

## NEUTROPENIA ONSET, SEVERITY AND THEIR ASSOCIATION WITH DEMOGRAPHIC DATA

BASSAM ABDUL RASOOL HASSAN,\* ZURAIDAH BINTI MOHD YUSOFF, SAAD BIN OTHMAN

**Introduction:** Neutropenia is a decreased in the absolute neutrophil count lower than the normal that is  $< 1500$  cell/  $\mu\text{l}$ .**Objective:** The aim of this study is to find the association between neutropenia onset and severity with neutropenic patients demographic data.**Material and Methods:** This is an observational retrospective study conducted on solid cancer patients admitted to Penang Hospital in the period between 2003-2006 who were treated with chemotherapy and as a result became neutropenic. The main statistical test used were Chi-square test and Fisher's Exact test and the result was considered significant when  $P < 0.05$ .**Results:** The main result of this study was there was an insignificant association between onset and severity of neutropenia with patients demographic data.**Conclusion:** Demographic data is not a risk factor for neither neutropenia onset nor severity. The main reason for this insignificant association in this study is the small sample size.**Keywords :** Demographic data; Neutropenia; Gender; Ethnic group; Age; Association; Insignificant.

## INTRODUCTION

Clinically neutropenia is defined as a decreased in the absolute neutrophil count (ANC) below  $1500$  cell/  $\mu\text{l}$ . The term febrile neutropenia is used when the patient became feverish with body temperature  $38.5^{\circ}\text{C}$  and  $\text{ANC} = 500$  cell/  $\mu\text{l}$  or body temperature =  $38^{\circ}\text{C}$  for at least 2 hours with  $\text{ANC} = 500$  cell/  $\mu\text{l}$ .<sup>1,2</sup> Factors that play a major role in causing neutropenia are demographic factors, hematological disorder, autoimmune diseases, infection, drugs reactions and chemotherapy or radiotherapy.<sup>1-3</sup> Neutrophils production decrease in the elderly since they have a lower ability to produce mature neutrophils than younger people. Besides that the neutrophil count in white man is higher than that in the black man. Also neutropenia incidence seems to be more in women than men.<sup>1,2,4</sup>

## MATERIAL AND METHOD

This is an observational retrospective study conducted on solid cancer patients who were treated with chemotherapy and as a result of that they suffered from neutropenia. Those patients were admitted to Penang Hospital between 2003-2006. Data were collected from patients files by specific data sheet form designed for this study. The total number of the files reviewed was 4503 files. While the number of those patients who fulfilled the inclusion criteria for this study was 117 patients. The inclusion criteria were adult = 18 years old, male or female, solid cancer and treated with chemotherapy and as a result of that became neutropenic ( $\text{ANC} < 1500$  cell/  $\mu\text{l}$ ). The statistical tests used were Chi-square test and Fisher's Exact test. Significant was set at  $P < 0.05$  and the power of this study was more than 87.5%. Sampling method used for this study was

convenience sampling method.

## RESULTS

## Patient's Gender

Among this 117 patients, female patients seems to develop neutropenia (86; 73.5%) more than the male patients (31; 26.5%) as shown in **Table-1**.

However the association between both neutropenia onset and severity with gender were insignificant. The  $P$  values for Chi-square test for onset and severity were 0.284 and 0.438 respectively. While Fisher's Exact test  $P$  values for onset was 0.208 and for severity was 0.469 respectively too.

## Patient's Ethnic Group

Looking at the ethnic group, the Chinese (82; 70.1%) seemed to be mostly prone to neutropenia followed by the Malays (22; 18.8%) and lastly by the Indian ethnic group (13; 11.1%). These are shown in **Table-2**.

Chi-square value for ethnic group association with neutropenia onset and severity were  $P = 0.971$  and  $P = 0.214$  respectively. While Fisher's Exact test  $P$  values for association of ethnic group with neutropenia onset and severity were  $P = 0.587$  and  $0.214$  respectively. Both results showed an insignificant association since both  $P$  values  $> 0.05$ .

