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iGFBP-1 Rapid Test Cassette (Vaginal Secretion): Performance Characteristics and Clinical Application in Detecting Rupture of Fetal Membranes

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Abstract: The iGFBP-1 Rapid Test Cassette (Vaginal Secretion) is a visually interpreted, qualitative immunochromatographic assay designed for the detection of insulin-like growth factor-binding protein 1 (iGFBP-1) in vaginal secretions of pregnant women. As a major protein marker of amniotic fluid, iGFBP-1 serves as an indicator for the diagnosis of rupture of fetal membranes (ROM). This study aims to do clinical studies of iGFBP-1 Rapid Test Cassette (Vaginal secretion) with the iGFBP-1 positive specimens and negative specimens which confirmed with other Rapid Test. A total of 230 vaginal swab specimens (100 iGFBP-1 positive and 130 iGFBP-1 negative, confirmed by another commercial iGFBP-1 rapid test) were analyzed. The results demonstrated high relative sensitivity (98.0%, 95%CI: 93.0%-99.8%), relative specificity (97.7%, 95%CI: 93.4%-99.5%) and overall accuracy (97.8%, 95%CI: 95.0%-99.3%). Intra-assay and inter-assay precision were excellent, with >99% correct identification of specimens across three lots. No cross-reactivity was observed with common vaginal microorganisms and no interference was detected from substances such as globulin, hemoglobin or bilirubin at clinically relevant concentrations. These findings indicate that the iGFBP-1 Rapid Test Cassette is a reliable, rapid, and practical tool for the qualitative detection of iGFBP-1 in vaginal secretions, aiding in the timely diagnosis of ROM and supporting clinical decision-making in obstetric care.

1. Introduction

Rupture of fetal membranes (ROM), characterized by the spontaneous rupture of the amniotic sac prior to the onset of labor, occurs in approximately 8-10% of all pregnancies[1]. This condition is linked to considerable maternal and fetal complications, including chorioamnionitis, preterm birth, neonatal sepsis and umbilical cord prolapse, which can significantly impact perinatal health[2]. Consequently, prompt and precise diagnosis of ROM is critical for optimizing obstetric management strategies and enhancing overall perinatal outcomes[3]. Traditional diagnostic approaches, such as clinical examination (e.g., observing pooled amniotic fluid in the vagina),

nitrazine testing (based on pH detection) and fern testing (microscopic observation of amniotic fluid crystallization), have notable limitations: nitrazine tests may produce false positives due to the presence of blood, semen, or vaginal infections, while fern tests require specialized technical expertise and are prone to subjectivity[4].

Insulin-like growth factor-binding protein 1 (iGFBP-1), primarily synthesized by the fetal membranes and decidua, exhibits a significantly higher concentration in amniotic fluid compared to maternal serum or vaginal secretions[5]. This distinct distribution makes it a specific marker for identifying amniotic fluid leakage into the vaginal tract[6]. Clinical studies have demonstrated that detecting iGFBP-1 in vaginal secretions shows a stronger correlation with ROM than traditional diagnostic methods[7]. The iGFBP-1 Rapid Test Cassette, a qualitative immunochromatographic assay designed for vaginal swab specimens, provides results within 5 minutes, making it well-suited for point-of-care settings like obstetric clinics and labor wards, in contrast to time-consuming quantitative methods such as enzyme-linked immunosorbent assay (ELISA)[8].

This study aims to evaluate the diagnostic performance of the iGFBP-1 Rapid Test Cassette using clinical specimens, with a commercial iGFBP-1 rapid test serving as the reference method. Key performance characteristics, including relative sensitivity, specificity, accuracy, precision, cross-reactivity and resistance to interfering substances, will be assessed to provide robust evidence supporting its clinical application in the diagnosis of ROM.

2. Materials and Methods

2.1 Specimen Collection

A total of 230 vaginal swab specimens were collected from pregnant women with suspected ROM across multiple obstetric clinics in China. All specimens were confirmed using a commercial iGFBP-1 rapid test (reference method) and clinical symptoms (e.g., vaginal fluid leakage, ultrasound evidence of oligohydramnios). The cohort included 100 iGFBP-1 positive specimens and 130 iGFBP-1 negative specimens.

Specimens were collected using sterile polyester swabs from the posterior fornix of the vagina during a sterile speculum examination; if no vaginal fluid was visible, specimens were taken from the cervix. Swabs were handled aseptically to avoid contamination, with no contact with non-vaginal surfaces before sampling. Each swab was left in the vagina or cervix for 10-15 seconds to absorb sufficient secretion [9].

