

FULL PAPER

Cross-cultural adaptation and validation of Kurdish version of the nasal obstruction symptoms evaluation (NOSE)

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Nasal obstruction can negatively impact the quality of life (QOL). The Nasal Obstruction Symptom Evaluation (NOSE) scale is a validated tool for assessing nasal obstruction symptoms. This study aimed to cross-culturally adapt and validate the NOSE questionnaire in Kurdish for patients undergoing nasal surgery in Iraq. This cross-sectional study was conducted from April 2022 to January 2023 at a publicly funded medical center located in Sulaymaniyah, Iraq. Using forward-backward translation, the NOSE questionnaire was translated into Kurdish. Psychometric evaluation was conducted in 136 patients who underwent rhinoplasty or septoplasty. Test-retest reliability and internal consistency were used to evaluate reliability. Responsiveness was determined by comparing pre-and post-operative scores. Cronbach's alpha for the NOSE-K total score was 0.9999, indicating excellent consistency. In the test-retest reliability assessment, the intraclass correlation coefficient (ICC; 0.9999, 95%CI: 0.9999-0.9999) and Kappa (0.995; 95% CI, 0.993-0.997) demonstrated excellent reliability. The validity of Lin's concordance correlation coefficient (CCC; 0.9999, 95%CI: 0.9998 to 0.9999) of the NOSE-K total score showed a strong correlation and concordance between the two measures, respectively. No ceiling or floor effects were observed (0%). The effect Size (ES) and Standardized Response Mean (SRM) of the NOSE-K total score were -0.003 (95%CI: -0.005 to -0.001) and -0.165 (95%CI: -0.246 to -0.079), respectively. The current study shows that the NOSE-K is a reliable and valid tool for assessing patients with septum-related symptoms. Concerning NOSE-K's strong validity, good internal consistency, repeatability, and reliability, its use is advised.

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KEYWORDS

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Introduction

Nasal obstruction, a disorder that affects approximately 15% of the general population,

can negatively impact a person's QOL [1]. It has a complex etiology and is frequently described as a sensation of blockage or inadequate airflow through the nose [2].

Nasal obstruction can be caused by several factors such as hypertrophic turbinates, nasal polyps, and septal deviation [3]. Its signs include breathing issues, sleep issues, snoring, headache, and a general decline in QOL [4].

Nasal airway obstruction (NAO) is often diagnosed clinically based on the patient's subjective symptoms and doctor's evaluation. Physicians and researchers have increasingly focused on patient-reported outcome measures to gauge the effectiveness of treatment because the objective assessment of nasal blockage typically does not correspond substantially with the patient's subjective sense of patency [5].

The ability to diagnose and measure nasal blockage requires certain equipment to effectively treat patients with these conditions. Assessments can be either objective (using tools such as rhinomanometry) or subjective (using patient reports). Patient-reported outcome measures (PROMS) have become more widely used for patient evaluation because there has been inconsistent estimation using objective measurements. Several QOL questionnaires linked to nasal function have been created in recent years, including the SNOT-22, the Nasal Symptom Questionnaire (NSQ), and Nasal Obstruction Symptom Evaluation (NOSE) scale [6-8].

The NOSE scale is one of the main tools used to evaluate the effect and severity of symptoms of nasal obstruction. This instrument has been extensively used in several clinical and scientific fields. It has been translated and modified into German [9], Turkish [5], Dutch [10], Polish [11], and Lithuanian languages [12], which shows its cross-cultural compatibility, validity, and wide global application. The NOSE scale is a straightforward, widely applied, and thoroughly verified QOL tool unique to the NAO. It comprises five nasal obstruction-related items that can be used to quickly assess the severity of a patient's problems during the last month. Each question uses a 5-point Likert scale, ranging from "0" (indicating no

problem) to "4" (indicating severe problems with breathing). A higher score indicates a more serious obstruction of the nasal airway. The total score ranged from 0 to 100 [8,9].

The NOSE scale has been shown to have high sensitivity and specificity for distinguishing between patients with nasal obstruction and healthy controls. For example, a study conducted by Carmel Neiderma *et al.* (2023) showed that the Hebrew version of the NOSE scale (H-NOSE) had a sensitivity and specificity of over 90%, with a significant difference in scores before and after surgical intervention for nasal obstruction [13]. Another study conducted by Prasertwit *et al.* (2023) focused on translating and validating the Thai version of the NOSE scale for patients with nasal septal deviation. The Thai-NOSE was found with high internal consistency (Cronbach's $\alpha = .942$) and was able to accurately discriminate between patients and healthy controls. This study confirmed the validity and reproducibility [14].

