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Immunohistochemistry Expression Gata3 Based on Subtypes of Ovarian Carcinoma at Haji Adam Malik General Hospital Medan 2019-2021

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ABSTRACT

Background
Ovarian carcinoma is a cancer with high mortality in women and although comprehensive management with surgery and chemotherapy at an advanced stage, the resistance rate is still low. GATA3 contributes to the progression of malignancy and its expression is one of the predictors in some malignancies, but the results are mixed in ovarian carcinoma. High GATA3 expression is associated with the aggressiveness of tumor growth and poor prognosis of ovarian carcinoma.

Methods
This research is an cross-sectional descriptive-analytical study with 33 histological specimens diagnosed with ovarian carcinoma from medical records/archives at H. Adam Malik Hospital Medan. Each sample specimen was stain with GATA3, and several various histopathological subtypes of ovarian carcinoma.

Results
From a total of 33 samples, 14 samples were serous carcinoma, 6 samples were mucinous carcinoma, 7 samples were endometrioid carcinoma, and 6 samples were clear cell carcinoma. GATA3 was expressed in 42.5% of serous carcinoma. Positive expression of GATA3 is mostly found in advanced ovarian carcinoma, older age, and histopathological type of serous carcinoma.

Conclusion
Immunohistochemistry GATA3 expression was expressed in 42.4% of serous carcinoma, 21.2% in endometrioid carcinoma, 18.2% in clear cell carcinoma, and 18.2% in mucinous carcinoma.

Keywords: ovarian carcinoma, GATA3, immunohistochemistry

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INTRODUCTION

Ovarian cancer is the second most common malignancy after breast cancer. The Global Burden of Cancer (GLOBOCAN) in 2020 stated that ovarian cancer ranks as the 8th most cancer in women worldwide with 313,959 new cases and an ovarian cancer death rate of 207,252. The incidence of ovarian cancer in Indonesia in 2020 ranks 10th, with 14,896 new cases and 9,581 deaths from ovarian cancer. Geographic variation in the incidence of ovarian cancer has increased in North America, Central-Eastern Europe, and Southeast Asia.[1-4]

The most commonly encountered histological picture of ovarian carcinoma is the high-grade serous carcinoma type. Other histological types of ovarian carcinoma are low-grade serous carcinoma, mucinous adeno-carcinoma, endometrioid adenocarcinoma, seromucinous carcinoma, clear cell adeno-carcinoma, malignant Brenner tumor carcino-sarcoma, and mixed cell adenocarcinoma. The morphology of the entity has a different etiology than the genetic characteristics, phenotype, and behavior of the tumor and includes a response to chemotherapy. Ovarian carcinoma (more than 70%) is more commonly diagnosed at an advanced stage, i.e., stage III or IV based on the FIGO stage, because there are still few effective screening strategies at an early stage as well as nonspecific early symptoms of carcinoma.[4-7]

GATA3 is a derivative of the trans-cription factor GATA, located on chromosome 10p14 is one of the 6 transcription factors in the DNA sequence functioning to regulate the process of differentiation during embryogenic development. GAT3 expression is associated with a poor prognosis in ovarian carcinoma. In ovarian carcinoma, GATA3 acts as an oncogenic protein related to TP53, which serves to stimulate the occurrence of apap-tosis. If GATA3 is strongly expressed in ovarian carcinoma, it will interfere with the work of TP53 so that there will be resistance to apaptosis.[10]

METHOD

This study is an analytical descriptive study that aims to assess the immunohisto-chemistry expression of GATA3 in ovarian carcinoma with a cross-sectional approach. Samples that met the inclusion and exclusion criteria were diagnosed with ovarian carcinoma with Hematoxylin & eosin staining, and then paraffin black was stained for GATA3 monoclonal antibodies (L50-823 clone primary mice). GATA3 expression positive was identified by staining brown granules in the nucleus of tumor cells using CX23 Olympus microscope. Assessment by means of assessing the area of the colored viewed at 20x magnification is categorized into: 0=≤5% cells, +1=6-25 % cells, +2=26-60 % cells, +3=61-100% cells, and the intensity of the colored verticality becomes: 0=negative, +1=weak, +2=medium, +3=strong. The expression from GATA3 is calculated using the following equation: H-score=Pi (i + 1), where I is the intensity of the colored tumor cells (0 to 3+), and Pi is the percentage of tumor cells colored for each intensity. We set the cut-off value at 150%, which corresponds to the H-score. Cases that have a value of 0% are considered negative GATA3 expressions, less than 150% are considered weak GATA3 expressions and those that equal to or exceed 150% are considered strong GATA3 expres-sions. Taking the average of the percentage of colored cells attenuated to 150%: low expression <150%, and high expression ≥150%.[74]

Data processing will be carried out using the statistical program "Statistical Package for the Social Sciences" (SPSS). The results of data processing are presented in the form of tables. The data in this study were analyzed with univariate analysis to see a frequency distribution that included each of the variables of age group, parity history, contra-ceptive history, clinical stage, histopathological type, and GATA3 expression. Data analysis in the form of mean, median, range, and standard deviation.

RESULTS

The samples used in this study were 33 samples diagnosed as ovarian carcinoma at the Anatomic Pathology Unit of H. Adam Malik General Hospital Medan in 2019-2021, where these 33 samples met the inclusion and exclusion criteria in this study.

The results of microscopic exami-nation of HE preparations showed that most of the samples had a histopathological type of serous carcinoma ovarian carcinoma 14 cases (42.4%), mucinous carcinoma 6 cases (18.2%), endometrioid carcinoma 7 cases (21.2%), and clear cell carcinoma 6 cases (18.2%). Most GATA3 immunohisto-chemistry expression was based on micro-scopic characteristics with low expression in 26 cases

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ovarian carcinoma (78.8%) and high expression in 7 cases (21.2%).

