pISSN: 2338-6401-eISSN: 2338-7335

INAJOG

Indonesian Journal of Obstetrics and Gynecology

Volume: 5, No. 2, page 67-126 April 2017

Founded 1974

Editorial

The Concept of Gynecologic Oncology Services in Jakarta Related to Academic Health System 68

Research Articles

The Impact of Educational Intervention of High-Risk Pregnancy and High-Risk Childbirth on Knowledge, Attitude, and Behavior in Recognizing Danger Signs in Pregnancy: A Single Blind Clinical Trial 69

Iron Deficiency Anemia, Cystitis, and Bacterial Vaginosis Increase the Risk for Developing Preterm Labor 73

Endothelin-1 Levels in Pregnant Women with Severe Pre-eclampsia and Normal Pregnant Women 77

Anti Müllerian Hormone as a Predictor of Metabolic Syndrome in Polycystic Ovary Syndrome 83

Post-laparoscopic GnRH-agonist Therapy does not Improve Spontaneous Conception Rates of Women with Endometriosis 87

The Efficacy of Monoplant® and Indoplant® as Contraceptive Methods: A Comparative Study 94

The Impacts of Pelvic Floor Dysfunction Counseling to Know-ledge Level and Atittude of Pregnant Women with Gestational [illegible] above Thirty Six Weeks in the Selection of Delivery Method

Vascular Endothelial [illegible]ctor-C Serum and Endo[illegible] Serum as Predictors of [illegible] Cervical Cancer

Evaluation of the Accuracy of Human Kall[illegible] Antigen-125, and Human Epididymis - 4 in Pred[illegible] Cancer 110

Human Papilloma Virus Self-testing as an Alternative Method for Cervical Cancer Screening 114

Human Papilloma Virus L1 Gene Methylation as a Potential Biomarker for Precancerous Cervical Lesion: a Preliminary Report 120

Official Publication of
Indonesian Society of Obstetrics and Gynecology

www.inajog.com

Accredited (2014 - 2019)
by the Directorate General of Higher Education of the Ministry of Education and Culture of the Republic of Indonesia
No.: 212/P/2014, 3 Juli 2014

INDONESIAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

Indones J Obstet Gynecol

Majalah Obstetri dan Ginekologi Indonesia

CONTENT

Volume 5, Number 2, Page 67 – 126, April 2017

Editorial

Sigit Purbadi, *Jakarta* — 68 — **The Concept of Gynecologic Oncology Services in Jakarta Related to Academic Health System**

Research Articles

JM Seno Adjie, Devi M Malik, *Jakarta* — 69 — **The Impact of Educational Intervention of High-Risk Pregnancy and High-Risk Childbirth on Knowledge, Attitude, and Behavior in Recognizing Danger Signs in Pregnancy: A Single Blind Clinical Trial**
The educational intervention gives significant impact in attitude and behavior.

Janet Sumampouw, I Ketut Suwiyoga, Ketut S Negara, *Bali* — 73 — **Iron Deficiency Anemia, Cystitis, and Bacterial Vaginosis Increase the Risk for Developing Preterm Labor**
Iron deficiency anemia, cystitis, and bacterial vaginosis increase the risk for developing preterm labor.

Yosiana Wijaya, John JE Wantania, Bismarck J Laihad, *Manado* — 77 — **Endothelin-1 Levels in Pregnant Women with Severe Preeclampsia and Normal Pregnant Women**
There was a significant difference between endothelin-1 level in severe preeclampsia and normotensive pregnancies.

Budi Wiweko, Cynthia A Susanto, *Jakarta* — 83 — **Anti Müllerian Hormone as a Predictor of Metabolic Syndrome in Polycystic Ovary Syndrome**
AMH can be used as a predictor of metabolic syndrome in PCOS.

Kevin D Tjandraprawira, Tono Djuwantono, *Bandung* — 87 — **Post-laparoscopic GnRH-agonist Therapy does not Improve Spontaneous Conception Rates of Women with Endometriosis**
Post-laparoscopic GnRH-agonist administration to women with endometriosis does not significantly improve their chances of spontaneous conception. In fact, such administration seems to delay it.

