

## Association Between Peritoneal Carcinomatosis and Histopathologic Type of Cancer

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### ABSTRACT

**Objective:** To evaluate histopathological subtypes and to assess age and gender wise differences in histopathological subtypes among patients with peritoneal carcinomatosis presenting at tertiary care hospital of Karachi, Pakistan.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** Medical Oncology Department, Jinnah Postgraduate Medical Center, Karachi Pakistan, from Apr 2019 to Apr 2020.

**Methodology:** One forty patients of age less than 70 years of any gender with peritoneal carcinomatosis were enrolled. The data regarding socio-demographic factors was collected on pre-designed questionnaire. Patients were undergone for CT scan and results were used to identify cancer type, stage and histological subtype of tumor.

**Results:** Of 140 patients, the mean age was 44.94±11.62 years. About 78 patients had ovarian cancer (55.7%), 27 had colorectal cancer (19.3%) and 35 patients had gastric cancer (25%) respectively. Most of the patients had serous histology 36(26%) followed by adenocarcinoma 33(24%). There was statistically significant difference in histological subtypes with respect to gender ( $p=0.001$ ).

**Conclusion:** Serous histology is the most common histology among patients with peritoneal carcinomatosis and gender-wise the proportions of histological sub-types varies significantly.

**Keywords:** Carcinoma, Colorectal Cancer, Gastric Cancer, Histopathology, Metastasis, Ovarian Cancer, Peritoneal Carcinomatosis.

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### INTRODUCTION

Invasion of serous membrane lining the abdominal cavity, coeloma and viscera by malignant cells in amniotes is termed peritoneal carcinomatosis (PC) or peritoneal surface malignancy.<sup>1</sup> PC is a rare advanced stage malignancy in the human body.<sup>2,3</sup> The frequent tumors metastasize to peritoneum are usually from the ovaries and gastrointestinal tract.<sup>4</sup> This disorder is highly associated with progression of disease and worse prognosis with no more than palliative treatment options.<sup>1</sup> Overall age-adjusted incidence of primary PC (origin of cancer in the mesothelium of the abdomen) is 6.8 per 1,000,000 and survival rate varies from 11 to 17 months.<sup>2,5</sup> Whereas in secondary PC (the dissemination of tumor cells in the peritoneal cavity from other sites), the median survival is 5 to 10 months for early stage (0-II) and 2 to 3.9 months for advanced stage (III-IV). According to site of the primary PC survival rates also vary; 2.9 months for pancreatic origin, followed by 6.9 months for colorectal origin and 6.5 months for gastric

respectively.<sup>5</sup>

Serous carcinoma is the most prevalent histological form of primary PC, responsible for 10% of all cancers found in the pelvis.<sup>6</sup> Whereas mesothelioma malignancy is a rare histology but highly fatal malignancy.<sup>1</sup> Pleural mesothelioma (PM) consists of a frequent number of cases and is accompanied by peritoneal mesothelioma (PM). MPM typically occurs in 10%-15% of cases of mesothelioma and nearly 50% of cases of leiomyosarcomas occur in the retroperitoneum.<sup>1</sup> The histological types of PC are significantly associated with prognosis of disease. The histological subtype such as epithelioid MPM has the best prognosis with median survival time as 55 months whereas biphasic subtype has median survival time of 13 months. Additionally, sacromatid characteristics, invasion depth, completeness of cytorreduction (2-3) and inflammatory stroma are other predictors of worse prognosis.<sup>1,7</sup>

Early and accurate detection of hidden malignant tumors in peritoneum and histology is critical in order to minimize the overall fatality risk of PC patients. The goal of this research was therefore to evaluate

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histopathological type and to assess age and gender wise differences in histopathological subtypes among patients with peritoneal carcinomatosis presenting at tertiary care hospital of Karachi, Pakistan. This research would help to produce evidence that could be helpful to avoid unresectable tumor treatment and damage from unnecessary chemotherapy medications.

### METHODOLOGY

It was a cross-sectional study conducted at the department of Medical Oncology of Jinnah Postgraduate Medical Center (JPMC), Karachi Pakistan, from April 2019 to April 2020. This research was approved by JPMC ethical review committee under the ERC#: NO.F.2-81-IRB/2019-GENL/18149/JPMC. The sample size of 140 was calculated using Raosoft online sample size calculator by taking statistics of serous carcinoma as 10%,<sup>6</sup> absolute precision as 5% and level of significance as 5%.

