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SHORT REPORT
Pregnant with HIV before age 25: data from a large national study in Italy, 2001–2016

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SUMMARY

Young pregnant women with HIV may be at significant risk of unplanned pregnancy, lower treatment coverage, and other adverse pregnancy outcomes. In a large cohort of pregnant women with HIV in Italy, among 2979 pregnancies followed in 2001–2016, 9·0% were in women <25 years, with a significant increase over time (2001–2005: 7·0%; 2006–2010: 9·1%; 2011–2016: 12·2%, $P < 0·001$). Younger women had a lower rate of planned pregnancy (23·2% *vs.* 37·7%, odds ratio (OR) 0·50, 95% confidence interval (CI) 0·36–0·69), were more frequently diagnosed with HIV in pregnancy (46·5% *vs.* 20·9%, OR 3·29, 95% CI 2·54–4·25), and, if already diagnosed

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with HIV before pregnancy, were less frequently on antiretroviral treatment at conception (<25 years: 56·3%; ⩾25 years: 69·0%, OR 0·58, 95% CI 0·41–0·81). During pregnancy, treatment coverage was almost universal in both age groups (98·5% *vs.* 99·3%), with no differences in rate of HIV viral suppression at third trimester and adverse pregnancy outcomes. The data show that young women represent a growing proportion of pregnant women with HIV, and are significantly more likely to have unplanned pregnancy, undiagnosed HIV infection, and lower treatment coverage at conception. During pregnancy, antiretroviral treatment, HIV suppression, and pregnancy outcomes are similar compared with older women. Earlier intervention strategies may provide additional benefits in the quality of care for women with HIV.

Key words: Antiretroviral treatment, HIV diagnosis, HIV testing, pregnancy, women's health.

INTRODUCTION

Young women (15–24 years) are particularly vulnerable to sexually transmitted infections and HIV [1]. In this particular population, pregnancy is commonly unplanned and undesired, and quite frequently occurs in women who had never been tested for HIV [1, 2]. Age, lower therapeutic adherence, and a combination of socio-economic factors pose young pregnant women with HIV at risk of adverse pregnancy outcomes, lower treatment coverage, less stringent suppression of HIV, and vertical transmission [3]. It is therefore of importance to better define the prevalence of undiagnosed HIV infection, unplanned pregnancy, adverse pregnancy outcomes and suboptimal HIV suppression in this fragile population. To address this issue, we used data from a large national cohort of pregnant women with HIV and explored temporal trends in the proportion of women with HIV with pregnancy at young age (<25 years), and assessed in this specific group the rates of planned pregnancy, HIV diagnosis in pregnancy, antiretroviral (ARV) treatment at conception and during pregnancy, HIV viral suppression at third trimester, HIV vertical transmission, and main pregnancy outcomes.

METHODS

Data from the Italian National Program on Surveillance on Antiretroviral Treatment in Pregnancy, an ongoing observational study established in Italy in 2001, were used [4]. Only HIV-positive pregnant women are eligible for the study, and treatment of HIV infection is decided by the treating physician, usually according to national guidelines. Women provide consent based on a patient information sheet approved by the competent Ethics Committee (deliberation 578, 28 September 2001, I.N. M.I. Lazzaro Spallanzani Ethics Committee, Rome). For the current analysis, all pregnancies with known maternal age and available date of HIV diagnosis were considered eligible. The study period (2001–2016) was divided in three intervals of 5 years each (2001–2005, 2006–2010, 2011–2016), and temporal trends were analyzed using the χ^2 test for trend. Other categorical variables were compared using the χ^2 test, with odds ratios (ORs) and 95% confidence intervals (CIs) calculated. In order to adjust for potential confounders, also defined in previous analyses [4, 5], the role of young age as predictor of unplanned pregnancy and undiagnosed HIV infection was further evaluated in multivariable logistic regression analyses. Gender- and gestational age-adjusted *Z*-scores for birthweight were calculated according to recent national references [6]. Major birth defects were defined according to the Antiretroviral Pregnancy Registry definition [7]. For all analyses, P values <0·05 were considered significant. All statistical analyses were performed with the SPSS software, version 22 (IBM Corp, Released 2013, Armonk, New York, USA).

