Neutrosophic Analysis of Complications Generated by Hypothyroidism during Pregnancy

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Abstract: Pregnancy process might be threaten by several complications. Affectations in the thyroid gland provoke that not enough thyroid hormone is produced, altering the heart rate, the body temperature and all the aspects of the metabolism. This research aims to develop a method that allows the estimation of complications generated by hypothyroidism during pregnancy. The method is based on the modeling of uncertainty using neutrosophic numbers under a multi-criteria approach. As the main result, a case study is carried out at the IESS Ambato Hospital in Ecuador, where the applicability of the proposed method is shown.

Keywords: Pregnancy; hypothyroidism; multi-criteria method; neutrosophic numbers.

1. Introduction

Pregnancy has a significant impact on the thyroid gland and thyroid function, often resulting in hypothyroidism in women with limited thyroid reserve or iodine deficiency. Clinical studies are producing critical data demonstrating the harmful effects of hypothyroidism in pregnant women [1-4].

Hypothyroidism is the most common condition in women of reproductive age [5, 6]. It is characterized by the decrease in the synthesis and secretion of thyroid hormones, giving a state of generalized hypo metabolism, therefore it causes important repercussions in the whole organism [7].

Although various studies have shown that hypothyroidism in pregnancy is quite common; Clinically, it requires specialized and urgent care, since it is associated with adverse pregnancy and perinatal outcomes. Thyroid stimulating hormones (TSH), especially free thyroxine (FT4), are crucial for early brain development in the embryo [8]. Epidemiological studies and case reports have shown that maternal hypothyroidism can have significant negative effects on pregnancy and fetal neurodevelopment [9].

The thyroid gland belongs to the endocrine system and has very important functions, the main one is to produce thyroid hormones as necessary to satisfy the demand of the peripheral tissues [10]. Thyroid hormones play a decisive role in brain development, somatic growth, and the regulation of numerous metabolic processes [5].

The decrease in the availability of maternal thyroid hormones can be a critical factor that damages the neurological development of the fetus in the initial stages of gestation, before the fetal thyroid gland is activated [11]. Several recent studies report increased fetal loss and preterm delivery in mothers with undiagnosed hypothyroidism [7, 8, 10, 12].

Considering the high levels of incidence, in Ecuador there have been several investigations dedicated to the advancement, understanding, prevention, diagnosis and treatment of thyroid disorders and thyroid cancer. However, hypothyroidism during the pregnancy period and its main maternal and infant consequences have not been sufficiently addressed by science; this is the main indicator that drives this research. The main objective
of this work is to perform a neutrosophic analysis of the complications generated by hypothyroidism during pregnancy.

As a methodology for the research, we decided to carry out a retrospective design, which allowed the collection of data from 80 medical records of pregnant patients diagnosed with hypothyroidism (defined as thyrotrphin (TSH) > 4.0 μIU/mL with normal levels of free thyroxine according to the guidelines of the American Thyroid Association of 2017), which have been admitted at the IESS Ambato Hospital in Ecuador, in the period January - September 2018. The bibliographic review was carried out on Ovid MEDLINE In-Process, in the journal Thyroid: the Official Journal of the American Thyroid Association, and in the academic databases Web of Science and Scopus. This methodological design allowed corroborating the main complications that occurred during pregnancy in the studied patients.

The paper is structured into the following sections: Preliminary, Materials and methods, Results and Conclusions. At the bibliographic references presented at the end. In the Preliminaries, we identify the main characteristics of hypothyroidism during pregnancy and analyze the main consequences that this condition may generate; the methodology to address decision-making problems is also introduced and the neutrosophic linguistic model that supports the main results of the research is formalized. The Materials section develops a method that allows estimating the complications generated by hypothyroidism during pregnancy. As a result, a case study is carried out at the IESS Hospital, where we show the applicability of the proposed method.

2. Preliminaries

This section introduces the main concepts associated with the problem domain. The main elements of Hypothyroidism during pregnancy are described as the core of the research. The section continues with the decision-making models as a form of inference for the proposed method. Finally, we introduce linguistic models for the representation of uncertainty.

2.1. Hypothyroidism during pregnancy

The thyroid gland belongs to the endocrine system, and has the function of producing thyroid hormones as necessary to satisfy the demand of the peripheral tissues. Thyroid hormones play a decisive role in brain development, somatic growth, and the regulation of numerous metabolic processes [13].

