Incidence and dietary risk factors of goitre in children in a rural area/ D.R.Congo

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ABSTRACT

Background: Although deficiency in dietary iodine remains the main cause of endemic and sporadic goitre, naturally occurring goitrogens in foods are additional factors that play a major role in developing goitre. In this study we focused on the relationship of different potential goitrogenous food and the development of goitre in preschool children in the rural area of Bwamanda, Democratic Republic of the Congo (DRC).

Objectives: First, to do a semi-systematic literature review on the incidence of goitre and the role of dietary pattern in its genesis. Second, describe the incidence of goitre in preschool children in DRC in relation to age, sex, and season. Third, examine the effects of specific food items on occurrence of goitre in these children.

Methods: For the 1st objective, we used a semi- systematic method to search for relevant published articles to the topic area. We searched four online databases, three online journals, five authors and the reference lists of the identified key articles. We did a secondary analysis of the data from an original dynamic population study which was done in the rural area of Bwamanda, DRC. That study included an open cohort of 5657 children which was followed up every 3 months throughout six survey rounds, during a period of three years from 1989-1991. All the investigations and clinical examination were done by trained doctors and interviewers at special under five clinics in the study setting.

Incidence of goitre among the children who were at risk of developing goitre was calculated for 5 survey intervals. The incidence of goitre was also assessed in relation to season, sex and age of the children.

For the 3rd specific objective, seven food items were selected to be investigated for their potential goitrogenic effects. The exposed group was those children who ate these foods and the unexposed group was the children who didn't eat these foods. Age, sex, height for age Z-score (HAZ), and weight for length Z-score (WLZ) were considered as potential confounders. All selected food items and confounders were analysed using logistic regression analysis.

Results: Four studies were included in the semi-systematic literature review; the conclusion was similar in all of them with iodine deficiency being the main cause of goitre in man, and cassava consumption being an important factor in addition to that.
Incidence of goitre was different in each survey interval and it was higher in rainy season. The incidence of goitre increased significantly when children got older but being a male or a female was statistically unrelated.
Eating cassava leaves, cassava tubers and maize played a major role in developing goitre especially in older children, while nuts reduced the risk of developing goitre in those children. Banana, fish and papaya had non-significant contributions.

Conclusion: This study confirms that goitre incidence in children (0-5years) in a rural area in Central Africa is significantly related with age as the older children had more risk to develop goitre than the younger children, but it had no relation to gender. The incidence of goitre increased also during rainy seasons.

This is the 1st longitudinal analysis showing the relationship between consumption of specific food items and the development of goitre in children (0-5 years) in a rural area in central Africa, where cassava and maize found to be important contributory factors while nuts may have a protective role in developing goitre in those children.

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LIST OF ABBREVIATIONS

CI	Confidence interval
DRC	Democratic Republic of the Congo
HAZ	Height for age Z score
ICCIDD	International Council for Control of Iodine Deficiency Disorders
ID	Iodine deficiency
IDD	Iodine deficiency disorders
IOC	Iodized oil capsules
OR	Odds ratio
RR	Relative risk
SCN	Thiocyanate
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
TGR	Total goitre rate
TGP	Total goitre prevalence
UI	Urine iodine
USI	Universal salt iodization
WHO	World Health Organization
WLZ	Weight for length Z score

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1. INTRODUCTION AND BACKGROUND

Iodine

Iodine is a necessary element for human beings and only small amounts (15-20 mg) are present in a healthy body (Hetzel, 1989). Iodine constitutes the thyroid hormones thyroxine and triiodothyronine, therefore, iodine is essential for the normal growth and development of the human body, and only 0.1-0.15 mg/day is enough to meet this requirement in adults (Hetzel, 1989). Iodine is found mainly in sea water and deep layers of the soil, and less found in old exposed soil and in mountainous areas like the Himalayas, the European Alps, and the Andes. Regions which are far from the oceans could be iodine deficient as well, like central Africa and Eastern Europe. Glaciations, flood, rain, snow and strong wind are causes for the loss of iodine from the soil. Plants grown in such soil would be iodine deficient and people who are totally dependent on that plants in their diet would be iodine deficient as well. The iodine concentration in iodine deficient soil or water could be 10 times less than the iodine concentration in soil or water which is not iodine deficient (Hetzel, 1989). Twenty-nine percent of world's population in almost 130 countries is living in iodine deficient areas (de Benoist et al., 2008).

Goitre and IDD

The enlargement in the thyroid gland is called goitre and it is mainly due to iodine deficiency which affects the normal production of thyroid hormones. Iodine deficiency is the primary cause of goitre where other causes like goitrogens can be presented as secondary factors that influence the effect of iodine deficiency (Delange, 1994). Goitre is the most common result of iodine deficiency in human in the world, yet iodine deficiency has a very wide spectrum of effects that start from fetal life up to the late adulthood period (Hetzel, 1989). Since goitre is the most obvious and significant manifestation of iodine deficiency, only the term 'goitre' was used previously, then in 1983, the term iodine deficiency disorders 'IDD' was suggested instead to include all the effects of iodine deficiency beside goitre on the health, development and growth of human beings (Hetzel, 1983). It is clear from the definition that all these effects and disorders can be prevented and treated by correction of iodine deficiency except those occurring during fetal stage (Hetzel, 1989). Neonatal effects of iodine deficiency are mainly on brain development during the first two years of life, while iodine deficiency is associated mostly with goitre in childhood and adulthood periods (Hetzel, 1989). Thyroid failure resulted from iodine deficiency during fetal stage and early childhood stage will lead to irreversible brain damage. Cretinism is the most damaging disorder of iodine deficiency along with irreversible mental retardation during these stages (Delange, 2001). In severely endemic areas, cretinism is estimated at 5-15% of the population, and iodine deficiency could result in IQ loss of 13.5 points, something that has a great effect on a population and an entire nation in severely endemic areas (Bleichrodt and Born, 1994)

Cretinism is the strongest manifestation of IDD, and it is of two types: neurological and myxedematous (Srivastav et al., 2012). Cretinism was reported to be very severe in Asia and less in Africa except for the formerly Zaire/ DRC that had one of the most extensive endemics of cretinism in the world (Delange et al., 1972).

Approximately, 1.6 billion or one about third of world population were at risk for ID, 30-70% of them had goitre, and 1-10% had cretinism (UNICEF, 1998). Estimated number of women who are at risk of IDD and getting pregnant is around 3 million, which resulted in around 15000 fetal death and around 30000 cretins birth (Kavishe, 1996).

Before 1990, Total Goitre Rate (TGR) or Total Goitre Prevalence (TGP) as the universally agreed terminology, was the main indicator used in the assessment of IDD prevalence (World Health, 1996). This is considered as a poor indicator with many limitations as TGP would take long time before returning to normal after the correction of iodine deficiency in the endemic areas (International Council for Control of Iodine Deficiency et al., 2001). However TGR can help in reflecting the population iodine nutrition status in the past, the severity of IDD at baseline and the long term impact of control programmes (World Health, 1996). Urine iodine (UI) is the recommended measurement over TGR, it is more sensitive indicator and many countries are using UI in their controlling programs to monitor the iodine status (International Council for Control of Iodine Deficiency et al., 2001). However, palpation of thyroid gland is the simplest way to assess goitre prevalence, although it is neither feasible nor practical way in neonates and young age group and misclassification can occur easily. Ultrasonography is the more precise and the recommended way to measure the thyroid volume yet it is not feasible in many regions around the world.

