



# Clinical Study the Relationship Between High-TSH Degree and Changes of LDL-C in Yunnan Plateau (China) Pregnant Patients' Serum

Li Bin \*, Kong Yan, Tian Meng

Department of Obstetrics and Gynecology, Kunming Angel Women's and Children's Hospital, Yunnan, China, 650032, Kunming, Yunnan, China.

\*Corresponding author: Li Bin; [abinzai@tom.com](mailto:abinzai@tom.com)

Received 10 February 2023;

Accepted 08 March 2023;

Published 12 March 2023

## Abstract

**Objective:** It was to investigate the relationship between high thyrotropin, thyroid stimulating hormone (TSH) degree and changes of low-density lipoprotein cholesterol (LDL-C) in Yunnan Plateau pregnant patients' serum in China; **Methods:** All pregnant woman were collected from the Kunming Angel Women's and Children's Hospital from January 2021 to October 2022, who were diagnosed by the endocrinology department, during their pregnancy. Then it analyzed their biochemical indicators levels and blood liquid parameters changes in their serum. Additionally, we investigated their epidemiological data, including the treatment history of hypothyroidism; **Results:** High-TSH degree and increasing of LDL-C level were both risk factors leading to hypertension, cardiovascular symptoms, symptoms of digestive tract, pregnancy ultrasound indicating small-sized fetus ( $P < 0.05$ ). Importantly, they reinforce each other on patients. Their increasing caused gestational diabetes mellitus, preterm birth history and autoimmune diseases in Yunnan plateau (China).  $TSH \geq 4.3$  m IU/L and  $DL-C \geq 3.6$  mmol/L in the pregnant patients' serum, which were approved by obstetric professional committee of that Hospital. Furthermore, only in high-TSH degree group, their high cholesterol could cause premature birth, elevated blood sugar, high blood pressure prenatal, postpartum infection and preeclampsia ( $P < 0.05$ ); **Conclusion:** These risk factors (high-TSH and LDL-C changes) could affect the health of pregnant, maternal and fetal, which should be taken to manage it so as to improve the perinatal health.

**Keywords:** high-TSH; LDL-C level; pregnant patients; perinatal period

## Introduction

Perinatal health care is a kind of system treatment science which is used to survey embryonic development, fetal physiology and pathology as well as the diagnosis and prevention of illnesses of new born babies and pregnant woman [1,2].

How to control their endocrine hormone levels during perinatal period is the new driving direction of control the risk of early clinical prevention in pregnancy adverse reactions. The thyroid stimulating hormone (TSH), coming from pituitary, is a kind of hormone promoting the growth and function of thyroid, but is also one of the fundamental risky factors to high-risk pregnancy. TSH helps thyroid hormone release and T4, T3 synthesise [3,4].

On the other field, thyroid hormone regulates the lipid metabolism. The abnormal expression of thyroxine might result the changes of various liquid metabolism and chronic disease [5-7]. Among patients with sub-clinical thyroid and thyroid reducing and dysfunction, the atherosclerosis accelerated by hyperlipidemia, affecting the danger of arterial disease. Sometimes, hypertensive disorders come together with pregnancy. And serious complications

also include the obstetric bleeding, infection and convulsions. Collectively, these above reasons causing death of maternal and perinatal women as well as infants [8,9].

In order to appropriately control the thyroid hormone levels, the relationship between the high-TSH and LDL-C level need to study clearly. The high expression level of TSH is expected to use as a high-risk warning indicator, which ensure the safety of pregnant women and infants. It was worth pointing out all results of postpartum of high-TSH pregnant had more than 12 gestational weeks. And these details of case report is as follows.

## Materials and Methods

### Subjects

**Involved:** All 270 pregnant patients were diagnosed in the Kunming Angel Women's and Children's Hospital from January 2021 to October 2022, who were diagnosed by the Endocrinology Department. Their ages were from 21 to 43, at average of  $27.32 \pm 3.40$ , years old. Their gestational time was above 12 weeks.

If they were less than 12 gestational weeks, and if they were not Yunnan (China) population, they were not involved in this study.

