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Evaluation of Serum Amylase as a Tumor Marker in Epithelial Ovarian Cancer

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ABSTRACT
Ovarian cancer poses a global mortality challenge due to early detection hurdles. This study, spanning April 2021 to April 2022, assesses serum amylase potential as an epithelial ovarian cancer marker. The study included fifty ovarian tumor patients in diverse departments provided informed consent. Preoperatively, 3 ml venous blood was collected, and serum amylase levels were analyzed within an hour. Histopathological subtypes categorize patients. The mean age of the participants was 40.8±11.4 years, and the mean duration of the disease was 2.4±1.2 months. Epithelial ovarian cancer was the most commonly diagnosed type (46.0%), followed by non-epithelial ovarian cancer (30.3%) and benign ovarian tumors (34.0%). High-grade serous cystadenocarcinoma (28.0%) was the most prevalent among the histopathological subtypes. Mean serum amylase levels were found to be significantly elevated in epithelial ovarian cancer compared to other groups ($p<0.05$). Serum amylase levels were 130.6±30.5 IU/L in the early stage and
155.3±29.2 IU/L in the advanced stage, although the difference was not statistically significant ($p>0.05$). Serum amylase demonstrated a sensitivity of 82.6%, specificity of 66.7%, the accuracy of 74.0%, and positive and negative predictive values of 67.9% and 81.8%, respectively. Receiver-operator characteristic (ROC) analysis yielded a cut-off value of ≥117.5 IU/L, with 82.6% sensitivity and 66.7% specificity for predicting epithelial ovarian cancer. High- grade serous cystadenocarcinoma, dermoid cyst, mucinous cystadenoma, dysgerminoma, low-grade serous, and yolk sac tumors were prevalent histological subtypes. Elevated serum amylase levels suggest its diagnostic potential in epithelial ovarian cancer.

Keywords: *Ovarian Cancer, Serum Amylase, Tumor Marker, Histopathology, Diagnostic Accuracy*

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I. Introduction

Ovarian cancer, comprising 35% of reproductive system malignancies in women, is the fifth leading cause of cancer- related deaths among them[1]. Late-stage diagnosis is common due to vague symptoms, resulting in a survival rate below 20% after five years[2]. Surgical removal of ovarian cancer tumors offers a high chance of survival[3]. In India and other developing countries, ovarian cancer accounts for 10-15% of all gynecological cancers, often diagnosed at advanced stages due to the lack of effective screening methods[4].

Current diagnostic methods, including pelvic exams, ultrasounds, and CA125 levels, are insufficient, particularly for early-stage detection when survival rates reach 90%[5]. New screening and detection methods are vital for improving patient outcomes. Ovarian neoplasms can originate from various ovarian tissues, and their malignant transformation is associated with biochemical changes[6]. Amylase, a non-conventional analyte, has shown potential as an ovarian cancer marker[7]. Studies have indicated elevated amylase levels in ovarian malignancies[8]. Some debate exists over which amylase gene encodes tumor-secreted amylase, but a unique ovarian cancer amylase isoenzyme has been suggested[9]. Previous research has characterized this isoenzyme and compared it with salivary and pancreatic amylases, highlighting its distinct properties[10].

This study aims to identify a novel diagnostic marker for epithelial ovarian cancer to enhance effective management and patient care. The source of tumor-secreted amylase in ovarian cancers remains debated, with some proposing AMY-2B as the encoding gene[11]. While others suggest salivary AMY-1A, -1B, or -1C[12]. Unique ovarian cancer amylase isoenzymes have been proposed[13]. Earlier research identified an acidic isoenzyme of amylase in human serous-type ovarian cancer[14], distinct from pancreatic and similar to salivary amylase. Characterization revealed differences in molecular mass, SDS-PAGE profile, specific activity, and sensitivity to alpha-amylase inhibitors. This study aims to identify a novel diagnostic marker for epithelial ovarian cancer[15]. Potentially improving patient management.

