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Original Article

Neutrophil Elastase as a Predictor of Delivery in Pregnant Women with Preterm Labour

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Abstract

Background and objectives: No previous study has been conducted in Nigeria on the role of neutrophil elastase in predicting preterm birth. The present study aimed to determine the role of the neutrophil elastase test in predicting birth in women with preterm labor.

Methods: The present prospective cohort study recruited 83 pregnant women with preterm labor between 28 and 36^{+6} weeks of gestation, and followed up these subjects for 14 days. The controls comprised 85 pregnant women without preterm labor. The cervicovaginal fluid was collected and tested using the neutrophil elastase test. Then, the sensitivity, specificity, and positive and negative predictive parameters were determined. Afterward, the data were scrutinized using the SPSS arithmetic software (Sort23).

Results: Among the 168 pregnant women analyzed in the present study, 83 pregnant women were assigned to the preterm labor group, and 85 pregnant women were assigned to the control group. Furthermore, among the 83 pregnant women in the preterm labor group, 11 women had spontaneous preterm delivery, leading to a spontaneous preterm birth proportion of 13.3%. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the neutrophil elastase test within 14 days post-enrollment were 93.8%, 61.2%, 36.6%, 97.6%, and 67.5%, respectively, for the general population, and 87.5%, 66.7%, 35.0%, 96.3%, and 70.2%, respectively, for subjects at <35 weeks of gestation. The positive and negative likelihood ratios for preterm birth prediction were 2.62 and 0.19, respectively.

Conclusion: The neutrophil elastase test exhibited high predictive accuracy in pregnant women with preterm labor, when compared to the controls, based on the sensitivity and negative predictive value, but this had poor positive predictive values. The neutrophil elastase test may be used as a screening test, but not as a potential predictive test, in the routine clinical setting.

Keywords: Elastase; Neutrophil; Prediction; Preterm labor; Sensitivity.

Abbreviations: BMI, body mass index; CI, confidence interval; NAUTH, Nnamdi Azikiwe University Teaching Hospital; NPV, negative predictive value; PPV, positive predictive value; OR, odds ratio; SCBU, specialized care baby unit.

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Introduction

Preterm labor refers to labor between the onset of fetal viability and the completion of 37 weeks of gestation.[1–4] This represents approximately 10% of all births and is responsible for 75% of perinatal mortality and 50% of long-term morbidity.[5,6] Preterm labor can lead to preterm birth. Preterm birth continues to be the principal reason for global perinatal near-misses and mortality.[7–10] This is also responsible for up to 70% of mortalities during the neonatal period and long-lasting neural problems.[8–11]

Preterm birth contributes to 5–13% of all deliveries. In the majority of cases, pregnant women with features of preterm labor are typically referred to hospitals with facilities for corticosteroids and uterine relaxants. However, following its presentation, up to 90% or 95% of women will not deliver within two weeks, and approximately 50% of women will carry their pregnancy until the term before delivery.[12] Subsequently, according to Hodgins, large volumes of pregnant women have been needlessly admitted for treatment for preterm labor. This causes unnecessary exposure to the adverse effects of steroid therapy and tocolytic therapy.[13] In order to overcome these challenges, the precise documentation of pregnant women who would remain undelivered within two weeks can be used as an important strategy.

The exact mechanism that leads to preterm labor remains elusive. A large proportion of evidence has pointed to infection or inflammatory changes as the processes that lead to preterm labor. Thus, it has been observed that half of preterm deliveries are mediated by infections.[14] No biological marker that allows for the accurate identification of high-risk patients has been identified, although several biomarkers have been identified in cervicovaginal secretions, such as interleukin 6, insulin-like growth factor binding protein 1, fetal fibronectin, and human chorionic gonadotropin.[15] However, other biomarkers, such as corticotropin-releasing hormone in maternal serum,[16] alpha-fetoprotein at 11–13 weeks in maternal serum,[17] serum ferritin,[2] maternal blood *EBF1*-based miRNA transcripts PremaQuick,[1,5] and neutrophil elastase, have been attempted to be used, either alone or in combination.[18–20] Several studies have reported some favorable outcomes with the use of neutrophil elastase.[18–21]