School-aged children (6-12 years) can be used as a proxy for the entire population, and a school-based sampling method for UI and TGP is recommended to monitor IDD in the general population (Hetzel, 1989). Iodine deficiency is considered to be a public health problem when the median UI is below100 μg/l or goitre prevalence is above 5% (International Council for Control of Iodine Deficiency et al., 2001). Other indicators are more expensive and difficult to implement in many settings (International Council for Control of Iodine Deficiency et al., 2001). The magnitude of IDD was assessed in 1999 in different WHO regions. The assessment was based on goitre prevalence in each region and it showed that the highest percentage of 32% found in the Eastern Mediterranean region where 152 out of 473 million people had goitre. Africa was the next highest with a percentage of 20; where124 out of 612 million people had goitre and the Americas were with the lowest percentage of 5 (International Council for Control of Iodine Deficiency et al., 2001). The prevalence of goitre had been investigated by palpation of thyroid gland and classified based on the WHO classification (International Council for Control of Iodine Deficiency et al., 2001).

The normal thyroid gland is non-palpable or slightly palpable with normal thyroid function. Goitre is 'a thyroid gland whose lateral lobes have a volume greater than the terminal phalanges of the thumb of the person examined' (Perez et al., 1960).

Goitre can be classified into 3 categories (International Council for Control of Iodine Deficiency et al., 2001):

- Grade 0: Neither palpable nor visible goitre

- Grade 1: A goitre that is palpable but not visible when the neck is in the normal position, even when the thyroid is not visibly enlarged. Thyroid nodules in a thyroid, which is otherwise not enlarged, fall into this category

- Grade 2: A swelling in the neck that is clearly visible when the neck is in a normal position and is consistent with an enlarged thyroid when the neck is palpated

Elimination of IDD

The global efforts to eliminate goitre or IDD started in 1932, after the meeting in Bern, Switzerland, where it had been correctly identified iodine deficiency as the cause of goitre problem in the world and iodine prophylaxis had been recommended on a national level to eliminate that problem (Assey, 2009).

So, the control of iodine deficiency became a part of the most national nutrition strategies and more than 120 countries were implementing salt iodation programs by 2006 (Assey, 2009). There are several interventions which have been used, Iodized Oil Capsules (IOC) were used as a short-term measure in areas with severe IDD, while the Universal Salt Iodation (USI) is the long-term measure to control IDD worldwide (Assey, 2009).

Africa and IDD

Iodine deficiency disorders are widely spread in Africa and it is an old problem there. Africa was ranked as the third most affected region in the world, after Western Pacific and South East Asia (Kavishe, 1996). Yet, not all the African countries have online data on goitre and IDD; this makes it difficult to address the real magnitude of the problem and the appropriate interference to solve it. However, methods of control would be the same for many countries in Africa and great efforts have been made to eliminate this significant health problem there. Iodized salt on long term basis has been found to be the most cost effective approach to combat IDD not only in Africa but in all regions affected by IDD around the world. Many success stories have been reported in different countries and IDD were eliminated in many regions including Africa. However, there are many countries on the African continent are still having IDD problems; this could be a big challenge since many of the African countries are in unstable political situation and armed conflicts. Additionally, harsh environmental factors and many natural disasters are happening there, with certain dietary habits of people living in remote or rural areas, all these factors can increase the influence of the IDD in these regions. According to WHO, 59.7 million children are suffering from insufficient iodine intake and its consequences in Africa with a prevalence of around 43% (WHO 2001).

Formerly Zaire/ The Democratic Republic of the Congo (DRC)

Formerly Zaire is the second largest country in sub-Saharan Africa with an estimated population of 68 million in 2011, and estimated annual growth rate of 3.39 percent (Worldbank, 2011) . The climate is tropical; hot and humid in equatorial river basin; cooler and drier in southern highlands; cooler and wetter in eastern highlands, north of equator has wet season from April to October and dry season from December to February, south of equator has wet season from November to March and dry season from April to October (Greenwich, 2013).

Life expectancy at birth estimated at 48 years for males and 50 years for females in 2011 (Worldbank, 2011). Infectious and parasitic diseases are prevalent and major health threat in the area, and according to the UN estimates, less than 50% of the population had access to health care and only 14% had access to safe water in 1990 (Meditz 1993). Malnutrition is widely spread and measurements show that at least one quarter of the children is undernourished; anemia and IDD are also prevalent in the region (Meditz 1993). The main cause of malnutrition there is poverty in addition to deficiency in food production and poor food quality. Also, despite large mineral resources, economy is very poor and is collapsing because of mismanagement and wide spread corruption in the country (Meditz 1993).

Agriculture is the main economic sector, yet it is neglected. Subsistence farming from the other hand is playing an important role in reducing the food insecurity of the rural households in parts of Africa (Baiphethi and Jacobs, 2009). The major food crops that people depend on are cassava and maize followed by corn, rice, millet, yams, potatoes, beans, bananas and fruits and cassava is the main staple food till our days. Cassava is grown nationwide, both roots and leaves are eaten and annual cassava production was estimated at 18.2 million tons in 1991 (Meditz 1993). Corn is also grown throughout the country and it is the preferred staple if available. Rice is grown in the humid climate in certain parts of the country; millet is grown in the savanna areas and important in dry parts of the country.

The DRC is one of the most affected regions in the world by IDD, the country is heavily populated so large number of people are at risk of iodine deficiency disorders and its devastating complications (ICCIDD, 2013). Population living with IDD is estimated at 13 million in DRC, and more than half of them are women in reproductive age and children (ICCIDD, 2013).

Goitrogens and goitrogenic food

Goitrogens are any active forces or substances that induce goitre (Hetzel 1989). With diet variation, goitrogens have no significant role in the development of goitre, however, goitrogens play an extremely important role in areas where population is with low dietary intake of iodine (Hetzel 1989). Goitrogenic food is likely a cause for the persistence of endemic goitre in different part of the world (Chandra et al., 2009).

Although the deficiency in the dietary iodine remains the main cause of endemic and sporadic goiter, naturally occurring goitrogens in foods like milk, millet, walnuts, along with bacterial and chemical water pollutants are additional factors that play a major role (Sidibe, 2007). In many papers that discussed the role of goitrogens in the etiology of goitre, cabbage and other vegetables that belong to the genus Brassica, were found to be a cause for the enlargement of thyroid gland in animal, with possible goitrogenic effect on man (Greer, 1957). Various foods had been investigated since long time ago for their antithyroid potency; peanuts, walnuts, bean, milk, grapefruit, orange, grape and many others had a questionable effect on development of goitre in human (Greer, 1957). Raw maize, taro, igname and nuts are others example among many other goitrogenous diet (Hetzel, 1989). There are also mineral goitrogens, which are absorbed through drinking water, and affect the iodine absorption in the body (Hetzel BS 1989).

