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Original Research

LONGER LAG TIME IN EARLY-STAGE RETINOBLASTOMA

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ABSTRACT

Retinoblastoma is a rare neoplasm disease that occurs in children, generally under the age of two. Retinoblastoma is more prevalent in developing countries and is often associated with a late diagnosis. Such delays can lead to a poor prognosis. The time from the appearance of symptoms of retinoblastoma (onset) to the time of diagnosis is called lag time. Early diagnosis of retinoblastoma by paying attention to factors such as age, clinical symptoms, and laterality can help improve retinoblastoma survival rates, especially in developing countries. The purpose of this study was to analyze the relationship between the lag time to the stage of retinoblastoma patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. This study was a retrospective analytical observational study using secondary data from retinoblastoma patients at the Ophthalmology Outpatient Unit at Dr. Soetomo General Academic Hospital, Surabaya, from January 2014 to December 2018. The data were analyzed using Kendall's tau-C test. No significant correlation was found between lag time and stage ($p = 0.339$). Patients with International Retinoblastoma Staging System (IRSS) I stage had the longest lag time (on average 28 months), and patients with stage IVB had the shortest lag time (on average four months). There was no correlation between lag time and retinoblastoma stage. However, there was a trend of patients with early stages delaying hospital visits, while patients with advanced stages in earlier to the hospital.

Keywords: Retinoblastoma; lag time; IRSS stage; disease; neglected disease

ABSTRAK

Retinoblastoma adalah suatu penyakit neoplasma langka yang terjadi pada anak, biasanya dibawah usia dua tahun. Prevalensi retinoblastoma paling banyak di negara berkembang. Retinoblastoma sering dihubungkan dengan diagnosis yang terlambat. Keterlambatan tersebut dapat menyebabkan prognosis yang buruk. Waktu dari munculnya gejala retinoblastoma (onset) hingga waktu saat diagnosis disebut lag time. Diagnosis dini pada retinoblastoma dengan memperhatikan faktor-faktor seperti umur, gejala klinis, maupun lateralitas dapat membantu meningkatkan survival rate retinoblastoma, terutama pada negara berkembang. Tujuan penelitian adalah menganalisis hubungan antara lag time terhadap stage pasien retinoblastoma di RSUD Dr. Soetomo Surabaya. Penelitian ini merupakan penelitian observasional analitik retrospektif menggunakan data sekunder dari pasien retinoblastoma di Instalasi Rawat Jalan Mata di RSUD Dr. Soetomo Surabaya bulan Januari 2014 hingga Desember 2018. Data dianalisis menggunakan uji kendall's tau-c. Tidak ditemukan korelasi yang signifikan antara lag time dan stage ($p=0,339$). Pasien dengan stage International Retinoblastoma Staging System (IRSS) I memiliki lag time paling panjang (rerata 28 bulan) dan pasien dengan stage IVB mempunyai lag time paling pendek (rerata 4 bulan). Tidak didapatkan korelasi antara lag time dan stage retinoblastoma, namun terdapat trend pasien dengan stage lebih awal lebih lama menunda kunjungan ke rumah sakit sedangkan pasien dengan stage lanjut lebih cepat berobat ke rumah sakit.

Kata kunci: Retinoblastoma; lag time; IRSS stage; penyakit; pengabaian penyakit

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INTRODUCTION

Cancer is the prominent cause of death in children. In high-income countries, the survival rate of cancer in children reaches 80%. Concurrently, in low and middle-income countries, the survival rate is only 25% (Kellie & Howards 2008). The most frequent cancer for children is retinoblastoma (Mattosinho et al. 2019). Retinoblastoma can be found in 1 out of 20,000 live births (Dimaras et al. 2012). Retinoblastoma causes account for 2% of all cancer in children. The disease is mainly found in children under five years old, with a five-year survival rate of approximately 94% (Hewitt et al. 2003).

The most common symptoms linked to Retinoblastoma are leukocoria and squint eyes (Mattosinho et al. 2019). Symptoms during the intraocular stage are more difficult to recognize. As the disease progresses, the tumor in the eye worsens (Ortiz & Dunkel 2015). Cases in developing countries are primarily at the extraocular stages due to metastasis, subsequently causing mortality (Navo et al. 2012).