Table 1. Distribution of ovarian carcinoma samples based on microscopic characteristics of histopathological subtypes of ovarian carcinoma and GATA3 expression.

Characteristic	Sum=n	Percentage (%)
Sum	33	100
Histopathological subtypes		
Serous carcinoma	14	42.4%
Mucinous carcinoma	6	18.2%
Endometrioid carcinoma	7	21.2%
Clear cell carcinoma	6	18.2%
GATA3 expressions		
Expression low	26	78.8
Expression high	7	21.2

Table 2. Distribution of positive GATA3 immunohistochemistry expression based on histopathological subtypes of ovarian carcinoma.

Histopathological subtypes	Sum=n	Presented (%)	GATA3 expressions					
			Expression low		Expression high		Total	
			n	%	n	%	n	%
Serous carcinoma	14	42.4	9	36.6	5	71.4	14	42.5
Mucinous carcinoma	6	18.2	6	23.1	0	0	6	18.2
Endometrioid carcinoma	7	21.2	6	23.1	1	14.3	7	21.1
Clear cell carcinoma	6	18.2	5	19.2	1	14.3	6	18.2
Total	33	100	26	100	7	100	33	100

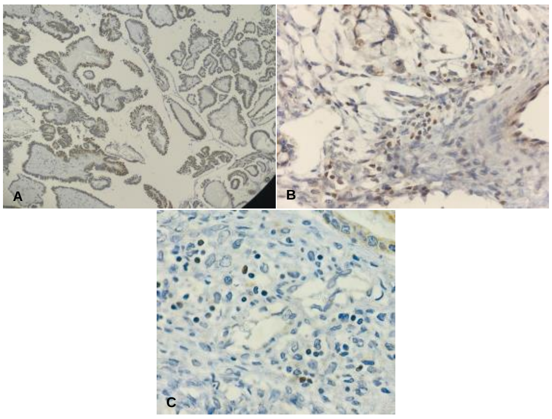

Figure 1. A, B, C. Immunohitochemistry expression GATA3 high expression.

The frequency distribution of GATA3 immunohistochemistry expression based on the histopathological subtype of serous carcinoma ovarian carcinoma was 14 cases (42.4%), mucinous carcinoma was 6 cases (18.2%), endometrioid carcinoma was 7 cases (21.2%), and clear cell carcinoma was 6 cases (18.2%). The results of the GATA3 immunocytochemistry examination showed that low expression majority of samples in the histopathological subtype of serous carcinoma were 9 cases (36.6%), mucinous carcinoma 6 cases (23.1%), endometrioid carcinoma 6 cases (23.1%), and clear cell carcinoma 5 cases (19.2%). The results of the GATA3 immunocytochemistry examination showed high expression in the histopathology subtype of serous carcinoma 5 cases (71.4,1%), no strong expression was found in mucinous carcinoma, endometrioid carcinoma 1 case (14.3%), and clear cell carcinoma 1 case (14.3%).

DISCUSSION

The immunohistochemistry GATA3 high expression in this study was found to be the most in the serous carcinoma type, which was 42.5% compared to other types. This is in line with the research of El-Arabey et al., where GATA3 is associated with the TP53 mutation in serous carcinoma. It is also supported by the same study by Espinosa et al., Chen et al., and Terzic et al., which states that overexpression of GATA3 using the lentiviral system in the HGSOC OVCAR5 cell line significantly improves expression in high-grade serous carcinoma. Where 6% of ovarian carcinoma expresses GATA3. The most common positive cases encountered are high-grade serous carcinoma with 3+ staining in more than 90% of malignant cells. Strong but less extensive staining is also seen in 2 mucinous adenocarcinomas that are positive in 50% and 20% of cells. In clear cell carcinoma, ovaries have a strong intensity in 30% of cells and weak staining in 20% of cells. However, this study is not in line with the research of Davis et al., and Ordo et al., which showed that serous carcinoma type and other histologic subtypes of ovarian carcinoma that did not have a positive expression of GATA3 were 0%.

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However, in this study, GATA3 was also found to have a low expression in mucinous carcinoma (3.1%), where mucinous carcinoma also has a TP53 mutation pathway, which should have GATA3 expression high. In the type of endometrioid carcinoma (3.1%) and clear cell carcinoma (3.1%), there is also a low expression of GATA3 with a minimal amount. So far researchers have not found mutations that are common in all of these subtypes; more research is needed to prove the relationship between GATA3 and these genes. In addition, researchers also suspect that the slight Tp53 mutation in the subtype affects GATA3 low expression.[60,61,65-67,72,85]

CONCLUSION

The results of the study on a total of 33 samples in this study conducted at the Anatomic Pathology Unit of H. Adam Malik General Hospital Medan, then it can be concluded as follows:

a. The frequency distribution of characteristics of people with ovarian carcinoma is most prevalent in the age group >50-60 years old (age range 58 years), history of nullipara parity, without a history of contraceptive use, and most in the group of stage III ovarian malignancy.
b. Based on the histopathology subtypes in this study, the most numerous are the serous carcinoma ovary subtype and GATA3 immunohistochemistry expression, which has a higher expression than the low expression.
c. GATA3 immunohistochemistry expression with high expression is most commonly displayed in the serous carcinoma ovary histopathology subtype, while low expression in the endometrioid carcinoma ovary and clear cell carcinoma ovary subtypes is only found in 1 case in each subtype.
d. GATA immunohistochemistry expression will be more widely displayed in the serous carcinoma ovary subtype due to the influence of the Tp53 mutation that occurs in the serous carcinoma ovary.

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ETHICAL APPROVAL

This research has been granted a research permit by the Health Research Ethics Committee of the Universitas Sumatera Utara.

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