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The evaluation of amnisure for the detection of premature rupture of membranes

Abstract

Objective: This study aims to evaluate the effectiveness of Amnisure test in detecting premature rupture of fetal membranes in comparison with other clinical methods.

Methods: A group of 154 pregnant ladies between 20-42weeks gestational age presented to our department with a history or a complain of PPROM. They underwent clinical examination (pooling from cervix, ferning test, nitrazine test, two out of three at least and ultrasound assessment for AFI) by the first examiner, after that patients were examined by Amnisure by a second examiner, all examiners were blinded to the results of each other. Sensitivity, specificity, negative and positive predictive values were all calculated.

Results: Sample size was 153patients, mean age was 26.6years (SD 6.8) and the mean gestational age was 35.6 week (SD4.7), of those patients 79 were less than 37 complete weeks (53%) and 70 were more than 37complete weeks (47%), 91patients had positive Amnisure test at 1st evaluation (60.7%), while patients with positive 1st clinical evaluation consists of 75(50%). Patients with the diagnosis of definite ROM made after delivery were 113 (75%). The sensitivity, specificity, positive and negative predictive values of the Amnisure test were found to be 93.6%, 75%, 80.2%, 91.5%, while they were 65.5%, 89.2%, 94.9% and 45.8% for clinical examination alone.

Conclusion: This study could support the evidence that Amnisure test performed to detect rupture of fetal membranes is an accurate, easy to perform and quick test.

Keywords: premature rupture of membranes, amnisure

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Abbreviations: PROM, premature rupture of membranes; PAMG, placental micro globulin; PPV, positive predictive value; NPV, negative predictive value; TP, true positives; FP, false positives; TN, true negatives; FN, false negatives

Introduction

Premature rupture of membranes (PROM) is defined as spontaneous rupture of the fetal membranes before the onset of uterine contraction and it consists for about 10%, while preterm PROM is defined as PROM before 37 weeks it is recorded in about 30% of women with PROM. The breakage of amniotic fluid is responsible for about 20-40% of preterm deliveries with its serious consequences such as cord prolapse and infectious morbidity (Chorioamnionitis, neonatal sepsis, neonatal pneumonia) and increased risk of neonatal death pulmonary hypoplasia of the fetus, development of fetal deformities, and postnatal endometritis, premature separation of placenta(abruption placenta).[1–3] It is very important to establish the diagnosis of PROM to avoid the unnecessary intervention in false positive results as the administration of antibiotics or corticosteroids or induction of labor, or not to have any delay in management in false negative patient.[4]

Disappointingly, the commonly used clinical methods for the diagnosis of PROM (pooling from the cervix, ferning test and nitrazine test) are unable to definitely establish the true diagnosis especially in cases of prolonged PROM with the sensitivity and specificity of the nitrazine test ranging from 90% to 97% and from 16% to 70%, respectively, it is designed to confirm only an alkaline PH in the cervicovaginal secretions and it is associated with high false-positive rates related to cervicitis, vaginit is, alkaline urine, and contamination with blood, semen, or antiseptic agent,[5–9] while the accuracy of The "fern test" (crystallization of amniotic fluid on drying) may give false-positive results due to fingerprints or contamination with semen and cervical mucus as well as false-negative results due to technical error (dry swab) or contamination with blood.[5–9] Reported sensitivity and specificity for the fern test were51% and 70%, respectively, in patients without labor and 98% and 88%, respectively, in patients in labor.[10] Further, clinical examination alone has a 12% false negative.[4,11] More recently, two commercial 'bedside' tests were developed, based on detecting high concentrations of amniotic fluid but not vaginal fluids.

Amnisure is an immunochromatographic assay measuring the placental alpha macroglobulin-1 (PAMG-1), while Actim PROM detects insulin-like growth factor-binding protein-1. Both of these bedside assays have been shown to have high sensitivity and specificity for the diagnosis of PROM and to be more accurate than clinical examination and nitrazine testing.[8,9,12,13] To establish the diagnosis two out of three tests should be positive, while it is confirmed with three positive results. When the diagnosis is still unclear, an invasive method maybe applied where amniocentesis is done and a dye (Evans Blue or Fluorescein) is injected and leakage from the cervix is visualized and assessed in 20-30 minutes. Although it is the most accurate diagnostic procedure with 100% accuracy rate but its limitations are the possibilities of infection, loss of pregnancy and induce PROM.[14] On the other hand, Alpha-fetoprotein, vaginal prolactin, fetal fibronectin, and Actim PROM are not answering questions such as the needed level of accuracy and needed noninvasiveness.[14]

