



AN ANALYSIS OF OXIDATIVE STRESS RESPONSE ELEMENTS AS A PRECURSOR TO CARCINOGENESIS IN PATIENTS WITH PCOS

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INTRODUCTION

Chronic inflammation and oxidative stress are hallmarks of PCOS. This persistent state may dysregulate key cellular defense and proliferation pathways, predisposing the endometrium and other tissues to malignant transformation. The specific role of oxidative stress response elements in this continuum is poorly defined.



RESEARCH OBJECTIVE

In this study, we aimed to investigate the gene expression of genes associated with PCOS, carcinogenesis, and oxidative stress in females.



METHODOLOGY

Study Design

This was a cross-sectional analytical study with patients enrolled according to the inclusion/exclusion criteria. The samples were collected from the Department of Oncology, Jinnah Hospital, Lahore.

Study Groups

Group 1: Healthy individuals taken as control samples.

Group 2: Patients diagnosed with gynaecological cancers.

Group 3: Patients diagnosed with PCOS

Data Collection

Data were collected through hospital-based sampling, blood sample collection, and review of relevant patient records/data.



Workflow Methodology



Blood collection → RNA extraction → cDNA synthesis → PCR → RT-qPCR → Gene expression analysis



GENE EXPRESSION ANALYSIS

The expression levels of eight target genes, CYP17A1, ESR1, GnRH1, IGF-2, IGF-1, NFE2, PTEN, and SOD2, were analyzed using RT-qPCR in three study groups: Reproductive Cancer patients (n=21), PCOS patients (n=5), and Healthy Controls (n=4). Gene expression was normalized to the reference gene β -Actin (ACTB), and the relative fold changes were calculated using the $2^{(-\Delta\Delta Ct)}$ method.



RESULTS

The heatmap illustrates gene expression patterns across reproductive cancer, PCOS, and healthy controls, with PTEN and NFE2 showing reduced expression in the cancer group. Overall, PTEN and NFE2 appear to be key differentiators between cancerous and non-cancerous reproductive conditions.

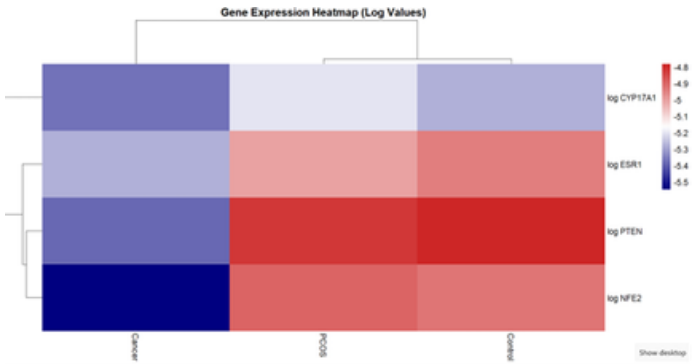
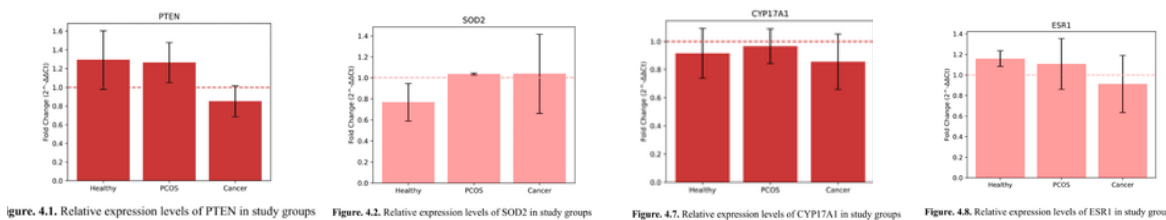


