



Analysis of Real Costs and INA-CBG of Hyperthyroidism in Hasanuddin University Hospital

Analisis Perbedaan Biaya Riil dan Tarif INA-CBG Pasien Hipertiroid di Rumah Sakit Universitas Hasanuddin

Siti Saharah Abdullah^{1*}, Amelia Lorensia¹, Suyanto²

¹Faculty of Pharmacy, Surabaya University

²Faculty of Business and Economics, Surabaya University

*Email korespondensi: abdullahsiti1593@gmail.com

ARTICLE INFO

Article History:

Received Aug, 6th, 2020

Revised form Nov, 18th, 2020

Accepted Des, 17th, 2020

Published online Des, 31st, 2020

Keywords:

Real costs;
hyperthyroidism;
INA-CBG;

Kata Kunci:

Biaya riil;
hipertiroid;
INA-CBG;

ABSTRACT

Hyperthyroid disease requires continuous treatment with not cheap medical costs. For JKN participants, the cost of treating hyperthyroidism has been fully covered by BPJS through the INA-CBG package. However, there is often a mismatch between the INA-CBG package and the real hospital costs thus causing losses for the hospital. This research is a comparative study with a hospital perspective and the purpose of this study is analyze difference between direct medical cost of hospitals and INA-CBG package for the treatment of JKN outpatient hyperthyroidism patient in Hasanuddin University Hospital (RSUH) Makassar using data from January 2017 to December 2018. Data collection was carried out by retrospective observational and data analysis using statistical non-parametric tests. The results showed that INA-CBG package cannot cover all components of the costs of treating hyperthyroid disease. The laboratory cost has a proportion of 83% of the total medical cost, which is an average of IDR 465.683,70 every patient. Meanwhile, the INA-CBG rate with code Q-5-44-0 only covers medical expenses of IDR 185.500 every patient. The conclusion of this study shows that there is a negative difference (-) between the real cost of the hospital and the INA-CBG rate, which is IDR 34.406.900,00 and an average of IDR 373.988.04 every patient. The recommendation is related to adjustment of the INA-CBG rate to cover the riil costs.

ABSTRAK

Penyakit hipertiroid memerlukan pengobatan secara berkesinambungan dengan biaya pengobatan yang tidak murah. Bagi peserta JKN biaya pengobatan penyakit hipertiroid telah di cover sepenuhnya oleh BPJS melalui paket INA-CBG. Namun, sering terdapat ketidak cocokan antara paket INA-CBG dengan biaya riil rumah sakit. Sehingga, menimbulkan kerugian bagi rumah sakit. Penelitian ini merupakan studi perbandingan dengan perspektif rumah sakit dan tujuan dari penelitian ini adalah menganalisis perbedaan antara biaya riil rumah sakit dengan tarif paket INA-CBG pada pasien hipertiroid rawat jalan peserta JKN di Rumah Sakit Universitas Hasanuddin (RSUH) Makassar menggunakan data periode Januari 2017 sampai dengan Desember 2018. Pengumpulan data dilakukan secara observasional retrospektif dan analisis data menggunakan statistic non parametric test. Hasil penelitian menunjukkan bahwa tarif paket INA-CBG tidak dapat menutupi semua komponen biaya pengobatan pada penyakit hipertiroid. Komponen biaya laboratorium memiliki proporsi sebesar 83% dari total biaya pengobatan yaitu rata-rata sebesar Rp. 465.683,70 per pasien. Sedangkan, tarif paket INA-CBG dengan kode Q-5-44-0 hanya menanggung biaya pengobatan sebesar Rp. 185.500 per pasien. Kesimpulan dari penelitian ini menunjukkan adanya selisih negatif (-) antara biaya riil rumah sakit dengan tarif paket INA-CBG yaitu sebesar Rp.34.406.900,00 dan rata-rata sebesar Rp.373.988,04 per pasien. Sehingga, memerlukan adanya rekomendasi penyesuaian tarif INA-CBG.

