

The incidence and prevalence of pelvic inflammatory disease and its impact in infertility, pelvialgia and surgical interventions

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ABSTRACT

Introduction. Pelvic inflammatory disease (PID) is considered a major cause of morbidity in women, but its epidemiology is little known in Albania.

Purpose. Investigation of the incidence and prevalence of pelvic inflammatory disease and its impact on infertility, pelvialgia and surgical interventions.

Objectives. The study is based on cases with acute and chronic PID, and not on asymptomatic ones. The literature review is based on studies and data from PubMed and Cochrane. We must emphasize the fact that the literature provides different data between developed and developing countries in terms of PID incidence. Data in Albania show that in addition to *C. trachomatis*, *N. gonorrhoeae* is also observed, which has a high incidence associated with PID. Other characteristics such as the age of the first relationship, having or not having many partners are similar to those of European Community countries.

Results. The highest incidence of patients diagnosed with PID was in women of reproductive age (1.7%). The diagnostic criteria were: the presence of abdominal pain and the exclusion of competitive diagnoses. The combined case-control and retrospective study showed that PID has the characteristics of a sexually transmitted disease. When compared with a control group who had undergone tubular ligation or the presence of IUD, the increased risk for PID was associated with: age group < 25 years; age at first sexual intercourse < 20 years; Roma or Egyptian population; parity; a previous history with SST and the presence of *C. trachomatis*. When the comparison was performed with the data obtained in the general population randomly, the increased risk is related to: age group < 25 years; age at first sexual intercourse < 15 years; low socio-economic status; having many partners; abortion; previous history of SSTs and exposure to *C. trachomatis*. Of the cases, 64% were not associated with any of the infectious agents measured in this study (idiopathic). Several idiopathic cases were associated with *Mycoplasma genitalium*.

Keywords: pelvic inflammatory disease (PID), infertility, pelvialgia, surgical interventions

INTRODUCTION

Pelvic inflammatory disease (PID) is defined as a clinical syndrome associated with upper genital tract infection in women. *Chlamydia trachomatis* is thought

to be a bacterial infection that is the most common, curable sexually transmitted infection. PID is a leading cause of health problems in women such as: ectopic pregnancies, tubular infertility factor and chronic ab-

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dominal pain and has been linked to ovarian cancer (1,2,3). A significant PID load is thought to exist in women of reproductive age, but little is known about the epidemiology of PID in Albania and other established market economies (EMEs). The burden of the disease and the risk factors associated with PID are poorly understood, but should be investigated to promote public health information and clinical practice. Recognition of the epidemiology of PID, which is the distribution and determinant of the occurrence of diseases within the population, is essential to understand reproductive morbidity and migration. PID should be monitored as part of a chlamydial intervention program.

OBJECTIVES

Investigation of the incidence and prevalence of pelvic inflammatory disease and its impact on infertility, pelvicgia and surgical interventions. The study is based on cases with acute and chronic PID, and not on asymptomatic ones. Data in Albania show that, in addition to *C. trachomatis*, *N. gonorrhoeae* is also observed, which has a significant incidence associated with PID. Other characteristics such as the age of the first relationship, having or not having many partners are similar to those of European Community countries.

1. Evaluation of the data of the outpatient or hospitalized cards in "Queen Geraldine" University Hospital and the clinics of the capital.
2. Comparison of these data with the literature.
3. Comparison of diagnostic methods, such as laboratory or surgical ones.
4. Comparison of diagnosis based on diagnosis and clinical framework.

MATERIALS AND METHODS

The research was conducted in Medline (PubMed) using the keywords 'pelvic inflammatory disease', 'endometritis', 'salpingitis', 'laparoscopy', 'endometrial biopsy', '*Chlamydia trachomatis*', '*Mycoplasma genitalium*' of well-known authors who have published studies related to PID and *C. trachomatis* (8). Research has shown that the literature is widely disseminated through Medline journals. Much of the literature review has been undertaken by requesting references cited in studies in the online library Cochrane, or by searching for them through the Internet. Clinical card-based studies in hospitalized or outpatient women at Queen Geraldine Hospital and the capital's leading clinics for the period 2011-2018. It is a cohort and retrospective study. Permission to use the cards has been

duly obtained from the Hospital Directorate. Patient surveys have always been conducted after they have given permission to perform data processing.

