



# Expression of iron metabolism-related genes is altered in Familial Hypercholesterolemia patients

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## Introduction

Atherosclerosis (ATH) is the major cause of cardiovascular diseases (CVD) causing great morbidity and mortality. Typically, ATH develops and progresses silently for years, without symptoms. Familial Hypercholesterolemia (FH) is an autosomal genetic disorder characterized by high levels of total and LDL cholesterol, a familial history of hypercholesterolemia and premature ATH. Atherogenesis is characterized by an early deposition of LDL in the artery walls, leading to the recruitment and activation of peripheral blood mononuclear cells (PBMC) to the plaque. In addition, monocyte-derived macrophages accumulate oxidized LDL and differentiate into foam cells, leading to the development of complex and unstable lesions. The oxidative modification of LDL, accelerated, or even initiated by transition metals as iron (Fe) has been implicated as an early step in the formation of atheromatous lesions.

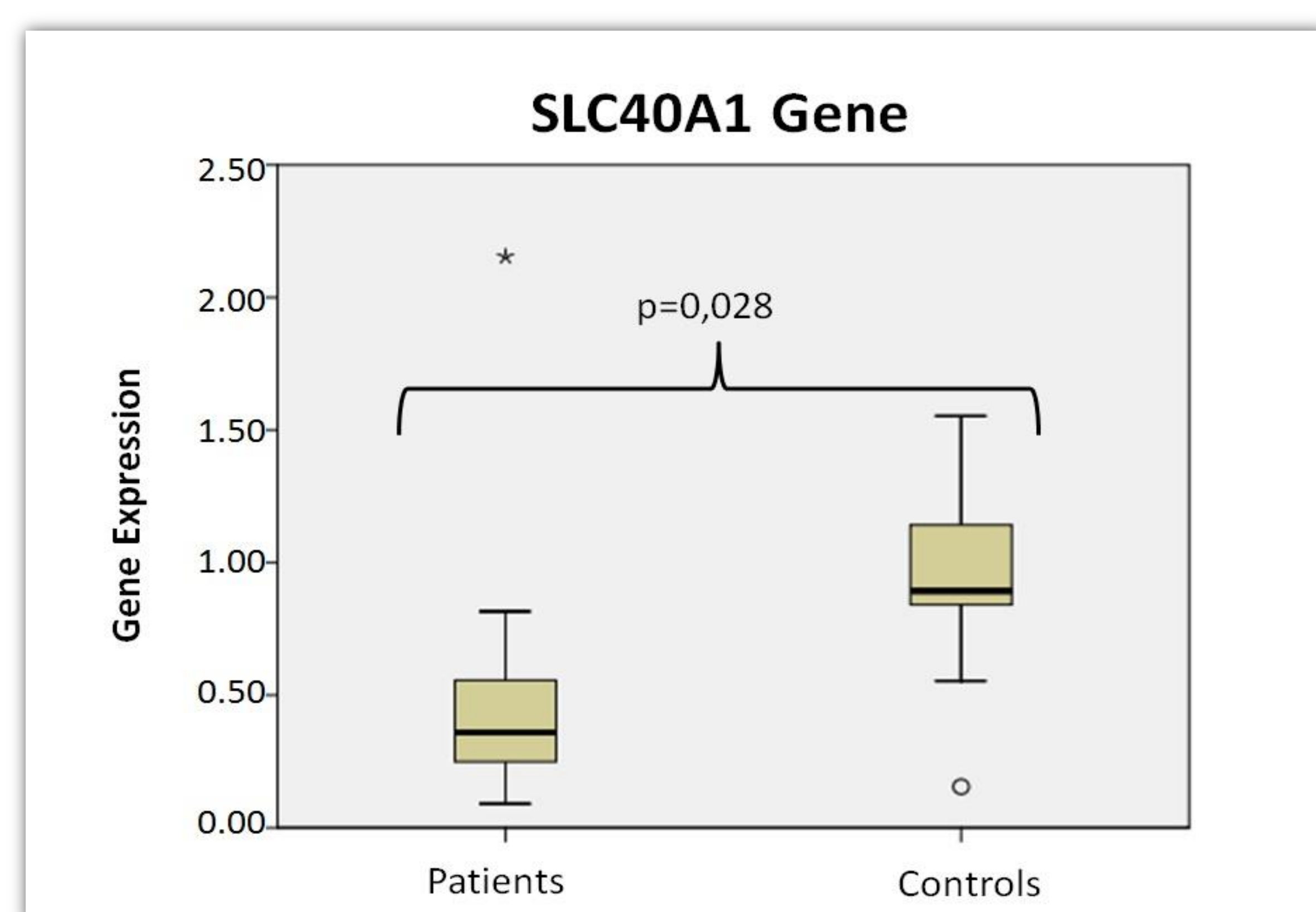
## Methods

The expression of several Fe metabolism-related genes involved in cellular Fe uptake (Transferrin Receptor 1, *TFR1*), efflux (Ferroportin, *SLC40A1*; Beta- Amyloid precursor protein, *APP*) and regulation (Interleukin 1beta, *IL1B*; Hepcidin, *HAMP*) was studied in Peripheral Blood Mononuclear Cells (PBMCs) isolated from 10 FH patients, used as clinical model of ATH, and 10 healthy controls. Gene expression was quantified using quantitative Real-Time PCR.

