International Journal of Medical Science and Clinical Research Studies

ISSN(print): 2767-8326, ISSN(online): 2767-8342

Volume 04 Issue 01 January 2024

Page No: 51-55

DOI: https://doi.org/10.47191/ijmscrs/v4-i01-11, Impact Factor: 6.597

The Relationship of Histopathological Features of the Fallopic Tubes with the Expression of P53 Mrna and YY1 Mrna in Mucinous Ovarian Carcinoma

Istikomah Noor [1], Gita Nawangtantrini[2], Aditiyono[3]

[1]Master of Biomedical Sciences, Faculty of Medicine, Jendral Soedirman University

[2]Department of Anatomical Pathology, Faculty of Medicine, Jendral Soedirman University

[3]Department of Obgyn Oncology, Faculty of Medicine, Jendral Soedirman University

ABSTRACT

Introduction: Ovarian cancer is the third most common cancer in Indonesia after breast cancer and cervical cancer. The global prevalence of mucinous ovarian carcinoma is lower than other subtypes, but the relative frequency of the mucinous subtype in Indonesia is the third highest after Singapore and South Korea. Ovarian cancer develops in the tubal fimbria before metastasizing to the ovaries. Genes involved in the carcinogenesis of mucinous ovarian carcinoma include KRAS, BRAF, p53. The expression of YY1 (Yin Yang 1) is associated with increased survival in ovarian cancer patients.

Objective: The aim of this study was to determine the relationship between histopathological features of the fallopian tubes and the expression of p53 mRNA and YY1 mRNA.

Methods: This study used a cross sectional research design. The sampling technique used was purposive sampling. The sample for this study were 27 mucinous ovarian carcinoma patients at Regional General Hospital Prof. Dr. Margono Soekarjo Purwokerto. Examination of p53 and YY1 expression using qPCR and tubal histopathology using hematoxylin eosin staining.

Results: . Of the 27 study samples, 24 patients had high p53 mRNA expression and 3 patients had low p53 mRNA expression. Meanwhile, 24 patients had low expression of YY1 mRNA expression, 3 patients had high expression. Based on the results of the Fisher's Exact statistical test analysis, there was no relationship between tubal histopathological features and p53 mRNA expression in mucinous ovarian carcinoma patients, with a significance value (p) of 0.231. There was no relationship between tubal histopathological features and YY1 mRNA expression with a significance value (p) of 0.569.

Conclusion: There is no relationship between the histopathological features of the fallopian tubes and the expression of p53 mRNA and YY1 mRNA

KEYWORDS : Mucinous Ovarian Carcinoma, p53 mRNA, Tubal Histopathological Features, YY1 mRNA

ARTICLE DETAILS

Published On:
12 January 2024

Available on:
https://ijmscr.org/

INTRODUCTION

Ovarian cancer is the third largest cancer in Indonesia after breast cancer and cervical cancer[(1)]. The prevalence of ovarian cancer in women is 10 cases per 100,000 individuals and the death rate is 6.6 cases per 100,000 individuals[(1).] Serous and mucinous histological types are the most common carcinomas found. The etiology of this disease is not yet known with certainty[(2).] The proposed pathogenesis of ovarian carcinoma, epithelial ovarian cancer originates from the surface epithelium of the ovary[(2).] Another study stated that ovarian cancer develops in the tubal fimbria before metastasizing to the ovaries.

Type I ovarian cancer is associated with molecular alterations of KRAS and BRAF treatment [(4).] TP53 mutations also occurred in mucinous ovarian carcinoma in 21 of 37 samples (56.8%)[(5).] The molecular profile of these tumors remains controversial but recent data show mutations in the KRAS, CDKN2A and p53 genes[(6).] TP53 mutations also occur in 64%, with the highest number of incidents originating from borderline mucinous tumors. This indicates that TP53 treatment is a sign of progression from borderline mucinous tumor to mucinous carcinoma[(7)].

