RESEARCH STUDY OPEN ACCESS

# Factors Associated with Goiter Incidence in Farmers in Kismantoro Sub-District, Wonogiri Regency

## *Faktor yang Berhubungan dengan Kejadian Gondok pada Petani di Kecamatan Kismantoro Kabupaten Wonogiri*

**Ahshaina Ramadhaningtiyas*[1], Yulia Lanti Retno Dewi[2], Sugihardjo[3]**

[1]Masters Degree Program in Enviromental Science, Graduate School, Universitas Sebelas Maret, Indonesia
[2]Departement of Nutrition, School of Medicine, Universitas Sebelas Maret, Surakarta, Indonesia
[3]Departement of Social Agricultural Economics, School of Agriculture, Universitas Sebelas Maret, Surakarta, Indonesia

***ARTICLE INFO***

***Received:*** *18-02-2021*
***Accepted:*** *13-09-2021*
***Published online:*** *06-06-2022*

***Correspondent:***
*Ahshaina Ramadhaningtiyas*
*ahshainatiyas@gmail.com*

***DOI:***
*10.20473/amnt.v6i2.2022.148-154*

***Available online at:***
*https://e-journal.unair.ac.id/AMNT*

***Keywords:***
*Goiter, Incidence, A Factor Associated, Kismantoro Sub-district*

**ABSTRACT**

**Background:** Kismantoro Sub-district has been an endemic area of severe goiter since 1982, with a total goiter rate of 35.5% until 2007, when was declared a mild endemic goiter area (TGR 10.79%). Monitoring in 2017 on salt circulating in Wonogiri exposed that there were still 26.01% of brands that did not meet the Indonesian national standard.
**Objective:** This study aimed to analyze the factors associated with goiter incidence in Kismantoro Sub-district, Wonogiri Regency.
**Methods:** This research applied analytic observational with a case-control design. The samples were 41 respondents in the case group and 41 respondents in the control group, taken by purposive sampling. The history of goiter was obtained from the medical records of Kismantoro Community Health Center. The data analysis method employed was logistic regression analysis.
**Results:** The results showed a significant correlation between age (p 0.005, OR 5.88, 95%CI 1.53-22.62), gender (p 0.003, OR 0.15, 95%CI 0.04-0.58), and salt iodine content (p 0.007, OR 0.14, 95%CI 0.03-0.68) with the goiter incidence in farmers in Kismantoro. Moreover, the multiple logistic regression test results revealed that age was the most dominant variable influencing the goiter incidence (p 0.006, OR 8.103, 95%CI (1.799-36.499).
**Conclusion:** There was a relationship between age and the goiter incidence, gender with the goiter incidence, and iodine content in household salt with the goiter incidence, the multiple logistic regression test results indicated that the age variable most influenced goiter incidence among farmers in Kismantoro Sub-District, Wonogiri Regency.

***ABSTRAK***

***Latar Belakang:*** *Kecamatan Kismantoro merupakan daerah gondok endemik berat sejak 1982 dengan angka Total Goiter Rate 35,5%, sampai pada tahun 2007 dinyatakan sebagai daerah gondok endemik ringan (TGR 10,79%). Monitoring tahun 2017 pada garam yang beredar di Kabupaten Wonogiri masih terdapat 26,01 % merek yang tidak memenuhi Standar Nasional Indonesia.*
***Tujuan:*** *Penelitian ini bertujuan untuk menganalisis faktor-faktor yang berhubungan dengan kejadian gondok pada petani di Kismantoro, Wonogiri.*
***Metode:*** *Penelitian ini bersifat observasional analitik dengan desain case control. Sampel sebanyak 41 responden kelompok kasus dan 41 responden kelompok kontrol, diambil dengan puposive sampling. Data riwayat gondok diperoleh dari data rekam medis Puskesmas Kismantoro. Metode analisis data yang digunakan adalah analisis regresi logistik berganda.*
***Hasil:*** *Hasil penelitian menunjukkan kolerasi yang signifikan antara umur (p 0,005, OR 5,88, 95% CI 1,53 – 22,62), jenis kelamin (p 0,003, OR 0,15, 95% CI 0,04 – 0,58), dan kandungan iodium garam (p 0,007, OR 0,14, 95% CI 0,03 – 0,68) dengan kejadian gondok pada petani di Kecamatan Kismantoro. Hasil uji regresi logistik berganda menunjukkan bahwa umur merupakan variabel paling dominan yang mempengaruhi kejadian gondok (p 0,006, OR 8,103, 95% CI (1,799-36,499).*
***Kesimpulan:*** *Ada hubungan antara umur dan kejadian gondok, jenis kelamin dengan kejadian gondok, dan kandungan iodium dalam garam dengan kejadian gondok, hasil tes regresi logistik berganda menunjukkan bahwa variabel umur adalah variabel yang paling dominan mempengaruhi kejadian gondok pada petani di Kecamatan Kismantoro, Kabupaten Wonogiri.*


