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ORIGINAL ARTICLE

Prognostic Impact of NANOG Immunohistochemical Expression in Endometrial Carcinoma: Clinicopathological Study

Mahmoud Wahied Emara, Hanaa M. Ibrahim, Aya G. Mohamed Sarhan, Doaa I. Abdelrahman
Pathology Department, Faculty of Medicine, Zagazig University

Corresponding author
Aya G. Mohamed Sarhan

Email:
sarhanaya10@gmail.com

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ABSTRACT

Background: Endometrial cancer (EC) stem cells play an important role in the development of endometrial cancer and they are responsible for tumor progression, invasiveness, metastasis and drug resistance. NANOG has been found to be surrogate indicators for cancer stem cells (CSCs). Therefore, in order to improve endometrial carcinoma management, we set out to assess the immunohistochemical expression of the cancer stem cell marker NANOG in endometrial carcinoma and their correlation with several clinicopathological features. **Methods**: This cohort study was conducted in the Pathology department, included tissue samples from 31 patients diagnosed with endometrial carcinoma, admitted and underwent hysterectomy at the obstetrics and gynecology department of Zagazig University, who have undergone hysterectomy to treat endometrial carcinoma. All study subjects were subjected to accurate and complete patient clinicopathological data from archives. Testicular seminoma was taken as a positive control to assess the expression of NANOG. NANOG expression is considered positive if nuclear staining was present in glandular epithelium of endometrium. **Results**: There was a statistically significant association between NANOG expression and clinicopathological characteristics among the studied group, as high NANOG expression was associated with high FIGO grade, high FIGO stage, and TNM stage (P=0.02), (P=0.005) and (P=0.005) respectively. Furthermore, there was no significant association between NANOG expression and tumor size (p=0.86). **Conclusion:** EC expressing high NANOG are highly aggressive tumors, therefore it could be promising therapeutic targets for EC as NANOG is highly expressed in most CSCs, NANOG is a desirable target for cancer therapy which could improve human health.

Keywords: Endometrial carcinoma, immunohistochemical expression, Cancer stem cells, NANOG

INTRODUCTION

EC is the second most common cancer in women globally and the third most common cause of death from gynecological cancer in women [1]. In recent years, there has been a rise in the prevalence of EC among Egyptian women [2]. Compared to the global incidence of 8.2 per 100,000, the age-standardized incidence rates of corpus uteri cancer in Egypt were 3.8 per 100,000[3].

Early menarche, late menopause, polycystic ovarian syndrome, infertility, obesity, diabetes, and genetic susceptibility with Lynch Syndrome are known risk factors for EC. These

factors are especially important for patients diagnosed before the age of 50 [4].

The majority of the cases are postmenopausal Although it is uncommon in younger people, 14–25% of EC patients are premenopausal, and 5% are under 40 years old [5].

Early diagnosis failure, late-stage anemia, weight loss, cachexia and metastasis are the primary causes of death for EC patients [6].

A tiny subset of malignant cells known as CSCs are responsible for the initiation and development of tumors. CSCs share similar characteristics with normal stem cells in the case of self-renewal and differentiation. Additionally, they aid in cancer cells' metastasis and chemoresistance, which results in therapeutic failure. Numerous cell surface markers, such as NANOG, which is present in high concentrations in various malignancies, have been described in order to identify CSCs [7].

An essential transcription factor for stem cells, NANOG plays a role in both cancer development and normal cell division. Its expression is intricate and subject to several levels of regulation. Furthermore, hundreds of target genes may be simultaneously regulated by the NANOG protein [8].

In order to control embryonic and fetal development, NANOG is essential for the preimplantation development phase and gradually diminishes throughout the differentiation of embryonic stem cells. The majority of human tissues are undetectable after birth, however a small percentage have low levels of expression in some cells in organs such as the testis, ovary, and endometrial glands [8].

Aim of the work:

This study aimed to evaluate the immunohistochemical expression of cancer stem cell marker NANOG in endometrial carcinoma and its correlation with different clinicopathological parameters for improving the management of endometrial carcinoma.

COVID-19 vaccines on the cardiovascular system.