RESULTS

As of 24 February 2017, 2979 pregnancies had available information and were included in the analysis. The median age at entry in pregnancy was 33 years (interquartile range 29–36), with 9·0% (269/2979) of the women <25 of age. Younger (<25 years) and older (⩾25 years) had identical mean CD4 count levels at entry (493/mm^3 in younger women *vs.* 494/mm^3 in older women, $P = 0{\cdot}966$), but younger women were more frequently of foreign origin (68·2% *vs.* 45·6%, OR 2·56, 95% CI 1·94–3·37, $P <$ 0·001). Only a small proportion of pregnancies were planned (925/2540, 36·4%), with a significantly lower probability of planned pregnancy among younger women (23·2% *vs.* 37·7%, OR 0·50, 95% CI

Table 1. *Temporal trends (2001–2016) in pregnancy planning, diagnosis of HIV in pregnancy, and treatment coverage in mothers and infants*

	2001–2016	2001–2005	2006–2010	2011–2016	*P* value*
Age lower than 25 (%)	9·0 (269/2979)	7·0 (82/1170)	9·1 (98/1079)	12·2 (89/730)	<0·001
Pregnancy planned (%):					
Overall	36·4 (925/2540)	34·3 (346/1009)	36·7 (338/922)	39·6 (241/609)	0·032
Age lower than 25	23·2 (51/220)	17·9 (12/67)	23·2 (19/82)	28·2 (20/71)	0·154
Age 25 or older	37·7 (874/2320)	35·5 (334/942)	38·0 (319/840)	41·1 (221/538)	0·031
Diagnosis of HIV in current pregnancy (%):					
Overall	23·2 (691/2979)	23·0 (269/1170)	24·4 (263/1079)	21·8 (159/730)	0·661
Age lower than 25	46·5 (125/269)	51·2 (42/82)	44·9 (44/98)	43·8 (39/89)	0·338
Age 25 or older	20·9 (566/2710)	20·9 (227/1088)	22·3 (219/981)	18·7 (120/641)	0·410
Mothers on treatment at conception† (%):					
Overall	68·2 (1553/2277)	61·9 (555/897)	66·9 (543/812)	80·1 (455/568)	<0·001
Age lower than 25	56·3 (81/144)	42·5 (17/40)	55·6 (30/54)	68·0 (34/50)	0·016
Age 25 or older	69·0 (1472/2133)	62·8 (538/857)	67·7 (513/758)	81·3 (421/518)	<0·001
Mothers on treatment in pregnancy (%):					
Overall	96·5 (2784/2885)	95·6 (1093/1143)	96·6 (1009/1044)	97·7 (682/698)	0·017
Age lower than 25	94·7 (248/262)	93·8 (76/81)	97·9 (92/94)	92·0 (80/87)	0·565
Age 25 or older	96·7 (2536/2623)	95·8 (1017/1062)	96·5 (917/950)	98·5 (602/611)	0·003
Infant prophylaxis (%):					
Overall	97·3 (1967/2021)	95·8 (789/824)	97·8 (719/735)	99·4 (459/462)	<0·001
Age lower than 25	97·2 (172/177)	96·6 (56/58)	96·9 (62/64)	98·2 (54/55)	0·604
Age 25 or older	97·3 (1795/1844)	95·7 (733/766)	97·9 (657/671)	99·5 (405/407)	<0·001

* χ^2 for trend.
† Women with HIV infection diagnosed before pregnancy only.

