MERIT RESEARCH JOURNALS
www.meritresearchjournals.org

Merit Research Journal of Medicine and Medical Sciences (ISSN: 2354-3238) Vol. 2(5) pp. 117-120, May, 2014
Available online http://www.meritresearchjournals.org/mms/index.htm

Original Research Article

HER-2/neu Expression is not correlated to stage of ovarian cancer

Ryan Saktika Mulyana*, I. Ketut Suwiyoga and I. Gede Mega Putra

Department of Obstetrics and Gynecology, Faculty of Medicine, Udayana University, Bali Sanglah

***Correspondence Author's Email: ryan_mul@yahoo.com; Tel: +6281805619588**

Abstract

Cross-sectional study, study was held in Obstetrics and Gynecology department, Anatomic Pathology and Medical Records of Sanglah General Hospital Denpasar, which was conducted from July 2011 until July 2013 with 44 pieces sample of paraffin blocks. Paraffin blocks sample are grouped based on the stage of ovarian cancer, namely: ovarian cancer stage I, II, III, and IV. Then each group of stage was examined the expression of HER2/neu by immunohistochemical techniques and assessing their correlation between HER2/neu expression and stage of ovarian cancer using the Spearman test. Mean age, Body Mass Index (BMI), parity, and history of hormonal contraceptives on four groups of ovarian cancer stage were homogeneous. Based on the correlation test was obtained that correlation r value was 0.203 (p = 0,185), indicated that there was no correlation between the stage of ovarian cancer and expression of HER2/neu. Her2/neu expression was not correlated with stage of ovarian cancer.

Keyword: Her2/neu expression and stage of ovarian cancer.

INTRODUCTION

Ovarian cancer is a common gynecological malignancy among women. Often cases of ovarian cancer had been found already spread out of ovarian and being difficult to be cured with surgery or chemotherapy. Ovarian cancer is an eighth most common of malignant disease among women and ranks fifth cause of deaths in women from cancer (American Cancer Society, 2009). Based on the results of a recent study found that incidence of ovarian cancer in the United States increased in the last 30 years (Chobanian and Dietrich, 2008). The incident in 2009 reached 21,500 cases with a mortality rate was 14,600 of women. By the end of 2009 cases increased to 21,550 cases of ovarian cancer, ovarian cancer accounts for approximately 3% of all cancers in women with the most common age group suffered from ovarian cancer was 55-64 years (American Cancer Society, 2009). The incidence of ovarian cancer in Sanglah hospital as much as 35% of all gynecological cancers, with 5-year survival rate was only 15% (Karyana, 2004). The difficulty in detecting, diagnosing and treating ovarian cancer is causing the low survival rate in women suffering from ovarian cancer, 46% of women with ovarian cancer survive at least 5 years after diagnosis (American Cancer Society, 2009). Until now there is no effective screening method in detecting ovarian cancer, besides the symptoms of ovarian cancer are not specific to be diagnosed as an ovarian cancer and often discovered in late stage, only a quarter of ovarian cancer was found in stage I (Chobanian and Dietrich, 2008). Biomarkers Ca-125 most frequently used by the clinician in determining ovarian cancer, but the Ca-125 is used widely to have a low sensitivity and the presence of a high false positive due to a variety of other conditions, such as pelvic inflammatory disease, endometriosis, ovarian cysts, and

Table 1. Distribution of Age, BMI, parity, and history Hormonal Contraception On Group of Ovarian Cancer Stage

Variables	Ovarian Cancer Stage				*p*
	I (n=7) mean±2SD	II (n=9) mean±2SD	III (n=21) mean ±2SD	IV (n=7) mean ±2SD	
Age (Years)	40,86±5,24	43,56±12,70	45,57± 9,77	57,86±8,78	0,814
BMI (kg/m^2)	19,9±1,51	25,15±4,04	21,76±4,95	21,38±3,75	0,304
Parity	1,57±0,78	1,33 ±0,70	2,00±1,30	2,43±0,97	0,057
Hormonal Contraception	1,71±0,48	1,78±0,44	1,90±0,30	1,71±0,48	0,562

