Clinical and Environmental Factors Affecting Goitre Growth in Sri Lanka

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ABSTRACT

Goitre, an enlarged thyroid gland, is a major health issue in tropical countries, primarily linked to Iodine deficiency. However, clinical, environmental, and genetic factors also contribute to the disease. This study explores the relationship between clinical and environmental factors influencing goitre occurrence in five districts of Sri Lanka: Anuradhapura, Colombo, Kurunegala, Nuwara Eliya, and Rathnapura, covering different climatic zones. The data consists of a hospital-based preliminary study conducted from 2012 to 2014, which involved 994 goitre patients from five base hospitals in Sri Lanka. A structured questionnaire survey recorded clinical examinations and investigation findings. Additionally, 562 water samples for Iodine and 147 samples for Selenium were collected from water sources used for drinking and cooking. The study included patients with a mean age of 43 years, predominantly females (98%), and 36% had a family history of goitre. Grades 3 and 4 were prevalent among the six goitre grades. All climatic zones showed an increasing trend of goitre grade with age. Notably, patients in the wet zone had higher goitre grades at younger ages compared to the other zones. Hierarchical cluster analysis based on environmental factors (Iodine and Selenium concentrations), clinical factors (thyroxine, triiodothyronine, and thyroid-stimulating hormone) and demographic factors identified seven clusters, categorizing patients based on dominant features. The most prominent cluster consisted of patients from Nuwara Eliya district, displaying a significant negative correlation between Iodine and Selenium levels with thyroxine. These clusters challenge the traditional methods of diagnosing endemic Goitre based solely on district and zone. The study provides valuable baseline data for effective planning and intervention strategies to prevent and treat goitre.

Keywords: Clinical factors, Environmental factors, Goitre, Hierarchical cluster analysis. Iodine deficiency

INTRODUCTION

Goitre is a swelling of the thyroid gland that causes a lump in the front of the neck. It can be associated with a thyroid that is not functioning properly. The thyroid gland produces the hormones thyroxine (T4) and triiodothyronine (T3) where most of the T4 is changed to T3 outside of the thyroid [1]. These hormones play a role in certain bodily functions, including body temperature, mood and excitability, pulse rate, digestion and others [2]. In Sri Lanka, Goitre is a complex condition with several unidentified environmental and clinical causes. Besides low Iodine in water, goitrogens in food and family history also play a role. Studies have revealed the disease passes from one female generation to the other [3]. Recent studies have also revealed the possible effect of Selenium on the disease [4]-[6]. Clinical studies conducted in Sri Lanka are mainly based on hospital setup and influential geographical factors are usually avoided. Diseases like Goitre where environmental factors are known to contribute, need different patient management than the conventional setup. Hence the main objective of this study is to investigate new patient clusters based on both clinical and environmental factors surrounding their households. Notably, Iodine and Selenium in natural water bodies of Anuradhapura, Kurunegala, Colombo, Kalutara and Nuwara Eliya along with histopathological studies of patients in respective districts were considered. The new clustering can be used for better medical intervention and future disease mitigation.

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MATERIALS AND METHODS

The present study evaluates 994 patients (36 men, 958 women) who attended the clinics for surgical treatment of Goitres during the period of year 2012 to 2014. Preliminary survey, collection of the details of Goitre patients from base hospitals and the collection of water samples were done in Nuwara Eliya, Anuradhapura, Kurunegala, Kalutara and Colombo districts. The survey was conducted to identify any factor behind the patients prior to identifying the places for water sampling. Prior to sample collection, a preliminary study was carried out in respective hospitals on Goitre patients. A hospital-based questionnaire was arranged to gather information on gender, age, family history of Goitre, age at menopause and menarche from female patients, while grade of Goitre, Clinical status and treatment methods (Fine Needle Aspiration Cytology (FNAC) or Ultrasound Scan (USS)) were collected from the medical authority in respective hospitals.

The prospective cohort study examined 221, 207, 145, 230 and 220 goiters from Colombo, Kurunegala, Anuradhapura, Nuwara Eliya and Rathnapura districts respectively, and 562 water samples for Iodine and 147 samples for Selenium were collected from running and stagnant water bodies in above mentioned districts. Descriptive statistical methods were carried out zone wise and district wise to understand the behavior of clinical and environmental factors. Variation of Iodine and Selenium concentration in each district were visualized using Geographic Information Systems (GIS) software (ArcMap 10.7.1).

