

PATHOGEN NEGATIVE PELVIC INFLAMMATORY DISEASE: IS IT PID?

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Background: Pelvic inflammatory disease (PID) occurs when pathogens (often sexually transmitted) ascend from the cervix to the upper genital tract. However no infectious agent is identified in up to two thirds of PID cases.^{1,2} We assessed the characteristics of PID of unknown aetiology (PID with no pathogen detected) among female sexual health clinic attendees.

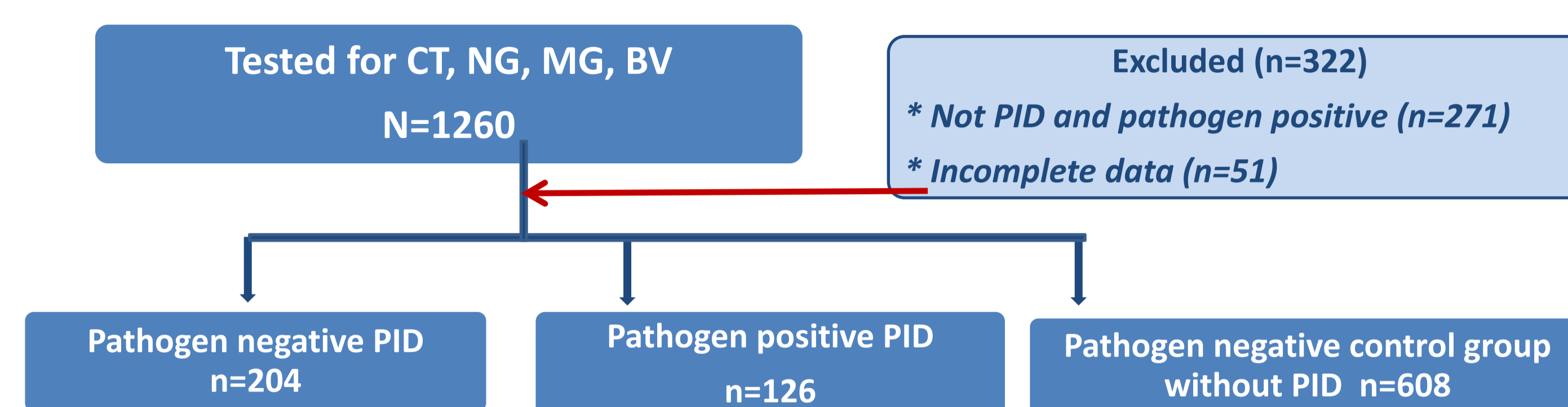
Methods

- Women aged 16-49 years (not reporting sex work) at first visit to Melbourne Sexual Health Centre (January 2006-June 2013) were eligible if tested for chlamydia(CT), gonorrhoea(NG), Mycoplasma genitalium(MG) and bacterial vaginosis(BV).
- Demographic, behavioural and clinical data, and diagnosis code were extracted from the electronic patient database.
- PID diagnosis was clinical: based on uterine, cervical motion, or adnexal tenderness in sexually active women with pelvic pain where no cause beside PID was identified. PID cases were classified as 'pathogen-negative' if testing negative for the four infections and 'pathogen-positive' if one or more infection was diagnosed.
- Vaginal inflammation was assessed by the presence of increased polymorphonuclear leukocytes (PMNL) on high vaginal swab and defined as ≥ 5 PMNL per 1000 high powered field.

Analysis

- Three analysis groups were created (figure 1):
 1. Pathogen negative PID,
 2. Pathogen positive PID, and
 3. Pathogen negative controls without a PID diagnosis
- Univariable and multivariable logistic regression with robust standard errors (to account for clustering by doctor) was conducted to identify factors associated with pathogen-negative PID compared with pathogen-positive PID, and pathogen-negative controls without PID.

Figure 1: Flow chart of the number of women in the three analysis groups



Results

- Of a total of 330 PID cases; 204 (62%; 95%CI:56%-67%) were 'pathogen-negative', and 126 were 'pathogen-positive', of whom 49.2% (95%CI:40.4-58.1) had CT, 6.3% (95%CI:2.0-10.7) had NG, 11.9% (95%CI:6.2-17.6) had MG, and 56.3% (95%CI:47.6-65.1) had BV.
- A further 608 pathogen-negative patients without a PID diagnosis comprised the control group.
- Compared with 'pathogen-positive PID', 'pathogen-negative PID' cases were older, less likely to have vaginal inflammation (AOR=0.5, 95%CI: 0.3-0.8) and less likely to report unprotected sex with non-regular sexual partners (past 3 months) (AOR=0.7, 95%CI:0.4-1.0) (table 1).
- Compared with 'pathogen-negative controls without PID', 'pathogen-negative PID' cases were more likely to have an IUD insitu (AOR=4.5, 95%CI:1.2-16.2) and to report unprotected sex with non-regular sexual partners (past 3 months) (AOR=1.4, 95%CI:1.1-1.9) (table 1).