**Ethical Approval:** All study participants provided written informed consent. The study was according to the declaration of Helsinki and world health organization guidelines to implement. It was under the supervision of the Ethics Committee of the Kunming Medical University (No. NMGU 2021090243). The patients' data were recorded, including symptoms, history and physical examination. Even discharged from hospital, the physicians performed a monthly telephone following-up for patients' condition.

**Grouping:** According to the level distribution of pregnant patients' TSH degree, all 270 subjects were divided into two groups. In the control group, there were 127 cases with normal TSH level (0.4 to 4.3mIU/L) during pregnancy. Ages varied from 20 to 41,  $29.04 \pm 4.40$ , years old at average. In the high-TSH group, it was consisting of 143 cases. Their ages varied from 24 to 44, with average ages of  $29.53 \pm 4.80$  years old. If their TSH degree was above 4.3mIU/L, they were considered as high-TSH group. There is no statistic differences between normal control and high-TSH pregnant in age construction and gestational weeks. All materials involved were matched and tested.

**Initial Condition:** All these subjects were tested in pregnancy-induced hypertension and gestational diabetes mellitus, nephropathy and hypothyroidism and other diseases affecting blood liquid metabolism. Previous medical history of the patients was evaluated by obstetrician. The hypothyroidism was treated during pregnancy, according to Chinese Maternal health care work specification [10]. The diagnosis standards were based on the obstetric diagnostic guild-line of The International Federation of Gynaecology and Obstetrics (FIGO).

#### Survey methods

Patients' information was analyzed retrospectively and we designed special forms for this study. Two trained professional and technical staffs have access to the patients' medical records. We surveyed their age, body weight, blood pressure, blood liquids, medical history and genetic history. Furthermore, the patients' epidemiological data were obtained by telephone following-up.

#### Serological analysis

Peripheral venous blood sample collection schedule was based on weekly pregnancy time collected once three weeks. 3 ml peripheral venous blood was collected in the morning before eating. Then separated the serum under 3,500 rpm/min centrifuged for 30 min at 4°C, which were stored under -20°C for the next test.

The test of serum (indicator including FT3, FT4 and TSH) was taken by the Central Testing Laboratory of the First Affiliated Hospital of Kunming Medical University. All tests were used the Chemiluminescence immunoassay methods. And the Automatic Chemiluminescence Analyzer was purchased from Jiangsu ZeCheng Biotechnology Co., Ltd. (Model: CIA1200) (China).

The detection reagent using for TC and LDL-C testing was purchased from Sichuan Bayer Company (Cat.No.2016071798). The inter variation and intra variation of the reagents in the experiment for quality-testing should be under 5%.

Statistical analyses were performed using IBM SPSS version 20.0 statistical software (IBM Corporation, Armonk, NY, USA). Data were expressed as means and standard deviations. Analysis of variance (ANOVA) was used to compare the epidemiological data in each group. The paired test method was used to analyze the difference in the level changes of LDL-C. Additionally, Fisher's least significant difference test was used to

compare the means between the groups. Values of  $P < 0.05$  were considered statistically significant.

## Results

### General Information

Firstly, it confirmed that high-TSH degree had a clear correlation with LDL-C level increasing by laboratory serum testing, pregnant patients' physical examination and epidemiological investigation. And importantly, both of them were high risk factors for the patients healthy. Furthermore, in this study, we defined the threshold value for these indicators as following:  $TSH \geq 4.3$  mIU/L and  $LDL-C \geq 3.6$  mmol/L in the pregnant patients' serum, which were approved by obstetric professional committee of the First Affiliated Hospital of Kunming Medical University.

Additionally, the survey results data on low density cholesterol threshold, along with the clinical performances of the 143 high TSH and 127 normal TSH which were shown in Table 1. As for the complications of high-TSH, it included pregnancy hypertension, cardiovascular symptoms, digestive tract system symptoms and small-sized fetus indicated by ultrasound, and they were related to each other ( $P < 0.05$ ). However, there was no significant difference in the gestational diabetes mellitus, preterm birth history and autoimmune diseases between them ( $P > 0.05$ ). So, it could make a conclusion that high-TSH degree was related to the growth of the fetus and vascular physiological changes of pregnant women, which should be paid more attention to and take measure to prevent it.