Amnisure® is a test designed to detect ruptured fetal membranes by using monoclonal antibodies; it can detect even a miniscule

amount of Placental Micro globulin (PAMG -1), which is an amniotic fluid protein that has been found to be present in cervico-vaginal secretions after the breakage of fetal membranes. AmniSure is easy to use test. As it gives highly accurate results when the test is performed in clinics, exam rooms either in in-patient and outpatient basis or by the patient at home. In a study conducted in obstetric clinics of San Diego and Oakland CA, sensitivity and specificity of the Amnisure test were found to be 99% and 100%, respectively.[3,4,8,13]

The need of a diagnostic approach which meets conditions such as high accuracy, less time consuming, easy to obtain and use even as outpatient or at home, and costly effective has risen the hypothesis of our study to evaluate Amnisure as a first choice for diagnosing PPROM even in some cases with subclinical coarse.

Study design

A group of 154 pregnant ladies between 20-42weeks gestational age presented to our department with history or complain of PROM went through clinical examination (pooling from cervix, ferning test, nitrazine test, two out of three at least and ultrasound assessment for AFI) by the first examiner. After that patients were examined by Amnisure as written in the leaflet by a second examiner. All examiners were blinded to the results of each other (double blind study). Patients with discrepant results were reevaluated (if negative clinical evaluation and positive Amnisure results and vice versa), and followed up till delivery for confirmation of diagnosis. The sensitivity, specificity, negative and positive predictive values were calculated for the Amnisure and for the other clinical examination methods. Women with obvious vaginal bleeding were excluded from our study because of the defect in Amnisure to establish the diagnosis in such cases. A verbal consent to participate in our study was obtained. This study was approved by the ethical committee of Jordanian Ministry of Health and by Al-Bashir hospital ethical committee. The filled questionnaire sheet was stored in place where only people with scientific reason have access to it.

Study finance

The company producing Amnisure provided kits for the study; other clinical examinations were part of our routine evaluation of patients in examination rooms.

Statistical analysis

Data were entered and analyzed using the Statistical package for Social Science (SPSS version 17). The sensitivity, specificity, positive and negative predictive values for both Amnisure test and clinical examination were then calculated separately. A comparison was done of the results of Amnisure examination if rupture of membranes had occurred within 12 or more than 12hours, and if the test was accompanied with clinical examination or not. P-value<0.05 was considered statistically significant.

Results

Of the 153patients who were examined the mean age was 26.6years (17-43yy, SD 6.8) and the mean gestational age was 35.6weeks (20-41ww, SD4.7). Seventy nine patients were less than 37 gestational weeks (53%) and 70 were more than 37complete gestational weeks (47%). Ninety-one patients had positive Amnisure test at 1st evaluation (60.7%), while only 75 patients (50%) had positive 1st clinical evaluation. The definite diagnosis of ROM was made after delivery. Those who had definite ROM were 113patients (75%). Three patients dropped out of the study because no follow up data were available at the time of analyses. As shown in Tables 1-3 The sensitivity, specificity, positive and negative predictive values of the Amnisure test were found to be 93.6%, 75.0%, 80.2%, 91.5%, while they were 65.5%, 89.2%, 94.9% and 45.8% for clinical examination alone.

Tables 4-6 show results of Amnisure test and clinical examination results of patients who were tested before or after 12hours since the onset of PROM. The results were as follows 94.8%, 69%, 86% and 87% for patients who had ROM before 12hours and 90%, 79.1%, 66.7% and 94.4% for those who were tested 12hours after the onset of ROM. Table 7 shows the results of discrepant cases (23 cases); those with positive clinical examination and negative Amnisure test and vice versa.

Table 1 Summary of patients tested with amnisure and clinical methods

		Uncorrected clinical test results			Corrected clinical test results		
		+	-	Total	+	-	Total
Amnisure test results	+	70	21	91	73	18	91
	-	5	54	59	5	54	59
	Total	75	75	150	78	72	150

Table 2 Summary of patients tested with clinical examination alone

		Uncorrected final diagnosis			Corrected final diagnosis		
		ROM	Intact	Total	ROM	Intact	Total
Clinical examination results	+	71	4	75	74	4	78
	-	42	33	75	39	33	72
	Total	113	37	150	113	37	150

Citation: Kan'an A, Emar D, Liswi M, et al. The evaluation of amnisure for the detection of premature rupture of membranes. *MOJ Womens Health.* 2015;1(1):7–10. DOI: 10.15406/mojwh.2015.01.00003

Table 3 Performance metrics

Test type		**Amnisure**		**Clinical examination**	
Metric		**Derivation (All Data)**	**Value**	**Derivation (All Data)**	**Value**
Sensitivity	TP/(TP+FN)	73/78	93.6%	74/113	65.5%
Specificity	TN/(TN+FP)	54/72z	75.0%	33/37	89.2%
PPV	TP/(TP+FP)	73/91	80.2%	74/78	94.9%
NPV	TN/(TN+FN)	54/59	91.5%	33/72	45.8%

PPV, positive predictive value; NPV, negative predictive value; TP, true positives; FP, false positives; T, true negatives; FN, false negatives.