Eka R Gunardi, Frista Ballo, *Jakarta* — 94 — **The Efficacy of Monoplant® and Indoplant® as Contraceptive Methods: A Comparative Study**
There are no significant differences in efficacy and side effects using Monoplant® and Indoplant® during the 6-month follow-up. However, the insertion time of Monoplant® is shorter compared to Indoplant®'s. Monoplant® can be considered for use as contraception with the effectiveness and side effects are almost the same, but with shorter time of insertion compared to Indoplant®.

Surahman Hakim, Fajar Ekaputra, *Jakarta* — 99 — **The Impacts of Pelvic Floor Dysfunction Counseling to Knowledge Level and Atittude of Pregnant Women with Gestational Age above Thirty Six Weeks in the Selection of Delivery Method**
There is a change scores better in knowledge about pelvic floor dysfunction after counseling. There was no significant difference between selecting the desired method of delivery before the after counseling.

Andhinna Rusmardiani, Syahrul Rauf, Efendi Lukas, *Makassar* — 105 — **Vascular Endothelial Growth Factor-C Serum and Endostatin Serum as Predictors of Lympho Vascular Invasion in Early Stage Cervical Cancer**
The level of VEGF-C and VEGF-C/ endostatin ratio was higher in patients with early stage cervical cancer with positive LVSI than negative LVSI.

Yongki Wenas, Ketut Suwiyoga, I Nyoman H Sanjaya, *Bali* — 110 — **Evaluation of the Accuracy of Human Kallikrein-6, Cancer Antigen-125, and Human Epididymis - 4 in Predicting Ovarian Cancer**
There was no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) found between hK6, CA125, HE4 compared to histopathology examination in predicting ovarian cancer.

Richard Chandra, Syahrul Rauf, Umar Malinta, *Makassar* — 114 — **Human Papilloma Virus Self-testing as an Alternative Method for Cervical Cancer Screening**
HPV self-testing is very potential to be used as an alternative method for cervical cancer screening.

Suzanna P Mongan, Andrijono, Hartono Tjahadi, *Manado, Jakarta* — 120 — **Human Papilloma Virus L1 Gene Methylation as a Potential Biomarker for Precancerous Cervical Lesion: a Preliminary Report**
HPV 16 infection were most commonly found in the form of single or multiple. Co-infection of HPV 16 and 18 were found in the majority of the samples. There were no significant correlation between HPV type and the severity of cervical lesions. Until now, the examination of DNA methylation HPV L1 already obtained eight samples of HPV 16 with a thin band on electrophoresis but the result could not be concluded because it is still in the process of optimization.

Editorial Board

Indonesian Journal of Obstetrics and Gynecology

Indones J Obstet Gynecol

Research Article

Evaluation of the Accuracy of Human Kallikrein-6, Cancer Antigen-125, and Human Epididymis - 4 in Predicting Ovarian Cancer

Evaluasi Akurasi Human Kallikrein-6, Cancer Antigen-125, dan Human Epididymis-4 dalam Memprediksi Kanker Ovarium

Yongki Wenas, Ketut Suwiyoga, I Nyoman H Sanjaya

Department of Obstetrics and Gynecology
Faculty of Medicine Universitas Udayana/
Sanglah Hospital
Bali

Abstract

Objective: To evaluate the accuracy of hK6, HE4, and CA125 in predicting the malignancy of ovarian mass.

Methods: The design of this study was cross-sectional. This study was conducted in the Obstetrics and Gynecology Clinic, Sanglah Hospital, Denpasar, between the period of September 2014 and August 2016. Samples were all patients with ovarian tumors who underwent surgery at Sanglah Hospital, Denpasar. Data analysis was performed using McNemar and chi square test in SPSS for windows version 17.0.

Results: 22 samples were obtained. P > 0.05 value of age and parity variables indicated no differences between the two groups. There is no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) of hK6 compared to histopathology examination in diagnosing ovarian cancer (p = 1). There is no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) of HE4 compared to histopathology examination in diagnosing ovarian cancer (p = 1). There is no accuracy difference (sensitivity, specificity, positive predictive value, negative predictive value) of CA125 compared to histopathology examination in diagnosing ovarian cancer (p = 0.687).