Neutrophil elastase is a serine protease of the chymotrypsin superfamily, which works by hydrolyzing the "fibrous connective tissues outside cells during the process of inflammation". Furthermore, neutrophil elastase may work by correlating inflammation to preterm delivery.[19,20,22] Elastase is located in polymorphonuclear neutrophils. Furthermore, elastase vitiates collagen cross-links, elastin fibers, and type III collagen, which strengthens the tissues of the cervix. Its release from granulocytes may lead to cervical dilatation, which would ultimately lead to preterm labor. A study reported that the specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) of granulocyte elastase in preterm deliveries were 75%, 53%, 92%, and 22%, respectively.[18]

Since accurate epidemiological and prediction data remain invaluable, there is a need for a multidimensional approach that involves the prediction of problems and interventions performed. To the best of our knowledge, most local studies have essentially focused on prevalence and risk factors, and not on the prediction of preterm labor. Hence, the present study aims to determine the role of neutrophil elastase in improving the likelihood of delivery within 14 days in pregnant women with preterm labor at 28–36 weeks of gestation.

Materials and methods

Study site

The present study was conducted at Nnamdi Azikiwe University Teaching Hospital (NAUTH) (Nnewi, Nigeria) and Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (Awka, Nigeria). These institutes serve as transfer centers for various cases of preterm labor. Furthermore, these institutes have equipment for neonatal intensive care following preterm labor and preterm birth.

Study design

The present prospective cohort study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and comprised consecutive pregnant women who presented to the Obstetrics Complex of NAUTH (Nnewi, Nigeria) and Chukwuemeka Odumegwu Ojukwu University Teaching Hospital (Awka, Nigeria).

Sampling approach

The convenience sampling method was used. Consecutive, eligible, and consenting pregnant women with symptoms of preterm labor, who presented in the antenatal clinic and emergency obstetrics unit, and subjects who were admitted to the ward were enrolled.

Study population

The cohort comprised of pregnant women who presented with symptoms, signs, or complaints that were suggestive of preterm labor between 24 and 36^{+6} weeks of gestation. Preterm labor was defined, as follows: subjects with intact membranes; subjects who had contractions, with or without increasing intensity and frequency; subjects with an uneffaced or partially effaced cervix, and a cervical os of ≤3 cm.

Inclusion criteria

Only women who provided consent were recruited. Consenting pregnant women, who were at least 18 years of age, and had a diagnosis of preterm labor, were included in the present study. Consenting pregnant women, who were at least 18 years of age, and had no preterm labor, were included as controls.

The inclusion criteria also included participants who were enrolled between 24 and 36^{+6} weeks of pregnancy. To be qualified for the study, the menstrual date and ultrasound-established gestational age need to be agreed. For pregnant women who presented with significant variations (the last menstrual period, and an ultrasound-based gestational age variance of at least 10 days in 20 weeks), the gestational age was centered on the ultrasound investigation.

Exclusion criteria

The following subjects were excluded: pregnant women with triplets, prenatal rupture of membranes, prior cervical examination, prior tocolysis, placenta previa, moderate or heavy vaginal bleeding, or cervical cerclage, or pregnant women with co-existing fetal congenital anomalies; pregnant women with diabetes, hypertension, kidney or heart diseases, or genital tract anomalies; pregnant women who had deliveries prior to 14 days of enrollment due to maternal or fetal reasons (iatrogenic reasons).

Outcome measures

The primary outcome measures included the sensitivity and specificity of neutrophil elastase. The secondary outcome measures included spontaneous preterm delivery, which was defined as birth before 37 completed weeks of gestation, PPV, NPV, positive likelihood ratio, and negative likelihood ratio for neutrophil elastase.