Table 4 Results of patients who were tested within less than 12 hours of the onset of PROM symptoms.

	Uncorrected clinical test results				**Corrected clinical test results**		
		+	-	Total	+	-	Total
Amnisure test results	+	53	11	64	55	9	64
	-	3	20	23	3	20	23
	Total	56	31	87	58	29	87

Table 5 Results of patients who were tested after 12 hours of the onset of PROM symptoms

	Uncorrected clinical test results				**Corrected clinical test results**		
		+	-	Total	+	-	Total
Amnisure test results	+	17	10	27	18	9	27
	-	2	34	36	2	34	36
	Total	19	44	63	20	43	63

Table 6 AmniSure performance metrics for patients with symptoms of PROM

Duration		**Less than 12 hours**		**More than 12 hours**	
Metric		**Derivation (all data)**	**Value**	**Derivation (all data)**	**Value**
Sensitivity	TP/(TP+FN)	55/58	94.80%	18/20	90.00%
Specificity	TN/(TN+FP)	20/29	69.00%	34/43	79.10%
PPV	TP/(TP+FP)	55/64	86.00%	18/27	66.70%
NPV	TN/(TN+FN)	20/23	87.00%	34/36	94.40%

Table 7 Discrepant cases after 2nd examination (n=23)

		Final Diagnosis	
		Intact	**ROM**
Amnisure	Negative	1	4
	Positive	0	18
Clinical examination	Negative	0	18
	Positive	1	4

Citation: Kan'an A, Emar D, Liswi M, et al. The evaluation of amnisure for the detection of premature rupture of membranes. *MOJ Womens Health.* 2015;1(1):7–10. DOI: 10.15406/mojwh.2015.01.00003

Discussion

This study was the first study to detect the effectiveness of Amnisure test in a developing country. It included pregnant women from several age groups on both second and third trimesters. To the best of our knowledge this was the first study to compare the accuracy of Amnisure test between patients who had ROM symptoms for less than 12 hours and those who had the symptoms for more than or equal to 12hours. Eighteen cases with negative clinical examination were found to have PROM (Amnisure positive). While in Amnisure there was only 4cases (clinically positive). Some researchers could link such results to the ability of the test to detect very small amounts of the placental microglobulin-1 in vaginal secretion. And the only case evaluated by Amnisure as negative and clinically as positive was finally diagnosed as having intact membranes, which gives an advantage to the Amnisure test again (Table 7).

In Cousins et al.,[13] found that the sensitivity and specificity of Amnisure test was 98.9% and 100%, respectively, while in this study the sensitivity was 93.6% and the specificity was 75.0%. The difference between these results could be explained by the difference in ethnic groups. In addition, maybe Cousins et al.[13] study had higher sensitivity and specificity percentages because they based their gold standard test simply on reviewing obstetric reports of one clinical assessment at the time of participants' evaluation.[13]

Moreover, Lee et al.[8] obtained relatively similar sensitivity and specificity results in comparison with this study results (98.7% and 87.5% vs 93.6% and 75.0%).[8] In regard to the positive and negative predictive values of Amnisure test, our study results were lower than Birkenmaier et al.[3] results (80.2% and 91.5% vs 92.9% and 90.6%). This is again could be explained by differences in ethnic groups between the two studies and maybe when Birkenmaier et al.,[3] excluded women with some types of pregnancy complication this lead to achieving better positive and negative predictive values.[3]

These are some of the strength and weakness points of the study

Strength points: According to our knowledge it was the first study to compare Amnisure effectiveness in a Middle Eastern country, and this study was done in real medical practice situation.

Weakness points: It was a convenient sample so selection bias cannot be avoided, and the Amnisure test cannot be used when there is active vaginal bleeding.

Conclusion

More clinical studies are needed to evaluate the accuracy of Amnisure test but this study could support the evidence that Amnisure test performed to detect rupture of fetal membranes is an accurate, easy to perform and quick test.

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None.

Conflict of interest

The author declares no conflict of interest.

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