Retinoblastoma is often associated with a late diagnosis, which causes delays that may lead to a poor outcome (Brasme et al. 2012). The interval between the first appearance of symptoms and the time of diagnosis is called lag time. Based on research conducted in China, the duration of lag time in extraocular tumors is more significant than in intraocular tumors. Furthermore, extraocular tumors are related to unfavorable prognoses (Chang et al. 2006, Gao et al. 2016). These tumors can cause various complications, from vision loss to death (Shields & Shields 1993).

Retinoblastoma is more prevalent in children living in developing countries (Chintagumpala et al. 2007). The incidence of retinoblastoma accounts for the highest mortality rate in Taiwan due to a high number of parents stalling or denying therapy (Chang et al. 2006). Meanwhile, retinoblastoma's incidence in Indonesia is still unknown due to the lack of epidemiology research regarding this disease. Early diagnosis of retinoblastoma by noting factors such as age, clinical symptoms, and laterality can help improve the survival rate of retinoblastoma, especially in developing countries (Maki et al. 2009, Naseripour et al. 2009). This study aimed to find the relationship between lag time and stage in retinoblastoma patients.

MATERIALS AND METHODS

This study was a retrospective analytical observational study using secondary data. The inclusion criteria were retinoblastoma patients at the Ophthalmology

Outpatient Unit in Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January 2014 to December 2018. Lag time data was categorized into 5 groups; ≤ 1 month, >1 month - 6 months, >6 months - 12 months, >12 months - 24 months, and >24 months. The stages were grouped based on IRSS staging; groups I, II, III-A, III-B, IV-A, and IV-B. The correlation between lag time and staging was statistically analyzed using Kendall's Tau-c.

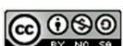
RESULTS

A total of 42 medical records were collected from the Ophthalmology Outpatient Unit. Out of those, 11 medical records had insufficient data, while 2 medical records were later diagnosed not as retinoblastoma. These data did not meet the criteria for sample inclusion. Therefore, the samples that fit the inclusion criteria were 29 samples. Subjects consisted of 14 males and 15 females. The average age of the subjects was 34.59 months (range 4 - 83 months). These patients originated from several regions in East Java and East Indonesia. As shown in Figure 1, no remarkable differences in cases are found in each region. The highest number of patients came from Gresik, Probolinggo, and East Kalimantan.

Table 1. Distribution of lag time and staging of retinoblastoma patients

Parameter	Frequency	Percentage (%)
Lag time		
≤ 1 month	3	10.3
$>1 - 6$ months	9	31.0
$>6 - 12$ months	7	24.1
$>12 - 24$ months	6	20.7
>24 months	4	13.8
IRSS staging		
I	3	10.3
II	6	20.7
III A	10	34.5
III B	6	20.7
IV A	0	0
IV B	4	13.8
Total of patients	29	100

Table 1 shows the frequency of patients based on lag time and staging. The shortest lag time was found in patients with a lag time of ≤ 1 month with an occurrence of 10.3%, while the longest lag time was found in patients with a lag time of 1-6 months and 31.0% of incidents. The average lag time in this study was 11.45 months (ranging from 1-36 months). The average duration of lag time for IRSS stages I, II, III-A, III-B, and IV-B were 28.0, 6.0, 12.4, 10.8, and 4 months, respectively. Most patients were categorized into stage III-A (34.5%), followed by stages II and III-B with 20.7%.



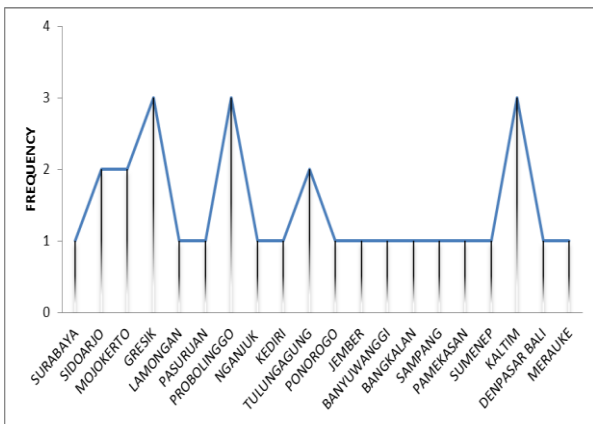


Figure 1. The frequency of cases per region in Dr. Soetomo General Academic Hospital

