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Ensemble Classifiers for Acute Leukemia Classification Using Microarray Gene Expression Data under uncertainty

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Abstract: One of the most prevalent cancers in children and adults, acute leukemia has the potential to lead to death if left untreated. Within a few weeks after diagnosis, childhood ALL has spread throughout the body, posing a serious health risk to the patient. Evaluation of acute leukemia contains uncertainty and incomplete information. Due to the subjective nature of the expectations, this rating procedure incorporates ambiguity and inaccuracy. To illustrate the ambiguity of our subjective judgments, we can use the triplet T, F, and I, truth, falsity, and indeterminacy (I). Therefore, a Single-Valued Neutrosophic Sets (SVNSs) approach based on AHP, TOPSIS, and VIKOR is designed and implemented in this article. Neutrosophic AHP is used to determine the weighting of criteria in this methodology. A neutrosophic TOPSIS and VIKOR model are used to rank alternatives. There is further validation and verification of the proposed methodology in the application. To demonstrate the adaptability of the offered decisions under various circumstances, sensitivity assessments and comparative analyses were carried out.

Keywords: AHP; TOPSIS; VIKOR; Acute Leukemia; Neutrosophic; MCDM

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1. Introduction and Background

There are a wide variety of blood-related diseases known as acute leukemia, which are defined by aberrant growth of blast cells in bone marrow, which results in the replacement of healthy cells and a decrease in the 3 hematopoietic types in peripheral blood.

Approximately 300,000 people are expected to die from them in 2018, making them the 11th and 10th greatest common causes of cancer in the world, respectively. There are 3.7 new cases of acute myeloid leukemia per 100,000 residents in Europe each year, with only 19 percent of those patients surviving for five years[1]. A precise and appropriate diagnosis is essential to successful disease control. In the bone marrow, immature lymphocytes cause acute lymphoblastic leukemia (ALL), also known as acute lymphocytic leukemia [2], [3]. Upon entering the bloodstream, leukemic cells move rapidly to several organs and tissues, including the spleen, liver, lymph nodes, brain, and the neurological system. The bone marrow and blood are primarily affected by ALL, which is a disease of the immune system [4], [5]. It is also known as acute pediatric leukemia because it is the most prevalent kind of leukemia in children since chronic and myeloid leukemias are rare in children.

For an accurate diagnosis of acute leukemia, the World Health Organization (WHO) recommends combining morphology with additional tests like immunophenotype, cytogenetics, and molecular biology[6]. As a result, finding blasts in the blood is still the first step in their diagnosis. It is true that smear review takes a long time, requires well-trained staff, and is subject to base on inter variability, which is especially important when dealing with the blast. Indeed, leukemia types have small interclass morphological variations, which results in low specificity scores during routine screening[7]. There's little doubt that clinical pathologists have difficulty distinguishing between different types of blasts and the subjective nature of their morphological identification. Leukemia lineage identification is critical since the prognosis and acute treatment effects are heavily dependent on this differentiation. Although automated blood cell image analyzers tend to underestimate the amount of blast cells, this complex topic hasn't been addressed in the literature[8], [9].

Medical diagnosis has been refrained by statistical approaches, pattern recognition, artificial intelligence, and neural networks[10]–[14]. To make medical diagnoses easier, another tool called a "MCDA" was developed. The MCDA approach uses the preference relational system proposed by Roy in 1996 [15] and Vincke in 1992 [16] to compare the individuals to be categorized and prototypes (prototypes are the reference points of classes).

It is so possible to use both qualitative and quantitative criteria in the MCDA approach. Additionally, it aids in overcoming some of the challenges associated with expressing data in several units.

In addition, several researchers provide certain improvements and enhancements to improve acute leukemia classification performance by better representing and reflecting acute leukemia data. Reviewing the above expansions reveals that the various types of uncertainty in the data set are primarily to blame for these additional versions. Different forms of fuzzy set extensions are used to address the uncertainty in the data set since it may contain vagueness, imprecision, indeterminacy, and hesitant information. There is no middle ground in classical set theory, optimization, and Boolean logic. An element can either belong to a set or not, and a statement can only be true or false[17]. The problem is that in the real world, hardly anything is accurate and it's all a relative term that cannot be characterized by classical reasoning. This type of ambiguity was addressed by Zadeh's fuzzy sets theory [18]. Since its inception in 1965, it has been reimagined in some ways. By introducing type-2 fuzzy sets, the mathematical procedures of Zadeh were able to better depict their imprecision [19]. A concept called "intuitional fuzzy sets" (also known as "membership degrees") was first developed by Atanassov in 1986 [20].