With the increasing rates of rhinoplasty and septoplasty surgeries in the Middle East, particularly in Iraq, there is a growing need for valid adaptation of the NOSE questionnaire in Kurdish. To date, no studies have been conducted regarding the cross-cultural adaptation and psychometric evaluation of the Kurdish version of the NOSE questionnaire. Therefore, it is essential that the present study is conducted to examine the cultural adaptation and validation of the NOSE scale in Kurdish among patients undergoing nasal or septal surgery in Iraq.

Methods

In this cross-sectional study, participants were randomly recruited from April 2022 to January 2023 from a publicly funded medical center located in Sulaymaniyah, Iraq. A total of 136 participants (94 females and 44 males) aged 18-48 years were recruited. All the participants underwent rhinoplasty or septorhinoplasty. All participants provided

informed consent, and the study was approved by the regional institutional review board. Age \geq eighteen or older, prior rhinoplasty or septoplasty, and proficiency in reading and comprehending Kurdish were among the inclusion criteria. The existence of cognitive or psychiatric disorders that impair one's capacity to complete questionnaires and incomplete questionnaires were excluded.

Sample Size

The NOSE questionnaire's test-retest reliability of 0.90 served as the basis for calculating the sample size. Several factors were considered to determine the appropriate sample size. A dropout rate of 20% was considered, with an alpha level of 5% and a beta level of 90%. Consequently, it was calculated that 136 participants would be the necessary sample size.

Instruments

The NOSE scale, a validated and widely used self-report instrument, was selected as the primary tool to assess nasal obstruction symptoms. This tool is designed to evaluate the severity and frequency of nasal obstruction and related symptoms using five items: nasal stuffiness or congestion, nasal obstruction, breathing problems through the nose, sleeping problems, and breathing problems during exercise. Each item is scored on a 5-point Likert scale from 0 (not a problem), 1 (very mild problem), 2 (moderate problem), 3 (fairly bad problem), and 4 (severe problem). Each item's total score ranges from 0 to 20, with higher values denoting more severe nasal blockages [14].

Translation and adaptation of NOSE to Kurdish (NOSE-K)

The NOSE questionnaire was translated and adapted into Kurdish based on the forward-backward translation approach outlined by Beaton *et al.* (2000) [15]. A five-step approach

involving translation, synthesis, reverse translation, expert committee evaluation, and pre-testing was used to modify the NOSE scale for use across cultures. The NOSE scale was initially translated from English to Kurdish by two separate bilingual translators whose mother tongues were Kurdish. A consensus version was created after resolving discrepancies. Two more international translators who were unfamiliar with the original NOSE scale, translated the synthesized version back into English. Following that, a committee of experts, language specialists, healthcare professionals, and methodology experts conducted a thorough review of all translations. The committee's primary objective was to address any inconsistencies, elucidate any uncertainties, and reach unanimous agreement on the cultural and semantic alignment between the original NOSE scale and its translated counterparts. The back-translation was compared to the original English version to identify and resolve any inconsistencies to produce a pre-final version.

The pre-final Kurdish NOSE version was pilot-tested on a sample of 10 native Kurdish speakers with nasal obstruction symptoms. Participants were interviewed about their interpretation of the questionnaire items, and their responses were used to make final refinements to produce the final Kurdish NOSE version.

Psychometric evaluation

The psychometric properties of the translated NOSE scale were assessed using a sample of 136 participants who underwent rhinoplasty or sept rhinoplasty surgery at a publicly funded private clinic, private hospital (Anwarshexa Hospital), and Sulaymaniyah Burn and Plastic Hospital, Iraq.

Each patient completed the K-NOSE questionnaire before and three months after the surgical procedure. Previous research has provided the basis for choosing a three-month time frame [5]. The analysis only included

completed surveys. When answering queries about the questionnaire's components or completion, the researchers were on hand to help and support the participants.

Data analysis

All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). To encapsulate the clinical and demographic features of the research sample, descriptive statistics, such as means, standard deviations, frequencies, and percentages, were computed.