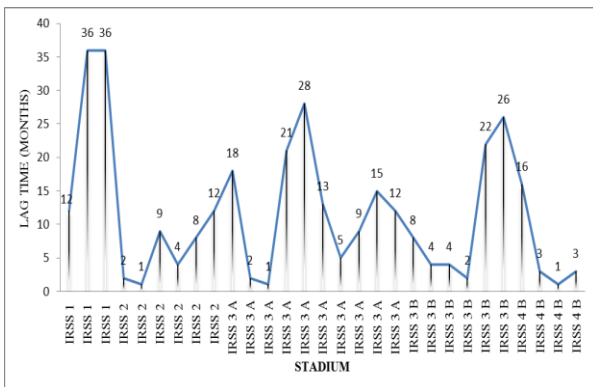


Figure 2. Lag time and stage of each retinoblastoma patient based on IRSS staging

Figure 2 illustrates the lag time and stage of each patient. The highest lag time duration was found in patients with stage IRSS I. Meanwhile, the shortest lag period was found in patients with stage IV-B. The correlation between lag time and the stage was tested using Kendall's Tau-c test. In this study, the result showed $p=0.339$, $r=0.134$, which indicated no relationship between lag time and stage.

DISCUSSION

Leukocoria is an early symptom most commonly found in retinoblastoma patients. Leukocoria is an abnormal white reflex in pupils that occurs due to light reflection from retinal lesions. Besides leukocoria, the second most frequent early symptom in retinoblastoma is strabismus (Balmer & Munier 2007). Retinoblastoma can precipitate strabismus if a mass interferes with vision (Murthy et al. 2004). Strabismus is the misalignment of the eyes. In most people, unevenly aligned eyes are visible, making them easy to detect (Helveston 2010).

In this study, 28 children (96.6%) out of 29 children with retinoblastoma had an early symptom of leukocoria according to their anamnesis. The other patient came in with an early symptom of no response to light. Research in India found that the frequency of leukocoria was as much as 98% (Sahu et al. 1998), 87% in Ghana (Essuman et al. 2010), 50% in Singapore (Aung et al. 2009), and 65% in America (Butros et al. 2002). Meanwhile, strabismus was found in 9 retinoblastoma patients (31%) in this study, as compared to research in Iran with an incidence of 28.2% (Naseripour et al. 2009), 6.6% of the incident happened in Singapore (Aung et al. 2009), and 26% in America (Butros et al. 2002). There were no recorded data regarding the type of strabismus in this research. Another study found that exotropia was the most common type of strabismus in retinoblastoma patients. At the same time, it was also found to be the most prevalent type (67%), followed by esotropia (13%), and combined with vertical strabismus (10%) (Fabian et al. 2017). Exotropia was also the most frequent (62%), followed by esotropia (28%), and an alternate exotropia/ esotropia type (10%) (Fabian et al. 2018).

In low-income countries, retinoblastoma can occur accompanied by apparent extraocular symptoms (Chantada et al. 2006). In some patients, advanced symptoms appear in the period from the first appearance of the symptoms to the time of diagnosis. Proptosis (44.8%) and red eyes (37.9%) were symptoms that were often found when patients visited the Ophthalmology Outpatient Unit at Dr. Soetomo General Academic Hospital. This finding was comparable to a study of 23 patients in Ghana, which found 34.8% proptosis and 21.7% red eyes (Essuman et al. 2010). All patients with proptosis have extraocular tumors, while those with red eyes can have both intraocular and extraocular tumors. One patient from our study initially came in with an intraocular tumor, decided not to undergo eye enucleation, and tried alternative treatments. When the patient returned to the hospital a few months later, the patient's tumor had progressed to proptosis. The tumor protruded outside the eyeball, a similar finding reported in Reddy's research (Reddy & Anusya 2010).