## Patient's Age

The patient's age distribution ranged from 18 to 93 years old. The mean age of the neutropenic patients was 51.33 years old and the median was 53 years as shown in **Table-3**. In this study, neutropenia occurred mostly in cancer

\*Corresponding author:

e-mail: bassamsunny@yahoo.com

patients above 40 years old (97) as compared to younger group. Most of the cancer patients with neutropenia were between 50-59 (46) years old, followed by those between 40-49 (27) years old, 60-69 (18) years old, 30-39 (12) years old, 20-29 (6) years old, = 70 (6) years old and lastly patients less than 20 (2) years old. The value for Chi-square test was  $P=0.468$  and Fisher test is  $P=0.311$  for association between neutropenia onset and patients age. While for association with severity the value for Chi-square test was  $P=0.185$  and is Fisher's Exact test  $P=0.193$ . Both results showed insignificant association since  $P$  values  $> 0.05$ .

**TABLE -1 Gender of neutropenic patients (N=117)**

Gender	Number	Percentage
Male	31	26.5
Female	86	73.5
<b>Total</b>	<b>117</b>	<b>100</b>

**TABLE -2 Ethnicity of neutropenic patients (N=117)**

Ethnic Group	Number	Percentage
Chinese	82	70.1
Malay	22	18.8
Indian	13	11.1
<b>Total</b>	<b>117</b>	<b>100</b>

**TABLE - 3 Age distribution of neutropenic patients admitted to penang hospital (N=117)**

Age Group (years)	Number of Patients	Percentage
? 18	2	1.7
20-29	6	5.1
30-39	12	10.3
40-49	27	23.1
50-59	46	39.3
60-69	18	15.4
?70	6	5.1
<b>Total</b>	<b>117</b>	<b>100</b>

## DISCUSSION

The possible reason for the higher number of female than male observed is that generally the incidence of cancer in female is higher the male by a ratio of 1:1.35. Also the Penang Cancer Registry (2003) reported that cancer occurrence in female is much more than male that is 3,745 (53.2%) of cancer cases were females and 3,294 (46.8%) were males 6. Lyman and Wilmot also reported that female gender is one of the risk factor that play a role in the development or occurrence of neutropenia and febrile neutropenia as observed in this present study 3. It has also been reported that 49% of the solid cancer patients who developed neutropenia at different levels of chemotherapy were those diagnosed with breast cancer. Since breast cancer occurs mostly in female so this could also explain the higher number of female seen with neutropenia 7. However, there was an insignificant association between gender and severity of neutropenia observed. This could be due to the small sample size which is insufficient to give a significant association 8. Among the races, Chinese seemed to develop neutropenia more than the Malay and the Indian. According to the National Cancer Registry of Malaysia the incidence of cancer is highest among the Chinese as compared to the Malay and Indian. Hence this could be one explanation for the Chinese being the major race observed in this study 5. Also it has been reported by Wolf that breast cancer is the solid cancer most highly associated with neutropenia and according to Kaur the breast cancer in Penang occur mostly among the Chinese (62.5%) followed by the Malays (26.7%) and the Indians (10.2%) 9,10. So this could also explain the results of this present study whereby the Chinese was the highest ethnic group experiencing neutropenia as compared to the Malays and finally the Indians. However there was no significant association obtained between the ethnic group and neutropenia onset as well as with severity this could be because of the insufficient sample size in this study 11. Munshi reported that patients between 50-59 years of age have the highest risk of occurrence of neutropenia than other age groups 12. The main reason for this could be that in this study majority of the patients suffered from breast cancer (Table-3) which had been reported to be more common in the elderly. According to the National Cancer Registry of Malaysia cancer especially breast cancer is more predominant at age of 50 years or more 5. Also Yip and Omar Hasan Kasule reported that neutropenia occurred mostly in the 50-59 years old patients and 75% of the neutropenic patients in their study were diagnosed with breast cancer. Another reason for the high occurrence