The main function of this gland is to synthesize and secrete thyroid hormone which is necessary to regulate basal metabolism. The functioning of this gland is based on processes such as: iodine metabolism; thyroid hormone production, storage, and secretion [12]. Iodine is extracted from the blood, oxidized and coupled intramuscularly with tyrosine radicals to form thyroglobulin, which is a mixture of iodine tyrosine, triiodothyronine (T3) and thyroxine (T4) stored as a colloid in the lumen of the follicle [14].

The thyroid stimulating hormone works by increasing the cells and vascularization of the gland; In addition, it intervenes in all the processes that control the synthesis and release of thyroid hormone [15]. Thyroid stimulating hormones are regulated by the concentration of free thyroid hormone in peripheral blood by a negative feedback mechanism [16].

Several studies have shown that pregnant women with clinical hypothyroidism are generally at increased risk of complications such as preeclampsia, placental abruption, and postpartum hemorrhage [6, 12-14]. Hence the interest in knowing about the main complications that can occur in pregnant patients who fail to comply with adequate treatment for hypothyroidism [17].

During normal pregnancy, as in all organs, several physiological changes occur that affect thyroid function, which is modulated by three factors [18]:

i. The increase in urinary iodide excretion, secondary to the physiological hyperfiltration of pregnancy, producing a decrease in its plasma concentration and, therefore, the uptake of iodine by the thyroid is increased [19].

ii. Increased Human Chorionic Gonadotropin (HCG) stimulates the thyroid [12].

iii. Increased thyroid hormone transport globulin (TBG): Increased levels of estrogens result from increased production at the liver level, decreased clearance and degradation, and increased glycosylation of this protein [20].

The complications generated by hypothyroidism during pregnancy are multiple and therefore are the reason for prescribing treatment; the main complications are described below:
- Preeclampsia: thyroid hormones have various actions on cardiovascular physiology and in the regulation of blood pressure. Exposure to altered hormonal concentrations can modify these functions. Studies of pregnant women have shown that as serum levels of thyroid stimulating hormones increased, the frequency of hypertensive disorders also increased [20, 21].
- Intrauterine growth restriction (IUGR): research results suggest an interrelation between thyroid hormones and intrauterine growth factors [15]. Other authors claim that treatment for hypothyroidism has led to intrauterine growth restriction, fetal bradycardia, and neonatal hypoglycemia [22].
- Recurrent abortions: the possible causes of abortion are multiple and can be caused by: anatomical, genetic, autoimmune, endocrine, infectious alterations, and due to the exposure to toxic substances [17]. Several literatures determine that hypothyroid women who are in treatment, and maintain normal TSH concentrations, have 4% abortions, while those who remain without treatment have a risk of 31.4% of abortion. The risk of abortion in women with thyroid stimulating hormones is 4.5-10 mIU / L is higher, so they recommend close monitoring and improve the delivery of hormone replacement.
- Preterm delivery: preterm delivery is a situation that can be caused by multiple factors. The literature review identified a possible association between preterm delivery and thyroid disease [18].
- Abruption placenta: it is considered a catastrophic event since the premature separation of the normal inserted placenta can generate high morbidity and mortality in the mother and the neonate. Although hypothyroidism is not the only cause of abrupt placental, several studies report that this pathology may increase the risk of abrupt placental [16].
- Recurrent Urinary Tract Infection (UTI): Thyroid disorders induce alterations at multiple levels. The heart and kidneys are the main targets for thyroid hormones [14]. The deterioration of renal function secondary to hypothyroidism implies heterogeneous mechanisms with dominance of hemodynamic alterations: negative isotropic effect on the heart, reduction in circulating intravascular volume and increase in peripheral resistance with renal vasoconstriction [23].

### 2.2. Decision making

Decision-making has historically been approached by multiple disciplines, from the classics such as philosophy, statistics, mathematics and economics, to the most recent, such as Artificial Intelligence. The theories and models developed point to rational support for making complex decisions. They include basic activities such as[24-27]:

1. Define the problem of decision making.
2. Analyze the problem and identify the alternative solutions $X = \{x_1, x_2, x_n\}, (n \geq 2)$
3. Establish evaluation criteria.
4. Select the experts.
5. Evaluate the alternatives.
6. Sort and select the best alternative.
7. Implement and follow up.

When the number of criteria satisfies that $C = \{c_1, c_2, c_m\}, (m \geq 2)$ it is considered a multi-criteria decision-making problem. When the number of experts is such that $K = \{k_1, k_2, k_n\}, (n \geq 2)$ it is considered a group decision-making problem. Figure 1 shows a diagram with the workflow for solving decision-making problems.