INTRODUCTION

Hyperthyroid disease is an abnormalities dysfunction of the thyroid gland, and this disease is found in many societies. The prevalence of hyperthyroid disease in Europe is 0,8% and in the United States is 1,3%.¹ Meanwhile, the prevalence of hypothyroidism in Indonesia is 0,4% and in the South of Sulawesi is 0,5%.^{2,3} Hyperthyroidism is a condition when the thyroid gland is hyperactive in producing thyroid hormones so that the thyroid hormone levels in the blood increase and are above normal limits.⁴

Treatment of hyperthyroid disease must be carried out continuously with antithyroid drug therapy for at least 1-2 years so that it requires expensive medical costs, and causing the low level of public awareness to check themselves and take medication when experiencing clinical symptoms of hyperthyroidism are social and economic factors.^{2,5} The untreated hyperthyroid disease can lead to serious clinical complications and disadvantage patients so, increasing health care costs.^{6,7}

However, for JKN participants, all costs for treating hyperthyroidism are borne by BPJS. JKN stands for National Health Insurance which functions to meet the needs of proper health for the community.⁸ The implementation of claim payments for treatment provided by the hospital as an advanced health facility uses the Indonesian Case Based Groups (INA-CBG) prospective payment package system.⁹ Determination of the hospital real cost rate serves to

minimize losses from each cost of activities and services which include operating costs, maintenance, development and improvement of the quality of hospital services.¹⁰ In addition, the determination of the hospital service tariff must be in line with the increase in the value of hospital services and the ability of the community to pay for each of these services.¹⁰ Since the JKN system was implemented in several hospitals there has often been a mismatch between the real hospital costs and the INA-CBG package,¹⁰ so it is necessary to do research on the analysis of the difference in real hospital costs and INA-CBG on hyperthyroidism.

This research is an extension of the research that has been conducted by Dian Ayu Juwita, Suhatri and Risa Hestia, in two things, that is the differences in the focus of observation and differences in research methods. This study has the advantage of the method used in analyzing direct medical cost comparisons with an INA-CBG package from BPJS. While the focus of observation focuses on the component of outpatient hyperthyroid treatment costs at the Hasanuddin University Hospital (RSUH). Because, from the medical record data of outpatient RSUH it is known that the total of patients with a diagnosis of hyperthyroidism is increasing every year.¹¹ The use of new methods that support the comparison of recent costs in this study. The purpose of this study was to analyze the real hospital costs with the INA-CBG package for outpatient hyperthyroidism participating in JKN at RSUH.

MATERIAL AND METHOD

This study used a retrospective observational with a hospital perspective and used two types of data that is, qualitative data and quantitative data. Qualitative data are descriptive data obtained from Hospital medical records, quantitative data is the form of numbers or nominal information on the results of tracing, medical costs and the INA-CBG package for outpatient hyperthyroid patients JKN participant using data from January 2017 to December 2018. Direct medical costs or real hospital costs are costs incurred in accordance with valid proof of expenditure as compensation received by the hospital for services provided to patients.¹² Meanwhile, the INA-CBG package is a system of claim fee packages by BPJS which functions as hospital claim costs based on grouping of diseases and therapies that have similarities.¹² Cost data are obtained from the Hospital Management Information System (SIM-RS) in the casemix unit, the research was conducted in July 2019-June 2020 and has obtained an ethical approval recommendation from the Hasanuddin University Medical Faculty (FKUH) with a number 6/UN4.6.4.5.31/PP36/2019.

The population in this study was outpatient hyperthyroidism with a total population of 1,139 and the sampling technique used was purposive sampling.¹³ The total of samples in this study was 92 respondents who were determined based on the results of calculations using the Yamane formula.¹³ The data were collected by tracing secondary data in

the form of medical records and data on medical bills through SIM-RS in the casemix unit and outpatient pharmacy installation of RSUH. The collected data is then processed with statistical software in the form of Statistical Package for Social Sciences (SPSS) version 23 that is, using univariate data analysis and descriptive statistics to describe the characteristics and components of the real hospital costs and test the difference between two or more groups of variables using a non parametric test that is, mann whitney u test and kruskall wallis.¹³ The data analysis to see a comparison between real hospital costs and INA-CBG rates analyzed using the mann whitney u test.