Procedure

The Institutional Review Board of the two hospitals approved the protocol. Before the digital cervical inspection, a cervical swab sample was collected for the neutrophil elastase assay. During the sterile speculum examination, cervicovaginal specimens were collected, according to the manufacturer's instructions, using a Dacron swab, which was inserted into the posterior fornix of the va-

gina for 30 seconds (in order to allow for swab saturation). Then, the tube that contained 1 ml of extraction buffer with proprietary concentrations and the cotton swab were combined. Afterward, the sample wells were fixed in a flat, horizontal position, and timed for 10 minutes using a timer, and the findings were analyzed.

Next, a pelvic examination was carried out. A Cusco's speculum was used during the pelvic examination before any digital vaginal examination was performed. The parameters documented at the presentation included the following: cervical dilatation, contraction frequency, membrane status, cervical effacement, patient history (age, number of prior births and miscarriages, prior preterm births, and number of antenatal checks), and test findings. The study data was not given to the physician who cared for the subject, except for cases of fetal mortality, membrane rupture, and advanced cervical dilatation (4 cm).

Principle of neutrophil elastase detection

Neutrophil elastase was detected using the immunological antigen-antibody approach. Briefly, the findings were read within 15 minutes after the swab was immersed in buffer for 10 minutes. The results were represented by either a positive line or a negative line.

Sample size determination

Using this approach, Buderer (a sample size calculation in diagnostic accuracy studies at a required absolute precision level for sensitivity) determined the sample size for the cohort study with a sensitivity endpoint:

$$N = \frac{Z^2_{1-\alpha/2} \times S_N \times (1 - S_N)}{L^2 \times \text{Prevalence}}$$

where: n refers to the minimum sample size in each group; S_N refers to the anticipated sensitivity, which was 85.0% in a previous study conducted by Hatakeyama *et al*.[23]; α refers to the size of the critical region (1−α was the confidence level); $Z_1-\alpha/_2$ refers to the standard normal deviation that corresponds to the specified size of the critical region (α), which is 1.96; L refers to the absolute precision desired on either side (half-width of the confidence interval) for sensitivity, which was 25%; P refers to the prevalence of preterm delivery in Nigeria (prevalence rate for preterm delivery in a previous study conducted in Nigeria by Mokuolu *et al*.,[24] which was set at 12.0%).

Substituting the above formula:

$$N = \frac{(1.96)^2 \times [0.85 \times (1 - 0.85)]}{0.25 \times 0.25 \times 0.12}$$

$$N = \frac{3.842 \times 0.85 \times 0.15}{0.0075}$$

N = 65.3 which is approximately 66.

The 20% attrition resulted in 66 + 13.2 = 79.2, which is approximately 80 pregnant women. Therefore, at least 160 pregnant women (80 pregnant women in each group) were recruited for the study.

Operational definition of terms

Preterm birth: refers to a delivery before 37 completed weeks of gestation; Preterm labor: occurs when painful uterine contractions are accompanied with or without cervical changes after 28 weeks of gestation, and before 37 weeks of gestation; Sensitivity: this is also called the true positive rate, which measures the proportion of actual positives that are correctly identified in the test; Specificity: in a test, this refers to the proportion of healthy patients who are known not to have the disease or condition, and tested negative; False positives: occurs when a test result incorrectly shows the presence of a condition, such as a disease (the result is positive), when in fact it is not; False positive: these refer to errors in data reporting; False negative: according to the National Institutes of Health, this test result claims that a person does not have an illness or condition, even though the person actually has.

Ethical considerations

The present study conformed to the ethics guidelines of the Helsinki Declaration (revised in 2013), and was approved by the NAUTH, Nnewi Ethics Committee (Approval number: NAUTH/CS/66/Vol.12/003/2019/003), and Chukwuemeka Odimegwu Ojukwu University Teaching Hospital, Awka Ethics Committee (Approval number: COOUTH/CMAC/ETH.C/Vol.1/0054). A written informed consent was obtained from all individual participants, and these participants provided consent for publication. The manufacturer of the product, Biosynex SA (France), provided all the neutrophil elastase antibody immunoassays used for the present study, free of charge.

