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Comparison Between Body Mass Index and Side Effect Incidence in Bladder Cancer Patients Treated with Gemcitabine-Cisplatin at Dr. Saiful Anwar General Hospital Malang, Indonesia

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Abstract*--Gemcitabine-Cisplatin chemotherapy is one of bladder cancer treatment available in Dr. Saiful Anwar General Hospital Malang, although chemotherapy are beneficent, it also gave many unwanted side effect. Body Mass Index (BMI) said to have roles in cancer development and therapy outcome. This study aimed to compare BMI with side effect incidence in bladder cancer patients receiving six course of Gemcitabine-Cisplatin chemotherapy. Eighteen bladder cancer patients receiving Gemcitabine-Cisplatin chemotherapy by urology oncologist from 2016 to 2018 were recorded. The patients were followed during their six series of chemotherapy and any possible side effect were recorded. The data then analysed with chi square and T-test using SPSS programme. Body mass index (BMI) including normal weight, underweight, overweight and obese, account to 73.3%; 6.67%; 13.3%; and 6.67% respectively . Pathology finding consist of Transitional Cell Carcinoma high grade (46.7%) and low grade (53.3%). All 15 patients underwent six series of Gemcitabine-Cisplatin chemotherapy, side effects occurred during the whole series including, nausea(80%), fatigue(87%), vomiting(27%), alopecia(13.3%), infection(20%). Hematologic side effect including anemia, leucopenia, thrombocytopenia and nephrotoxicity Hematologic side effects such as: anemia, leucopenia and thrombocytopenia and also nephrotoxicity occurred in all 15 patients, minimally once of the six series of chemotherapy. When those side effect compared with BMI there were no statistical significant between the them with (p = 0.360), (p = 0.310), (p = 0.634), and (p = 0.423) respectively. Body Mass Index has no relation with side effect occurrence in bladder cancer patients receiving Gemcitabine-Cisplatin chemotherapy.*

Key words*--BMI, bladder cancer, Gemcitabine-Cisplatin, side effects*

I. INTRODUCTION

Bladder cancer is the fourth most common malignancy in men and eighth most common in women. In Indonesia bladder cancer ranked 13 out of all malignancy with 6978 Indonesian are diagnosed with bladder cancer over the past decade. In Dr. Saiful Anwar General Hospital Malang, there were approximately 287 inpatient was diagnosed with bladder cancer for the past 5 years. Gemcitabine-Cisplatin chemotherapy is the most common used regiment available at Dr. Saiful Anwar General Hospital Malang to treat bladder cancer, although chemotherapy is beneficent, it also gave many unwanted side effect including nausea, fatigue, vomiting, anaemia,

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leucopenia, thrombocytopenia due to bone marrow suppression and also nephrotoxicity. Body Mass Index (BMI) acclaimed to have associated with bladder cancer, high BMI and certain dietary factors have also been hypothesized to be associated with bladder cancer prognosis. Excess body fat is associated with increased circulating concentrations of insulin and insulin-like growth factor-1, as well as systemic inflammation, all of which may be related to worse bladder cancer outcomes [1,2]. The majority of chemotherapeutic agents can cause myelosuppression in a dose-dependent manner [3]. This study aimed to compare between Body Mass Index with side effect incidence in bladder cancer patients receiving six course of Gemcitabine-Cisplatin chemotherapy.

II. MATERIAL AND METHOD

Eligible bladder cancer patients including; patient with any BMI (WHO BMI classification: Underweight (<18.5 kg/m^2); Normal (18.5-24.9 kg/m^2); Overweight (25-29.9 kg/m^2); and Obese (≥30 kg/m^2)); fulfil six series of Gemcitabine-Cisplatin Chemotherapy by urology oncologist at Dr. Saiful Anwar General Hospital from 2016 to 2018; underwent TURB Staging were recorded in this study. There were total of 18 patients, but only 15 patients were able to make it until the end of the series. The patient underwent six course of Gemcitabine-Cisplatin chemotherapy, one course consist of day 1,2,8,15 where Gemcitabine are given on day 1,8 and 15, meanwhile Cisplatin are given on day 2. Chemotherapy dose are based on body surface area with Gemcitabine dose of 1000mg/m^2 , while cisplatin dose is 70mg/m^2 [4]. Whole Blood Count and Blood Urea Nitrogen/Serum Creatinine were measured before chemotherapy admission. The patients were followed during their six course of chemotherapy and any possible side effect were recorded. The data then analysed using chi square and T-test equation.

III. RESULTS

There were a total of 18 patient enrolled for this study, 2 patients passed away during follow up, while 1 patient had dropped out from chemotherapy programme. Fifteenth patient were eligible for the study, 10 of them were male, while the other 5 were female. With mean age of 66.6 years. Body mass index (BMI) including normal weight, underweight, overweight and obese, account to 73.3%; 6.67%; 13.3%; and 6.67% respectively. Pathology finding consist of Transitional Cell Carcinoma high grade (46.7%) and low grade (53.3%). All 15 patients underwent six series of Gemcitabine-Cisplatin chemotherapy, side effects occurred during the whole series including; nausea (80%), fatigue (87%), vomiting (27%), alopecia (13.3%), infection (20%).