II. Objectives

General:

To evaluate the serum amylase as a tumor marker in epithelial ovarian cancers.

Specific:

- To estimate the level of pre-operative serum amylase in patients with ovarian neoplasm.
- To find out the level of serum amylase in histopathologically confirmed epithelial ovarian cancer, non- epithelial ovarian cancer, and benign ovarian tumor.
- To compare serum amylase levels in patients with confirmed epithelial ovarian cancer, non-epithelial ovarian cancer, and benign ovarian tumor.
- To determine the sensitivity, specificity, positive predictive values, negative predictive values, and accuracy of the serum amylase in detecting epithelial ovarian cancer.

III. Materials And Method

Study Design: This study followed a cross-sectional analytical design and was conducted from April 2021 to April 2022. The study was carried out at the Department of Gynecological Oncology, Department of Obstetrics & Gynaecology, Bangabandhu Sheikh Mujib Medical University (BSMMU), and NICRH, Dhaka. The participants included women diagnosed clinically with ovarian tumors who were admitted for surgical management at, Department of Obs & Gynae, BSMMU, and Department of Gynecological Oncology, NICRH.

Inclusion criteria

- Patients who were diagnosed clinically as a case of ovarian tumor and planned for surgery.

Exclusion criteria

- Women who received chemotherapy in ovarian neoplasm
- Pregnant women,
- Secondary neoplasm in the ovary,
- Women with any other known malignancy,
- Patients having salivary disease by history and clinical examination excluded
- Patient with a history of pancreatitis
- Patients with a history of respiratory disease.

Data Collection

A day before surgery, venous blood samples (5ml) were collected from eligible participants in an EDTA container, adhering to strict aseptic protocols. Following collection, samples were centrifuged at 3000 rpm for 10 minutes within an hour. Serum amylase estimation was performed at the Department of Biochemistry in BSMMU and NICRH on the same day as collection. The recorded serum amylase levels were utilized for analysis. Additionally, laparotomy and surgical procedures were conducted as necessary, with specimens sent for pathological examination.

Estimation of Serum Amylase

Amylase was determined by α amylase color test employing 2-chloro-4 nitro phenyl – α-D-malto trioxide (CNPG3) as substrate. This substrate reacts directly with α amylase and does not require the presence of ancillary enzymes. The release of 2-chloro-4 nitro phenol (CNP) from the substrate and the resulting absorbance increase at 410 nm is directly proportional to the α amylase activity in the sample. Chemical reaction scheme.

Data Analysis

The collected data, including serum amylase levels and histopathological findings, were thoroughly analyzed using SPSS version 23. Descriptive statistics such as means and standard deviations were calculated for

continuous variables. Categorical variables were summarized using frequencies and percentages. Comparative statistical tests assessed differences among various groups, such as t-tests and chi-square tests for categorical variables. Receiver- operator characteristic (ROC) analysis was conducted in SPSS to establish diagnostic cutoff values for serum amylase in identifying epithelial ovarian cancer. The significance level was set at $p<0.05$.

Ethical Considerations

This study rigorously adhered to ethical principles throughout its execution. Institutional Review Board (IRB) approval was obtained from BSMMU. Informed consent was obtained from all participants, who were thoroughly informed about the study's purpose, design, and their right to withdraw at any time. Privacy and confidentiality were strictly maintained, with only the researcher accessing collected data. The study complied with the Helsinki Declaration for Medical Research involving Human Subjects (1964), prioritizing the participants' well-being and ethical standards in research involving human subjects.