RESULTS

Analysis of basic characteristics was carried out on each research respondent grouped by gender, age, education level and type of worker. The results of the characteristics respondent's analysis are presented in Table 1. The distribution of the basic characteristics of research respondents based on the female gender group was more than that of male respondent that is, as much 77 patients. The highest distribution of characteristics in the age group of 26-35 years and the lowest in the 56-65 years age group with 11 patients. The distribution of the characteristics of the highest education level that is, the Senior High School group of 45 patients and the education level group with the least total of respondents of the Junior High School group with 8 patients. The distribution of the characteristics of the types of workers was mostly in the unemployed group as

many as 58 patients and for the not working group most of the housewives (IRT) were 34 patients (Table 1).

The results of the analysis of the components of treatment costs in Table 2, it can be concluded that, of 92 outpatient hyperthyroid patients who completed one treatment cycle included administration costs, doctor consultation costs, laboratory examination costs and drug costs. The cost component that has the largest cost of the total real hospital costs, sequentially, is the laboratory cost of 83% or an average of IDR 465.683,70 every patient, doctor

consultation fee 12% or an average of IDR 69.347,83 every patient. Patients, the cost of drugs is 3% or an average of IDR 14.347,83 every patient and 2% administration fee with an average of IDR. 10.108,70 every patient (Table 2).

The results of statistical analysis in Table 3. Can be concluded that the INA-CBG package cannot cover all components of the costs incurred by hyperthyroid patients, causing the difference (-) IDR 373.988,04 every patient.

Table 1. Characteristics of Respondents

Characteristics	n = 92	Total Cost (IDR)	Average Cost (IDR)	St. Dev (IDR)	p
Gender					
Male	15	7.926.600,00	528.440,00	87699,1676	0,173
Female	77	43.546.300,00	565.536,36	102447,77	
Age (Years)					
17-25	18	10.118.100,00	562.116,67	69701,9896	0,603
26-35	26	14.353.400,00	552.053,85	108629,794	
36-45	21	12.017.700,00	572.271,43	114699,273	
46-55	16	8.523.100,00	532.693,75	110283,172	
56-65	11	6.460.600,00	587.327,27	86285,3416	
Level of Education					
Elementary School	14	8.138.500,00	581.321,43	97915,9937	0,555
Junior High School	8	4.039.600,00	504.950,00	99806,9852	
Senior High School	45	25.285.100,00	561.891,11	111646,817	
University	25	14.009.700,00	560.388,00	78802,5926	
Type of Workers					
Working	34	18.475.300,00	543.391,18	94214,0225	0,547
Not Working	58	32.997.600,00	568.924,14	103933,404	

Source: Secondary Data of the Hospital SIM, 2017-2018

Table 2. Component of Real Cost in Hyperthyroid Patients

Cost component	Total (IDR)	Average (IDR)	Proportion (%)	St. Dev (IDR)
Administrative Costs	930.000,00	10.108,70	2	3550,1324
Doctor Consultation Costs	6.380.000,00	69.347,83	12	25615,6866
Laboratory Costs	42.842.900,00	465.683,70	83	98125,5602
Drug Costs	1.320.000,00	14.347,83	3	9605,3268

Source: Secondary Data of the Hospital SIM, 2017-2018

Table 3. Difference between Real Hospital Costs and INA-CBG Package Rates

Total Respondents	Total Real Costs (IDR)	INA-SBG Package (Q-5-44-0)	p	Total Difference (IDR)	Difference in Average (IDR)
92	51.472.900,00	17.066.000,00	0,000	(-) 34.406.900,00	(-) 373.988,04

Source: Secondary Data of the Hospital SIM, 2017-2018

DISCUSSION

Hyperthyroid disease is a type of autoimmune disease caused by an increase in the synthesis and secretion of thyroid hormones in the thyroid gland so that thyroid hormone levels increase in the blood.⁴ Thyroid hormone has an important role in growth, nerve development, reproductive system, and regulation of energy metabolism.¹⁴