Table1. Characteristic distribution of bladder cancer patients receiving Gemcitabine-Cisplatin chemotherapy

Characteristic Distribution	**N**	**%**
Age		
40-49	1	6.7
50-59	3	20
60-69	7	46.7
70-79	2	13.3
>80	2	13.3
Sex		

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Male	10	66.7
Female	5	33.3
Body Mass Index		
Normal	11	73.3
Underweight	1	6.67
Overweight	2	13.3
Obese	1	6.67
Tumor Pathology		
TCC High Grade	8	53.3
TCC Low Grade	7	46.7
Side Effect		
Nausea	12	80
Vomiting	4	26.7
Alopecia	2	13.3
Fatigue	13	86.7
Infection	3	20
Anemia	5	33.3
Thrombocytopenia	9	60
Low Absolute Neutrophil	8	53.3
Increased of Creatinine Serum	13	86.7

Hematologic side effects such as: leucopenia and thrombocytopenia, also nephrotoxicity side effect occurred in all 15 patients, minimally once of the six series of chemotherapy with ($p = 0.360$), ($p = 0.310$), ($p = 0.634$), and ($p = 0.423$) respectively when compared to BMI. There are no statistical significant between Body Mass Index and the presence of hematologic side effects and nephrotoxicity.

Table 2. Comparison between body mass index (BMI) with the occurrence of side effect

(significant = $p < 0.05$)

BMI vs Side Effect	**p-value**
Anemia	0.360
Leucopenia	0.310
Thrombocytopenia	0.634
Nephrotoxicity	0.423

Comparing occurrence of side effect before and after admission of Gemcitabine-Cisplatin chemotherapy, despite of BMI there were no statistically significant in anemia ($p = 0.082$). Statistic significant occurred in side effect including; leucopenia ($p = 0.01$); thrombocytopenia ($p = 0.01$); and nephrotoxicity ($p = 0.00$).

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Table 3. Side effect occurrence before and after Gemcitabine-Cisplatin chemotherapy

(significant = $p < 0.05$)

Side Effect Before and After Gemcitabine Cisplatin Chemotherapy	**p-value**
Anemia	0.082
Leucopenia	0.01
Thrombocytopenia	0.01
Nephrotoxicity	0.00

IV. DISCUSSION

The incidence of bladder cancer is increasing, an estimated 386,300 new cases and 150,200 deaths from bladder cancer occurred in 2008 worldwide. Bladder cancer occurred in the majority of cases in males with a male/female sex ratio of 3:1, with the average age of diagnosis is 65 years. Transitional cell carcinoma (TCC) is the most predominant histological type which represents more than 90% of the cases [5]. In this study male to female ratio was 2:1 this condition is mainly due to tobacco smoking as the greatest risk factor in bladder cancer, smoker had threefold higher risk of bladder cancer than non-smokers, male smoker are higher in number than female smoker. Therefore bladder cancer incidence occurred much higher in men than women [6]. Mean age in this study are also similar which is 66.6 years old.

Transitional cell carcinoma (TCC) is the only pathology finding existed (100%) in this study. High grade TCC account (53.3%) of pathologic finding in this study. More than 90% of bladder cancer instances represent urothelial carcinomas, which can be subdivided by grade, stage, and subtype. Such pathologic finding is due to bladder nature's consist of urothelial epithelium [7]. Over the past twenty years, there has been a dramatic increase in obesity rates in adults and children. Obesity has long been recognized as a strong risk factor for many co-morbid conditions such as the metabolic syndrome, diabetes, the obesity-hypoventilation syndrome, and cardiovascular diseases. A previous prospective study of over 400,000 women found that women in the heaviest cohort (BMI 40 kg/m2) had a cancer death rate that was 62% higher than that of women with normal weight.Overweight patients experienced fewer complications(1). According to study by Hourdequin, et al. The large majority of reported toxic effect and survival outcomes did not statistically differ between obese and normal-weight .

Previous analysis by Hunter et al. and recent consensus guidelines by Griggs et al. concluded that obese patients receiving full-dose chemotherapy do not experience more myelosuppression and other toxic effects than normal-weight patients. In this study BMI does not correlate with side effect occurrence ($p<0.05$), while side effect itself significantly occurred after six series of Gemcitabine-Cisplatin chemotherapy ($p<0.05$) except for anemia ($p>0.05$) Dosing of obese patients using BSA, the shortfalls of BSA-based dosing, which has been shown

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to have little correlation with pharmacokinetic (PK) measurements for most chemotherapeutic. Additionally, there is some evidence that doses adjusted for BSA do not produce the same plasma drug concentrations in normal and obese patients. Since as early as 1996, experts have been advising against dosing based on BSA and instead proposing alternate dosing schemes. Therapeutic drug monitoring using pharmacokinetics (PKs) continues to be examined as a more accurate, individualized way to determine dose .

V. CONCLUSION

Body Mass Index has no relation with side effect, occurring in bladder cancer patients receiving Gemcitabine-Cisplatin chemotherapy. Nevertheless, Gemcitabine-Cisplatin chemotherapy significantly produce hematologic side effect such as anemia, thrombocytopenia and leucopenia.

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