Conclusion: There was no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) found between hK6, CA125, HE4 compared to histopathology examination in predicting ovarian cancer.

[Indones J Obstet Gynecol 2017; 5-2: 110-113]

Keywords: cancer antigen 125, human epididymis-4, human kallikrein 6, ovarian cancer

Abstrak

***Tujuan**: Untuk mengetahui akurasi hK6, CA125 dan HE4 dalam memprediksi keganasan ovarium pada massa ovarium.*

***Metode**: Rancangan penelitian ini adalah uji diagnostik (cross sectional) yang dilaksanakan di Poliklinik Kebidanan dan Kandungan RSUP Sanglah, Denpasar. Sampel penelitian ini adalah semua penderita dengan tumor ovarium yang datang ke Poliklinik Kebidanan dan Kandungan RSUP Sanglah dan menjalani operasi di RSUP Sanglah, Denpasar. Pengambilan sampel dilakukan dengan cara consecutive sampling mulai September 2014 sampai Agustus 2016. Analisis data memakai uji Chi Square dan McNemar dengan bantuan SPSS for windows 17.0 version.*

***Hasil**: Didapatkan sebanyak 22 sampel penelitian variabel usia dan paritas didapatkan nilai p > 0,05, yang menyatakan bahwa tidak adanya perbedaan antara kedua kelompok. Tidak ada perbedaan kurasi hK6 (sensitivitas, spesivisitas, nilai prediksi positif, nilai prediksi negatif) dibandingkan dengan hasil pemeriksaan histopatologi dalam mendiagnosis kanker ovarium (p=1). Tidak ada perbedaan kurasi HE4 (sensitivitas, spesivisitas, nilai prediksi positif, nilai prediksi negatif) dibandingkan dengan hasil pemeriksaan histopatologi dalam mendiagnosis kanker ovarium (p=1). Tidak ada perbedaan kurasi CA125 (sensitivitas, spesifisitas, nilai prediksi positif, nilai prediksi negatif) dibandingkan dengan hasil pemeriksaan histopatologi dalam mendiagnosis kanker ovarium (p=0,687).*

***Kesimpulan**: Tidak ada perbedaan kurasi antara hK6, CA125, HE4 (sensitivitas, spesifisitas, nilai prediksi positif, nilai prediksi negatif) dibandingkan dengan hasil pemeriksaan histopatologi dalam memprediksi kanker ovarium.*

[Maj Obstet Ginekol Indones 2017; 5-2: 110-113]

***Kata kunci**: cancer antigen 125, human epididymis-4, human kallikrein 6, kanker ovarium*

Correspondence: Yongki Wenas, dokter.yongki@gmail.com

INTRODUCTION

Ovarian cancer is a major burden in the field of gynecology oncology, due to high rate of mortality resulted from this cancer.[1] Increasing ratio of morbidity and mortality in ovarian cancer patients is due to progression of disease that shows no symptoms found until metastasis. 70% of women with ovarian cancer are diagnosed at advanced stage. The five year survival rate of ovarian cancer is 85% when diagnosed at early stage (stage I and II), but may decrease to less than 20% if diagnosed at advanced stage (stage III or IV).[2]

Serum of CA125 tumor marker to predict the presence of malignancy in patients with ovarian mass has lower sensitivity and specificity in pre and postmenopausal women.[3] Several studies conducted to diagnose ovarian cancer in patients with ovarian mass using tumor marker HE4 and combination of HE4 and CA125 have shown that HE4 has higher sensitivity and specificity compared to CA125.[4]

Kallikrein 6 gene is a trypsin-like serine protease of human gene, family kallikrein that has great potential to be developed as a tool for early detection for ovarian cancer and various preliminary research have been conducted to support towards it and result of the research can be used as rationale that hK6 can be used as a medium or tool for early detection of ovarian cancer.[5]

Based on explanation elaborated above, assessment of the correlation or relationship between hK6 with ovarian cancer will be performed. This study is expected to be a reference or additional consideration to support usage hK6 as the early detection of ovarian cancer diagnostic.