IV. RESULT

Table 1: Distribution of the study subjects by demographic characteristics (n=50)

Demographic Characteristics	Number of Patients	Percentage
Age (years)		
20-29	12	24.0
30-39	9	18.0
40-49	14	28.0
50-59	13	26.0
≥60	2	4.0
Mean±SD	40.8 ±11.4	
Range (min-max)	20.0 - 62.0	
Educational Status		
Illiterate	18	36.0
Primary	13	26.0
Secondary	18	36.0
Graduate	1	2.0
Marital Status		
Married	33	66.0
Unmarried	6	12.0
Divorced	6	12.0
Widow/Widower	5	10.0

Displays the distribution of study subjects by age, educational status, marital status, and relevant numerical data and percentages

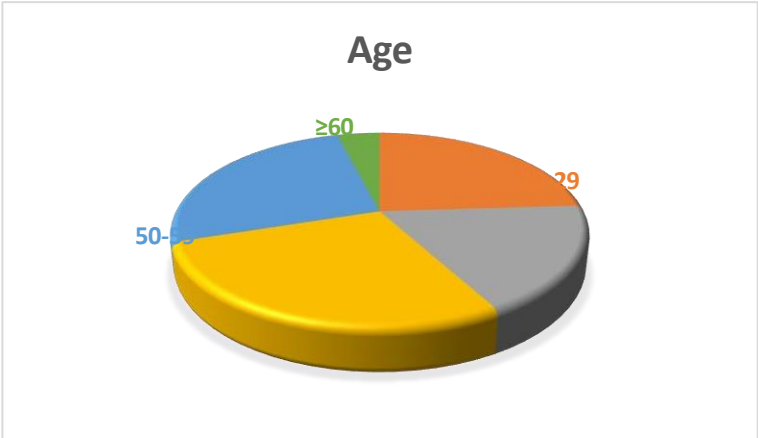

Figure 1: Age Distribution Overview

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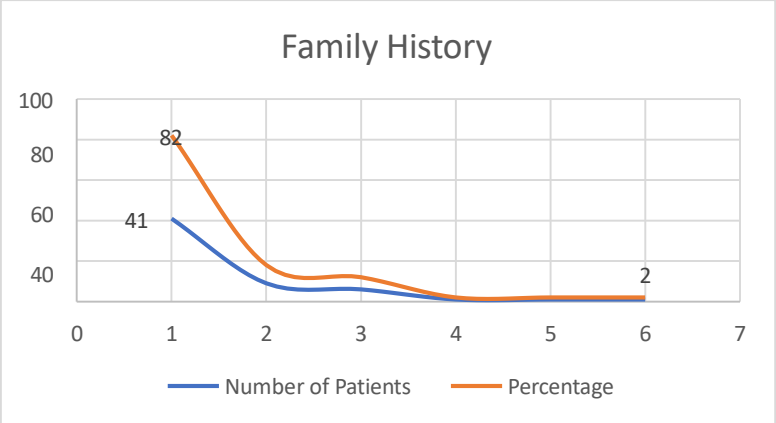

Figure 2: Family history of ovarian cancer among the study

Table 2: Distribution of the study subjects according to duration with histopathological disease with pathological type (n=50)

Duration of Disease (months)	**Number of Patients**	**Percentage**
≤3	42	84.0
>3	8	16.0
Mean±SD	2.4 ±1.2	
Range (min-max)	1.0 - 6.0	
Histopathological Diagnosis		
Malignant	33	66.0
Benign	17	34.0
Type of Histopathological		
Epithelial Ovarian Cancer	23	46.0
Non-Epithelial Ovarian Cancer	10	20.0
Benign Ovarian Tumor	17	34.0

These tables provide information on family history of ovarian cancer, the duration of the disease, histopathological diagnosis, and pathological type among the study subjects.

Table 3: Level of serum amylase in the study subjects (n=50)

Serum Amylase (IU/L)	**Number of Patients**	**Percentage**
25-115 (Normal)	22	44.0
≥116 (Elevated)	28	56.0
Mean±SD	111.3 ±43.6	
Range (min-max)	35.0 - 200.0	

Shows that 28(56.0%) patients had elevated serum amylase levels (≥116 IU/L). The mean serum amylase was found to be 111.3±43.6 IU/L, with a range from 35 to 200 IU/L.