Data analysis

The data was entered in a Microsoft Excel 2016 spreadsheet (Redmond, Washington, USA). Then, Epi Info 2008 version 3.5.1 (Centres for Disease Control and Prevention, Atlanta, GA, USA) was used for the analysis. Cross-tabulation was performed to further examine the results, and identify the intervariable statistical correlations. Continuous variables were analyzed using the student's test. Fisher's exact test was used to evaluate the difference in proportions and determine the statistical significance of the difference between groups for continuous variables. The statistics were considered to be significant when the p-value was <0.05. Compared to women without preterm labor, the baseline characteristics of women who experienced preterm labor, and tested positive or negative for neutrophil elastase were examined. According to the study conducted by Olusanya *et al*.,[25] the social class stratification was determined, as follows: Classes 1, 2, and 3 were considered as high social class, while classes 4 and 5 were considered as low social class. The test properties of the neutrophil elastase test (*e.g.,* sensitivity, specificity, PPV, NPV, and likelihood ratios) were determined using software (available at vassarstats.net/clin1.html).

Results

In the present study, a total of 193 subjects were evaluated for eligibility. Among these subjects, 174 subjects were recruited, while 19 subjects were excluded due to non-compliance with the inclusion criteria (n = 16) and declining to provide consent (n = 3). Preterm labor was identified in 87 (50.0%) of the enrolled subjects, while the 87 (50.0%) subjects who were not diagnosed with preterm labor were assigned to the control group. Due to the iatrogenic deliveries that occurred 14 days after enrollment, four subjects in the premature labor group and two subjects in the control group were further eliminated from the study.

Finally, a total of 168 subjects were examined (85 subjects in the control group and 83 subjects in the preterm labor group). Figure 1 presents the flow pattern. The demographic characteristics of these subjects were examined, and the difference was not statistically significant between the preterm labor group and the control group (Table 1). The mean maternal age, gestational age, frequency of nulliparity, and body mass index were similar between the two groups.