According to gender of the Hyperthyroid outpatient the total of female is bigger than male. Hyperthyroid disease is diagnosed both of male and female but, in the female more risk to suffer from the Hyperthyroid disease it causes some factor and one of them is the effect of estrogen hormone. Estrogen hormone increases the level of Thyroxine Binding Globulin (TBG) it causes the level of T4 and T3 to be increased, that can be Hyperthyroid.^{1,15} While in male, Hyperthyroid disease can be affected by unhealthy lifestyle for example smoking.² Average cost incurred by the female and male patient did not show significant difference. Prevalence of Hyperthyroid disease in South Sulawesi is 0,5% and in Indonesia the prevalence of population that is diagnosed with Hyperthyroid is higher in the female which is 0,6%.² Signs and symptoms of Hyperthyroid disease are palpitation, exhaustion, the tremor of extremities, sleep disturbance anxiety, losing weight, high temper intolerance, sweating, polydipsia and tachycardia.¹

Base on the age characteristic, age group between 26-35 years more than the other age groups. Hyperthyroid disease can occur in all ages but the risk of Hyperthyroid disease is

higher in between 20-40 years old because it is in a fertile age with high productivity so it raises anxiety, stress and depression. Hyperthyroid disease has been linked with psychiatric morbidity increase, hormone thyroid increase in blood (Hyperthyroid) can cause anxiety and depression.¹⁶ Previous researches have been proved that there is impact and significant relation between Thyroid Stimulating Hormone (TSH) and Thyroid Receptor Antibodies (TRAb) of anxiety, stress and depression.¹⁶ Besides the stress factor, 26-35 years old are a fertile age or a reproductive period and in this period estrogen hormone will increase thus causing enhancement of thyroid hormone production in blood (Hyperthyroid).^{17,18,19} Average medical expenses incurred of the respondents with age group 56-65 years (elderly) more than the age group 26-35 years because, elderly Hyperthyroid patients are often accompanied with atrial fibrillation disease that can cause heart failure disease and stroke. So, the type of laboratory tests are more numerous and need more costs before starting therapy and after giving antithyroid drug therapy.²⁰ In previous researches also concluded that there were 5% atrial fibrillation cases caused by Hyperthyroid disease.²⁰ Hyperthyroid disease in Indonesia is more dominant in patients with age range 45-75 years as much as 0,5%.² Hyperthyroid disease in the elderly is a cause of the reduction function of the thyroid gland so, the level of TSH decreased.²¹

According to the level of education characteristic, it shows that patients in the senior high school more than patients in the

junior high school as much as 45 patients. This research is in line with previous research that said in senior high school more risk attached thyroid disorders than in elementary school and junior high school.²² The other research also concluded that, Hyperthyroid patients in Indonesia with education level D1, D3 and bachelor have prevalence as much as 0.5%.² Even there is not previous research that proves the impact and relation between Hyperthyroid patients and education level.²² According to jobs characteristics, show that the respondent who does not work more than the respondent with a job. Characteristics of the not-working patients on average are house wife while the working patients are civil servants, police, army, private employees and self-employed. Hyperthyroid disease poses more risk to the house wife because the change of estrogen hormone during and after pregnancy so it affects the function of thyroid.^{17, 23} Prevalence of Hyperthyroid disease patients in Indonesia have higher risk in the non-working group as much as 0,5% than in the working group as much as 0,4%.² Social and economic factors be the one of the cause of the lack of awareness and access to check their-self determination in the health facility (hospital) when they experiencing Hyperthyroid symptoms.² Previous researches conclude that there is nothing significant relation between jobs and anxiety, as much as 46,7% of house wives experiencing anxiety as the outcome of Hyperthyroid disease can be lowered with doing counseling. Because, when counseling the