The reliability of the translated NOSE scale was assessed by evaluating its internal consistency using Cronbach's alpha and test-retest reliability using Intraclass Correlation Coefficients (ICC). ICC values above 0.70 were considered acceptable.

Standardized Response Means (SRM) and ES between the preoperative and postoperative NOSE scores were computed to assess responsiveness. Large effect sizes and SRMs were defined as those exceeded 0.8.

The percentage of patients who received the highest and the lowest possible ratings on the NOSE scale was used to compute the ceiling and floor effects. Less than 15% of the ceiling and floor effects were deemed appropriate.

The responsiveness of the NOSE-K questionnaire was evaluated by assessing the ES and SRM. These metrics gauge the questionnaire's capacity to detect the extent of improvement resulting from treatment. Another statistical measure used to assess

responsiveness is Standard Error in Measurement (SEM). SEM helps to differentiate genuine changes in a patient's clinical status from measurement errors during the follow-up period. Consequently, we computed the Minimal Detectable Change (MDC) with 95% confidence (MDC95) and 90% confidence (MDC90), to ascertain this distinction.

Minimal Clinically Important Difference (MCID) was estimated by calculating the SEM and minimal detectable change at MDC95. SEM was calculated as $SD \times \sqrt{(1-ICC)}$. MDC95 was calculated as $SEM \times 1.96 \times \sqrt{2}$. Statistical significance was set at $P < 0.05$.

Ethical considerations

Before being included in the study, each participant provided informed consent. Participants' privacy was respected, and all data collected were anonymized to ensure confidentiality.

Results

This study included 136 patients, of which 44 (32.4%) were male and 92 (67.6%) were female. The mean age at participation was 26.698 ± 8.742 years. 61 (44.9%) were married. 49 (36%) were smokers and 16 (11.8%) consumed alcohol. 100 (73.5%) of the participants lived in Sulaymaniyah city, 25 (18.45) lived in Kalar City, 2 (1.5%) lived in Erbil, and the rest of the people, 9 (6.6%) lived outside of Iraq (Table 1).

TABLE 1 Demographic characteristics of participants

Characteristics	Value
N	136
Age (mean \pm SD; year)	26.698 ± 8.742
Sex (n, %)	
Male	44 (32.4%)
Female	92 (67.6%)
Marital status (n, %)	
Married	61 (44.9%)
Unmarried	75 (55.1%)
Smoking status (n, %)	
Yes	49 (36%)

No	87 (97%)
Alcohol consumption (n, %)	
Yes	16 (11.8%)
No	120 (88.2%)
Residency status (n, %)	
Sulaimani City	100 (73.5%)
Kalar City	25 (18.45%)
Erbil City	2 (1.55)
Outside City	9 (6.6%)

SD:Standard deviation

In the second assessment, the mean total score of the NOSE-K was 15.94 ± 1.7 in the first and 2.35 ± 1.25 in the second assessment that the mean of the first and second assessments was significantly different ($P \leq 0.001$). As subscales of the Nasal congestion of stuffiness score (2.77 ± 1.12) in the first and (0.85 ± 0.9) in the second assessment that the mean of the first and second assessment had a significant difference ($P \leq 0.001$). The Nasal blockage or obstruction score (3.35 ± 0.64) in the first and (0.35 ± 0.41) in the second assessment that the mean of the first and second assessment had a significant difference ($P \leq 0.001$). The breathing problem through the nose score (3.71 ± 0.86) and (0.27 ± 0.15) in the first and

second assessments, respectively, indicated that the mean of the first and second assessments was significantly different ($P \leq 0.001$). The score of the Sleeping problem was (2.37 ± 0.65) in the first and (0.24 ± 0.53) in the second assessment that the mean of the first and second assessment had a significant difference ($P \leq 0.001$) and the score of the breathing problem during exercise was ($3.74 \pm .42$) in the first and (0.64 ± 0.26) in the second assessment that the mean of the first and the second assessment had a significant difference ($P \leq 0.001$). The second evaluation brought about minimal alterations to all subscale scores (Table 2).