***Joinly Published by IAGIKMI & Universitas Airlangga***

***Kata kunci:*** *Gondok, Kejadian, Faktor yang Berhubungan, Kecamatan Kismantoro.*

**INTRODUCTION**

Iodine Deficiency Disorder (IDD) is one of the public health problems that can hinder the improvement of human resources quality[1]. Iodine is an essential substance for the body because it is a component of the thyroxine hormone, which is vital for thyroid hormone formation[2]. The body's need for iodine per day, according to WHO, Recommended Dietary Allowances (RDA) 2019 is around 90 µg to 150 µg. However, if it is not fulfilled continuously and lasts a long time, it will cause goiter. Goiter is a human way of adapting to the lack of iodine in food and beverages[3].

Factors that affect iodine deficiency include physical factors such as soil type, high rainfall, topography, deforestation, and erosion. Biologic factors include natural and synthetic goitrogenic substances. Erosion, for any reason, will erode iodine from the ground and bring it to sea[4,5]. Natural goitrogenic is a source of food consumed, such as cassava and cabbage plants. Synthetic goitrogens such as organochlorine (DDT, DDD, and Dieldrin), exposure to environmental pollution, namely Pb, Hg, Cd, pesticides, and nitrogen fertilizers[5,6,7] Pesticides can interfere with the synthesis and metabolism of thyroid hormones through several mechanisms. They are first disrupting TSH receptors (TSH-r) in the thyroid gland so that TSH that will spur the synthesis of thyroid hormones cannot enter the gland and impact the inhibition of thyroid hormone synthesis. Second, pesticides inhibit the work of enzymes deiodinase type one (D1), which catalyzes the change of T4 into T3 (the active form of the hormone in the body). Third, the similarity of the chemical structure of pesticides and thyroid hormones causes competition in binding by thyroid hormone receptors (TH-r) in cells. The four pesticides are suspected of spurring the work of the enzyme T4 into rT3 (an inactive form of thyroid hormone), resulting in the body's lack of the active form of thyroid hormone (T3)[8]

Chemical pesticides are toxic substances designed explicitly for the control of pests, weeds, or plant diseases. The application of pesticides is still the most effective way to protect crops from pests and has contributed significantly to increased agricultural productivity and yields[9]. Of most farmers in Indonesia, 95.29% use chemical pesticides to control Plant Destruction Organisms (OPT) because it is considered the most effective[10]. Farmers often use pesticides even many times during crop growth and sometimes still used them when leading up to harvest to improve crop yields and improve quality[11].

Kismantoro subdistrict is one of the largest chili-producing agricultural areas in the Wonogiri Regency. In 2017 Kismantoro District produced chili peppers of 1300.5 tons and 1665.8 tons in 2018, with a chili harvest area of 205 ha in 2017 and 203 ha in 2018. The favorable natural situation is that the mountains cover almost all villages with state forests and land as farmland. Most of the population in the Kismantoro subdistrict has a livelihood as farmers and chili peppers as the most produced horticultural products. Cassava becomes the most widely planted crop as a food.

The data shows that farmers in Kismantoro often use pesticides to fertilize crops, and cassava is a food that is usually consumed. This explains that the activities and food consumed by farmers in Kismantoro are strongly related to the factors that cause iodine deficiency. In addition to activities, the state and natural conditions in Kismantoro are also proven not to contain much iodine, one example of iodine content in the water.

The iodine content of well water consumed in Kismantoro Sub-District, Wonogiri Regency, was on average 0.9-4.9 µg/l[13]. From these data, it could be assumed that the source of well water consumed by the community in the Kismantoro Sub-District was categorized as a lack of iodine. The water iodine content is classified as 1) less, if≤ 3 µg/l and 2) sufficient if> 3 µg/l. Kismantoro Sub-District has soil formed by the weathering process of tertiary volcanic rocks and has an iodine content of 2.79-4.30 mg/kg, an area with the soil characteristics formed from volcanic rock, which has the potential to be exposed to IDD (Iodine Deficiency Disorders) because iodine content in the soil is very low[14].