Previous studies suggested that flavonoids (what gives the fruits and plants their colors), humic substances originating from the organic residues in the soil, smoking habits could have a contributory effect in the development of goiter especially in non-endemic areas (Delange, 1988). Many papers showed that consumption of poorly detoxified cassava resulted in thiocyanate overload which is a goitrogenic factor that aggravates iodine deficiency and contributed to the prevalence of goitre (Ermans, 1981, Thilly et al., 1992, Gbadebo and Oyesanya, 2005).

Cassava leaves and roots are the main staple food that is widely consumed in developing countries, like Africa. Cassava consumption was found to be an important factor in development of goitre in these areas. People especially children who frequently consumed cassava were significantly affected by goitre and reported to have other health in addition to that (Abuye et al., 2008). Although cassava has been extensively investigated as a goitrogenic food, some studies showed that cassava consumption decreased the risk of thyroid cancer in population with high thyroid cancer incidence rate in the world (Cléro et al., 2012). To our knowledge, reports on protective foods and diet that may reduce or treat the enlargement of thyroid gland are very rare, and all previous studies were investigating the correlation between the consumption of certain food items and the prevalence not the incidence of goitre. Further studies are needed to focus on the relationship of these potential goitrogenous food and the development of goitre, with specific focus on preschool children as the most vulnerable group in the population.

2. GENERAL OBJECTIVE AND RATIONALE

2.1 General objective

To bring together the existing evidence in literature about the incidence of goitre and dietary factors related to goitre development, to describe longitudinal occurrence pattern of goitre in children (0-5 years) in rural Democratic Republic of the Congo (DRC) and explore the role of consumption of specific food items in its aetiology.

2.2 Rationale

Most previous studies showed only the prevalence of goitre, not the incidence. Cross-sectional studies have looked at the relation between dietary factors and goitre prevalence, and longitudinal studies on this relationship between diet and goitre are rare. In this thesis we will do a semi-systematic literature review to summarize evidence from these studies and to bring together all the available evidence, if any, on incidence of goitre. In addition, we will do a longitudinal study of the relation between dietary determinants and development of goitre in children (0-5 years), using an existing dataset from Central Africa.

3. SPECIFIC OBJECTIVE

1. To conduct a semi-systematic literature review about the incidence of goitre and the role of dietary pattern in its genesis.

2. To describe the incidence of goitre among 0 to 5 year old children in relation to age, sex and season in rural central African environment.

3. To examine the effect of specific food items on occurrence of goitre in 0 to 5 year old children.

4. SEMI-SYSTEMATIC REVIEW OF LITERATURE

4.1 Objective and rationale of the literature review

The prevalence of goitre has been explored extensively in literature but not the incidence, and the relationship between goitre and consumption of specific food items was examined in only cross- sectional studies. Our objective is to focus on the longitudinal relationship between food consumption and development of goitre, with a research question "what is the impact of consumption of specific food items on the incidence of goitre?"

4.2 Search strategy and selection criteria

A semi-systematic approach has been adapted, with a non-strict protocol that has been followed to incorporate as much as possible the online available evidences in the review. A setting of criteria was used to help us identify the relevant published articles to our topic and research question within the limited time and resources.

Inclusion criteria

  i. Literature related directly to the research question
  ii. All types of study design
  iii. All age groups

Exclusion criteria

  i. Literature not related directly to the research question
  ii. Literature not in English
  iii. Unpublished literature
  iv. Animal or lab studies

4.3 Methods for searching the literature

The four main methods described by Aveyard in her book, have been used (Aveyard, 2007) . These are electronic searching of databases, reference list searching, relevant journal searching, and author searching.

4.3.1 Electronic searching of databases

Four databases have been searched: Pubmed, Embase, Cinahl, and Google scholar. Limitations were English language and human studies in all, with no time or age restriction.

Table 1 presents the strategy that has been used in searching the electronic databases.

Table 1: Electronic databases searching record

Electronic databases	Keywords and searching terms	Limitations	Total number of hits
Pubmed (June 2012)	-[Mesh terms] goitre AND [All fields] diet AND [Mesh sub terms] toxicity -[Mesh terms] goitre AND [All fields] food -[All fields] goitrogens] AND [All fields] goitre incidence -[Mesh terms] incidence AND [All fields] goitre AND [All fields] diet	English language Human studies	829
Embase (June 2012)	-*goitre incidence , *goitre, *etiology AND *diet -*goitre AND *food	English language Human studies	57
Cinahl (June 2012)	Cinahl headings -*goitre AND *food OR *diet -*Incidence of goitre AND *food -*goitrogens	English language Human studies	15
Google scholar (June 2012)	-[All of the words] *food and *diet AND [Exact phrase] *goitre incidence -*food OR *diet OR *goitrogens OR * goitrogenic AND *goitre incidence	English language Human studies	313

Summary

Totally 1214 articles were identified by searching the four electronic databases. The title of all the 1214 hits were screened initially and 185 were potentially relevant from title assessment. The online available abstracts were assessed for these185 articles; articles with unavailable online abstract were excluded. After abstract assessment, only 20 papers were identified to be relevant to our topic area. Finally full text analysis was carried out for those 20 articles, and only 3 were included in the review. Articles were not relevant after full text assessment either because they were not directly relevant to the topic area or of poor quality. Many studies mentioned incidence in the title and/or abstract, but later only the prevalence had been measured. Multiple publications of same study were also not included in the literature review.

4.3.2 Relevant online journal searching

The 20 key articles identified after abstract assessment were found to be located in different journals. Yet, 2 of them were published in the East African Medical journal. Also, it has been noticed throughout the entire search that many interesting articles were published in the European Journal of Endocrinology and the American Journal of Clinical Nutrition. As a result the content lists of these three journals were searched online:

1. The east African medical journal (2000-2011)

2. American journal of clinical nutrition (2000-2011)

3. The European journal of endocrinology (1948-2012)

No additional articles were found to be relevant to the topic area.

4.3.3 Author searching

Throughout the electronic searching of databases, it has been noticed that many of the relevant and/or interesting articles were written by the same authors. Author searching was carried out for Delange F, Ermans AM, Gaitan E, Hetzel BS and Bourdoux P. In all, searching was limited to English language, human studies but no time restriction. No further articles were included from author searching; results are presented in table 2.

Table 2: Summary of author searching

Author name	Total number of hits	Potentially Relevant articles	Number of articles included	Comments on the potentially relevant articles
Delange, F	116	6	0	5 unavailable online abstracts, 1 duplicate
Ermans, AM	53	6	0	4 unavailable online abstracts, 2 duplicates
Gaitan, E	42	1	0	Unavailable online abstract
Hetzel, BS	90	0	0	Unavailable online abstracts, not relevant
Bourdoux, P	76	2	0	Not relevant

4.3.4   Reference list searching

Reference lists of the 20 identified articles from abstract assessment were searched for further references that could be relevant to our topic. As a result one additional article was selected and included in the review.