**Inclusion Criteria:** All patients of age less than 70 years of any gender with PC were enrolled in the study using consecutive sampling method.

**Exclusion Criteria:** Patients with poor performance status and recurrent disease were excluded from the study.

Written informed consent was obtained from all the eligible participants. The data regarding socio-demographic factors was collected on pre-designed questionnaire. Patients were undergone for CT scan and results were used to identify cancer type, stage and histological subtype of tumor and peritoneal cancer index score was calculated.

SPSS version 25 was used to analyze data. Numeric variables like age, BMI and peritoneal cancer index score. Frequency and percentage were reported for gender, religion, educational status, socio-economic status, marital status, addiction, family history of cancer, types of cancer, histopathological type and other CT scan findings. Association between age and gender with histopathological subtypes was assessed using chi-square test. The *p*-value of  $\leq 0.05$  was considered as statistically significant.

### RESULTS

Of 140 patients, the mean age was  $44.94 \pm 11.62$  years (Range: 20-72 years). Most of the patients were females 93(66.4%), Urdu speaking 63(45%), married 115(82.1%), had monthly income 15,000-30,000 PKR 78(55.7%) and uneducated 71(50.7%) respectively.

Only 17(12.1%) patients had positive family history of cancer (Table-I).

**Table-I: Characteristics of Patients with Peritoneal Carcinomatosis**

Variables	Mean $\pm$ SD
Age (years)	44.94 $\pm$ 11.62
<b>Gender</b>	<b>n(%)</b>
Male	47(33.6)
Female	93(66.4)
<b>Ethnicity</b>	<b>n(%)</b>
Urdu	63(45)
Sindhi	40(28.6)
Punjabi	12(8.6)
Balochi	10(7.1)
Pashto	8(5.7)
Others	7(5)
<b>Marital status</b>	<b>n(%)</b>
Single	24(17.1)
Married	115(82.1)
Divorced	1(0.8)
<b>Monthly income</b>	<b>n(%)</b>
<15,000 PKR	54(38.6)
15,000-30,000 PKR	78(55.7)
>30,000 PKR	8(5.7)
<b>Education status</b>	<b>n(%)</b>
Uneducated	71(50.7)
Educated	69(49.3)
<b>Family history of cancer</b>	<b>n(%)</b>
Yes	17(12.1)
No	123(87.9)

Of 140 patients with PC, 78 patients had ovarian cancer (55.7%), 27 had colorectal cancer (19.3%) and 35 patients had gastric cancer (25%) respectively. Eighty one patients had stage III of cancer (57.9%) and 59 patients had stage IV of tumor (42.1%).

About 36 patients had serous histology (26%), 33 patients had adenocarcinoma (24%), 23 patients had endometrioid (16%), 21 patients had signet ring cells and mucinous (15%) and 6 patients had clear cell (4%) (Figure).

In patients of age <45 years, majority of the patients had adenocarcinoma (29%) followed by serous (27%), whereas in patients of age  $\geq 45$  years, serous was the most frequent histology (25%) followed by adenocarcinoma and endometrioid each (19.8%) respectively. There was statistically insignificant difference in histological subtypes with respect to age (*p*=0.641). Among males adenocarcinoma was the most common histology whereas, in females serous histology was the most frequent type. There was statistically significant difference in histological subtypes with respect to gender (*p*=0.001) (Table-II).

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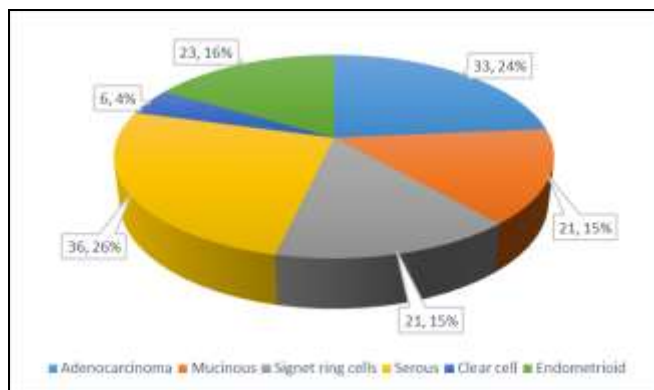