Table 4: Association between pathological stage with serum amylase (n=33)

Histopathological Stage	**Number of Patients**	**Serum Amylase (IU/L)**	**P Value**
Early (I+II)	27	130.6±30.5	0.080 (ns)
Advance (III+IV)	6	155.3±29.2	

Table 4 shows that the mean serum amylase was found to be 130.6±30.5 IU/L in the early stage and 155.3±29.2 IU/L in the advanced stage. The difference between the two groups was not statistically significant (p>0.05).

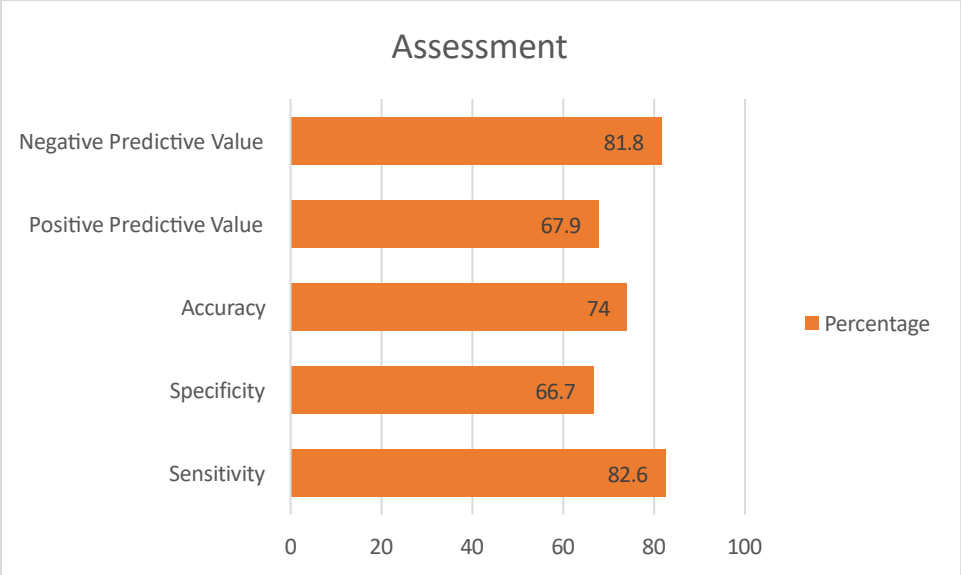

Figure 3: Serum Amylase Level's Predictive Performance in Ovarian Cancer Assessment

The sensitivity of serum amylase level vs histopathology diagnosis was 82.6%, specificity 66.7%, accuracy 74.0%, positive predictive value 67.9%, and negative predictive value 81.8%.

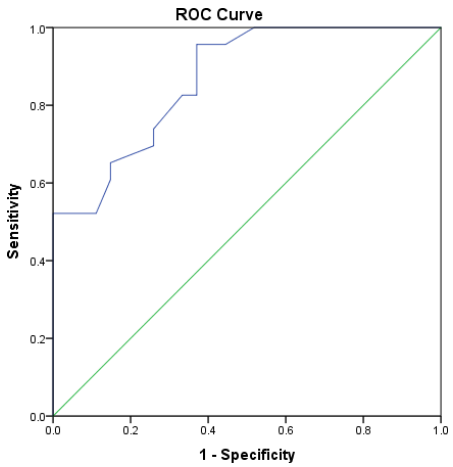

Figure 4: Receiver-operator characteristic curves of serum amylase level.

V. DISCUSSION

We analyze the findings from a cross-sectional analytical study involving 50 clinically diagnosed ovarian neoplasm patients admitted to various departments for surgical management. The study population had a mean age of 40.8±11.4 years, and a significant proportion belonged to the 40-49 age group. Similar age distributions have been reported in previous studies[16]. Education levels varied, with approximately 36% having completed secondary education. Around 66% of patients were married, and 76% came from middle-class families. These demographics align with the diverse socio-economic backgrounds typically observed in ovarian cancer patient populations.