The low iodine content in water and soil commonly used for drinking and irrigation of food crops can lead to low levels of iodine in planted plants. The content of iodine in plants depends on the soil where the plant is grown. The higher the iodine level in the ground, the higher the iodine found in the plant[15,16]. It explains the mechanism that ecologically, an endemic area of iodine deficiency will have soil and water characteristics that are low in iodine[17]. Moreover, Kismantoro Sub-District has been an endemic area of severe goiter since 1982, with a total goiter rate of 35.5% until 2007, which was declared a mild endemic goiter area, with a total goiter rate of 10.79%.

Based on UPT Puskesmas Kismantoro until 2017, goiter sufferers in Kismantoro subdistrict as many as 147 people. In 2018 as many as 138 sufferers, and in 2020 as many as 128 sufferers. In 2018, there were as many as 706 mumps sufferers in the target of implementing the activities of Wonogiri free of goiter with the highest number of sufferers, namely from Kismantoro Subdistrict as many as 132 people. Iodine intake can be obtained by consuming iodized salt, which is added to food or drinks consumed daily. Hence, iodine deficiency disorders can be measured using iodized salt in the household. In 2017, Wonogiri District also implemented an IDD prevention program with coordination meetings and consultations.

The socialization carried out included socialization on the importance of consuming iodized salt, the benefits of iodine for development and growth, testing of iodine content in consumption salt, monitoring, and testing of consumption salt in the Wonogiri Regency area. The monitoring activities results obtained samples of consumption salt of as many as 44 brands, with various types of fine salt (table salt), brick salt, and coarse salt. After a test utilizing mini lab equipment, it was found that there were several salt brands whose iodine content did

not meet the set standards, namely 30 ppm. Based on the monitoring and testing results, it was also known that consumption salt circulating and marketed in Wonogiri Regency still did not meet the $KIO_3$ content requirements according to SNI standards for as many as eight brands out of 44 brands, or around 26.01%[20]. Based on this explanation, the researchers were interested in examining the factors related to goiter incidence in Kismantoro, Wonogiri. This study also aimed to provide information on the distribution of iodized salt consumed in farmer households and the incidence of goiter so that it can be an input for the local government to plan and overcome goiter incidence.

## METHODS

This type of research was case-control with a sample size of 82 respondents. The sampling technique employed was purposive sampling, using a 1: 1 ratio between the case group and the control group[21,22]. In this study, the case population was all people who tested positive for goiter and were recorded at the Kismantoro Sub-District Community Health Center, Wonogiri Regency, in 2020, with as many as 128 respondents. Meanwhile, the control population was all people who tested negative for goiter, did not live in the same house as the case group, and had the same risk factors as the case group. Selection of samples used inclusion criteria: samples willing to become respondents, resided in Kismantoro Sub-District, and worked as farmers or got involved in agricultural activities.

Goiter's diagnosis was carried out through a grading system for physical signs and clinical symptoms by examining the thyroid gland using the palpation method in the thyroid gland area[23], by doctors and midwives at Kismantoro Health Center. Household salt quality data were acquired from each respondent, whose samples were taken from each house, and then checked for iodine levels utilizing an iodine test kit, by dropping 1-2 drops of iodide test kit solution into the sample salt, with the standard test, namely ≤30 ppm, not bright purple; ≥30 pm dark purple-black. Respondent characteristics data were obtained by interview using a questionnaire and medical data from the Kismantoro Sub-District Community Health Center. The process of retrieving data with an iodine content test kit in salt and interviews were conducted by researchers.

The analysis in this study used bivariate analysis using simple logistic regression and multivariate tests employing multiple logistic regression tests. This study's independent variables consisted of the respondents' characteristics: age, gender, education level, and iodine content in the household salt of farmers. The dependent variable was goiter incidence. The researchers provided an informed consent form to be read and signed by the respondents. Respondents volunteered to participate in the research. The confidentiality of all data and information provided by the respondents will be maintained and used for research purposes. All actions have obtained permission from the code of ethics committee, Faculty of Medicine, Universitas Sebelas Maret, Surakarta Indonesia, No.01/UN27.06.6.1/KEPK/EC/2021.

## RESULTS AND DISCUSSION

### Respondent Characteristics

#### Age

The data analysis results on the age variable can be seen in the following table.

