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# Adult Hodgkin's Lymphoma in Indonesian National Cancer Center Hospital: An Observational Study

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ABSTRACT

**Background:** Hodgkin's lymphoma (HL) is a malignancy of lymphatic glands whose incidence is higher in Asia than in other continents and it is highly curable amongst other hematological malignancies. Our study aims to establish distribution data among HL patients in the Indonesian National Cancer Hospital.

**Method:** A cohort retrospective was conducted from 2017 to 2021 on HL patients. Data on demographic and clinical characteristics were collected and described.

**Result:** From 177 HL subjects, 52.5% were men with a median age of 32 years. B-symptoms occurred in 30.1% of subjects. Most subjects have great performance status (44%) and normal body mass index (39.6%). Comorbidities found were diabetes mellitus (10.3%) and hypertension (8.1%). By hematological examination, lactate dehydrogenase (LDH) level was found 85.7% more than 240 U/dL, hemoglobin (Hb) level 71.6% non-anemic, leukocytosis in 33.5%, and thrombocytosis in 59.4%. The disease stage is mostly in stage 2 (51%), with 19.2% having extra nodal lesions which are commonly found in bone marrow (32.2%). The outcome showed that 69.2% of subjects survived.

**Conclusion:** In general, the majority of subjects were young adult males, with no B-symptoms, great performance status, no comorbidity, elevated LDH levels, normal Hb and white blood cell counts, high platelet counts, and were diagnosed with stage 2 disease. Most patients with Hodgkin's Lymphoma survived for 5 years.

## INTRODUCTION

Hodgkin's lymphoma (HL) is a malignancy of lymphatic glands that was found in 83,000 people globally in 2020 with prevalence stands 26th position among other malignancies [1]. It is less frequent when compared to other cancers, yet incidence in Asians has a 2% higher rate than in other continents. In Indonesia, HL occupies 28th place among the other malignancy incidents [2,3].

The 5-year survival rate for HL at stage I and IIa is 90% while at stage IV with extranodal involvement decreased to 60%. There is international prognostic scoring (IPS) of HL that determines factors affecting survival including gender, age, hemoglobin, white blood cell count, serum albumin, and lymphocyte count [2]. Other factors suggesting a negative prognostic factor are lactate dehydrogenase (LDH), performance status, and extranodal involvement [3]. Hodgkin's lymphoma incidence has a bimodal age distribution in the age group 20 to 24 and 75 to 79 years which could differentiate the clinical features of each group [1,4,5]. In recent years, the incidence at young ages has risen. Age is the most significant factor in terms of survival because it is linked to the biological characteristics of the lymphoma, prevalence of comorbid conditions, and adherence to therapy [6]. LDH is used to elevate due to malignancies and is indicative of a poor outcome [6,7]. This knowledge was crucial and served as the foundation for future HL research and development. Hence, our study aims to establish distribution data among HL patients in Indonesia.

## METHODS

### Design and participation of the study

This descriptive study conducted a retrospective cohort design on HL patients at Dharmais National Cancer Hospital, Jakarta, Indonesia. Data was collected from January 2017 to December 2021 using total sampling. Patients aged 18 or older and diagnosed with

HL in any subtype based on histopathological examination from nodal and/or extranodal were eligible to participate. Patients with multiple malignancies were excluded. Demographic data was obtained including age and gender. Clinical features include B-symptoms, ECOG, BMI, comorbidity, LDH, hemoglobin, leukocyte, platelet, extranodal, extranodal location, stage, and chemotherapy. Outcome recorded from diagnosis to the end of the study either alive, deceased, or lost to follow up. B-symptoms refer to symptoms of fever, night sweats, and unintentional weight loss. Information obtained from the medical records.

### Statistical analysis

The data obtained were processed using the Statistical Package for the Social Science (SPSS) version 25.0 program. Numeric data is presented as descriptive data without any statistical test. Demographic information and clinical characteristics were presented descriptively.

## RESULTS

### Demographic characteristics

Based on inclusion and exclusion criteria, during five years, the number of subjects with HL was 177. **Table 1** shows the demographic distribution of subjects. The distribution of male subjects was 52.5% and 47.5% for women. The median age of subjects was 32 years within the range of 18 to 75 years. Stratification was performed based on the nearest median value with ≤ 30 years comprising 71 subjects (41.6%) and > 30 years comprising 92 subjects (56.4%).