Afterward, Smarandache presents neutrosophic sets that have three distinct subsets to reflect different sorts of uncertainty [21]. Each element in the cosmos has a degree of truthiness, indeterminacy, and falsehood between 0 and 1, and these degrees are independent subsets of the neutrosophic sets [21]. To discriminate between degrees of belonging and non-belongingness and to depict absoluteness from relativeness, indeterminacy functions are used in neutrosophic sets. Neutrosophic sets use this notation to deal with the system's uncertainty and lessen the indecision caused by conflicting data. The neutrosophic sets have the most essential benefit over other fuzzy extensions in this regard. Three functions of neutrosophic sets give a domain area that can be used to undertake mathematical operations with varying degrees of uncertainty.

Analytic Hierarchy Process (AHP), developed by Saaty [22], is a well-known technique for solving complicated problems by breaking them down into subproblems and then combining the solutions of these subproblems. It is critical to ensure that the judgments are consistent in this procedure, which uses pairwise comparisons of experts. According to the literature [23]–[32], AHP is frequently utilized as a standard procedure.

When faced with uncertainty and incomplete information, one popular decision-making technique is the TOPSIS approach, which allows for a wide range of alternatives and criteria to be considered in the decision-making process [33]. Consequently, TOPSIS is an excellent method for determining the predicted usefulness of a scenario that is ambiguous, lacking information, or vague. Using the TOPSIS technique, it is possible to identify a short distance from the ideal solution and a long distance from the negative-ideal solution, but these distances are not reflected in their proportionate significance.

Serafim Opricovic (1998) first developed the VIKOR technique, which was first applied in 2004 by Opricovic and Tzeng to solve multicriteria decision-making problems. To begin, there is a compromise solution, which is closer to an ideal answer than any other option available.

Many studies employ the SVNS technique. Distance measurement for SVNSs was first proposed by ahin and Küçük [34] using the neutrosophic subset idea. Several steps in the analysis of Ye [35] were shown to be unrealistic by Peng et al. [36]. Making decisions using machine learning methods has recently become popular [37]. There is also a growing usage of deep learning and other types of learning-based methodologies in the field of decision-making [38] in engineering research [39]–[44]. Machine learning, on the other hand, has its drawbacks, such as the fact that it requires a distinct training phase each time and is only applicable to the data it is trained on. The current scoring function and distance measure utilized in many research with SVNSs yielded erroneous results, according to an analysis of the literature. As a result of this research, we have devised a new score function and a new distance measure.

The remainder of this paper is structured as follows: Section 2 outlines the method that will be taken and lays the groundwork for it. Applicability is shown in Section 3, which includes problem definitions, computations, and results. Section 4 provides comparative assessments and section 5 provides sensitivity analysis. Section 6 concludes with some final thoughts and ideas for future research.

2. Methodology

By Saaty, the AHP approach was invented, which allows for comparisons between two variables. This study proposes a single-valued neutrosophic (SVN) AHP approach.

Step 1: Build the comparison matrix between criteria as:

$$X = \begin{pmatrix} X_{11} & \cdots & X_{1b} \\ \vdots & \ddots & \vdots \\ X_{a1} & \cdots & X_{ab} \end{pmatrix} \quad (1)$$

Where $a = 1,2,3 \ldots, e\ (alternatives), b = 1,2,3 \ldots, f(criteria)$

Step 2: Compute the score function as:

$$S(X) = \frac{2+a-b-c}{3} \quad (2)$$

Which, a, b and c present truth, indeterminacy, and falsity values.

Step 3: Normalize the comparison matrix as:

$$N(A) = \frac{A_a}{\sum_{a=1}^{e} A_a} \quad (3)$$

where, A_a value in comparison matrix and $\sum_{a=1}^{e} A_a$ sum all values in each column.

Step 4: Compute the weights of criteria by taking the average row.

