Hyaluronan Binding Assay (HBA®) and Maternal Age Serve as Positive Predictors of Clinical Outcomes in Assisted Reproductive Technology (ART)

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Hyaluronan Binding Assay (HBA®) and Maternal Age Serve as Positive Predictors of Clinical Outcomes in Assisted Reproductive Technology (ART)

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INTRODUCTION:

- Initial evaluation of the infertile couple includes a thorough assessment of their history, etiology and parameters specific to ovarian and spermatozoon potential. Clinical and laboratory review of these parameters directs the clinician towards the selection of the optimal ART treatment for each couple facing infertility. Established andrology assays assist in this critical process.
- The HBA assay assesses the ability of the seminal population to bind to an immobilized substrate of hyaluronan. Hyaluronan is a major component of the cumulus oophorous matrix and may serve to select functionally competent sperm for in vivo fertilization.
- Research has demonstrated that hyaluronan bound (HB) sperm exhibit an increased expression of the HspA[2] chaperone protein and decreased levels of cytoplasmic inclusions[1], persistent histones, active caspase-32, DNA fragmentation[3] and chromosomal aberrations[1], each critical in the paternal contribution to preimplantation embryogenesis.
- The relationship between HB-sperm and potentially enhanced levels of functional competence led to the current study examining sperm binding potential as determined by the HBA index, seminal parameters as determined by established andrology assays, specific descriptive parameters of the male and female partners, history and etiology, and their individual predictive value and contribution to IVF outcome.
- The study sought to explore the potential association between the HBA index, morphology (M), total number of motile sperm (MS), ART treatment, hemizona assay index (HZA), age, etiology (E), parity (P), follicle stimulating hormone (FSH) level, number of dominant follicles (DF), number of Metaphase II oocytes and the likelihood of a clinical pregnancy (CP).

MATERIALS AND METHODS:

- Using an IRB-approved protocol, a retrospective analysis of 253 infertility couples was performed. Each parameter was statistically evaluated as to its contribution to a CP. The study population consisted of patients receiving intrauterine insemination (IUI) (n=76), IVF (n=93) and intracytoplasmic sperm injection (ICSI) (n=84).
- The HBA score, M, MS, HZA, E, P, FSH, DF, number of Metaphase II oocytes, maternal and paternal age, and ART treatment served as the independent variables (IV) and were recorded for each patient. To evaluate morphology, three slides were prepared per patient and a minimum of 300 sperm was assessed. All slides were read twice by two independent technicians. The HBA score was calculated as # bound MS/# total MS.
- Using the presence or absence of a CP as the dependent variable, the data was subjected to logistic regression analysis employing asymptotic, double-sided criteria. The likelihood of determining a clinical pregnancy was calculated for each parameter adjusting for the remaining terms of the model. Pearson's and Spearman's rho (ρ) correlations were used to test for linear associations among independent variables.

RESULTS:

Table 1. Logistic Regression Model Likelihood of Determining a Positive Clinical Pregnancy

Factor	Adjusted OR	95% CI	
Hyaluronan Binding Assay HBA® Score*	1.029	1.003	1.057
Female Age*	.886	.791	.993
ICSI*	41.91	9.41	186.59
IVF*	15.26	3.93	59.28
IUI (reference)	1.0		
Male Age	.951	.867	1.044
Total Motile Sperm (M/mL)	1.000	.998	1.003
FSH	1.113	.960	1.291
Hemizona	1.002	.989	1.016
Oocytes	1.0114	.913	1.125
Dominant Follicles	1.076	.954	1.215
Morphology	1.049	.935	1.177
Etiology	.559	.278	1.124
No Etiology (Reference)	1.0		

*p<0.05

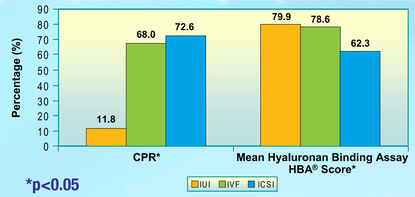
- Independent of the ART method used, the hyaluronan binding assay HBA® index and maternal age are the single most robust predictors of a positive clinical outcome.
- Of the three ART methods evaluated, use of ICSI was 41.91 X and IVF 15.26 X more likely to result in a CP over that of an IUI.

Table 2. Correlation of Hyaluronan Binding Assay HBA® Score with Sperm Parameters and Clinical Characteristics

Indicator	Person Correlation	pvalue	N
IUI Attempts	.362	<.001	247
IVF Attempts	.219	0.001	243
ICSI Attempts	-.488	<.001	241
Male Age (yr)	-.193	0.002	253
Total Motile Sperm M/ml	.488	<.001	253
Dominant Follicles	-.140	0.026	253
Number of Oocytes	-.162	0.010	253

- A statistically significant relationship exists between the value of the HBA index, TMS, paternal age and the number of ICSI cycles necessary to achieve a clinical pregnancy. A positive correlation exists between the HBA index and TMS (Pearson's correlation = .488, p<.001). A negative correlation exists between the HBA index, paternal age (Pearson's correlation = -.193, p=0.002) and the number of ICSI cycles necessary (Pearson's correlation = -.488, p<.001).

Figure 1. Hyaluronan Binding Assay HBA® Score and CPR by Method



*p<0.05

- In addition to the statistically significant relationship existing between the ART method selected and the resulting clinical pregnancy rate, a statistically significant relationship was demonstrated between the ART treatment and the mean HBA score associated with the patients within the ART group.

CONCLUSIONS:

- Logistic regression demonstrated that the HBA assay was the single most robust and objective prognostic indicator of clinical outcomes and optimal ART treatment. Use of the HBA index in the evaluation of the infertile couple may increase the efficiency of the infertility diagnosis and direct the clinician to select more effective ART procedures, thus improving the level of patient care offered.
- Paternal age, TMS, M, FSH, HZA, # Metaphase II oocytes, DF, P and etiology demonstrated no statistical significance in their ability to predict a positive clinical outcome.
- Pearson's correlation demonstrated that there was a statistically significant relationship between the dynamic value of the HBA index and the number of ICSI cycles necessary to achieve a positive clinical outcome. The negative correlation demonstrated that as the value of the HBA index increased, the number of ICSI cycles necessary for a successful outcome decreased.
- Pearson's correlation demonstrated that there was a statistically significant relationship between paternal age and the HBA score of the associated semen. The negative correlation indicated that as the paternal age increased, the associated HBA score decreased.
- A statistically significant and positive correlation was demonstrated between the HBA index and TMS. The values of the HBA index and TMS increased concomitant with one another.
- The predictive value of the HBA index may be a reflection of the influence HB-sperm exert on preimplantation embryogenesis. Use of the refined criteria for the HBA index may serve to better predict the functional capacity of a seminal population and direct the technologies selected for improved patient care.

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