**Table 1.** Demographic data

| Variable | N (%) |
|---|---|
| Gender (N = 177) | |
| Female | 84 (47.5) |
| Male | 93 (52.5) |
| Age (N = 163) | |
| Median (Min–Max) | 32 (18–75) |
| > 30 | 92 (56.4) |
| ≤ 30 | 71 (43.5) |

N: number of subjects, Min: minimum, Max: maximum

### Clinical features

The main clinical features of HL are shown in **Table 2** with the occurrence of B-symptoms (n= 136). There 30.1% of subjects presented with B-symptoms and 69.6% did not. The performance status based on Eastern Cooperative Oncology Group (ECOG; n = 136) was predominantly scored at 0 for 44.4% of subjects. Body mass index (BMI; n = 144) within the normal range was found in 39.6%, obesity 22%, overweight 19.4%, and underweight 18.8%. Comorbidities of the subject prior diagnosed with HL were diabetes mellitus (DM) at 10.3%, hypertension at 8.1%, end-stage renal disease at 1.5%, and each 0.7% for heart failure, acute coronary syndrome, hepatitis B, and epilepsy.

Hematological examination with reference limits based on the International Prognostic Score (IPS) for HL. The lactate dehydrogenase (LDH; n = 140) average between subjects was 460.37 U/dL with 85.7% having LDH > 240 U/dL and 14.3% LDH ≤ 240 U/dL. Hemoglobin (Hb; n = 155) average level was 11.4 g/dL with 28.4% having Hb < 10.5 g/dL and 71.6% had Hb ≥ 10.5 g/dL. White blood cell (WBC; n = 155) had an average of 14,328/μL with 33.5% having WBC > 15,000/μL and 66.5% had WBC ≤ 15,000/μL. Platelet count (PLT; n = 155) with average of 400,412/μL with 59.4% having PLT > 350,000/μL and 40,6% PLT ≤ 350,000/μL.

Based on the Ann-Arbor stage classification, radiological examinations were done for stage determination (n = 149). Most subjects were identified in stage II for 51.0%, followed by stage III for 28.2%, stage IV for 20.1%, and the least stage I for 0.7%. Extranodal lesions (n = 30) were identified as most frequent in bone for 32.2%.

The administration of chemotherapy (n = 110) primarily consisted of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD) given to 92.7% of subjects. Other subjects received second, third, and fourth as they had received their first-line in previous treatment before admitting to our hospital. There were 47 subjects (26.6%) lost to follow-up. The outcome (n = 130) for our study showed 69.2% alive and 30.8% deceased until the end of the study period.

## DISCUSSION

The results Our study took place over five years and obtained 177 subjects with HL. The median age found in our study is 32 years and the majority male gender. Resemblance to Meng et al. [8], in a retrospective study in China, the median age of HL was found to be 38 years. According to Huang et al. [9], the incidence of HL new cases has increased in those aged 44 and younger since 2019. In line with our study, Basudan et al. [10], through a study in Saudi Arabia, found that males are more prevalent in HL than females. Anggorowati et al. [11], who conducted a study in the province of Yogyakarta, Indonesia, also found males dominate in HL. According to Roemer et al. [12], the estrogen hormone, which is abundant in women, is one of the protective factors against lymphomagenesis.

B-symptoms were found in 30% of HL patients in our study. In line with Kaseb et al. [4], who stated that B-symptoms in HL were found up to 30% and are common in stages III and IV. A study by Boo et al. [13] in Malaysia