Yin-Yang 1 (YY1) is a Zinc transcription factor Yin-Yang 1 (YY1) which is ubiquotus and has an important role in

controlling the cell cycle[8]. YY1 plays a role in the regulation of cell growth, development and differentiation by increasing the interaction between MDM2 and P53, thereby causing p53 ubiquitination and degradation. In some tumors, increased YY1 expression is associated primarily with poor prognosis. However, Meliala and Hosea et al, found that increased YY1 expression had a good survival prognosis in ovarian cancer[9,10]. In line with the research of Matsumura et al., reported that increased expression of YY1 (Yin Yang 1) had a positive correlation with increased Survival in epithelial ovarian cancer patients[12]. There are different expression profiles of YY1 in several cancers, so investigating molecular expression patterns related to the YY1 and p53 genes in ovarian cancer presents an interesting avenue for further research.

The aim of this study was to determine the relationship between ovarian tube histopathology and P53 and YY1 mRNA expression through PCR (Polymerase Chain Receptor) examination in mucinous ovarian carcinoma.

METHODS & MATERIALS

his research uses a cross sectional research design. The sampling technique used was purposive sampling. The sample for this study were 27 mucinous ovarian carcinoma patients at Prof. Regional Hospital. Dr. Margono Soekarjo Purwokerto. Examination of p53 and YY1 expression using qPCR and tubal histopathology using hematoxylin eosin staining. mRNA expression is divided into low expression (<0.01) and high expression (>0.01). The histopathological appearance of the tube is seen from the criteria for grade 1 and grade 2 lesions. It is said to be grade 1 if the lesion is intermediate, normal architecture, mild atypia, reduced cilia, while grade 2 if it consists of neoplastic cells, changes in architecture, no cilia. Data analysis used the Fisher exact test.

RESULT

This study examined the relationship between histopathological features of the ovarian tube and the expression of p53 mRNA and YY1 mRNA in mucinous ovarian carcinoma. The samples in the study were 27 patients suffering from mucinous ovarian carcinoma who had undergone surgery during the period 1 January 2020 – 31 December 2022 at RSUD Prof. Dr. Margono Soekardjo Purwokerto.

The presentation of the results or outcomes of this study can be seen in detail in table 1, while p53 mRNA expression and YY1 mRNA expression based on tubal histopathology are presented in table 2. In this study it was concluded that the outcome of this study was that there was no relationship between p53 mRNA expression (p> 0.05) and YY1 mRNA (p>0.05) with histopathological features of the fallopian tubes are presented in tables 3 and 4. In this study, from 27 samples, 12 grade 1 samples were obtained with normal architecture, mild atypia, reduced cilia and 15 samples grade 2 with the appearance of neoplastic cells, architectural changes and no cilia.

Table 1

	Variable	F	%
Age	15-25 years	4	14,8%
	26-35 years	2	7,4%
	36-45 years	2	7,4%
	46-55 years	11	40,7%
	56-65 years	7	30%
	65-75 years	1	3,7%
Total		27	100%
Histopathological Features	Grade 1	12	44,4%
	Grade 2	15	55,6%
Total		27	100%
P53	*Low expression*	3	11,1%
	High expression	24	88,9%
Total		27	100%
YY1	*Low expression*	24	88,9%
	High expression	3	11,1%
Total		27	100%

Table 2. Expression of p53 and YY1 based on hisopathological features of the ovarian tube

Variable	n	Mean ± SD	Range (Median)
Ekspresi p53	27	91.7189 ± 180,087	0,12-814,16 (17,030)
Grade 1	12	65,8942±88,872	
Grade 2	15	112,37±230,206	

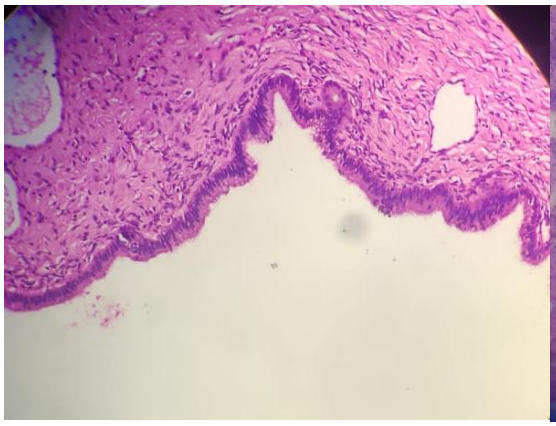
Ekspresi YY1	27	3,3304±11,379	0,00-55,33 (0,01)
Grade 1	12	5,485±15,971	
Grade 2	15	1,606±5,734	

