LAMPIRAN

Lampiran 1.

Prosedur kerja pemeriksaan feritin serum menggunakan metode ECLIA *(Electro-Chemiluminescence Immunoassay)*

Alat dan Bahan:

1. Serum
2. Reagen *elecsys ferritin*
3. Alat Cobas e411

Prinsip : prinsip feritin dalam sampel akan berikatan dengan antibodi spesifik feritin monoklonal biotinilasi dan antibodi spesifik feritin yang dilabel dengan komplek rhutenium. Penambahan Streptavidin coated mikropartikel akan menempel pada kompleks tersebut. Kompleks yang terikat akan ditangkap oleh permukaan elektroda. Zat-zat yang tidak berikatan akan dicuci oleh procell dan emisi chemiluminescent. Pengukuran konsentrasi feritin diukur dengan photomultiplier dan hasil ditentukan menggunakan kurva kalibrasi.

Cara Kerja :

1. Masukkan 10 µl sampel berupa serum ke dalam cuvet.
2. Masukkan cuvet ke dalam disk alat.
3. Masukkan sampel ID lalu tekan enter
4. Masukkan nomor posisi sampel di *Disk Position* lalu tekan enter.
5. Tandai tes yang akan dipilih dengan menekan nama tes dan ditekan new sampel untuk sampel selanjutnya.
6. Tekan start untuk memulai proses pemeriksaan sampel.

(Sumber: Ningrum, 2020)

Lampiran 2.

KARTU KONSULTASI

Nama : Tias Idamatu Rizkia Fitri

Judul KTI : Gambaran Kadar Feritin Serum pada Penderita Talasemia Mayor yang Menjalani Transfusi Rutin (Studi Pustaka)

Pembimbing Utama : Sri Nuraini, S.Pd.,M.Kes

No.	Hari/Tanggal	Materi	Keterangan	Paraf
1.	28 Desember 2020	Bab I, II, dan III	Perbaikan	
2.	8 Januari 2021	Bab I, II, dan III	Perbaikan	
3.	12 Januari 2021	Bab I, II, dan III	Perbaikan	
4.	18 Januari 2021	Bab I, II, dan III	Perbaikan	
5.	28 Januari 2021	Penulisan	Acc Seminar	
6.	26 Februari 2021	Perbaikan	ACC penelitian	
7.	28 Mei 2021	Bab IV dan V	Perbaikan	
8.	7 Juni 2021	Bab IV dan V	Perbaikan	
9.	10 Juni 2021	Bab IV dan V	Perbaikan	
10.	14 Juni 2021	Bab IV dan V	Acc seminar	
11.	29 Juli 2021	Bab I-V dan jurnal	Perbaikan	
12.	4 Agustus 2021	Bab I-V dan jurnal	Perbaikan	
13.	5 Agustus 2021	Bab I-V dan jurnal	Acc cetak	

Ketua Prodi TLM Program Diploma Tiga

Misbahul Huda, S.Si.,M.Kes

NIP. 196912221997032001

Lampiran 3.

KARTU KONSULTASI

Nama : Tias Idamatu Rizkia Fitri

Judul KTI : Gambaran Kadar Feritin Serum pada Penderita Talasemia Mayor yang Menjalani Transfusi Rutin (Studi Pustaka)

Pembimbing Pendamping : Putri Dwi Romodhyanti, SKM

No.	Hari/Tanggal	Materi	Keterangan	Paraf
1.	19 Desember 2020	Bab I, II, dan III	Perbaikan	
2.	6 Januari 2021	Bab I, II, dan III	Perbaikan	
3.	11 Januari 2021	Bab I, II, dan III	Perbaikan	
4.	18 Januari 2021	Penulisan	ACC seminar	
5.	28 Februari 2021	Perbaikan	ACC penelitian	
6.	21 Mei 2021	Bab IV dan V	Perbaikan	
7.	28 Mei 2021	Bab IV dan V	Perbaikan	
8.	10 Juni 2021	Bab IV dan V	Perbaikan	
9.	11 Juni 2021	Bab IV dan V	ACC seminar	
10.	25 Juni 2021	Bab I - V	ACC cetak	

Ketua Prodi TLM Program Diploma Tiga

Misbahul Huda, S.Si.,M.Kes

NIP. 196912221997032001

Lampiran 4.

Original article:

Estimation of serum ferritin and TSH levels in thalassemia patients undergoing iron chelation therapy.

Soma Ghosh[1], Dwaipayan Chakrabarti[2]

Abstract:

Objectives & introduction: Thalassemia, heterogenous group of disorders of haemoglobin, characterised by reduced or absent production of one or more of globin chains.Regular red cell transfusion with chelation therapy for iron overload are cornerstones of therapy for ß thalassemia major. Serum ferritin assay is widely available, relatively inexpensive method for assessing body iron burden and monitoring response to chelation process which in turn also improves TSH levels in thalassemic subjects .The objective of this study was to assess prechelation and postchelation levels of serum ferritin and TSH and correlating post chelation levels of serum ferritin and TSH in thalassemic patients >6yrs undergoing chelation therapy. ***Materials & methods***: Serum TSH measured by Enzyme linked fluorescent assay and serum ferritin measured by enzyme linked immunosorbent assay. ***Results:*** Amongst 500 participants, 47% were males & 53% females. Mean age was 9.04 yrs ;prechelation ferritin and TSH levels were 2995.78ng/ml with SD of 802.53 and 5.07 µU/ml with SD of 2.52. The postchelation ferritin and TSH levels were 2168.80 ng/ml with SD of 1335.89 and 4.51µU/ml with SD of 4.76. Paired t test with respect to pre and postchelation ferritin and TSH levels showed 2 tailed p as 0.000 and t>3, both of which considered significant. While correlating post chelation ferritin with TSH levels; they showed a linear correlation (Pearson coefficient of .836). ***Conclusion***: Serum ferritin and TSH estimation in prechelation and postchelation periods give an estimate of iron overload with effect of chelation on it. Both levels decrease post chelation presenting a linear correlation between the two.

Keywords: Thalassemia; iron; chelation; ferritin; TSH.

Bangladesh Journal of Medical Science Vol. 20 No. 01 January'21. Page : 130-135
DOI: https://doi.org/10.3329/bjms.v20i1.50357

Introduction: Thomas Cooley and Lee described the homozygous or compoundheterozygous state for a recessive Mendelian disorder not confined to the Mediterranean,But occurring widely throughout tropical countries. In the past 20 years, the two important Forms of this disorder,α- and β-thalassemia, resulting from the defective synthesis of the α-and β-globin chains of hemoglobin, respectively, have been recognized as the most common monogenic diseases in humans.[1,2,6]

Under physiologic conditions, the concentration of iron in the human body is carefully regulated and normally maintained at approximately 40 mg iron/ kg body weight in women and approximately 50 mg iron/kg body weight in men, distributed among functional, transport and storage components.[2,3,7]

Chronic blood transfusion is associated with many untoward complications like blood borne infections, isoimmunisation, febrile reactions and iron overload. Iron overload causes serum ferritin level to be raised in thalassemia. A single transfusion of two units of packed RBCs is about equal to a 1 to 2 year intake of iron. There are no mechanisms for increasing the excretion of iron beyond normal daily losses.Iron thus rapidly accumulates in chronically transfused patients. Common clinical complaints in iron overload include lethargy, weight loss, change in skin color, loss of libido abdominal pain and joint pain.[4,5,7,8]

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2. Dr. DwaipayanChakrabarti, Postgraduate trainee, dept. of pathology, Burdwan Medical College, Burdwan.