patient can tell or express their emotion, feeling and their mind.²⁴

According to the proportion of the real cost components, the component of laboratory cost has the biggest proportion than administration cost, doctor consultation cost and drugs cost is as much as Rp. 42.842.900,00 and average of Rp. 465.683,70 for each patient or as much as 83% from the total real cost of the hospital. Hyperthyroid disease is a disease that often occurs without realizing it. One of the clinical symptoms is the front of the neck enlargement and heart palpitations (tachycardia).^{25,26} Hyperthyroid disease only can detected through primary laboratory test those are TSHs, FT4 or FT3.²⁷ The test of FT4 (Free Thyroxine), TSHs (Thyroid Stimulating Hormone serum) and FT3 (Free Triiodothyronine) are primary laboratory test in diagnosis Hyperthyroid disease because, the these three test for knowing the level of thyroid hormone in blood.⁵ Beside that, using *USG Thyroid* also for evaluation the condition of organs in te thyroid gland.⁵

The test of the thyroid gland in blood periodically is very needed to monitor the therapy result with antithyroid drugs and for knowing the level of thyroid hormone in blood.²⁶ The secondary laboratory test to view the harm of the other organ which causes Hyperthyroid disease or *adverse effect* from the use of *thionamide* class (PTU and *Methimazole* or *Thiamazole*) antithyroid drugs those are liver function test, kidney function test and blood test. Every laboratory test needs quite an expensive cost.^{5,28}

The use of antithyroid for Hyperthyroid disease can be used as the main therapy or the therapy before surgery of the thyroid gland (radiotherapy).²⁹ Methimazole is the first time therapy of Hyperthyroid disease while, Propylthiuracil (PTU) is the first time therapy of Hyperthyroid disease in the early trimester of pregnancy.³⁰ Hyperthyroid disease needs treatment continuously. But, the use of antithyroid drugs on a prolonged basis will cause a negative effect on the patient body. *Methimazole* has minor adverse drugs reactions like rash, itching of the skin, vertigo and swelling of the salivary glands. While, major adverse drugs reactions like Thrombocytopenia, Agranulocytosis, Carcinogenesis and Hepatotoxic.³¹ Propylthiouracil (PTU) has minor nausea adverse drugs reaction, like gag and edema. And major adverse drugs reaction like agranulocytosis and hepatotoxicity.³² With these negative effects, so the cost that needed in the laboratory test will increase. Except the primary laboratory test, secondary laboratory test is also required. The type of secondary laboratory test before and after giving the therapy antithyroid which is the test of SGOT (*Serum Glutamic Oxaloacetic Transaminase*), SGPT (*Serum Glutamic Pyruvic Transaminase*), direct bilirubin, total bilirubin, automatic routine hematology, urine test, urea and creatinine and EKG (electrocardiogram).³³

EKG test of the Hyperthyroid patients is very important because it very much help in diagnosis, prognosis or determination of drugs therapy. Hyperthyroid disease has clinic

symptoms like tachycardia, because the thyroid hormone has a role directly or indirectly on the cardiovascular system.^{21,34} Thyroid hormones gives electrophysiology and inotropic effects of heart so it can increase atherosclerosis risk, increased cardiac contractility, increased cardiac output and decreased systematic vascular resistance.³⁴

Based on result of the researches show that there are significant different between real cost of the hospital and package cost INA-CBG, total real cost from 92 hospital respondent is IDR 51.472.900,00 with average IDR 559.488,04 for each patient and total cost covered by the BPJS through package cost INA-CBG with code Q-5-44-0 as much as IDR 185.500,00 for each patient and total cost INA-CBG is IDR 17.066.000,00. The results showed that the laboratory costs were 85% of the total real hospital costs, so the INA-CBG package was unable to cover all components of the cost of treatment hyperthyroidism. This resulted in losses for the hospital of (-) IDR 34.406.900,00 and an average of (-) IDR 373.988,04 every patient. The results of this study are different from previous studies regarding hyperthyroid disease, because this study focuses on the component of the cost of treatment hyperthyroidism with a comparative study method.