TABLE 2 Total score of the NOSE in the first assessment and the second assessment

NOSE-K	First assessment		Second assessment		P-value*
	Range	Mean \pm SD	Range	Mean \pm SD	
Nasal congestion of stuffiness	1-4	2.77 ± 1.12	1-4	0.85 ± 0.9	0.001
Nasal blockage or obstruction	2-4	3.35 ± 0.64	2-4	0.35 ± 0.41	0.001
Breathing problem through the nose	1-4	3.71 ± 0.86	1-4	0.27 ± 0.15	0.001
Sleeping problem	0-4	2.37 ± 0.65	0-4	0.24 ± 0.53	0.001
Breathing problem during exercise	2-4	$3.74 \pm .42$	1-4	0.64 ± 0.26	0.001
Total NOSE score	10-20	15.94 ± 1.7	10-20	2.35 ± 1.25	0.001

P-value, Wilcoxon signed-rank test; SD: Standard deviation. NOSE = Nasal Obstruction Symptom Evaluation Kurdish version.

Reliability

Cronbach's alpha for the NOSE-K total score was 0.9999, indicating excellent consistency. In the test-retest reliability assessment, the intraclass correlation coefficient (ICC; 0.9999, 95%CI: 0.9999-0.9999) and Kappa (0.995;

95%CI, 0.993-0.997) demonstrated excellent reliability.

For the reliability assessment, nasal congestion of stuffiness, Cronbach's alpha (0.9999), ICC (0.9999, 95%CI: 0.9999-0.9999), and Kappa (0.997, 95%CI: 0.995-0.999) were indicative of excellent consistency and

reliability. In addition, Cronbach's alpha (0.9997), ICC (0.9997, 95%CI: 0.9996-0.9998), and kappa (0.998, 95%CI: 0.994-0.999) statistics for nasal blockage or obstruction showed excellent consistency and reliability. For the reliability assessment of breathing problems through the nose, Cronbach's alpha (0.9999), ICC (0.9999, 95%CI: 0.9999-0.9999), and Kappa (0.998, 95%CI: 0.995-0.999) were indicative of excellent consistency and reliability. Cronbach's alpha (0.9999), ICC (0.9999, 95%CI: 0.9998-0.9999), and kappa (0.995; 95%CI, 0.994-0.999) statistics of the sleeping problem showed excellent consistency and reliability. In addition, Cronbach's alpha (0.9999), ICC (0.9999, 95%CI: 0.9999-0.9999), and Kappa (0.995; 95%CI, 0.992-0.999) statistics of breathing problems during exercise showed excellent consistency and reliability (Table 3). NOSE-K showed a high degree of agreement between the test and retest times.

Validity

To evaluate the validity Lin's concordance correlation coefficient (CCC; 0.9999, 95%CI: 0.9998 to 0.9999) of NOSE-K total score showed a strong correlation and concordance between two measures, respectively. No ceiling effect nor floor effect was detected (0%).

Robust agreement between the two measurements was demonstrated in the CCC (0.9998, 95%CI: 0.9998 to 0.9999) pertaining to the nasal congestion of the stuffiness subscale. Zero percent ceiling effect and floor effect were also detected. Moreover, the analyses showed a strong concordance between different measures of nasal blockage or obstruction subscales according to CCC (0.9996, 95%CI: 0.9995-0.9997). Likewise, a zero percent ceiling effect and floor effect were detected in the pain subscale. In addition, CCC

(0.9999, 95%CI: 0.9998-0.9999) for breathing problems through the nose, CCC (0.9997, 95%CI: 0.9996-0.9998) for sleeping problems, and CCC (0.9999, 95%CI: 0.9998-0.9999) for breathing problems during exercise showed a strong correlation and concordance between the two measures. No ceiling effect nor floor effect was detected (0%) (Table 3).

Responsiveness

The ES and SRM of the NOSE-K total score were -0.003 (95%CI: -0.005 to -0.001) and -0.165 (95%CI: -0.246 to -0.079), respectively. SEM, MDC₉₀, and MDC₉₅ were 0.149, 0.351, and 0.685, respectively, for the NOSE-K total score.