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METHODS

This cohort study was conducted on tissue samples from 31 patients diagnosed with endometrial carcinoma grade I , grade II and grade III, all cases are admitted and underwent hysterectomy at the obstetrics and gynecology department of Zagazig University period from 2023 to 2025 in the Pathology department, all cases were obtained after receiving approval from the Faculty's local ethical committee and the institutional review board (IRB#:10583-21-3-2023) of Medicine, Zagazig University Hospital and a written consent from every patient participating in the study was taken. The study was done according to the code of ethics of the world medical association (Declaration of Helsinki 1979).

Tissue samples from patients with an endometrial cancer diagnosis were included in the study. Individuals with incomplete or inaccurate patient data, second malignancies, or a history of previous hormonal treatment or other medications for at least six months were excluded.

Age, tumor size, FIGO stage, grade, lymphovascular invasion, lymph node metastasis, and distant metastasis were among the precise and comprehensive patient clinicopathological data from archives that were applied to all research participants.

Histopathological study:

Using a rotatory microtome, paraffin blocks of each instance under study were cut into sections that were 3–4 μm thickness and stained with H&E. To assess tumor features, all cases' slides were examined. The current WHO classification of endometrial cancer was used to histologically classify all of the cases **[9]**.

Immunohistochemical study:

Anti-NANOG primary antibody (Rabbit polyclonal anti-NANOG antibody, isotype IgG, Catalogue number (A3232), diluted 1:100, ABclonal) was used to stain paraffin-embedded tissue blocks.

Immunohistochemical procedure:

After being serially sectioned into 3–4 μm, formalin-fixed paraffin-embedded blocks were deparaffinized in xylene and rehydrated in a

decreasing order of alcohols. Ten milliliters of citrate buffer (pH 6.0) was microwaved for about twenty minutes in order to perform the antigen retrieval. For ten minutes, 3% hydrogen peroxide was used to block endogenous peroxidase. Following several PBS washes, the slides were incubated with the primary antibody for Rabbit polyclonal anti-NANOG antibody. Overnight, the slides were stored between 2 and 8 ^{o}C in a humidity chamber. The slides were carefully rinsed with a buffer solution to avoid flowing directly on tissue. As stated earlier, wipe the slides after quickly tapping off any excess buffer. Subsequently, the sections were incubated with an immunohistochemistry kit including a streptavidin-linked peroxidase and a secondary antibody tagged with biotin for 15 minutes at room temperature. Following this, they were rinsed.

The diaminobenzidine (DAB) substrate was applied to tissue sections, which were then gently cleaned with distilled water after being incubated for five to ten minutes. Depending on the intensity of Mayer's hematoxylin, slides were immersed in a solution and incubated for two to five minutes. Slides were dipped ten times into an ammonia water bath and then gently rinsed in the distilled water bath to get rid of any remaining hematoxylin stains. Slides were cleaned in a bath of distilled water for two to five minutes. Slides were cleaned in xylene for three changes before being carefully mounted with a cover slip using D.P.X.

To measure NANOG expression, testicular seminoma was used as a positive control. PBS was used in place of the primary antibodies to create the negative control.

Evaluation of NANOG immunostaining:

If nuclear staining was seen in the endometrial glandular epithelium, NANOG expression is regarded as positive. Positive cells' staining strength was determined and categorized into four scores: 0 for no staining, 1 for weak staining, 2 for moderate staining, and 3 for strong staining. Additionally, a score of 0 indicated that there were no tumor cells, 1 indicated that there were 1–50% of positive tumor cells, and 2 indicated that there were 51–100% of positive tumor cells. The overall score, which varied from 0 to 6, was then calculated using the formula (% of positive tumor cells X staining intensity). The findings were divided into three categories: absent (0), low (1–3), and high (4–6) **[10,11].**

Ethical Consideration

A clear explanation of the study was made for all cases, and written consent was taken from each. All patient data was handled with strict confidentiality, adhering to relevant privacy regulations and protocols. The study protocol was approved by the ethical committee and the institutional review board (IRB) of Zagazig University. IRB#: 10583-21-3-2023. The study was done according to the code of ethics of the world medical association (Declaration of Helsinki 1979).