Tabel 2. The Correlation between HER2/neu expression and Ovarian Cancer Stage

Variables		Ovarian Cancer Stage				r	*p*
		I (n=7)	II (n=9)	III (n=21)	IV (n=7)		
Her2/neu	(+)	2	5	5	1		
expression	(-)	5	4	16	6	0,203	0,185

fibroids (Hogdall et al., 2007). Analysis of the expression of genes needed to monitor global gene expression profiles on ovarian cancer tissues, including primary cells, ovarian surface epithelial cells and cell cystadenomas (Colleen et al., 2000). Knowledge about the changing of gene expression during development and prognosis of ovarian tumors may provide a new paradigm regarding early detection and treatment of ovarian cancer strategies (Mayr et al., 2006). Factors that contribute independently to determine prognosis are tumor stage, degree of tumor differentiation and DNA ploidy. Another Factors such as the volume of residual tumor after reduction, ascites, rupture, tumor adhesion, increasing age and serum CA-125 levels are factors that affect prognosis independently (Seidman, 2002). However, until now only a few studies find a relationship between the HER2/neu expression and independent factors especially stage of ovarian cancer that has been proven in determining the prognosis and therapy of ovarian cancer and may provide predictive value for Her2/neu expression in each based on the stage of ovarian cancer cases.

METHOD

This study used observational analytic design (cross-sectional) in Obstetrics and Gynecology department, Anatomic Pathology and Medical Records of Sanglah General Hospital, Denpasar which was conducted from July 2011 until July 2013 with 44 pieces samples of paraffin blocks. Paraffin block samples are grouped based on the stage of ovarian cancer, namely: ovarian cancer stage I, II, III, and IV. Then each group of stage was examined for the expression of HER2/neu by immunohistochemical techniques and assessing their correlation between HER2/neu expression and stage of ovarian cancer using the Spearman test.

RESULT

In this research, test for normality data with Kolmogorov-Smirnov test and using Levene's test for homogeneity of the data to some variables such as age, Body Mass Index (BMI), parity and history of hormonal contraception. The analysis showed that the distribution of sample on the variables of age, BMI, parity, and history of hormonal contraceptives were normal with ($p > 0.05$) and homogeneous ($p > 0.05$), whereas to compare mean values of each variable used One Way Anova test. (Table 1)

Assessment of the correlation between HER2/neu expression and ovarian cancer stage was analyzed using the Spearman correlation test. The results of this analysis are presented in Table 2.

Table 2 shows that the overexpression of HER2/neu in stage I were 2 samples, 5 samples in stage II, stage III as much as 5 samples, and 1 sample in stage IV. Assessment test of the correlation between HER2/neu expression and stage of ovarian cancer was done by using the Spearman correlation test, where there was no correlation was obtained between HER2/neu expression and stage of ovarian cancer ($p > 0.05$).

DISCUSSION

In this study, the mean age in the group stage I ovarian cancer stage was 40,86 ± 5,24 years, stage II was 43,56 ± 12,70 years, stage III was 45,57 ± 9,77 years and stage IV is 57,86 ± 8,78 years. The mean parity in stage I ovarian cancer group was 1,57 ± 0,78, stage II was 1,33 ± 0,70, stage III was 2,00 ± 1,30, and stage IV was 2,43 ± 0,97. The mean BMI at each stage I ovarian cancer group was 19,9 ± 1,51 kg/m^2, stage II was 25,15 ± 4,04 kg/m^2, stage III was 21,76 ± 4,95 kg/m^2, and stage IV was 21,38 ± 3,75 kg/m^2. While mean sample for variable hormonal contraception stage I was 1,71±0,48, stage II was 1,78±0,44, stage III was 1,90±0,30 and stage IV was 1,71±0,48. Her2/neu over expression in ovarian cancer in this study was 29.54% (13 of 44 cases). 2 samples were obtained from stage I, 5 in stage II samples, 5 samples in stage III and only 1 sample in stage IV. This result is similar to several studies from around the world which found HER2/neu over expression in ovarian cancer was 15-30% (Zahra et al., 2010). Statistical analysis was not obtained the relationship between the expression of HER2/neu and ovarian cancer stage with p=0.185 (P> 0.05). Nowadays there are a difference of opinion about the correlation between HER2/neu expression and stage of ovarian cancer, there were several studies that support and some of them denied this hypothesis, as the research by Coronado in 2007 which found there were 24, 2% of cases of ovarian cancer with over expression of HER2/neu and it was correlated with advanced stages of ovarian cancer (Coronado et al., 2007). While the research is contrary to this hypothesis in several studies such as the study conducted Verri, et al in which the results of this study showed that Her2/neu expression was not associated with prognostic factors including stage ovarian cancer ovarian cancer (Tuefferd et al., 2007). Whereas in the study by Yun also found that the lack of correlation between HER2/neu over expression in early stage ovarian cancer (Yun et al., 2009). The lack correlation between ovarian cancer stage and HER2/neu expression in ovarian cancer in this study may be caused by another gene (protooncogene) mutations besides HER2/neu gene (protooncogene). One of the causes of cancer are the result of disruption of the four groups of normal regulation of regulatory genes, either the disruption in the gene that stimulates protooncogene growth, inhibition of tumor suppressor genes, regulation of apoptosis (Programmed cell death) or DNA repair genes involving (Kumar et al., 2010). All of the pathway is the main target of the genetic damage. Not only occur in the HER2/neu gene mutation alone but can be through various mutations involving other genes or mutations that occur simultaneously. like for example damage to tumor suppressor genes in the gene (P53, RB1, MSH2, MLH1. etc.) or damage to the DNA repair gene (bcl-2) or the presence of mutations in more than one gene, so that all the mechanisms of gene mutations will be able to improve progression ovarian cancer and provide clinical manifestations on the stage (Kumar et al., 2010). In this study, the number of sample is determined based on the data from "Badan Registrasi Kanker" in 2006, where the incidence of ovarian cancer in a population was 11.9%. Therefore, number of sample should be determined based on the highest number of samples obtained from the prevalence of each group of ovarian cancer stage, not based on the prevalence of ovarian cancer in the population, because the prevalence of each group from ovarian cancer stage in the population is not available, this study using ovarian cancer prevalence in the population as a data in determining the study sample.