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Lampiran 5.

Original Article

Growth pattern in thalassemic children and their correlation with serum ferritin

Vyas Kumar Rathaur[1], Ayesha Imran[2], Monika Pathania[3]

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Abstract

Background: This study was conducted to determine the effects of iron overload on growth and correlation of serum ferritin and growth disorders in children with thalassemia. **Methodology:** It was a crosssectional study conducted from January to June 2019 on 70 children age up to 18 years with transfusiondependent thalassemia. Detailed history, demographics, anthropometric parameters, clinical and laboratory details were evaluated. Data was analyzed by statistical package of social sciences (SPSS) software. Logistic regression model was used to determine the correlation between serum ferritin with short stature. **Results:** It included 46 male and 24 female, of which 65.71% had short stature and 77% were underweight. The mean serum ferritin level was 1,560.9 µg/L, 45.71% have serum ferritin level >2,500 µg/L, and 65.71% had hemoglobin levels of 5–8 g/dL before transfusion. The receiver operating curve value of serum ferritin was 1,107 µg/L with respect to the incidence of short stature and there was significant correlation between serum ferritin level and the incidences of short stature ($P = 0.001$). **Conclusion:** There was a significant correlation between serum ferritin level and growth disorders.

Keywords: Ferritin, growth, short stature, Thalassemia

Introduction

Thalassemia is prevalent in India.[1] Around 3.4% are carrier and 7,000–10,000 born with thalassemia per year.[2] In thalassemia, there is lifelong sequence of blood transfusions and chelation therapy leading to iron overload.[3,4]

With treatment, life expectancy can be prolonged. However, growth retardation affects quality of life. Many factors including iron overload causes growth delay.[5,6] High-serum ferritin leads to short stature.[7] Very few studies have reported problem of growth delay; so, present study is undertaken to determine effects of iron overload on height, body mass index (BMI) and ferritin and to determine correlation of ferritin and growth disorders in these children.

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Methodology

A crosssectional study was conducted on 70 children age up to 18 years (46 boys, 24 girls) with transfusion dependent thalassemia over a time period of 6 months from January 2019 to June 2019 after taking approval from ethics committee on 22 December 2018. Detailed history is evaluated. The following information is collected from medical records of the patients: demographics (age, gender, age at the time of diagnosis and at first transfusion), anthropometric parameters (weight, height, and BMI), and clinical details (blood transfusion history, last pretransfusion hemoglobin and last serum ferritin level). Serum ferritin is measured by chemi-luminescent micro-particle immunoassay.

Center of disease control and prevention (CDC) growth chart were used for boys and girls to assess their weight, height, and BMI percentiles. BMI is calculated as weight in kg/height

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Lampiran 6.

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e-ISSN: 2582-4597, CODEN (USA): GARRC2

Journal homepage: https://www.gsconlinepress.com/journals/gscarr

(RESEARCH ARTICLE)

Ferritin and genu joints ultrasound in major-beta thalassemia

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Article DOI: https://doi.org/10.30574/gscarr.2020.5.3.0132

Abstract

Objective: This study aims to determine whether there is a relationship between ferritin levels and the ultrasound of genu joints in Major-beta Thalassemia patients who undergo repeated transfusions.

Methods: 43 major-beta thalassemia patients who met the inclusion criteria had their genu joint examined by ultrasonography in the Radiology Department of Dr. Moewardi Hospital Surakarta. We analyzed several variables related to synovial thickening, synovial vascularization and joint effusion in these patients.

Results: From 43 samples, the median value of ferritin was 2976.8 (702.2-8897.7) ng/mL and the median of average transfusion was 15 (5-67) times. Analysis with Mann Whitney's non-parametric hypothesis test showed a statistically significant relation between ferritin levels and the presence or absence of ultrasonographic genu joint manifestations in general (p = 0.006) and hypoechoic synovial joint thickening (p = 0.020)

Conclusion: Major-beta thalassemia patients with ferritin levels> 2976.8 ng/mL had a 1.73 times higher risk for thickening of the synovial joints and 1.50 times higher for having genu joint manifestations. The frequency of transfusion showed a statistically significant relationship with the thickening of the synovial joint. Repeated transfusions more than 15 times increased the prevalence of the synovial joints thickening by 1.57 times.

Keywords: Ferritin; Genu; Beta-thalassemia; Ultrasound

1. Introduction

Thalassemia is a serious public health problem in the world, especially in Mediterranean countries, Malaysia, Thailand, and Indonesia.[1] More than 3% of the world's population has the thalassemia gene where the highest incidence rate that up to 40% of cases occurs in Asia.[2] In Indonesia, thalassemia is the most common disease among hemolytic anemia groups with intra-corpuscular causes. Major-beta thalassemia as a genetic disease that affects a lifetime will bring many problems for the patient. Starting from blood disorders due to anemia, the process of hemolysis, to abnormalities of various organs both caused by the disease itself or the side effects of the treatment. Hemoglobin (Hb) levels <10 gr% occur in 99.1% of major-beta thalassemia patients. To this day, blood transfusion is still the main treatment for managing anemia in major-beta thalassemia.[3,4]

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Lampiran 7.

DOI: https://doi.org/10.32539/BJI.V5I1.7986

Korelasi Antara Kadar Feritin Serum dan Status Gizi Pasien Talasemia-β Mayor

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ABSTRAK

Talasemia adalah penyakit kronik yang membutuhkan transfusi darah berulang, karena adanya gangguan sintesis hemoglobin akibat mutasi dari satu atau lebih gen globin. Transfusi secara terus menerus dapat menyebabkan terjadinya penimbunan besi dalam tubuh khususnya jantung, hati, dan organ endokrin, serta dapat menyebabkan pertumbuhan yang terhambat dan gizi kurang atau gizi buruk. Penelitian ini bertujuan untuk mengetahui korelasi antara kadar feritin serum dan status gizi pasien talasemia-β mayor di RSUP Dr. Moh. Hoesin Palembang. Penelitian ini merupakan penelitian observasional analitik dengan desain *cross sectional*. Sampel penelitian ini adalah pasien talasemia-β mayor yang menjalani rawat inap di Departemen Ilmu Kesehatan Anak RSUP Dr. Mohammad Hoesin pada bulan Oktober hingga November 2016 yang memenuhi kriteria keikutsertaan. Dari 43 pasien, sebagian besar (60.5%) pasien memiliki badan kurus sesuai dengan indeks berat badan menurut usia (BB/U) dan berperawakan pendek sesuai indeks tinggi badan menurut usia (TB/U), namun hanya 14.0% pasien memiliki gizi kurang menurut indeks BB/TB. Didapatkan nilai rata-rata kadar feritin serum 2837.69 µg/L, dengan rentang 278.7-13867 µg/L. Hasil uji korelasi antara kadar feritin serum dan status gizi menunjukkan nilai p=0.326 dan nilai r=0.153. Terdapat korelasi yang tidak bermakna antara kadar feritin serum dan status gizi pasien talasemia-β mayor.