**Table 1:** Distribution of the frequency relationship between age and the goiter incidence in farmers in Kismantoro Sub-district in 2020

| Age | Goiter Incidence | | | | p-value | 95% CI | OR |
|---|---|---|---|---|---|---|---|
| | Goiter | | No goiter | | | | |
| | n | % | n | % | | | |
| >40 years old | 38 | 57.6 | 28 | 42.4 | | | |
| ≤40 years old | 3 | 18.8 | 13 | 81.3 | 0.005 | 1.53-22.62 | 5.88 |
| Total | 41 | 50.0 | 41 | 50.0 | | | |

In Table 1, of the 41 respondents, the group that experienced goiter incidence was 38 respondents (57.6%) aged> 40 years, while the group that did not experience goiter incidence was 28 respondents (42.4%) aged> 40 years.

From the bivariate analysis of the relationship between age and the goiter incidence, a p-value of 0.005 was obtained. Thus, statistically, it could be stated that there was a significant relationship between age and goiter incidence. Besides, the cross-tabulation results showed an OR value of 5.88 (95% CI = 1.53-22.62). It could be said that farmers, who were more than 40 years old, had a risk of experiencing a goiter 5.88 times more than farmers who were less than or equal to 40 years.

#### Gender

The data analysis results on the gender variable can be seen in the following table.

**Table 3:** Distribution of the frequency relationship between education level and the goiter incidence in farmers in Kismantoro Sub-District in 2020

| Education Level | Goiter Incidence | | | | p-value | 95% CI | OR |
|---|---|---|---|---|---|---|---|
| | Goiter | | No goiter | | | | |
| | n | % | n | % | | | |
| Low | 40 | 51.3 | 38 | 48.7 | 0.308 | 0.32 – 31.70 | 3.16 |
| High | 1 | 25.0 | 3 | 75.0 | | | |
| Total | 41 | 50.0 | 41 | 50.0 | | | |

Low: Did not attend school, did not graduate from primary school or junior high school. High: Senior high school, college.

In Table 3, of the 41 respondents, for the group that experienced goiter incidence, there were 40 respondents (51.3%) with a low level of education. Meanwhile, 38 respondents (48.7%) did not experience goiter incidence with a low education level.

From the bivariate analysis of the relationship between education level and the goiter incidence, the p-value was 0.308. Therefore, statistically, it could be inferred that there was no significant relationship between education level and the goiter incidence. The cross-tabulation results uncovered an OR value of 3.16 (95% CI = 0.32-31.70).

**Iodine content in household salt of farmers**

The data analysis results regarding the variable iodine in salt can be seen in the following table.

**Table 4:** Distribution of the frequency relationship between the iodine content in salt and the goiter incidence among farmers in the Kismantoro Sub-district in 2020

| Iodine Content | Goiter Incidence | | | | p-value | 95% CI | OR |
|---|---|---|---|---|---|---|---|
| | Goiter | | No goiter | | | | |
| | n | % | n | % | | | |
| Yes | 30 | 43.5 | 39 | 56.5 | | | |
| No | 11 | 84.6 | 2 | 15.4 | 0.007 | 0.03 – 0.68 | 0.14 |
| Total | 41 | 50.0 | 41 | 50.0 | | | |

Table 4 displays that of the 41 respondents, 11 respondents (84.6%) of the group who experienced goiter incidence indicated no iodine in the salt they consumed. Meanwhile, the group that did not experience goiter incidence were two respondents (15.4%) who did not have iodine in the salt they consumed.

The bivariate analysis of the relationship between the iodine content in the salt consumed and the goiter incidence obtained a p-value of 0.007, so statistically, it could be asserted that there was a significant relationship between the iodine content in the salt consumed and the goiter incidence. The cross-tabulation results exhibited an OR value of 0.14 (95% CI=0.03-0.68).

**Table 5:** Risk factors for the goiter incidence in farmers in Kismantoro Sub-district, Wonogiri Regency

| Variables | Coefficient | P-Value | OR (95% CI) |
|---|---|---|---|
| Age | 2.092 | 0.006 | 8.103 (1.799-36.499) |
| Gender | -2.506 | 0.003 | 0.082 (0.016-0.427) |
| Iodine content | -2.781 | 0.010 | 0.062 (0.008-0.511) |
| Constant | 5.220 | 0.025 | 184.963 |

The multivariate analysis results determine the independent variables' influence on the dependent variable using logistic regression statistical tests. It was shown that the variable age, gender, and iodine content in salt had an effect on the goiter incidence, with the independent variable that most dominantly influenced the goiter incidence was the age variable (p = 0.006, OR = 8,103, 95% CI = 1,799-36,499). That could mean that the age group of the 40s and above have a greater chance of developing goiter disease by 8,103 times greater than the age of less than 40years.