Steps and results of the search strategy are presented in figure 1.
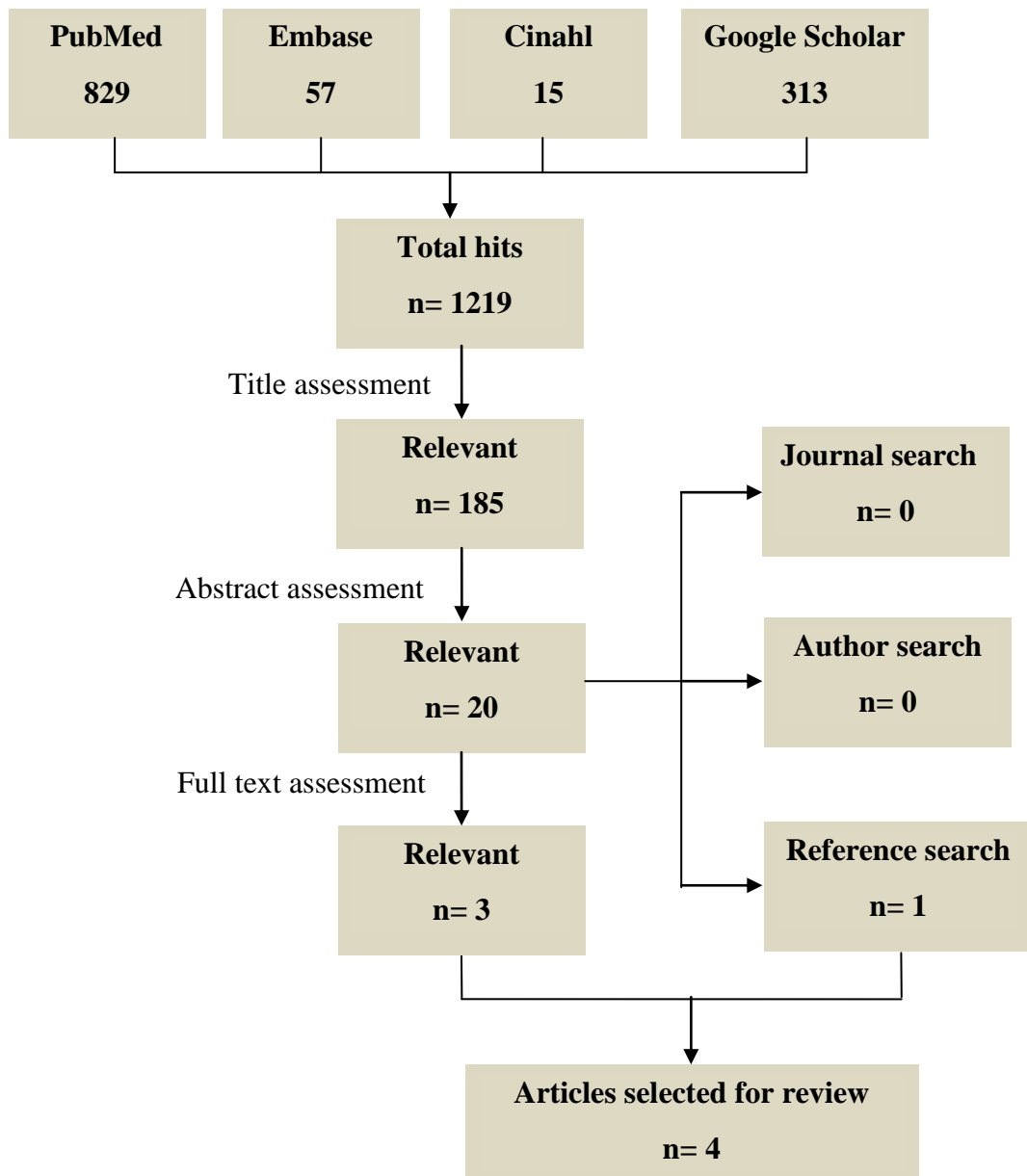
Figure 1: Flow chart of article selection in the semi-systematic literature review

4.4 Data extraction and critical appraisal

The methodological quality of each selected article was critically appraised using STROBE statement "The STrengthening the Reporting of OBservational studies in Epidemiology". STROBE recommendations were developed by a group of methodologist, researchers and editors at the University of Bern to improve the quality of observational studies reporting, through addressing of a check list of 22 items (von Elm et al., 2008). All studies were assessed according to whether they met these items. Characteristics of each study are presented in table 3.

Table 3: Characteristics of the selected articles

Year	Author	Title	Study type	Thyroid gland/ function assessment	Food and dietary habits assessment
1971	Delange, F et al.	Role of a dietary goitrogen in the etiology of endemic goiter on Idjwi Island	Trial	-Thyroid uptake of radioiodine -Urinary excretion of radioactive iodine	-Goitrogenous food vs control food administration.
Limitations of the paper		Study design was not mentioned/not clear in the title and/or in the abstract, and no clear information about what was done and what was found in the abstract. Eligibility criteria, study size, methods of selection, missing data, follow up, setting and dates were not mentioned. No efforts to address biases No discussion about results, limitations and external validity.			
1983	Vanderpas, J et al.	Endemic infantile hypothyroidism in a severe endemic goitre area of central Africa	Cohort	-Thyroid gland examination -Serum hormone level measuring	-24-hours food questionnaire.
Limitations of the paper		Eligibility criteria were not clear and no information on how they reached the study size. No information on potential confounders, biases, limitations.			

Year	Author	Title	Study type	Measurement	Method
1993	Osman, BA et al.	The effect of cassava intake on thyroid hormone and urinary iodine	Trial	-Serum hormone level measurement -Urinary excretion of iodine	-Cassava leaves administration.
Limitations of the paper		No information on the control group. No information on statistical methods used. Very limited information on the participants. Did not discuss the limitations and the external validity of the study.			
2005	Gbadebo, AM et al.	Assessment of iodine deficiency and goitre incidence in part of Yewa area of Ogun state, south-western Nigeria	Cohort	-Medical goitre incidence records analysis	-24-hours food questionnaire. -Samples analysis (soil, water, cassava).
Limitations of the paper		No efforts to address biases. No information on the study size, missing data and external validity.			

Summary of the characteristics of the included studies in the literature review

- The study design was not clear in the title and/or the abstract in all of them.

- Aim and objectives of the study were relatively clear in all of them.

- Study sample was not clearly defined in 3/4 studies, with no explanation on the study size decision.

- No information on eligibility criteria in 3/4 studies.

- Statistical analysis section was not included in 2/4 of the studies.

- Efforts to address bias, limitation and potential confounder were missing in all the studies.

- External validity had not been discussed in all the studies.

- Information on ethical approval and fund were not included in all the studies.

4.5 Results of the literature review

Iodine deficiency was found to be the major and most important factor that affects the prevalence of goitre, mainly in regions with low iodine content in soil and water accompanied by poor dietary habits and practices.

