed relatively greater redistribution toward higher expression groups compared to TPS, indicating substantial contribution from tumour-associated immune cells.

Table 3: Distribution of PD-L1 Expression Categories

Expression Category	TPS n (%)	CPS n (%)
Low	11 (34.3)	8 (25.7)
Moderate / Intermediate	15 (51.4)	15 (51.4)
High	4 (14.3)	7 (22.9)
Total	30 (100)	30 (100)

Strong diffuse membranous PD-L1 positivity was observed in a subset of tumours showing high expression scores.

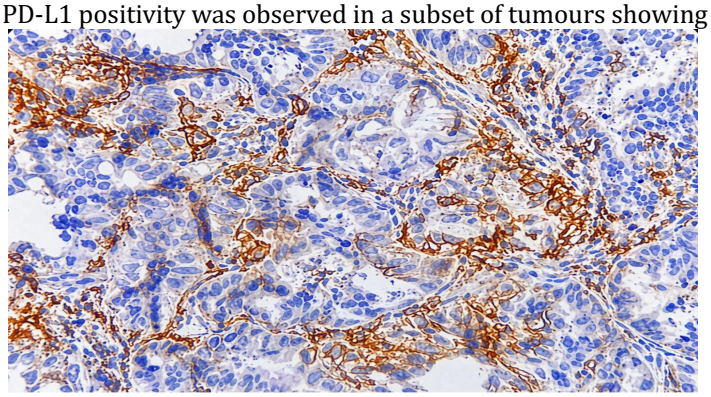


Figure 4: PD-L1 immunohistochemistry demonstrating strong diffuse membranous positivity in tumour cells (22C3, ×40)

Moderate membranous positivity was observed in tumours demonstrating intermediate expression categories.

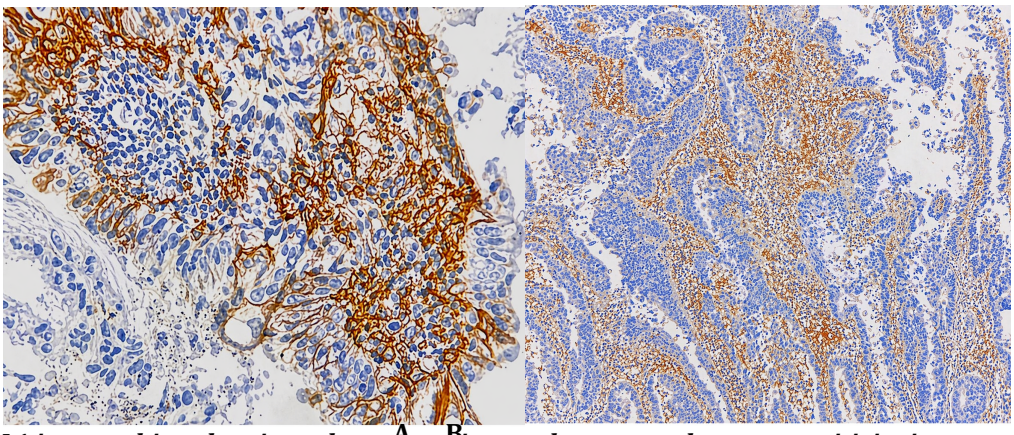


Figure 5: PD-L1 immunohistochemistry demonstrating moderate membranous positivity in tumour cells (22C3, ×40)

Analysis of the association between TPS and tumour grade demonstrated statistically significant correlation (p=0.048). Grade 1 tumours were predominantly confined to low and moderate TPS categories, whereas Grade 3 tumours demonstrated progressive redistribution toward higher TPS expression.