**Table 2.** Clinical features data

| Variable | N | % |
|---|---|---|
| B-Symptoms (N = 136) | | |
| Yes | 41 | 30.1 |
| No | 95 | 69.9 |
| ECOG (N = 136) | | |
| 0 | 60 | 44.4 |
| 1 | 56 | 41.5 |
| 2 | 17 | 12.6 |
| 3 | 3 | 1.5 |
| BMI (N = 144) | | |
| Underweight | 27 | 18.8 |
| Normal | 57 | 39.6 |
| Overweight | 28 | 19.4 |
| Obesity | 32 | 22.2 |
| Comorbidity | | |
| DM | 14 | 10.3 |
| Hypertension | 11 | 8.1 |
| CKD | 2 | 1.5 |
| Heart failure | 1 | 0.7 |
| Acute coronary syndrome | 1 | 0.7 |
| Hepatitis B | 1 | 0.7 |
| Epilepsy | 1 | 0.7 |
| LDH (N = 140) | | |
| Mean (SD) | 460.37 (290.023) | |
| Median (Min-Max) | 379.5 (117–2019) | |
| > 240 | 120 | 85.7 |
| ≤ 240 | 20 | 14.3 |
| Hemoglobin (N = 155) | | |
| Mean (SD) | 11.4 (2.20) | |
| Median (Min-Max) | 11.8 (5.2–16.5) | |
| < 10.5 | 44 | 28.4 |
| ≥ 10.5 | 111 | 71.6 |
| Leukocyte (N = 155) | | |
| Mean (SD) | 14,328,58 (8,849,45) | |
| Median (Min-Max) | 11,540 (2,400–41,540) | |
| > 15,000 | 52 | 33.5 |
| ≤ 15,000 | 103 | 66.5 |
| Platelet (N = 155) | | |
| Mean (SD) | 400,412 (165,555) | |
| Median (Min–Max) | 395,000 (28,000–1,052,000) | |
| > 350,000 | 92 | 59.4 |
| ≤ 350,000 | 63 | 40.6 |
| Extranodal (N = 156) | | |
| Yes | 30 | 19.2 |
| No | 126 | 80.8 |
| Extranodal location | | |
| Brain | 1 | 2.6 |
| Lung | 8 | 22.5 |
| Pleura | 6 | 16.1 |
| Bone marrow | 12 | 32.2 |
| Digestive tract | 1 | 2.6 |
| Liver | 2 | 5.3 |
| Lien | 5 | 13.4 |
| Pericardium | 2 | 5.3 |
| Stage (N = 149) | | |
| I | 1 | 0.7 |
| II | 76 | 51.0 |
| III | 42 | 28.2 |
| IV | 30 | 20.1 |
| Chemotherapy (N = 110) | | |
| ABVD | 102 | 92.7 |
| ICE | 4 | 3.6 |
| DHAP | 2 | 1.8 |
| BV | 2 | 1.8 |
| Outcome (N = 130) | | |
| Median | 65 months | |
| Death | 40 | 30.8 |
| Survive | 90 | 69.2 |
| Lost to follow-up | 47 | 26.6 |

N: number of subjects, Min: minimum, Max: maximum, ECOG: Eastern Cooperative Oncology Group, BMI: body mass index, DM: diabetes mellitus, CKD: chronic kidney disease, LDH: lactate dehydrogenase, SD: standard deviation, ABVD: adriamycin bleomycin vinblastine dacarbazine, ICE: ifosfamide carboplatin etoposide, DHAP: dexamethasone high dose cytarabine platinum, BV: brentuximab vedotin

found that 36.2% experienced B-symptoms. BMI in our study was mostly normal, followed by overweight, obese, and least underweight. Strongman et al. [14] stated that an increase in BMI will increase the risk of HL. This finding supports that many factors can influence the occurrence of HL and BMI can be considered as a supporting factor. The main comorbidities found in our study were diabetes mellitus and followed by hypertension. According to the International Diabetes Federation (IDF) in 2021, Indonesia occupies the second most countries for the number of people with diabetes in the Western Pacific Region [15]. In addition, according

to Mashuri et al. [16], among Southeast Asian countries, Indonesia had the highest prevalence of hypertension. Cokgezer et al. [17] found more hypertension comorbidities compared to diabetes mellitus in HL. According to van Spronsen et al. [18], the most common comorbidities are cardiovascular disease, followed by hypertension, obstructive lung disease, and diabetes mellitus, and the presence of comorbidities is not related to the stage of the disease [18,19].