This research is a development of previous research conducted by Dian Ayu Juwita, Suhatri and Risa Hestia.¹⁷ The results of this study also contain useful implications as input in the future for the government as the BPJS organizer to further calculate the cost

benchmark to cover all treatment costs and service claims in health facilities, especially hospitals. In addition, this study can contribute to the empirical literature regarding the cost-effectiveness of direct treatment and its comparison with the cost of the INA-CBG package that has not been carried out in previous studies. The limitation in this study is that the total of samples is still insufficient because this study was only conducted in one hospital.

CONCLUSION AND RECOMMENDATION

The INA-CBG package does not cover all components of hospital costs for hyperthyroid disease, causing hospital losses with a difference of (-) IDR 34.406.900,00 and an average of (-) IDR 373.988,04 every patient. So it is recommended of Hasanuddin University Hospital Makassar need to ask the government to adjust the INA-CBG by requesting an upgrade to the standard of the INA-CBG package to be able to reimburse hospital claims for outpatient treatment of hyperthyroid disease.

REFERENCES

1. Leo S De, Lee SY, Braverman LE, Unit E, Sciences C. Hyperthyroidism. *HHS Public Access Author*. 2016;388(10047):906-918.
2. Kemenkes RI. Situasi dan Analisis Penyakit Tiroid. Jakarta: Pusat Data dan Informasi Kementerian Kesehatan RI; 2015.
3. Kemenkes RI. Riset Kesehatan Dasar (Riskesdes). Jakarta: Kementerian Kesehatan RI; 2013.
4. Yu W, Wu N, Li L, Wang J, OuYang H, Shen H. Side Effects of PTU and MMI in The Treatment of Hyperthyroidism: A systematic Review and Meta-Analysis. *Endocrine Practice*. 2020;26(2):207-217.
5. Dipiro JoT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM. Pharmacotherapy, a Pathophysiologic Approach 9th Edition. New York: McGraw-Hill Education; 2015.
6. Caputo M, Pecere A, Sarro A, et al. Incidence and Prevalence of Hyperthyroidism: A Population-Based Study in The Piedmont Region, Italy. *Endocrine*. 2020;69(1):107-112.
7. Okosieme OE, Taylor PN, Dayan CM. Should Radioiodine Now Be First Line Treatment For Graves' Disease?. *Springer Sci Bus Media New York*. 2020;13(3):1-7.
8. BPJS Kesehatan. Paduan Praktis Administrasi Klaim Fasilitas Kesehatan BPJS Kesehatan. Jakarta: Badan Penyelenggara Jaminan Sosial; 2018.
9. BPJS Kesehatan. Panduan Praktis Pelayanan Kesehatan BPJS Kesehatan. Jakarta: Badan Penyelenggara Jaminan Sosial; 2017.
10. Wulan S, Herman A, Direja S, Reflisiani D. Penghitungan Biaya Satuan pada Instalasi Rawat Jalan di Rumah Sakit X Jambi menggunakan Metode Step Down. *Jurnal Ekonomi Kesehatan Indonesia*. 2017;3(1):43-50.
11. RS Universitas Hasanuddin. Data Rekam Medis Kunjungan Pasien Rawat Jalan. Makassar; Rumah Sakit Universitas Hasanuddin; 2018.
12. Rahayuningrum IO, Tamtomo DG, Suryono A. Analisis Tarif Rumah Sakit Dibandingkan dengan Tarif Indonesian Case Based Groups Pada Pasien Rawat Inap Peserta Jaminan Kesehatan Nasional Di Rumah Sakit. *Pros Semin Nas Int*. 2017;1(1):214-223.
13. Sugiyono. Metode Penelitian Kombinasi (Mixed Methods). Bandung: Alfabeta; 2018.
14. Taylor PN, Albrecht D, Scholz A, et al. Global Epidemiology of Hyperthyroidism and Hypothyroidism. *Nature Reviews Endocrinology*. 2018;14(5):301-316.
15. Chiovato L, Magri F, Carle A. Hypothyroidism in Context : Where We've Been and Where We're Going. *Adv Ther*. 2019;2019(36):47-58.
16. Bové KB, Watt T, Vogel A, et al. Anxiety and