The sociodemographic details of the subjects in the present

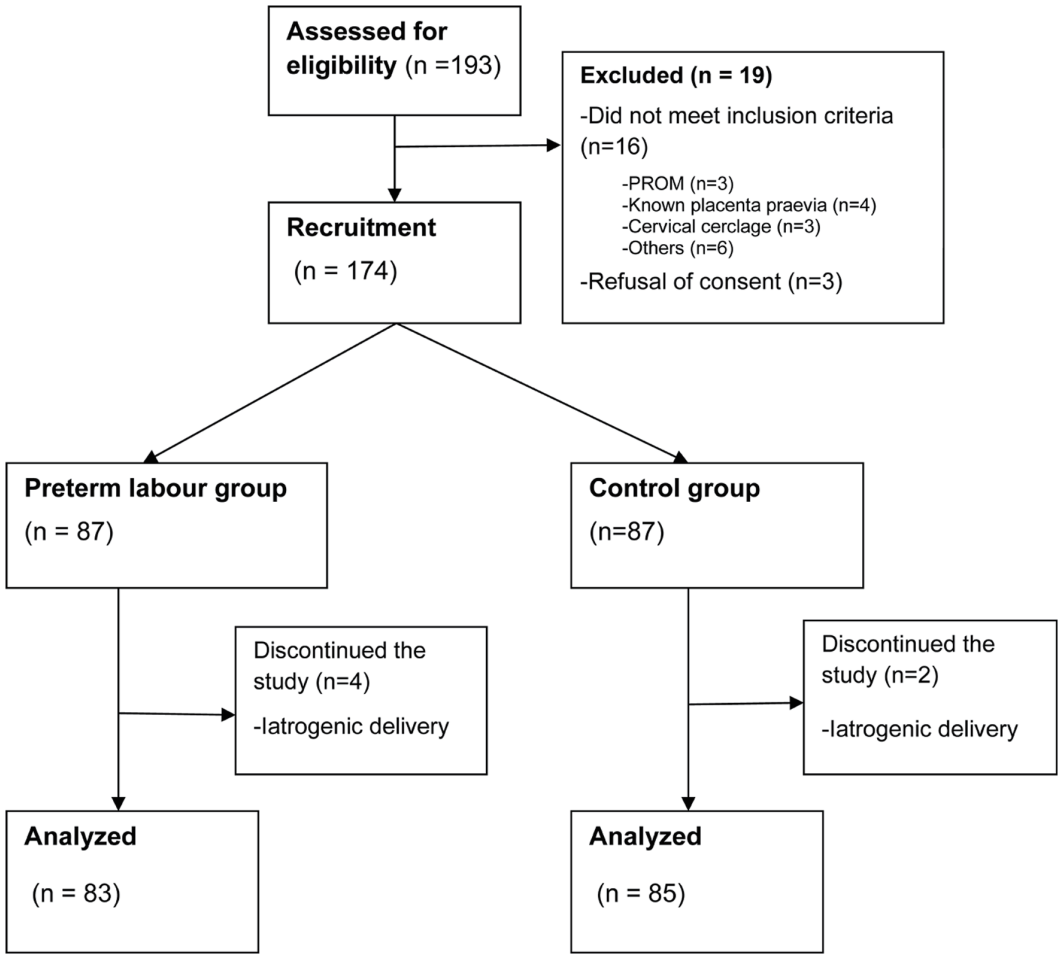

Fig. 1. Flowchart for the study participants.

study are presented in Table 1. For the preterm labor group and control group, the mean age was 29.9 ± 3.9 vs. 30.6 ± 5.5 years old, respectively. The socio-demographic profiles of the two groups were comparable, except for the socio-economic level and gestational age at delivery. Furthermore, 11 of the 83 pregnant women, who experienced preterm labor, spontaneously gave birth. Thus, the percentage of preterm laborers who spontaneously gave birth was 13.3%.

The neutrophil elastase test performance matrices for the general study participants (regardless of the gestational age) in predicting the delivery within 2, 7, and 14 days from enrollment are presented in Table 2. The neutrophil elastase test performance matrices for predicting delivery within two days are presented in Table 3.

Table 4 demonstrates how well neutrophil elastase predicts preterm birth in women who are in preterm labor, when compared to the controls, within 14 days from enrollment in the overall study. The neutrophil elastase test results revealed substantially better sensitivity values (93.8% vs. 50.0%, $p < 0.001$), but not the specificity values (61.2% vs. 57.5%, $p = 0.333$), in preterm labor cases, when compared to the controls.

The neutrophil elastase test performance matrices for predicting delivery within 2, 7, and 14 days from enrollment in women with preterm labor, who were enrolled at ≤35 weeks of gestation, are presented in Table 5. The performance matrices for the neutrophil elastase test in predicting pregnancy in women without preterm labor within 2, 7, and 14 days from enrollment are presented in Appendix 1.

Table 6 presents how well neutrophil elastase predicts premature birth within 14 days from enrollment in women who had preterm labor when compared to the controls, who were recruited at ≤35 weeks of pregnancy. For sensitivity (87.5% vs. 66.7%, $p < 0.001$), but not for specificity (66.7% vs. 60.0%, $p = 0.189$), the neutrophil elastase test results were considerably higher in preterm labor cases than in the controls. Table 7 presents the delivery outcomes for infants who were born at ≤35 weeks of gestation within 14 days from enrollment. The difference in newborn outcomes in both the preterm labor group and control group was not statistically significant ($p > 0.05$, for all cases).