Statistical Analysis:

The Statistical Package for Social Science (IBM SPSS Statistics for Windows, Version 23.0, IBM Corp., Armonk, NY, USA) was used to gather, edit, code, and enter the data. When the presumption that "less than 20% of cells have expected count less than 5" is not met, Fisher's exact test (f) is employed. At $P < 0.05$, the P-value was significant.

RESULTS

The included cases are 31 people having endometrial cancer diagnoses. With a mean ± SD of 63 ± 8.62, the ages varied from 48 to 79. Among the patients, 87.1% were in menopause and 58.1% were nullipara (table 1).

Our research revealed that the most commonly found FIGO stage was stage (I), and most cases were FIGO grade (III) and T 1 (41.9 % for all). Additionally, 83.9% of the cases were endometrioid, while all non-endometrioid cases were serous endometrial carcinoma. Furthermore, the majority (51.6%) had tumors larger than 4 cm in size. Most cases had a myometrial invasion that was more than 50% thick (74.2%) and no lymph node metastasis (67.7%). Necrosis, distant metastasis, cervical involvement, and lymphovascular invasion were noted in 41.9%, 51.6%, 12.9%, and 74.2% of the patients, respectively (table 2).

As regards NANOG immunohistochemical expression, 64.5% of the patients had a high NANOG expression (table 3).

Our study showed a statistically significant association between NANOG expression and clinicopathological characteristics among the studied group, as high NANOG expression was associated with high FIGO grade, high FIGO stage, and TNM stage (P=0.02), (P=0.005) and (P=0.005) respectively. Furthermore, there was no significant association between NANOG expression and tumor size (p=0.86). Also, high NANOG expression was associated with myometrial invasion ≥ 50% thickness, the presence of Lymph node metastasis, lymphovascular invasion, necrosis, and cervical involvement (P=0.02), (P=0.02), (P=0.005), (P=0.01) and (P=0.02) respectively (table 4).

Our study showed no significant association between NANOG expression and parity (P=0.28). Furthermore, there was a statistically significant association between NANOG expression and menopause, as (96.8%) of the patients with high NANOG expression were menopausal in comparison to (47.4%) of the patients with low NANOG expression and (11.6%) of the patients with absent NANOG expression (P<0.001) (table 5).

Case Presentation:

Figure 1: A): A case of endometrioid endometrial carcinoma FIGO (GI) showing closely backed malignant glands lined by atypical columnar epithelial cells with pseudostratified nuclei and cytological atypia (H&E X400 of Original magnification). B): A case of Endometrioid Endometrial carcinoma FIGO (GII) showing malignant glands lined by atypical columnar cells with large rounded nuclei and prominent nucleoli intermixed with malignant solid growth pattern (H&E X400 of Original magnification). C) A case of Serous endometrial carcinoma FIGO (GIII) showing complex papillary pattern of growth lined by high grade neoplastic cells. Numerous mitotic figures can be seen (H &E X 400 of Original magnification). D): A case of endometrioid endometrial carcinoma FIGO (GIII) showing high grade anaplastic cells in complex papillary and glandular growth pattern (H&E x 400 of Original magnification). E): A case of endometrioid endometrial carcinoma FIGO (GIII) showing invasion of the myometrium by malignant glands (H&E x 40 of Original magnification). F): A case of endometroid endometrial carcinoma FIGO (GIII) with lymphovascular invasion, revealed malignant cells infiltrating the lumen of a blood vessel (H&E X 400 of Original magnification).

Figure 2: A): the same case of figure 1A of endometrioid endometrial carcinoma FIGO (GI) showing low nuclear NANOG expression (IHC x 400 of Original magnification). B): the same case of figure 1B of endometrioid endometrial carcinoma FIGO (GII) showing high nuclear NANOG expression (IHC x 400 of Original magnification). C): the same case of figure 1C of serous endometrial carcinoma FIGO (GIII) showing high nuclear NANOG expression (IHC x 100 Original magnification). D): the same case of figure 1D of endometrioid endometrial carcinoma FIGO (GIII) showing high nuclear NANOG expression (IHC X 400 of Original magnification). E): the same case of figure 1E of endometrioid endometrial carcinoma FIGO (GIII) showing high nuclear NANOG expression in the invasive malignant glands (IHC x 100 of Original magnification). F): the same case of figure 1F of endometrioid endometrial carcinoma with lymphovascular invasion showing high nuclear NANOG expression in the invasive malignant epithelial cells (IHC x 100 of Original magnification).