Kata kunci: *talasemia, feritin serum, status gizi*

ABSTRACT

Thalassemia is a chronic disease that requires repeated blood transfusions, because of the haemoglobin production disorder due to defective synthesis of one or more globin chains. Repeated transfusions can lead to accumulation of iron in the body, especially the heart, liver, endocrine organs, and can cause stunted growth and malnutrition. The aim of this study was to determinate correlation between ferritin serum level and nutritional status of β-thalassemia major patients at RSUP Dr. Moh. Hoesin Palembang. This study was an analytic observational study using a cross sectional design. Samples in this study were all hospitalized β-thalassemia major patients in the Department of Pediatric Hospital Dr. Mohammad Hoesin Palembang in October to November which fits the inclusion criteria. From 43 patients, most (60.5%) patients had an underweight body according to weight-for-age index and short stature according to stature-for-age, but only 14.0% of patients had poor nutrition based on weight-for-stature index. The average value of serum ferritin levels 2837.69 µg/L, ranged from 278.7-13867 µg/L. The result of Spearman correlation test between serum ferritin levels and nutritional status indicates the value of p=0.326 and r=0.153. There is no significant correlation between serum ferritin levels and nutritional status of children with β-thalassemia major.

Keywords: *thalassemia, serum ferritin, nutritional statu*

Lampiran 8.

DOI: https://doi.org/10.32539/BJI.V5I1.7986

Korelasi Antara Kadar Feritin Serum dan Status Gizi Pasien Talasemia-β Mayor

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ABSTRAK

Talasemia adalah penyakit kronik yang membutuhkan transfusi darah berulang, karena adanya gangguan sintesis hemoglobin akibat mutasi dari satu atau lebih gen globin. Transfusi secara terus menerus dapat menyebabkan terjadinya penimbunan besi dalam tubuh khususnya jantung, hati, dan organ endokrin, serta dapat menyebabkan pertumbuhan yang terhambat dan gizi kurang atau gizi buruk. Penelitian ini bertujuan untuk mengetahui korelasi antara kadar feritin serum dan status gizi pasien talasemia-β mayor di RSUP Dr. Moh. Hoesin Palembang. Penelitian ini merupakan penelitian observasional analitik dengan desain *cross sectional*. Sampel penelitian ini adalah pasien talasemia-β mayor yang menjalani rawat inap di Departemen Ilmu Kesehatan Anak RSUP Dr. Mohammad Hoesin pada bulan Oktober hingga November 2016 yang memenuhi kriteria keikutsertaan. Dari 43 pasien, sebagian besar (60.5%) pasien memiliki badan kurus sesuai dengan indeks berat badan menurut usia (BB/U) dan berperawakan pendek sesuai indeks tinggi badan menurut usia (TB/U), namun hanya 14.0% pasien memiliki gizi kurang menurut indeks BB/TB. Didapatkan nilai rata-rata kadar feritin serum 2837.69 µg/L, dengan rentang 278.7-13867 µg/L. Hasil uji korelasi antara kadar feritin serum dan status gizi menunjukkan nilai p=0.326 dan nilai r=0.153. Terdapat korelasi yang tidak bermakna antara kadar feritin serum dan status gizi pasien talasemia-β mayor.

Kata kunci: *talasemia, feritin serum, status gizi*

ABSTRACT

Thalassemia is a chronic disease that requires repeated blood transfusions, because of the haemoglobin production disorder due to defective synthesis of one or more globin chains. Repeated transfusions can lead to accumulation of iron in the body, especially the heart, liver, endocrine organs, and can cause stunted growth and malnutrition. The aim of this study was to determinate correlation between ferritin serum level and nutritional status of ß-thalassemia major patients at RSUP Dr. Moh. Hoesin Palembang. This study was an analytic observational study using a cross sectional design. Samples in this study were all hospitalized ß-thalassemia major patients in the Department of Pediatric Hospital Dr. Mohammad Hoesin Palembang in October to November which fits the inclusion criteria. From 43 patients, most (60.5%) patients had an underweight body according to weight-for-age index and short stature according to stature-for-age, but only 14.0% of patients had poor nutrition based on weight-for-stature index. The average value of serum ferritin levels 2837.69 µg/L, ranged from 278.7-13867 µg/L. The result of Spearman correlation test between serum ferritin levels and nutritional status indicates the value of p=0.326 and r=0.153. There is no significant correlation between serum ferritin levels and nutritional status of children with ß-thalassemia major.

Keywords: *thalassemia, serum ferritin, nutritional statu*

Lampiran 9.

June 2018/ Vol 5/ Issue 6 Print ISSN: 2349-5499, Online ISSN: 2349-3267

Editorial

Study of Serum ferritin levels in β-Thalassemia major children

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Correspondence Author: Dr. Bablu Kumar Gaur, Assistant Professor, Flat No- 11, E Block, M.M Residential Complex, MMU, Mullana, Ambala (Haryana). E-mail ID- drbkgaur@gmail.com

Abstract

Background: Thalassemiais one of the most common inherited single-gene disorder in the world. Every year approximately 100,000 thalassemia major children are born all over the world, and there are about 65,000-67,000 β thalassemia major patients in India, with around 9,000-10,000 cases being added every year. Measurement of serum ferritin level can give idea regarding starting of Iron chelation therapy, which will reduce the concentration of serum ferritin and effective in preventing iron induced tissue injury and prolonging life expectancy. **Method:** This study was conducted on 60 children between 3 to 17 years, being regularly transfused at department of Pediatrics, Kamala Raja Hospital, Gajra Raja Medical College, Gwalior, for period of 1 year from 2011 to 2012, after taking the informed consent from the parents and explaining them the purpose of study. Detailed history weretaken and serum ferritin level weremeasured by ELISA based serum ferritin assay kit. **Results:** Serum ferritin level was found to be elevated in all the patients of beta thalassemia major with range from 1050 to 5029 µg/l and with a mean value of 3879µg/l. Out of 60 patients, 30 (50%) patients had serum ferritin level below 2000µg/l,20 (33.3%) patients had serum ferritin value between 2001 to 4000 µg/l and rest 10 (17.7%) patients had values above 4000 µg/l. Mean value of serum ferritin was found to be higher in patients who received frequent blood transfusion. **Conclusion:** Majority of the patients had very high ferritin levels, with a mean value of 3879 µg/l. 50% patients had serum ferritin levels more than 2000µg/l. This cut off value reflect either inadequate chelation therapy or non-affordability of parents to purchase oral chelation therapy.