Multivariate Analysis of Variance (MANOVA) is used to identify significant differences in thyroxine (T4), triiodothyronine (T3) and Thyroid-stimulating hormone (TSH) levels of the study participants which were recorded prior to the treatment. Moreover, the association between hormone levels with Iodine and Selenium contents in water was analyzed in terms of correlation techniques. Finally, hierarchical cluster analysis was used to achieve the specific objective of the study which was to identify new clusters to classify patients other than district or zone wise while breaking the traditional methods to diagnose or disease management from endemic Goitre.

RESULTS AND DISCUSSION

From the clinical survey, it was evident that the incidence of endemic Goitre is high in Nuwara Eliya, Colombo and Rathnapura with equal percentage of 22% of the population of the study. Among them the majority was females (93.64%) and the mean age of Goitre for the current population was 43 years. As the studies suggest that Goitre can be transmitted from generation to generation by hereditary characteristics, surprisingly the present study reveals the vice versa of the previous knowledge on Goitre carried via genes. When considering the progression of Goitre, the variation among districts is significant. Nuwara Eliya and Ratnapura (Wet Zone) have more Grade 1b and Grade 2 patients compared to Anuradhapura and Kurunegala Dry Zone) (Fig 1).

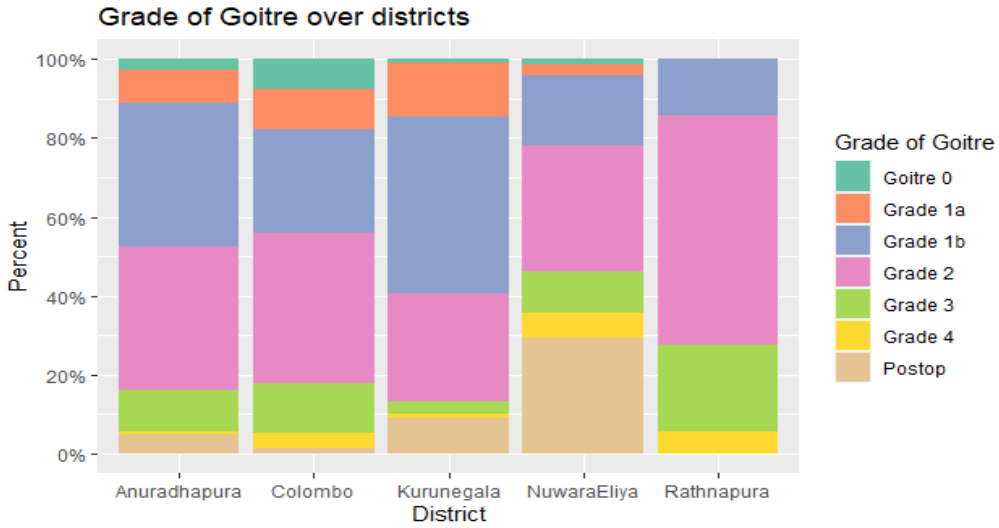

Fig. 1 Distribution of Goitre Grades over districts

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Moreover, Grades 3 and 4 were found to be more prominent among patients with mean age 40 and 42 respectively. Patients in Wet zone had higher grades of Goitre at younger ages compared with other two zones (Fig. 2).