Ghadebo et al. presented cassava as the potential cause of goitre in the relatively low lying villages in south-western Nigeria where iodine concentration is low in soil and water (Gbadebo and Oyesanya, 2005). Cassava is the most important staple food in these villages and generally, consumption of cassava produced thyroid gland dysfunction. Delange et al. and Osman et al., both found in their trials a significant decrease in serum thyroid hormones level in the cassava group of participants, although Osman et al. did not have a control group in their study. Change in urinary iodine excretion has also been noticed in both studies after introduction of cassava food to the healthy participants in addition to the change in the serum hormonal level (Delange and Ermans, 1971, Osman et al., 1993).

The frequency of cassava consumption is also important; goitre cases increase in populations with high frequency of cassava consumption, compared to others with less frequent cassava consumption and same method of preparation. Epigastric and abdominal complains are recorded to be associated with cassava consumption in addition to the thyroid gland problems.

Infantile hypothyroidism in severely endemic goitre area in Northern Zaire is found to be linked to the persistent dietary iodine deficiency in that area and the increase in the thiocyanate (SCN) overload from the consistent consumption of cassava. Thyroid function deterioration occurs during and after weaning, thus, less frequent cases of infantile hypothyroidism is recorded at birth and during the first year of life (Vanderpas et al., 1984).

4.6 Discussion and conclusion of the literature review

The objective of this semi-systematic literature review was to identify and critically appraise the online available literature on incidence of goitre in relation to dietary pattern. The most important expected finding from this investigation was that, out of the 1214 articles first identified, very few epidemiological studies were specifically designed to investigate the relationship between dietary pattern and development of goitre. Thus, the literature evidence on that matter was very poor.

Overall selected studies were only 4; three of them were in Africa and one in Asia. This clarified the health impact that might be induced by the type of food consumed in these regions. Cassava was the only investigated food in all the included studies; it is the main staple food in many developing countries especially in Africa. It was recorded that cassava has other gastrointestinal effects beside thyroid gland problem, both the amount and the frequency of consumption are important in producing these health effects.

No other food items beside cassava were investigated for their contributory effects on the development of goitre in these populations.

Identified studies were relatively old, they were of poor quality according to the STROBE statement which has been published in the nineties and recommended for reporting the observational studies. Papers included in the review mostly did not meet many of the 22 check items listed in the STROBE statement.

Sampling technique, sample size decision, efforts to address and reduce biases were not clearly mentioned in all the studies. This give the impression that internal and external validity were not reliable and the results of these studies were limited because they were not well designed.

However, it is still obvious that consumption of cassava in iodine deficient areas plays an important role in the thyroid gland dysfunction and development of goitre in their populations.

4.7 Limitations of the literature review

- Large number of articles was with unavailable online abstract and/or text and was excluded from the review.

- During the electronic searching of databases, many of the used search words/terms did not yield any hits, leaving a limited options in searching strategy.

- Many articles had unclear title and/or abstract regarding whether the incidence or the prevalence of goitre had been measured in the study.

- Few epidemiological studies were specifically designed to investigate the relationship between dietary pattern and development of goitre and little information was obtained regarding this longitudinal relationship.

- Studies were focusing on one food item and very little or no information was obtained on other food items which were consumed by people with high goitre occurrence.

- No protective food if any was investigated in the identified studies.

5. Methods

5.1 The original dynamic population study

The original study was an observational dynamic population study, in Bwamanda, DRC. Bwamanda is a rural town located in the north-western part of the country. Subsistence farming constitutes the main activity and source of income to the local population. The climate is tropical with rainy season from June to November and dry season from December to May. Dietary habits are very limited with almost two staple foods, cassava and maize.

The study was a prospective follow up on the maternal determinants of the child health and care, with an objective of studying the maternal factors that act upon the nutrition- morbidity- mortality triangle. So a cohort of 5657 children from 0- 72 months age was followed for every 3 months period from October 1989 to March 1991.

Random cluster sampling was done for a total of 52 villages and 16 villages were selected accordingly. A preliminary census of all the households of the 16 villages was done in August and September 1989, that yielded a list of 4238 preschool children for enrolment. Training of interviewer with secondary certificate was done also in this period at Bwamanda hospital on how to perform a simple physical examination and to complete a questionnaire from using an interviews manual. In September 1989 pre-surveys were done in the field to complete the training.

Six quarterly surveys were done, and observed variables were interval-morbidity, feeding practice, socio-economic conditions, mortality and anthropometric measures. In each survey all numbers of new-born and immigrants together with the number of deaths and emigrants were given. Interviews and examination were done at special under-5 clinics and data collection was continuously supervised. Examination of children was 75% done by two medical doctors.

Ethical approval was obtained by the University of Leuven's Tropical Childcare Health Working Group and funding provided by the Belgian Administration for Development Co-operation, and the Nutricia Research Foundation.

All the above information was taken and can be reviewed in details in the original paper (Van den Broeck, 1994).

5.2 Data handling and descriptive statistics

We utilize the pre-existing data on age, sex, goitre, food items, WAZ and WHZ from the original Bwamanda dynamic study. Data was already cleaned and variables were clearly defined.

Statistical analysis in this study was performed using the Statistical Package for Social Sciences (SPSS), version 19.0 for windows.

The demographic characteristics of the participants were calculated using basic statistical methods. Frequencies of males and females, age distribution, number of children in each round and other characteristics are presented.

5.3 Analysis plan for specific objective 2

5.3.1 Goitre incidence risk

For this specific objective we used the data from original Bwamanda study on goitre, age, sex, and season. Goitre incidence risk was the number of new cases developed during each survey intervals over the total number of children who had valid information on goitre and were at risk of developing it in this period. Calculation started from the 2nd survey interval where we can identify the new cases of goitre.

We used three age groups; group 1 included the children from new-born up to 11 months old, group 2 included children from 12 to 35 months old, and group 3 included children from 36 to 60 months old. Then we compared the incidence risk of goitre between males and females, between dry and rainy seasons, and between the three age groups.

The incidence risk of disappearing of goitre was also calculated, this represented the number of children who had been recorded to have goitre in one round and then no goitre in the following round, over the total number of children with valid information on goitre and were at risk of goitre disappearing during that period.

Direct age standardization was done, choosing the children in the first survey round (A) as the standard population. The age structure was the three age groups division that was used earlier.

5.4 Analysis plan for specific objective 3

A longitudinal study was done. Data from the original Bwamanda study on food items consumed during the previous 24-hours was used, and all children with history of eating these foods were taken as cases. Data on sex, age, HAZ, and WLZ were selected and tested for their potential confounding effects. Combined data from all survey rounds was used for this specific objective.

In Bwamanda study, the mothers of the children were interviewed with a questionnaire on the consumed foods during the 24-hours preceding the interview. Assumption was made from the 24-hour recall on dietary habits in the study population. Seven food items were selected and included in the study; they were cassava leaves, cassava tubes, maize, papaya, fish, nuts and banana. This selection was based on the frequency of consumption, and only food items with a frequency of consumption >10% were included in the analysis.
Test for multicollinearity was done, and then logistic regression was performed to assess the impact of a number of factors on the likelihood that children would develop goitre. The full model contained eleven independent variables; seven food items and four potential confounders. We did goodness of fit test and the predictive power of the set of seven food items was tested along with the assessment of the relative contribution of each individual food item.