of neutropenia at this advanced age of 50 years old or more is that at this age there is already a lowered ability for the production of mature neutrophil cells<sup>13</sup>. In addition the presence of myelosuppressive chemotherapy given to older cancer patients will further increase the occurrence of neutropenia as compared to the younger ages<sup>2,3,14</sup>. In this present study, the incidence of neutropenia was high among the 50-59 years old but then decreased among those more than 60 years old age. According to the American Society of Clinical Oncology (ASCO) at these advanced ages the chemotherapeutics doses will usually be reduced and the administration of granulocyte-colony stimulation factor (G-CSF, Filgrastim) will also be increased. So these two reasons could explain the reduced neutropenia incidence in these advanced ages of more than 60 years old<sup>3</sup>. The second highest age group of patient with neutropenia was 40-49 years old. The National Cancer Registry of Malaysia reported that nasopharyngeal and rectum cancers are considered as common cancers types in Malaysia which mostly occur at this age range, as was observed in this study<sup>5</sup>. However, there was no significant association relationship observed between the patient's age and onset and severity of neutropenia. The most possible reason for this insignificant association was again due to the small sample size available<sup>8</sup>. However, Dale reporting that there was an association between patients ages with neutropenia. The reason given for neutropenia to be highly presented in the old age patients suggested there was a decreased or the inability of their body to produce mature neutrophil cells<sup>1</sup>. Other studies suggested that demographic data (i.e., age, ethnic group and gender) have an effect on neutrophil count and therefore there is a relationship between these variables with the neutropenia<sup>2</sup>. However this was not seen in this present study.

#### **AKNOWLEDGMENTS**

We like to thank all the medical staff of Penang hospital for their efforts to help us in conducting this study especially for Dr. Fong Chin Heng and nursing staff in ward C19, oncology clinic and the record office of the hospital.

#### **REFERENCES**

1. Dale DC. Neutropenia. In: Herman NW, editor. *Encyclopedia of Life Sciences*. Chichester: John Wiley & Son's, Ltd.; 2005. p. 147-163.
2. Frey R, Granger J. Neutropenia. In: Thackery E, editor. *The Gale Encyclopedia of Cancer*. Detroit: Gale Group; 2002. p. 770-773.
3. Lyman GH, Wilmot JP. Risks and consequences of chemotherapy-induced neutropenia. *Clinical Cornerstone* 2006; 8: 12-18.
4. Linker CA. Blood. In: Tiernery LM, Mcphee SJ, Ppadakis MA. Editors. *Current Medical Diagnosis and Treatment*. New York: Appleton & Lange; 2000. p. 499-551.
5. National Cancer Registry of Malaysia. Second Report of the National Cancer Registry Cancer Incidence in Malaysia 2003. In: Ministry of Health Malaysia. *National Cancer Registry*; 2003. p. 1-141.
6. Penang Cancer Registry. Speech by Yb DATO' Chua Jui Meng, minister of health Malaysia, at the launch of the first 5-year report of the Penang cancer registry, 15 December 2003 at 12.00 Noon, Ministry of Health Malaysia. Penang: Penang Cancer Registry; 2003. p. 1-6.
7. Wolff D, Culakova E, Poniewierski MS, Lyman GH, Dale DC, Crawford J. Predictors of chemotherapy-induced neutropenia and Its complications: results from a prospective nationwide registry. *Journal of Supportive Oncology* 2005; 3: 24-25.
8. Frakkinga FNJ, Van De Weteringa MD, Brouwerb N, Dolmana KM, Geisslerb J, Lemkesa B, Carona HN, Kuijpersa TW. The role of mannose-binding lectin (MBL) in paediatric oncology patients with febrile neutropenia. *European Journal of Cancer* 2006; 42: 909 -916.
9. Wolff D, Crawford J, Dale CD, Poniewierski MS, Lyman GH. Risk of neutropenic complications based on a prospective nationwide registry of cancer patients initiating systemic chemotherapy. *Journal of Support Oncology* 2005; 3: 56-57.
10. Kaur G, Rosli Ismail, Lee Suk Kam, Sabaratnam S, Noorani Ahmad. Assessment of correlation between clinico pathological features and lymph node metastases in breast cancer. *The Internet Journal of Pathology* 2007; 5: 1528-8307.
11. Crawford J, Wolff D, Culakova E, Poniewierski MS, Selby C, Dale D, Lyman GH. First-cycle risk of severe and febrile neutropenia in cancer patients receiving systemic chemotherapy: results from a prospective nationwide study. *Supportive Oncology* 2005; 3: 52-53.
12. Munshi HG. Severe neutropenia: a diagnostic approach. *Western journal of medicine* 2000; 172: 248-252.
13. Yip C, Omar Hasan Kasule. Epidemiology of breast cancer in Malaysia. *International medical journal* 2005; 4: 1.
14. Dale DC. Neutropenia and the problem of fever and infection in patients with cancer. In: Morstyn G, Lieschke GJ, editors. *Hematopoietic growth factors in oncology*. New Jersey: Human Press; 2004. p. 219-233.