Key words: β-Thalassemia major, Serum ferritin, Blood transfusion

Introduction

Thalassemia is one ofthe most common inherited single-gene disorder in the world. Reportedly there are about 240 million carriers of beta thalassemia world wide and in India alone, the number is approximately 30 million with a mean prevalence of 3.3%. Every year approximately 100,000 thalassemia major children are born all over the world, and there are about 65,000-67,000β thalassemia major patients in India, with around 9,000-10,000 cases being added every year[1,2]

The name Thalassemia is derived from a combination of two Greek words: Thalassa meaning the sea, i.e. the Mediterranean, and anemia ("weak blood")[3]. It is characterized by deficient or absent synthesis of normal globin chains owing to inherited mutations of β- globin genes, where more than 200 mutations, mostly point mutations are seen in β thalassemia. There is an excess of alpha globin chains relative to beta and gamma globin chains and alpha globin tetramer formed that cause damage to both developing RBC and mature RBC. The gamma and delta globin are produced in increased amount leading to an elevated HbF and HbA2. Since β chains are not present in fetal hemoglobin, beta thalassemia major does not manifest itself in newborns. Beta thalassemia presents at 6 months of age when adult hemoglobin has replaced fetal hemoglobin.

The clinical course is characterized by severe anemia, failure to thrive, typical facies (also called chipmunk facies/thalassemic facies), marked hepatosplenomegaly,

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Lampiran 10.

REVISTA BRASILEIRA DE HEMATOLOGIA E HEMOTERAPIA

Artigo / Article

Determination of iron-overload in thalassemia by hepatic MRI and ferritin

Determinação da sobrecarga de ferro na talassemia pela IRM hepática e ferritina

Ivan L. Angulo[1]
Dimas T. Covas[2]
Antonio A. Carneiro[3]
Oswaldo Baffa[4]
Jorge Elias Junior[5]
Guilherme Vilela[6]

Accumulation of iron in thalassemia causes organ damage and reduces patient survival due to heart lesions in the second decade of life. Iron deposits are monitored by direct (biopsy) and indirect methods (ferritin) with sequential data being better than isolated measurements. This paper compares two indirect measurements of iron overload; a single hepatic iron concentration (HIC) by magnetic resonance and mean ferritin levels over four years. A retrospective study of 25 patients from the Centro Regional de Hemoterapia in Ribeirão Preto, Brazil was carried out. High HIC (above 7 mg per gram of dry weight) was found in 20 patients and high mean serum ferritin (above 2500 µg/L) in 10 patients. Stratification into three levels (low, moderate and high) of iron overload gave similar results in both tests. Many other factors influence de degree of iron overload in thalassemia. No correlation was found using a non-parametric statistical test between HIC and mean serum ferritin. Both methods provide better planning of chelation therapy. Rev. Bras. Hematol. Hemoter. 2008;30(6):449-452.

Key words: *Iron overload; thalassemia; magnetic resonance imaging; ferritin; chelation.*

Introduction

The accumulation of iron in thalassemia causes organic injuries and a reduction in survival and must be treated with iron chelators such as deferoxamine. The success of treatment depends essentially on patient adherence and can be evaluated by determining iron loading by direct or indirect methods. The accumulation of transfusional and absorbed iron in thalassemia is approximately 7 to 14 grams per year. The measurement of iron is important for the prognosis (risk of organic and associated injuries) and monitoring chelation.[1,2]

Ferritin is the principal iron storage protein, found in the liver, spleen, bone marrow, and to a small extent in the blood (serum ferritin - SF).[3] In the majority of clinical centers, the standard method of evaluating the total amount of body iron is measurement of the SF concentration in the blood.[4] However, the correlation between SF and body iron is not sufficiently precise to be of high prognostic value, especially when associated with inflammation or tissue damage. Moreover, alterations in the relationship between blood serum ferritin concentration and body iron content by chelation and vitamin C treatment are complex. For example, the relationship between serum ferritin and body iron appears to be singular for different hematologic conditions.[5] SF has been the primary clinical measure of iron stores in thalassemic patients undergoing transfusions. It is non-invasive, widely available, inexpensive, but has not been systematically compared to validated quantitative measurements of liver iron using techniques such as MRI.[6]

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Lampiran 11.

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Iron overload in beta thalassemia major patients

Atthanayaka Mudiyanselage Dilhara Sewwandi Karunaratna, JG Shirani Ranasingha, Rasnayaka Mudiyanselage Mudiyanse

ABSTRACT

Aims: Beta thalassemia is the most common monogenic hereditary hemoglobin disorder, which poses a major health burden to Sri-Lanka. Regular transfusions of erythrocytes required for survival of these patients lead to inevitable iron overload, which is manifested, by elevated serum ferritin levels. Progressive deposition of iron leads to dysfunction and failure of the major organs. The aim of this study was to evaluate the iron overload of the beta thalassemia major patients in one of the thalassemia centres in Sri Lanka and to find its effect on growth status of the patients. Methods: The study included forty patients with confirmed diagnosis of beta thalassemia major, undergoing any chelation treatment. The mean age of the study group was 10.97±5.9 years with a range of 2–20 years. The patients were interviewed for the socio-demographic variables and their medical histories were obtained from the hospital files. Serum ferritin concentration, height and weight of the patients were measured and body mass index (BMI) was calculated. Results: The mean serum ferritin concentration was 2992.2±1575.35 ng/ml which showed a significant correlation with age and duration of blood transfusion. The mean z-score for height was -2.3±1.06 and 50% of the patients were stunted. The mean z-score for BMI was -1.32±1.28 and 35% of the patients were wasted. Both height and BMI had no significant correlation with iron overload of the patients. Conclusion: Iron overload and growth retardation were common in beta thalassemia major patients of the treatment center evaluated in this study in Sri Lanka. However, there was no significant relationship between physical growth and iron overload.

Keywords: Beta thalassemia major, Growth status, Iron overload

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INTRODUCTION

Beta thalassemia is the most common monogenic hereditary hemoglobin disorder, which poses a major health burden in Sri Lanka. The national incidence of 60–80 cases per year together with the estimated life span

Lampiran 12.

Profil Pertumbuhan, Hemoglobin Pre-transfusi, Kadar Feritin, dan Usia Tulang Anak pada Thalassemia Mayor