Table 4: Association between Tumour Grade and TPS Expression

Tumour Grade	Low TPS	Moderate TPS	High TPS	Total
Grade 1	5	2	0	7
Grade 2	5	6	1	12
Grade 3	2	5	4	11

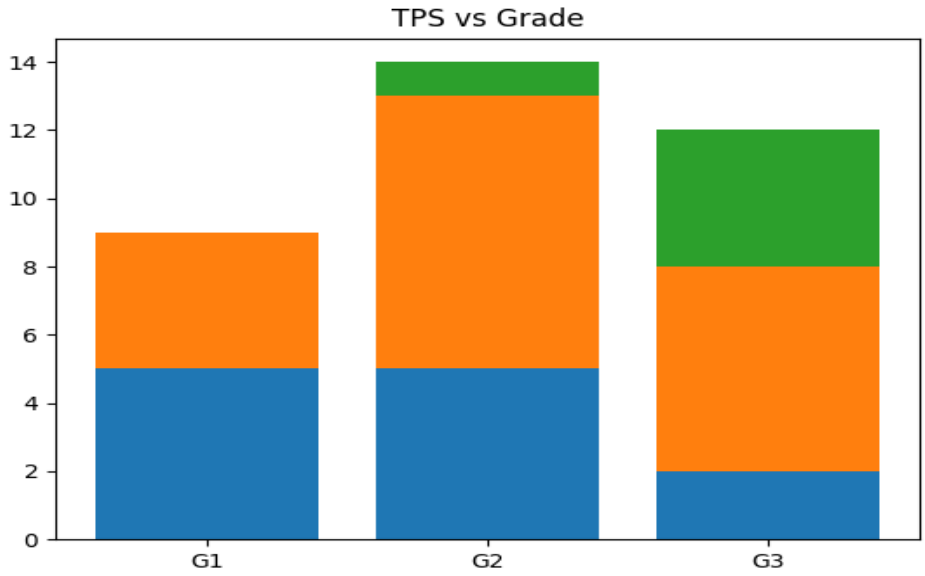


Figure 6: Comparative distribution of TPS expression across FIGO grades

Association between CPS and LVSI demonstrated statistically significant correlation (p=0.021). LVSI-positive tumours demonstrated substantially higher CPS expression compared to LVSI-negative tumours.

Table 5: Association between LVSI and CPS Expression

LVSI Status	Low CPS	Intermediate CPS	High CPS	Total
Present	1	4	5	10

Absent	6	12	2	20

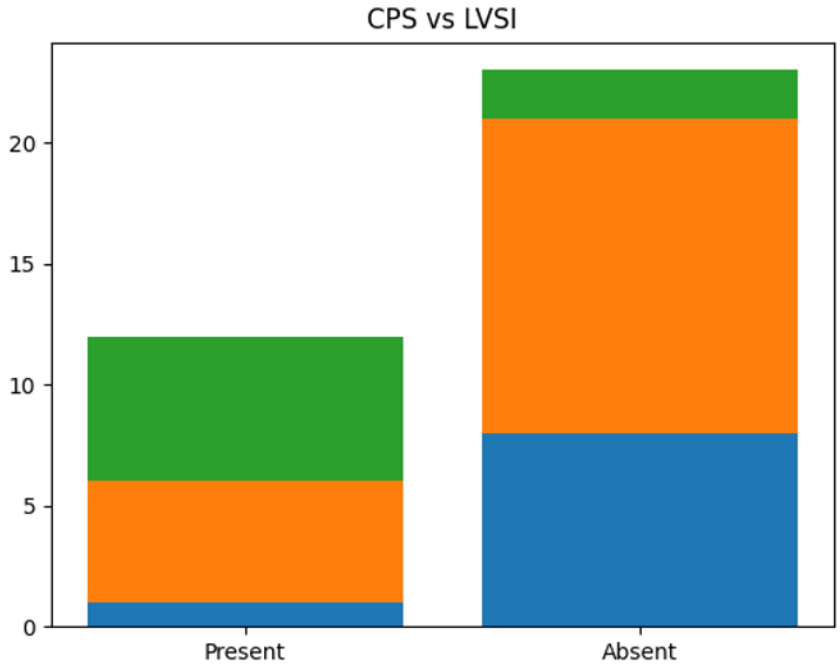


Figure 7: Comparative distribution of CPS expression in relation to lymphovascular space invasion

Association between CPS and myometrial invasion did not achieve statistical significance (p=0.062); however, tumours with deep myometrial invasion demonstrated relatively higher CPS expression.

Table 6: Association between Myometrial Invasion and CPS Expression

Myometrial Invasion	Low CPS	Intermediate CPS	High CPS	Total
<50% invasion	6	8	2	16
≥50% invasion	2	6	6	14

p-value = 0.062

Correlation analysis demonstrated moderate positive correlation between PD-L1 expression and tumour aggressiveness. CPS demonstrated stronger correlation with adverse histopathological parameters compared to TPS.