Discussion

The present study evaluated the clinical value of a single bedside test kit for detecting neutrophil elastase to predict preterm birth. The present study revealed that the proportion of women with preterm labor, who progressed to spontaneous preterm birth, was 13.3% in the present study. The neutrophil elastase test exhibited the following predictive performance for sensitivity, specificity,

Table 1. Demographic variables for women with and without preterm labor

Variables/Subgroup	Preterm labor group (*n* = 83)	Control group (*n* = 85)	*p*-value
Mean age	29.9 ± 3.9 years old	30.6 ± 5.5 years old	0.344
Parity			
Nulliparous	40(48.2)	41 (48.2)	0.559
Parous	43 (51.8)	44 (51.8)	
Socio-economic class			
High	36 (50.0)	50 (58.8)	0.032*
Low	47 (50.0)	35 (41.2)	
History of preterm delivery			
Yes	7 (8.4)	3 (3.5)	0.155
No	76 (91.6)	82 (96.5)	
BMI (kg/m^2)			
<30	58 (69.9)	65 (76.5)	0.215
≥30	25 (30.1)	20 (23.5)	
Gestational age at delivery			
≥37 weeks	67 (80.7)	81 (95.3)	0.003*
<37 weeks	16 (19.3)	4 (4.7)	

BMI, body mass index.

PPV, NPV, and accuracy at 14 days post-enrolment: 93.8%, 61.2%, 36.6%, 97.6%, and 67.5%, respectively, for the general population; 87.5%, 66.7%, 35.0%, 96.3%, and 70.2%, respectively, for women recruited at <35 weeks gestation. The PPVs were poor (<37%) in both groups.

In perinatology practice, preterm birth continues to be the leading cause of morbidity and mortality, and its severe effects place an undeniable burden on society and families. In the present study, 13.3% of the subjects started preterm labor, and ultimately gave birth to a preterm baby on their own. This result is consistent with the result reported by Nakai et al., which revealed that 12% of women who experienced preterm labor prematurely gave birth before 34 weeks of gestation.[20] Furthermore, the outcome was consistent with the prevalence of 3.4% to 49.4% for preterm birth in sub-Saharan Africa.[26] This result was analogous to the results of a prior multi-center study conducted by Eleje *et al*. on preterm labor.[1] In a preceding study conducted by Tanaka *et al.*, 22.2% of women, who were assessed for preterm labor, prematurely gave birth before 34 weeks of gestation, despite the fact that the study population was on twin gestations.[21]

Table 2. Performance of the neutrophil elastase test in predicting preterm delivery in women with preterm labor within 2, 7, and 14 days post-enrollment

Test characteristics	Delivery within two days	Delivery within seven days	Delivery within 14 days
True Negative	42	41	41
True positive	10	12	15
False Negative	1	1	1
False positive	30	29	26
Total	83	83	83
Specificity (%)	58.3	58.6	61.2
Sensitivity (%)	90.9	92.3	93.8
NPV (%)	97.7	97.6	97.6
PPV (%)	25.0	29.3	36.6
Accuracy (%)	62.7	63.9	67.5
Positive likelihood ratio	2.18	2.23	2.42
Negative likelihood ratio	0.16	0.13	0.10

NPV, negative predictive value; PPV, positive predictive value.

Table 3. Performance of the neutrophil elastase test in predicting preterm delivery in women without preterm labor (control group) within 2, 7, and 14 days post-enrollment

Test characteristics	Delivery within two days	Delivery within seven days	Delivery within 14 days
True Negative	44	46	47
True Positive	1	1	2
False Negative	3	2	2
False Positive	37	36	34
Total	85	85	85
Specificity (%)	54.3	56.1	57.5
Sensitivity (%)	25.0	33.3	50.0
NPV (%)	93.6	95.8	95.9
PPV (%)	2.6	2.7	5.6
Accuracy (%)	52.9	55.3	57.6
Positive likelihood ratio	0.55	0.76	1.18
Negative likelihood ratio	1.38	1.19	0.87

NPV, negative predictive value; PPV, positive predictive value.

Table 4. Performance comparison of neutrophil elastase test characteristics for predicting preterm delivery between women with and without preterm labor within 14 days post-enrollment

Test characteristics	Preterm labor group	Without preterm labor group	OR (95% CI)	*p*-value
True negative	41	47	-	
True positive	15	2	-	
False negative	1	2	-	
False positive	26	34	-	
Total	83	85	-	-
Specificity (%)	61.2	57.5	1.18 (0.67–2.08)	0.333
Sensitivity (%)	93.8	50.0	15.67 (6.28–29.06)	<0.001

OR, odds ratio; 95% CI, confidence interval.