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Latar belakang. Thalassemia adalah kelainan bawaan sintesis hemoglobin, dan salah satu penyakit monogenetik paling banyak dijumpai. Di Indonesia diperkirakan akan lahir 2500 anak dengan thalassemia mayor setiap tahunnya. Berkat kemajuan penanganan medis, sebagian besar pasien akan mengalami pertumbuhan normal pada masa anak-anak namun selanjutnya akan terjadi gangguan pertumbuhan dan keterlambatan pubertas secara signifikan.
Tujuan. Mengetahui gambaran tinggi badan, kecepatan tumbuh, usia tulang, kadar hemoglobin pretranfusi, dan kadar feritin serum pasien thalassemia.
Metode. Laporan serial kasus pada anak yang menjalani rawat inap di Sub-bagian Hematologi Bagian Ilmu Kesehatan Anak FK UNUD/RSUP Sanglah Denpasar dari bulan Desember 2010-Februari 2011. Data yang diperoleh disajikan dalam bentuk tabel.
Hasil Limabelas subyek thalassemia mayor, berumur antara 1,9 tahun – 13,5 tahun, 7 laki-laki dan 8 perempuan. Dua anak berumur kurang dari 3 tahun dan 7 anak telah memasuki usia pubertas. Semua pasien telah menjalani terapi kelasi besi deferioksamin namun kualitasnya tidak memadai. Perawakan pendek ditemukan pada 4 anak (26%), semua subjek mempunyai kecepatan tumbuh <5 cm/tahun. Secara klinis satu orang dikategorikan sebagai pubertas terlambat. Kadar hemoglobin rata-rata pre-transfusi dapat dipertahankan ≥8 mg/dl (10), sisanya (5) memiliki hemoglobin rata-rata di bawah 8 mg/dl. Empat anak dengan feritin serum di atas 3000 ng/ml, dan semua subjek mempunyai perawakan pendek. Pada evaluasi radiologi manus sinistra 5 anak memiliki usia tulang terlambat.
Kesimpulan. Perawakan pendek didapatkan pada 26% kasus dan semua subjek telah memasuki usia pubertas. Semua subjek mempunyai perawakan pendek dan memiliki kadar feritin serum >3000 ng/ml.
Sari Pediatri 2011;13(4):299-304.

Kata kunci: thalassemia, pertumbuhan terhambat, ferritin, kelasi deferioksamin

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Thalassemia adalah kelainan bawaan sintesis, dan salah satu penyakit monogenetik paling banyak di dunia. Pada tahun 1994 *World Health Organization* (WHO) menyatakan

Lampiran 13.

Annals of the College of Medicine Vol. 36 No. 1 & 2 2010

Serum ferritin level in transfusion dependent β-thalassaemia patients in Mosul

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(Ann. Coll. Med. Mosul 2010; 36 (1 & 2): 72-78).
Received: 10th Jan 2010; Accepted: 10th Nov 2010.

ABSTRACT

Objectives: To establish a correlation between serum ferritin and different clinical, biochemical and haematological parameters and to determine the efficacy of chelation therapy using desferrioxamine measured by serum ferritin.

Patients and Methods: A case-series of one hundred patients with transfusion dependent β-thalassaemia were included in the study during a period of one year (Nov. 2007-Nov.2008). The study included clinical evaluation, routine haematological tests and serum ferritin level.

Results: Mean value of serum ferritin in our patients was 1886.74 ng/ml. It was found that serum ferritin was higher in older patients, those who received higher number of blood transfusions to date and those of higher annual blood consumption. β-thalassaemic patients with serum ferritin level equal or higher than 2500 ng/ml were older, of shorter stature, had higher percentage of splenectomy, higher number of blood transfusions to date and higher annual blood consumption than patients with serum ferritin level less than 2500 ng/ml. It was found that patients with good compliance to chelation therapy with desferrioxamine had lower mean serum ferritin than patients with poor compliance. Thirty seven percent of our patients had growth retardation regarding weight for age and 57% were low in height for their age.

Conclusions: Serum ferritin was higher in older patients, those with higher annual blood consumption and those with poor compliance to desferrioxamine therapy when compared to patients with good compliance. Patients with serum ferritin equal to or more than 2500 ng/ml were older and of shorter stature for their age than patients with serum ferritin less than 2500 ng/ml.

الخلاصة

الاهداف:

١- إيجاد قيم حديدين المصل في مرضى الثلاسيميا نوع بيتا المعتمدين على نقل الدم في الموصل.

٢- تم تطبيق ارتباط بين حديدين المصل ومختلف القياسات السريرية والمخبرية (الدموية والكيماوية).

٣- قياس كفاءة دواء الدسفريوكسامين في القدرة على طرح عنصر الحديد من الجسم باستخدام حديدين المصل.

الحالات والطرق: شملت الدراسة ١٠٠ مريض بالثلاسيميا نوع بيتا المعتمدين على نقل الدم خلال الفترة الممتدة من (تشرين الثاني ٢٠٠٧- تشرين الثاني ٢٠٠٨). تضمنت الدراسة تقييماً سريرياً وفحص الدم الكامل بالإضافة إلى فحص حديدين المصل.

النتائج: معدل حديدين المصل لدى مرضانا هو ١٨٨٦,٧ نانوغرام/ملليتر. وجد أن حديدين المصل كان أعلى عند المرضى الأكبر سناً وأولئك الذين استلموا العدد الأعلى من قناني للدم حتى وقت أجراء الفحص وأولئك الذين يكون استهلاك الدم السنوي لديهم عالياً. وجد أيضاً أن مرضى الثلاسيميا نوع بيتا المعتمدين على نقل الدم الذين كان لديهم حديدين المصل مناظراً أو أعلى من ٢٥٠٠ نانوغرام/ملليتر كانوا أكبر سناً وأقصر قامة ولديهم نسبة أعلى من عمليات رفع الطحال واستلموا عدداً أكبر من قناني الدم حتى وقت اجراء الفحص واستهلاكهم السنوي للدم كان أعلى من أولئك الذين كان لديهم

Gambaran Kadar Feritin Serum pada Penderita Talasemia Mayor yang Menjalani Transfusi Rutin (Studi Pustaka)

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Abstrak
Talasemia merupakan penyakit genetik yang ditandai adanya kelainan pada sintesis hemoglobin sehingga banyak terjadi pemecahan sel darah merah dan menimbulkan anemia. Untuk menangani anemia tersebut diperlukan transfusi darah yang rutin. Penderita talasemia mayor yang menerima transfusi berulang akan mengalami penumpukan zat besi dan terjadi peningkatan kadar feritin serum. Pemeriksaan feritin serum merupakan pemeriksaan yang paling sering digunakan untuk mengevaluasi kelebihan zat besi pada penderita talasemia mayor. Tujuan penelitian ini adalah untuk mengetahui gambaran kadar feritin serum pada penderita talasemia mayor. Jenis penelitian ini adalah studi pustaka. Hasil studi pustaka didapatkan bahwa rata-rata kadar feritin serum pada penderita talasemia mayor dari penelitian Ghosh (2021): 2995.78 ng/ml, Rathaur: 1560.9 ng/ml, Soewondo: 2976.8 ng/ml, Amelia: 2842.85 ng/ml, Rafika: 2837.69 ng/ml, Koreti: 3879 ng/ml, Angulo: 2337 ng/ml, Karunaratna: 2992.2 ng/ml, Made: 2703.18 ng/ml, dan Faris: 1886.74 ng/ml. Sedangkan rentangnya dari penelitian Ghosh: 1804 – 6231 ng/ml, Rathaur: 207 – 9848.9 ng/ml, Soewondo: 702.2 – 8897.7 ng/ml, Amelia: 647 – 9978 ng/ml, Rafika: 278.7 – 13867 ng/ml, Koreti: 1050 – 5029 ng/ml, Angulo: 481 – 7595 ng/ml, Karunaratna: 875.5 – 7625 ng/ml, Made: 1180.0 – 6383.3 ng/ml, dan Faris: 380 – 7990 ng/ml.

