

# Early detection of ovarian cancer through urinary CA 125.

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## ABSTRACT

Ovarian cancer is the most lethal among all gynecologic cancers, causing more deaths than any other cancer of the female reproductive system (Alzheimer's Association, 2009). It is the fifth leading cause of cancer deaths in females and account approximately 50% of all death from gynaecologic cancers. We proposed detection of urinary Ca-125 in a case of ovarian mass for early detection of ovarian cancer. Urine CA-125 and serum CA-125 were measured by commercially available standard ELISA kits method using kit for CA-125 levels (Calbiotech). **Histopathology**: Adnexal masses were excised and tissue obtained was fixed in 10% buffered formalin, embedded in paraffin. Sections were cut and stained with H & E for routine histopathological diagnosis and the grading in the cases of malignant lesion was done. We found that maximum serum as well as urinary CA-125 value was in a case of papillary serous adenocarcinoma (histologically High grade) with serum CA-125 957 U/ml and urinary CA 125 207.54 U/ml whereas the lowest levels were recorded in a case of mucinous cystadenoma with serum CA-125 9.5 U/ml and Urinary CA-125 2.36 U/ml.

We also found that there was a significant and definite correlation in serum and urinary CA-125 values. The serum CA-125 values were lower in the cases of benign tumors and higher in the cases of malignant tumors, similarly the urinary CA-125 values were lower in benign cases and higher in malignant cases.

## INTRODUCTION:

Ovarian cancer is the most lethal among all gynecologic cancers, causing more deaths than any other cancer of the female reproductive system (Alzheimer's Association, 2009)<sup>1</sup>. It is the fifth leading cause of cancer deaths in females and account approximately 50% of all death from gynaecologic cancers. (cai et al)<sup>2</sup>. Not all the ovarian growths are cancer and most of them cannot be diagnosed by histo & cytopathology. Despite several genetic and immunohistochemical markers, early detection of ovarian cancer, which is life threatening, is still lacking.

Till date, CA-125 is the serum marker that has received the most attention in identifying methods for early detection. It is the first serum tumor marker test for epithelial cancer of the ovary, was introduced by bast et al, in 1983.<sup>3</sup> CA-125 was originally developed to monitor patients previously diagnosed with ovarian cancer and not for screening. CA-125 levels are elevated in 80-90% of advanced-stage ovarian cancers.<sup>4</sup>

We proposed detection of urinary Ca-125 in a case of ovarian mass for early detection of ovarian cancer.

## REVIEW OF LITERATURE:

A female has approximately 1 in 72 lifetime risk (1.6%) of developing ovarian cancer, with the majority of affected women developing epithelial tumors.<sup>5</sup> Tumor markers differ in their usefulness for screening, diagnosis, prognosis, assessing therapeutic response and detecting recurrence. CA-125 is considered as gold standard tumor marker in ovarian cancer<sup>6</sup>. A cancer antigen 125 (CA-125) is a protein found on the surface of many ovarian cancer cells. It also can be found in other cancers like cancer of colon, breast, lung, endometriosis, uterine fibroids, pelvic inflammatory disease and in small amounts in normal tissue. Pathological diagnosis of ovarian cancer is difficult without laprotomy. In ovarian cancer CA-125 serum levels correlate with the state of the disease and can be used in the prediction of survival. (Cohen AD et al)<sup>7</sup>.

CA-125 is very useful method to discriminate between benign and malignant cases.<sup>8</sup> Most oncology societies recommend the use of CA-125 for differential diagnosis of a suspected pelvic mass, monitoring efficacy of treatment and detection of recurrence of ovarian cancer (Strugeon et al., 2008).<sup>9</sup> Tumor markers such as CA-125 in addition to diagnostic imaging are useful in preoperative evaluation of ovarian cancer. However detection of biomarkes in urine can provide a less and more convenient way of identifying ovarian cancer.

With this aim we had taken the evaluation of urinary CA-125 marker for early detection of ovarian cancer.

We could find only one reference of Tay SK et al<sup>10</sup> who studied the correlation of serum, urinary and salivary CA 125 levels in patients with adnexal masses. They found that both serum and urinary CA 125 levels were significantly higher in the ovarian cancer group. However there was no correlation in CA 125 concentrations between serum and urine.