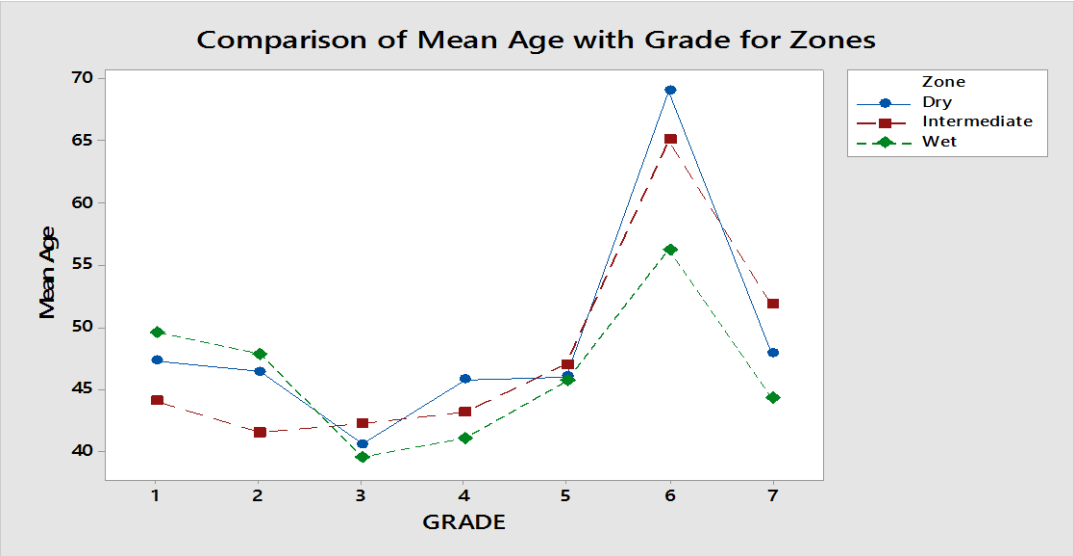

Fig. 2 Comparison of mean age and TSH levels among climatic zones

A clear decrease in TSH values for patients in Wet zone was observed while T4 values behave similarly for Dry and Intermediate zones but a deviation was expected in Wet zone (see Fig. 3 & Fig. 4).

