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## The trend of hemoglobin levels in nasopharyngeal cancer patients treated with chemotherapy in low human development index region in Indonesia

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# The trend of hemoglobin levels in nasopharyngeal cancer patients treated with chemotherapy in low human development index region in Indonesia

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**Abstract.** Nasopharyngeal cancer (NPC) is a malignant tumor in the epithelial cell of the nasopharynx. Globally, the incidence was around 80,000 new cases annually or it composed 0.7% of cancer cases in the world. In locally advanced cases, chemotherapy and radiotherapy is a treatment of choice for this cancer. Chemotherapy could be given before the radiotherapy, or simultaneous, or after the radiotherapy. Chemotherapy can affect the hemoglobin levels by inducing a suppressive effect on bone marrow and a toxic effect on erythrocytes. Thus, this study aimed to explore the trend of hemoglobin levels in every cycle of chemotherapy in patients with NPC. This study is a retrospective study with secondary data collection of patients with NPC who received chemotherapy at the West Nusa Tenggara, one of the regions with low human development index (HDI) in Indonesia, during the period 2017-2019. The data obtained were analyzed descriptively and repeated measurement ANOVA test to explore the difference of hemoglobin levels during every cycle of chemotherapy. The results showed a trend of decreasing mean hemoglobin levels in six series of chemotherapy, with p-value = 0.06 on repeated measurement test. There was a trend of decreasing mean haemoglobin levels in patients with nasopharyngeal cancer who received chemotherapy in low HDI region in Indonesia.

**Keyword:** haemoglobin level, nasopharyngeal cancer, chemotherapy, trend

## 1. Introduction

Nasopharyngeal cancer is a malignant tumor that attacks the epithelial cells in the nasopharynx [1]. This cancer has a strong association with Epstein-Barr virus infection, as well as a strong tendency to metastasize to regional and distant lymphatic organs, as well as chemo-radio-sensitive [2]. The incidence is rare globally, with around 80,000 new cases per year or 0.7% of all cancer cases in the world. The incidence is only about 1 case per 100,000 globally; however, this cancer is endemic in Asia, especially in Southeast Asia, where the incidence was more than 30 cases per 100,000 population [3]. There were around 6.2 cases per 100,000 population in Indonesia, with the number of new cases as many as 12,000 cases [4]. However, this figure was still below the actual figure because many Indonesia cases are not properly registered.

This cancer causes inflammation of the oral mucosa and mucus membranes of the digestive system, pain, and reduced of saliva secretion, psychological stress, and dental abnormalities. Decreased of nutritional intake due to difficulty on oral intake, persistent bleeding, and persistent chemotherapy may lead to anemia [5,6]. Anemia is a frequent complication of malignancy and exacerbated by



chemotherapy. Up to 90% of cancer patients experience anemia during the disease [7]. However, the frequency varies according to the type and stage of the tumor and its treatment.

Treatment of NPC depends on the severity of cancer itself, but in general, the management of nasopharyngeal cancer includes surgery, radiotherapy, and chemotherapy [8]. In locally advanced (stage 3 and 4), the management is mainly radiotherapy and chemotherapy. Chemotherapy is carried out to control the malignant cells. However, chemotherapy have several side effect due to its potency on destruction of normal cells with fast regenerating cycles, such as skin cells, hair cells, and hematology cells [9].

Chemotherapy reduces hemoglobin levels through a suppressive effect on bone marrow and a toxic effect on erythrocytes. The incidence of anemia has been directly correlated with the chemotherapy. On the other hand, anemia has the adverse effects on the patient functional capacity, quality of life, prognosis, and cancer survival [10]. Pre-clinical studies showed that anemia is associated with the resistance to antineoplastic therapy, partly due to anemia's hypoxic effect. Anemia also correlated with ionizing radiation and some types of chemotherapy agents. Both depend on tissue oxygenation adequacy for their ability to destroy cancer cells. This study aims to determine the trend of red blood cell damage by assessing patients' hemoglobin levels after chemotherapy.