Specimens were processed immediately after collection. For delayed testing, specimens were stored at 2-8 ℃ for up to 72 hours; if testing was delayed beyond 72 hours, specimens were frozen at -20 ℃ or below. Thawed specimens were equilibrated to room temperature (15-30 ℃) before testing. All specimen handling and transportation complied with regulations for etiological agents [10].

2.2 Test Kit and Procedure

This study used iGFBP-1 Rapid Test Cassettes from Hangzhou AllTest Biotech Co., Ltd., including cassettes (with anti-iGFBP-1 antibodies immobilized in T and C regions), sterile polyester swabs, extraction solution tubes and instructions (timer and gloves required separately). The reference method was a clinically validated commercial iGFBP-1 rapid test. Based on the double-antibody sandwich immunochromatographic principle, the cassette's specimen pad has colloidal gold-conjugated anti-iGFBP-1 monoclonal antibodies. Specimens react with these to form complexes, which migrate via capillary action. A visible T band (positive) appears if iGFBP-1 ≥25 ng/mL; the C band always appears (valid test). A T-negative/C-positive result is negative; no C band

means invalid retesting.

Tests followed the manual: equilibrate to 15-30 ℃, rotate swabs in extraction solution 20 times (then discard), add 3 drops to the cassette, read results at 5 minutes (invalid after 20 minutes). Performance evaluation included: sensitivity, specificity, and accuracy (with 95% CIs via Clopper-Pearson method, using the reference as gold standard); intra-assay (3 concentrations, 10 replicates/run, 3 runs, 3 lots) and inter-assay (3 assays, 3 lots) precision; cross-reactivity with 11 bacteria, 1 fungus and 1 parasite (no false T bands = non-reactive); interference testing with 6 substances (e.g., globulin, hemoglobin) at clinical concentrations.

3. Results and Discussion

3.1 Results

3.1.1 Sensitivity, Specificity, and Accuracy

A total of 230 specimens (100 positive, 130 negative by the reference method) were tested with the iGFBP-1 Rapid Test Cassette. The results are summarized in Table 1.

Table 1: Clinical Study Results (Comparison with Reference Rapid Test)

iGFBP-1 Rapid Test Cassette	Reference Method		Total
	Positive	Negative	
Positive	98 (True Positives)	3 (False Positives)	101
Negative	2 (False Negatives)	127 (True Negatives)	129
Total	100	130	230

Relative sensitivity: 98.0% (95%CI: 93.0%-99.8%)

Relative specificity: 97.7% (95%CI: 93.4%-99.5%)

Overall accuracy: 97.8% (95%CI: 95.0%-99.3%)

These results indicate strong agreement between the iGFBP-1 Rapid Test Cassette and the reference method. The high relative sensitivity (98.0%) suggests that the test effectively identifies true positive cases of ROM, minimizing false negatives that could delay intervention. The high specificity (97.7%) reduces the risk of false positives, which might lead to unnecessary medical procedures (e.g., induction of labor).

The accuracy of 97.8% is comparable to or exceeds that of other commercial iGFBP-1 tests. For example, Rutanen et al. (1993) reported a sensitivity of 95% and specificity of 97% for an iGFBP-1 immunoassay, while our study shows slightly improved performance, likely due to advancements in immunochromatographic technology.

3.1.2 Precision

Intra-assay and inter-assay precision results are shown in Table 2.

Table 2: Precision of the iGFBP-1 Rapid Test Cassette.

iGFBP-1 Concentration	Intra-Assay (3 lots, 10 replicates/run, 3 runs)	Inter-Assay (3 lots, 3 independent assays)
0 ng/mL (Negative)	100% correct identification	100% correct identification
25 ng/mL (Positive)	99.3% correct identification	99.0% correct identification
50 ng/mL (Positive)	100% correct identification	100% correct identification

Table 2 shows the precision of the iGFBP-1 Rapid Test Cassette: for intra-assay precision (3 lots, 10 replicates per run across 3 runs) and inter-assay precision (3 lots, 3 independent assays), the

correct identification rates were 100% for 0 ng/mL (negative) and 50 ng/mL (positive) in both, 99.3% for 25 ng/mL (positive) in intra-assay and 99.0% for 25 ng/mL in inter-assay. Across all concentrations, the test achieved >99% correct identification, indicating excellent precision, which is critical for clinical reliability as it ensures consistent results in repeated tests on the same specimen or those with similar iGFBP-1 levels.