METHOD

We used cross-sectional study design. This study was conducted at the Obstetrics and Gynecology Clinic, Sanglah Hospital, Denpasar, during the period between September 2014 and August 2016. The subjects were all patients with ovarian tumors who came to Obstetrics Clinic of Sanglah Hospital and underwent surgery in Sanglah Hospital, Denpasar. Data analysis was performed using SPSS for Windows version 17.0.

RESULT

In this study, T-independent test was conducted toward age and parity variable between the two groups. As seen in Table 1, p value> 0.05 of age and parity was obtained, indicated no differences between both groups.

To determine diagnostic test of hK6 toward histopathology in the diagnosis of ovarian cancer, it was analyzed using Chi-Square test. The results of the analysis are presented in the following table.

Table above with 2x2 cross table, showed 80.0% sensitivity, 75.0% specificity, 72.7% positive predictive value, 81.8% negative predictive value, 27.3% false positive, 18.2% false negative values, and 77.3% accuracy. McNemar test showed no accuracy differences of hK6 (sensitivity, specificity, positive predictive value, negative predictive value) compared to histopathology examination in diagnosing ovarian cancer (p = 1.00)

To determine diagnostic test of HE4 compared to histopathology in diagnosis of ovarian cancer, Chi-Square test analysis was conducted. Results are presented in Table 3.

Table 1. General and Parity Characteristics Comparison between both Groups

Risk factor	Malignancy group (n=10)		Benign tumor group (n=12)		p
	Mean	DS	Mean	DS	
Age (year)	52.80	16.72	50.50	14.94	0.737
Parity	2.10	1.10	2.08	1.88	0.981

Table 2. Diagnostic Test of hK6 toward Histopathology in Diagnosing Ovarian Cancer

		Ovarian cancer		Total
		Malignant	Benign	
hK6	High	8	3	11
	Low	2	9	11
Total		10	12	22

Table 3. Diagnostic Test of HE4 toward Histopathology in Diagnosing Ovarian Cancer

		Ovarian cancer		Total
		Malignant	Benign	
HE4	High	7	2	9
	Low	3	10	13
Total		10	12	22

Table 4. Diagnostic Test of CA125 toward Histopathology in Diagnosing Ovarian Cancer

		Ovarian cancer		Total
		Malignant	Benign	
CA125	High	6	2	8
	Low	4	10	14
Total		10	12	22

Table above with a 2x2 cross table showed 70.0% sensitivity, 83.3% specificity, 77.8% positive predictive value, 76.9% negative predictive value, 22.2% false positive, 23.1% false negative values, and 77.3% accuracy. McNemar test showed no differences of accuracy (sensitivity, specificity, positive predictive value, negative predictive value) HE4 compared to histopathology examination in diagnosing ovarian cancer (p = 1.00).

To determine diagnostic test of CA125 compared to histopathology in diagnosis of ovarian cancer, Chi-Square test analysis was conducted. The results of analysis is presented in Table 4.

Table above with a 2x2 cross table showed 60.0% sensitivity, 83.3% specificity, 75.0% positive predictive value, 71.4%, negative predictive value, 25.0%, false positive, 28.6%, false negative values, and 72.7% accuracy. McNemar test showed no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) of HE4 compared to histopathology examination in diagnosing ovarian cancer (p = 1.00).

DISCUSSION

Result of the research revealed p value > 0.05 of age and parity variable, suggesting no differences between the two groups.