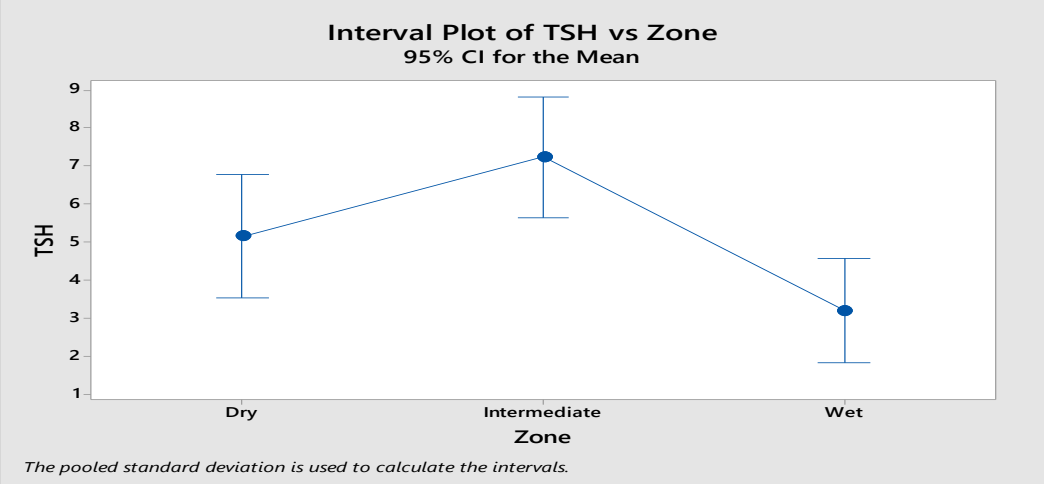

Fig. 3 Interval Plot of Tsh Levels Across Different Zones

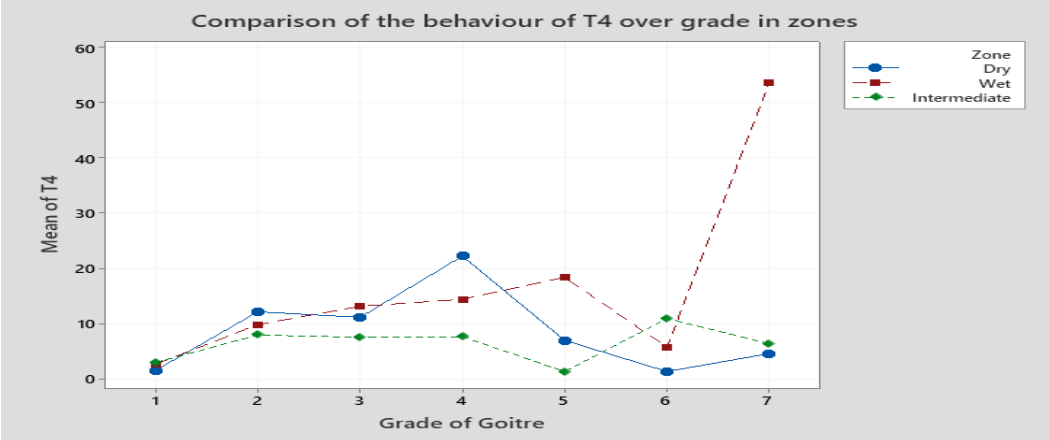

Fig. 4 Comparison of T4 Levels across Grades of Goitre in different

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The Iodine concentration levels of water samples collected from each district indicate significant differences as in indicated in Table 1. Nuwaraeliya indicates the lowest mean concentation complard to all other istricts followed by Kalutara.

TABLE 1 Distribution of Iodine Levels (µg/L) across Districts

District	Sample Size	Mean Iodine Level (µg/L)	Standard Deviation	Confidence Interval (95%)
Anuradhapura	321	235.54	131.8	(223.86, 247.22)
Kalutara	73	26.85	16.82	(2.36, 51.34)
Kurunegala	153	233.4	129.8	(216.50, 250.3)
Nuwara Eliya	175	5.398	9.46	(0.00, 21.216)

The geographical formation in hill country and the complex distribution of waterbodies can be the main reason for this difference. According to correlation analysis for TSH with Selenium levels indicated a weak positive correlation for Nuwara Eliya district ($r = 0.2$, $P\_val<0.05$), but there was no significant correlation with iodine levels. None of the other districts indicated significant associations to hormone levels with Iodine or Selenium. This leads to the need for different categorizations of patients other than district or climatic zones.

Hierarchical cluster analysis was then performed, which resulted in seven clusters, as shown in Fig. 5 and features of each cluster are summarized in Table 2.

Out of the seven identified clusters, Cluster 1 is primarily composed of patients residing in the dry zone region. This region is characterized by arid or semi-arid climates with limited rainfall and high temperatures. The patients in this cluster have an average age of 45 years, indicating that they belong to the middle-aged population.

Although patients in Cluster 1 have a considerable amount of T4 and TSH recorded, the occurrence of Goitre among them may be influenced by several reasons. If there is insufficient Iodine intake in the diet, arid climates may limit the natural sources of Iodine, such as seafood and Iodine-rich soil. Cluster 2 primarily consists of patients residing in the wet zone region. The wet zone is characterized by high levels of rainfall and humidity. The patients within this cluster exhibit distinctive characteristics in terms of their thyroid function, with the lowest TSH levels and high levels of T4 and Iodine-Selenium imbalance.

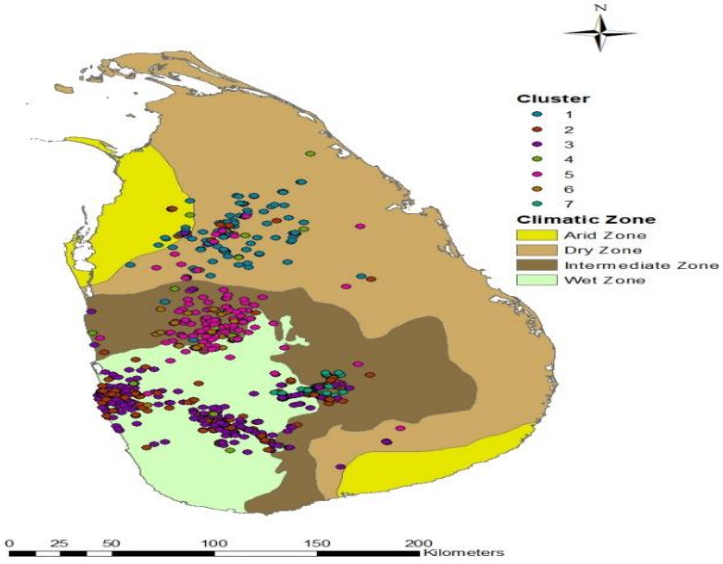

Fig. 5 Map of Patient Locations according to Cluster

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TABLE 2 Mean Values of Clinical and Environmental Factors According to Cluster

Cluster	Age (Years)	T4 (ng/ml)	TSH (µg/ml)	Iodine(µg/L)	Selenium (µg/L)
1	45.105	13.19	5.536	214.719	2.482
2	42.913	25.033	3.395	35.938	15.479
3	43.219	7.843	5.561	25.116	1.55
4	**45.778**	14.169	3.567	115.506	7.296
5	44.222	9.009	5.67	**256.757**	1.976
6	42.667	2.755	4.221	245.848	1.926
7	42.158	**39.712**	**9.064**	2.225	**86.318**

Since TSH is the major regulator of thyroid function, this is crucial for the modulation of thyroid hormone release and growth of the thyroid gland.

