POSITIVE PREDICTIVE VALUE OF ENDOMETRIAL BCL6 OVEREXPRESSION IN PATIENTS WITH PATHOLOGY-CONFIRMED ENDOMETRIOSIS.

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BACKGROUND: Endometriosis affects approximately 10% of reproductive age women[1,2]. It is implicated as a leading cause of unexplained infertility but remains underdiagnosed in this setting[2]. ReceptivaDx™ detects endometrial BCL6 overexpression in asymptomatic women, indicating an in-flammatory process most likely caused by undiagnosed endometriosis. A positive test has been associated with progesterone resistance, implantation failure, poor IVF outcomes, and recurrent miscarriage[2]. By treating the cause of endometrial inflammation, studies have shown improvement in subsequent pregnancy rates[2,3].

OBJECTIVE: To evaluate the positive predictive value (PPV) of the ReceptivaDx™ test in a cohort of women with unexplained infertility, and
pregnancy outcomes following surgical management of endometriosis.

MATERIALS & METHODS: Clinical data were obtained from women with unexplained infertility who presented to our institution after a positive ReceptivaDx™ test. Only women who underwent surgery for confirmation of endometriosis were included. Statistical analysis was performed using Microsoft® Excel.

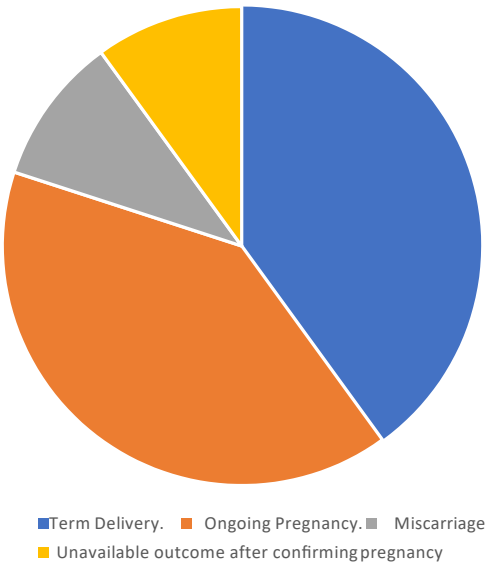
Table 1. Characteristics of Endometrial BCL6-positive Patients

ReceptivaDx™ positive N =62

Age (years)	Average ¼ 37.32	Nulliparous	49/ 79.03%
	SD ¼ 4.1 [31-47]	Parous	13/ 20.97% [0-2]
		Parity	
BMI (Kg/m^2)	Average ¼ 23.15	Infertility (years)	Average TTC = 2.34
	SD ¼ 3.55 [17-29]		SD = 1.61 [0-10]
Overall pain symptoms	N ¼ 46/74.19%	Only IUI	N=9/ 14.52% / [0-13]
Urinary symptoms	Dysmenorrhea N ¼ 36/58.06%	Only IVF	N=18/ 29.03% / [0-5]
GI Symptoms	NMPP n ¼ 30/48.39%	None	N=20 / 32.26%
	N ¼ 7/11.29%	Both	N=14 / 22.58%
	N ¼ 31/50.00%		
Asymptomatic	N ¼ 7/11.29%		
PPV for ReceptivaDx(TM)	82.26%	PPV for symptoms	81.81%

NMPP ¼ Non-menstrual Pelvic Pain, IUI ¼ Intrauterine insemination, SD ¼ Standard Deviation, GI - Gastrointestinal symptoms, IVF ¼ In vitro fertilization, TTC ¼ Trying to conceive

Table 2. Pregnancy Outcomes



RESULTS: We included a total of 62 women, with an average age of 37.3 4.1 years (Table 1). Most (79.0%) were nulliparous, and average time trying to conceive was 2.3 1.6 years. Fifty-one patients had pathology consistent with endometriosis, resulting in a PPV of the ReceptivaDx™ test of 82.3%. Of the remaining 11 patients, 9 had fibrosis or fibrous adhesions on pathology. Interestingly, 88.7% of women previously thought to be asymptomatic had at least mild symptoms consistent with endometriosis, whether dysmenorrhea (58.1%), non-menstrual pelvic pain (48.4%), gastrointestinal (50.0%) or urinary symptoms (11.3%). Only 7 patients (11.3%) were truly asymptomatic. Presence of any symptom consistent with endometriosis had a PPV of 81.8%. Average post-operative follow-up was 5.8 4.2 months [0-21]. To assess reproductive outcomes, we selected women with a post-operative period of at least four months (n 45). A clinical pregnancy was confirmed in 10 women (22.2%), all of whom had pathology-proven endometriosis. All the women conceived within 1 year of surgery. All pregnancies were conceived through IVF; half of these women (50.0%) had not under- gone previous ART. Of the women with known outcomes, 1 had a miscarriage, 4 have ongoing pregnancies and 4 had live-births (Table 2).

CONCLUSIONS: The PPV of the ReceptivaDx™ test was 82.3% in this study. Interestingly, PPV for the presence of symptoms (81.8%) was similar in predicting endometriosis. These findings suggest endometriosis may be underdiagnosed in women with mild symptoms, in particular in those with unexplained infertility. Although PPV was lower than previously described for ReceptivaDx™, previous studies had only considered visual diagnosis and not pathology-confirmed disease[1]. Furthermore, some ovarian lesions consistent with endometriosis were deliberately not biopsied to preserve ovarian function. Most (81.8%) women who had negative pathology for endometriosis had pathologic specimens consistent with fibrosis or fibrous adhesions, possibly associated with other undiagnosed inflammatory processes leading to positive BCL6 testing. Our results highlight the potential role of ReceptivaDx™ testing in unexplained infertility, as well as the importance of recognizing endometriosis symptoms prior to ART cycles.

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