Comparison of eight commercial PROM tests: ACTIM® PROM IS THE ONLY TEST NOT REPORTING PROM FALSE POSITIVES FOR MATERNAL SERA, AND NOT EXHIBITING HOOK EFFECT

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- The rate of false positive reporting of premature rupture of fetal membranes (PROM) was evaluated for eight commercial PROM tests.
- Actim® PROM (Medix Biochemica) was the only test not reporting PROM false positives for two maternal sera, and not exhibiting the hook effect in presence of high IGFBP-1 concentrations.
- Actim® PROM recognized purified human IGFBP-1 at very high concentrations of up to 500,000 µg/L.

Background

Premature rupture of fetal membranes (PROM) is a serious complication occurring in approximately 10% of pregnancies[1]. Pre-term PROM (<37 weeks' gestation) is associated with an elevated risk of chorioamnionitis, leading to increased maternal and perinatal mortality and morbidity[2]. Pre-term PROM is associated with approximately a third of all premature births[3].

Dipstick tests are a quick, reliable and non-invasive method of detecting PROM from vaginal fluid[4] (Figure 1). The majority of diagnostic PROM tests detect insulin-like growth factor binding protein-1 (IGFBP-1) present in vaginal amniotic fluid. Amniotic fluid contains both non- and less phosphorylated isoforms of IGFBP-1, whereas highly phosphorylated (phIGFBP-1) and less phosphorylated isoforms dominate in maternal serum[5]. The concentration of IGFBP-1 is 100–1,000-fold higher in amniotic fluid than in serum[6,7].

Distinction between the amniotic fluid and maternal serum IGFBP-1 isoforms is crucial, since up to 20% of women with suspected PROM have vaginal bleeding[8]. Accordingly, PROM test validation studies that have excluded from the study population women with bleeding may not accurately demonstrate test performance in a clinical setting[9].

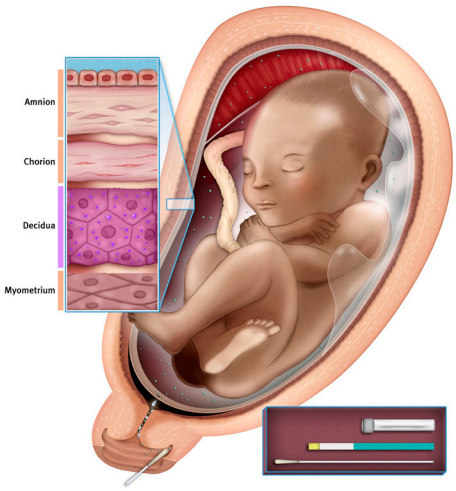


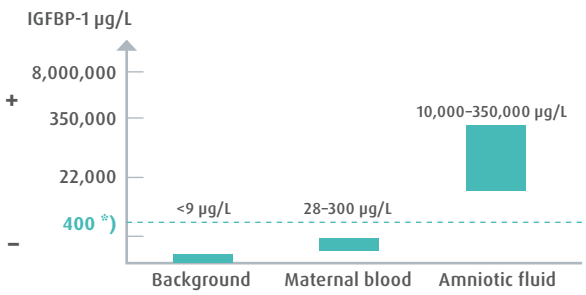
FIGURE 1. Rapid PROM dipstick tests detect premature rupture of fetal membranes (PROM) from amniotic fluid in the vagina.

Actim® PROM

Actim® PROM is a qualitative immunochromatographic dipstick test with monoclonal antibodies specific for the amniotic isoforms of IGFBP-1. Therefore, the test is not affected by the presence of maternal blood in the specimen[4,6,8,10].

Actim® PROM has a wide detection range for IGFBP-1 (400–8,000,000 µg/L in the original sample), covering all clinically relevant concentrations from the smallest membrane microruptures to larger volumes of amniotic fluid (Figure 2).

The lower cut-off limit of Actim® PROM has been set to exclude IGFBP-1 concentrations commonly found in maternal blood[11], which further increases the specificity of Actim® PROM for amniotic IGFBP-1.