**Factors associated with the goiter incidence among farmers in Kismantoro Sub-District, Wonogiri, comprising age, gender, education level, and iodine content in salt consumed in farmer households.**

**The effect of age on the goiter incidence among farmers in Kismantoro Sub-District, Wonogiri**

Goiter incidence can affect sufferers of all ages, but getting older will increase disease risk. It is because the body's immune system and immunity decrease with age[24]. From the research conducted by Díez (2005), goiter was most common in patients aged 55 years and over. It aligns with the study carried out by Rehman et al. (2006), which found that goiter was common in older adults, and its incidence increased with age.

Based on Asturiningtyas et al. (2016) research in patients at IDD Litbang clinic Magelang regarding the

characteristics of thyroid dysfunction, patients found that the adult age group of women dominated cases of hyperthyroidism. Hormonal changes during pregnancy can affect thyroid function. Research conducted by Barbesino (2019) at Massachusetts General Hospital, Harvard Medical School shows that the pattern that arises is a decrease in thyroid function in the elderly, leading to slightly higher levels of thyroid-stimulating hormone (TSH) compared to young age. The incidence of mild hyperthyroidism also increases in adulthood, especially in populations with a history of iodine deficiency.

Increased levels of TSH characterize hypothyroidism. TSH circulating has been shown to increase with age. References to TSH also increase with age, as the distribution of the TSH concentration population increases with age[28,29]. Thyroid hormones are under the control of TSH levels making the latter a sensitive marker of thyroid function. The aging process leads to reduced absorption and organization of iodine with an altered thyroid response to TSH. This makes old age more susceptible to goiter disease than at a young age[29].

Non-toxic goiter, commonly referred to as endemic goiter, was found in areas where the drinking water content was very low in iodine. Usually, the thyroid has begun to enlarge at a young age and develops into multinodular in adulthood. However, most sufferers did not experience complaints because there was no hypothyroidism or hyperthyroidism[30]. Patients only came for treatment because they experienced changes in the neck's shape and were afraid of malignancies. Thus, most patients registered at the Community Health Center were older patients or 40 years and over.

**The effect of gender on the goiter incidence among farmers in Kismantoro Sub-District, Wonogiri**

From a study conducted by Malboosbaf et al. (2012), the results uncovered that goiter's proportional prevalence was more significant in women than in men. Based on the research results found in Prof. Dr. R. D. Kandou Manado, patients with thyroid disorders were mostly women, namely 80.3%, while men were 19.7%, with a ratio of 4.1: 1[32]. Based on research conducted by Dauksiene et al. (2017) in Kaunas, Lithuania, on factors related to the prevalence of thyroid nodules and goiter in middle-aged euthyroid subjects found that female gender, thyroid nodules, smoking, BMI, and TSH levels were identified as potential predictors of goiter. Female gender, TSH levels, and thyroid volume predict the presence of thyroid nodules.

Gender and age play a role in determining thyroid disease incidence and clinical course[34]. Meng et al. (2015) researched the impact of gender and age on the relationship between thyroid function and metabolic syndrome in China. They found that women with excessive TSH and excessive $FT_3$ had a higher risk of metabolic syndrome than men. TSH and $FT_3$ significantly increased the risk of metabolic syndrome in both sexes, with women (4,408–58,455) higher than males (2,588–4,943). Aging is a risk for metabolic syndrome, especially for women.

Based on research conducted by Calcaterra et al. (2020) on gender differences at the onset of Autoimmune Thyroid Diseases in children and adolescents in Pavia, Italy found that women are more susceptible to Autoimmune Thyroid Diseases (ATD) during puberty. The influence of hormones on women is one of the predisposing factors for the increasing number of female patients than men. Estrogen can increase thyroid-binding globulin (TBG) levels, which acts as a $T_4$ and $T_3$ transport in the blood resulting in a decrease in free $T_4$ and free $T_3$ levels. It stimulates TSH so that gland hyperplasia occurs as a compensatory mechanism, forming more thyroid hormone so that serum $T_4$ and $T_3$ levels can return to normal[37]. Research carried out by Darmayanti et al. (2012) uncovered that goiter cases were more common in women than men, but with increasing endemic weight, the gender difference was almost non-existent.