Table 3. Correlation between ovarian tube histopathology and YY1 mRNA expression

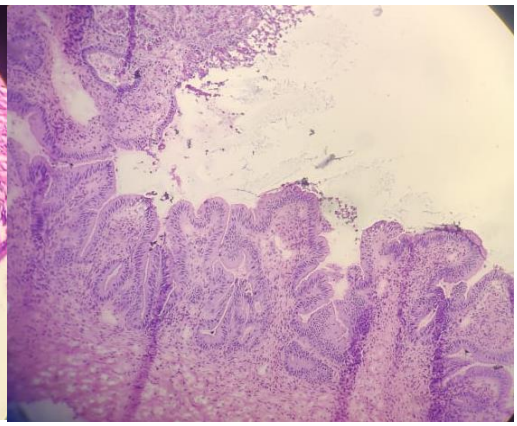
	Exact Sig. (2-sided)	*Exact Sig. (1-sided)*
Fisher's Exact Test	0.569	0.414

Table 4. Correlation between ovarian tube histopathology and p53 mRNA expression

	Exact Sig. (2-sided)	*Exact Sig. (1-sided)*
Fisher's Exact Test	0.231	0.156



Picture 1. Grade 1



Picture 2. Grade 2

DISCUSSION

One of the risk factors for ovarian cancer is age. Characteristics of mucinous tumors are that they are diagnosed in patients who are younger than other epithelial ovarian carcinomas. Based on SEER (the Surveillance, Epidemiology, and End Results) data, mucinous ovarian carcinoma is diagnosed in young women over 44 years old[4]. This research shows the majority of cases of mucinous ovarian cancer at General Region Hospital Prof. Dr. Margono Soekardjo was seen in individuals aged between 46 and 55 years, accounting for 11 cases (40.7%). The prevalence of ovarian cancer is among women aged 45 years and over, with the highest frequency seen during the 10-20 year period after menopause. This may be associated with increased gonadotropin concentrations in menopausal or postmenopausal women. Increased gonadotropin levels in women after menopause have the potential to alter ovarian surface epithelial cells [13].

There are several other risk factors for ovarian cancer such as reproductive, environmental and genetic factors. A family history of breast or ovarian cancer has significant relevance, as it has been shown that 10% of individuals affected by these cancers have a genetic predisposition. Additional variables that have been identified as potential risk factors for ovarian cancer include nulliparity, early menstruation, delayed menopause, advanced age, use of hormone replacement treatment, and others. Smoking is the only risk factor for mucinous ovarian cancer[4].

Based on previous studies, mutations in TP53 are rarely seen in type I ovarian tumors, except for mucinous carcinomas where TP53 mutations occur relatively frequently[14]. Research by Ryland et al., 2015, which aims to determine the genetic etiology of mucinous ovarian carcinoma from 24 samples, 5 benign, 8 borderline and 11 carcinomas. As many as 52% of carcinomas have p53 mutations [16]. In line with research by Mackenzie et al., 2015, p53 mutations in mucinous ovarian tumors occur more frequently in carcinomas than borderline tumors (56.8% and 11.5%)[5].