IRSS staging was used to classify stages of intraocular and extraocular retinoblastoma (Chantada et al. 2006). Patients with enucleated eye were grouped into stage I category, retinoblastoma patients who had been enucleated and followed by chemotherapy were grouped into stage II, retinoblastoma patients with tumors that had metastasized out of the eyeball were grouped into stage III-A, retinoblastoma patients with metastasis to lymph nodes into stage III-B, patients with hematogenous metastasis stage into IV-A, and



patients with metastasis to brain tissue were grouped into stage IV-B.

IRSS is a staging system created in 2006, covering the entire stage of retinoblastoma, unlike Reese-Ellsworth (Reese & Ellsworth 1963) and Murphree's IIRC, which can only be used for intraocular retinoblastoma (Dimaras et al. 2015). In addition, IRSS also considers tumor extension or metastasis along with a response to therapy into stage classification (Chantada et al. 2006). Therefore, this staging system is the most appropriate classification for the data in the medical records at Dr. Soetomo General Academic Hospital.

Our study found no significant correlation between lag time and the stage ($p=0.339$), although we noted that patients with IRSS stage I had a significantly longer average lag time than those in IRSS stage IV-B. Therefore, there was a tendency for the early stage to be presented late, while the advanced stage had the earliest presentation. This study's results followed a study by Posner et al. (2017). Meanwhile, Faranoush et al. (2014) found a significant link between lag time and IIRC tumor grouping. Another study found a link between lag time and mutated retinoblastoma (IRSS stage IV) (Rodrigues et al. 2004). It can be assumed that other factors were involved beyond this research's scope. Parents' awareness and knowledge of this disease, the doubts and fears in undergoing enucleation or exenteration, and economic difficulties may contribute to the lag time (Xiao et al. 2019). The laterality of the disease was found to have an effect in the relationship between lag time and disease staging but only found in patients with bilateral retinoblastoma.

In this study, there was no correlation between lag time and staging in unilateral disease. Another factor taken into consideration was the family's socioeconomics. However, socioeconomic factors were found not to correlate with lag time, but there was a relationship between socioeconomic factors and the advanced disease (Ramirez-Ortiz et al. 2014).

This study might not be perfect due to the small number of samples. Also, some medical records contained a lack of information required. The medical record data were taken only from the Ophthalmology Outpatient Unit at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. In addition, the stage used was only IRSS due to a lack of data to classify according to the Reese-Ellsworth classification.

CONCLUSION

No correlation between lag time and retinoblastoma stage was found in this study. However, this study

could reveal a trend where patients of stage I demonstrated the longest lag time duration, and the shortest duration of lag time was demonstrated by patients with the most advanced staging of IRSS.

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REFERENCES

- Aung L, Chan Y, Yeoh E, et al (2009). Retinoblastoma: A recent experience at the National University Hospital, Singapore. *Ann. Acad. Med. Singapore* 38, 693–698.
- Balmer A, Munier F (2007). Differential diagnosis of leukocoria and strabismus, first presenting signs of retinoblastoma. *Clin. Ophthalmol.* 1, 431–439.
- Brasme J, Morfouace M, Grill J, et al (2012). Delays in diagnosis of pediatric cancers: A systematic review and comparison with expert testimony in lawsuits. *Lancet Oncol.* 13, 445–459.
- Butros L, Abramson D, Dunkel I (2002). Delayed diagnosis of retinoblastoma: analysis of degree, cause, and potential consequences. *Pediatrics* 109, 1–5.
- Chang C, Chiou T, Hwang B, et al (2006). Retinoblastoma in Taiwan: Survival rate and prognostic factors. *Jpn. J. Ophthalmol.* 50, 242–249.
- Chantada G, Doz F, Antoneli C, et al (2006). A proposal for an international retinoblastoma staging system. *Pediatr. Blood Cancer* 47, 801–805.
- Chintagumpala M, Chevez-Barrios P, Paysse E, et al (2007). Retinoblastoma: Review of current management. *Oncologist* 12, 1237–1246.
- Dimaras H, Corson T, Cobrinik D, et al (2015). Retinoblastoma. *Nat. Rev. Dis. Prim.* 1, 1–22.
- Dimaras H, Kimani K, Dimba E, et al (2012). Retinoblastoma. *Lancet* 379, 1436–1446.
- Essuman V, Ntim-Amponsah C, Akafo S, et al (2010). Presentation of retinoblastoma at a pediatric eye clinic in Ghana. *Ghana Med. J.* 44, 10–15.
- Fabian I, Naeem Z, Stacey A, et al (2017). Long-term visual acuity, strabismus, and nystagmus outcomes following multimodality treatment in group D retinoblastoma eyes. *Am. J. Ophthalmol.* 179, 137–144.
- Fabian I, Stacey A, Naeem Z, et al (2018). Strabismus in retinoblastoma survivors with long-term follow-up. *J. Am. Assoc. Pediatr. Ophthalmol. Strabismus* 22, 1–7.