The classification of the ethnic group was simplified into: white, colored. The analysis included 781 women aged 16 to 46 years. The duration of patients registered with their GP varied from one day to one year. No distinction was made whether these were new diagnoses or a consultation for an episode diagnosed for the first time outside the study period. Thus, the analysis gives an estimate of the spread. Interactions were undertaken and a model of key effects was used to describe the data. Non-regulated and regulated rate ratios (RRs) are calculated.

RESULTS

The data show that there was an increase in the diagnosis of gonorrhea in women during 2012 and 2013, which was followed by a decrease during 2015, 2016 and 2017. The diagnosis of PID has been steadily increasing since 2012 and in 2014, while ectopic pregnancies have gradually increased since mid-2014. Data from the age group show that the highest diagnostic rates in hospital records are seen continuously in the 16-24 age group. Analysis of the data group shows that the rate of diagnosis of PID in women aged 16 to 46 years following general practice was 167/10,000 persons at risk (13/781) or 1.7%. The number of diagnoses and the rate per 100,000 people at risk were calculated. The RRs adjusted for other variables in regression analysis were calculated together with 95% confidential intervals (CI). The data were re-coded to avoid problems with rare data in some categories. There was a significant difference between the age groups, with women aged 35 to 39, at half the risk of PID diagnosis ($p < 0.0001$, adjusted RR = 0.54, 95% CI 0.40 to 0.72) and those aged 40 to 46 years were in a quarter of the risk (RR adjusted = 0.26 95% CI 0.19 to 0.36) compared to the 16-19 age group.

Smokers were at higher risk of PID than non-smokers ($p < 0.0001$, RR adjusted = 1.85, 95% CI 1.65 to 2.09). Patients in socioeconomic groups III to V were all at higher risk of PID than those in socioeconomic group I / II ($p < 0.0001$). Compared to patients who were married, the increased risk of PID was also associated with those patients who were widowed, separated or divorced and not cohabitants (RR adjusted = 1.62, CI 1.35 to 1.97), and with those who were unmarried but cohabitants = 1.32; 95% CI 1.11 to 1.56.

The difference in PID risk between ethnic groups was not statistically significant ($p = 0.0994$), but there was evidence of increased risk in the color group (RR adjusted 1.65, 95% CI 0.97 to 2.79) 1.53; 95% CI 0.84 to 2.78) compared with white patients.

TABLE 1. Expectations for patients with hospitalized PID, according to age groups

Variable	Prevalence (cases/100,000 persons per year)	RR adjusted (95%CI)	P value (RR adjusted)
Age			
16-19	223	1.00	< 0.0001
20-24	251	1.07 (0.84- 1.36)	
25-29	220	0.94 (0.72- 1.21)	
30-34	188	0.80 (0.61- 1.05)	
35-39	127	0.54 (0.40- 0.72)	
40-46	63	0.26 (0.19- 0.36)	
Etnicity			
White	167	1.00	0.0994
Other	264	1.65 (0.97- 2.79)	
Civil status			
Married	131	1.00	< 0.0001
Cohabitant	262	1.32 (1.11- 1.56)	
Divorced/ widow	236	1.62 (1.35- 1.97)	
Single	192	0.88 (0.75- 1.05)	
Social class			
I/II	114	1.00	< 0.0001
III	157	1.22 (1.04- 1.43)	
III	223	1.59 (1.28- 1.97)	
IV	239	1.65 (1.38- 1.97)	
V	196	1.52 (1.17- 1.98)	
Smoking			
Yes	122	1.00	< 0.0001
No	266	1.85 (1.65- 2.09)	

Prevalence of PID, RR and 95% CI (data group)

Five categories have been proposed that include symptoms, signs, microbiological investigations, antibiotic therapy, and partner notification. The answers from general practices were compared to this 'gold standard'.