### LDL-C level of the median

High-TSH interfered the median of LDL-C level. The dynamic trend change was analyzed, during each gestational week, by testing low density cholesterol level in the high-TSH group. It found that TSH increasing was accompanied by the continuation of the week. But by analyzing its average trend, it had no sign to decrease. When analyzed the changes of LDL-C level in the same pregnancy week time, it suggested that the increasing trend was from the beginning to the fourth week, but no continuation till childbirth.

However, regarding the slope of the growth trend of LDL-C level, it was not as large as the high-TSH degree, which might be affected by endocrine regulations of various hormone levels (Figure 1).

### Comparison of postnatal outcomes

In this detection schedule, they were monitored during total pregnancy period. All patients were grouped again by the non-sequential triglyceride (TG) level, according to the pregnant specificity. The 95% reliable data of pregnant TG should be taken as normal referenced to the value of T4. The 143 high-TSH patients were re-divided into low blood lipid group (31 patients) and high blood lipid group (112 patients). Then it compared the postnatal outcomes both of pregnant mothers and children.

There were significant differences in the premature delivery, prenatal hyperglycemia incidence, prenatal hypertension and postpartum infection ( $P < 0.05$ ) between low and high blood lipid groups. High level of blood lipid could be a high risk for the high-TSH degree pregnant patients. But, it had no difference in the premature rupture of membranes, postpartum hemorrhage, fetal distress and placental abruption ( $P > 0.05$ ). (Table 2).

### Relationship between TSH with FT3/4 FT4 in high blood lipids group

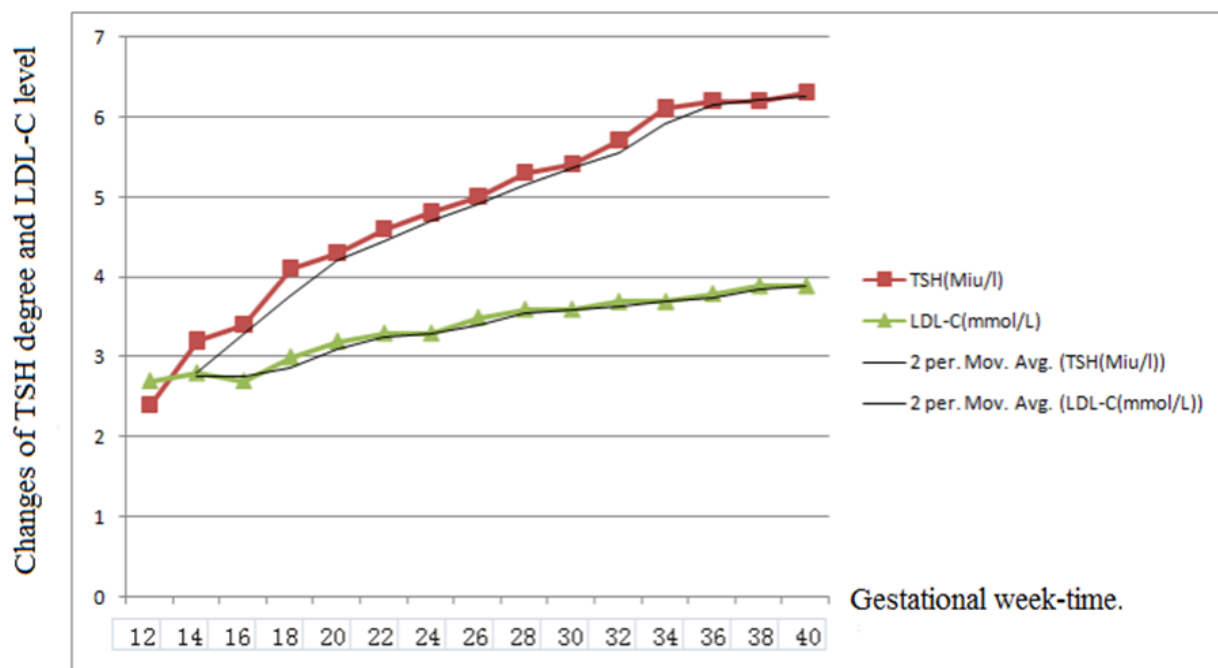
It was to understand the direct relationship between high TSH and FT3/4 in their serum. It took tracking analysis of the high-TSH group

patients from 12 to 40 weeks by biochemical testing, whose results were listed in Table 2.

