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 fertile couple includes a thorough assessment of their history, and 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 pool 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 vitro fertilization.

Research has demonstrated that hyaluronan bound (HB) sperm exhibit an increased expression of the HsP40 chaperone protein and decreased levels of cytoplasmic inclusions, persistent histones, active caspase-3, DNA fragmentation, and chromosomal aberrations, each critical in the paternal contribution to preimplantation embryogenesis.

The relationship between HB-sperm and potentially enhanced levels of functional sperm was investigated. Research has demonstrated that hyaluronan bound (HB) sperm exhibit an increased expression of the HsP40 chaperone protein and decreased levels of cytoplasmic inclusions, persistent histones, active caspase-3, DNA fragmentation, and chromosomal aberrations, each critical in the paternal contribution to preimplantation embryogenesis.

In addition to the statistically significant relationship existing between the HBA index, TMS, paternal age, and the number of ICSI cycles necessary to achieve a clinical pregnancy. A positive correlation exists between the HB-sperm index and TMS (Pearson’s correlation = .488, p<.001). A negative correlation exists between the HB-sperm index and age (Pearson’s correlation = -.303, p<.001). A statistically significant relationship exists between the complete hyaluronan binding assay (HBA) and male age (Pearson’s correlation = .488, p<.001). The negative correlation indicated that as the paternal age increased, the associated HBA score decreased.

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.

Materials and Methods:

Using an IRB-approved protocol, a retrospective analysis of 253 infertility couples was performed. Each patient was statistically evaluated as to its contribution to a CP. The study population consisted of patients receiving intratubal insemination (ITI) and IVF.

The HBA score, MS, HZA, age, and ART treatment served as the independent variables. ICSI and intracytoplasmic sperm injection (ICSI) were recorded for each patient. Evaluating 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-logit criteria. The likelihood of determining a clinical pregnancy was calculated for each parameter adjusting for the remaining terms in the model. Pearson’s and Spearman’s rho (φ) correlations were used to test for linear associations among independent variables.

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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Likelihood Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBA Score</td>
<td>2.083</td>
<td>.001</td>
</tr>
<tr>
<td>TMS</td>
<td>1.029</td>
<td>.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.003</td>
<td>.001</td>
</tr>
<tr>
<td>MS</td>
<td>1.076</td>
<td>.001</td>
</tr>
<tr>
<td>P</td>
<td>1.076</td>
<td>.001</td>
</tr>
<tr>
<td>FSH</td>
<td>1.016</td>
<td>.001</td>
</tr>
<tr>
<td>HZA</td>
<td>1.124</td>
<td>.001</td>
</tr>
</tbody>
</table>

Results:

- A statistically significant relationship exists between the complete hyaluronan binding assay (HBA) and male age (Pearson’s correlation = .488, p<.001).
- A negative correlation exists between the HB-sperm index and age (Pearson’s correlation = -.303, p<.001).
- A statistically significant and positive correlation was demonstrated between the HBA index and TMS. The values of the HBA index and TMS increased concomitantly with each other.
- 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.

Conclusions:

- Logistic regression demonstrated that the HBA assay was the single most robust and objective prognostic indicator of infertility diagnosis and directed patients to select more effective ART procedures, thus improving the level of patient care offered.
- Paternal age, TMS, 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.

Support: Hyaluronan Binding Assay HBA® chambers were provided by Biocost, Inc.