Table 1: Associations for pathogen negative PID compared with pathogen-positive PID and pathogen-negative controls without PID

		Pathogen-negative PID (N=204)	Pathogen positive PID (N=126)	Associations for pathogen-negative PID compared with pathogen-positive PID		Pathogen negative and no PID (N=608)	Associations for pathogen-negative PID compared with pathogen-negative controls without PID	
		n (%)	n (%)	Univariable OR (95%CI)	Multivariable AOR (95%CI)	n (%)	Univariable OR (95%CI)	Multivariable AOR (95%CI)
Age group	16-29 years	165 (80.9)	111 (88.1)	1.0	1.0	454 (74.7)	1.0	1.0
	30-49 years	39 (19.1)	15 (11.9)	1.7 (1.0-3.0)	1.8 (1.0-3.2)	154 (25.3)	0.7(0.5-1.0)	0.7 (0.5-1.0)
Born in Australia	No	111 (54.4)	76 (60.3)	1.0		365 (60.0)	1.0	
	Yes	93 (45.6)	50 (39.7)	1.3 (0.8-2.1)		243 (40.0)	1.3 (1.0-1.7)	
STI contact	No	193 (94.6)	112 (88.9)	1.0		579 (95.2)	1.0	
	Yes	11 (5.4)	14 (11.1)	0.5 (0.2-1.1)		29 (4.8)	1.1 (0.7-2.0)	
IUD present	No	197 (96.6)	120 (95.2)	1.0	1.0	603 (99.2)	1.0	1.0
	Yes	7 (3.4)	6 (4.8)	0.7 (0.2-2.0)	0.7 (0.2-2.0)	5 (0.8)	4.3 (1.2-15.1)	4.5 (1.2-16.2)
>1 MSP past 3 months ^a	No	120 (58.8)	61 (48.4)	1.0		397 (65.3)	1.0	
	Yes	84 (41.2)	65 (51.6)	0.7 (0.4-1.0)		211 (34.7)	1.3 (1.0-1.8)	
>12 MSP past 12 months ^a	No	55 (27.0)	27 (21.4)	1.0		202 (33.2)	1.0	
	Yes	149 (73.0)	99 (78.6)	0.7 (0.4-1.4)		406 (66.8)	1.3 (1.0-1.9)	
Unprotected sex with non-regular MSP, past 3 months	No	127 (62.3)	64 (50.10)	1.0	1.0	430 (70.7)	1.0	1.0
	Yes	77 (37.8)	62 (49.2)	0.6 (0.4-1.0)	0.7 (0.4-1.0)	178 (29.3)	1.5 (1.1-1.9)	1.4 (1.1-1.9)
Unprotected sex with non-regular MSP, past 12 months ^a	No	67 (32.8)	34 (27.0)	1.0		260 (42.8)	1.0	
	Yes	137 (67.2)	92 (73.0)	0.8 (0.4-1.5)		348 (57.2)	1.5 (1.1-2.1)	
Vaginal inflammation	No	135 (66.2)	65 (51.6)	1.0	1.0	392 (64.5)	1.0	1.0
	Yes	69 (33.8)	61 (48.4)	0.5 (0.3-0.9)	0.5 (0.3-0.8)	216 (35.5)	0.9 (0.6-1.4)	0.9 (0.6-1.3)

STI, sexually transmitted infection; IUD, intra-uterine device; MSP, male sexual partner; a. Variables omitted from multivariable analysis due to collinearity

Conclusion: Pathogen-negative PID cases had a lower sexual risk and reduced presence of vaginal inflammation than PID cases with a genital infection detected. PID cases were more likely to have an IUD insitu, raising the possibility of detection bias.

References: 1. Simms I, et al. Risk factors associated with pelvic inflammatory disease. STI 2006;82:452-7; 2. Paavonen J, et al. Pelvic Inflammatory Disease In: Holmes K, et al, editors. Sexually Transmitted Diseases. 4th ed: McGraw Hill; 2008. p. 1017-50.

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