Kata Kunci: Talasemia Mayor, Transfusi Darah, dan Feritin Serum

Serum Ferritin Levels in Thalassemia Major Receiving Routine Blood Transfusions (Literature Review)

Abstract
Thalassemia is a genetic disease characterized by abnormalities in the synthesis of hemoglobin so that a lot of red blood cell breakdown occurs and causes anemia. To treat anemia in patients with thalassemia major, regular blood transfusions are required. Patients with thalassemia major who receive repeated transfusions will experience a buildup of iron in the body and an increase in serum ferritin levels. Serum ferritin is the most frequently used test to evaluate iron overload in patients with thalassemia major. The purpose of this study was to determine the description of serum ferritin levels in patients with thalassemia major. This type of research is a literature study using 10 scientific journal articles. The results of the literature study showed that the average serum ferritin level in patients with thalassemia major from Ghosh's study (2021): 2995.78 ng/ml, Rathaur: 1560.9 ng/ml, Soewondo: 2976.8 ng/ml, Amelia: 2842.85 ng/ml, Rafika: 2837.69 ng/ml, Koreti: 3879 ng/ml, Angulo: 2337 ng/ml, Karunaratna: 2992.2 ng/ml, Made: 2703.18 ng/ml, and Faris: 1886.74 ng/ml. Meanwhile, the research ranges from Ghosh: 1804 – 6231 ng/ml, Rathaur: 207 – 9848.9 ng/ml, Soewondo: 702.2 – 8897.7 ng/ml, Amelia: 647 – 9978 ng/ml, Rafika: 278.7 – 13867 ng/ml, Koreti : 1050 – 5029 ng/ml, Angulo: 481 – 7595 ng/ml, Karunaratna: 875.5 – 7625 ng/ml, Made: 1180.0 – 6383.3 ng/ml, and Faris: 380 – 7990 ng/ml.

Keywords*: Thalassemia Major, Blood Transfusion, and Serum Ferritin*

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Pendahuluan

Talasemia merupakan salah satu penyakit turunan terbanyak yang menyerang hampir semua golongan etnik dan terdapat pada hampir seluruh negara di dunia. Data dari WHO menunjukan bahwa 7% dari populasi dunia merupakan pembawa sifat talasemia. Setiap tahun sekitar 300.000-500.000 bayi baru lahir disertai dengan kelainan hemoglobin berat dan 50.000 hingga 100.000 anak meninggal akibat talasemia (Kemenkes, 2018).

Indonesia termasuk salah satu negara dengan angka pembawa sifat talasemia yang tinggi. Hal ini terbukti dari penelitian epidemiologi di Indonesia yang mendapatkan bahwa frekuensi gen talasemia berkisar 3-10%.

Talasemia adalah kelainan genetik yang ditandai dengan adanya gangguan sintesis rantai protein globin pada produksi hemoglobin. Hal ini menyebabkan gangguan pembentukan hemoglobin sehingga banyak pemecahan sel darah yang menimbulkan anemia (Rochman dkk, 2019). Pada penderita talasemia tubuh tidak dapat membentuk sel darah merah yang normal, sehingga sel darah merah mudah rusak atau berumur pendek kurang dari 120 hari (Rachmaniah, 2012).

Talasemia diklasifikasikan berdasarkan genotifnya menjadi 2 yaitu talasemia α dan talasemia β. Sedangkan berdasarkan derajat berat ringannya gejala klinisnya talasemia dibagi menjadi talasemia minor, talasemia intermedia, dan talasemia mayor. Talasemia α terjadi karena akibat berkurangnya atau tidak diproduksi sama sekali rantai globin-α, sedangkan talasemia β terjadi akibat berkurangnya atau tidak diproduksi sama sekali rantai globin-β (Nuari, 2013). Talasemia minor atau pembawa sifat, hidup seperti orang normal, tidak bergejala sama sekali dan tidak membutuhkan transfusi darah. Talasemia intermedia tetap dapat hidup normal tetapi memerlukan transfusi darah tapi tidak rutin. Sedangkan talasemia mayor dapat hidup dengan normal jika mendapatkan pengobatan optimal dengan transfusi darah rutin, konsumsi obat kelasi besi teratur dan pemantauan ketat oleh dokter (Kemenkes, 2018).

Mayoritas penderita talasemia mayor memiliki kadar hemoglobin < 10 g/dL. Manajemen utama anemia pada pasien talasemia mayor adalah transfusi darah. Pemberian transfusi darah bertujuan untuk mempertahankan hemoglobin pada kisaran kadar normal atau mendekati normal (Bulan, 2009). Transfusi ini harus dilakukan sepanjang hidup bagi para penderita talasemia mayor dan dilakukan secara rutin dalam periode 4-5 minggu sekali. Transfusi darah berulang jangka panjang menyebabkan kelebihan besi di berbagai organ sehingga menyebabkan kerusakan organ tersebut bahkan dapat menimbulkan kematian (Permatasari, 2019).

Zat besi dalam tubuh beredar dalam darah berikatan dengan transferin, kemudian digunakan oleh sumsum tulang dalam proses eritropoesis. Tubuh sendiri mempunyai kemampuan terbatas untuk mengekskresikan zat besi (Kohgo et al, 2008). Pada manusia normal, zat besi yang tertinggal dalam tubuh digunakan untuk membentuk sel darah merah yang baru. Lain halnya dengan pasien talasemia, zat besi akan menumpuk dalam organ tubuh seperti hati, limpa, kulit dan jantung sehingga dapat mengganggu fungsi organ tersebut.

Feritin merupakan protein yang berperan menyimpan zat besi di dalam tubuh. Kadar feritin sangat berguna untuk mendiagnosis keadaan defisiensi zat besi atau keadaan kelebihan zat besi. Kadar feritin normal berkisar antara 20 ng/ml sampai 200 ng/ml. Pada pasien talasemia yang mengalami kelebihan besi akibat transfusi darah berulang, feritin serum akan meningkat. Pemeriksaan feritin serum adalah salah satu pemeriksaan yang digunakan untuk mendeteksi kelebihan zat besi dan mengevaluasi efektivitas terapi kelasi besi dan yang paling banyak digunakan (Ikram et al, 2014).

Metodologi Penelitian

Jenis dan racangan yang digunakan pada penelitian ini adalah studi kepustakaan yang didapat dengan menelaah artikel, jurnal ilmiah, dan buku yang berkaitan dengan kadar feritin serum pada penderita talasemia mayor, yang dipublikasikan secara nasional maupun internasional dalam waktu 10 tahun terakhir. Terdapat dua kriteria dalam penelitian ini yaitu kriteria inklusi yang mendukung penelitian yaitu jurnal yang memenuhi syarat yang menjawab semua tujuan penelitian ini, sedangkan kriteria eksklusi adalah yang tidak mendukung penelitian ini yaitu jurnal yang hanya menjawab salah satu tujuan atau tidak menjawab semua tujuan penelitian ini. Waktu yang digunakan peneliti untuk

melakukan penelitian kepustakaan ini yaitu dilaksanakan dari Maret – Juni 2021.