ES and SRM of Nasal congestion of stuffiness subscale were -0.004 (95%CI: -0.002 to -0.0006) and -0.136 (95%CI: -0.207 to -0.008), respectively. In addition, SEM, MDC₉₀, and MDC₉₅ were 0.154, 0.368, and 0.729, respectively. Similar ES (-0.002; 95%CI: -0.008 to -0.0006) and SRM (-0.132, 95%CI: -0.116 to 0.081) were observed in the nasal blockage or obstruction subscale. The SEM, MDC₉₀, and MDC₉₅ of the nasal blockage or obstruction subscale were 0.084, 0.183, and 0.346, respectively.

ES and SRM of Breathing problems through the nose subscale were -0.002 (95%CI: -0.005 to -0.0006) and -0.129 (95%CI: -0.205 to -0.017). In addition, SEM, MDC₉₀, and MDC₉₅ were 0.164, 0.387, and 0.759, respectively. ES and SRM of Sleeping problem subscale were -0.003 (95%CI: -0.007 to -0.0009) and -0.120 (95%CI: -0.192 to -0.021). In addition, SEM, MDC₉₀, and MDC₉₅ were 0.164, 0.387, and 0.758, respectively. Similar ES (-0.002; 95%CI: -0.005 to -0.0006) and SRM (-0.123, 95%CI: -0.202 to 0.018) were observed for breathing problems during the exercise subscale. Breathing problems during the exercise subscale SEM, MDC₉₀, and MDC₉₅ were 0.164, 0.389, and 0.758, respectively (Table 3).

TABLE 3 The psychometric characteristics of the Kurdish NOSE version

Properties	Value (95% CI)					
	NOSE total score	Nasal congestion of stuffiness	Nasal blockage or obstruction	Breathing problem through the nose	Sleeping problem	Breathing problem during exercise
Reliability						
Cronbach alpha	0.9999	0.9999	0.9997	0.9999	0.9999	0.9999
ICC	0.9999 (0.9999 to 0.9999)	0.9999 (0.9999 to 0.9999)	0.9997 (0.9996 to 0.9998)	0.9999 (0.9999 to 0.9999)	0.9999 (0.9998 to 0.9999)	0.9999 (0.9999 to 0.9999)
Kappa	0.995 (0.993 to 0.997)	0.997 (0.995 to 0.999)	0.998 (0.994 to 0.999)	0.998 (0.995 to 0.999)	0.995 (0.993 to 0.998)	0.995 (0.992 to 0.999)
Validity						
Ceiling effect	0%	0%	0%	0%	0%	0%
Floor effect	0%	0%	0%	0%	0%	0%
CCC	0.9999 (0.9998 to 0.9999)	0.9998 (0.9998 to 0.9999)	0.9996 (0.9995 to 0.9997)	0.9999 (0.9998 to 0.9999)	0.9997 (0.9996 to 0.9998)	0.9999 (0.9998 to 0.9999)
Responsiveness						
ES	-0.003 (-0.005 to -0.001)	-0.004 (-0.002 to -0.006)	-0.002 (-0.008 to 0.0006)	-0.002 (-0.005 to -0.0006)	-0.003 (-0.007 to -0.0009)	-0.002 (-0.005 to -0.0006)
SRM	-0.165 (-0.246 to -0.079)	-0.136 (-0.207 to -0.008)	-0.132 (-0.116 to 0.0815)	-0.129 (-0.205 to -0.017)	-0.120 (-0.192 to -0.021)	-0.123 (-0.202 to -0.018)
SEM	0.149	0.154	0.084	0.164	0.072	0.164
MDC 90	0.351	0.368	0.183	0.387	0.171	0.389
MDC95	0.685	0.729	0.346	0.758	0.335	0.758

The correlation and agreement for each question and the total score on the test-pretest showed a strong and significant correlation. The correlation of the total score on the test-pretest was strong and significant ($r = 0.986$, $P \leq 0.001$). The correlation between nasal congestion and stuffiness in the first and the second assessments was strong and significant ($r = 0.982$, $P \leq 0.001$). In addition, in the first and

the second assessments, the correlation between nasal blockage and obstruction was strong and significant ($r = 0.988$, $P \leq 0.001$). For Breathing problems through the nose, sleeping problems, and breathing problems during exercise, a strong and significant correlation was obtained. The results are shown in (Table 4).