## AIM:

**To detect Ca-125 in urine in a case of ovarian mass to diagnose malignancy.**

## OBJECTIVES & RESEARCH QUESTION:

**Research Question:** Can urinary Ca-125 detect ovarian cancer.

## Objectives:

1. To detect urinary Ca-125 in all patients of ovarian mass including benign and malignant.
2. To confirm ovarian cancer on histopathology.
3. To correlate histopathological grade and urinary CA-125 levels.

**METHODOLOGY:****MATERIAL AND METHODS:-**

Radiological : CT/Ultrasound abdomen was done for detecting ovarian mass.

Biochemical Assay : Urine CA-125 and serum CA-125 were measured by commercially available standard ELISA kits method using kit for CA-125 levels(Calbiotech).

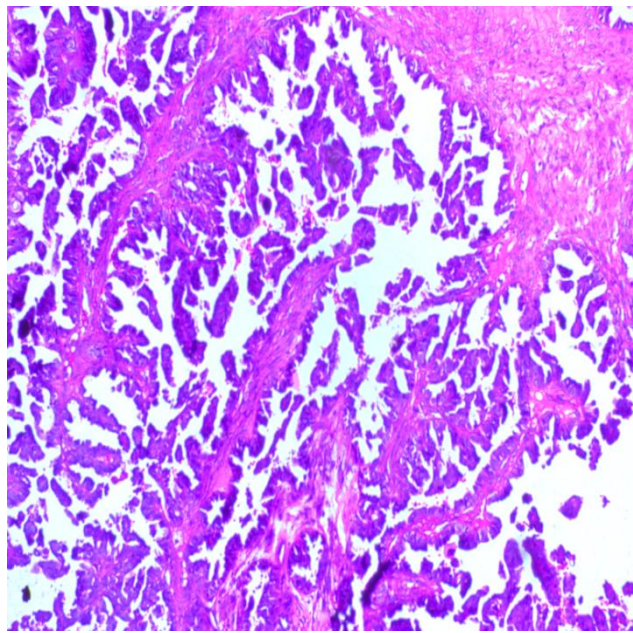
Histopathology :Adnexal masses were excised and tissue obtained was fixed in 10% buffered formalin, embedded in paraffin. Sections were cut and stained with H & E for routine histopathological diagnosis and the grading in the cases of malignant lesion was done.