Table 5. Performance of the neutrophil elastase test in predicting preterm delivery in women with preterm labor (<35 weeks of gestation) within 2, 7, and 14 days post-enrollment

Test characteristics	Delivery within two days	Delivery within seven days	Delivery within 14 days
True negative	29	27	26
True positive	3	6	7
False negative	1	1	1
False positive	14	13	13
Total	47	47	47
Specificity (%)	67.4	67.5	66.7
Sensitivity (%)	75.0	85.7	87.5
NPV (%)	96.7	96.4	96.3
PPV (%)	17.6	31.6	35.0
Accuracy (%)	68.1	70.2	70.2
Positive likelihood ratio	2.30	2.64	2.62
Negative likelihood ratio	0.37	0.21	0.19

NPV, negative predictive value; PPV, positive predictive value.

Table 6. Performance comparison of neutrophil elastase test characteristics for predicting preterm delivery within 14 days between women with and without preterm labor (recruited at gestational age <35 weeks)

Test characteristics	Preterm labor group	Without Preterm labor group	OR (95% CI)	*p*-value
True negative	26	27	-	
True positive	7	2	-	
False negative	1	1	-	
False positive	13	18	-	
Total	47	48	-	-
Specificity (%)	66.7	60.0	1.35 (0.76–2.41)	0.189
Sensitivity (%)	87.5	66.7	3.61 (1.74–7.52)	<0.001

CI, confidence interval; OR, odds ratio.

In the present study, the neutrophil elastase test had a sensitivity, specificity, PPV, and NPV of 87.5%, 66.7%, 35.0%, and 96.3%, respectively, for preterm birth. Thus, the present study supports the findings reported by Nakai *et al.*,[20] which revealed a sensitivity, specificity, PPV, and NPV of 53%, 75%, 22%, and 92%, respectively, for premature delivery. However, the neutrophil elastase test, which is a stand-alone screening test for singleton pregnancies, is not supported by its weak positive predictive accuracy for premature birth. Furthermore, poor PPVs continue to be a problem in preterm labor prediction test kits in the market, including fetal fibronectin.

The neutrophil elastase test had strong NPVs (up to 96.3%) for predicting preterm birth, and the findings reported by Ai *et al.* further support this conclusion.[18] Furthermore, the neutrophil elastase test had a high NPV, which means that for pregnant women who exhibit symptoms and signs of premature labor, there is a low likelihood that preterm deliveries would occur. An infection that involves the cervix may predispose to local invasion, significant accumulation of inflammatory cells, and the discharge of inflammatory cytokines in response to inflammatory factors, which are followed by neutrophil activation and degranulation, and the release of neutrophil elastase.[27] Therefore, the absence of the inflammatory cytokines indicated above may ensure resistance to cervical alterations.

According to the findings, a positive likelihood ratio of 2.6 translates to a probability gain of >15%. As a result, a positive screen test would be insufficient to confirm the incidence of preterm delivery (PPV = 35%), due to the large number of false positives and small number of false negatives in the present study. Therefore, additional studies or interventions are required. The sensitivity allowed for its identification was 87.5% of all occurrences. As a predictor test, a negative result would be quite effective in assuring the patient that she would not ultimately prematurely give birth (NPV = 96.3%). The initial prediction identified 66.7% of patients who would not prematurely give birth (specificity).