Table (1): Age and clinical data among the studied cases

Variables		Cases (n=31)
Age (years)	*Mean ± SD*	63 ± 8.62
	Range	(48 – 79)
Parity (n. %)	Nullipara	18 (58.1%)
	Multipara	13 (41.9%)
Menopause (n. %)	No	4 (12.9%)
	Yes	27 (87.1%)

Table (2): Clinicopathological characteristics of the endometrial carcinoma cases.

Variables (n. %)		Endometrial carcinoma (n=31)	
		No.	%
FIGO grade	Grade (I)	8	25.8%
	Grade (II)	10	32.3%
	Grade (III)	13	41.9%
FIGO stage	Stage (I)	13	41.9%
	Stage (II)	8	25.8%
	Stage (III)	6	19.4%
	Stage (IV)	4	12.9%
Histological subtype	Endometrioid	26	83.9%
	Non-Endometrioid	5	16.1%
TNM stage	T 1	13	41.9%
	T 2	8	25.8%
	T 3	6	19.4%
	T 4	4	12.9%
Size	< 4 cm	15	48.4%
	> 4 cm	16	51.6%
Myometrial invasion	Less than half	8	25.8%
	More than half	23	74.2%
Lymph node metastasis	Negative	21	67.7%
	Positive	10	32.3%
Lymphovascular invasion	Negative	18	58.1%
	Positive	13	41.9%
Necrosis	Absent	15	48.4%
	Present	16	51.6%
Distant metastasis	Absent	27	87.1%
	Present	4	12.9%
Cervical involvement	Negative	8	25.8%
	Positive	23	74.2%

Table (3): Immunohistochemical expression of NANOG among the studied cases.

Variables		Cases (n=31)
NANOG	Absent	4 (12.9%)
	Low	7 (22.6%)
	High	20 (64.5%)

Table (4): Association between clinicopathological characteristics and NANOG expression among the endometrial carcinoma cases.

Variables			NANOG expression			P Value
		No	Absent (n=4)	Low (n=7)	High (n=20)	
FIGO grade	Grade (I)	8	2 (50%)	4 (57.1%)	2 (10%)	0.02
	Grade (II)	10	2 (50%)	2 (28.6%)	6 (30%)	
	Grade (III)	13	0 (0%)	1 (14.3%)	12 (60%)	
FIGO stage	Stage (I)	13	4 (100%)	6 (85.7%)	3 (15%)	0.005
	Stage (II)	8	0 (0%)	1 (14.3%)	7 (35%)	
	Stage (III)	6	0 (0%)	0 (0%)	6 (30%)	
	Stage (IV)	4	0 (0%)	0 (0%)	4 (20%)	
Histological subtype	Endometrioid	26	4 (100%)	7 (100%)	15 (75%)	0.26
	Non-endometrioid	5	0 (0%)	0 (0%)	5 (25%)	
TNM stage	T 1	13	4 (100%)	6 (85.7%)	3 (15%)	0.005
	T 2	8	0 (0%)	1 (14.3%)	7 (35%)	
	T 3	6	0 (0%)	0 (0%)	6 (30%)	

	T 4	4	0 (0%)	0 (0%)	4 (20%)	
Size	≤ 4 cm	15	2 (50%)	4 (57.1%)	9 (45%)	0.86
	> 4 cm	16	2 (50%)	3 (42.9%)	11 (55%)	
Myometrial invasion	< 50 %	8	2 (50%)	4 (57.1%)	2 (10%)	0.02
	≥ 50 %	23	2 (50%)	3 (42.9%)	18 (90%)	
Lymph node metastasis	Negative	21	4 (100%)	7 (100%)	10 (50%)	0.02
	Positive	10	0 (0%)	0 (0%)	10 (50%)	
Lymph-vascular invasion	Negative	18	3 (75%)	7 (100%)	8 (40%)	0.005
	Positive	13	1 (25%)	0 (0%)	12 (60%)	
Necrosis	Absent	15	4 (100%)	5 (71.4%)	6 (30%)	0.01
	Present	16	0 (0%)	2 (28.6%)	14 (70%)	
Distant metastasis	Absent	27	4 (100%)	7 (100%)	16 (80%)	0.58
	Present	4	0 (0%)	0 (0%)	4 (20%)	
Cervical involvement	Absent	8	2 (50%)	4 (57.1%)	2 (10%)	0.02
	Present	23	2 (50%)	3 (42.9%)	18 (90%)	