Along with the rise of TSH degree, FT3 and FT4 showed a decreasing trend, even FT4 decreased greatly during 12-18 weeks. Thus, it needed medicine to prevent this downward trend.

**Table 1: Analysis of the difference of the clinical symptoms in pregnancy with high-TSH group between low and high LDL-C level subgroups.**

Clinical symptoms	Number	High-TSH group		Normal TSH group		X2	P
		Low LDL-C level	high LDL-C level	Low LDL-C level	high LDL-C level		
Pregnancy-induced hypertension	21	4	16	0	1	12.61	p<0.01
Gestational diabetes mellitus	12	3	4	2	3	0.22	p>0.05
Cardiovascular symptoms	48	11	30	3	4	17.00	p<0.01
Digestive tract symptom	64	12	22	14	16	1.13	p>0.05
Pregnancy Ultrasound indicating small fetus	76	16	43	8	9	46.42	p<0.01
Pregnant women with abnormal body weight	83	18	38	12	15	20.27	p<0.01
Personal or family history	17	4	5	5	3	0.12	p>0.05
The history of premature birth or spontaneous abortion	14	4	3	3	4	0.00	p>0.05
Autoimmune disease	11	3	3	3	2	0.18	p>0.05



**Figure 1: The changes in TSH degree and LDL-C level at different gestational week-time.**

**Table 2: Control Study of high-TSH blood lipid group with normal TSH degree.**

Group	Low blood lipid group	High blood lipid group
Number	31	112
Premature delivery	9	57#
Increased blood sugar	11	66#
Increased blood pressure	14	89&
Premature rupture of membranes	2	4
Postpartum hemorrhage	3	4
Cesarean section	3	6
Fetal distress	1	7
Placental abruption	2	3
Puerperal infection	3	32#
Gestational hypertension in later life	2	2
Abnormal liver function	7	16

**Note:** # when compared with low blood lipid group, there were statistic differences ( $P<0.05$ ); & compared with low blood lipid group, there were notable statistic differences.