In the present study, the therapeutic implications suggested that a persistently low level of neutrophil elastase may reduce the likelihood of premature birth. On the contrary, persistent positives may signal a higher likelihood of preterm birth. This would necessitate intensive treatment, such as the encouragement of fetal lung maturity, in order to improve the survival of preterm newborns. Preterm labor and birth present a significant concern, in terms of scope and severity. Preterm birth has been listed as one of the "top 10" research priorities for reduction by the World Health Organization by 2025.[11] In addition, the United Nations (UN) has positioned preterm labor research as essential to meet the proposed Sustaina-

Table 7. Delivery outcomes for babies delivered within 14 days from enrollment at <35 weeks of gestation

Variables/Subgroup	Preterm labor group (*n* = 11)	Control group (*n* = 3)	*p*-value
Birth weight			
<2.5 kg	8 (72.7)	2 (66.7)	1.000
≥2.5kg	3 (27.3)	1 (33.3)	
Apgar score			
<7	2 (18.2)	1 (58.8)	1.000
≥7	9 (81.8)	2 (66.7)	
Need for SCBU admission			
Yes	11 (100.0)	3 (100.0)	0.253
No	0 (0.0)	0 (0.0)	
Condition at discharge			
Alive	10 (90.9)	2 (66.7)	0.396
Dead	1 (9.1)	1 (33.3)	

SCBU, specialized care baby unit.

ble Development Goals by 2030, and decrease neonatal fatalities.[11] The majority of studies were conducted in high-income countries, while few studies have been conducted in Nigeria. Evidence has revealed that the incidence of preterm labor is globally rising.[1–7] This can be more keenly felt in this environment due to the lack of sophisticated equipment and technology for enhancing the survival of preterm babies. Therefore, there is a need to stem this tide.

To the best of our knowledge, the present study is the first study conducted in Nigeria that assesses the effectiveness of neutrophil elastase bedside tests for predicting preterm births in pregnant women. Most of the data were thoroughly analyzed 14 days after enrollment of the subjects, although the outcome of preterm delivery, which was not fully investigated, may have been of greater clinical importance. Furthermore, only the patients were blinded to the assessments, while the care providers were informed of the study. Therefore, the likelihood of bias might have increased in the present study. Moreover, multivariable regression was not conducted to determine the association of neutrophil elastase with preterm labor delivery. This would be conducted in future studies with larger sample sizes.

Future direction

The present long-term follow-up multisite longitudinal study would have a clear future direction for the novel research effort of the investigators. Although the present study was the first study conducted in Nigeria that compared neutrophil elastase for predicting delivery in women with or without preterm labor, according to the present literature, more similar studies must be conducted in other locations before a generalization can be made.

Conclusions

Compared to the controls, the neutrophil elastase test had strong predictive accuracy, in terms of sensitivity and NPV. Therefore, although the positive predictive accuracy was low for preterm delivery, the neutrophil elastase test appears to be a useful bedside tool, which can be employed as a screening test for predicting preterm births in women with premature labor. In regular clinical environments with preterm labor, the neutrophil elastase test may be used as a screening test, rather than as a potential predictive test, when available.

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Conflict of interest

The authors have no conflicts of interest to declare. Biosynex SA, which supported the study by supplying the neutrophil elastase tests, was not involved and did not participate in the study design, collection, and project development.

Author contributions

GUE: designed the study and carried out the procedures for the project, and wrote and revised the manuscript; UIN: supervised the overall conceptual design implementation of the project, and the revision of the manuscript; GUE, UIN, IUE, EOU, KEE, JII, ECE and ACE: wrote and revised the manuscript. The authors have read and approved the final manuscript and agreed to be accountable for all aspects of the work.

Ethical statement

The study conforms to the ethics guidelines of the Helsinki Declaration and was approved by the Nnamdi Azikiwe University Teaching Hospital, Nnewi Ethics Committee (Approval number: NAUTH/CS/66/Vol.12/003/2019/003), and the Chukwuemeka Odimegwu Ojukwu University Teaching Hospital, Awka Ethics Committee (Approval number: COOUTH/CMAC/ETH.C/Vol.1/0054). A written informed consent was obtained from all individual participants, and all participants provided consent for publication.

Data sharing statement

All relevant data are included in the manuscript and its supporting information files. The datasets used and/or analyzed in the study are available from the authors upon reasonable request.

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