Step 5: Check the consistency ratio (CR)

Apply the Steps of the TOPSIS method

The steps of the TOPSIS approach are as follows:

A. A decision matrix should be built.

B. Make the decision-making matrix uniform.

C. Make a decision matrix that is normalised and weighted.

D. Decide on the ideal remedies for the positive and negative scenarios you're dealing with.

E. The ideal solutions, both positive and negative, are at a certain distance from each alternative.

F. Distance measurements can be used to calculate the relative closeness coefficients.

G. Rank alternatives

Step 6: Build the decision matrix between criteria and alternatives as Eq. (1), then convert the neutrosophic values to one value by Eq. (2).

Step 7: Normalize the decision matrix as:

$$Nor_{ef} = \frac{X_{ef}}{\sqrt{\sum_{f=1}^{b} X_{ef}^2}} \quad (4)$$

Step 8: Compute the weighted normalized decision matrix as:

$$WN_{ef} = Nor_{ef} * W_f \quad (5)$$

where W_f the weights of the criteria

Step 9: Compute the positive and cost ideal solution as:

$$PI_e^+ = \max_e WN_{ef} \text{ for positive criteria} \quad (6)$$

$$PI_e^- = \min_e WN_{ef} \text{ for cost criteria} \quad (7)$$

$$PI_e^- = \min_e WN_{ef} \text{ for positive criteria} \quad (8)$$

$$PI_e^- = \max_e WN_{ef} \text{ for cost criteria} \quad (9)$$

Step 10: Compute the distance of each alternative from the positive and cost criteria as:

$$DI_f^+ = \sqrt{\sum_e^b (WN_{ef} - PI_e^+)^2} \quad (10)$$

$$DI_f^- = \sqrt{\sum_e^b (WN_{ef} - PI_e^-)^2} \quad (11)$$

Step 11: Compute the closeness coefficient as:

$$CC_f = \frac{DI_f^-}{DI_f^- + DI_f^+} \quad (12)$$

Step 12: Rank alternatives according to descending values of CC_f

Apply the steps of the VIKOR method

Step 13: Compute the positive and cost ideal solution as:

$$CI_e^+ = \max_e X_{ef} \text{ for positive criteria} \quad (13)$$

$CI_e^- = \min_e X_{ef}$ for cost criteria (14)

$CI_e^- = \min_e X_{ef}$ for positive criteria (15)

$CI_e^- = \max_e X_{ef}$ for cost criteria (16)

Step 14: Compute the value of C_e and D_e as:

$$C_e = \sum_{f=1}^{b} W_f * \frac{CI_e^+ - X_{ef}}{CI_e^+ - CI_e^-} \quad (17)$$

$$D_e = \max_f W_f * \frac{CI_e^+ - X_{ef}}{CI_e^+ - CI_e^-} \quad (18)$$

Step 15: Compute the value of G_e as:

$$G_e = i * \left(\frac{C_e - \min_e C_e}{\max_e C_e - \min_e C_e}\right) + (1 - i) * \left(\frac{D_e - \min_e D_e}{\max_e D_e - \min_e D_e}\right) \quad (19)$$

Where the value of i is in the range 0 to 1. It refers to the utility degree. We use the i =0.5.

Step 16: Rank alternatives according to ascending value of G_e.

3. Application

To validate the steps of the methodology, we apply them with the application. We collected the criteria and alternatives from previous studies as in Fig 1. The decision-makers are selected according to their experts in this field to evaluate the criteria and alternatives by using the single-valued neutrosophic numbers (SVNNs) as [45]. Then we convert the SVNNs into one value by applying Eq. (2) score function. This matrix is called a comparison matrix where data between criteria. Then compute the normalized comparison matrix in Table 1. Then compute the weights of criteria where $w_1 = 0.138656, w_2 = 0.163386, w_3 = 0.168678, w_4 = 0.227536, w_5 = 0.301744$. According to [46] the opinions of experts are consistent. Then go-ahead to apply the steps of the TOPSIS method.

