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Pitout JDD, Church DL, Gregson DB, Chow BL, McCracken M, Mulvey M, Laupland KB (2007). Molecular epidemiology of CTXM-producing Escherichia coli in the Calgary Health Region: emergence of CTX-M-15-producing isolates. Antimicrob. Agents Chemother. 51: 1281-1286.

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Full Length Research Paper

Demographic characteristics of stroke patients in developing countries: Example from Jordanian government hospitals

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The aim of this study was to identify for the first time, the characteristics of stroke patients in Jordan. In this retrospective study, the case records of 1,287 stroke patients admitted to Al-basher Hospital during a three-year period were reviewed. The stroke patient cohort included 60% men and 40% women. The mean age for men was 59.5±9.7 and 58.95±10.7 for women. Three quarters of all stroke patients were diagnosed as having ischemic strokes and 14% were diagnosed as having haemorrhagic. The most common risk factors were high blood pressure, diabetes and heart disease. The present data established important information about stroke characteristics in Jordanian hospitals. There was missing information in patients' records which made it difficult to calculate important epidemiological data which is necessary to plan for and provide better services for patients. This study has demonstrated the need for further research to explore reasons for inadequacies in services and to identify the best way of fully recording accurate information in developing countries.

Key words: Stroke patients, developing countries, government hospitals, stroke type, risk factors, demographic characteristics.

INTRODUCTION

Stroke is a leading cause of death and, for those who survive a stroke, the condition is a major cause of functional disablement (Bonita et al., 1990). Understanding demographic characteristics of patients is necessary in order to assess patients' needs, to improve the quality of life of patients and their careers, and to develop new services for stroke survivors (Ebrahim and Harwood, 1999). However, there are only a limited number of studies in developing countries which have investigated the demographic characteristics of stroke patients in hospitals (Bonita et al., 1997). In Jordan, there is as yet no information available relating to the stroke profile. Reports from Middle East Arabian countries (Al-Rajeh et al., 1991, 1993; Yaqub et al., 1991) where the lifestyle, religion and cultural traditions are similar to those in Jordan, indicates that stroke incidence increases with increased age and that it is higher in men than in women. Hypertension, smoking, diabetes and a trial fibrillation have also been found to be important risk factors in the incidence of stroke both in developing and developed countries.

The lack of information about stroke characteristics in developing countries including Jordan highlights the importance of demographic studies as they may provide a key to help in the planning of health care services and necessary preventive actions in a community. Thus, the present study was undertaken to establish the demographic characteristics of stroke patients in Jordan. The Hashemite Kingdom of Jordan is situated in the Middle East with an estimated population of nearly 5.7 million in 2007. Al-Basher Hospital was selected because it is the main and largest state referral general hospital in Jordan; the majority of stroke patients in Jordan are admitted to it and it maintains relatively reliable medical registers. This makes this hospital well suited for demographic study on stroke in Jordan.

METHODS

In this retrospective study, the case records of all stroke patients admitted to Al-basher Hospital, during the three-year period from 2008 to 2010 were reviewed. Al-basher Hospital is a 928 bed

Table 1. Numbers and percentages of stroke patients by age and gender at Al-basher Hospital, Amman.

Age group (years)	Male patients		Female patients	
	Number	%	Number	%
25-34	12	44	15	56
35-44	42	62	26	38
45-54	146	53	127	47
55-64	278	63	161	37
65-74	288	60	192	40
Total	766	60	521	40

tertiary care teaching hospital providing health care to a large section of Jordanian population. As the major and main hospital in Jordan, it serves as a principal referral centre for the entire Jordanian population.

The definition of stroke given by the World Health Organization (WHO) as 'rapidly developing clinical signs of focal disturbance of cerebral function, with symptoms lasting 24 h or longer or leading to death, with no apparent cause other than vascular origin' were applied (WHO, 1989). It was not possible to record stroke subtype in this study due to missing information about CT scans. In Al-basher Hospital, CT scan reports included only information as to whether the stroke was ischemic or haemorrhagic, and not the subtype.

Findings on CT scans of brain, performed within 1 week of the onset of stroke were used for classification of the type of stroke. Ischemic type was diagnosed based on typical CT scan findings of infarct or a normal CT scan when it was performed within 2 days of the onset of stroke or the presence of a potential source of cerebral emboli such as the heart or carotid artery relevant to the side of stroke (Awada, 1994). Hemorrhagic was diagnosed based on clinical and CT scan findings. Where none of these criteria were fulfilled or information was not available, the cases were classified as 'no data '. Hypertension was considered to be present if the patient was already receiving antihypertensive therapy or if the systolic blood pressure (BP) was >160 mmHg and/or diastolic BP was >95 mmHg at the time of admission and persisted even after that during the hospital stay (NCEP, 2001; TECDCM, 1999). Diabetes mellitus was considered to be present if the patient was already diagnosed and receiving medication for the same, or if at least 2 fasting blood glucose values were 7.8 mmol/L or above during the patient's hospital stay (JNCPDE, 1997).

The relevant data was retrieved from the case records of the patients and was entered on a standardized computer record form, comprising items like age, gender, CT services, stroke type, and length hospital stay, history of hypertension, diabetes mellitus, cardiac disease and stroke in the past.

RESULTS

Approximately 186,000 patients were admitted to Al-basher Hospital between 2008 and 2010; of these, 1,287 stroke patients satisfied the definition of stroke.

Age and gender

Table 1 shows the age and gender distribution of stroke patients. The stroke patient cohort included 766 men (60%) and 521 women (40%), giving a male-to-female ratio of 3:2. The mean age for men was 59.5±9.7 and 58.95±10.7 for women.

Figure 1 shows that the number of stroke patients admitted to Al-basher Hospital increased steeply with age. In the 25 to 34 age group, the number of patients who had had strokes was similar for both sexes. This number increased sharply in the 65 to 74 age group. As this figure shows, more men than women in all age groups had strokes except those aged between 25 and 34. The number of men affected by strokes peaked in the 55 to 64 and 65 to 74 age groups.

Diagnostic CT scanning

At Al-basher Hospital, three quarters of stroke patients underwent a diagnostic CT scan to help identify the type of stroke they had sustained and to ensure that necessary treatment was given as soon as possible. The mean time before stroke patients in Al-basher Hospital had their CT scan was approximately 27 days.

Classification of stroke type

Figure 2 shows that at Al-basher Hospital, about three quarters of all stroke patients were diagnosed as having ischaemic strokes and 14% were diagnosed as having haemorrhagic strokes. There was no data available for 11% of the stroke patients.

Length of stay

Figure 3 shows that the majority of stroke patients admitted to AL-basher Hospitals stayed for one week or less.

Risk factors

Figure 4 shows that the most common risk factors recorded for stroke patients in this study were high blood

