ABSTRACT

Endometriosis, a common benign gynecological disease, is characterized by proliferation of functional endometrial glands and stroma outside the uterine cavity. The clinical symptoms often appear late during the disease process thus making early diagnosis challenging. Currently, laparoscopy, a surgical procedure, followed by biopsy is used for definitive diagnosis of endometriosis. The need for non-invasive/minimally invasive marker (s) is thus well recognized.

The first part of this study involves investigation of alterations in the serum proteome of endometriosis patients compared to healthy controls. Discovery and validation phase results indicate that haptoglobin, Ig kappa chain C region, alpha-1β-glycoprotein hold promise as effective serum protein markers for the diagnosis of endometriosis. Further, while alpha-1β-glycoprotein showed similar expression profile, haptoglobin showed an inverse relationship in endometrial tissue indicating their involvement in disease progression.

The second part of the study involves investigation of serum metabolome alterations in endometriosis patients. A large panel of metabolite and lipid markers including proline, phosphatidylcholine, phenylalanine, 2-hydroxybutyrate, lysine and several branched chain amino acids showed significant diagnostic potential. We also report metabolic perturbations in eutopic endometrial tissue associated with different stages of endometriosis. The dysregulated metabolites were found to be mostly associated with oxidative stress and angiogenesis, major hallmarks of the disease.

The third part of the study involves a mass spectrometry-based lipidomics approach to investigate the alterations in serum lipid profiles of mice induced with endometriosis. Several dysregulated lipids such as phosphatidylcholines, sphingomyelins, phosphatidylethanolamines and triglycerides were found to be altered in serum of mice induced with endometriosis. Also, alteration in the phosphatidylethanolamine N-methyltransferase (PEMT) pathway is suggestive of changes in the phosphatidylcholine/phosphatidylethanolamine ratio in serum of endometriosis mice. This finding provides a new insight to the etiology of endometriosis.

Finally, the study shows that the sensitivity and specificity of the panel of markers when used together increased significantly to ~ 90% for early stage diagnosis compared to that of the markers, when used individually. The differentially regulated proteins and metabolites found in this study provide an important step towards developing effective bioassays for diagnosing endometriosis.

Keywords: Endometriosis, minimally invasive diagnosis, proteomics, metabolomics