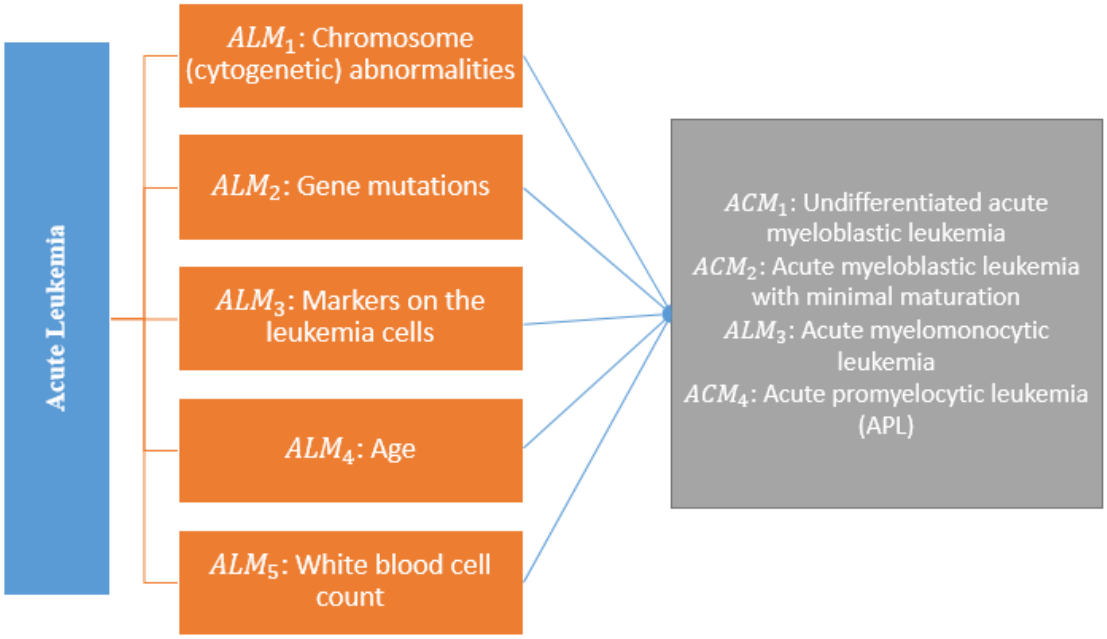

Fig 1. The criteria and alternatives in this study.

Table 1. Normalized comparison matrix by the AHP method.

Criteria	ALM_1	ALM_2	ALM_3	ALM_4	ALM_5
ALM_1	0.076252	0.128138	0.113528	0.242515	0.132848
ALM_2	0.186664	0.07842	0.048313	0.22015	0.283385
ALM_3	0.16945	0.409503	0.063071	0.103204	0.098162
ALM_4	0.16945	0.19197	0.329354	0.134731	0.312175
ALM_5	0.398184	0.19197	0.445734	0.299401	0.17343

Let experts build the decision matrix between criteria and alternatives. Then normalize the decision matrix as Eq. (4) in Table 2. Then compute the weighted normalized decision matrix as Eq. (5). All criteria are positive so, we apply Eqs. (6 and 8) to obtain a positive and cost ideal solution. Then compute the distance of each alternative from the positive and cost ideal solution as Eq. (10) in Table 3. Then compute the closeness coefficient as Eq. (12). Finally rank alternatives according to the biggest value of the closeness coefficient as $ACM_3 \succ ACM_1 \succ ACM_4 \succ ACM_2$. Fig 2. Show the rank of alternatives by the TOPSIS method.

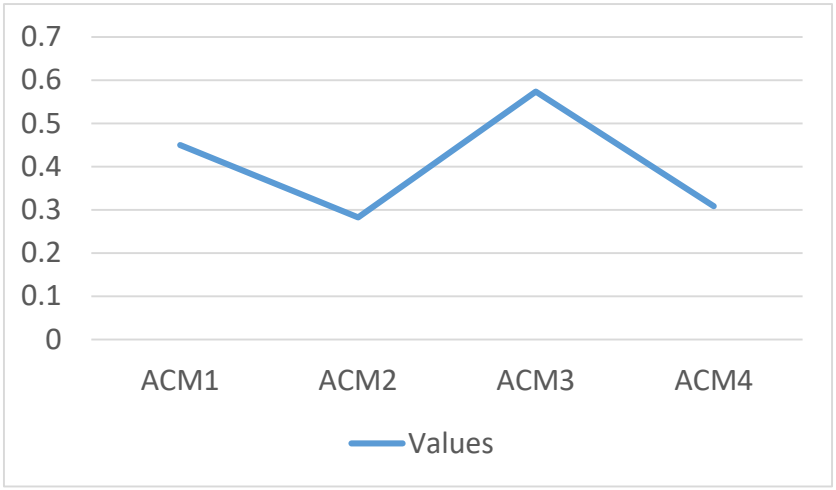

Fig 2. The rank of alternatives by the TOPSIS method.