0·36–0·69, $P < 0·001$). The main temporal trends in pregnancy planning, diagnosis of HIV in pregnancy, and ARV treatment coverage in mothers and infants are summarized in Table 1. The proportion of young women increased significantly over time, from 7·0% in 2001–2005 to 12·2% in 2011–2016. The proportion of planned pregnancy also increased over time, but this increase was statistically significant only in the entire group and in the subgroup of older women. The rate of HIV diagnosis in current pregnancy did not change over time, but young women were significantly more likely (46·5% compared with 20·9% in older women) to have HIV diagnosed in pregnancy (OR 3·29, 95% CI 2·54–4·25, $P <$ 0·001). Among the women with HIV already known, overall treatment coverage at conception was 68·2%, with a significant increase in recent years, from 61·9% in 2001–2005 to 80·1% in 2011–2016 ($P <$ 0·001). This significant temporal trend was present in both age groups (Table 1), but younger women were significantly less likely to be on treatment at conception (overall: 56·3% *vs.* 69·0%, OR 0·58, 95% CI 0·45–0·81, $P = 0·002$). Subsequent treatment coverage in pregnancy was almost universal, with ARV treatment administered in 96·5% of all pregnancies (details in Table 1), and in 99·2% (2177/2195) of the pregnancies that did not end in miscarriage, stillbirth, or voluntary termination (98·5% in women <25 years *vs.* 99·3% in older women, $P = 0·240$). ARV prophylaxis in infants also showed no difference by maternal age (97·2% and 97·3% in infants from younger and older women, respectively; OR 0·94, 95% CI 0·37–2·39, $P = 0·895$). The main pregnancy outcomes, reported in Table 2, showed no major differences by age group. Among the pregnancies that ended in a live birth, the two age groups had similar rate of undetectable HIV viral load at third trimester (58·2% *vs.* 65·2%, Table 2). Given the possible role of some confounders in the significant differences observed, we performed two logistic regression analyses that analyzed the role of other potential relevant cofactors as predictors of pregnancy planned and HIV diagnosis in pregnancy. Such analyses confirmed the independent role of young age as a predictor of unplanned pregnancy and undiagnosed HIV infection before pregnancy. The details of univariate and multivariate analyses for

Table 2. *Pregnancy outcomes in the two age groups*

	Overall	Age lower than 25	Age 25 or older	OR (95% CI)	*P* value*
HIV viral load <50 copies/ml at third trimester (*n*:1737), %:	64·6 (1122/1737)	58·2 (92/158)	65·2 (1030/1579)	0·74 (0·53–1·04)	0·080
Pregnancy not ending in a live birth (*n*: 2556), %	13·7 (351/2556)	12·2 (27/221)	13·9 (324/2335)	0·86 (0·57–1·31)	0·494
Pre-term delivery (<37 weeks) (*n*: 2175), %	20·4 (443/2175)	15·8 (30/190)	20·8 (413/1985)	0·71 (0·48–1·07)	0·102
Very pre-term delivery (<32 weeks) (*n*: 2175), %	2·4 (53/2175)	1·6 (3/190)	2·5 (50/1985)	0·62 (0·19–2·01)	0·426
Low birthweight (<2500 g) (*n*: 2096), %	23·3 (489/2096)	21·7 (39/180)	23·5 (450/1916)	0·90 (0·62–1·30)	0·581
Very low birthweight (<1500 g) (*n*: 2096), %	3·1 (66/2096)	1·7 (3/180)	3·3 (63/1916)	0·50 (0·15–1·60)	0·243
Small by gestational age (*n*: 1923), %†	12·2 (235/1923)	14·3 (24/168)	12·0 (211/1755)	1·22 (0·77–1·92)	0·393
HIV transmission (*n*: 1685), %	1·3 (22/1685)	2·8 (4/145)	1·2 (18/1540)	2·40 (0·80–7·18)	0·118
Birth defects (*n*: 2185), %‡	3·8 (84/2185)	4·8 (9/187)	3·8 (75/1998)	1·30 (0·64–2·63)	0·473

OR, odds ratio; CI, confidence interval.
* χ^2.
† Birthweight <10th percentile by age and gender, singletons only.
‡ Livebirths only.

Table 3. *Factors associated with planning of pregnancy and diagnosis of HIV in pregnancy in univariate and multivariate analyses*