Cluster 3 consists predominantly of patients residing in the wet zone of Sri Lanka, specifically in districts such as Colombo and Rathnapura. Notably, this cluster exhibits the lowest Selenium levels among the patients. Furthermore, Cluster 3 can be considered a subset of Cluster 2. Cluster 4 represents a diverse group of patients spread across all five districts under consideration. This cluster encompasses individuals from various regions, potentially representing a wide range of backgrounds and environments. Notably, the patients in Cluster 4 have the highest recorded average age of 46 years. Cluster 5 consists of patients primarily residing in the Kurunegala district, which is part of the intermediate zone in Sri Lanka. The intermediate zone is characterized by a combination of environmental conditions found in both dry and wet zones.

Notably, patients in Cluster 5 have the highest recorded Iodine levels and low T4, TSH levels. It was observed that the coincidence of lower Iodine content with high amount of T4, TSH and Selenium levels which is evidence of Goitre prevalence. Therefore, it suggests that there was a strong inverse relationship between TSH and Iodine levels in water sources. This indicates that irrespective of climatic zones, Goitre patients are reported where low Iodine and high amount of T4 and TSH. Further, it suggests that the climate plays a secondary role for the Goitre progression.

Cluster 6 shares several similarities with Cluster 5, including a concentration in the same geographical region. However, Cluster 6 is distinguished by the lowest recorded T4 levels with high Iodine levels. Moreover, these Goitres are formed from genetically induced ones from family to family. The highest mean for Iodine is due to low rainfall pattern seen in Kurunegala district, since tanks and stagnant bodies are dominant in this district, which lead to have more Iodine content within them. Since Iodine is concentrated, people who use water from open lakes in Kurunegala seem to be in less danger from Goitre.

Cluster 7 represents the final cluster and primarily consists of patients residing in the Nuwara Eliya district, which falls within the wet zone of Sri Lanka. This cluster exhibits several distinctive factors, including the lowest Iodine levels, highest Selenium levels, highest T4 and TSH levels, and the lowest average age group recorded (42 years). Being concentrated in the Nuwara Eliya district, Cluster 7 focuses on a specific region within the wet zone characterized by its unique environmental conditions. The wet zone, with its high rainfall and humidity, presents different health considerations compared to other zones in Sri Lanka. One notable feature in Cluster 7 is the lowest Iodine levels among the patients. Conversely, Cluster 7 shows the highest Selenium level, which is an essential mineral in thyroid function. Understanding the relationship between the Nuwara Eliya district, the wet zone with its notable features in Cluster 7 is crucial for identifying potential health challenges and informing targeted interventions. The Iodine and Selenium concentration in Nuwara Eliya district clearly indicates the findings confirming Cluster 7 (Fig. 6).

CONCLUSION

The main objective of this study is to investigate the association between clinical and environmental factors

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affecting goiters in Sri Lanka after identifying similar patient groups using cluster analysis. Seven clusters were identified based on clinical and environmental factors which has different patient groupings other than districts or zone only. The analysis considers only clinical factors and drinking water quality of the patients. Including the dietary patterns of the patients can further improve the findings of this study.