Regarding BMI, 64% of patients had normal BMI (18.5-24.9 kg/m2), with a mean BMI of 22.8±2.9 kg/m2. This distribution is consistent with the variation in BMI observed in the general population[17]. Only 6% of patients were obese, suggesting that obesity may not be a prominent risk factor in this study group. Histopathological findings revealed that 46% of patients had epithelial ovarian tumors, 20% had non-epithelial ovarian tumors, and 34% had benign ovarian tumors. This distribution is in line with previous studies highlighting epithelial tumors as the majority of ovarian cancer cases[18]. High-grade serous cystadenocarcinoma was the most common histological subtype observed, consistent with its prevalence in ovarian cancer cases[19,20].

Regarding cancer staging, 66.7% of malignant ovarian tumor patients were in FIGO stage I, indicating early-stage diagnosis. This high percentage of early-stage diagnoses could be attributed to the study population

selected from a tertiary referral hospital, where patients may have more access to advanced medical care and early detection[21]. The key finding of this study was the significant elevation of serum amylase levels in epithelial ovarian cancer cases. Mean serum amylase levels were 141.2±32.9 IU/L in epithelial ovarian cancer, 121.0±23.1 IU/L in non-epithelial ovarian cancer, and 65.1±20.7 IU/L in benign ovarian tumors. These results are consistent with previous research indicating elevated serum amylase levels in malignant ovarian tumors[22].
The study also assessed the diagnostic potential of serum amylase levels in identifying epithelial ovarian cancer. The sensitivity of serum amylase level vs. histopathological diagnosis was 82.6%, with a specificity of 66.7%[23-25]. The accuracy was 74.0%, and the positive and negative predictive values were 67.9% and 81.8%, respectively[26]. These results suggest that serum amylase may be a useful diagnostic marker for epithelial ovarian cancer, particularly when combined with other diagnostic modalities.

Receiver-operator characteristic (ROC) analysis was performed, revealing an area under the curve (AUC) of 0.867 for serum amylase levels[27,28]. The ROC curve identified a cut-off value of ≥117.5 IU/L, providing a sensitivity of 82.6% and a specificity of 66.7% for predicting epithelial ovarian cancer[29]. These findings support the potential utility of serum amylase as a diagnostic marker for early detection of ovarian cancer. Comparisons with previous studies indicated variations in serum amylase cut-off values and diagnostic performance. A similar study identified a cut-off threshold of 46 U/L for salivary amylase level, yielding a sensitivity of 66.7% and a specificity of 76.7%[30]. These differences may stem from variations in study populations and methodologies.

This study demonstrated that elevated serum amylase levels were significantly associated with epithelial ovarian cancer. The sensitivity and negative predictive values of serum amylase support its potential as a diagnostic marker for early detection of epithelial ovarian cancer. Further research and validation studies are warranted to confirm these findings and establish serum amylase as a valuable tool in ovarian cancer diagnosis and prognosis.

VI. CONCLUSION

Mean serum amylase was higher in patients with epithelial ovarian cancer (141.2±32.9 IU/L) in comparison to non- epithelial ovarian cancer (121.0±23.1 IU/L) and benign ovarian neoplasm (65.1±20.7 IU/L). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 82.6%, 66.7%, 67.9%, 81.8%, and 74.0%, indicating that serum amylase can be used as a tumor marker in diagnosing epithelial ovarian cancer.

Limitations

- The study population was selected from two tertiary-level hospitals in Dhaka city, so the study's results may not reflect the exact picture of the country.
- The present study was a cross-sectional study conducted in a very short time.
- The small sample size was also a limitation of the present study. Therefore, in the future, further study may be undertaken with a large sample size.

Recommendation

- Serum amylase can be used as a tumor marker for screening in epithelial ovarian cancer.
- Further studies involving the integrated use of CA-125 and serum amylase as a diagnostic tool in ovarian cancer are required.
- Further study using salivary serum amylase can be performed, which can be used as a noninvasive method in the future.

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Conflict of interest: None declared

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