Of the 781 questionnaires sent to patients, 297 (38%) returned. There was no significant statistical difference between those who responded and those who did not respond in terms of practice size ($p = 0.47$), the Carstairs index ($p = 0.55$), and the sex of the contact physician ($p = 0.33$). Of male physicians, 40% responded compared to 33% of female physicians.

Of those practices that have been answered, 95% are computerized, 66% are based in urban areas, 13% in rural areas and 21% in mixed urban/rural areas. Immunization coverage of 90% or more was achieved with 86% of practices and an 80% cervical cytological target was achieved with 87% of practices. 72% of internships said they would refer patients to Queen Geradine Hospital.

Comparison of current practice against the „gold standard“ showed that 100 (34%) called at least 2

signs and 2 symptoms, 160 (54%) called the correct antibiotic therapy, 64 (22%) usually treated the partner and 252 (85%) usually undertook microbiological investigations (91%) received an endocervical buffer. Only 21 (7%) answered all parts of the „gold standard“ correctly. Unfortunately, only 11% (34/297) of respondents completed part C of the questionnaire and thus this data was excluded from the analysis.

Adjustment for other variables reinforces the effects observed in the single variable analysis. The lowest quality of management ($p < 0.01$) was related to non-computerized practices compared to those that were computerized (OR 0.07: 95% CI 0.005 to 0.96). The quality was significantly higher ($p = 0.05$) when the clinician was female compared to males (OR 2.34: 95% CI 1.19 to 4.63) and the quality increased by 12% (95% CI 5% to 21%) No interaction statistically significant was not found between the variables.

All patients included in the study had an initial clinical diagnosis based on clinical presentation (signs and symptoms), the criteria were bilateral abdominal or pelvic pain lasting less than 3 weeks, along with 2 or more of the following: abnormal vaginal discharge, fever $> 38^{\circ}\text{C}$, vomiting, menstrual irregularities, persistent bleeding, urethritis symptoms, rectal temperature $> 38^{\circ}\text{C}$, tenderness of pelvic organs on bimanual examination, adnexal mass and ESR ≥ 15 mm/hour. Laparoscopy has been used to verify the clinical diagnosis, the criteria used are hyperemia of the tubular surface, edema of the tubal wall, and exudates on the tubal surface and the edges of the fimbriae.

A total of 157 patients were included in this analysis, 124 patients were laparoscopically confirmed as PID and 33 were not. There were no significant statistical differences between these groups regarding: age ($p = 0.649$), number of pregnancies ($p = 0.447$), births ($p = 0.375$), and whether an IUD was used ($p = 0.675$) or inserted six weeks from the index laparoscope ($p = 0.100$).

None of the variables had specificity and high sensitivity. Some achieved high sensitivity of the pelvic organs in bimanual examination and ESR or high specificity (proctitis and vomiting symptoms), but most had low specificity and sensitivity.

The pretest probability of confirming PID laparoscopically was 79%, 95% CI 76% to 82%. All probability ratios were positive and there was little difference between the variables in terms of probability ratios or probabilities after the test (Table 2). For example, the lowest probability ratio (0.98) produced a probability after Test of 79% (95% CI 74% to 81%), while the highest probability ratio (1.73) has a probability after test of 84% (CI 81% to 87%). Consequently, for all variables studied, probability after trial was not significantly different from pre-trial probability.