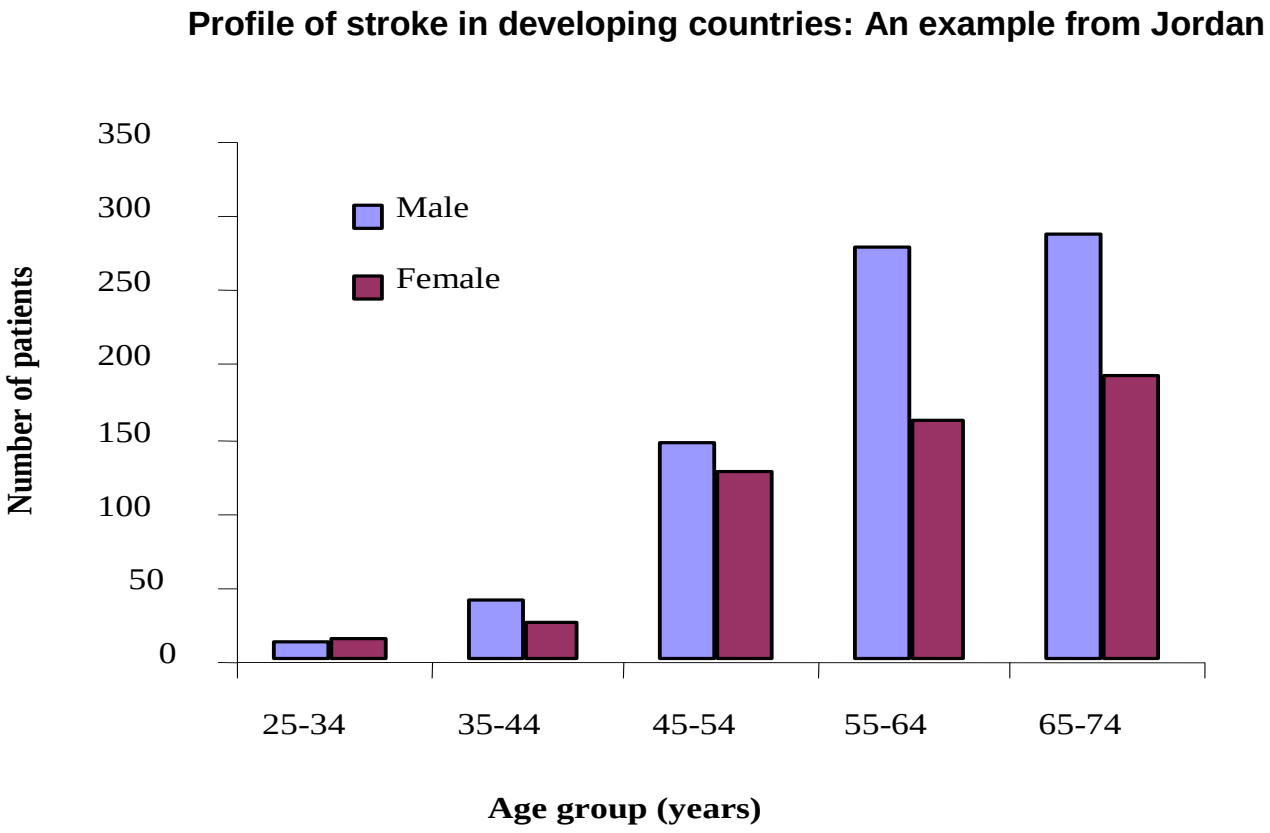

Figure 1. Stroke admissions to Al-basher Hospital (n=1287).

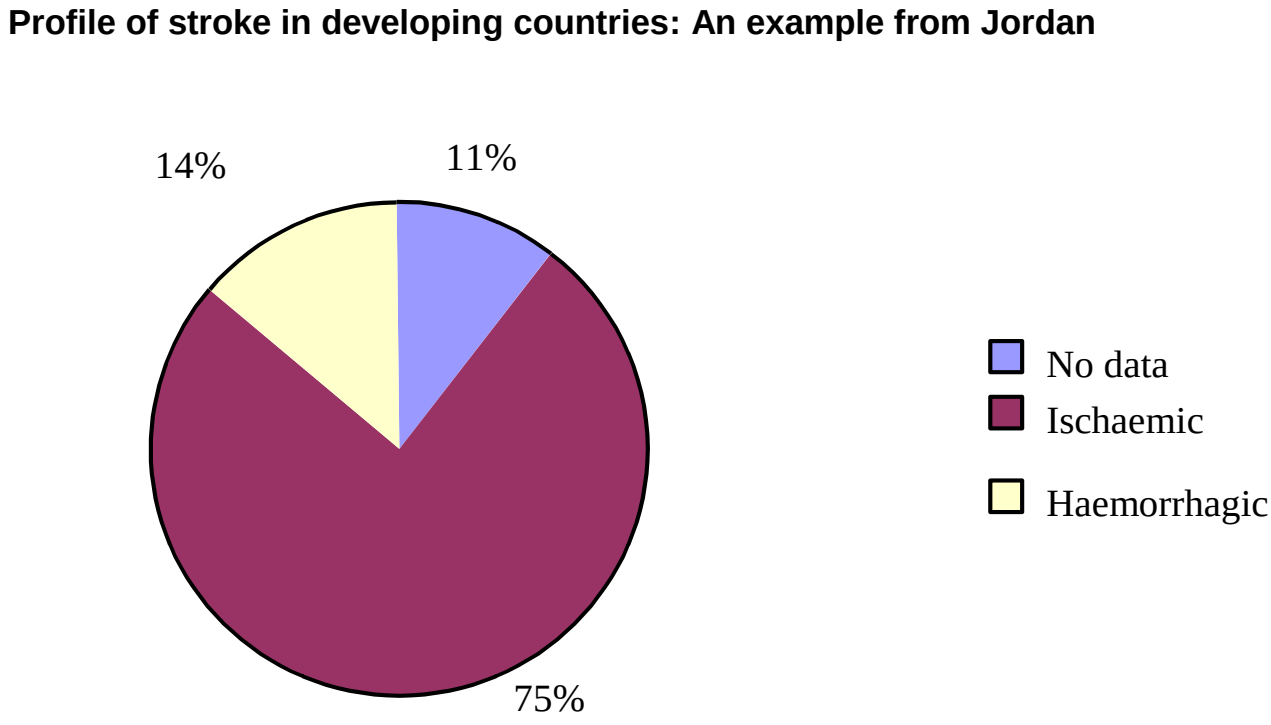

Figure 2. Classification of stroke type: Al-basher Hospital (n=1287).

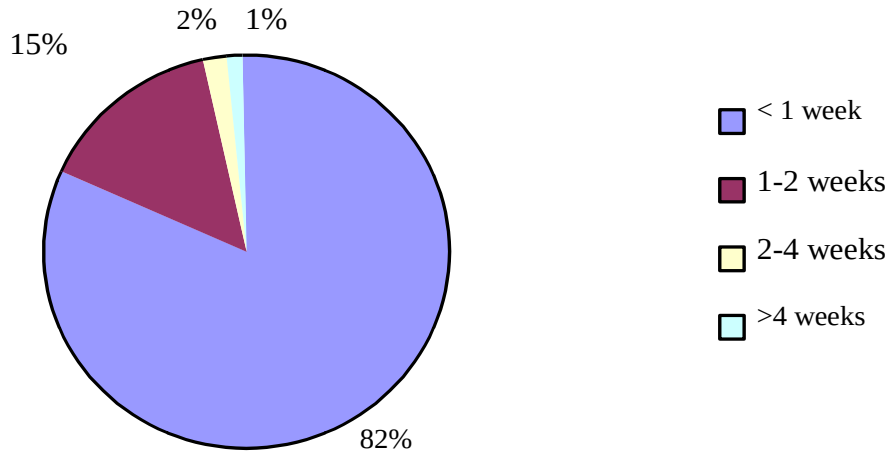

Figure 3. Length of in-patient stay for stroke patients at Al-basher Hospital (n=1287).

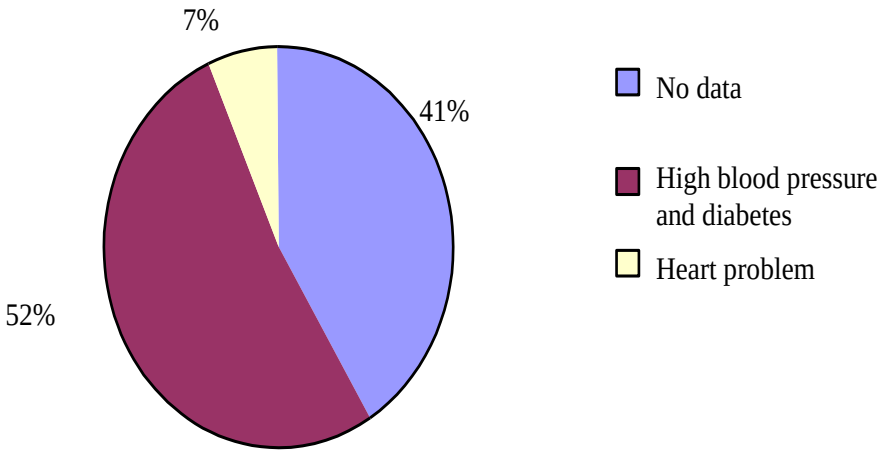

Figure 4. Risk factors for patients at Al-basher Hospital (n=1287).

pressure, diabetes and heart disease.

Stroke events

Table 2 shows that 81% of stroke occurrences were classified as first events and 17% as recurrent events. There was no information available for 2% of the stroke patients admitted to Al-basher Hospital.

DISCUSSION

The aim of this study was to identify the demographic characteristics of stroke patients admitted to state hospital in Jordan. This retrospective hospital-based study examined the records of 1,287 stroke patients who had been admitted to Al-basher Hospital in Amman-Jordan. Despite the limitations of hospital-based and retrospective studies, the findings of the study revealed very important information relating to the stroke profile in Jordanian hospitals such as age and gender, classification of stroke type, length of hospital stay and risk factors.

Age and gender

Stroke in this study affected more men than women and increased with increased age. The percentages of men

Table 2. Numbers and percentages of patients having first and recurrent strokes at Al-basher Hospital, Amman.

Age group (years)	First stroke		Recurrent strokes		Missing data (%)
	Number	%	Number	%	
25-34	23	86	3	7	7
35-44	66	97	0	0	3
45-54	232	85	22	8	7
55-64	350	80	87	20	0
65-74	366	76	104	22	2
25-74	1032	81	215	17	2

with stroke who were admitted to hospitals were about 60%. These findings were in accordance with other studies carried out in developed countries (Johansson et al., 2000; Stewart et al., 1999). These studies found that the stroke incidence rate was higher in older age groups and in men rather than in younger age groups and in women.