* The Actim® PROM test has an IGFBP-1 measurement range of 400–8,000,000 µg/L. 400 µg/L corresponds to 25 µg/L in extracted sample.

FIGURE 2. Actim® PROM's detection range covers all clinically relevant concentrations of IGFBP-1 in vaginal amniotic fluid.

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Materials and methods

This study evaluated the rate of false positive PROM reporting for eight commercially available rapid immunochromatographic PROM dipstick tests.

All tests were performed according to manufacturers' instructions on two maternal sera with IGFBP-1 concentrations of (A) 6.1 µg/L and (B) 6.4 µg/L in sample buffer. Sample buffer was used as a negative control and purified human IGFBP-1 (25 µg/L) as a positive control. Additionally, three of the tests were evaluated for the hook effect on ascending concentrations of purified human IGFBP-1 (200–77,000 µg/L).

Results

Actim® PROM (Medix Biochemica) and IGFBP-1 Qualitative Test Kit (Komdary/Tianjin Xinwan Jiezhun) were the only two tests that did not report either maternal sera as false positives for PROM (Table 1). IGFBP-1 Detection Kit and IGFBP-1 / fFN Combo test (BioHermes), IGFBP-1 (ZyBio) and Amnioquick Rapid PROM Test (Biosynex) reported serum A as PROM-positive, while AmniSure ROM test (Qiagen), IGFBP-1 test kit (Anhui Deep Blue Medical Technology) and Amnioquick Rapid PROM Test (Biosynex) reported serum B as PROM-positive. All tests reported negative and positive controls accurately (data not shown).

Actim® PROM retained its ability to recognize purified human IGFBP-1 in a remarkably wide concentration range of 12.5–500,000 µg/L (data not shown). On the contrary, IGFBP-1 test kit (Anhui Deep Blue Medical Technology) and IGFBP-1 Qualitative test Kit (Komdary/Tianjin Xinwan Jiezhun) exhibited a notable hook effect – a decrease in IGFBP-1 detection for high IGFBP-1 concentrations (Table 1).

FIGURE 3. An example of a vaginal swab sample and a diluted specimen from a pregnant woman with bleeding.

TABLE 1. Premature rupture of fetal membranes (PROM) reporting for eight commercial PROM tests on two maternal sera (A and B). Hook effect was assessed on ascending concentrations of purified human insulin-like growth factor binding protein-1 (IGFBP-1).

		SERUM		IGFBP-1 (µg/L)			
PROM TEST	MANUFACTURER	A	B	200	1,000	7,700	77,000
Actim® PROM	Medix Biochemica	–	–	+	+	+	+
AmniSure ROM Test*	Qiagen	ND	+	ND	ND	ND	ND
IGFBP-1 Detection Kit	BioHermes	+	ND	ND	ND	ND	ND
IGFBP-1 / fFN Combo test	BioHermes	+	ND	ND	ND	ND	ND
IGFBP-1	Zybio	+	ND	ND	ND	ND	ND
IGFBP-1 test kit	Anhui Deep Blue Medical Technology	–	+	+	+	+	–
Amnioquick Rapid PROM Test	Biosynex	+	+	ND	ND	ND	ND
IGFBP-1 Qualitative Test Kit	Komdary/Tianjin Xinwan Jiezhun	–	–	+	+	+	–

A Maternal serum specimen (IGFBP–1 6.1 µg/L)
B Maternal serum specimen (IGFBP–1 6.4 µg/L)
+ Positive
– Negative
ND Not determined
***** Detects placental α-microglobulin-1 (PAMG-1).

Conclusions

In this study, Actim® PROM outperformed seven other commercial PROM tests and exhibited a remarkably wide detection range.

Actim® PROM was the only PROM test not reporting PROM false positives for maternal sera, and not exhibiting a hook effect at high concentrations of purified human IGFBP-1.

The data demonstrates that Actim® PROM is an exceptionally specific test for the detection of IGFBP-1 – even in the presence of maternal sera – and aids in the rapid and accurate care of pregnant women experiencing PROM.

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