The majority of p53 expression examination results in 27 mucinous ovarian cancer patients at RSUD Prof. Dr. Margono Soekardjo Purwokerto had high expression in 24 patients and low expression in 3 patients. The results of the Fisher exact statistical test showed that there was no relationship between the histopathological appearance of the ovarian tube and the expression of p53 in mucinous ovarian carcinoma in patients with mucinous ovarian cancer at RSUD Prof. Dr. Margono Soekardjo Purwokerto (p=0.231). The research results are in line with research by Erickson et al., 2013 which states that the origin of mucinous tumors is not from the fallopian tubes but from the gastrointestinal tract or appendix [17]. Piek et al., 2001 reported that examination of tubal segments taken from women who underwent bilateral salpingo oophorectomy (BSO), of 12 women with BRCA mutations and a family history of ovarian cancer, 6 showed dysplasia, 5 hyperplastic lesions and 1 had no histological abnormalities. on the tube. In addition, there was a high accumulation of p53, Ki67, p27 expression in dysplastic

lesions compared to normal epithelium in women with a predisposition to ovarian cancer. Dysplastic and hyperplastic lesions are histologically similar to high-grade serous ovarian cancer. Areas of dysplasia within the tubal epithelium are called "tubal intraepithelial carcinoma" (TIC) and these areas show high levels of p53 accumulation[18]. Research by Przybycin et al., 2010 in 52 cases of epithelial ovarian cancer, the TIC frequency rate was 59% in patients with serous tumors, no TIC was identified on mucinous histology, endometrioid, or carcinosarcoma. This provides strong support that TIC is specifically associated with serous rather than nonserous carcinoma [19].

The majority of YY1 expression examination results in 27 mucinous ovarian cancer patients at Prof. Hospital. Dr. Margono Soekardjo Purwokerto had low expression in 27 patients and high expression in 3 patients. The results of the Fisher exact statistical test showed that there was no relationship between the histopathological appearance of the ovarian tube and the expression of YY1 in mucinous ovarian carcinoma in patients with mucinous ovarian cancer at RSUD Prof. Dr. Margono Soekardjo Purwokerto (p=0.569). In contrast to previous research which stated that YY1 expression had a negative correlation with the survival of ovarian carcinoma patients[20]. YY1 expression was significantly increased in ovarian carcinoma cells compared with normal epithelial ovarian cells [20]. YY1 decreases miR-99a levels by increasing deacetylation of miR-99a via recruitment of HDAC5 (Histone deacetylase) to the miR-99a promoter [20].

Some literature supports the oncogenic function of YY1, but there are several reports of opposing roles of YY1 in tumorigenesis. YY1 in some cases of ovarian cancer displays upregulation and is associated with poor prognosis, but there are also those that show the opposite [11]. The mechanism underlying this paradox is related to the dual function of YY1 in regulating gene expression, namely as an oncogene activator and also as a suppressor [8]. Further research remains to be done to reveal whether the role of YY1 as an oncogene or tumor suppressor is related to the type of cancer, or even the subtype of cancer, especially when designing antitumor therapy strategies [21].

CONCLUSION

Based on the above research, it can be concluded that there is high p53 mRNA expression in mucinous ovarian carcinoma, while Yin-Yang 1 mRNA expression is low in mucinous ovarian carcinoma. There was no relationship between the histopathological features of the ovarian tube and p53 mRNA expression and YY1 mRNA expression in patients with mucinous ovarian carcinoma at Regional General Hospital Prof. Dr. Margono Soekarjo Purwokerto.

REFERENCES

I. GLOBOCAN. Ovarian Cancer Incidence and Mortality. Int Agency Res Cancer GLOBOCAN [Internet]. 2020;5–6. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/25-Ovary-fact-sheet.pdf

II. Reid BM, Permuth JB, Sellers TA. Epidemiology of ovarian cancer: a review. Cancer Biol Med. 2017;14(1):9–32.

III. Shih IM, Kurman RJ. Ovarian Tumorigenesis: A Proposed Model Based on Morphological and Molecular Genetic Analysis. Am J Pathol. 2004;164(5):1511–8.

IV. Morice P, Gouy S, Leary A. Mucinous Ovarian Carcinoma. N Engl J Med. 2019;380(13):1256–66.

V. Mackenzie R, Kommoss S, Winterhoff BJ, Kipp BR, Garcia JJ, Voss J, et al. Targeted deep sequencing of mucinous ovarian tumors reveals multiple overlapping RAS-pathway activating mutations in borderline and cancerous neoplasms. BMC Cancer [Internet]. 2015;15(1):1–10. Available from: ???