TABLE 4 Correlation of mean score of the NOSE-K Scale for each question (test–pretest)

NOSE-K	Correlation Between First and Second Assessment	
	r	P-value
Nasal congestion or stuffiness	0.982	0.001
Nasal blockage or obstruction	0.988	0.001
Breathing problem through the nose	0.965	0.001
Sleeping problem	0.941	0.001
Breathing problem during exercise	0.914	0.001
Total NOSE score	0.986	0.001

P value Pearson correlation, NOSE-K= Nasal Obstruction Symptom Evaluation Kurdish version

Discussion

This study aimed to cross-culturally adapt the Kurdish version of the NOSE questionnaire and assess its psychometric properties. The study findings show that the NOSE-K exhibits excellent internal consistency and validity when assessing patients who have undergone rhinoplasty or septoplasty, demonstrating its effectiveness in this patient population.

The findings of the present study clearly demonstrate that the questionnaire exhibits a very high level of reliability, allowing for consistent results under similar conditions and at different time points. Additionally, the values of Cronbach's alpha, ICC, and Kappa indicate that the questionnaire has a high degree of reliability. The results from the ES and SRM, based on the obtained values, suggest that the questionnaire can be effectively used for clinical change detection. Furthermore, concerning the results of SEM, MDC90, and MDC95, this questionnaire can be employed to detect slight clinical changes. In addition, the results from the analysis suggest a strong validation of the questionnaire

The NOSE scale was first published by Stewart *et al.* (2004) [8]. The NOSE questionnaire includes five items: congestion, obstruction, breathing problems, sleep, and exercise. The questions are rated on a 5-point Likert scale. Owing to its ease of use and validity, it has been translated into many other languages, including Greek [16], Portuguese [17], Turkish [18], Spanish [19], French [20], Polish [11], Italian [21], German [9], Dutch

[10], Lithuanian [12], Thai [14], Slovenian [22], Arabic [23], and Hebrew [8].

In the present study, the reliability coefficient was approximately 1. This indicates that the translated Kurdish version of the NOSE questionnaire demonstrated excellent test-retest reliability. In a validation study of the German version of the NOSE scale (D-NOSE) conducted by Spiekermann *et al.* (2018), an ICC of 0.9 was reported, consistent with the results of the present study [9]. In another validation study of the Arabic version of the NOSE scale conducted by Amer *et al.* (2017) to assess validity and cross-cultural adaptation, a Cronbach's alpha of 0.995 was reported for the Arabic version [23]. Based on these findings, the Kurdish version of the questionnaire, similar to the other translated versions, exhibited very good reliability. Furthermore, based on Cronbach's alpha, the reliability of the Kurdish version was higher than that reported for the Hebrew version (0.716-0.76) in a study by Daoud *et al.* (2023) [8].

The validity of the Kurdish version was also demonstrated to be excellent in this study, indicating that this version measures what it intends to measure. The results of this study are consistent with the study conducted by Kawai *et al.* (2021), which showed that the NOSE instrument has good validity [24]. In addition, a study conducted in Mexico by Portillo-Vásquez *et al.* (2022) also demonstrated that the NOSE instrument has very good validity for assessing nasal obstruction [25]. Accordingly, it can be

concluded that the NOSE can be used across diverse societies and cultures.

The present study's findings have shown that there are substantial and favorable correlations between the Test-Pre-test examination's overall score and each of the questionnaire's separate components. This indicates that the questionnaire possesses a very good structural validity. A study conducted in Turkey by Celebi *et al.* (2018), aimed at validating the Turkish translation of the NOSE questionnaire, revealed that in addition to excellent reliability and validity, the Turkish version also exhibits excellent structural validity. This finding aligns with the results of the present study [18].

It is important to note that the validity and reliability of the NOSE questionnaire have been assessed in various languages. Accordingly, in Greek [16], Spanish [19], and Polish [11], versions of the questionnaire, similar to the Kurdish version in the present study, it was demonstrated that this questionnaire exhibits excellent validity and reliability. This indicates the utility of the questionnaire across diverse cultures and societies.

Conclusion

It appears that this is the first study to investigate the adaptation and assessment of the Kurdish version of the NOSE questionnaire. The study shows that NOSE-K is a dependable and effective tool for evaluating individuals with septum-related symptoms. Due to its solid internal consistency, reliability, repeatability, and strong validity, it is suggested that NOSE-K be used in medical procedures and rhinology research within the Kurdish-speaking community experiencing nasal blockages. Further research is crucial to confirm the results of this study.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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