Further analysis within this cluster can shed light on the

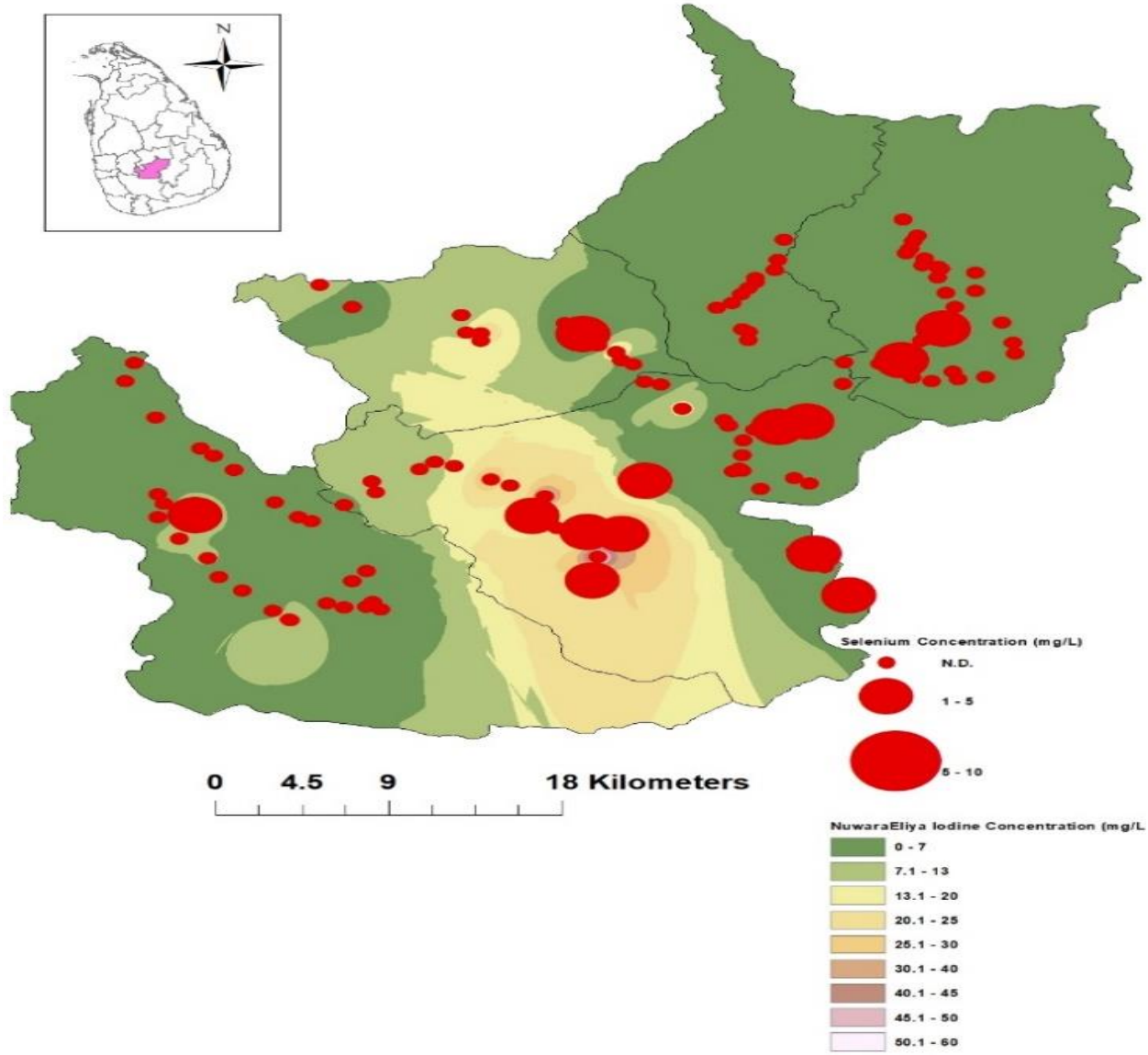

Fig. 6 Variation of Iodine and Selenium Concentrations in Nuwara Eliya

specific factors contributing to the observed hormonal profiles, age-related health conditions, and the impact of environmental and dietary factors in the wet zone.

The clustering can be finetuned by including a control group to the study and validating with new cases in future. Furthermore, the highest recorded T4 and TSH levels within Cluster 7 suggest potential hyperthyroidism, a condition characterized by excessive thyroid hormone production. This knowledge can guide public health efforts aimed at addressing Iodine deficiency, optimizing Selenium intake, managing hyperthyroidism, and addressing the unique health needs of the younger population in the Nuwara Eliya and the wet zone. The identified features within these clusters challenge the traditional methods of diagnosing endemic Goitre solely based on district or zone. This classification provides valuable insights for improved planning and prevention strategies in tackling Goitres effectively. By considering factors beyond geographical boundaries, healthcare professionals can develop more targeted approaches to avoid and treat Goitres, leading to better outcomes for affected individuals.

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