Figure: Histopathological Analysis (n=140)

peritoneum, as well as the embryological continuity of the development of ovarian epithelial cells with peritoneal mesothelial cells.<sup>12</sup> In the present study, 55.7% of the patients had ovarian cancer, 25% had gastric cancer and 19.3% had colorectal carcinoma. Literature also showed that 75% of patients with ovarian cancer, 17% with gastric cancer and 10% of the patients with colorectal carcinoma had peritoneal metastases at the time of first diagnosis.<sup>13-15</sup> Dirisamer *et al.*, found in their study that 19 patients had ovarian carcinoma with confirmed peritoneal lesions, 3 patients had colorectal carcinoma with confirmed peritoneal lesions and only 1 patients had gastric

Table-II: Association of Age and Gender with Histological Subtypes (n=140)

	Adenocarcinoma	Mucinous	Signet ring cells	Serous	Clear cell	Endometrioid	p-value
<b>Age groups</b>							
<45 years	17	7	9	16	3	7	0.641
	28.8%	11.9%	15.3%	27.1%	5.1%	11.9%	
≥ 45 years	16	14	12	20	3	16	
	19.8%	17.3%	14.8%	24.7%	3.7%	19.8%	
<b>Gender</b>							
Male	26	5	16	0	0	0	0.001*
	55.3%	10.6%	34.0%	0.0%	0.0%	0.0%	
Female	7	16	5	36	6	23	
	7.5%	17.2%	5.4%	38.7%	6.5%	24.7%	

## DISCUSSION

PCs are a very broad and generally metastatic group of malignancies diagnosed with loco-regional involvement at an advanced stage. PCs are typically lethal and incurable conditions, where curative resection is no longer a good choice.<sup>8</sup> However, in recent decades, modern resection technologies and advances in PC control have significantly altered the trajectory of the disease. Efficient approaches have advanced, allowing improvements in overall and disease free survival.<sup>9</sup>

In both female and male patients, PC is widespread, where malignant peritoneal tumor deposits may derive from the lungs, gastrointestinal tract, genital system, or breast. Because of the high incidence of general colorectal carcinomas, colorectal carcinomas contribute to a higher incidence of peritoneal involvement. Around 7% of patients diagnosed with synchronous PCs.<sup>10</sup> Gastric cancer appears to enter a late stage at first diagnosis, and 14% of those tumors may have peritoneal metastasis.<sup>11</sup> In 46% of cases, ovarian carcinoma also leads to peritoneal metastasis due to the anatomical location of the ovaries and their strong contact with the

carcinoma with confirmed peritoneal lesions.<sup>16</sup>

Mucinous, serous, clear cell, signet ring or endometrioid, which depend on the organ of origin, are the typical PC tumour histology.<sup>8,12</sup> However, the most common subtype of PC patients with serous carcinoma deposits accounts for 60% of all PC cases.<sup>17</sup> In this study, we have find serous (26%) as the most frequent histology, accompanied by adenocarcinoma (24%) and endometrial carcinoma (16%). Because most serous tumors originate from the fallopian tube or ovary, females with peritoneal lesions should be promptly given a gynecological diagnostic work-up.<sup>17</sup> In our study majority of the patients with PC were females (66.4%). In a study by Klos *et al.*, also found that females were more affected with PC than males (78% versus 22%). They also found almost similar proportion of PC in colorectal tumors.<sup>8</sup> In the present study we found males had higher proportion of adenocarcinoma than females ( $p=0.001$ ). A large study conducted at Ireland showed annual incidence of PC increased from 228 to 402 (1994-2012) and females were predominant and 70% of them were older than 59 years at the time of first presentation.<sup>18</sup>

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## CONCLUSION

Serous histology is the most common histology among patients with peritoneal carcinomatosis and gender-wise the proportions of histological sub-types varies significantly. It is important for the planning of treatment strategies.

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**Funding Source:** None.

## Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HP & GH: Data acquisition, data analysis, critical review, approval of the final version to be published.

KM & SZ: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

PK & MEK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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