**Figure 1:** Diagram with the flow for decision-making problems.
According to the decision environment, decision-making problems can be classified into three situations or decision environments:

- **Environment of certainty**: the elements and/or factors involved in the problem are known precisely. An exact utility value can be assigned to the alternatives involved.
- **Risk environment**: Some of the elements or factors involved are subject to changes. They are usually solved by assigning probabilities to the alternatives according to the theory of probabilities.
- **Uncertainty environment**: the available information is vague or imprecise, generally associated with sensory or subjective appraisals from experts.

### 2.3. Linguistic model

The criteria for the evaluation of complications generated by hypothyroidism may have different characteristics. Therefore, it is appropriate to express each criterion in the appropriate domain (numerical or linguistic). In this context, the extension of the 2-tuple linguistic model proposed in [28] constitutes a way of increasing the interpretation of the data that are introduced in the decision-making problem.

The linguistic representation model based on 2-tuples defines a set of transformation functions for linguistic 2-tuples to carry out the decision-making process without loss of information. Since \( \beta \in [0, g] \) is a value that represents the result of a symbolic operation, a linguistic tuple can be assigned to express the information equivalent to that given by \( \beta \).

**Definition 1.** Let \( S = \{s_0, s_g\} \) be a set of linguistic terms. The set of 2 tuples associated with \( S \) is defined as \( \langle S \rangle = S \times [-0.5, 0.5] \). We define the function \( \Delta: [0, g] \rightarrow S \times [-0.5, 0.5] \) given by:

\[
\Delta \beta = (s_i, \infty), \text{ with } f(x) = \begin{cases} s_i, & i = \text{round}(\beta) \\ \alpha = \beta - i, & \text{otherwise} \end{cases}
\]

where the round assigns to \( \beta \) the integer \( i \in \{0, 1, \ldots, g\} \) closest to \( \beta \).

Note that the function \( \Delta \) is bijective and \( \Delta^{-1}: [0, g) \rightarrow s \times [-0.5; 0.5] \) is defined by \( \Delta^{-1}(s_i, \infty) = i + \infty \).

Numeric values can be transformed to the \( S_t \) language domain in a two-step process. First, transforming numerical values in \([0, 1]\) to \( f(S_t) \) using the numerical linguistic transformation function.

**Definition 2.** Let \( V \in [0, 1] \) be a numerical value and \( S_t = \{s_0, s_1, s_g\} \) a set of linguistic terms. The numerical linguistic transformation function \( tNS_t: [0, 1] \rightarrow f(S_t) \) is defined by:

\[
tNS_t(v) = \{(s_0, y_0), (s_1, y_1), (s_g, y_g)\}
\]

With:

\[
y_i = \mu_{si} = \begin{cases} 0, & \text{if } v < \alpha \text{ or } v > d, \\ \frac{v-a}{b-a}, & \text{if } a < v < b, \\ 1, & \text{if } b \leq v \leq c, \\ \frac{d-v}{d-c}, & \text{if } c < v < d, \end{cases}
\]

Where \( y_i \in [0, 1] \) and \( f(S_t) \) is the set of fuzzy sets in \( S_t \) and \( \mu_{si} \) is the membership function of the linguistic label \( S_t \in S_t \).

The unified previous information in fuzzy sets in \( S_t \) is subsequently transformed to facilitate the interpretation of the results. This transformation is carried out by the function \( \chi: F(S) \rightarrow [0, g] \).

**Definition 3.** Given the set of linguistic terms \( S_t = \{s_0, s_1, s_g\} \) the function \( \chi: F(S) \rightarrow [0, g] \) is defined by:

\[
X: (f(s_t)) = X\{(s_j, y_j), j = 0, \ldots, g\} = \frac{\sum_{j=0}^{g} y_j}{\sum_{j=0}^{g}} = \beta
\]

where the fuzzy set \( F(S_t) \) could be obtained from \( tNS_t \).

Applying the function \( \Delta \) a \( \beta \) (Definition 1) we can assign a tuple of 2 that expresses the information equivalent to that given by \( \beta \).

### 2.4. 2-tuple linguistic neutrosophic number

In [29] the concept of 2-tuple linguistic neutrosophic number sets (2TLLNSs) is proposed to solve this problem based on the SVNS and 2-tuple linguistic sets (2TLSs) [26, 30, 31].