**Fisher exact test, Non-significant: P >0.05, Significant: P ≤0.05*

Table (5): Association of NANOG expression and clinical data among the studied patients

Variables			NANOG expression			P value
		No	Absent (n=43)	Low (n=19)	High (n=31)	
Parity (n. %)	Nullipara	32	12 (27.9%)	6 (31.6%)	14 (45.2%)	0.28[2]
	Multipara	61	31 (72.1%)	13 (68.4%)	17 (54.8%)	
Menopause (n. %)	No	49	38 (88.4%)	10 (52.6%)	1 (3.2%)	<0.001[3]
	Yes	44	5 (11.6%)	9 (47.4%)	30 (96.8%)	

**[1]One way ANOVA, [2]Chi-square test, [3]Fisher exact test, Non-significant: P >0.05, Significant: P ≤0.05*

Figure 1: Histopathological finding of endometrial carcinoma with different grades in H & E stained sections.

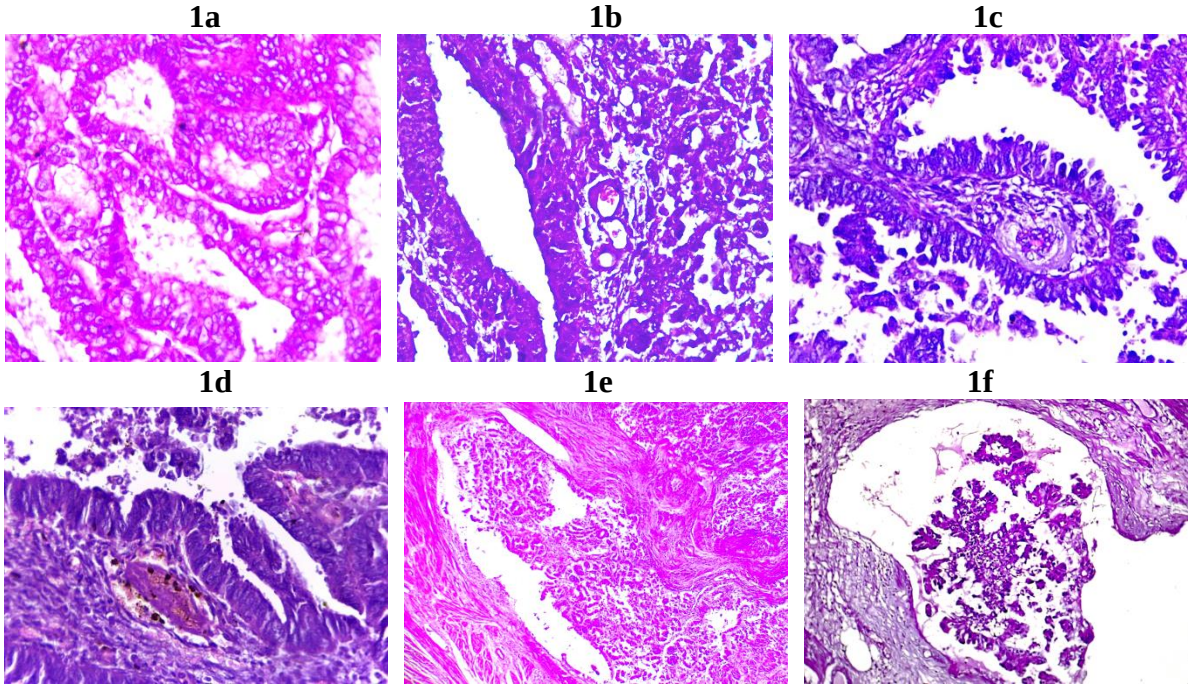
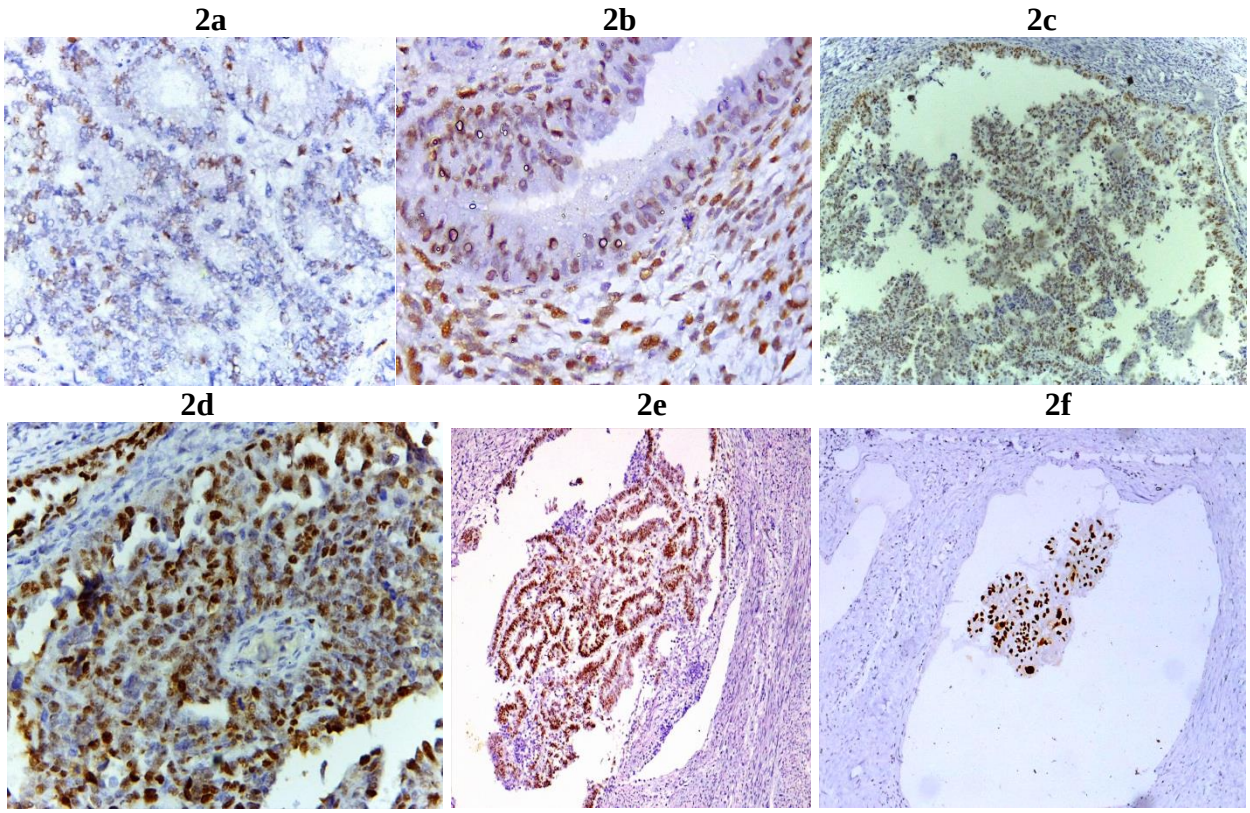


Figure 2: histopathological finding of endometrial carcinoma with different grades in immunohistochemical stained sections.



DISCUSSION

High NANOG expression was linked to both high FIGO grade and high FIGO stage (P=0.02) and (P=0.005), respectively, indicating a statistically significant relationship between NANOG expression and clinicopathological features. These results are in coordinate with **Al-Kaabi et al. [11**], who found a substantial correlation with negative prognostic indicators such as high FIGO grade and high FIGO stage. Additionally, **Saravi et al. [10]** showed a strong correlation with histological grade and disease stage. In contrast to our findings, **Sibghatullah et al. [12**] found no significant relationship with histological grade ($p > 0.05$). Additionally, **Roudi et al. [13**] demonstrated no significant connection with illness stage. The disparities may be caused by variations in the sensitivity and specificity of detection techniques as well as intratumor and inter-tumor heterogeneity.

Our research revealed no meaningful correlation between histological subtypes and NANOG expression.