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of this study it can be concluded that HER2/neu expression was not associated with stage of ovarian cancer. Based on this conclusion it is necessary to do further research for detecting multiple pathways of carcinogenesis that have mutations in ovarian cancer. because the carcinogenesis pathway of ovarian cancer are Multi-step, then in order to support the development of the idea of the use of genes and gene expression in the early detection and diagnostic of ovarian cancer follow-up studies are needed to assess another the carcinogenesis pathway, such as the oncogene pathway, changes of apoptotic genes, and genes involved in DNA repair.

REFERENCES

American Cancer Society (2009). Detailed Guide: *Ovarian Cancer.* [citied 2010 okt 18]. Available from : http://nccu.cancer.org

Chobanian N, Dietrich CS (2008). Ovarian cancer, *Surgical Clinics of North America,* PP. 285-299.

Colleen D, Cheryl A, Sherman B, Ellen S, Pizer FJ, Montz D (2000). "Large-Scale Serial Analysis of Gene Expression Reveals Genes Differentially Expressed in Ovarian Cancer", *Cancer Research 60,* 6281–6287.

Coronado M, Fasero L, García S, Ramírez M, Vidart A (2007). Overexpression and prognostic value of p53 and HER2/neu proteins in benign ovarian tissue and in ovarian cancer. *Medicina Clinica* 2007, 128(1):1-6

Hogdall EVS, Christensen L, Kjaer SK (2007). *CA125 Expression Pattern, Prognosis and Correlation with Serum CA125 in Ovarian Tumor Patients. From The Danish "MALOVA" Ovarian Cancer Study*. (serial online), [cited 2010 Aug. 21]. Available from: URL: http://info.cancerresearchuk.org/cancerstats/types/ovary/riskfa ctors/.

Karyana K (2004). *Profil Kanker Ovarium Di Rumah Sakit Sanglah Denpasar Periode Januari 2002 – Desember.* PPDS I obstetric dan ginekologi FK UNUD/RSUP Sanglah Denpasar 205:13-6.

Kumar V, Abbas A, Fausto N, Aster J (2010). *Robbins and Cotran Pathologic Basis of Disease*. 8th ed, Saunders Elsevier, Philadelphia.

Mayr D, Kanitz V, Ammann G, Engel J, Burges AU, Diebold (2006). *HER2/neu gene amplification in ovarian tumors: a comprehensive immunohistochemical and FISH analysis on tissue microarrays",* Histopathology, 48 149 – 156.

Seidman JD (2002). *Surface Epithelial Tumos of The Ovary.* In: Kurman, R J., editor: Blaustein's Pathology of The Female Genital

Track. 5th ed. New York: Springer. pp. 791 – 904.
Tuefferd M, Couturier J, Penault F, Vincent SA, Broet P (2007). HER2 Status in Ovarian Carcinoma. A Multicenter GINECO Study of 320 patients, Gineco J. 2(11): e1138. doi: 10.1371/journal. pone.0001138.
Yun WA, Robert A, David S, Mario L, Beiyun C (2009). Her-2/neu expression and amplification in early stage ovarian surface epithelial neoplasms. *Gynecologic Oncology*, 570–575.
Zahra M, Sharareh SD, Alamtaj SD, Minoo R, Ahmad M, Mohammad JF, Abbas G (2010). Serum HER2/neu level in epithelial ovarian cancer. *Middle East Journal of Cancer,* 1(2): 65-68.