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A 2TLNSS is defined as follows [29]: Suppose that $S = \{s_0, s_1\}$ is a 2TLSs with odd cardinality $t + 1$. It is defined for $(S_t, \infty), (S_t, b), (S_t, c) \in L$ and $a, b, c \in [0, t]$, where $(S_t, \infty), (S_t, b), (S_t, c) \in L$ independently express the degree of truth, indeterminacy and falsehood by 2TLSs, then 2TLNSSs is defined as follows:

$$l_j = \{(S_t, \infty), (S_t, b), (S_t, c)\}$$

(5)

Where:

$$0 < \Delta^{-1}(S_{tj}, a) \leq t, 0 < \Delta^{-1}(S_{tj}, b) \leq t, 0 < \Delta^{-1}(S_{tj}, c) \leq t$$

and

$$0 < \Delta^{-1}(S_{tj}, a) + 0 < \Delta^{-1}(S_{tj}, b) + 0 < \Delta^{-1}(S_{tj}, c) \leq 3t$$

(6)

The Scoring and Accuracy feature allows 2TLNN to be classified as:

Let:

$$l_1 = \{(S_{t1}, \infty), (S_{t1}, b), (S_{t1}, c)\}$$

2TLNN in $L$ the scoring and precision function is defined as follows:

$$S_{t1} = \Delta \left\{ \frac{2t + \Delta^{-1}(S_{t1}, \infty) - \Delta(S_{t1}, b) - \Delta(S_{t1}, c)}{3} \right\}, \Delta^{-1}(S(l_1)) \in [0, t]$$

(7)

$$H_{t1} = \Delta \left\{ \frac{t + \Delta^{-1}(S_{t1}, \infty) - \Delta(S_{t1}, c)}{2} \right\}, \Delta^{-1}(H(l_1)) \in [0, t]$$

(8)

3. Materials and Methods

This section describes the structure and operation of the method for estimating complications generated by hypothyroidism during pregnancy. The method operates on a neutrosophic environment based on the linguistic decision analysis scheme that can address criteria of different nature and provide linguistic results. Figure 1 illustrates the general structure of the proposed method.

![Figure 1. Structure of the method to estimate the complications generated by hypothyroidism during pregnancy.]

1. Evaluation framework:

In this phase, the assessment framework is defined for medical complications caused by hypothyroidism during pregnancy. The framework is established as follows:

Let $E = \{e_1, e_2, \ldots, e_n\}, (n \geq 2)$ be a set of experts.

Let $C = \{c_1, c_2, \ldots, c_k\}, (k \geq 2)$ be a set of criteria.

Let $R = \{r_1, r_2, \ldots, r_m\}, (m \geq 2)$ be a set of medical complications.

2. Obtaining information:

Once the framework has been defined, the knowledge of the experts group must be obtained. Each expert provides his preferences through the use of utility vectors. The utility vector is represented as follows:

$$P^n_\ell = \{P^n_\ell_1, P^n_\ell_2, \ldots, P^n_\ell_h\}$$

(9)

where $P^n_\ell_h$ is the preference given by the $c_h$ criteria of the $r_m$ requirement of the $e_n$ experts.

3. Classification of medical complications.

The objective of this phase is to obtain an easily interpretable collective linguistic global assessment. To do so, the information is unified and aggregated. Finally, a prioritization process is carried out. This phase develops the approach reviewed in Section 2.3 for dealing with heterogeneous information and giving linguistic results. Unification of information.

The information is unified in a specific linguistic domain $(S_t)$. The numerical information is transformed to the linguistic domain $(S_t)$, following these steps:

a) Select a specific linguistic domain, called a set of basic linguistic terms $(S_t)$.
b) Transformation of numerical values in [0, 1] to $f(S_t)$.
c) Transformation of fuzzy sets $S_t$ into a linguistic 2-tuple.

Information aggregation
The aggregation process is developed in two steps with the aim of calculating a global evaluation of each criterion that affects medical complications.

Assessment of medical complications.
The final step in the prioritization process is to rank the medical complications. This classification makes it possible to select the complication with the highest value. The most critical complication is the one that has the most effective collective evaluation of the $\text{Max}\{r_j, a_j = 1, 2, 3, n\}$ process. Requirements are prioritized based on this value in descending order.

4. Results
In this session an illustrative example is developed to show the applicability of the proposed method. The study was carried out using data from the medical history of a pregnant patient treated at IESS Ambato Hospital in Ecuador, and who was diagnosed with hypothyroidism in Outpatient Consultation and Hospitalization.

1. Evaluation framework
In this case study, the evaluation framework is made up of: 3 experts $E = \{e_1, e_2, e_3\}$ who evaluate the main medical complications recorded in the scientific literature composed of 5 complications $R = \{r_1, r_2, r_3, r_4, r_5\}$ where:

- $r_1$: Hypertensive disorders such as preeclampsia,
- $r_2$: Threat of preterm labor,
- $r_3$: Recurrent urinary tract infection,
- $r_4$: Intrauterine growth restriction,
- $r_5$: Threat of abortion.