Table 7: Correlation of PD-L1 Expression with Histopathological Parameters

Variables	Spearman Correlation (ρ)	p-value
TPS vs Tumour Grade	+0.42	0.032
CPS vs Tumour Grade	+0.48	0.018
CPS vs LVSI	+0.51	0.012

Overall, the present study demonstrates substantial heterogeneity in PD-L1 expression in endometrial carcinoma and identifies significant association between increased PD-L1 expression and adverse histopathological parameters, particularly tumour grade and lymphovascular space invasion.

DISCUSSION

Endometrial carcinoma continues to demonstrate increasing global incidence due to obesity, metabolic syndrome, and ageing populations [1,2]. Recent advances in molecular pathology and cancer immunology have substantially altered the understanding of EC biology, particularly regarding tumour–immune interactions and immune checkpoint pathways [7-9].

In the present study, universal PD-L1 positivity was observed, although expression levels varied considerably. This finding highlights substantial heterogeneity in PD-L1 expression among EC cases. Similar variability has been

reported by Wahba et al. and Yusof et al., who demonstrated marked differences in PD-L1 positivity rates across studies due to differences in scoring systems, antibody clones, and tumour heterogeneity [23,24].

The present study demonstrated statistically significant association between TPS and tumour grade. High-grade tumours showed increased PD-L1 expression compared to low-grade tumours. Similar observations were reported by Zong et al. and Zhang et al., who demonstrated elevated PD-L1 expression in aggressive and poorly differentiated tumours [27,28].

The biological basis for this association may relate to increased genomic instability and mutational burden in high-grade tumours, resulting in increased neoantigen formation and immune activation [8,29]. Interferon-gamma-mediated adaptive immune resistance may subsequently induce PD-L1 expression as a mechanism of tumour immune evasion [19,20].

Importantly, CPS demonstrated stronger correlation with tumour grade compared to TPS, suggesting that immune cell contribution significantly influences overall PD-L1 expression. This finding supports observations by Pasanen et al., who emphasised the importance of evaluating both tumour and immune cell PD-L1 expression [22].

A significant association was also observed between CPS and LVSI. Tumours demonstrating vascular invasion exhibited markedly higher CPS expression. Siraj et al. similarly identified PD-L1 as an independent predictor of lymph node metastasis and tumour dissemination [26]. The association between elevated CPS and LVSI may reflect increased interaction between tumour cells and stromal immune components during metastatic progression.

Although the association between CPS and myometrial invasion did not achieve statistical significance, deeply invasive tumours demonstrated higher CPS expression. Nishio et al. similarly observed increased PD-L1 expression in tumours with deeper myometrial invasion and increased immune infiltrates [17]. The lack of statistical significance in the present study may be attributed to limited sample size.

Another important finding was the consistently higher CPS values compared to TPS. This observation indicates that the tumour microenvironment significantly contributes to PD-L1 expression. Sulaiman et al. demonstrated that stromal and immune-cell PD-L1 expression may substantially influence immunotherapy response [39]. Therefore, CPS may better represent tumour–immune interactions than TPS alone.

Recent molecular studies have shown that PD-L1 expression is highest in MMR-deficient and POLE-mutated tumours because of high neoantigen load and immune activation [21,29]. Although molecular subtyping was not performed in the present study, the observed heterogeneity in PD-L1 expression may reflect underlying molecular diversity.

The present study has important clinical implications. Immune checkpoint inhibitors have emerged as effective therapeutic options in advanced and recurrent EC [38,81]. In resource-constrained settings where comprehensive molecular profiling is unavailable, PD-L1 immunohistochemistry may provide a practical surrogate biomarker for identifying patients who may benefit from immunotherapy.

However, the study has certain limitations. The relatively small sample size limits statistical power and subgroup analysis. Molecular classification and mismatch repair testing were not performed. Additionally, long-term follow-up and survival analysis were not available.

Despite these limitations, the study demonstrates meaningful associations between PD-L1 expression and adverse clinicopathological parameters, reinforcing the role of tumour immune microenvironment in EC progression.