5.5 Ethical considerations

For the original study, approval was obtained from the Zairian Ministry of Health, with the support of the Nutricia Research Foundation.

Data from the original study was anonymous and no ethical approval was required for the current longitudinal analysis.

6. RESULTS

6.1 Descriptive statistics

The demographic characteristics of the study population are presented in the tables below.

Table 4: Basic demographic characteristics

		Frequency	Percentage
Gender	Female	2756	48.7
	Male	2899	51.3
Age of the child at the 1st survey round (A)	0-1 year	631	17.7
	1-3 years	1566	44.0
	3-5 years	1365	38.3
The survey round when the child was first seen	Round A	4240	75.0
	Round B	287	5.1
	Round C	342	6.1
	Round D	292	5.2
	Round E	344	6.1
	Round F	152	2.7
Goitre cases at the 1st round (A)/ prevalence	No goitre	3407	91.4
	Palpable goitre	292	7.8
	Visible goitre	29	0.8

Table 5: Sex and age distribution in each survey round

Survey Rounds	Gender		Age group		
	Female	**Male**	**0-1yr**	**1-3yrs**	**3-5yrs**
Round A	49% n=(2077)	51.0% n=(2162)	17.7% n=(631)	44.0% n=(1566)	38.3% n=(1365)
Round B	48.9% n=(2214)	51.1% n=(2311)	19.2% n=(698)	42.9% n=(1563)	37.9% n=(1379)
Round C	48.7% n=(2371)	51.3% n=(2496)	20.4% n=(749)	42.0% n=(1541)	37.6% n=(1380)
Round D	48.4% n=(2499)	51.6% n=(2660)	20.5% n=(764)	41.5% n=(1551)	38.0% n=(1419)
Round E	48.7% n=(2679)	51.3% n=(2824)	19.0% n=(712)	41.0% n=(1534)	40.0% n=(1496)
Round F	48.7% n=(2756)	51.2% n=(2899)	16.5% n=(553)	41.7% n=(1399)	41.8% n=(1401)

Summary of table 4 and 5

- Total number of children in the original study was 5657 and the majority was seen in the first survey round (75%).

- There are 2756 females (48.7%) and 2899 males (51.2%) in the original study sample, with almost same sex ratio in all survey rounds. Only two cases were with missing information for the variable sex in the whole study.

- In the 1st survey round (A), age information was valid for 3562 out of 4240. The age was ranging from new-borns to almost 6.5 years, with a mean of 2.8 years and standard deviation of around 1.6 years (information not presented in the above tables).

- Totally, missing information on age ranges from 33.9% to 40.7% throughout the six survey rounds.

- Age distribution was with little difference in the different rounds and the majority of children were in the second age group (1-3 years) in all survey rounds.

- Most of the children who were 1st seen in the 1st survey round (A) had no goitre (91.4%). The rest had mostly the mild palpable type of goitre.

6.2 Results for the specific objective 2

6.2.1 Goitre incidence risk

Goitre incidence risk was calculated for each survey round and comparison was done between females and males, between the three age groups (0-1yr), (1-3yrs), (3-5yrs) and finally between rainy and dry seasons. Results are presented in the tables below.

Table 6: Goitre incidence risk (crude)

	Round B	Round C	Round D	Round E	Round F
Number of new goitre case	262	293	510	392	315
Incidence risk of goitre	9.8%	11.4%	19.8%	17.1%	15.1%
95% CI	(8.67-10.93)	(10.17-12.63)	(18.26-21.34)	(15.56-18.64)	(13.56-16.64)

Summary

- The incidence risk of goitre increased gradually during the three survey intervals B, C, and D, from 9.8% to 11.4%, being the highest in the 4th survey interval D with a percentage of 19.8 which is more than the double from the 1st measurement in round B. Then, it decreased again throughout the last two survey intervals from 17.1% to 15.1%.

Table 7: Goitre incidence risk according to sex

Survey round	Gender	Incidence risk	Relative risk (RR) Female/male	95% confidence interval (CI) of RR
Round B	Female	8.1%	0.91	**(0.55 – 1.27)**
	Male	8.9%		
Round C	female	10.0%	1.17	**(0.75 – 1.59)**
	Male	8.6%		
Round D	Female	15.8%	0.98	**(0.60 – 1.36)**
	Male	16.1%		
Round E	Female	11.0%	0.82	**(0.45 – 1.19)**
	Male	13.5%		
Round F	Female	10.5%	0.94	**(0.53 – 1.35)**
	Male	11.2%		

Summary

- There is no clear relationship between sex and the incidence risk of goitre in children throughout the five survey intervals.

Table 8: Goitre incidence risk according to age

Survey round	Age group	Incidence risk	RR	95% CI of RR
Round B	0-1 year	0.0%		
	1-3 year	4.4%	Ref	
	3-5 year	16.1%	3.6	**(2.89 – 4.31)**
Round C	0-1 year	0.0%		
	1-3 year	6.1%	Ref	
	3-5 year	16.4%	2.7	**(2.07 – 3.33)**
Round D	0-1 year	0.6%	Ref	
	1-3 year	12.1%	20.2	**(18.65 – 21.75)**
	3-5 year	25.6%	42.7	**(40.79 – 44.61)**
Round E	0-1 year	0.3%	Ref	
	1-3 year	7.6%	25.3	**(23.52 – 27.08)**
	3-5 year	20.3%	67.7	**(65.78 – 69.62)**
Round F	0-1 year	0.6%	Ref	
	1-3 year	9.5%	15.8	**(14.23 – 17.37)**
	3-5 year	15.6	26.0	**(24.11 – 27.89)**

Summary

- The lowest valid risk in the youngest age group has been chosen as the reference in each survey round.

- There is a strong relationship between age and the incidence of goitre in children in all rounds. Risk of developing goitre increased greatly with increasing in age, thus, the incidence of goitre was highest in the oldest children

- Using gender as a layer factor in the cross tabulation between age and incidence of goitre did not affect the results. So, being a male or a female did not change the positive relationship between age and developing of goitre in these children.

Table 9: Goitre incidence risk according to season

	Round B	Round C	Round D	Round E	Round F
Incidence risk	9.8%	11.4%	19.8%	17.1%	15.1%
95% CI	**(8.67-10.93)**	**(10.17-12.63)**	**(18.26-21.34)**	**(15.56-18.64)**	**(13.56-16.64)**
Season	Dry	Dry	Rainy	End of rainy	Dry

Summary

- There is a difference in the incidence risks between rainy and dry seasons. The incidences of goitre were higher in rainy season. The highest percentages of 19.8 and 17.1 were in survey round D and E respectively which represented the rainy season.

6.2.2   Direct age standardization

Direct age standardization procedure was applied and standardized incidence risks were obtained by adopting the age distribution of the population in the 1st survey round A as the standard population.

For the standardization process, children in each round were divided in to three age groups (strata), group 1 (0-1 year), group 2 (1-3 years) and group 3 (3-5 years).