However, these studies used incidence rates. In the current study, it was not possible to calculate the incidence rate because in order to calculate this rate, the population in the area must be known and there should be a system where there is no duplication of registration. In the Amman area, there are four major state and 18 private hospitals and because of the health system and insurance provision in Jordan, patients can be treated at more than one hospital, leading to possible duplication of patient information.

In studies carried out in Saudi Arabia and Libya, countries where the lifestyle, religion and cultural traditions are similar to those in Jordan, the incidence rate of stroke was also higher for men than for women and stroke incidence increased with increased age (Ashok et al., 1986; El Sayed et al., 1999). The consistency of the findings of studies carried out in developed and developing countries and the current study indicate that age and gender may not be related to the cultural backgrounds of stroke patients.

Classification of stroke

The findings of this study showed that three-quarters of stroke patients admitted to Al-basher Hospital had ischaemic strokes and 14% of the patients had haemorrhagic strokes. These findings were slightly different from the findings of other studies undertaken in both developed and developing countries (Ebrahim and Harwood, 1999; El Sayed et al., 1999; Burn et al, 1997). These studies found that approximately 80% of strokes were ischaemic and 20% were haemorrhagic. Missing information in hospital records may explain the difference between the findings of these studies and the current study. There was no information available about stroke type for 11% in Al-basher Hospital.

In the current study, diagnostic CT brain scanning was used to identify the type of stroke and 72% of stroke patients in Al-basher Hospital underwent brain scans. However, the time before stroke patients had their CT scan was about 27 days, indicating that not all patients who were admitted to Jordanian hospitals underwent brain scanning and that those who did had their scans delayed. A possible reason for patients not having scans might be that many people were still not covered by health insurance, so could not afford the cost of scanning. A possible explanation for the delay in having CT scans might be that Al-basher Hospital is crowded, leading to long waiting times for scans.

The implications of not having CT scans or delays in having a CT scan are serious and can include delayed or inappropriate treatment. Both could be dangerous. Kelson et al. (1998) suggested that before treatment, accuracy of diagnosis is important, not only to define type of stroke but also to differentiate vascular from non-vascular stroke.

Length of hospital stay

The majority of stroke patients in the AL-basher Hospital stayed less than one week with an average stay of 3.1 days. This average stay is different from the average length of stay for stroke patients in developed countries; for example, the length of hospital stay for stroke patients was 95.2 days in Sweden (Holmqvist et al., 1993). The enormous difference between the average length of hospital stay in Jordan and in developed countries could be explained by different factors reported by Mawjdeh et al. (1997).

In Jordan, approximately 32% of the population are not covered by any health insurance (Suhimat, 2001), so, shorter hospital stays could be related to the financial status of the patients, leading them to request an early hospital discharge, while in developed countries such as Sweden, health and social insurance are covered by the state, so there was no worry about the cost of staying in hospital. Another possible explanation for the shorter

length of stay might be related to the quality of services in public hospitals, where crowding may lead to patients requesting an early discharge from hospital. About 20% of the patients in this study discharged themselves against medical advice. The implication of short hospital stays is that the responsibility of caring for patients at the very early stage and during the recovery stage is placed almost entirely on their families.

Risk factors

In this study, the major risk factors for stroke were found to be the combined effects of hypertension and diabetes mellitus.

This observation is consistent with studies carried out with stroke patients in countries with cultures similar to the Jordanian culture (Al-Rajeh et al., 1993; El Sayed et al., 1999). Heart disease constituted an important risk factor in this study, accounting for about 10% of all cases. In approximately 41% of stroke patients, no risk factors were found or recorded.

However, risk factors reported in other studies such as smoking, diabetes, limited physical activity; alcohol abuse and poor nutrition (Goldstein et al., 2001; Wolf et al., 1991) were not found in the current study. This does not mean that Jordanian stroke patients are free from these risk factors, but it may be that the missing information and the recording system made it impossible to identify these factors.

Recurrent stroke events

In this study, 17% of stroke patients admitted to Al-basher Hospital were classified as 'recurrent strokes'. The literature contains limited information about rates of recurrent stroke. In a Finnish World Health Organisation project, the percentage of recurrent strokes was lower than the findings of this part of the study, which was approximately 10% of stroke events (Mähönen et al., 1999). However, the Finnish study was carried out over ten years while the current study was carried out over three and the different research designs between the two studies may have influenced the findings.

A possible explanation of the different rates of recurrent stroke in these two studies could be the different health systems and cultural backgrounds of the people in these two countries. It has been suggested that the main factors associated with a higher risk of recurrent stroke are uncontrolled high blood pressure, a trial fibrillation and diabetes (Gubitz and Sandercock, 2000). The problems of access to services which can help control these factors may increase the chance of people who have had first strokes having second strokes. Due to the health care and health insurance systems in Jordan and the country's poor economic situation, patients may have difficulties accessing medical clinics and medicines, and may therefore be at high risk of recurrent stroke.

The clinical implications of recurrent stroke are important in developing care services for stroke patients because recurrent strokes leave patients with greater disabilities than a first stroke, and patients show poorer outcomes (Samsa et al., 1999). Because of the low standards of care in Jordanian hospitals and the lack of support in the community, it could be expected that the burden of recurrent stroke on families and on the community would be higher than the burden of first stroke. In order to reduce the effects and impact of recurrent stroke, health policy makers should provide better community support for carers and survivors, reduce the likelihood of recurrent stroke by providing information about preventative measures and make medication and necessary therapeutic interventions available to stroke patients.

Missing information

This study found a considerable amount of missing information in patients' medical records; there was no information about brain scanning available for 5%, about reasons for discharge for 12%, about risk factor for 41% and about classification of stroke for 11% of stroke patients admitted to Al-basher Hospital. One possible explanation for this missing information might be that in Jordan, medical records are paper-based and are kept manually and as such, lack consistency and completeness. Missing information in stroke patients' medical files may affect practice and research. In practice, as discussed earlier, the lack of information about stroke type may affect appropriate and timely intervention. Research may be affected because missing information such as correct diagnosis, date of birth and cause of death may make it impossible to calculate epidemiological data such as incidence and mortality rates. These are important indicators in planning community services for stroke patients (Ebrahim and Harwood, 1999).

Conclusion

This paper has presented a profile of stroke patients admitted to hospitals in Jordan, including stroke occurrence, accessibility to diagnostic tools such as brain scanning, length of hospital stay, and risk factors of stroke. Strokes occurred more frequently in men than in women and the risk increased with age. The major known risk factors were high blood pressure and diabetes. Comparisons with the profiles of stroke patients admitted to hospitals in other countries shows that stroke patients in Jordan stay less time in hospitals; more Jordanian stroke patients are readmitted to hospitals because of a second stroke, and Jordanian patients had difficulties accessing CT services. Furthermore, there was missing

information in patients' hospital records on the classification of stroke and the presence of risk factors.

The problems of access to services in Jordanian hospitals may lead to misdiagnosis and inaccurate intervention and, as a result, poor outcome. The missing information in patients' medical records made it difficult to calculate important demographic data which is necessary to plan for and provide better services for patients.

In order to provide better services, health policy makers need first, to make available all necessary diagnostic tools to enable appropriate intervention and second, to make sure that health professionals who work with stroke patients document all available information in their patients' medical records. Because family carers may take on the responsibility of caring in the early stages, when patients need a lot of attention and support, health professionals need to provide them with suitable information to allow them to play their role effectively and safely. This study has demonstrated the need for further research to explore reasons for inadequacies in services and to identify the best way of fully recording accurate information in developing countries.

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Full Length Research Paper

Female genital mutilation in Southeast Nigeria: A survey on the current knowledge and practice

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Female genital mutilation (FGM) has been recognised as a major reproductive health problem and a dehumanising practice that has resisted change especially in developing countries. The study reviews the current knowledge and practice of FGM in Southeast Nigeria. This is a questionnaire based descriptive study involving women of reproductive age in Abakaliki, South east Nigeria. A semi-structured questionnaire was distributed to 320 women by simple random sampling. Information sought included the socio-demographic characteristics, and personal information on FGM with regards to knowledge and practice. Two hundred and sixty (81.3%) were appropriate for analysis. The mean age of the respondents was 28.6 years ± 5.4 SD. Most had formal education, with tertiary education contributing 60.8%. A high percentage was aware of FGM, and the problem associated with it was 91 and 72%, respectively. Half of the respondents (49.6%) were genitally mutilated while almost the same number (47.7%) affirmed that FGM is still practised today. Eighty – two percent do not support FGM but were not doing anything about it and 36% were not aware of any problem associated with FGM. The prevalence rate of FGM of 50% is high. Though most did not support the practice, nothing has been done to change the practice. Serious advocacy, government support and legislation are needed to curb this serious health problem as significant proportions are still not aware of the problems of FGM.