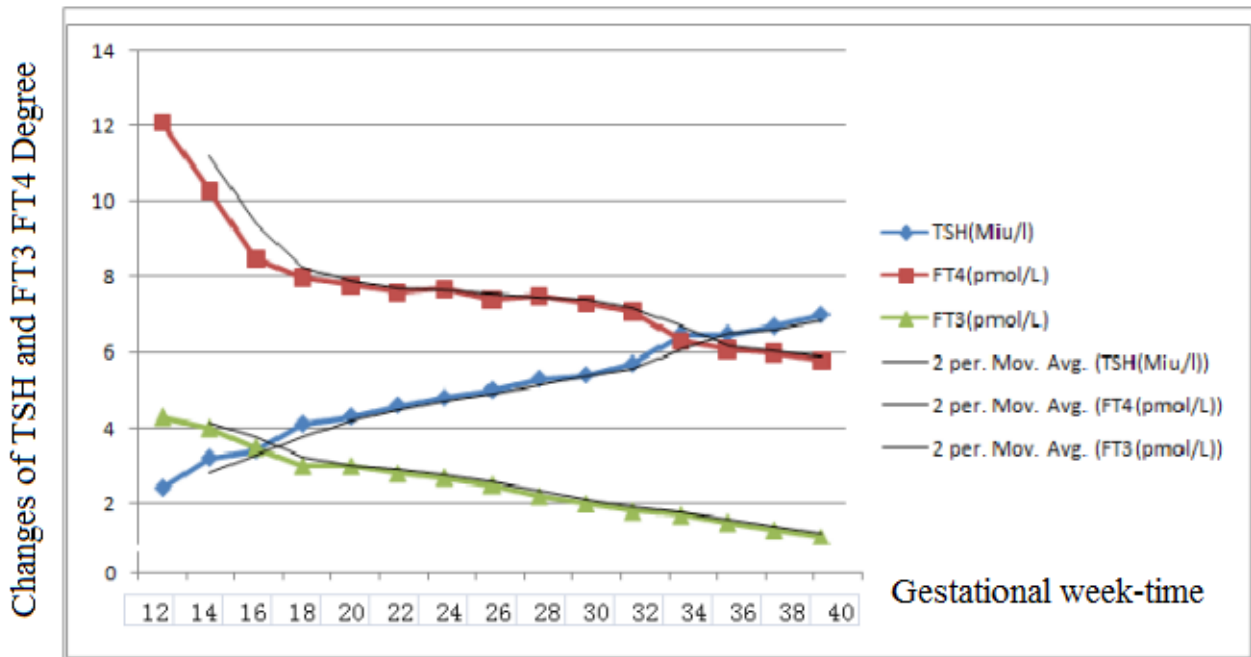


Figure 2: The changes in TSH and FT3 FT4 degree at different gestational week-time.

## Discussion

Perinatal health care is an important part of perinatal medicine, whose aim is to decline the death rate of perinatal children and prevent the incidence rate of pregnant women. Regarding the perinatal medicine, the scientist pays more focus on secretion regulation because women in pregnant period greatly influence the growth of fetus.

TSH plays an important role in the pregnancy period. Clinical and non-clinical hypothyroidism as well as perinatal health care have been well discussed in recent years [3-5]. The high-TSH degree further influences the normal metabolism of blood lipid, forming endocrine systemic diseases.

This study analyzed the serum indications for thyroid function retrospectively, and discussed the basic strategies of thyroid function screening methods. We set some thresholds of clinical risk factors with TSH and LDL-C, which both of them had relationship with hypothyroidism.

The scientist from the Third Military Medical University (China) indicated that thyroid dysfunction of women childbearing age had an important impact on the process and results of pregnancy [11]. The clinical hypothyroidism or sub-hypothyroidism might lead to infertility. It was also related to spontaneous abortion, hypertensive disorder complicating pregnancy, premature labor, placental abruption, fetal distress and low birth weight infants by their survey. On the other side, it might cause new born babies with low intelligence. This result was consistent with our research.

Ph.D. Li Jianan [12] found that blood lipid was higher in the late pregnancy than that in postpartum period. It was obviously that lipid was higher than the non-pregnant group, if pregnant. The difference had been significant. However, Ph.D. Chen Shuo [10] found that the increase of blood lipid in pregnant women serum was a normal issue. The higher lipid levels are well known in pregnancy, but the regular checking is useless, since all the effective lipid lowering agents are contraindicated in pregnancy. Our regular checking results might suggest the most suitable healthy diet for pregnant women.

Furthermore, it might be influenced by estrogen levels. The increasing of blood lipid does not cause illness, because it would be decrease when postpartum period.

Study from the First Hospital of Peking University (China) [13] showed that the screening indications of thyroid function or sub clinical hypothyroidism, had an impact on the pregnant results among 548 pregnancy cases, for early warning of hyperlipidemia. FT4 with TSH among 111 showed dropping. This trend and the sub clinical hypothyroidism were important in disease screening.

Many hormone levels were changing when pregnancy, which clearly influences lipid and apolipoprotein metabolism. Firstly, estrogen declined the LDL-C level, while progesterone declined TG, but up-regulated the LDL-C level. Then the increase of LDL-C leads to arteriosclerosis. The incidence rate of sub clinical hypothyroidism in worldwide is 2.2% for pregnant women, but it is up to 5.32% in China, which is higher.

But by now, scientist still have not reached an agreement on the strategies of screening indicators of thyroid function during pregnancy [14,15]. The key issue was no standard on clinical reference for thyroid function during pregnancy in the world, neither is sub clinical hypothyroidism [16,17]. The exact relationship between sub clinical hypothyroidism and adverse pregnancy outcome is uncertain, making it hard to get a standard in drug intervention time, drug intervention dose and the effect achieved after intervention. This research approved by committee of the First Affiliated Hospital of Kunming Medical University, had been properly discussed and made an effective method by retrospective analysis. We defined the threshold value for these indicators as following:  $TSH \geq 4.3 \text{ mIU/L}$  and  $DL-C \geq 3.6 \text{ mmol/L}$  in the pregnant patients' serum. Additionally, we further analyzed the risk factors of adverse outcomes in low-density cholesterol in serum by testing the degree of TSH and combining FT3 and FT4 degree. We look forward to more effective interventions in the future to help address these risk factors for pregnant women.