**The effect of iodine content on the goiter incidence among farmers in Kismantoro Sub-District, Wonogiri**

The research results found by Kasih et al. (2015) disclosed a relationship between salt iodine levels and the goiter incidence in WUS in Purbosono Village, Kertek Sub-District, Wonosobo Regency. It corroborates Hidayah's (2018) research, which discovered that as many as 65% of respondents used salt in the wrong size and method and causing goiter in grades IV and V at SD Sidorejo 2, Kendal Sub-District, Ngawi Regency. On the other hand, Assey (2009), in a study in Tanzania, stated that there was a rapid increase in iodine status in Tanzania because people consumed iodized salt. Meanwhile, the low household level of iodized salt in Wolaita, Southern Ethiopia, was studied by Kumma et al. (2018), showed that the influencing factors included low education, monthly income, and improper storage of salt, namely by leaving it open.

According to Liang et al. (2017), iodine intake deficiency is the leading cause of idd-related diseases. The strategy to increase iodine intake is to add iodine salt to the diet. Although his research in China on whether the incidence of thyroid disorders is related to salt intake by promoting universal salt iodization (USI) is not proven, iodine deficiency is still a common cause of goiter disease.

Kusrini et al. (2020) conducted a study in Magelang, Central Java, on iodine status in pregnant women. This study compares a pregnant woman who previously lived in areas with severe iodine deficiency with pregnant women living in areas with enough iodine. The study proved that pregnant women in both regions are careful to meet their iodine needs by consuming iodine salts.

Research conducted by Abebaw et al. (2020) on Ethiopian schoolchildren, in Ethiopia, about 12 million school-age children do not get adequate iodine intake. Iodine deficiency is significantly associated with the incidence of goiter in school-age children in Ethiopia. The contributing factor to the iodine deficit in school-age children in Ethiopia is that they consume non-iodized salt and consume cabbage more than twice per week. Nurrakhmawati (2012) stated that storing the salt for one year could reduce iodine levels by 20% in a closed container at a relative humidity of 60% and a temperature of 400 C; instead, the salt should be kept at room

temperature, out of the sun, and in the heat of the fireplace.

## CONCLUSION

There was a relationship between age and the goiter incidence, gender with the goiter incidence, and iodine content in household salt with the goiter incidence. The multiple logistic regression test results indicated that the age variable most influenced goiter incidence among farmers in Kismantoro Sub-District, Wonogiri Regency.

## RECOMMENDATION

Society should also be more aware of the importance of using iodized salt. Education for the community about the storage of iodized salt should also always be monitored by local authorities. Program efforts to ensure the sustainability of iodine intake's adequacy in endemic areas of mumps need to be maintained continually.

Efforts for law enforcement and monitoring, ranging from production to sale of iodized salt, need improvement. Every citizen can benefit from the presence of iodized salt. Further research needs to by adding variables such as dietary habits. Researchers should use a semi-quantitative FFQ questionnaire to get a complete picture of diet and other factors that cause iodine deficiency in further research.

## ACKNOWLEDGEMENT

We would like to thank all of the authors for the hard work and for finishing the article. We would also say our gratitude to the stakeholders of Kismantoro Sub-District Community Health Center, Wonogiri Regency.