Key words: Female genital mutilation, prevalence rate, knowledge, practice, Abakaliki, Southeast Nigeria.

INTRODUCTION

The practice of Female Genital Mutilation (FGM) is regrettably persistent in many parts of the world. This occurs commonly in developing countries where it is firmly anchored on culture and tradition, not minding many decades of campaign and legislation against the practice (Onuh et al., 2006; WHO, 2008). Female genital mutilation comprises any procedure involving partial or total removal of the external female genitalia or other injury to the female genital organs for cultural, religious or other non-therapeutic reason (WHO, 2008; WHO, 1996). The World Health Organization (WHO) estimates that between 100 and 140 million girls and women worldwide are presently living with female genital mutilation and every year about three million girls are at risk (WHO, 2008). In Africa, it is estimated that about 92 million girls from 10 years of age and above have undergone female genital mutilation (WHO, 2010). FGM is practised in one form or the other in 28 African Countries including Nigeria. It is also practised in a few countries on the Arab Peninsula, among minority community in Asia, and among migrants from these areas who have settled in Europe, Australia and North America (WHO, 2010; Toubia, 1994). In Nigeria, the prevalence of female genital mutilation averages 50% but ranges from 0% in parts of Kogi, Fulani and Ogun States to 100% in Benue and Kebbi States (Onuh et al., 2006; Toubia, 1994). With an overall national prevalence of 50%, Nigeria has the highest absolute number of genitally mutilated women throughout the world (Okonofua, 1998).

Female genital mutilation is classified into four major types (WHO, 1996). The most common type of the female genital mutilation is type 2 which account for up to 80% of all cases while the most extreme form which is type 3 constitutes about 15% of the total procedures

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(WHO, 1996; Oduro et al., 2006). Types 1 and 4 of FGM constitute the remaining 5%. The consequences vary according to the type of FGM and severity of the procedure (Onuh et al., 2006; Oduro et al., 2006).

The practice of FGM has diverse repercussions on the physical, psychological, sexual and reproductive health of women, severely deteriorating their current and future quality of life (Oduro et al., 2006; Larsen, 2002). The immediate complications include: severe pain, shock, haemorrhage, urinary complications, injury to adjacent tissue and even death (Onuh et al., 2006; Oduro et al., 2006; Larsen, 2002). The long term complications include: urinary incontinence, painful sexual intercourse, sexual dysfunction, fistula formation, infertility, menstrual dysfunctions, and difficulty with child birth (Akpuaka, 1998; Okonofua et al., 2002; Oguguo and Egwuatu, 1982). The physical and psychological sequelae of female genital mutilation have been well highlighted in many literatures (Onuh et al., 2006; Oduro et al., 2006; Badejo, 1983; Klouman et al., 2005; ACHPR, 2003; Ibekwe, 2004). Recently, there has been serious concern on the increased rate of transmission of Human Immunodeficiency Virus (HIV) following this practice (WHO, 1996; Klouman et al., 2005). The practice is also a violation of the human rights of the women and girl child. FGM categorically violates the right to health, security and physical integrity, freedom from torture and cruelty, inhuman or degrading treatment and the right to life when the procedure results in death. It constitutes an extreme form of violation, intimidation and discrimination.

Despite its numerous complications, this harmful practice has continued unabated, not withstanding that Nigeria ratified the Maputo Protocols and was one of the countries that sponsored a resolution at the 46th World Health Assembly calling for the eradication of female genital mutilation in all nation (Klouman et al., 2005; ACHPR, 2003; Idowu, 2008).

In Ebonyi State, South-East Nigeria, FGM is viewed differently from their wide indigenous cultural inclinations and traditional beliefs. This study surveys the current opinion of women of reproductive age in the capital city of Ebonyi State, Abakaliki, South-East Nigeria on their knowledge and practice of FGM.

METHODOLOGY

The study was carried out in the Obstetrics and Gynaecology Department of the Federal Medical Centre, Abakaliki, Ebonyi State, Southeast Nigeria. Women who attended antenatal and postnatal care were recruited for the study between June to September 2010.

The hospital is located in Abakaliki the Capital city of Ebonyi State and receives referrals from all parts of the State and neighbouring States of Benue, Enugu, Cross River and Abia. Ebonyi State created in 1996 from the old Abakaliki division of Enugu State and old Afikpo division of former Abia State has 13 Local Government Areas (LGA's), one urban, one semi-urban and the rest rural. It has estimated population of about 4.3 million and occupies a land mark of 5935 km. About 75% of the population dwell in the rural areas with farming as their major occupation.

The study was conducted using a semi structured questionnaire which was administered using simple random sampling. The questionnaire was pretested, and validated by a pilot study. Written consent was obtained from the respondents before the study. The questionnaires were administered by trained nurses and doctors over a period of four months. Information sought included the socio-demographic characteristics, personal information on FGM with regard to the respondents' knowledge on the past and current practice of FGM and their suggestions on the best way to deal with the problem.

A total of 320 questionnaires were given out to the highly motivated respondents (antenatal and postnatal women) at the clinics, of which 260 were fit for analysis.

Data collation and analysis were done using Epi-Info 2007 Statistical Analysis Software package (CDC-Atlanta USA).

The study was certified by the Ethics and Research committee of the hospital. There was no conflict of interest.

RESULTS

Of the 320 questionnaires distributed, 260 (81.25%) were appropriately filled and returned for analysis.

Table 1 shows the socio-demographic characteristics of the respondents. The mean age of the respondents was 28.6 ± 5.4 years with range of 15 to 40 years. Majority of the respondents (61.5%) were in the age bracket of 20 to 29 years. 90% (294) of them were married while 10% (26) were not married. The literacy level was quite high in this study. About 60.8% had tertiary education while 3.8% had no formal education. Majority were civil servants (41.2%) by occupation. Regarding parity, 126 (48.5) were para 14, nulliparae 117 (45%), while 16 (6.2%) were grandmultiparae.

Table 2 shows the degree of awareness, attitude, and practice of FGM by respondents. Greater percentage (90.5%) was aware of FGM. Similarly, a significant percentage (71.5%) was aware that FGM is being discouraged. On the other hand, 166 (63.8%) were aware of the side effects or problems associated with FGM, 94 (36.2%) did not know of any side effects or problems associated with FGM. Forty-six (17.7%) of the respondents supported FGM, while 214 (82.3) did not support FGM.

Approximating half of the respondents (49.6%) were circumcised at various stages of their life giving a prevalence rate of 49.6%. On the current practice of FGM, 136 (53.3%) asserted that FGM is not currently practiced while 124 (47.7%) opined that FGM is still being currently practised. Majority 231(88.80%) of the respondents would not want their wife circumcised if they were to assume the responsibility of being a man, while a lower percentage 29 (11.20%) will still advocate that their wife should be circumcised if made a man.

Table 3 shows reasons for persistent practice of FGM among those who affirmed that FGM is still practiced currently. Out of the 260 respondents analysed, 124 (47.7%) affirmed that FGM is still practised currently. However, there were 145 reasons for the persistent practice of FGM. This was because multiple entries were

Table 1. Sociodemographic characteristics of respondents.

Variables	No (260)	% (100)	C/I
Age (years)			
10 – 29	5	1.9	0.6 – 4.4
20 – 29	160	61.5	55.3 – 67.5
30 – 39	88	33.8	28.1 – 39.9
≥ 40	7	2.9	1.1 – 5
Marital status			
Single	26	10	7.2 – 15.5
Married	234	90	85.6 – 93.1
Separated	Nil	Nil	Nil
Widowed	Nil	Nil	Nil
Education status			
No formal education	10	3.8	1.9 – 7.0
Primary	11	4.2	2.1 – 7.0
Secondary	81	31.2	25.6 – 37.2
Tertiary	158	60.8	54.5 – 66.7
Occupation			
Trader	30	11.5	7.9 – 16.1
Civil Servant	107	41.2	35.1 – 47.4
Student	47	18.2	13.6 – 23.3
Corper	3	1.2	0.2 – 3.3
Applicant	4	1.2	0.4 – 3.9
Other*	69	26.5	2.1 – 32.3
Parity			
None	117	45	38.8 – 51.3
1 – 4	126	48.5	42.2 – 54.7
≥ 5	16	6.2	3.6 – 9.8

* Represent farmers, seamstress, hairdressing and fashion designers.

Table 2. Degree of awareness, attitude and practice of FGM.

Variables	N (260)	% (100)	C/I
Are you aware of FGM			
Yes	235	90.5	86.1 – 93.7
No	25	9.5	6.3 – 13.9
Are you aware that FGM is being discouraged			
Yes	186	71.5	65.6 – 76.9
No	74	28.5	23.1 – 34.4
Are you aware of any side effect or problem associated with FGM			
Yes	166	63.8	57.7 – 69.7
No	94	36.2	30.3 – 42.3
Do you support FGM			
Yes	46	17.7	13.3 –22. 9

Table 2. Contd.