Hb levels in HL in our study were 62.7% more than 10.5 g/dL. Similar to Bierman et al. [20], it was found that 60.4% had Hb ≥ 10.5 g/dL. According to Hohaus et al. [21], anemia in HL is associated with the overproduction of hepcidin stimulated by cytokine IL-6 when there is an increase in disease activity. However, an increase in hepcidin alone is not enough to induce anemia so not all patients experience it. Subjects with WBC levels more than 15,000/μL in our study were fewer compared to ≤ 15,000/μL. The result was in line with Porrata et al. [22] who found only 12% of HL patients who have WBC > 15,000/μL. According to Akdeniz et al. [23], platelets in HL patients are higher compared to healthy individuals with platelet count > 321,000/μL being a predictive value for HL diagnosis [23]. HL patients tend high LDH levels. According to Ruan et al. [24], an increase in LDH levels in HL patients can be a biomarker for the occurrence of sepsis or disease progression that is associated with poor prognosis. The mortality rate in our study tends to be higher compared to other studies [25,26]. Almost half of the subjects in our study were in the advanced stage, supported with high LDH levels and the most metastasis found were in bone marrow that lowered WBC level increase the risk of death.

The limitation of our study was some uncompleted data caused by the not well-organized medical record administration during the transition period between manual to electronic medical records. The number of subjects is also limited to a single center. A multi-centered study for larger distribution data and deeper analysis associated with mortality should need to be done.

## CONCLUSION

Our study investigates the distribution of clinical features among HL patients in Dharmais Hospital an Indonesian National Cancer Center. Generally, most subjects were male in the young adult stage, unpresented B-symptoms, great performance status, normal BMI, no comorbidity, high level of LDH, normal Hb, normal WBC, high Plt count, and stage 2 disease. The majority of individuals with Hodgkin's lymphoma lived for 5 years.

## DECLARATION

### Competing interest

There is no conflict of interest in our study.

### Ethics approval and consent to participate

Our study has been approved by the ethical committee in Dharmais National Cancer Center Hospital with reference number DP.04.03/11.7/376/2023.

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## REFERENCES

1. International Agency for Research on Cancer. Global Cancer Observatory Indonesia Fact Sheet 2022 [Internet]. [cited 2024 Feb 23]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/360-indonesia-fact-sheet.pdf
2. Moccia AA, Donaldson J, Chhanabhai M, Hoskins PJ, Klasa RJ, Savage KJ, et al. International Prognostic Score in Advanced-Stage Hodgkin's Lymphoma: Altered Utility in the Modern Era. J Clin Oncol. 2012 Sep 20;30(27):3383–8.
3. Cojbasic I, Macukanovic-Golubovic L. Analysis of Prognostic Factors In Hodgkin ' S Lymphoma with Regard to Response to Treatment. Facta Universitatis. 2007;14(3):117–20.
4. Kaseb H, Babiker HM. Hodgkin Lymphoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 [cited 2023 Nov 23]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK499969/
5. Cancer Research UK. Hodgkin lymphoma incidence statistics [Internet]. 2015 [cited 2024 Feb 23]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/hodgkin-lymphoma/incidence
6. Qi J, Gu C, Wang W, Xiang M, Chen X, Fu J. Elevated Lactate Dehydrogenase Levels Display a Poor Prognostic Factor for Non-Hodgkin's Lymphoma in Intensive Care Unit: An Analysis of the MIMIC-III Database Combined With External Validation. Front Oncol. 2021 Oct 28;11:753712.
7. Cancer Research UK. Survival [Internet]. [cited 2024 Feb 28]. Available from: https://www.cancerresearchuk.org/about-cancer/hodgkin-lymphoma/survival