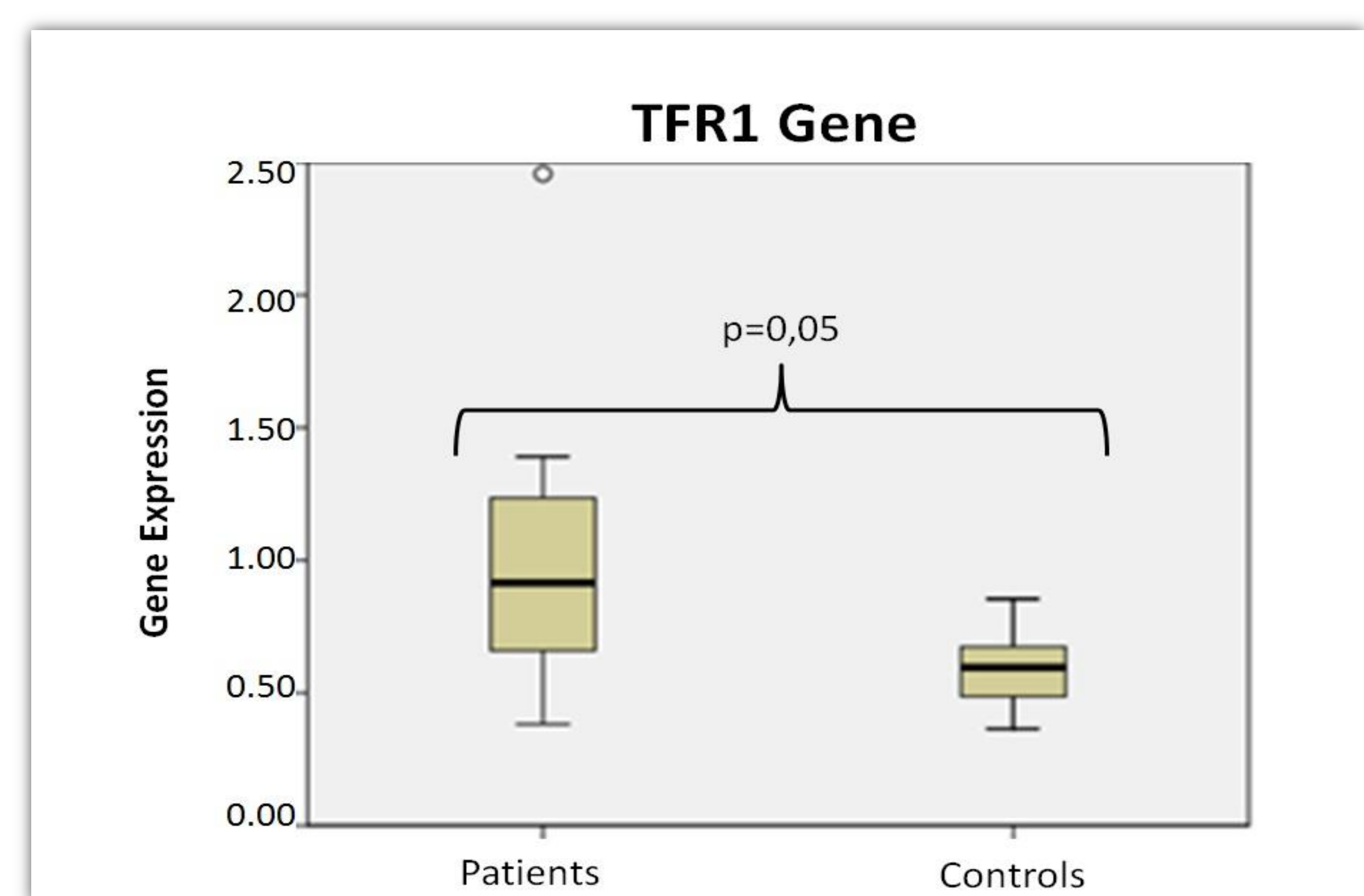
## Results

The results obtained showed that mRNA levels from the Fe exporter *SLC40A1* gene were significantly decreased in PBMCs from FH patients compared to controls ( $p=0.028$ ), while no significant differences were found in the other genes analyzed.

Interestingly, a tendency for an increase ( $p=0.05$ ) in the expression of *TfR1* (involved in iron uptake) was found in these patients.



**Fig.1** –Expression of ferroportin gene in FH patients and controls (n=10,  $p=0.028$ ).



**Fig.2** – Expression of transferrin receptor 1 in FH patients and controls (n=10,  $p=0.05$ ).

## Discussion and Conclusion

The results obtained in this study support Fe homeostasis deregulation in FH at transcriptional level. The decreased expression of *SLC40A1* gene along with the tendency of *TFR1* gene expression increase in PBMC from FH patients could suggest monocyte-derived macrophage Fe accumulation in the atheromatous plaque, thus promoting the development of unstable lesions.

In conclusion, we hypothesize that impaired cellular Fe transport could be implicated in the physiopathology of ATH.