- Depression Are More Prevalent in Patients with Graves' Disease than in Patients with Nodular Goitre. *European Thyroid Journal*. 2014;3(3):173-178.
17. Juwita DA, Suhatri, Hestia R. Antithyroid Drug Use Evaluation on Hyperthyroid Patients in Dr. M. Djamil Hospital Padang, Indonesia. *Jurnal Sains Farmasi dan Klinis*. 2018;5(1):49-54.
 18. Meng Z, Liu M, Zhang Q, et al. Gender and Age Impacts on The Association Between Thyroid Function and Metabolic Syndrome in Chinese. *Medicine (United States)*. 2015;94(50):1-9.
 19. Zhang J, Huang C, Meng Z, et al. Gender-Specific Differences on the Association of Hypertension with Subclinical Thyroid Dysfunction. *International Journal Endocrinology*. 2019;2019:1-9.
 20. Samuels M. Hyperthyroidism in Aging. In: *Thyroid Disease Manager*; 2018.
 21. Barbesino G. Thyroid Function Changes in The Elderly and Their Relationship to Cardiovascular Health: A Mini-Review. *Gerontology*. 2019;65(1):1-8.
 22. Ngurah IG, Dwi G, Sudarsa IW. Faktor-Faktor Yang Mempengaruhi Kualitas Hidup Pasien Kanker Tiroid Berdiferensiasi Baik (DTC) Paska Tiroidektomi Total di Rumah Sakit Umum Pusat (RSUP) Sanglah, Denpasar. *Intisari Sains Medis*. 2019;10(1):197-204.
 23. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum. *Thyroid*. 2017;27(3):315-389.
 24. Yunitawati D, Santi K. Psychological Counseling And Anxiety In Patients With Hyperthyroidism In Klinik Litbang GAKI Magelang. *Media Gizi Mikro Indonesia*. 2014;6(1):53-62.
 25. Liu J, Fu J, Xu Y, Wang G. Antithyroid Drug Therapy for Graves' Disease and Implications for Recurrence. *International Journal of Endocrinology*. treatment; 2017:1-8.
 26. Kamsyakawuni A, Gernowo R, Sarwoko EA. Aplikasi Sistem Pakar untuk Diagnosa Penyakit Hipertiroid dengan Metode Inferensi Fuzzy Mamdani. *Jurnal Sistem Informasi Bisnis*. 2012;2(2): 58-66.
 27. Burch HB, Cooper DS. Management of Graves Disease. *Journal American Medical Association*. 2016;314(23):2544-2554.
 28. Klaver EI, Loon HCM Van, Stienstra R, et al. Thyroid Hormone Status and Health-Related Quality of Life in the LifeLines Cohort Study. *Thyroid Journal*. 2013;23(9):1066-1073.
 29. Brown DC. Thyroid Hormones, Antithyroid Drugs [Chapter 37]. *Clinical Pharmacology* 11th Vol. 4 ed. Elsevier Ltd; 2018.
 30. Tjay TH, Rahardja K. Obat-Obat Penting Khasiat, Penggunaan, dan Efek Samping Edisi Ke 7. Jakarta: Elex Media Komputindo ; 2015.
 31. Iglesias P, Bajo MA, Selgas R, Díez JJ. Thyroid Dysfunction and Kidney Disease : An Update. *Reviews in Endocrine and Metabolic Disorders*. 2017;18:131-144.
 32. Akmal A, Kung J. Expert Opinion on Drug Safety Propylthiouracil, and Related Hepatotoxicity. *Journal Expert Opinion on Drug Safety*. 2014;13(10):1397-1406.
 33. Siddiqui MF, Anwer H, Batool Z, Hasnain S, Imtiaz M. Assessment of Carbimazole, Propylthiouracil & L-Thyroxine For Liver Markers in Thyroid Patients From Punjab, Pakistan. *Journal of Applied Pharmacy*. 2015;7(1):105-113.
 34. Baladi IH, Rai AA, Ahmed SM. ECG Changes in Patients With Primary Hyperthyroidism. *Pan African Medical Journal*. 2018;30:1-5.