Hasil dan Pembahasan

Penelitian ini menggunakan metode kepustakaan dengan mengkaji beberapa literatur yang relevan dengan tema penelitian. Literatur yang diperoleh dari penelusuran yang digunakan adalah literatur yang dipublikasikan secara nasional dan internasional. Berdasarkan hasil review dari 10 literatur didapatkan hasil sebagai berikut.

No.	Penulis Jurnal	Rata-rata Kadar (ng/ml)	Rentang Kadar (ng/ml)
1.	Ghosh (2021)	2995.78	1804 – 6231
2.	Rathaur (2020)	1560.9	207 – 9848.9
3.	Soewondo (2020)	2976.8	702.2 – 8897.7
4.	Amelia (2020)	2842.85	647 – 9978
5.	Rafika (2019)	2837.69	278.7 – 13867
6.	Koreti (2018)	3879	1050 – 5029
7.	Angulo (2018)	2337	481 – 7599
8.	Karunaratna (2017)	2992.2	875.5 – 7625
9.	Made (2011)	2703.18	1180.0 – 6383.3
10.	Faris (2010)	1886.74	380 – 7990

Berdasarkan tabel dari penelusuran 10 artikel yang terkait dilakukaan pembahasan untuk menjawab tujuan penelitian sebagai berikut:

Dari hasil penelitian didapatkan 10 jurnal menyatakan bahwa terdapat kadar feritin serum yang tinggi di atas nilai normal pada penderita talasemia mayor yang menjalani transfusi rutin. Tingginya kadar feritin serum pada penderita talasemia mayor disebabkan oleh transfusi berulang yang diterimanya (Permatasari, 2019). Penderita talasemia mayor memerlukan transfusi darah secara rutin untuk mengatasi anemia yang disebabkan oleh pemecahan sel darah merah akibat adanya gangguan pada sintesis rantai protein globin saat pembentukan hemoglobin (Bakta, 2014). Mayoritas penderita talasemia mayor memiliki kadar hemoglobin kurang dari nilai normal (Bulan, 2009). Hal tersebut sejalan dengan penelitian Made (2011) yang menunjukkan hasil bahwa penderita talasemia mayor memiliki kadar hemoglobin pre-transfusi yang rendah yaitu <10 g/dL.
Namun, transfusi yang berulang akhirnya meyebabkan dampak lain yaitu kelebihan zat besi di dalam tubuh (Safitri, 2015). Kelebihan zat besi akibat transfusi berulang merupakan efek samping yang tidak bisa dihindari lagi oleh penderita talasemia mayor. Hal ini dikarenakan tiap 450 ml darah yang ditransfusikan mengandung sekitar 200 – 250 mg besi, sedangkan kemampuan tubuh untuk mengekskresikan zat besi sangat terbatas. Kelebihan zat besi di dalam tubuh ditandai dengan peningkatan kadar feritin serum (Hoffbrand, 2013).

Penderita talasemia mayor yang menjalani terapi transfusi darah harus melakukan serangkaian pemeriksaan laboratorium, salah satunya adalah pemeriksaan feritin serum (Atmakusuma, 2014). Feritin serum menjadi marker penting dalam penentuan jumlah besi total dalam tubuh. Pemeriksaan feritin serum merupakan pemeriksaan yang paling sering digunakan untuk mengevaluasi kelebihan zat besi pada pasien talasemia mayor, sebab pemeriksaan ini mudah dilakukan jika dibandingkan dengan pemeriksaan kadar besi lainnya (M Shah, 2014).

Berdasarkan hasil penelitian dari 10 jurnal yang berkaitan dengan kadar feritin serum pada penderita talasemia mayor, didapatkan bahwan kadar feritin serum pada penderita talasemia mayor yang menjalani transfusi rutin mengalami peningkatan sehingga berada diatas nilai normal. Pada hasil kajian di tabel 4.1 didapatkan bahwa rata-rata kadar feritin serum pada pada penderita talasemia mayor yaitu >1000 ng/ml. Nilai tersebut merupakan nilai yang sangat tinggi jika dibandingkan nilai normal feritin serum yaitu yang berkisar antara 20 – 200 ng/ml (Ikram et al, 2014).

Kemudian untuk rentang kadar didapatkan kadar feritin serum dengan kadar terendah yaitu 207 ng/ml, sedangkan untuk kadar tertinggi yaitu 13867 ng/ml. Menurut penelitian Faris (2010) kadar feritin serum yang lebih tinggi ditemukan pada penderita talasemia yang menerima transfusi darah lebih banyak. Begitupula dengan penelitian Koreti (2018) dan Karunaratna (2017) yang mengatakan bahwa penderita yang menerima transfusi darah lebih banyak

memiliki kadar feritin serum yang lebih tinggi. Semakin banyak penderita talasemia mayor menerima transfusi darah, maka kadar feritin serum akan semakin tinggi. Hal ini dikarenakan kadar feritin serum meningkat sejalan dengan pertambahan akumulasi zat besi di dalam tubuh yang terjadi karena transfusi yang berulang (Ningrum, 2020).

Tingginya kadar feritin serum pada penderita talasemia mayor merupakan masalah serius yang harus ditangani dengan tepat karena jika tidak maka akan terjadi penumpukan zat besi dan dapat menyebabkan kerusakan beberapa organ dan jaringan di dalam tubuh. Kondisi ini dapat dicegah dengan pemberian terapi kelasi besi (Oktavia, 2017). Ketika kadar feritin serum sudah melebihi dari 1000 ng/ml atau biasanya setelah menerima 10 – 12 kali transfusi, maka dibutuhkan terapi kelasi besi (Kemenkes, 2018).

Terapi kelasi besi berfungsi untuk mengurangi kelebihan zat besi dengan cara mengikat zat besi dan mengeskresikan sebagian besar melalui feses dan urin. Beberapa penelitian menunjukkan bahwa penderita talasemia mayor yang menerima kelasi besi memiliki kadar feritin serum yang lebih rendah dibandingkan penderita yang tidak menerima kelasi besi. Hasil penelitian oleh Riaz (2011) menunjukkan hasil nilai rata-rata kadar feritin serum mengalami penurunan setelah pemberian obat kelasi besi dibandingkan sebelum pemberian kelasi besi.

Kesimpulan

1. Rata-rata kadar feritin serum pada penderita talasemia mayor yang menjalani transfusi rutin dari penelitian Ghosh (2021): 2995.78 ng/ml, Rathaur: 1560.9 ng/ml, Soewondo: 2976.8 ng/ml, Amelia: 2842.85 ng/ml, Rafika: 2837.69 ng/ml, Koreti: 3879 ng/ml, Angulo: 2337 ng/ml, Karunaratna: 2992.2 ng/ml, Made: 2703.18 ng/ml, dan Faris: 1886.74 ng/ml.
2. Rentang kadar feritin serum pada penderita talasemia mayor yang menjalani transfusi rutin dari penelitian Ghosh: 1804 – 6231 ng/ml, Rathaur: 207 – 9848.9 ng/ml, Soewondo: 702.2 – 8897.7 ng/ml, Amelia: 647 – 9978 ng/ml, Rafika: 278.7 – 13867 ng/ml, Koreti: 1050 – 5029 ng/ml, Angulo: 481 – 7595 ng/ml, Karunaratna: 875.5 – 7625 ng/ml, Made: 1180.0 – 6383.3 ng/ml, dan Faris: 380 – 7990 ng/ml.