LIMITATIONS

1. Small sample size limited subgroup analysis.
2. Molecular classification and MMR/MSI testing were not performed.
3. Survival analysis and therapeutic response assessment were unavailable.
4. Single-centre study design may limit generalisability.

CONCLUSION

PD-L1 expression in endometrial carcinoma demonstrates substantial heterogeneity and shows significant association with tumour grade and lymphovascular space invasion. CPS demonstrated stronger correlation with tumour aggressiveness compared to TPS, highlighting the importance of tumour microenvironment assessment. PD-L1 immunohistochemistry may serve as a useful adjunctive biomarker for prognostication and therapeutic stratification, particularly in settings where advanced molecular testing is not routinely available.

REFERENCES

1. Gynecologic Oncology Siegel RL, Miller KD, Jemal A. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17–48.

2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN. CA Cancer J Clin. 2021;71(3):209–249.
3. Brooks RA, Fleming GF, Lastra RR, et al. Endometrial cancer recommendations. CA Cancer J Clin. 2019;69(4):258–279.
4. Setiawan VW, Yang HP, Pike MC, et al. Type I and II endometrial cancers: risk factors. J Clin Oncol. 2013;31(20):2128–2135.
5. Ryan AJ, Susko AM, Massi D. Hormonal & metabolic drivers of EC. Nat Rev Endocrinol. 2021;17(11):695–713.
6. Bokhman JV. Two pathogenetic types of EC. Gynecol Oncol. 1983;15(1):10–17.
7. Murali R, Soslow RA, Weigelt B. Classification of EC beyond two types. Lancet Oncol. 2014;15:e268–278.
8. Cancer Genome Atlas Research Network. Integrated genomic characterization of EC. Nature. 2013;497:67–73.
9. Talhouk A, McConechy MK, Leung S, et al. Molecular subtype & outcomes in EC. Clin Cancer Res. 2018;24(10):2247–2258.
10. Keir ME, Butte MJ, Freeman GJ, Sharpe AH. PD-1 & ligands in immunity. Annu Rev Immunol. 2008;26:677–704.
11. Pardoll DM. Immune checkpoint blockade. Nat Rev Cancer. 2012;12:252–264.
12. Sharma P, Allison JP. Future of checkpoint therapy. Science. 2015;348:56–61.
13. Sloan EA, Ring KL, Willis BC, et al. PD-L1 in MMR-deficient EC. Am J Surg Pathol. 2017;41(3):326–333.
14. Pasanen A, Ahvenainen T, Pellinen T, et al. PD-L1 in EC tumour & immune cells. Am J Surg Pathol. 2019;43(5):689–697.
15. Wahba MG, Soliman SS, Salama ME, et al. PD-L1 in Egyptian EC. Asian Pac J Cancer Prev. 2024;25:1441–1450.
16. Mamat Yusof MN, Ab Mutalib NS, Mokhtar NM. PD-L1 in EC: meta-analysis. Cancers (Basel). 2022;14:659.
17. Siraj AK, Parvathareddy SK, Bu R, et al. PD-L1 predicts LN metastasis. Diagnostics. 2021;11:888.
18. Zong L, Zhang Q, Zhang Y, et al. PD-L1 in high-risk EC. Gynecol Oncol. 2021;162:50–58.
19. Zhang S, Zhao J, Zhang T, et al. PD-L1 and CD4 in EC prognosis. BMC Cancer. 2020;20:945.
20. Howitt BE, Shukla SA, Sholl LM, et al. POLE-mutated & MSI-H EC immune activation. JAMA Oncol. 2015;1:1319–1327.
21. Nishio H, Iwaya T, Kaneko J, Kuroda M. PD-L1 & immune infiltrates in EC. Pathol Int. 2019;69:325–334.
22. Sulaiman R, Mahajan V, Prasad P, et al. PD-1/PD-L1 microenvironment in EC. Int J Mol Sci. 2023;24:8759.
23. Makker V, et al. Pembrolizumab + Lenvatinib EC. N Engl J Med. 2022;386:437–448.
24. WHO Classification of Tumours Editorial Board. Female Genital Tumours. 5th ed. Lyon: IARC; 2020.