**H&E Staining was done by following method**

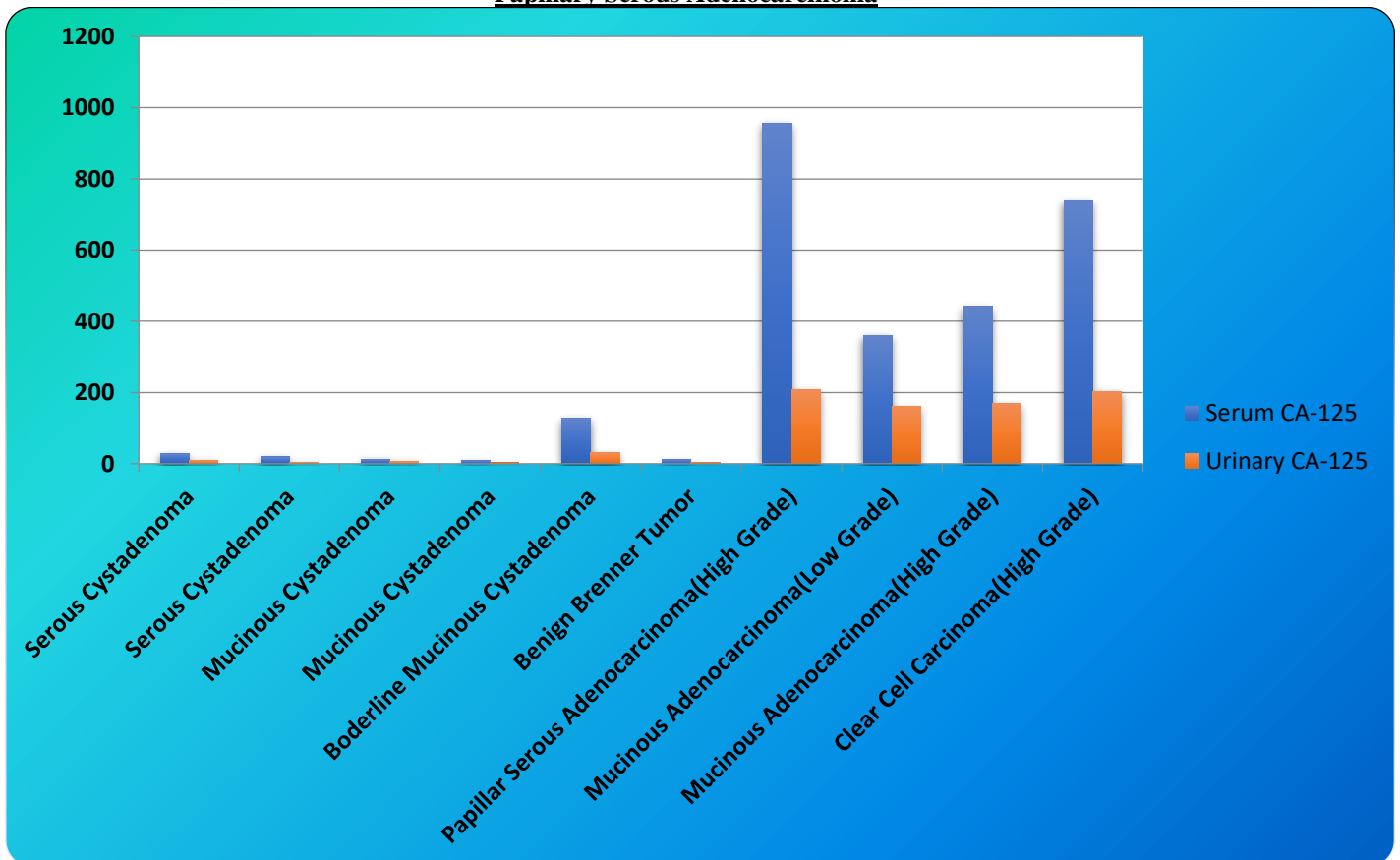
- Dewax sections, hydrate through alcohols to water.
- Remove fixation pigments if necessary.
- Stain in an alum hemotoxylin of choice for a suitable time.
- Wash well in running tap water until sections are again 'Blue' for 5 minutes or less.
- Differentiate in 1% acid alcohol 91% HCl in 70% alcohol for 5-10 seconds.
- Wash well in tap water until sections are again 'Blue' (5-10 minutes), or
- Blue by dipping in an alkaline solution(e.g. Ammonia water), followed by a 5 minutes tap water wash.
- Stain in 15 eosin Y for 10 minutes.
- Wash in running tap water for 1-5minutes.
- Dehydrate through alcohol, clear and mount.

**OBSERVATIONS AND RESULTS:-****OBSERVATIONS**

S.No.	Histopathological diagnosis	Serum CA 125	Urinary CA 125
1.	Serous cystadenoma	28	9.90
2.	Serous Cystadenoma	19.22	4.36
3.	Mucinous Cystadenoma	12.56	7.03
4.	Mucinous Cystadenoma	9.5	2.36
5.	Boderline Mucinous Cystadenoma	128	29.97
6.	Benign Brenner Tumor	11.86	3.14
7.	Papillary serous adenocarcinoma (High Grade)	957	207.54
8.	Mucinous Adenocarcinoma (Low Grade)	360	160.21
9.	Mucinous Adenocarcinoma (High Grade)	442	168.74
10.	Clear Cell Carcinoma (High Grade)	740	203.37



**Papillary Serous Adenocarcinoma**



**RESULTS:-**

In 4 months study we came across 18 cases with adnexal masses, however due to our inclusion and exclusion criteria we could include only 10 cases. The inclusion criteria included only those cases of Ovarian neoplasm who had not received any treatment till admission and were not complicated by any other malignancy while the exclusion criteria was:-

- (A) Metastasis in ovary from any other organ malignancy.
- (B) Any cases of ovarian mass with AIDS/ TB/ Leprosy.