Table 2. Normalized decision matrix by the TOPSIS method.

Criteria/alternatives	ALM_1	ALM_2	ALM_3	ALM_4	ALM_5
ACM_1	0.310344828	0.166521739	0.268576544	0.461775269	0.160249151
ACM_2	0.097586207	0.355217391	0.243807819	0.145202668	0.216874292
ACM_3	0.310344828	0.123043478	0.243807819	0.196511031	0.462627407
ACM_4	0.281724138	0.355217391	0.243807819	0.196511031	0.160249151

Table 3. Distance of each alternative from positive and cost criteria.

Criteria/alternatives	ALM_1	ALM_2	ALM_3	ALM_4	ALM_5
ACM_1	0	0.000950507	0	0	0.008324884
ACM_2	0.000870268	0	1.74551E-05	0.005188551	0.005498891
ACM_3	0	0.001438991	1.74551E-05	0.003642981	0
ACM_4	1.57485E-05	0	1.74551E-05	0.003642981	0.008324884

By using the decision matrix from the TOPSIS method, the VIKOR method used the Eqs. (13 and 15) to compute the positive and cost ideal solution in Table 4. Eqs. (17 and 18) are used

to compute the values of C_e, D_e. Then Eq. (19) is used to compute the values of G_e. Then rank alternatives according to ascending values of G_e. $ACM_3 \succ ACM_1 \succ ACM_2 \succ ACM_4$. Fig 3 shows the rank of alternatives by the VIKOR method.

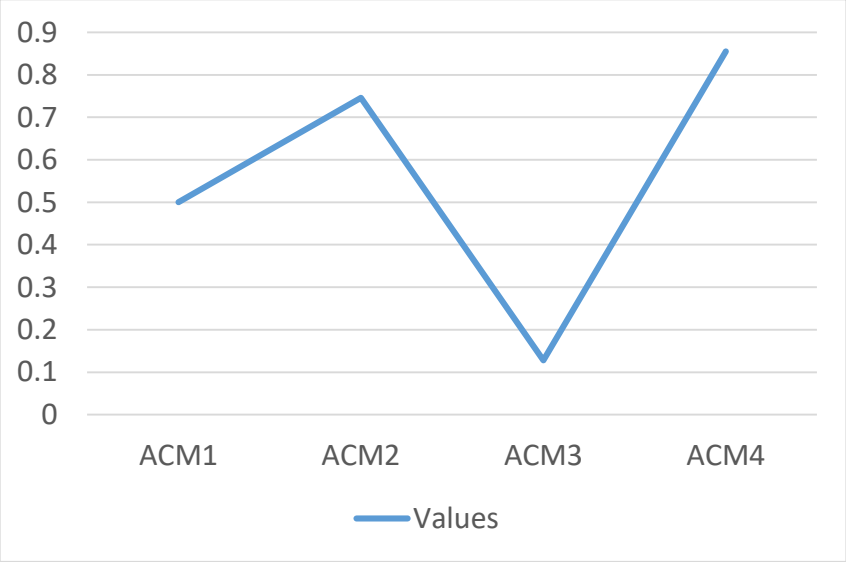

Fig 3. Rank of alternatives by the VIKOR method.

Table 4. The positive and cost ideal solution by the VIKOR method.

Criteria/alternatives	ALM_1	ALM_2	ALM_3	ALM_4	ALM_5
ACM_1	0	0.13279	0	0	0.301744
ACM_2	0.138656	0	0.168678	0.227536	0.245238
ACM_3	0	0.163386	0.168678	0.190658	0
ACM_4	0.018652	0	0.168678	0.190658	0.301744

4. Comparative analysis

In this section, we compare our methods (SVNNs TOPSIS and VIKOR) with Bipolar Neutrosophic Numbers (BNNs VIKOR and TOPSIS) [47] to show the validity of our proposed model. We used the same weights. Fig 4. Show the rank of alternatives under four methods. Table 5 shows the best and worst alternatives. All four methods show the ACM_3 is the best alternative. The SVNNs TOPSIS show ACM_2 is the worst alternative and other three methods show ACM_4 is the worst alternative. Table 5 show the correlation between four methods. The correlation between the four methods is strong.