3.1.3 Cross-reactivity and Interference

None of the tested microorganisms (e.g., Candida albicans, Chlamydia trachomatis, Group B Streptococcus) caused false positive results. This indicates that the test specifically detects iGFBP-1 without cross-reacting with common vaginal pathogens, reducing the risk of misdiagnosis in women with vaginal infections.

No interference was observed with globulin, hemoglobin, bilirubin, uric acid, mucoprotein or human serum albumin at the tested concentrations. This is particularly important because vaginal secretions often contain mucin or trace blood (e.g., from cervical irritation), which could potentially affect test performance. The lack of interference supports the test's robustness in clinical settings.

3.2 Discussion

3.2.1 Performance Characteristics

The iGFBP-1 Rapid Test Cassette (Vaginal Secretion) demonstrated high relative sensitivity, specificity and accuracy for the detection of iGFBP-1 in vaginal secretions, with performance metrics comparable to other commercial iGFBP-1 rapid tests. It has a defined detection threshold of 25 ng/mL, which aligns with the concentration of iGFBP-1 in amniotic fluid, making it clinically relevant for identifying rupture of fetal membranes (ROM). The relative sensitivity was 98.1% and relative specificity was 98.0% , with an overall accuracy of 98.0% , confirming its reliability in distinguishing ROM cases.

A clinical study with 230 specimens (100 iGFBP-1 positive and 130 iGFBP-1 negative, confirmed by another rapid test) further validated its performance. The test showed a relative sensitivity of 98.0%, relative specificity of 97.7% and overall accuracy of 97.8%. These results indicate a low rate of false negatives and false positives, which is critical for avoiding missed ROM diagnosis or unnecessary clinical interventions, both of which pose risks in obstetric care.

Notably, the test exhibits no cross-reactivity with common vaginal microorganisms, including M.urealyticum, Candida albicans, Chlamydia trachomatis and Group B Streptococcus, at concentrations up to 1.0×10^9 organisms/mL. It also supports flexible specimen handling: extracted specimens can be tested within 4 hours, stored at 2-8 ℃ for up to 72 hours or frozen and thawed for later testing, enhancing its practicality in diverse clinical settings.

3.2.2 Limitations

Despite its strong performance, the test has limitations: it is qualitative and cannot quantify iGFBP-1 levels, thus failing to differentiate between mild and severe membrane rupture; its results depend on specimen quality, with inadequate collection (e.g., insufficient secretion) or improper storage (e.g., prolonged room temperature exposure) potentially causing false results; it should not be used within 72 hours of vaginal treatments (e.g., antifungal agents) as these may interfere with antigen-antibody binding ; excessive blood in specimens (e.g., from placental abruption) may lead to false positives, requiring correlation with clinical findings and like all diagnostic tests, its results must be interpreted alongside clinical symptoms (e.g., fluid leakage) and other findings (e.g., ultrasound) to confirm ROM.

3.2.3 Comparison with Other Markers

Fetal fibronectin (fFN) is another marker used for ROM and preterm birth prediction. However, fFN is more commonly associated with preterm labor risk rather than acute ROM and its detection window is narrower (up to 24 hours post-ROM). In contrast, iGFBP-1 remains detectable in vaginal secretions for longer periods after ROM, making it more reliable for delayed presentation. Additionally, iGFBP-1 testing is less affected by cervical manipulation (e.g., during speculum examination) compared to fFN, which can be falsely elevated by such procedures.

4. Conclusion

The iGFBP-1 Rapid Test Cassette (Vaginal Secretion) is a reliable and practical tool for the qualitative detection of iGFBP-1 in vaginal secretions, with high relative sensitivity (98.0%), specificity (97.7%) and accuracy (97.8%). Its excellent precision, lack of cross-reactivity with common vaginal microorganisms, and resistance to interfering substances further validate its clinical utility.

This test addresses the need for rapid, point-of-care diagnosis of ROM, particularly in settings where advanced laboratory facilities are unavailable. By enabling timely identification of ROM, it supports informed obstetric management, reducing maternal and fetal complications.

Future studies should evaluate its performance in larger, diverse populations (e.g., preterm vs. term pregnancies) and compare it directly with other diagnostic methods (e.g., ultrasound) to further establish its role in clinical practice.

Overall, the iGFBP-1 Rapid Test Cassette represents a valuable advancement in obstetric diagnostics, contributing to improved perinatal care.

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