No	214	82.3	77.1 – 86.7
Were you circumcised			
Yes	129	49.6	43.4 – 55.9
No	131	50.4	44.1 –56. 6
Is FGM still currently practiced			
Yes	124	47.7	41.5 – 54.0
No	136	52.3	46.6 – 38.5
If you are a man, will you want your wife circumcised			
Yes	29	11.20	7.6 – 15.6
No	231	88.80	84.4 – 95

Table 3. Reasons for persistence of the practice of FGM among the 124.

Variables	No (145)**	% (100)	C/I
Culture	32	22.07	9.1 – 17.7
Tradition	22	15.17	4.1 – 14.9
Ignorance	25	17.24	6.3 – 13.9
Reduced sexual desire	6	4.14	0.9 – 5.0
Lack of awareness	2	1.38	0.1 – 2.8
Easy vaginal delivery	1	0.69	0.0 – 2.1
Do not know	57	39.31	46.0 – 58.5

Table 4a. Reasons adduced for supporting the practice.

Reasons	No (64)**	%
Increased female hygiene	9	14.06
Reduced sexual desire	14	21.88
Safe delivery	5	7.81
Risk to baby (could kill baby)	5	7.81
Tradition/Culture	21	32.81
Do not know	10	15.63

allowed. Majority 57 (30.30%) did not know the reason for the persistence of FGM. Culture, ignorance and tradition were significant reason for the practice of FGM with proportion of 32 (22.07%), 25 (17.27%) and 22 (15.17%), respectively. Other reasons for the persistence of FGM were reduce sexual desire - 6 (4.14%), lack of awareness - 2 (1.38) and easy vaginal delivering -1 (0.69%).

Table 4a shows reasons adduced for supporting FGM. Tradition and culture 32.81% were the main reasons given for supporting FGM. This was followed by 21.88% who affirmed that it will reduce sexual desires. Other reasons given for supporting FGM include increased female hygiene -14.06%, safe delivery - 7.81% among others. A significant percentage (15.63%) of the respondents did not know the reason but they still supported FGM.

Table 4b shows reasons adduced by the respondent for not supporting FGM. Out of the 260 respondents analyzed, 214 (82.3%) did not support FGM but the adduced reason given for not supporting FGM, were 277. This was because multiple entries were allowed. Majority 20.22% did not support the practices because it could lead to difficulty labour and delivery. Others were bleeding - 18.05%, religious reasons - 12.64%, barbaric (uncivilized) - 10.47%, reduced sexual satisfaction - 8.30%, culture and tradition - 7.22%, painful coitus - 5.42%, infection - 4.70%, death - 3.97%, fistula formation e.g VVF - 2.89%, genital scarification - 2.17%, HIV/AIDS - 1.81%. Small percentage of the respondents (2.17%) did not know the reason for not supporting FGM.

Table 4b. Reason adduced for not supporting the practice of FGM.

Reason	No (277)**	%
Difficult labour/delivery	56	20.22
Bleeding	50	18.05
Not biblical	35	12.64
Barbaric (uncivilized)	29	10.47
Culture/tradition	20	7.22
Painful coitus	15	5.42
Infection	13	4.70
Death	11	3.97
Fistula formation (v v f)	8	2.89
Genital scarification/keloid	6	2.17
HIV/AIDS transmission	5	1.81
Do not know	6	2.1

Table 5. Knowledge of side effects of FGM.

Reason	No (216)**	% (100)
Difficult labour/delivery	68	31.48
Bleeding	48	22.22
Infection	28	12.96
Painful coitus	15	6.94
Reduced sexual satisfaction	16	7.41
Fistula formation (v v f)	12	5.56
Risk to baby	9	4.17
HIV/AIDS transmission	8	3.70
Death	12	5.56

Table 5 illustrates the knowledge of side effects of FGM among those who are aware of side effects or problems associated with FGM. Of the 260 respondents analyzed, 166 (63.8%) were aware of side effects or problems associated with FGM. Difficult labour and delivery 31.48% were the main problem noted to be associated with FGM. Others were: bleeding (22.22%), infection (12.96%), reduced sexual satisfaction (7.41%), and painful coitus (6.94%). The remaining reasons in descending orders include death - 5.56%, fistula formation - 5.56%, risk to baby - 4.17% and HIV/AIDS - 3.70%.

Table 6 illustrates how best to prevent the practice of FGM. Majority (31.25%) of the respondents did not know how best to prevent the practice of FGM. Increasing literacy level (20.40%) was given as the best way to prevent practice of FGM. Others include awareness campaign (19.08%), mass media (10.53%), health education (7.24%), capital punishment (5.92%), Government intervention (3.29%) and advocacy (2.30%).

In this study, 218 (83.8%) of the respondents expressed their desire to ban FGM if they are in position of authority whereas 42 (16.4%) will still advocate for it if placed in a position of authority.

Table 6. How best to prevent the practice of FGM.

Variables	n (304)**	% (100)
Public enlightenment	62	20.40
Awareness campaign	58	19.08
Mass media	32	10.53
Health education	22	7.24
Capital punishment	18	5.92
Government intervention	10	3.29
Advocacy	7	2.30
Do not know	95	31.25

** Multiple answers allowed.

DISCUSSION

Female genital mutilation remains an unending public health problem in many societies and cultural groups despite the concerted efforts and laws forbidding the practice. The prevalence rate of 49.6% in this study laid credence to this. This figure is approximately equal to the national average of 50% but higher than the 37% in the South-south (Briggs, 2002). The implication of this finding is that the prevalence rate of female genital mutilation is rather on the increase. This figure is also higher than other regional findings in Nigeria of 48% South-West, 16% North-Central, 3% North-West and 2% North-East (Briggs, 2002).

The socio-demographic analysis indicates that the mean age of the female respondents was 28 ± 5.4 years.

Surprisingly, a higher number of respondents attained tertiary education (62%), a factor that ideally would have reduced the prevalence rate. However, it was not possible to ascertain the educational status of their parents as the circumcision was done in infancy in almost all the respondents.

A higher percentage of the respondents were aware of female genital mutilation and the problem associated with it (91 and 72%, respectively) and yet 48% affirmed that FGM is still currently practiced. This has been sustained by various reasons which included: culture, tradition, ignorance, misconception (reduced sexual desire, easy vaginal delivery) among others. This is in conformity with the findings in Somalia where FGM connote symbol of female womanhood and an instrument for the control of female promiscuity/sexuality (Ntiri, 1993). Okonofua et al. (2002) in a cross sectional study, affirmed that FGM has nothing to do with attenuating sexual feeling or desire and that it may predispose women to adverse sexual outcomes. This study also collaborates with the findings by Meyers et al. (1985), Caldwell et al. (1997) and Osifo and Eubuomwan, (2009) which supports that FGM is shrouded on culture and tradition.

Eighty-two percent of the respondents do not support FGM yet 50% of them were circumcised. Thus, it may be assumed that most FGM would not have been performed

if they were given options of making a choice by themselves. Most of the reasons adduced for supporting FGM sounded absurd but they reflect the level of ignorance, unenlightenment and myth (most of which are enshrined in the culture and tradition), that are still prevalent in our society. These reasons were also noted in previous studies (Osifo and Eubuomwan, 2009; Anuforo et al., 2004; Odimegwu et al., 2001; Oyeledum et al., 1997; WHO, 2000; Ragheb et al., 1978). Haemorrhage, infection, difficult labour have been noted as major problems associated with FGM in other studies (Osifo and Eubuomwan, 2009; Oyeledum et al., 1997; Yount and Abraham, 2007).

Despite the national, international, governmental and non-governmental organisations (NGOs) efforts to eliminate this practice, it has persisted in many communities today. The practice remains highly prevalent in 28 countries across Africa and the Middle East. Public enlightenment, awareness campaign, mass media, health education and advocacy on the negative health implications of FGM are suggested as best ways of eliminating the practice.

Some respondents in this study suggested capital punishment and Government intervention as best ways of curbing the practice. In Nigeria, there is no Federal Law against FGM unlike in France, Canada, Belgium, Ghana, Sweden and United Kingdom among others. In late 1999, the advocacy efforts of the Edo State government in Nigeria government resulted in the successful passage of state legislation making FGM punishable by fine and/or 6 months imprisonment. Capital punishment (prosecution) has been adopted by four out of the 28 Countries where FGM is prevalent (Onuh et al., 2006).