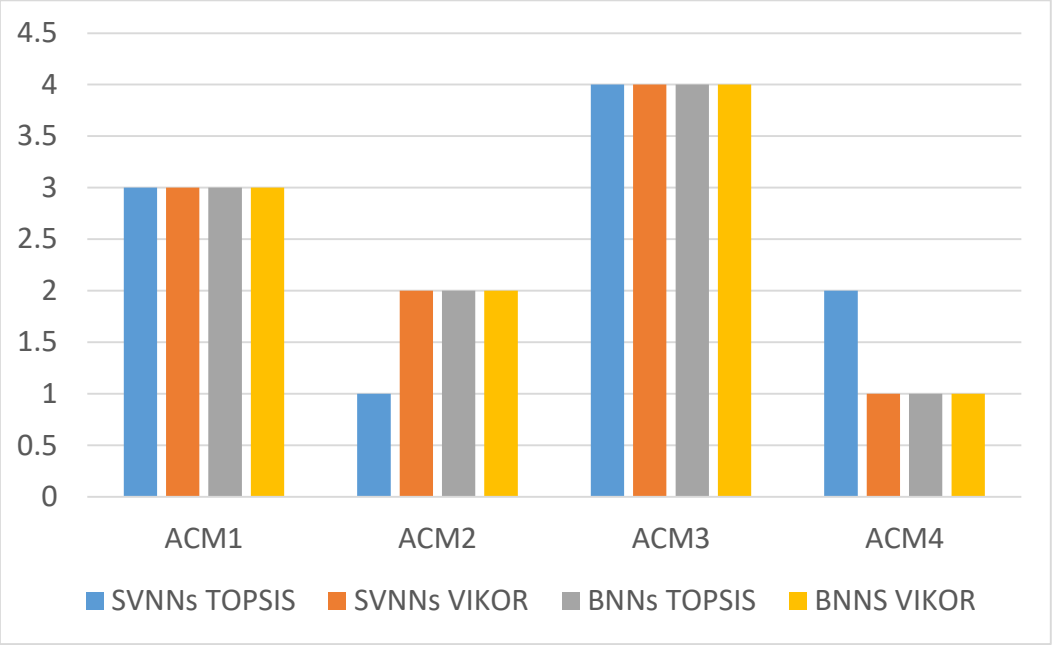

Fig 4. The rank of alternative under comparative analysis.

Table 5. The rank of alternatives by the four methods.

Methods	***Rank***
SVNNs TOPSIS	$ACM_3 \succ ACM_1 \succ ACM_4 \succ ACM_2$
SVNNs VIKOR	$ACM_3 \succ ACM_1 \succ ACM_2 \succ ACM_4$
BNNs TOPSIS	$ACM_3 \succ ACM_1 \succ ACM_2 \succ ACM_4$
BNNS VIKOR	$ACM_3 \succ ACM_1 \succ ACM_2 \succ ACM_4$

Table 6. Pearson correlation between methods.

Methods	**Correlation**
SVNNs TOPSIS and SVNNs VIKOR	0.8
SVNNs TOPSIS and BNNs TOPSIS	0.8
SVNNs TOPSIS and BNNs VIKOR	0.8
SVNNs VIKOR and BNNs TOPSIS	1
SVNNs VIKOR and BNNs VIKOR	1

5. Sensitivity Analysis

In this section, we change the weights of criteria and then compute the rank of alternatives. Table 7 shows the five cases in changing weights of criteria. In Fig 5. The weights of criteria under five cases. In each case we put the weight by 0.5 and the rest of 0.5 is disrupted to all other criteria. For example, in case 1, the first criteria is 0.5 and the other criteria have 0.125 weights. Fig 6. Show the rank of alternatives under five cases by the TOPSIS method. Fig 7. Show the rank of alternatives under five cases by the VIKOR method. Table 8 and Table 9. Show the rank of alternatives by the TOPSIS and VIKOR methods under five cases. In case 1, we put the first criteria with 0.5 weight and the other four criteria have 0.125. In case 2, the second criteria have 0.5 and the other four criteria have 0.125. In case 3, the third criteria have 0.5 and the other four criteria have 0.125. In case 4, the fourth criteria has 0.5 and the other four criteria have 0.125. In case 5, the fifth criteria have 0.5 and the other four criteria have 0.125.

Table 7. The five cases change the weights of the criteria.