Outcome: planning of pregnancy	Univariate analysis			Multivariate analysis (*n*: 2443)		
Predictive variables	UOR	95% CI	*P* value	AOR	95% CI	*P* value
Age (reference category <25 years)	0·50	0·36–0·69	<0·001	0·60	0·43–0·85	0·003
Foreign origin	0·59	0·50–0·70	<0·001	0·69	0·58–0·83	<0·001
HIV undiagnosed before pregnancy	0·44	0·35–0·55	<0·001	0·52	0·41–0·65	<0·001
Outcome: diagnosis of HIV in pregnancy	Univariate analysis			Multivariate analysis (*n*: 2496)		
Predictive variables	UOR	95% CI	*P* value	AOR	95% CI	*P* value
Age (reference category <25 years)	3·29	2·54–4·25	<0·001	1·88	1·35–2·61	<0·001
Foreign origin	3·88	3·21–4·71	<0·001	3·53	2·79–4·46	<0·001
No preconception counseling	35·96	20·17–64·10	<0·001	30·64	16·20–57·95	<0·001
Primigravida	2·44	2·03–2·94	<0·001	3·15	2·47–4·02	<0·001
Asymptomatic HIV disease	5·63	3·66–8·65	<0·001	4·81	2·94–7·87	<0·001

Univariate analyses, contingency tables with χ^2 test; UOR, unadjusted odds ratio; CI, confidence interval; multivariate analysis, multivariable logistic regression models; AOR, adjusted odds ratio.

these two outcomes, with adjusted ORs for age and the other covariates are reported in Table 3.

DISCUSSION

This longitudinal study provided new findings on HIV and pregnancy in young women. First, we showed that within the population of pregnant women with HIV in Italy, the proportion of younger women is increasing. This finding is consistent with the high number of new HIV infections reported by WHO in young people [1], and with other local studies that reported a recent increase in the proportion of young pregnant women with HIV [8]. We also showed

that, despite a positive temporal trend indicating increasing rates of planned pregnancy, a very high proportion of pregnancies (63%) remain unplanned among women with HIV. National data are scarce, but the rate of planned pregnancy in the general population is likely to be higher [9]. In terms of predictors, younger age and foreign origin were two strong and independent determinants of both unplanned pregnancy and diagnosis of HIV in pregnancy. This significant role of younger age and foreign origin in pregnancy planning is consistent with the marked differences reported in fertility and abortion rates between Italian and foreign women [10], and with the higher rate of induced abortion observed in younger women with HIV [11]. Overall, these findings underline the urgent need to promote more efficiently HIV testing and reproductive counseling among young [12, 13] and migrant women [14].

It has already been shown that women with HIV are less likely to receive adequate and timely prenatal care compared with women without HIV [15]. The later entry in HIV care observed for younger women indicates an even more vulnerable subgroup within a population who already receives suboptimal care. Although the analysis of maternal treatment coverage and pregnancy outcomes showed no significant differences by maternal age in all the outcomes considered, younger women, being quite commonly unaware of their HIV infection status at booking in pregnancy, were less frequently on ARV treatment at conception, as already described, with a later entry in HIV care and treatment [8]. Given the strong consequential associations that link late maternal HIV diagnosis and later start of treatment to unsuppressed HIV viral load and mother-to-child transmission, a later entry in HIV care may potentially translate in some infants infected with HIV [8, 16], and should not be therefore underestimated. In this study, the number of infants vertically infected with HIV was very low, not allowing any conclusion, but younger women had slightly lower rates of viral load suppression at third trimester, and slightly higher rates of vertical transmission.

The present findings therefore confirm the urgency of implementing as much as possible the WHO recommendations, with particular attention to promoting and enhancing HIV testing before pregnancy among young women and among foreign women [1, 17]. Women's knowledge of their own HIV-positive status is a significant predictor of family planning [18], and there is evidence that women already aware of being infected before pregnancy have an earlier attendance of antenatal care, with potential significant benefits [19]. Although HIV testing in pregnancy is extremely relevant and effective, earlier interventions may provide additional benefits to young and foreign women in terms of family planning and engagement in care. Potentially relevant strategies include promotion of testing and antenatal counseling by cross-cultural phone counseling [20], wider and better implementation of contraception counseling in pre- and post-natal maternal care [14], immediate testing in the presence of HIV indicator diseases [21], and rapid HIV testing in outpatients belonging to vulnerable/at-risk populations [22].

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DECLARATION OF INTEREST

None.

ETHICS APPROVAL

Ethics approval was obtained from the Ethics Committee of the I.N.M.I. Lazzaro Spallanzani in Rome (ref. deliberation 578/2001, 28 September 2001).

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