Diagnostic test of HK6 toward histopathology in diagnosis of ovarian cancer revealed sensitivity, specificity, positive predictive value, negative predictive value, false positive value, negative value, and accuracy of 80%, 75%, 72.7%, 81.8%, 27.3%, 18.2%, and 77.3%, respectively. McNemar test showed p-value of diagnostic tests of hK6 toward histopathology examination in diagnosing ovarian cancer is p = 1.00. It shows that no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) of hK6 compared to histopathology examination in diagnosing ovarian cancer. This can be explained that, in ovarian cancer, the increment of hK5, hK6, hK8, hK10, hK11 and hK14 in serum make kallikrein become a potential biomarker. Several studies on the association of hK6 with ovarian cancer showed that among many types of cancer, only in ovarian cancer, hK6 levels in circulation showed remarkable increase.[6]

Diagnostic test of HE4 toward histopathology showed 70.0% sensitivity, 83.3% specificity, 77.8% positive predictive value, 76.9% negative predictive value, 22.2% false positive, 23.1% false negative values, and 77.3% accuracy. McNemar test showed no differences of accuracy (sensitivity, specificity, positive predictive value, negative predictive value) HE4 compared to histopathology examination in diagnosing ovarian cancer (p = 1.00). This result is supported by another research conducted Wang et al which examined HE4 level in the differential diagnosis of pelvic mass in the population of Chinese women. The

study demonstrated that the sensitivity and specificity of HE4 were 86.7% and 98.0%, respectively.[7]

Diagnostic test of CA125 toward histopathology showed 70.0% sensitivity, 83.3% specificity, 77.8% positive predictive value, 76.9% negative predictive value, 22.2% false positive, 23.1% false negative values, and 77.3% accuracy. McNemar test showed no differences of accuracy (sensitivity, specificity, positive predictive value, negative predictive value) CA125 compared to histopathology examination in diagnosing ovarian cancer ($p = 1.00$). In initial report, it is known that level of CA125 increased by about 80% in women with advanced ovarian cancer and only 1-2% in the normal population. While in stage I ovarian cancer, CA125 level increased less than 50%. Specificity of CA125 is also low in differentiating between benign and malignant cases. In a retrospective study of 9233 women, sensitivity 62% of CA125 was obtained.[8]

CONCLUSION

There were no accuracy differences (sensitivity, specificity, positive predictive value, negative predictive value) between hK6, CA125, HE4 compared to histopathology examination in diagnosing ovarian cancer. Each of hK6, CA125 and HE4 value can be used as an ovarian cancer biomarker.

REFFERENCES

1. Azis MF. Gynecological Cancer In Indonesia. J Gynecol Oncol, 2009; 20(1): 8-10.
2. Diamandis E, Scorilas A, Fracchioli S, Van Gramberen M, de Bruijn H, Henrik A, et al. Human Kallikrein 6 (hK6): A New Potential Serum Biomarker for Diagnosis and Prognosis of Ovarian Carcinoma. J Clin Oncol, 2003; 21: 1035-43.
3. Moore RG, McMeekin DS, Brown AK, Disilvestro P, Miller MC, Allard WJ, et al. A novel multiple bioassay utilizing HE4 and CA125 for the prediction of ovarian cancer in patients with a pelvic mass. Gynecol Oncol, 2009; 112: 40-6.
4. Montagnana M, Lippi G, Ruzzenente O, Bresciani V, Danese E, Scevarolli S, et al. The Utility of Human Epididymis Protein 4 (HE4) in Patients with a Pelvic Mass. J Clin Lab Analy, 2009; 23: 331-5.
5. Magklara A, Mellati A, Wasney GA, Little SP, Sotiropoulou G, Becker GW, et al. Characterization of the Enzymatic Activity of Human Kallikrein 6: Auto activation, Substrate Specificity, and Regulation by Inhibitors. Biochem Biophysical Research Communications, 2003; 307: 948-55.
6. Pampalakis G, Kurlender L, Diamandis EP, Sotiropoulou G. Cloning and Characterization of Novel Isoforms of The Human Kallikrein 6 gene. Biochemical and Biophysical Research Communication. Elsevier. 2004; 320: 54-61.
7. Wang S. The Application of HE4 in Diagnosis of Gynecological Pelvic Malignant Tumor. Clin Oncol Cancer Res. 2009; 6: 72-4.
8. Daniel N. and Urban, N. CA125 in ovarian cancer. Biomark Med, 2006; 1(4): 513-23.