TABLE 2. Prediction of laparoscopically diagnosed PID, sensibility and specific signs and symptoms, likelihood ratio and probabilities post-tests

Signs and symptoms	Sensitivity% (95%CI)	Specificity% (95%CI)	PID laparoscopically diagnosed	PID non laparoscopically diagnosed	Likelihood ratio + (positive)	Prob. post-tests
			Present(n=124) Number (%)	Absent(n=33) Number (%)		
Vaginal discharge	74(69.99- 77.90)	24(16.95- 32.34)	91 (74)	25(76)	0.98	0.79
Temperature	47(42.49- 51.47)	64(55.43- 72.58)	58(47)	12(36)	1.30	0.83
Vomiting	14(11.03- 17.34)	88(81.55- 93.34)	34(14)	4(12)	1.11	0.81
Menstrual disorder	45(40.49- 49.45)	57 (48.36- 66.03)	17(45)	14(43)	1.04	0.80
Bleeding	25(21.34- 29.17)	77 (68.49 - 83.73)	31(25)	7(22)	1.12	0.81
Urinary symptoms	35(30.81- 39.41)	64(55.43- 72.58)	18(35)	11(36)	0.98	0.79
Proctis symptoms	10(7.43- 12.90)	92(86.21- 96.22)	13(10)	3(8)	1.31	0.83
Sensitivity of pelvic organs in vaginal examination	99(97.65- 99.67)	0.007(<0.01- 2.84)	123(99)	32(99)	1.00	0.79
Adnexial mass	52(47.52- 56.51)	70(61.06- 77.54)	64(52)	9(30)	1.73	0.84
ESR \geq 15 mm/h	81(77.23- 84.34)	33(25.28- 42.17)	201(81)	21(66)	1.22	0.82

Discriminatory analysis showed that three variables significantly affected the predicted presence of PID: ESR (correlation value = 0.669, $p < 0.0001$), fever (CV = 0.584, $p < 0.0001$) and adnexal sensitivity (CV = 0.540, $p < 0.0001$). These variables correctly classified 65% of patients with laparoscopic PID diagnosis (95% CI 61% to 69%). Other variables have not reached the significance, so the presence of these variables did not increase the probability that the patient had PID.

The diagnosis of PID in primary and hospital care is focused on the syndrome diagnosis and the exclusion of competitive diagnoses (9-11). Recommended diagnostic criteria are based on the definition proposed by Hager et al. (12), which focuses on clinical presentation. The accuracy with which the signs and symptoms predict the presence of PID has been assessed using a gold laparoscopic standard.

Interpretation of the probability ratio: > 10 and < 0.1 (large difference between pre- and post-test options), 5 to 10 and 0.1 to 0.2 (modified change), 2 to 5 and 0.5 to 0.2 (small), 1 to 2 and 0.05 to 1 (market change).

TABLE 3. Classification of results from the discriminatory analysis of the previous phase

		Absent	Present	Total
PID laparoscopically diagnosed	Absent	22	11	33
	Present	44	80	124
	Total	66	91	157

High diagnostic accuracy is essential for effective patient management. Evaluation of the evidence base

shows that the most effective diagnostic criteria are the presence of low abdominal pain and the exclusion of competitive diagnoses. The simplicity of these diagnostic criteria makes it appropriate as a case-by-case definition of supervision, but unfortunately, there is no specificity and sensitivity. The results of this investigation will be useful in guiding a reassessment of PID diagnostic criteria and formulating a new definition of case surveillance.

DISCUSSION

Few surveillance data were available and most are limited to coverage and scope, even in environments that specialize in sexual health. Data quality varies significantly between clinical settings, tertiary hospital settings, and data sets cannot be compared or combined due to differences in collection methods. In particular, the severity of clinical presentation varies between clinical conditions: patients who receive primary care generally have low chronicity, while patients in hospital services will be women who experience acute and chronic pain and long-term reproductive health problems associated with PID. During the years 2011-2018 in Albania, variations in the number of cases of gonorrhoea, episodes of hospitalization for PID and ectopic pregnancy have followed a pattern similar to that seen in Sweden. Interpreting long-term tendencies of gonorrhoea, SIP, and ectopic pregnancy is difficult because ecological analyzes cannot be used to establish a causal link between conditions. There are

some shortcomings in reporting due to changes in collection methods or lack of data. Another concern is that the steep increase in gonorrhoea seen after 2012 is not reflected in an expected increase in SIP patients. This question represents the accuracy of the PID hospital data collected. In addition, the decline in episodes of hospitals viewed in Sweden, the Netherlands, Canada and the US in 2016 was not seen in our data (4,5,6,7).