The current investigation found a statistically significant correlation (P=0.005) between TNM stage and NANOG expression. **Liang et al. [14]** found a correlation between TNM stage. Similar findings were found by **Huang et al. [15],** who demonstrated a strong correlation (P=0.001). **Kołodziej et al. [16]** found no significant correlation. NANOG's significance in tumor cell survival and proliferation can be explained by its ability to prevent apoptosis and activate several signaling pathways to promote angiogenesis **[17].** Transcription factor 3 (TCF3), OCT4, and SOX2 were discovered to influence NANOG expression in endometrial CSCs **[4].**

According to our findings, myometrial invasion > 50% thickness was linked to high NANOG expression (P=0.02). According **to Al-Kaabi et al. [11],** there was a substantial correlation

between NANOG expression and profound myometrial invasion.

NANOG expression and tumor size did not significantly correlate in our study (P=0.86). In line with our results, **Saravi et al. [10]** demonstrated that there was no meaningful relationship between tumor size and NANOG expression. In contrast to our findings, **Sibghatullah et al. [12]** found a significant correlation with tumor size ($p < 0.05$). Additionally, **You et al. [18**] demonstrated a positive correlation (R=0.169, p=0.036).

Our findings indicated that the presence of lymphovascular invasion was linked to high NANOG expression (P=0.005). **Sibghatullah et al. [12]** and **Roudi et al. [13]** found no significant link with lymphovascular invasion ($p > 0.05$). Additionally, **Saravi et al. [10]** demonstrated that there was no discernible link.

NANOG expression and distant metastasis did not significantly correlate, according to our results (p=0.58). Similar findings were made by **Roudi et al. [13]** and **Kołodziej et al.[16],** who found no evidence of a significant relationship.

NANOG expression and lymph node metastasis were found to be statistically significantly correlated in this study (p=0.02), which was comparable with **Saravi et al. [10]** and **Sibghatullah et al. [12]** Results showed that NANOG expression and lymph node involvement were significantly correlated ($p < 0.05$). According to reports, NANOG controls the epithelial-mesenchymal transition **Yun et al. [19]** which explains how it contributes to EC metastasis. Additionally, it has been demonstrated that NANOG lowers E-cadherin expression, which may cause metastasis **[17].** Thus, for cancer patients, focusing on NANOG and associated pathways may be a beneficial approach.

Our research revealed no significant correlation between NANOG expression and parity (P=0.28).

The current investigation found a statistically significant correlation between NANOG expression and menopause, as (96.8%) of the patients with high NANOG expression were menopausal in comparison to (47.4%) of the patients with low NANOG expression and (11.6%) of the patients with absent NANOG expression (P<0.001). Different from our result **Ibrahim et al. [20]** showed that there was no significant correlation between NANOG expression and menopause (p = 0.104).

Methodological differences in detection systems, clones of antibodies, and scoring might explain the disagreement between studies.

CONCLUSIONS

Since NANOG is substantially expressed in the majority of CSCs, it is a desired target for cancer therapy, which could benefit human health. Additionally, NANOG expression significantly correlated with bad prognostic signs like high grade, deep myometrial invasion, positive lymph node, and high stage. This implies that NANOG affects endometrial carcinoma oncogenesis.

Recommendations:

We recommend evaluation of our marker (NANOG) in all other histopathologic subtypes of endometrial carcinoma.

Conflicts of Interest

The authors report no conflicts of interest.

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None declared

REFERENCES

1- **Liu J, Yin J, Wang Y, Cai L, Geng R, Du M et al.** A comprehensive prognostic and immune analysis of enhancer RNA identifies IGFBP7-AS1 as a novel prognostic biomarker in Uterine Corpus Endometrial Carcinoma. Biol Proced Online. 2022 Jul 15;24(1):9.

2- **Rashad HM, Abd El-Fattah GA, Elosaily GM.** Relation of autophagy to apoptosis and progesterone receptor expression in endometrial carcinoma type I. Egypt J Pathol. 2019 Jan 1;39(1):165-70.

3- **Saad AM, Robert MC, Ahmed HM.** Impact of hysterectomy on uterine cancer incidence rates in Egypt. Obstet Gynecol Int J. 2021;12(1):34-8.

4- **Giannone G, Attademo L, Scotto G, Genta S, Ghisoni E, Tuninetti V et al.** Endometrial cancer stem cells: role, characterization and therapeutic implications. Cancers. 2019 Nov 19; 11(11):1820.