## REFERENCES

1. Marwanto, A., Setiani, O., Suhartono. Hubungan Pajanan Pestisida dengan Kejadian Goiter pada Anak Sekolah Dasar di Area Pertanian Hortikultura Kecamatan Ngablak Kabupaten Magelang. *Jurnal Kesehatan Lingkungan Indonesia*. **2**, 104-111 (2018).
2. Kholifah S. *Kuliah Psikologi FAAL.* (Prodi Psikologi Fakultas Dakwah IAIN Sunan Ampel, 2004).
3. Djokomoeljanto R. *Book Teaching of Internal Medicine* (*Buku Ajar Ilmu Penyakit Dalam). (*Interna Publishing, 2009).
4. Djokomoeljanto R. *Penyakit Kelenjar Gondok*. (Universitas Diponegoro Press Semarang, 2007).
5. Dewi, Y. L. R. Senyawa Goitrogenik dalam Bahan Makanan (Goitrogenic Substances in Foodstuffs). *Bioedukasi.* **2,** 24-27 (2015)
6. Sudargo, T., Aini, N. K., Laily, N. H. *Defisiensi Yodium, Zat Besi, dan Kecerdasan*. (Gadjah Mada University Press Yogyakarta, 2015).
7. Saidin, S. Hubungan Keadaan Geografi dan Lingkungan dengan Gangguan Akibat Kurang Yodium (GAKY). *Media Litbang Kesehatan*. **2,** 101-108 (2009).
8. Koibuchi, N. *Mechanism of Chemical Destruptors of Thyroid Function*. (Department of Integrative Physiology Gunma University Graduate School of Medicine Japan, 2010).
9. Kumar, L. P., Panneerselvam, N. Toxic Effects of Pesticides: A Review on Cytogenetic Biomonitoring Studies. *Facta Universitatis Series: Medicine and Biology*. **2,** 46-50 (2008).
10. Andesgur I. Analisa Kebijakan Hukum Lingkungan dalam Pengelolaan Pestisida. *Jurnal Bestuur*. **2,** 93-105 (2019).
11. Adriyani, R. Environmental Pollution Control Effort Due to The Use of Agricultural Pesticides. *Jurnal Kesehatan Lingkungan*. **1,** 95-106 (2006).
12. Badan Pusat Statistik Wonogiri. *Kismantoro dalam Angka 2018*. (BPS Kabupaten Wonogiri, 2018).
13. Mutalazimah, Asyanti S. Kadar Yodium Air, Ekskresi Yodium Urin dan Goiter di Daerah Endemis Defisiensi Yodium. *The 2nd University Research Coloquium.* **2015,** 28-34 (2015).
14. Harijoko A. Hubungan Antara Kandungan Yodium di Tanah dan Endemi Gangguan Akibat Kekurangan Yodium. (Prosiding IAGI, 2009)
15. Gibney, M.J, Michael, Margetts M, Barrie, Kearney M, John and Lenore. *Public Health Nutrition (Gizi Kesehatan Masyarakat)*. (Penerbit Buku Kedokteran EGC Jakarta, 2009).
16. Kapil, Umesh, Preeti, and Sing. Status of Iodine Content of Salt and Urinary Iodine Excretion Levels in India. *Pakistan Journal of Nutrition*. **6,** 361-373 (2003).
17. Johnson C. C, Fordyce F. M, Stewart A. G. *Environmental Controls in Iodine Deficiency Disorders Project Summary Report.* British Geological Survey Commissioned Report CR/03/058N. BGS, Keyworth, Nottingham, UK (2003).
18. *UPT Puskesmas Kismantoro. Data Gondok Kretin UPT Puskesmas Kismantoro Tahun 2020 Data Gondok Kretin Rekap Kecamatan Kismantoro* (2020)
19. *UPT Puskesmas Kismantoro. Data Wonogiri Bebas Gondok UPT Puskesmas Kismantoro Tahun 2018. Target Waktu Pelaksanaan Kegiatan Wonogiri Bebas Gondok Tahun 2018* (2018).
20. Jarwadi S. *Laporan Pelaksanaan Program Penangguangan GAKY Kabupaten Wonogiri Tahun 2017. (*Wonogiri: Dinas Kesehatan Kabupaten Wonigiri, 2017).
21. Notoatmodjo S. *Promosi Kesehatan Teori dan Aplikasi.* (PT Rineka Cipta, 2010).
22. Notoatmodjo S. *Ilmu Perilaku Kesehatan.* (PT Rineka Cipta, 2010).
23. Lewinski A. The Problem of Goitre with Particular Consideration of Goitre Resulting from Iodine Deficiency (I): Classification, Diagnostics, and Treatment. *National Library of Medicine.* **4,** 351-355 (2002).
24. Díez J. J. Goiter in Adult Patients Aged 55 Years and Older: Etiology and Clinical Features in 634 Patients. *Journal of Gerontology: Medical Science*. **7,** 920–923 (2005).
25. Rehman S. U, Hutchison F, Basile J. N. Goiter in Older Adults. *Aging Health*. **2,** 1-5 (2005).
26. Asturiningtyas I. P, Kumorowulan S. Karakteristik Pasien Disfungsi Tiroid : Studi Epidemiologi. *Media*

*Gizi Mikro Indonesia Jurnal Litbang Kemkes*.**1,** 43-54 (2016).