In Conclusion, there is great awareness on FGM and the side effects/problems are well known. However, the practice is still persistent in Abakaliki South-East Nigeria, sustained perhaps by culture, tradition and misconceptions. Serious advocacy is vital to stop the menace of this problem. The society and the nation should look for strategies to curb the practice of FGM. These may include education of the girl child, woman empowerment, and legislation against FGM. All government, non-governmental organisation (NGOs), supporters of reproductive health issues are called upon to initiate authentic programmes that will end this menace of reproductive ill-health.

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Full Length Research Paper

Diagnosis of invasive squamous cell carcinoma: Impact of opportunistic screening in >70 year-old women in Trentino (Northern region of Italy)

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The objective of this paper is to assess the value of opportunistic screening in diagnosis of invasive squamous carcinoma found in >70 years old women in Trentino (Italy). From 2007 to 2010, the Cytopathology Section of Institute of Anatomic Pathology of Rovereto Hospital have been examined; 28589 opportunistic pap-smears was performed in all histological specimens with diagnosis of low, high grade intraepithelial lesions and invasive cervical carcinoma. 111 cases (0.38%) of cervical intraepithelial neoplasia-3-squamous cell carcinoma have been identified in 28589 opportunistic pap smears. The cytological diagnosis of cervical intraepithelial neoplasia-3 was performed in three cases, confirmed by cone biopsy in two patients with presence of HPV-16 and HPV-58. The diagnosis of squamous cell carcinoma was performed with pap-smear in three patients; non-keratinizing squamous cell carcinoma was diagnosed with pap-smear in two cases. An estimated 2,927 new cases of cervical cancer occurred in Italy in 2005. 34.64% of cases has been diagnosed in >65 years old women. Consequently, early diagnosis is necessary to the decrease mortality, morbidity and direct management costs of disease. The present study should be support the screening policy to perform Pap test every 3 years until aged 69 years, independently to sexual activity.

Key words: Invasive cervical carcinoma, opportunistic screening, cancer in elderly women.

INTRODUCTION

Since 1996, Italian national guidelines have recommended to regions, the implementation of organised screening programmes for cervical cancer. These recommendations, largely based on European guidelines, include personal invitations to women aged 25 to 64 years for a Pap smear every three years, a monitoring system, and quality assurance for each phase of the programme. Surveys designed to assess the level of implementation of organised programmes in Italy and to collect process indicators have been conducted by Italian Group for Cervical Screening since 1997 (Ronco et al., 2007). Their results have been published by the Osservatorio Nazionale Screening (ONS) (National Centre for Screening Monitoring) since 2002. Since 1993, in Trentino province (North Italy) an organized screening (OrS) exists for women aged 25 to 65. The target population comprises of 146737 women. In the period 1993 to 2006, the pap-smears of OrS were examined in the Institutes of Anatomic Pathology and Cytopathology of S. Chiara Hospital Trento and Rovereto Hospital. Since 2007, the Cytopathology Section of Institute of Anatomic Pathology of Rovereto Hospital has examined only pap-tests of Opportunistic Screening (OpS), that is, left to the woman's initiative. OpS may be considered as all pap-test performed outside an OrS program. For example, some women have pap-test at their doctor's office during their physical examination, independent of personal letter invitation of OrS. An estimated 2,927 new cases of cervical cancer occurred in Italy in 2005 (crude incidence 9.7/100,000; world age-standardized incidence 6.0/100,000). 1014 (34.64%) has been diagnosed in >65

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Table 1. Opportunistic screening: decades of age of 28.589 women in the period 2007 to 2001.

Total number opportunistic pap-tests	≤ 20 years (%)	21 – 40 years (%)	41 – 70 years (%)	> 70 years (%)
28.589	892 (3.2)	11240 (39.3)	14848 (51.9)	1620 (5.6)

years old women (AIRTum: I Tumori in Italia – Rapporto, 2006; ISTAT, 2005). Early diagnosis is necessary to decrease the direct management costs of disease. In the present study, we have examined the screening histories, treatment, human papillomavirus (HPV) detection of cervical intraepithelial neoplasia(CIN)3- invasive squamous cell carcinoma in >65 years-old women, diagnosed in the period 2007 to 2010 with opportunistic pap-tests in the Cytopathology Section of Institute of Anatomic Pathology of Rovereto Hospital.

MATERIALS AND METHODS

The pap-smear was performed by gynaecologist to the woman's initiative. An experienced cytopathologist (TP) whose diagnostic experience exceeds 20 years have examined all abnormal smears and 10% of the normal smears were previously observed by a senior cytotechnologist. Colposcopic and cervical biopsies were taken by an experienced colposcopist (in practice for more than 10 years) and review by a senior colposcopist as part of the routine.

Consensus polymerase chain reaction (PCR) and direct sequencing of PCR products (DNA HPV typing) were used to determinate the type or types of human papillomavirus (HPV) in histological specimens.

RESULTS

The distribution of women for decades is reported in Table 1. Between the women >64 years-old with CIN3-squamous carcinoma, the cytological diagnosis all were > 70 years-old and were not invited to OrS because of age, > 64 years. We have reported in Table 2, the age, histological diagnosis, treatment and HPV detection of 8 patients over 70 years, with CIN 3 squamous cell carcinoma cytological diagnosis.

DISCUSSION

There are approximately 493,000 new cases of invasive cervical cancer worldwide and 274,000 women die of the disease annually (Waterhouse et al., 1982). The highest rates are reported in Latin America, where cervical cancer accounts for half of all female cancers. The annual incidence of invasive cervical cancer in women between 30 and 50 years of age in high-risk areas is 1/1,000. In developing countries throughout the world, cervical cancer is a major public health problem and is one of the leading causes of death (Carmichael et al., 1986). From an epidemiological point of view, an HPV infection meets the criteria as a causal agent for cervical cancer (Schiffman et al., 1993; Bosch et al., 2002). Having sexual contact is the main source of HPV infection. HPVs are a group of host specific DNA virus with remarkable epithelial cell specificity. More than 120 different HPV genotypes have been identified and almost 45 subtypes, isolated from the low genital tract, have been grouped into high- and low- risk HPV types, considering their risk potential to induce an invasive cervical cancer. In a recent study, Muñoz et al. (2003) classified HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82 as high risk viruses, detectable in high grade squamous intraepithelial lesions or in invasive cancer; HPV 26, 53 and 66 as potential high risk with a not well known oncogenic potential; while types 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and 89 can be considered as viruses with low oncogenic risk and they can be isolated from low grade epithelial lesions. Functionally, high risk HPV-types infection contributes to carcinogenesis and tumour progression predominantly through the action of two viral oncogenes, E6 and E7. The E6 protein exerts rapid degradation of p53, in corporation with E6-associated protein (E6-AP), via ubiquitin-mediated proteolysis pathway (Scheffner et al., 1993; Huibregtse et al., 1993). The E7 protein mediates the release of the E2F transcription factor from pRb-E2F complex (Nevins, 1992). Mutational analysis of HPV 16 E6 protein revealed that a certain level of the activity to degrade p53 is required for E6 to manifest its transforming function (Nakagawa et al., 1992). The p53 mutations are the most frequent genetic abnormalities found in a wide variety of human malignant tumours (Harris, 1993). Once DNA damage occurs, p53 protein is induced and arrests cells in the G1 phase to enhance DNA repair (Kuerbitz et al., 1992), or triggers apoptosis following DNA damage (Lowe et al., 1993). These functions of p53 protein are important to maintain the genomic integrity. Mutant p53 proteins are devoid of these functions, because they lose the ability of DNA contact or destabilize the structure of the core domain (Cho et al., 1994). In this way, once p53 is mutated, DNA damage is fixed and subsequent genetic rearrangement progress may be putative mechanisms to initiate cancer. Thus far, exceptionally low prevalence (0 to 6%) of the p53 mutations had been documented in cervical carcinomas (Fujita et al., 1992; Choo and Chong, 1993; Helland et al., 1993; Paquette et al., 1993; Miwa et al., 1995). The p53 protein in cervical carcinoma is thought to be inactivated presumably due to complex formation with HPV E6 oncoprotein. The most common member of the high-risk group is HPV 16, which accounts for more than 60% of all cervical cancers. The high- risk types account for more than 95% of all cases of cervical

Table 2. Age, treatment, histological diagnosis, HPV detection in women over 70 years-old with CIN3-squamous cell carcinoma.