## 2. Materials and Methods

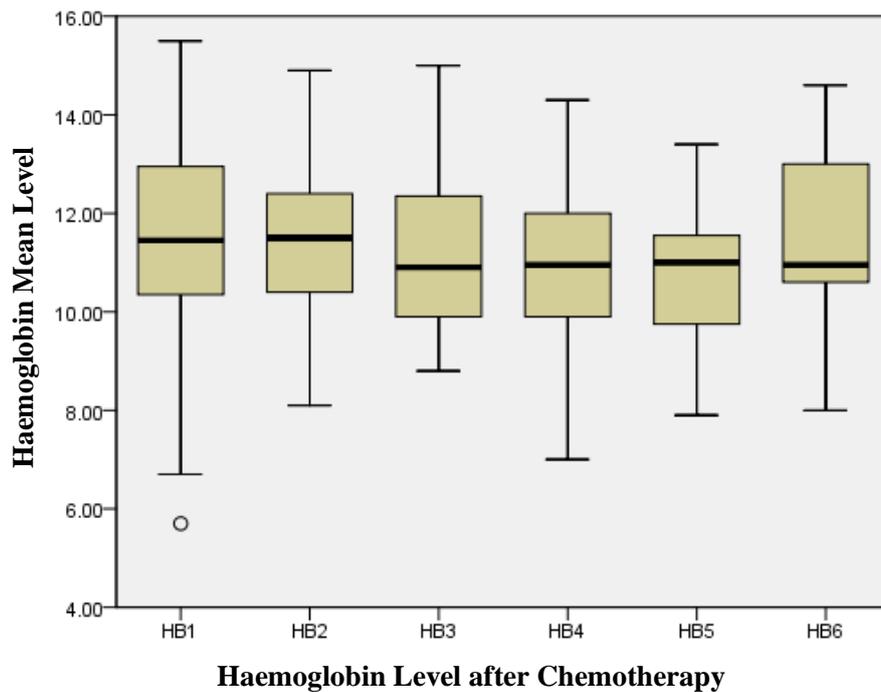
This study is a retrospective study using a secondary data which was taken from medical records at West Nusa Tenggara General Hospital. The data collection using total sampling from patients who was diagnosed as NPC and chemotherapy was given. The data will be collected on the period 2017-2019. The stage was defined according AJCC 2018. The hemoglobin level was measure using the routine hematology analyzer and available on the medical record. The hemoglobin level was documented from the initial NPC diagnosis and followed until the last chemotherapy series. The data obtained then analyzed with SPSS software to explore the trends of the mean hemoglobin levels in patients with NPC who received chemotherapy. The differences mean of hemoglobin levels in each cycle of chemotherapy was analyzed by repeated measurement Anova test.

## 3. Results and Discussion

During the study period, there were 94 patients with NPC, however, only 92 subject who has a complete routine hematology laboratory test. The patients mainly male with the male and female ratio 3:1. Particularly the stage NPC on this research is stage 3 followed by stage IVA, the detailed data can be seen in table 1.

**Table 1.** Patient characteristics.

Characteristic		N (%)
Gender	Male	65 (69,1)
	Female	29 (30,9)
	Total	94 (100)
Stage	II	12 (12,8)
	III	34 (36,2)
	IVA	26 (27,7)
	IVB	17 (18,1)
	IVC	5 (5,3)
	Total	94 (100)



**Figure 1.** The average of hemoglobin level on chemotherapy series.

Figure 1 shows that the average haemoglobin level has decreased from the first chemotherapy to fifth chemotherapy, and increases again at the 6th chemotherapy. The number of patients who continued the chemotherapy therapy until the 6th chemotherapy was 18 subject from the initial 92 subject. During chemotherapy, two patients did not continue the chemotherapy due to died or experienced a decrease in hemoglobin levels and lead to transfusion or patients dropped out.

In this study, the figure of the average haemoglobin level showed a trend decreased by the number of chemotherapy cycles. To determine the difference in hemoglobin levels in each chemotherapy series, a further test analysis was performed using *repeated measurement anova* test and found  $p = 0.06$ . There was no significant difference but showed a trend of decreasing hemoglobin levels in each chemotherapy treatment.

The characteristics of NPC patients in this study was like another previous research. The incidence of nasopharyngeal cancer globally is 1.2 per 100,000 (in men, 1.7 per 100,000; in women, 0.7 per 100,000) [11] where cases in men are more than in women's cases. In the European region, there are generally less than two cases per 100,000 in 1 year among men and less than one case per 100,000 among women. In contrast, in China, Southeast Asia, and the Arctic region and among immigrants from these regions, the incidence was 30 cases per 100,000 in men and 10 cases per 100,000 in female subjects [12]. Indonesia has around 6.2 cases per 100,000 population, with the number of new cases as many as 12,000 cases [4]. The incidence of nasopharyngeal cancer is 2-3 times greater in men; this may be due to differences in lifestyle between men and women (for example, alcohol consumption and smoking habits) [13]

According to the stage, the result of this study was comparable with the other research worldwide. (Wang and Lu, 2017) was found the incidence of stage I-II was 35 (26.9%) patients and stage III-IV 75 (57.7%) patients. On the other study found that according to 650 participants there were subsequently 4 (0.6%), 59 (9.1%), 429 (66.0%), and 158 (24, 3%) patients at stage I, II, III, and IV A and B [15].

The interesting finding in this study was the mean haemoglobin levels decreased from the first chemotherapy to the fifth chemotherapy, but the average increased at the sixth chemotherapy. Guo et

al., found in their study, the mean baseline haemoglobin levels were 14.1 g / dl, (from 7.5 g / dl to 18.1 g / dl). About 64 (9.8%) patients had anemia before chemotherapy out of 650 patients. The mean haemoglobin level during chemotherapy was 12.9 g / dl, ranging from 7.4 g / dl to 15.9 g / dl, and the mean haemoglobin level after chemotherapy was 12.0 g / dl, with a range of 5, 8 g / dl to 12.2 g / dl [15]. In this study, the mean baseline haemoglobin level was 11.51 g / dl (from 5.70 g / dl to 15.50 g / dl). After receiving chemotherapy on the 5<sup>th</sup> cycle, the mean haemoglobin level was decreased to 10.71 g / dl (from 7.60 g / dl to 13.40 g / dl). This mechanism could be due to chemotherapy's effect on hematologic cells. The compression of the bone marrow by chemotherapy agents will affect the hematopoiesis, including the erythropoiesis process. Monitoring the routine haemoglobin levels is a mandatory to be done before delivering the chemotherapy agents.