## Acknowledgment

This work was supported by the Fundamental Research Project of Science and Technology Planning Project in Yunnan Province (202201AT070243).

## Conflicts of Interest

All authors declare no competing interests.

## References

- [1] GBD 2013 Mortality and Causes of Death, Collaborators (17 December 2014). "Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.". *Lancet*. 385: 117–171.
- [2] Reiter RJ, Tan DX, Korkmaz A, Rosales-Corral SA (2014). "Melatonin and stable circadian rhythms optimize maternal, placental and fetal physiology". *Hum. Reprod. Update*. 20 (2): 293–307.
- [3] Merck Manual of Diagnosis and Therapy, Thyroid gland disorders.
- [4] The American Heritage Dictionary of the English Language, Fourth Edition. Houghton Mifflin Company. 2006. ISBN 0-395-82517-2.
- [5] Beck-Peccoz P, Persani L (Oct 1994). "Variable biological activity of thyroid-stimulating hormone". *Eur J Endocrinol*. 131 (4): 331-40.
- [6] Sergi I, Papandreou MJ, Medri G, Canonne C, Verrier B, Ronin C (Jun 1991). "Immunoreactive and bioactive isoforms of human thyrotropin". *Endocrinology*. 128 (6): 3259–68.
- [7] Duntas LH, Tsakalakos N, Grab-Duntas B, Kalarritou M, Papadodima E (2003). "The use of recombinant human thyrotropin (Thyrogen) in the diagnosis and treatment of thyroid cancer". *Hormones*. 2 (3): 169-74.
- [8] Dashti M, Kulik W, Hoek F, Veerman EC, Peppelenbosch MP, Rezaee F (2011). "A phospholipidomic analysis of all defined human plasma lipoproteins.". *Sci Rep*. 1 (139).
- [9] Dashty M, Motazacker MM, Levels J, de Vries M, Mahmoudi M, Peppelenbosch MP, Rezaee F (2014). "Proteome of human plasma very low-density lipoprotein and low-density lipoprotein exhibits a link with coagulation and lipid metabolism.". *Thromb Haemost*. 111: 518-530.
- [10] Cite as:  
<http://www.nhfpc.gov.cn/zwgkzt/wsbysj/201107/52320.shtml>
- [11] Sun Xiao, Zhang Lei, Yang Huixia, Zhou Yingfang, Sun Weijie. The screening indication of thyroid function of 548 cases and the effects of subclinical hypothyroidism on pregnancy outcomes. *Chin J Clin Obstet Gynecol* 2014;15(1):45-50.
- [12] Cheng Shuo Ma Wuxiang Liu Guohua. Analysis of Changes of Blood Lipid in Normal Pregnant Women during Pregnancy "The 10th National Military Medical Laboratory Paper Proceedings" 2005.
- [13] Moncayo R, Moncayo H.A post-publication analysis of the idealized upper reference value of 2.5 mIU/L for TSH: Time to support the thyroid axis with magnesium and iron especially in the setting of reproduction medicine. *BBA Clin* 2017;7:115-119.
- [14] Wang S, Teng WP, Li JX, Wang WW, Shan ZY. Effects of maternal subclinical hypothyroidism on obstetrical outcomes during early pregnancy. *J Endocrinol Invest* 2012 ;35(3):322-5.
- [15] Cai Y, Zhong L, Guan J, Guo R, Niu B, Ma Y, Su H. Outcome of in vitro fertilization in women with subclinical hypothyroidism. *Reprod Biol Endocrinol* 2017;15(1):39.
- [16] Zhang Y, Wang H, Pan X, Teng W, Shan Z. Patients with subclinical hypothyroidism before 20 weeks of pregnancy have a higher risk of miscarriage: A systematic review and meta-analysis. *PLoS One* 2017;12(4):e0175708.
- [17] "Reproductive Health and Research Publications: Making Pregnancy Safer". World Health Organization Regional Office for South-East Asia. 2009.



**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third-party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>.

© The Author(s) 2023