5- **Gullo G, Etrusco A, Cucinella G, Perino A, Chiantera V, Laganà AS et al.** Fertility-sparing

approach in women affected by stage I and low-grade endometrial carcinoma: an updated overview. Int J Mol Sci. 2021 Oct 31;22(21):11825.

6- **Su D, Li L, Zhong M, Xia Y.** Capacity of endometrial thickness measurement to diagnose endometrial carcinoma in asymptomatic postmenopausal women: a systematic review and meta-analysis. Ann Palliat Med. 2021 Oct;10(10):108400848-10848.

7- **Vasefifar P, Motafakkerazad R, Maleki LA, Najafi S, Ghrobaninezhad F, Najafzadeh B et al.** Nanog, as a key cancer stem cell marker in tumor progression. Gene. 2022 Jun 15;827:146448.

8- **Grubelnik G, Boštjančič E, Pavlič A, Kos M, Zidar N.** NANOG expression in human development and cancerogenesis. Exp Biol Med. 2020 Mar;245(5):456-64.

9- **Akhtar M, Al Hyassat S, Elaiwy O, Rashid S, Al-Nabet AD.** Classification of endometrial carcinoma: new perspectives beyond morphology. Adv Anat Pathol. 2019; 26(6), 421-7.

10- **Saravi OE, Naghshvar F, Torabizadeh Z, Sheidaei S.** Immunohistochemical expression of nanog and its relation with clinicopathologic characteristics in breast ductal carcinoma. Iran Biomed J. 2019 May;23(3):184.

11- **Al-Kaabi M, Noel K, Al-Rubai AJ.** Evaluation of immunohistochemical expression of stem cell markers (NANOG and CD133) in normal, hyperplastic, and malignant endometrium. J Med Life. 2022 Jan;15(1):117.

12- **Sibghatullah H, Verma H, Memon RA, Ujjan ID.** MAR Pathology & Clinical Research (2023) 2: 5 Research Article.

13- **Roudi R, Barodabi M, Madjd Z, Roviello G, Corona SP, Panahi M.** Expression patterns and clinical significance of the potential cancer stem cell markers OCT4 and NANOG in colorectal cancer patients. Mol Cell Oncol. 2020 Sep 2;7(5):1788366.

14- **Liang X, Zeng H, Chen S, Jiang M, Liu S, Fan J.** Ovarian metastasis risk factors in endometrial carcinoma: a systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2021 Dec 1;267:245-55.

15- **Huang W, Zhong Z, Luo C, Xiao Y, Li L, Zhang X et al.** The miR-26a/AP-2α/Nanog signaling axis mediates stem cell self-renewal and temozolomide resistance in glioma. Theranostics. 2019 Jul 28;9(19):5497.

16- **Kołodziej-Rzepa M, Biesaga B, Słonina D, Mucha-Małecka A.** Nanog expression in patients with squamous cell carcinoma of oropharynx in relation to immunohistochemical score. Pol J Pathol. 2022 Jan 1;73(1):60-71.

17- **Najafzadeh B, Asadzadeh Z, Motafakker Azad R, Mokhtarzadeh A, Baghbanzadeh A, Alemohammad H et al.** The oncogenic potential of NANOG: An important cancer induction mediator. J Cell Physiol. 2021 Apr;236(4):2443-58.

18- **You L, Guo X, Huang Y.** Correlation of cancer stem-cell markers OCT4, SOX2, and NANOG with clinicopathological features and prognosis in operative patients with rectal cancer. Yonsei Med J. 2018 Jan 1;59(1):35-42.

19-**Yun H, Han GH, Kim J, Chung JY, Kim JH, Cho H.** NANOG regulates epithelial–mesenchymal transition via AMPK/mTOR signalling pathway in ovarian cancer SKOV-3 and A2780 cells. J Cell Mol Med. 2022 Oct;26(20):5277-91.

20- **Ibrahim F. A., El Feky S. E., Kadhim K. K., et al. (2019).** Gene Expression of OCT4 and NANOG Correlated with Advanced Stage and Worse Survival in Breast Cancer Patients. Journal of CancerResearch, 7(2),36-43.

Citation

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