27. Barbesino G. Thyroid Function Changes in the Elderly and Their Relationship to Cardiovascular Health: A Mini-Review. Gerontology. **65,** 1-8 (2018).
28. Leng O, Razvi S. Hypothyroidism in the older population. *Thyroid Research.* **2,** 1-10 (2019).
29. Calsolaro V, Niccolai F, Pasqualetti G, Calabrese A. M, Polini A, Okoye C, Magno S, Caraccio N, Monzani F. Overt and Subclinical Hypothyroidism in the Elderly: When to Treat?. *Frontiers in Endo*crinology. **177,** 1-8 (2019).
30. Darmayanti N. L. A, Setiawan I. G, Maliawati S. Endemik Goiter. *SMF Ilmu Bedah Fakultas Kedokteran Universitas Udayana Rumah Sakit Umum Pusat Sanglah Denpasar,* 1-18 (2012).
31. Malboosbaf R, Hosseinpanah F, Mojarrad M, Jambarsang S. Relationship between Goiter and Gender: A Systematic Review and Meta-analysis. *PubMed.* **3,** 1-10 (2012).
32. Crosby H, Pontoh V, Merung M. A. The Pattern of Thyroid Abnormalities at RSUP Prof. Dr. R. D. Kandou Manado for the Period January 2013 until December 2015. *Jurnal e-clinic (eCl)*. **1,** 430-437 (2015).
33. Dauksiene D, Petkeviciene J, Klumbiene J, Verkauskiene R, Vainikonyte-Kristapone J, Seibokaite A, Ceponis J, Sidlauskas V, Daugintyte-Petrusiene L, Norkus A, Zilaitiene B. Factors Associated with the Prevalence of Thyroid Nodules and Goiter in Middle-Aged Euthyroid Subjects. *Hindawi International Journal of Endocrinology*. **8401518,** 1-8 (2017).
34. Castello R, Caputo M. Thyroid diseases and gender. *Itali Journal Gender-Specific Med*. **3,** 136-141 (2019).
35. Meng Z, Liu M, Zhang Q, Liu L, Song K, Tan J, Jia Q, Zhang G, Wang R, He Y, Ren X, Zhu M, He Q, Wang S, Li X, Hu T, Liu N, Upadhyaya A, Zhou P, and Zhang J. Gender and Age Impacts on the Association Between Thyroid Function and Metabolic in Chinese. *Medicine Journal.* **50,** 1-9 (2015).
36. Calcaterra V, Nappi R. E, Regalbuto C, Silvestri A. D, Incardona A, Amariti R, Bassanese F, Clemente A. M, Vinci F, Albertini R, Larizza D. Gender Differences at the Onset of Autoimmune Thyroid Diseases in Children and Adolescents. *Frontiers in Endocrinology.* **229,** 1-6 (2020).
37. Nagarkar R, Roy S, Akheel M, Palwe V, Kulkarni N, Pandit P. Incidence of Thyroid Disorders in India: An Institutional Retrospective Analysis. *International Journal of Dental and Medical Specialty*. **2,** 19-23 (2015).
38. Kasih L. M, Pranowowati P, Widyawati S. A. Hubungan Antara Kadar Yodium Garam Dengan Kejadian Gondok Pada Wanita Usia Subur (WUS) Di Desa Purbosono Kecamatan Kertek Kabupaten Wonosobo. *Jurnal Gizi dan Kesehatan*. **13**, 112-118 (2015).
39. Hidayah N. Hubungan Konsumsi Garam Beryodium Dengan Kejadian Gondok Pada Anak Kelas IV Dan V Di SD Sidorejo 2 Kecamatan Kendal Kabupaten Ngawi. *Cakra Medika*. **1,** 18-25 (2018).
40. Assey V. D. Controlling Iodine Deficiency Disorders Through Salt Iodization in Tanzania. *Thesis for the Degree of Doctor of Philosophy at the University of Bergen* (University of Bergen, 2009).
41. Kumma W. P, Haji Y, Abdurahmen J, Adinew Y. M. Factors Affecting the Presence of Adequately Iodized Salt at Home in Wolaita, Southern Ethiopia: Community Based Study Wondimagegn. *Hindawi International Journal of Food Science*. **2018,** 1-9 (2018).
42. Liang Z, Xu C, Luo Y. J. Association of iodized salt with goiter prevalence in Chinese populations: a continuity analysis over time. *MMR Military Medical Research*. **8,** 1-8 (2017).
43. Kusrini I, Farebrother J, Mulyantoro D. K. Adequately iodized salt is an important strategy to prevent iodine insufficiency in pregnant women living in Central Java, Indonesia. *Journal Plos One*. **11,** 1-13 (2020).
44. Abebaw B, Oumer A. Determinants of iodine deficiency among school age children in Guraghe Zone, Southwest Ethiopia. *International journal of public Health Science (IJPHS).* **2,** 90-96 (2020).
45. Nurrakhmawati EY. *Pola Konsumsi Pangan dan Kejadian Gondok di Daerah Gondok Endemis Gondok Berat*. (Amd.Gizi KTI, Politeknik Kesehatan, Malang, 2012)