There is a significant PID reservoir undiagnosed in the general population. The 1.7% prevalence of the first PID diagnosis in the analysis of the collected data set suggests that in 2015, there would be more cases diagnosed with PID while in reality the number was much smaller. This finding shows that general practice provides an important focus for the diagnosis and treatment of PID. The 41% increase in the diagnosis of the first PID in general practice in 2015-2016 suggests that PID may be increasingly managed in this environment, although this increase may also reflect an increase in the incidence of cases. The data showed that only 30% of those diagnosed with PID had participated in clinic services, indicating that most cases of PID were seen in hospital. Although the specific age of hospitalized patients suggests that higher diagnostic rates and higher growth rates were consistently seen in the 16-24 age group. Consequently, while the peak of genital infection with chlamydia is in adolescent women, the following morbidity women's reproductive health is considerable. The analysis of the collected data group supports previous observations that women who smoke are at significantly higher risk of PID. A relationship between PID risk and divorced marital status has also been reported in studies in England and Wales (10,11). For example, age at first sexual intercourse and the number of sexual partners during life are known to vary with marital status, cohabitant, and socioeconomic group. Unfortunately, measures of sexual behavior were not included in the data set, and this severely limits interpretation, as aspects of sexual behavior can be potentially confusing in observed relationships. Recent studies have speculated whether other than white ethnic groups have a high load of reproductive morbidity and some evidence of increased risk in them has been seen in the analysis. The other ethnic group is under representation, accounting for only 1.6% of the sample. After adjusting for socio-economic status, these groups were not found to be at higher risk of PID than whites. However, the presence of RRs higher than 1 along with lower confidence limits that includes only 1 for the other ethnic group category indicates that the risk of PID was approaching the importance for that category. These data suggest that the PID load in different ethnic groups should be further investigated.

The analysis was the first study to be undertaken in a primary care setting and there are no international comparisons. The analysis provides an overview of the epidemiology of PID but has a number of limitations. First, the data group is dedicated to overseeing general illness and does not include information on factors that are either known to be associated with PID, or are potential confusions. Second, clinical samples have not been collected so the etiology of PID cases is unknown. Third, the study findings are limited to data collection time. The epidemiological changes of PID over time and thus the results of the study cannot be used as a basis for evidence except for the time period studied. The available surveillance data do not provide an accurate picture of the PID epidemiology. They are one-sided because: some rarely accumulate; little or no data on behavioral, demographic, and reproductive health are collected; standard diagnostic criteria are not used; methodologies cannot be modified; and diagnostic samples cannot be collected. However, although the diagnosis of PID in general practice is likely to have a lower specificity and sensitivity than that diagnosed in hospital, surveillance data show that information from general practice is likely to provide a more complete picture of PID epidemiology. National representative, future data are needed to produce accurate and precise information on the PID epidemiology needed to guide control and prevention strategies. Two areas of further work need to be addressed: a new custom monitoring system and a case-by-case definition of PID supervision.

CONCLUSIONS

Most of cases with PID seen by clinical services follow general practice. Systematic collection of timely, representative oversight data from primary care is necessary if future prevention needs are addressed. However, this study showed that the diagnostic accuracy is low. Epidemiological studies and intervention initiatives will only be effective if diagnostic accuracy is improved and standardized.

High diagnostic accuracy is essential for effective patient management. Evaluation of the evidence base shows that the most effective diagnostic criteria are the presence of low abdominal pain and the exclusion of competitive diagnoses. The simplicity of these diagnostic criteria makes it appropriate as a case-by-case definition of supervision, but unfortunately there is no specificity and sensitivity. The results of this investigation will be useful in guiding a reassessment of PID diagnostic criteria and formulating a new definition of case surveillance.

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