Table 10: Age standardized incidence risk

Round	B	C	D	E	F
Crude risk	9.8%	11.4%	19.8%	17.1%	15.1%
Age standardized risk	10.8%	12.4%	21.1%	17.4%	17.6%
95% CI for the age standardized risk	(9.62-11.98)	(11.13-13.67)	(19.52-22.68)	(15.85-18.95)	(15.96-19.24)

Summary

- After elimination the effect of the difference in the age structure in all survey rounds, we obtained an adjusted incidence risk that is almost similar to the crude risk .This support the finding of almost equal age distribution in all survey rounds.

6.2.3 Incidence risk of disappearing of goitre

Incidence risk of disappearing of goitre was calculated for each interval starting from the 2nd round B, and then comparison was done between females and males, between the three age groups and between dry and rainy seasons. Results are presented in the tables below.

Table 11: Incidence risk of disappearing of goitre

Survey Round	Round B	Round C	Round D	Round E	Round F
Number of cases	99	190	165	255	284
Disappearing risk	48.3%	55.5%	40.2%	40.6%	46.9%
95% CI	**(33.59-47.01)**	**(50.23-60.77)**	**(35.45-44.95)**	**(36.76-44.44)**	**(42.93-50.87)**
Season	Dry	Dry	Rainy	End of rainy	Dry

Summary

- The incidence risk of disappearing ranged from 40.2% to 55.5%; the lowest percentages were in the 4th round D and 5th round E which represented the rainy season.

Table 12: Incidence risk of disappearing of goitre according to sex

Survey round	Risk in female	Risk in male	RR Female/Male	95% CI
Round B	3.2%	2.4%	1.3	**(0.25 – 2.85)**
Round C	5.4%	5.2%	1.0	**(0.05 – 2.05)**
Round D	4.1%	5.0%	0.8	**(0.06 – 1.66)**
Round E	7.6%	6.7%	1.1	**(0.28 – 1.92)**
Round F	7.5%	9.2%	0.8	**(0.09 – 1.51)**

Summary

- There is no clear significant relationship between sex and the incidence risk of disappearing of goitre in children (0-5 years).

Table 13: Incidence risk of disappearing of goitre according to age

Survey round	(0-1 yr)	(1 -3 yrs)	(3 -5 yrs)	Relative Risk (RR)	95% CI
Round B	.0%	0.9% ref	5.7%	6.3	**(2.97 – 9.63)**
Round C	.0%	1.9% ref	10.8%	5.7	**(3.24 – 8.16)**
Round D	.0%	2.6% ref	8.3%	3.2	**(1.50 – 4.90)**
Round E	.0%	5.2% ref	11.2%	2.2	**(1.05 – 3.35)**
Round F	.0%	3.2% ref	15.9%	5.0	**(3.26 – 6.74)**

Summary

- The lowest valid risk was chosen as the reference to calculate for the relative risk.

- The risk of disappearing of goitre was significantly increasing with age, as goitre was more likely to disappear in older children than in younger children.

6.3 Results for the specific objective 3

Binary logistic regression was performed to assess the impact of a number of factors on the incidence of goitre in children (0-5 years) in the rural area of Bwamanda, DRC. The full model contained seven food items (cassava leaves, cassava tubers, maize, banana, nuts, fish and papaya) and four potential confounders (age, sex, HAZ and WLZ). Test of multicollinearity was taken and all the predictor variables showed a correlation < 0.5, therefore, all the variables were retained in the model.

The results are presented in tables 14, 15.

Table 14: Food consumed at baseline associated with the odds of goitre development, with and without controlling for age

Predictor variable	P-value	OR	95% CI	Controlling for age		
				P-value	OR	95% CI
Cassava leaves	.000	1.77	**(1.51-2.07)**	.007	1.26	**(1.07-1.48)**
Cassava tubers	.000	1.56	**(1.34-1.83)**	.000	1.53	**(1.30-1.79)**
Maize	.000	2.21	**(1.66-2.95)**	.049	1.34	**(1.00-1.79)**
Banana	.002	1.25	**(1.09-1.44)**	.084	1.14	**(0.98-1.32)**
Nuts	.911	0.18	**(0.80-1.04)**	.038	0.86	**(0.75-0.99)**
Fish	.207	1.08	**(0.96-1.23)**	.211	0.92	**(0.80-1.05)**
Papaya	.374	0.93	**(0.79-1.09)**	.091	0.87	**(0.74-1.02)**

Table 15: Food consumed at baseline associated with the odds of developing goitre, with controlling for age, sex, HAZ and WLZ

Predictor variable	Controlling for age and sex			Controlling for age, sex, HAZ			Controlling for age, sex, HAZ and WLZ		
	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI
Cassava leaves	.007	1.26	**(1.07-1.48)**	.005	1.27	**(1.08-1.50)**	.004	1.27	**(1.08-1.50)**
Cassava tubers	.000	1.53	**(1.30-1.79)**	.000	1.51	**(1.29-1.77)**	.000	1.51	**(1.29-1.77)**
Maize	.049	1.34	**(1.00-1.79)**	.034	1.37	**(1.02-1.83)**	.032	1.37	**(1.03-1.84)**
Banana	.084	1.14	**(0.98-1.32)**	.107	1.13	**(0.97-1.31)**	.109	1.13	**(0.97-1.31)**
Nuts	.038	0.86	**(0.75-0.99)**	.029	0.85	**(0.74-0.98)**	.032	0.86	**(0.74-0.99)**
Fish	.210	0.92	**(0.80-1.05)**	.167	0.91	**(0.79-1.04)**	.159	0.91	**(0.79-1.04)**
Papaya	.091	0.87	**(0.74-1.02)**	.083	0.86	**(0.73-1.02)**	.083	0.86	**(0.73-1.02)**

Summary of table 14 and 15

- Hosmer and lemeshow goodness of fit test for the whole model with the set of 7 food items and 4 confounders shows poor fit with a significant value <.000

- However, binary logistic regression analysis shows that cassava leaves, cassava tubers and maize made a statistically significant contribution to the model, where maize being the strongest predictor with an odd ratio of 2.21.

- In general, children who ate more cassava and maize were 1 ½ and 2 times respectively, more likely to develop goitre than children who didn't eat cassava and maize.

- Nuts, fish and papaya showed a protective effect against the development of goitre in children with non-significant values except for nuts with an odd ratio of 0.86.

- The odd ratios of the predictor variables were changed significantly after controlling for age; this indicates the confounding effect of increasing in age in developing goitre in those children. While controlling for sex, HAZ and WLZ had no significant confounding effects on the results.

7. Discussion

7.1 Discussion of results from specific objectives

Specific objective two

The aim of this objective was to measure the incidence risk of goitre in a cohort of children (0-5 years) in the rural area of Bwamanda, DRC. This longitudinal study showed that the incidence risk was ranging from 9.8% - 19.8% in five survey intervals (table 6). The incidence risk of goitre was calculated for each 3 months period throughout 5 consequential survey rounds, starting from the 2nd survey round B.

The incidence risk was low in the beginning period and started to increase with the following rounds being the highest during the 4th interval D. Afterward, the incidence risk decreased to 15.1% during the last interval F which is still higher than the 1st measurement.