FIG 4.2: GENE EXPRESSION HEATMAP

TABLE: SIGNIFICANT ASSOCIATIONS BETWEEN GENE EXPRESSIONS

Gene	Expression Pattern	Statistical Result	Biological Implication
PTEN	Downreg. in Cancer	$p < 0.01$	Loss of tumor suppressor activity - promotes oncogenesis
NFE2	Downreg. in Cancer	$p < 0.05$	Reduced antioxidant defense - oxidative
CYP17A1	Stable	$p > 0.4$	Steroidogenic enzyme unaffected
ESR1	Stable	$p > 0.1$	Estrogen receptor signaling unchanged

CANCER PREVALENCE AND GENE EXPRESSION ANALYSIS



In this study, 42 patients with reproductive cancers, 10 patients with PCOS, and 8 healthy individuals were evaluated for the relative expression of selected genes. Ovarian cancer was the most prevalent cancer type (62%), followed by cervical (23%), endometrial (10%), and vaginal cancer (5%). Gene expression analysis showed significant downregulation of PTEN, CYP17A1, and ESR1 in the Cancer group compared with the Healthy and PCOS groups, whereas SOD2 expression remained relatively stable across the study groups. These findings demonstrate distinct gene-expression changes associated with reproductive cancers in comparison with PCOS and healthy controls.

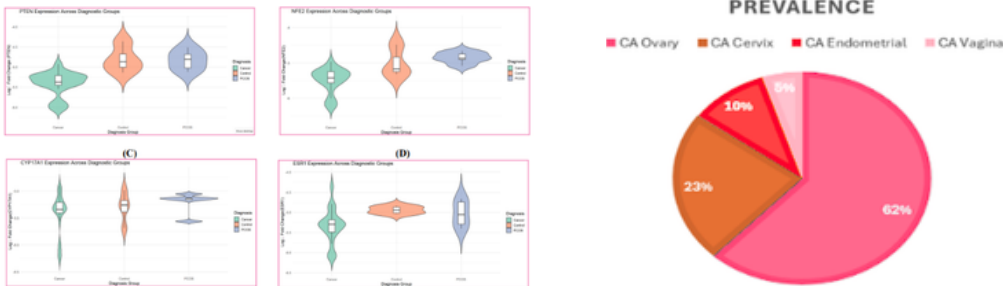
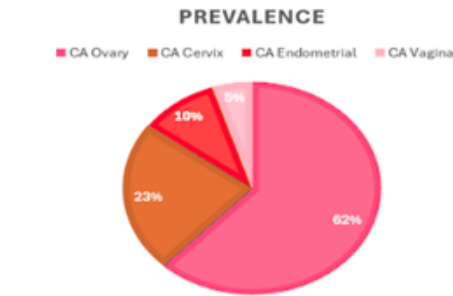


Figure 1. Violin plots of $\log_2$ fold-change expression for (A) PTEN, (B) NFE2, (C) CYP17A1, and (D) ESR1 across Cancer, PCOS, and Control groups. PTEN (A) and NFE2 (B) are significantly downregulated in Cancer, indicating loss of tumor-suppressor and antioxidant activity. CYP17A1 (C) and ESR1 (D) show overlapping distributions with no significant differences.



42 patients with reproductive cancers were enrolled, 10 patients with PCOS along with 8 healthy individuals taken as control. Subjects were divided into groups for comparative analysis between cancers and PCOS. All samples were females. Patients were aged 18 to 70 years.



CONCLUSION

In conclusion, this study demonstrates that the relationship between PCOS and reproductive cancer is not a simple matter of progressive gene dysregulation from a pre-disease state to malignancy. Instead, our findings suggest a more complex model. Young women with PCOS may exhibit an adaptive, protective upregulation of key defense systems, including the antioxidant regulator NFE2 and the tumor suppressor PTEN. In contrast, established reproductive cancers, particularly of non-endometrial origins, are characterized by a loss of estrogen receptor expression.

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STUDY LIMITATIONS

- The small sample size, particularly for the PCOS (n=5) and control (n=4) groups, increases the risk of Type II errors, where real biological differences are missed.
- The dramatic age difference between the cancer group and the others remains a fundamental confounder.
- Peripheral blood may not adequately capture the localized gene regulatory events central to PCOS pathophysiology.