S/no. of patient	Age	Treatment	Histological diagnosis (pT)	HPV finding
1	81	Hysterectomy with bilateral salpingo-oophorectomy	CIN3	HPV16
2	82	Cone biopsy	CIN3	Negative
3	71	Cone biopsy	CIN3	HPV58
4	79	Cone biopsy + radiotherapy	Keratinizing squamous cell carcinoma NOS	Negative
5	75	Hysterectomy with bilateral salpingo-oophorectomy	Non keratinizing squamous cell carcinoma (pT1b1)	Negative
6	82	Biopsy	Keratinizing squamous cell carcinoma NOS	Negative
7	72	Biopsy + radiotherapy	Keratinizing squamous cell carcinoma NOS	HPV58
8	75	Hysterectomy with bilateral salpingo-oophorectomy + radiotherapy	Non keratinizing squamous cell carcinoma (pT1b1)	Negative

NOS = not other specified.

cancer. One of the main differences between high- and low-risk types is the possibility of integration in the genome. Approximately 1% of the high-risk HPV types and only 0.1% of the low-risk HPV types will lead to the development of cervical cancer (Ferlay et al., 2001). In our case, HPV 16 and HPV 58 were detected in two cases of CIN3 and HPV 58 and in one case of squamous cell carcinoma. In one case of CIN3 and in 4 cases of squamous cell carcinoma, the HPV type has been not detected. Two hypotheses may be made. There is a subset of squamous cell carcinomas that is unrelated to HPV. The other hypothesis takes into account that HPV 16 is only integrated in 72% of all invasive cervical cancers (Walboomers et al., 1999). The finding of the absence of HPV 16 DNA integration in some carcinomas implies that integration is not always required for malignant progression, but does not exclude the importance of HPV integration in the initiation of cervical cancer. Hypothetically, after the development of a carcinoma, the abnormal clone could lose the viral DNA. HPV 18, on the other hand, shows 100% integration.

In light of recent studies demonstrating that mutation of p53 gene was found in over 20% of the patients with vulvar carcinoma (Lee et al., 1994; Milde-Langosch et al., 1995), a disease of elderly women and a known HPV- related malignancy, Nakagawa et al. (1999) analysed mutation of the p53 gene in 46 women with cervical carcinomas at the age of 60 or more (mean; 71 years, range; 60 to 96 years). Of the 46 patients, 41 had squamous cell carcinoma and five had adenocarcinoma. Point mutation of the p53 gene was detected in 5 out of 46 (11%) cervical carcinomas: 1 of 17 (6%) samples associated with high-risk HPVs (HPV 16 and HPV 18) and 4 of 27 samples (15%) with intermediate-risk HPVs, whereas no mutation was found in 2 HPV negative cases. Although falling short of statistical significance reduces the strength of the conclusion, data presented by Nakagawa et al. imply that p53 gene mutations may constitute one pathogenetic factor in cervical carcinoma affecting elderly women. To clarify the age-related genetic events in cervical cancer in elderly (>65 years) women, Saito et al. (2000) have analyzed for HPV typing via polymerase chain reaction, the expression of p53, the 66 tissue specimens obtained from patients with stage Ib-IIb cervical carcinoma.

Of this group, 50 women aged 64 years and younger were designated as the younger group (mean age 46.7), and 16 women aged 65 years and older were designated as the older group (mean age 67.6)

The prevalence of HPV DNA was higher in the younger group than in the older group (84.0 vs. 50.0%) as was the detection rate of HPV 16 (44.0 vs. 6.3%). In contrast, HPV 18, 33, 52, 58 were frequently detected in older patients. The positive rate of p53 overexpression in the older group was similar to that in the younger group (46.7 vs. 48.8%). There was no significant difference in the incidence of lymph node metastasis, histology, and the distribution of clinical stage between the two groups.

EGFR and Cox-2 overexpression have been reported in many neoplasms (Tsujii et al., 1995; Tsujii et al., 1997). To find information on invasive squamous cervical carcinoma in the elderly,

Giordano et al. (Giordano et al., 2011) have analyzed 110 invasive squamous cervical carcinomas obtained from 2 groups of patients for HPV status

Table 3. Organised cervical cancer screening programmes in Italy: value of some process indicators in Trentino region between 2006 to 2009(National Centre for Screening Monitoring).

Process indicator	Trentino			
	2006	2007	2008	2009
Nominal extension (%)	30	30.1	29.8	29.6
Number of invited woman	43.455	45.104	44.852	42.249
Adhesion rate of invited women (%)	36.2	37	53.2	48.0
Inadequate citology (%)	5.7	5.5	5	4.4
Colposcopy recommendation (%)	1.3	1.3	1.2	1.3
Compliance colposcopy with referral for ASCUS+	78.5	79	76	82.8
Standardised DR°for cytologyc lesions CIN2+	2.4	3.2	2.4	3.3
PPV for CIN2+ of ASCUS+ referred to colposcopy	23.9	31.5	28.3	35.3

by polymerase chain reaction study, for immunohistochemical EGFR, Cox-2 expression, and clinicopathologic features.

In this study, 64 women 60 years or younger were designated as the younger group and 46 who were 61 years or older were designated as the older group. The HPV status and the expression of Cox-2 and EGFR in the younger and older women were compared and correlated with the grading, staging neoplasm, lymph nodal status and overall survival.

The number of neoplasms with higher staging was significantly greater than those in the younger women. The mortality was higher in the older group than in the younger patients. In the elderly, the presence of HPV DNA in 65% of cases, and in the absence of sexual activity, could be due to reactivation of latent HPV infection.

In accordance with data provided by the literature, this finding demonstrated that HPV DNA can be detected in elderly women and can be associated with cervical carcinoma (Baay et al., 2001; Garcia-Pineres et al., 2006; Subbaramaiah and Dannenberg, 2007). Thus, it is possible that, in elderly women, HPV presence, in the absence of sexual activity, could be due to reactivation of latent HPV infection because of impairment of host immunologic response (Mubiayi et al., 2002).

Inadequate immunologic control of HPV infection resulting in viral persistence is likely an important determinant of risk of progression to cervical neoplastic disease. Immunologic competence has been reported to decrease with aging (81 to 93). Garcia Piňeres et al. (2006) examined the association between lymphoproliferative responses to antigens/mitogens and persistent HPV infection in women older than 45 years. Women included in this study were participants in a 10,000-woman population-based cohort study of cervical neoplasia in Costa Rica. Women older than 45 years and HPV DNA positive at a screening visit were selected as cases (n = 283). Garcia Piňeres et al. selected a comparably sized control group of HPV DNA–negative women, matched women, matched to cases on age and time since enrollment (n = 261). At an additional clinical visit, women were cytologically and virologically rescreened and cervical and blood specimens were collected. Proliferative responses to phytohemagglutinin (PHA), influenza virus (Flu), and HPV16 virus-like particle (VLP) were lower among women with persistent HPV infection than for the control. The decreases were most profound in women with long-term persistence and were only observed for the oldest age group (≥65 years). The results of this study indicate that impairment in host immunologic responses is associated with persistent HPV infection.

Since 1993, at least 7 studies have described the screening histories of women with invasive cervical cancer (Ciatto et al, 1993; Kenter et al., 1996; Stuart et al., 1997). In 2007, the almost 30% of the Italian population not included in organised programmes is partly the result of an implementation process still in progress in some regions in Southern Italy, but mainly of a very limited or completely absent implementation in a few regions in Northern Italy. In 2007, 121 active programmes had a target population of 11,872,810 women, corresponding to 71.8% of Italian women aged 25 to 64 years compared to 69% in 2006. During 2007, 39.8% of invites women were screened compared to 38.5% in the previous year. The last report of National Centre for Screening Monitoring as been published in 2008 and various process indicators of all regions have been described with exclusion of Liguria. Only 39.7% of invited women were screened, compared to 39.8% in the previous year. The data of Trentino Region has been reported in Table 3. The data of other Italian regions has been described in Table 4. The nominal extension varied from 8% (Puglia 2007) to 65.9% (Basilicata 2009), the inadequate cytology from 0.8% (Valle D'Aosta 2008) to 12.1% (Molise 2008). The main examined process indicators have been not reported in all the regions. In conclusion, the data of National Centre for Screening Monitoring provides information regarding the deluded performance of the organized screening programmes

Table 4. Organised cervical cancer screening programmes in Italy: Value of some process indicators in single regions between 2006-2009 (National Center for Screening Monitoring)