VI. Bouri S, Simon P, D'Haene N, Catteau X, Noël JC. P53 and PIK3CA Mutations in KRAS/HER2 Negative Ovarian Intestinal-Type Mucinous Carcinoma Associated with Mature Teratoma. Case Rep Obstet Gynecol. 2020;2020:8–11.

VII. Hirst J, Crow J, Godwin A. Ovarian Cancer Genetics: Subtypes and Risk Factors. Ovarian Cancer - From Pathog to Treat. 2018;(May 2019).

VIII. Wai DCC, Shihab M, Low JKK, Mackay JP. The zinc fingers of YY1 bind single-stranded RNA with low sequence specificity. Nucleic Acids Res. 2016;44(19):9153–65.

IX. Meliala ITS, Hosea R, Kasim V, Wu S. The biological implications of Yin Yang 1 in the hallmarks of cancer. Theranostics. 2020;10(9):4183–200.

X. Hosea R, Hillary, Sharon, Wu S. Targeting Transcription Factor YY1 for Cancer Treatment : Current Strategies and Future Directions. 2023;

XI. Matsumura N, Huang Z, Baba T, Lee PS, Barnett JC, Mori S, et al. Yin Yang 1 modulates taxane response in epithelial ovarian cancer. Mol Cancer Res. 2009;7(2):210–20.

XII. Hada T, Miyamoto M, Ishibashi H, Matsuura H, Sakamoto T, Kakimoto S, et al. Survival and biomarker analysis for ovarian mucinous carcinoma according to invasive patterns: retrospective analysis and review literature. J Ovarian Res. 2021;14(1):1–12.

XIII. Rampersad AC, Wang Y, Smith ER, Xu X. Menopause and ovarian cancer risk : mechanisms and experimental support. Am J Clin Exp Obs Gynecol. 2015;2(1):14–23.

XIV. Rojas V, Hirshfield KM, Ganesan S, Rodriguez-

Rodriguez L. Molecular characterization of epithelial ovarian cancer: Implications for diagnosis and treatment. Int J Mol Sci. 2016;17(12).

XV. Ryland GL, Hunter SM, Doyle MA, Caramia F, Li J, Rowley SM, et al. Mutational landscape of mucinous ovarian carcinoma and its neoplastic precursors. Genome Med [Internet]. 2015;7(1):1–12. Available from: http://dx.doi.org/10.1186/s13073-015-0210-y

XVI. Cheasley D, Wakefield MJ, Ryland GL, Allan PE, Alsop K, Amarasinghe KC, et al. The molecular origin and taxonomy of mucinous ovarian carcinoma. Nat Commun. 2019;10(1):1–11.

XVII. Erickson BK, Conner MG, Landen CN. The role of the fallopian tube in the origin of ovarian cancer. Am J Obstet Gynecol [Internet]. 2013;209(5):409–14. Available from: http://dx.doi.org/10.1016/j.ajog.2013.04.019

XVIII. Piek JMJ, Van Diest PJ, Zweemer RP, Jansen JW, Poort-Keesom RJJ, Menko FH, et al. Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. J Pathol. 2001;195(4):451–6.

XIX. Przybycin CG, Kurman RJ, Ronnett BM, Shih IM, Vang R. Are all pelvic (Nonuterine) serous carcinomas of tubal origin? Am J Surg Pathol. 2010;34(10):1407–16.

XX. Qian S, Wang W, Li M. Transcriptional factor Yin Yang 1 facilitates the stemness of ovarian cancer via suppressing miR-99a activity through enhancing its deacetylation level. Biomed Pharmacother [Internet]. 2020;126(March):110085. Available from: https://doi.org/10.1016/j.biopha.2020.110085

XXI. Sarvagalla S, Kolapalli SP, Vallabhapurapu S. The Two Sides of YY1 in Cancer: A Friend and a Foe. Front Oncol. 2019;9(November):10–3.