Criteria	Case 1	Case 2	Case 3	Case 4	Case 5
ALM_1	0.5	0.125	0.125	0.125	0.125
ALM_2	0.125	0.5	0.125	0.215	0.125
ALM_3	0.125	0.125	0.5	0.125	0.125
ALM_4	0.125	0.125	0.125	0.5	0.125
ALM_5	0.125	0.125	0.125	0.125	0.5

Fig 5. The weights of criteria under five cases.

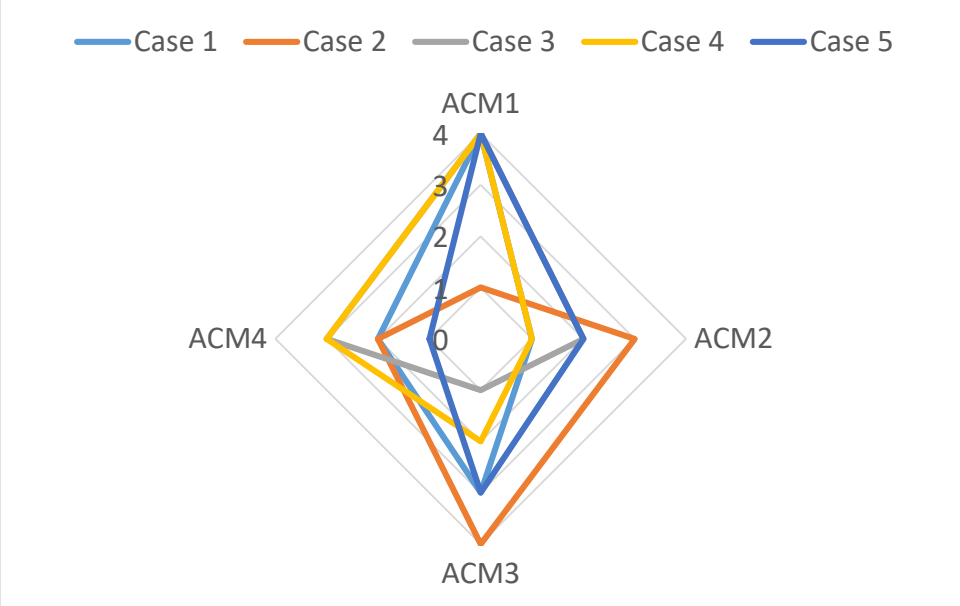

Fig 6. The rank of the TOPSIS method under five cases.

Fig 7. The rank of the VIKOR method is under five cases.

Table 8. The rank of alternatives by the TOPSIS method under five cases.

Cases	**Rank by the TOPSIS method**
Case 1	$ACM_1 \succ ACM_3 \succ ACM_4 \succ ACM_2$
Case 2	$ACM_4 \succ ACM_2 \succ ACM_1 \succ ACM_3$
Case 3	$ACM_1 \succ ACM_3 \succ ACM_4 \succ ACM_2$
Case 4	$ACM_1 \succ ACM_4 \succ ACM_3 \succ ACM_2$
Case 5	$ACM_1 \succ ACM_3 \succ ACM_2 \succ ACM_4$

Table 9. The rank of alternatives by the VIKOR method under five cases.

Cases	**Rank by the TOPSIS method**
Case 1	$ACM_1 \succ ACM_3 \succ ACM_4 \succ ACM_2$
Case 2	$ACM_4 \succ ACM_2 \succ ACM_1 \succ ACM_3$
Case 3	$ACM_1 \succ ACM_3 \succ ACM_4 \succ ACM_2$
Case 4	$ACM_1 \succ ACM_4 \succ ACM_3 \succ ACM_2$
Case 5	$ACM_3 \succ ACM_1 \succ ACM_2 \succ ACM_4$

6. Conclusions

According to the results of this study, a new method to prioritize acute leukemia based on their weight is proposed. Neutrosophic AHP and neutrosophic TOPSIS and VIKOR are used in the suggested approach to rank alternatives in acute leukemia. Because the relationships between acute leukemia data are likewise represented using neutrosophic numbers, the integration of all these components is also carried out using neutrosophic operations.

This methodology can be employed in future research on any other MCDM problems. Furthermore, additional forms of fuzzy sets, such as intuitionistic, hesitant, and Pythagorean fuzzy sets, which reflect uncertainty in different ways, can be added to this strategy. The use of many decision-making methodologies, such as multi-criteria decision-making, can also be used for acute leukemia.

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