- Faranoush M, Hedayati A, Mehrvar A, et al (2014). Consequences of delayed diagnosis in treatment of retinoblastoma. *Iran. J. Pediatr.* 24, 381–386.
- Gao J, Zeng J, Guo B, et al (2016). Clinical presentation and treatment outcome of retinoblastoma in children of South Western China. *Medicine (Baltimore)*. 95, 1–7.
- Helveston E (2010). Understanding, detecting, and managing strabismus. *Community Eye Heal.* 23, 12–14.
- Hewitt M, Rowland J, Yancik R (2003). Cancer survivors in the United States: Age, health, and disability. *J. Gerontol.* 58, 82–91.
- Kellie S, Howards S (2008). Global child health priorities: What role for pediatric oncologists? *Eur. J. Cancer* 44, 2388–2396.
- Maki J, Marr B, Abramson D (2009). Diagnosis of retinoblastoma: How good are referring physicians? *Ophthalmic Genet.* 30, 199–205.
- Mattosinho C, Moura A, Oigman G, et al (2019). Time to diagnosis of retinoblastoma in Latin America: A systematic review. *Pediatr. Hematol. Oncol.* 36, 55–72.
- Murthy R, Honavar S, Naik M, et al (2004). Retinoblastoma. In: *Modern Ophthalmology*. New Jaypee Brothers, New Delhi, pp. 849–859.
- Naseripour M, Nazari H, Bakhtiari P, et al (2009). Retinoblastoma in Iran: Outcomes in terms of patients' survival and globe survival. *Br. J. Ophthalmology* 93, 28–32.
- Navo E, Teplisky D, Albero R, et al (2012). Clinical presentation of retinoblastoma in a middle-income country. *J. Pediatr. Hematol. Oncol.* 34, 97–101.
- Ortiz M, Dunkel I (2015). Retinoblastoma. *J. Child Neurol.* 31, 227–236.
- Posner M, Jaulim A, Vasalaki M, et al (2017). Lag time for retinoblastoma in the UK revisited: A retrospective analysis. *BMJ Open* 7, 1–6.
- Ramirez-Ortiz M, Ponce-Castañeda M, Cabrera-Muñoz M, et al (2014). Diagnostic delay and sociodemographic predictors of stage at diagnosis and mortality in unilateral and bilateral retinoblastoma. *Cancer Epidemiol. Biomarkers Prev.* 23, 784–792.
- Reddy S, Anusya S (2010). Clinical presentation of retinoblastoma in Malaysia: A review of 64 patients. *Int. J. Ophthalmol.* 3, 64–68.
- Reese A, Ellsworth R (1963). The evaluation and current concept of retinoblastoma therapy. *Trans. - Am. Acad. Ophthalmol. Otolaryngol.* 67, 164–172.
- Rodrigues K, Latorre M, de Camargo B (2004). Atraso diagnóstico do retinoblastoma. *J. Pediatr. (Rio. J)*. 80, 511–516.
- Sahu S, Banavali S, Pai S, et al (1998). Retinoblastoma: Problems and perspectives from India. *Pediatr. Hematol. Oncol.* 15, 501–508.
- Shields J, Shields C (1993). Ocular tumors of childhood. *Pediatr. Clin. North Am.* 40, 805–826.
- Xiao W, Ye H, Zeng H, et al (2019). Associations among socioeconomic factors, lag time, and high-risk histopathologic features in eyes primarily enucleated for retinoblastoma. *Curr. Eye Res.* 44, 1144–1149.