We found that age is a strong predictor of the incidence risk of goitre in children (0-5 years) living in that area; this might support other studies' findings where age being strongly related to the prevalence of goitre (Bjoro et al., 2000). On the other hand, some studies found only a week positive relationship between age and the prevalence of goitre (Muller-Leisse et al., 1988). Yet, we could not assume that the difference in the incidences of goitre between the 5 survey intervals was due to the age difference. Age distribution was almost similar in all survey rounds (table 5); and there was no substantial changes in the estimate after direct age standardization. Moreover, the children who turned over 5 years were not included in the analysis.

We did not find a clear relationship between gender and the incidence of goitre. Previous cross-sectional studies showed inconsistent findings on the effect of gender on the prevalence of goitre in populations with different iodine status (Malboosbaf et al., 2013). Some studies suggested that the prevalence of goitre is more in females (Kimiagar et al., 1990, Bazrafshan et al., 2005), but others showed no difference between female and males (Muller-Leisse et al., 1988, Chanoine et al., 1991). A recent meta-analysis study suggests that goitre prevalence is higher in females, and this gender difference becomes more prominent in iodine-deficient areas and after puberty, this could be due to the sex steroids that affect the volume of thyroid gland; where male hormones usually decrease the enlargement of the gland (Malboosbaf et al., 2013).

Regarding seasonal variation, each survey round represented either a dry or a rainy season on average. This considered as a limitation in our study, since each survey round was of a three months period, and could include both rainy and dry months. However, we found that the incidence of goitre in children (0-5 years) was higher during the two survey intervals D and E which represented rainy seasons on average, with a percentages of 19.8 and 17.1 respectively (table 10). Many studies suggested that health and nutritional problems are more prevalent during rainy season (Van den Broeck et al., 1993), this could be due to the shortage of the dietary resources during these periods.

Children could be eating less during rainy season because of less food stock and limit diet variation during rainy. Therefore, we assumed that iodine deficiency could be higher as well in rainy season and that might affect the incidence of goitre in these children, in addition to the type and amount of food they are consuming during rainy season. We found that the consumption of potential goitrogenic food like cassava and maize was more frequent during these two rainy survey rounds comparing to the frequency of consumption of other food items.

Goitre in newborns and pre-school children may disappear completely on a variable period of time (Carswell et al., 1970). Small goitre can be easily treated and disappear after iodine supplementation, on the other hand, larger goitre and goitre in adults rather than in children are more persistent and difficult to disappear completely (Zimmermann et al., 2003). Literature reported goitre disappearance after iodine supplementation in IDD endemic areas and in some cases after changing the dietary habits in mild to moderate iodine deficient population. In this study we found that goitre disappeared more in older children, and to our knowledge, no iodine supplementation was given in that period when the study was conducted. Therefore, we assume that the disappearance of goitre in the study population might be due to less potential goitrogenic food consumption and better dietary habits and better health condition in general. This might also contribute to the difference in goitre disappearing risk between rainy and dry season.

Specific objective three

This objective was concerned with the causal relationship between specific food items and the development of goitre in children (0-5 years) in the rural area of Bwamanda, DRC. From investigating the original data, cassava leaves, cassava tubers and maize were found as expected to be the most frequent consumed foods by the study population followed by nuts, fish and papaya.

Cassava is the main staple food in Central African countries, it is the everyday food of the people in the DRC (Banea-Mayambu, 1997). Cassava has many agricultural advantages, it can tolerate harsh environmental conditions and considered as a famine crop in these areas (Banea-Mayambu, 1997). The DRC is one of the main producers of cassava in the world (Nweke, 1994), and cassava is of a great importance for both food and economic security in the country. Cassava leaves and roots contain cyanogenic glucosides, the higher the concentration of glucosides the more bitter the taste (Sundaresan et al., 1987). Cyanogens can be toxic to man if they are eaten in an insufficiently processed cassava (Hahn, 1989). Limited information was available from the original data on the ways people processed, stored and transported cassava they consumed. Previous studies indicate that exposure to cyanogens in poorly processed cassava with high level of cyanogens is a major contributory factor to IDD (Bourdoux et al., 1978). The thiocyanate ion (SCN) in poorly processed cassava acts in a similar way to the iodine ion and it interferes with the normal function of the thyroid gland. Therefore, SCN is considered as a goitrogen (Bourdoux et al., 1978). Yet, the goitrogenic effect of SCN applies only if the consumption of insufficiently processed cassava is over a long period of time and in an iodine deficient population (Banea-Mayambu, 1997). Consumption of insufficiently processed cassava in a population with an adequate daily iodine intake will not interfere with the their normal thyroid function (Cliff et al., 1986).

In our study population, the extent of exposure to cyanogens from the eaten cassava was unknown. The exposure to cyanogens could be related to many factors like the content of cyanogens in cassava consumed by them, the degree of removal during processing of cassava, the frequency of cassava consumption, the amount consumed at each meal and finally the duration of exposure (Banea-Mayambu, 1997). Children during and after weaning, could be more exposed to the toxic material in the consumed food than the children during 1st year of life. Information on food was obtained only by using a 24-hour recall method, the mothers were asked to recall the foods her child consumed during the past 24-hours. No information on cooking and preparing methods, neither on the quantities of foods consumed was included. Moreover, no urine samples were provided by the participants to measure for the SCN level and/or the iodine level in them. Therefore, causal relationship between cassava and other investigated food items and the development of goitre in these children cannot be justified.

7.2 Limitations of the study

The study population were preschool children, and the only technique used to examine the thyroid gland in them was palpation. Palpation of thyroid gland in children can be challenging and extremely difficult in infant and children under 5 years of age, so the chance of misclassification is high in our study. Additionally, the observer could have a steep learning curve to identify goitre throughout the study period, all this could have changed sensitivity and specificity of goitre identification in this study.

Limited information was available from the original study on iodine status and cyanogens exposure level in the study population, so it was difficult to interpret the results of our study. A the dietary habits of the participants were estimated from a 24-houres recall only.

Limited online data and/or data in English on the iodine status in the DRC, other information on the preventive measures interventions and their effects in the country are also limited.

Limited literature is available in relation to our topic area, to interpret and discuss the results of our study and this affects the external validity of the study.

8. Conclusions

Goitre incidence in children (0-5years) in a rural area in Central Africa increases with age but has no relationship with gender, and the risk of developing goitre in children is increasing during rainy season.

This is the 1st longitudinal analysis showing a longitudinal relationship between consumption of specific food items and the development of goitre in children (0-5 years) in a rural area in central Africa. Cassava and maize are important contributory factors while nuts have a protective role in developing goitre in those children.

9. Recommendations

The simplest eradication procedure in this area is to implement iodized salt and iodine supplementation programs. In addition, promotion of effective cassava processing can play an extremely important role in elimination of IDD in cassava eating populations and in areas where iodized salt is not easily to access.

Further studies are needed to investigate the causal relationship between cassava, maize and other food items and the incidence of goitre in man, especially in areas where iodised salt programs are not yet implemented.

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