8. Meng J, Chang C, Pan H, Zhu F, Xiao Y, Liu T, et al. Epidemiologic characteristics of malignant lymphoma in Hubei, China. Medicine (Baltimore). 2018 Aug 21;97(35):e12120.
9. Huang J, Pang WS, Lok V, Zhang L, Lucero-Prisno DE, Xu W, et al. Incidence, mortality, risk factors, and trends for Hodgkin lymphoma: a global data analysis. J Hematol OncolJ Hematol Oncol. 2022 Dec;15(1):1–11.
10. Basudan AM, Althani M, Abudawood M, Farzan R, Alshuweishi Y, Alfhili MA. A Comprehensive Two-Decade Analysis of Lymphoma Incidence Patterns in Saudi Arabia. J Clin Med. 2024 Jan;13(6):1652.
11. Anggorowati N, Indrawati, Dhyanti AL, Arkananda H, Rizki SH, Setiawan SA, et al. Sociodemographic and Clinicopathological Features of Lymphoma Patients in Indonesia: A report from Special Region of Yogyakarta Province. Asian Pac J Environ Cancer. 2021;4(1):33–8.
12. Roemer K, Pfreundschuh M. How do estrogens control lymphoma? Blood. 2014 Mar 27;123(13): 1980–1.
13. Boo YL, Ting HSY, Yap DFS, Toh SG, Lim SM. Clinical features and treatment outcomes of Hodgkin lymphoma: A retrospective review in a Malaysian tertiary hospital. Blood Res. 2019 Sep 30;54(3): 210–7.
14. Strongman H, Brown A, Smeeth L, Bhaskaran K. Body mass index and Hodgkin's lymphoma: UK population-based cohort study of 5.8 million individuals. Br J Cancer. 2019 Apr;120(7):768–70.
15. Karakas. IDF Western Pacific Members [Internet]. International Diabetes Federation. [cited 2020 Mar 4]. Available from: https://idf.org/our-network/regions-members/western-pacific/members/104-indonesia.html
16. Mashuri YA, Ng N, Santosa A. Socioeconomic disparities in the burden of hypertension among Indonesian adults - a multilevel analysis. Glob Health Action. 15(1):2129131.
17. Çokgezer S, Elverdi T, Salihoğlu A, Ar MC, Öngören Ş, Başlar Z, et al. Treatment Responses, Toxicity, and Survival in Patients with Classical Hodgkin Lymphoma Aged ≥50 Years: A Single-Center Experience Over Two Decades. Cancer Manag Res. 2022 Jun 7;14:1911–21.
18. van Spronsen DJ, Janssen-Heijnen ML, Breed WP, Coebergh JW. Prevalence of co-morbidity and its relationship to treatment among unselected patients with Hodgkin's disease and non-Hodgkin's lymphoma, 1993-1996. Ann Hematol. 1999 Jul;78(7):315–9.
19. National Comprehensive Cancer Network. Hodgkin Lymphoma [Internet]. [cited 2024 Aug 14]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf
20. Bierman PJ, Lynch JC, Bociek RG, Whalen VL, Kessinger A, Vose JM, et al. The International Prognostic Factors Project score for advanced Hodgkin's disease is useful for predicting outcome of autologous hematopoietic stem cell transplantation. Ann Oncol. 2002 Sep 1;13(9):1370–7.
21. Hohaus S, Massini G, Giachelia M, Vannata B, Bozzoli V, Cuccaro A, et al. Anemia in Hodgkin's Lymphoma: The Role of Interleukin-6 and Hepcidin. J Clin Oncol. 2010 May 20;28(15):2538–43.
22. Porrata LF, Ristow K, Colgan JP, Habermann TM, Witzig TE, Inwards DJ, et al. Peripheral blood lymphocyte/monocyte ratio at diagnosis and survival in classical Hodgkin's lymphoma. Haematologica. 2012 Feb;97(2):262.
23. Akdeniz A, Mehtap Ö, Karakuş V, Ünal S, Aygün K, Temel GÖ, et al. Are Platelet-related Parameters Predictive of the Prognosis of Hodgkin's Lymphoma?
24. Ruan GJ, Gandhi S, Abeykoon JP, Schram S, Habermann TM, Sandefur BJ, et al. Elevated Serum Lactate in Patients With Lymphoma: It Is Not Always Infection. Mayo Clin Proc Innov Qual Outcomes. 2021 Apr 1;5(2):423–30.
25. Huang J, Pang WS, Lok V, Zhang L, Lucero-Prisno DE, Xu W, et al. Incidence, mortality, risk factors, and trends for Hodgkin lymphoma: a global data analysis. J Hematol OncolJ Hematol Oncol. 2022 May 11;15:57.
26. International Agency for Research on Cancer. 360-indonesia-fact-sheet.pdf [Internet]. [cited 2024 Jul 5]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/360-indonesia-fact-sheet.pdf