In our selected 10 cases we were fortunate to obtain the biopsies of adnexal masses as well as the urinary and serum CA-125 values. Our study on the 10 cases comprised of 5 cases of benign tumors, 1 case of boderline tumor and 4 cases of malignant tumors. Out of the 5 benign tumors 2 cases were of serous cystadenoma, 2 cases were of mucinous cystadenoma and 1 case of Benign Brenner tumor.

The malignant tumors included 2 cases of Mucinous Adenocarcinoma, 1 case of Papillary Serous Adenocarcinoma and 1 case of Clear Cell Carcinoma. We also had a tumor of which the histological diagnosis of Boderline mucinous Cystadenoma was made.

The maximum serum as well as urinary CA-125 value was in a case of papillary serous adenocarcinoma (histologically High grade) with serum CA-125 957 U/ml and urinary CA 125 207.54 U/ml whereas the lowest levels were recorded in a case of mucinous cystadenoma with serum CA-125 9.5 U/ml and Urinary CA-125 2.36 U/ml.

We also found that there was a significant and definite correlation in serum and urinary CA-125 values. The serum CA-125 values were lower in the cases of benign tumors and higher in the cases of malignant tumors, similarly the urinary CA-125 values were lower in benign cases and higher in malignant cases.

#### **Discussion:-**

Until today the diagnostic as well as the prognostic marker for ovarian cancers is serum CA-125 levels and is considered as a gold standard tumor marker in ovarian cancer.<sup>5</sup>

However we proposed a study of detection of urinary CA-125 levels in the cases of ovarian mass for early detection of ovarian cancer.

With this aim we studied 10 cases of adnexal masses and detected urinary CA-125 levels, serum CA-125 levels of the patient and correlated it with the histopathological grade (in case of malignant tumors). We found that there was a significant and definite correlation in serum and urinary CA-125 values. Both serum and urinary CA-125 values were lower in the cases of benign tumors and higher in the cases of malignant tumors.

Tay SK et al<sup>10</sup> studied the correlation of serum, urinary and salivary CA 125 levels in patients with adnexal masses. They found that both serum and urinary CA 125 levels were significantly higher in the ovarian cancer group. However there was no correlation in CA 125 concentrations between serum and urine. Our study also states that the serum and urinary CA-125 levels are higher in malignant cases whereas in contrast to the study of Tay SK et al we found a significant correlation between urinary and serum CA-125. However we feel that a study with larger population of adnexal masses should be done to support our view.

#### **CONCLUSION:-**

##### **From our study we concluded that:-**

- Urinary CA-125 can be an important non-invasive diagnostic tool for early detection of ovarian cancer.
- Serum and urinary CA-125 levels are lower in benign ovarian tumors and there is a significant correlation between their levels.
- Serum and urinary CA-125 levels are higher in malignant ovarian tumors and there is a significant correlation between their levels.
- Urinary and Serum CA-125 levels are higher in histologically high grade malignant lesions.

#### **SUMMARY:-**

- Serum CA-125 is the Gold standard for the detection of ovarian neoplasms.
- We proposed the detection of Urinary CA-125 and its correlation with serum CA-125 levels as well as Histological grading of the ovarian cancers.
- The study comprised of a total of 10 cases out of which 5 were histologically confirmed benign, 4 were malignant and 1 Borderline benign tumor.
- On serum and urine analysis of CA-125 it was found that a malignant tumor (Papillary Serous Adenocarcinoma High Grade) had the highest serum and urinary reading of CA-125 (907 U/ml and 207.54 U/ml respectively) and a benign tumor (Mucinous cystadenoma) with the lowest serum and urinary CA-125 values (9.5 U/ml and 2.36 U/ml respectively).
- Thus it shows that urinary CA-125 levels show a definite correlation with serum CA-125 levels.
- Urinary CA-125 was also found to be higher in histologically high grade ovarian cancer and lower in low grade ovarian cancer, thus it parallels the increase in serum CA-125 levels.
- Urinary CA-125 can be an important non-invasive diagnostic tool for detection of early ovarian carcinoma.

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