Saran

1. Untuk klinisi, perlu dilakukannya pemantauan dan pemeriksaan feritin serum secara rutin dan dilakukan terapi kelasi besi ketika kadar feritin serum sudah melebihi 1000 ng/ml.
2. Untuk peneliti selanjutnya dapat dilakukan penelitian lanjutan mengenai analisis hasil pemeriksaan status zat besi selain feritin serum seperti besi serum, saturasi transferin dan kapasitas ikat besi total pada penderita talasemia mayor.

Daftar Pustaka

Angulo, I.L. 2018. *Determination of Iron Overload in Thalassemia by Hepatic MRI and Ferritin.* Brazilian Journal of Hematology and Hemotherapy.

Agustina, R., Mandala,Z., & Sahara, R. 2020. *Hubungan Kadar Feritin Serum dan Kejadian Stunting pada Anak Talasemia Beta Mayor*. Jurnal Ilmiah Kesehatan Sandi Husada.

Amelia, S., et al. 2020. *The Relation Between Types of Iron Chelators and Ferritin on Osteocalcin of Thalassemia Patients with Repeated Transfusions.* Diponegoro Medical Journal.

Atmakusuma, D & Setiyaningsih, I. 2014. "Dasar-dasar Thalassemia: Salah Satu Jenis Hemoglobinopati" di dalam *Buku Ajar Ilmu Penyakit Dalam.* Fakultas Kedokteran Universitas Indonesia, Jakarta.

Bakta, I.M. 2014. *Hematologi Klinik Ringkas. Jakarta* : EGC.

Bulan, S. 2009. *Faktor-faktor yang Berhubungan dengan Kualitas Hidup Anak Thalassemia Beta Mayor*. Skripsi. Fakultas Kedokteran Universitas Diponegoro. Semarang.

Faris, Y., & Sadoon, O.A. 2010. *Serum Ferritin Levels in Transfusion Dependen Beta Thalassemia Patients in Mosul.* Annals of the College of Medicine.

Ghosh, S., & Chakrabarti, D. 2021. *Estimation of Serum Ferritin and TSH Levels in Thalassemia Patients Undergoing Iron Chelation Therapy*. Bangladesh Journal of Medical Science.

Herdata, H.N. 2008. *Thalasemia Mayor*. Welcome and Joining Pediatric Hematology Oncology in Indonesia.

Hoffbrand, A.V & Moss, P.A.H. 2013. *Kapita Selekta Hematologi*. Jakarta : EGC.

Ikram, N., et al. 2014. *Feritin Levels in Patient of Beta Thalasemia Major.* International Journal of Pathology.

Karunaratna, A.M.D.S., Ranasingha, J.G.S., & Mudiyanse, K.M. 2017. *Iron Overload in Beta Thalassemia Major Patients.* International Journal of Blood and Immunohematology.

Kementrian Kesehatan RI. 2018. *Apakah Pasien Thalassemia Dapat Hidup Normal.*

Koreti, S., et al. 2018. *Study of Serum Ferritin Levels in Beta Thalassemia Major Children.* International Journal of Pediatric Research.

Made, A., & Ketut, A. 2011. *Profil Pertumbuhan, Hemoglobin Pre-Transfusi, Kadar Feritin, dan Usia Tulang Anak pada Thalassemia Mayor. Sari Pediatri.*

M Shah, A., et al. 2014. *Iron Overload Status in Beta Thalassemia Major.* International Journal Medical Research.

Naseh, S., 2013. *Keunggulan dan Keterbatasan Beberapa Metode Penelitian Kesehatan.* Media Litbangkes.

Ningrum, I.P. 2020. *Gambaran Kadar Feritin Serum pada Penderita Talasemia Beta Mayor yang Melakukan Transfusi Rutin.* Karya Tulis Ilmiah. Jurusan Teknologi Laboratorium Medis, Politeknik Kesehatan Jakarta III. Jakarta.

Nuari, A. 2013. *Hubungan Kadar Feritin Serum dengan Aktivitas Enzim Aspartar Aminotransferase (AST), Alanin Aminotransferase (ALT) dan Status Gizi pada Anak Talasemi B mayor.* Journal of Chemical Information and Modeling.

Oktavia, S., Widajanti, L., & Aruben, R. 2017. *Faktor-faktor yang Berhubungan dengan Status Gizi Buruk pada Balita di Kota Semarang Tahun 2017.* Jurnal Kesehatan Masyarakat.

Partinah, Raden. 2017. *Gambaran Kadar Feritin Serum Wanita Hamil Trisemester I di Rumah Sakit Umum Hasanah Graha Afiah Depok Periode April 2016-Juli 2017*. Skripsi. Fakultas Kedokteran dan Ilmu Kesehatan Universitas Islam Negeri Syarif Hidayatullah. Jakarta

Permatasari, T.D., dkk. 2019. *Hubungan Antara Kadar Feritin dengan Kadar Malondialdehyde pada Pasien Talasemia Beta Mayor di RSD dr. Soebandi Jember.* e-Journal Pustaka Kesehatan.

Permono, B., dkk. 2012. *Buku Ajar Hematologi-Onkologi Anak*. Jakarta : IDAI.

Rachmaniah, D. 2012. *Pengaruh Psikoedukasi terhadap Kecemasan dan Koping Orang Tua dalam Merawat Anak dengan Thalasemia Mayor di RSU Kabupaten Tangerang Banten.* Tesis. Fakultas Ilmu Keperawatan Universitas Indonesia. Depok.

Rafika, dkk. 2019. *Korelasi antara Kadar Feritin Serum dan Status Gizi Pasien Talasemia Beta Mayor.* Biomedical Journal of Indonesia: Fakultas Kedokteran Universitas Sriwijaya.

Rathaur, V.K., Imran, A., & Pathania, M. 2021. *Growth Pattern in Thalassemia Children and Their Corelation with Ferritin Serum.* Journal of Family Medicine and Primary Care.

Riaz, H., et al. 2011. *Serum ferritin levels, socio-demographic fators and desferrioxamine therapy in multi-transfused thalassemia major patients at a government tertiary care hospital of Karachi, Pakistan.* BMC Research.

Rochman, F., Mulyantari, N.K., & Sutirtayasa, I.W.P. 2019. *Hubungan Jumlah Transfusi Darah dan Penggunaan Kelasi Besi dengan Kadar Feritin pada Pasien Talasemia.* Jurnal Medika Udayana.

Rujito, Lantip. 2019. *Genetik Dasar dan Pengelolaan Terkini*. Purwokerto: Universitas Jendral Soedirman.

Soewondo, W., et al. 2020. *Ferritin and Genu Points Ultrasound in Beta Thalassemia Major.* GSC Advanced Research and Reviews.