From which 3 evaluative criteria are identified $C = \{c_1, c_2, c_3\}$ which are shown below:

- $c_1$: Heart rate,
- $c_2$: Body temperature,
- $c_3$: Disorder in metabolism.

Each expert could give the information numerically or linguistically, taking into account the nature of the criteria. A common linguistic domain $S_t$ is chosen to verbalize the results. Figure 2 shows the linguistic domain used.

![Figure 2: Domain of linguistic values $S_t$](image)

For numerical values, the following linguistic scale is used with single-value neutrosophic numbers as shown in Table 1

<table>
<thead>
<tr>
<th>Linguistic terms</th>
<th>SVN number</th>
</tr>
</thead>
<tbody>
<tr>
<td>(EG) Extremely Good</td>
<td>(1.0,0)</td>
</tr>
<tr>
<td>(VVG) Very Very Good</td>
<td>(0.9, 0.1, 0.1)</td>
</tr>
<tr>
<td>(VG) Very Good</td>
<td>(0.8,0.15,0.20)</td>
</tr>
<tr>
<td>(G) Good</td>
<td>(0.70,0.25,0.30)</td>
</tr>
<tr>
<td>(MG) Moderate Good</td>
<td>(0.60,0.35,0.40)</td>
</tr>
<tr>
<td>(M) Medium</td>
<td>(0.50,0.50,0.50)</td>
</tr>
<tr>
<td>(MB) Moderate Bad</td>
<td>(0.40,0.65,0.60)</td>
</tr>
<tr>
<td>(B) Bad</td>
<td>(0.30,0.75,0.70)</td>
</tr>
<tr>
<td>(VB) Very Bad</td>
<td>(0.20,0.85,0.80)</td>
</tr>
<tr>
<td>(VVB) Very Very Bad</td>
<td>(0.10,0.90,0.90)</td>
</tr>
<tr>
<td>(EB) Extremely Bad</td>
<td>(0,1,1)</td>
</tr>
</tbody>
</table>

Table 1. Linguistic Terms Used to Provide Assessments [32].
2. Obtaining information

Once the information on medical complications has been gathered, an evaluation framework is made. Table 2 shows the result obtained. The evaluation criteria are carried out on the $S_2$ scale.

<table>
<thead>
<tr>
<th>$e_1$</th>
<th>$e_2$</th>
<th>$e_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$c_1$</td>
<td>(1.0,0)</td>
<td>(0.9,0.1)</td>
</tr>
<tr>
<td>$c_2$</td>
<td>(0.70,0.25,0.30)</td>
<td>(0.80,15.0,20)</td>
</tr>
<tr>
<td>$c_3$</td>
<td>(0.80,15.0,20)</td>
<td>(1.0,0.1)</td>
</tr>
</tbody>
</table>

Table 2. Information gathering.

Information is transformed to unify heterogeneous information. Subsequent fuzzy sets $S_2$ are transformed into linguistic 2-tuples. In this example, a two-step aggregation process is applied to calculate a collective assessment of medical complications. For this investigation, we used the weighting average of the 2-tuples linguistic neutrosophic numbers. 2-TLNNWA is used to add evaluations for each expert. The weighting vectors we used were $W=(0.4,0.3,0.3)$.

To calculate the collective evaluation, the 2-TLNNWA operator is used with the weighting vector $V=[0.5,0.2,0.3]$ (see table 2).
Pregnancy
C. Antonio Escobar Suárez, R. Oliva Torres, L. Espinoza Freire.

Conclusions
The complications generated by hypothyroidism during pregnancy demonstrate the need for thyroid studies to be performed on all pregnant women in order to reduce the morbidity and mortality caused by the complications that may occur if not diagnosed and treated in time. Early diagnosis of thyroid dysfunction during pregnancy and initiation of rational therapy can alleviate adverse pregnancy outcomes.

Our study identified that maternal hypothyroidism was associated with various pregnancy and perinatal complications, including gestational diabetes mellitus, gestational hypertension, severe preeclampsia, caesarean section, preterm birth, major congenital anomalies, and admission to the neonatal intensive care unit.

With the implementation of the proposed method, it was possible to estimate the incidence of complications generated by hypothyroidism during pregnancy. The method operates by modeling the uncertainty using neutrosophic numbers under a multi-criteria approach. The case study was carried out at IESS Ambato Hospital in Ecuador, where the applicability of the proposed method is corroborated.

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