Objective
Endometriosis is a complex gynecological condition that affects approximately 5-11% of reproductive age women. It is generally accepted that endometriosis is influenced by both genetic and environmental factors. Genetic factors make up about half of the variation in endometriosis. In 1980, Simpson et al. published the first study on the polygenic/multifactorial inheritance pattern of endometriosis. Among 123 patients with endometriosis, he observed 6.9% recurrence risk for all first-degree relatives. Subsequent study by Lamb et al. (1986) based on 491 endometriosis members (USA), found a positive family history in 18% of the responders. Here, we present the case of a familial cluster composed of 6 members, all affected by endometriosis, a novelty among the 150 patients that are being treated in our department.

Methods
We describe the only family ever found in Crete with multiple members suffering from endometriosis. The diagnosis was histologically confirmed and staging was performed according to the revised ASRM classification. Case 1, the grandmother (now aged 65) gave birth to three children, between age of 16 and 24. She underwent total abdominal hysterectomy for bilateral ovarian endometriosis (stage IV) at the age of 32. Case 2, the first daughter of the case 1, had two childbirths (the first when she was 14 years and the second when she was 18 years). She had a laparotomy for bilateral ovarian endometriosis (stage IV) at the age of 31. Two years later, she underwent total surgical hysterectomy due to failure of conservative management. Case 3, the second daughter of case 1, gave birth to two children, between age of 17 and 22. Laparoscopy at the age of 28 years for infertility investigation, revealed endometriosis stage III. Case 4, the third daughter of case 1, also had histologically confirmed stage II endometriosis at the age of 25, after diagnostic laparoscopy due to 4-year history of severe dysmenorrhea and infertility. Case 5, the granddaughter of case 1 and the daughter of case 2 (now 32 years old) suffer from severe dysmenorrhea. Elevated level of CA-125 raised the suspicion of endometriosis. She is scheduled for laparoscopy due to primary infertility. Case 6, the 26 year old sister of the case 5, underwent laparoscopy for primary infertility and was diagnosed with endometriosis stage III.

Results
In this study, we clearly demonstrate the familial aggregation of endometriosis, as we present a high incidence rate among first degree relatives. Our data is in accordance with several linkage studies in families with multiple affected women, which demonstrate a genetic association to the disease. Previous reports cannot exclude a Mendelian inheritance pattern for endometriosis, despite the fact that the causative gene(s) and mechanisms remain elusive due to the multifactorial pattern of inheritance of this disease.

Conclusion
We conclude that further studies are necessary in order to identify the hereditary pattern in endometriosis patients, although it is also possible that environmental factors play a role in this condition. This would ultimately result in better and earlier methods for detection, diagnosis and prevention amongst family members with endometriosis. In this context, genetic studies focusing on various endometriosis-associated gene polymorphisms are in progress. This case report highlights our attempt to shed light on the contribution of these genetic factors in the development of this gynecological condition within this family. Further investigations on more families could provide further insight into the pathogenesis of endometriosis.

Figure 1: The family tree of endometriosis (red circles depict the members with histologically confirmed endometriosis)