The aim of chemotherapy is to destroy the malignant cells. However, chemotherapy have side effects and can also destroy the cells with fast regenerating cycles, including hematological cells [9]. Hematologic cells consist of erythrocyte, leukocyte, and platelet cells. These cells easily regenerate and proliferate in the process of hematopoiesis. Chemotherapy agents can suppress the process of hematopoiesis, furthermore, the blood cell production will be decrease. The standard requirement of chemotherapy should be the haemoglobin level more than 8 g / dl to avoid tissue hypoxia, in the meantime, the body will lose many erythrocytes during chemotherapy. If the haemoglobin level was less than 8 g / dl, a transfusion will be performed first [16]. In the analysis of the difference in haemoglobin levels statistically using repeated measurement tests, the results were not significant ( $p = 0.06$ ). This was possible because some patients received blood transfusions which increased their haemoglobin levels prior to chemotherapy. As a result, the mean haemoglobin levels in the sixth chemotherapy cycles found 11.57 gr/dl. The limitation of this study was that it did not analyze the nutritional intake and history of blood transfusions.

West Nusa Tenggara General Hospital is lies in the one of region with low HDI in Indonesia. According national statistics bureau 2019, West Nusa Tenggara Province stand on 29<sup>th</sup> from 34 province in Indonesia [17]. One of the indicators in establishing the HDI is health status. Thus, this condition may contribute to the anemia incidence in population and may altered the trend of hemoglobin level in NPC patients. However, an advanced research should be delivered to explored this issue.

#### 4. Conclusion

This study shows a trend of decreasing haemoglobin levels in nasopharyngeal cancer patients receiving chemotherapy in low HDI region in Indonesia although it's not significant. The further research should be done to explore this phenomenon.

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**Preface: Proceedings of the 3<sup>rd</sup> International conference on bioscience and biotechnology (3<sup>rd</sup> ICBB 2020), 12<sup>th</sup> – 14<sup>th</sup> October 2020****Prof. Ir. H. Sunarpi, PhD***Chairman of ICBB2020 Organizing Committee*

This issue of IOP conference proceedings contains papers presented at the 3rd International Conference on Bioscience, Biotechnology and Biometrics (ICBB) 2020 conducted on 12<sup>th</sup> and 14<sup>th</sup> October 2020. It covers a broad range of research in the field of agriculture, bioscience, health and food science which relates to environmental sustainability. The COVID-19 pandemic situation made the organizers conduct the conference through online. The conference was hosted by Lab of Bioscience and Biotechnology, University of Mataram, Indonesia.

Interactive online presentations were arranged through Zoom Video Communications for the participants to present their ideas. The conference was divided into two main sessions: Main session for Keynote speakers and Panel Sessions for participants. A time of 30 minutes was given for Keynote speakers to present their fabulous work. For panel session, 10 minutes were given for participants to share their research and findings. A total of 102 participants from Universities, Research Institutes and also Government Departments joined the conference. All the selected papers were peer reviewed by expert reviewers in a single blind review system as per the review policy given by IOP Conference Series.

On the first day of the conference (12<sup>th</sup> October) invited talks were presented by Prof Lim Phaik Eem from Malaya University on "*Assessing the genetic diversity of Eucheumatoids in Indonesia: Exploration and Conversation for a sustainable seaweed cultivation industry*" and Prof Julian Heyes from Massey University New Zealand on "*The food safety risks associated with fresh products: perception vs reality*". The second day of the conference presented talks by Prof Akihiro Hazama from Fukushima Medical University Japan on "*Electrophysiological technique for the evaluation of mammalian oocytes used for the artificial fertilization*", Prof Jong-Min Lee from Nanyang Technological University Singapore on "*Recovery of feedstock chemicals and fuels from contaminated electronic and electrical waste plastics*" and Eka Sunarwidhi Prasedya, PhD from University of Mataram on "*Elaborating macroalgae potentials to combat COVID-19*". The final day of the conference included talks by Prof Deo Florence Onda from University of Philippines on "*Plastisphere: Understanding the implications of microbial colonization of plastics in the marine environment*" and Prof Ir H Sunarpi PhD from University of Mataram Indonesia on "*Diversity and Potency of Indonesian seaweed as source of hydrocolloid, UV-protector, and biofertilizer*".

Our special gratitude also goes to the Rector of Mataram University for the support given to this conference. Also, we are thankful for the enormous support of IOP conference proceedings for supporting us in every step.

*Editor-in-Chief, ICBB2020***Eka Sunarwidhi Prasedya, Ph.D.***Associate Editors, ICBB2020***Prof. Ir. Sri Widyastuti, M.App.Sc., Ph.D.****apt. Anggit L. Sunarwidhi, MSc, Ph.D.**

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