Process indicator	Abruzzo				Basilicata			
	2006	2007	2008	2009	2006	2007	2008	2009
Nominal extension (%)	33.5	20.2	23.8	20.88	64.6	54.9	54.4	65.9
Number of invited woman	118.054	73.981	88.974	74.607	111.808	96.613	95.476	112.961
Adhesion rate of invited women (%)	32.9	18	31.5	21.5	36.1	36.9	33.4	33.2
Inadequate citology (%)	2.4	3.2	3.9	4.2	2.2	3	1.8	1.5
Colposcopy recommendation (%)	3.7	4.3	4.5	5.2	2.1	4.3	2.4	2.5
Compliance colposcopy with referral for ASCUS+	60.4	68.7	77.2	85.3	95.8	68.7	97.1	96.9
Standardised DR°for cytologyc lesions CIN2+	2.5	3	4.2	4.8	1.1	1.1	0.9	1.0
PPV for CIN2+ of ASCUS+ referred to colposcopy	16.2	10.8	12.1	10.7	5.5	3.5	4.3	4.3
	Campania				**Emilia Romagna**			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	14.9	17	18.5	22.0	31.4	30.8	33.4	32.0
Number of invited woman	241.649	283.007	285.593	335.561	377.409	379.162	409.376	394.285
Adhesion rate of invited women (%)	26.1	27	27.2	25.2	50.8	56	56.5	57.6
Inadequate citology (%)	2.6	2.6	2.7	1.8	1.7	2	2	1.7
Colposcopy recommendation (%)	1.8	2.3	1.6	1.9	2.9	2.7	3.1	2.9
Compliance colposcopy with referral for ASCUS+	63.9	40	63.4	55.3	83.2	85.9	88.8	88.8
Standardised DR°for cytologyc lesions CIN2+	1.3	1. 4	1.5	0.9	3.8	4	4.4	4.3
PPV for CIN2+ of ASCUS+ referred to colposcopy	11.7	12.8	17.2	11.0	15.7	17.9	16.4	16.4
	Lazio				**Lombardia**			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	22.1	24.2	23.3	27.0	27.1	29.7	25.7	30.7
Number of invited woman	303.896	299.466	360.688	375.511	154.165	164.979	198.728	235.119
Adhesion rate of invited women (%)	21.8	31.3	30.3	25.5	41.5	41	39.7	42.0
Inadequate citology (%)	1.9	2.6	3.9	4.3	2.4	2.5	2.4	2.3
Colposcopy recommendation (%)	2.4	2.7	2.7	2.3	1.4	2	1.9	1.9
Compliance colposcopy with referral for ASCUS+	86.6	91.3	87.6	92.9	83.9	93	86	87.8
Standardised DR°for cytologyc lesions CIN2+	1.8	2. 4	2.7	3.2	3	4	4	3.5
PPV for CIN2+ of ASCUS+ referred to colposcopy	10.2	12.3	12	15.4	27.0	21.5	22.3	18.0

Table 4. Contd.

Process indicator	Molise				Piemonte			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	18.6	-	21.5	29.1	27	30	31.8	30.9
Number of invited woman	15.908	-	23.459	24.850	330.188	371.226	396.661	383.010
Adhesion rate of invited women (%)	14.4	-	19.3	21.5	42.9	43	44.7	44.9
Inadequate citology (%)	6.3	-	12.1	6.7	2.6	3	3.2	3.0
Colposcopy recommendation (%)	2.2	-	2.5	2.7	1.9	2	2	2.4
Compliance colposcopy with referral for ASCUS+	37.1	-	63.1	48.2	91.6	92.2	90.5	91.8
Standardised DR°for cytologyc lesions CIN2+	0.62	-	1	0.35	2	2.2	2.3	2.5
PPV for CIN2+ of ASCUS+ referred to colposcopy	7.7	-	5.9	2.9	15.1	17.2	17.2	15.8

	Sardegna				Sicilia			
Nominal extension (%)	**2006**	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Number of invited woman	24.6	20.4	26.4	23.1	24.6	21.1	21.2	16.8
Adhesion rate of invited women (%)	35.368	29.329	74.765	86.556	126.905	131.256	133.590	121.224
Inadequate citology (%)	23.7	31.4	33.7	42.3	29.1	25.4	19.7	19.8
Colposcopy recommendation (%)	5.8	6	6.1	7.2	3.5	0.3	1.9	3.4
Compliance colposcopy with referral for ASCUS+	5.6	5.7	3	3.2	3.2	3.8	4	4.3
Standardised DR°for cytologyc lesions CIN2+	93.1	8 8.2	91.1	86.3	73.4	81	83.9	80.5
PPV for CIN2+ of ASCUS+ referred to colposcopy	4.5	5.7	4.2	4.5	2.6	3.1	3	3.7

	Toscana				Umbria			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	29.8	31.3	29.9	28.5	29.3	23.5	31.5	32.7
Number of invited woman	303.307	319.444	309.365	296.965	73.206	58.556	78.215	81.980
Adhesion rate of invited women (%)	46.6	48	49.6	49.7	47.1	58.2	47.5	48.1
Inadequate citology (%)	2.1	1.8	1.5	1.5	3.4	1.3	2.3	2.9
Colposcopy recommendation (%)	1.6	1.5	1.5	1.5	2	1.6	1.6	1.0
Compliance colposcopy with referral for ASCUS+	77.6	81.3	82.7	83.3	70.7	66.1	78	70.1
Standardised DR°for cytologyc lesions CIN2+	2.9	2. 8	3	3.2	4.2	2.4	4.2	3.6
PPV for CIN2+ of ASCUS+ referred to colposcopy	25.1	24.2	23.9	23.8	29.1	22.6	34.2	52.7

Table 4. Contd.

Process indicator	Valle d'Aosta				Veneto			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	32.6	28	26.7	32.0	24.1	24.4	25.7	25.8
Number of invited woman	11.486	9.728	9.478	11.378	315.619	321.378	346.496	353.688
Adhesion rate of invited women (%)	63.8	59.4	73.8	59.5	43.8	44.8	41.8	46.9
Inadequate citology (%)	4.5	1	0.8	1.5	4.7	5.4	5.4	5.4
Colposcopy recommendation (%)	4.5	2.4	1.6	2.9	2.8	3	3.1	2.7
Compliance colposcopy with referral for ASCUS+	94.1	93.9	95.2	95.6	91.6	92.3	91.6	91.0
Standardised DR°for cytologyc lesions CIN2+	2.5	3. 8	1.6	2.7	2.9	2.8	3.3	3.4
PPV for CIN2+ of ASCUS+ referred to colposcopy	12.9	20.8	13.9	11.2	13.3	13.1	14.0	15.0
	Friuli Veneziagiulia				**Marche**			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	-	25.2	29.4	27.1	31.8	32.7	33.4	32.3
Number of invited woman	-	86.085	100.548	93.166	134.799	140.035	142.600	139.135
Adhesion rate of invited women (%)	-	56.2	59.2	56.7	36.2	35.2	40.6	41.6
Inadequate citology (%)	-	6.0	4.1	5.3	1.1	2.0	1.7	1.4
Colposcopy recommendation (%)	-	2.1	3.0	2.1	1.8	2.0	2.0	1.9
Compliance colposcopy with referral for ASCUS+	-	88.0	85.8	99.9	79.7	84.7	82.5	86.6
Standardised DR°for cytologyc lesions CIN2+	-	4.6	4.4	4.3	1.05	2.1	1.7	2.7
PPV for CIN2+ of ASCUS+ referred to colposcopy	-	24.7	17.3	20.0	12.1	17.1	17.7	20.6
	Alto Adige (Sudtirol)				**Calabria**			
	2006	**2007**	**2008**	**2009**	**2006**	**2007**	**2008**	**2009**
Nominal extension (%)	13.4	26.1	24.3	-	24.2	35.6	23.8	25.6
Number of invited woman	18.542	37.699	34.871	-	94.105	162.164	117.597	145.294
Adhesion rate of invited women (%)	34.0	32.2	33.5	-	25.0	24.4	23.9	23.5
Inadequate citology (%)	0.75	0.85	1.8	-	2.3	3.6	2.8	3.9
Colposcopy recommendation (%)	-	-	-	-	2.2	2.7	2.7	3.0
Compliance colposcopy with referral for ASCUS+	-	-	-	-	75.5	81.7	64.4	69.6
Standardised DR°for cytologyc lesions CIN2+	-	-	-	-	2.24	1.3	1.7	0.8
PPV for CIN2+ of ASCUS+ referred to colposcopy	-	-	-	-	9.5	6.3	11.2	4.0

Table 4. Contd.

Process indicator	Puglia			
	2006	2007	2008	2009
Nominal extension (%)	-	8.0	9.9	19.3
Number of invited woman	-	41.094	105.599	205.443
Adhesion rate of invited women (%)	-	36.2	17.2	28.3
Inadequate citology (%)	-	3	4	4.4
Colposcopy recommendation (%)	-	4.4	1.2	1.2
Compliance colposcopy with referral for ASCUS+	-	45.9	59.2	40.7
Standardised DR°for cytologyc lesions CIN2+	-	0.3	0.7	-
PPV for CIN2+ of ASCUS+ referred to colposcopy	-	1.6	9.2	-

The data of Liguria region have not been reported.

programmes for cervical cancer. The distinction between OpS and OS screening has not been done. Ricciardi et al. (2009) examined the direct cost of managing invasive cervical cancer in Italy. An estimated 2,927 new cases of cervical cancer occurred in Italy in 2005. The estimated numbers of new cases by FIGO stage were: FIGO I, 1,927; FIGO II, 556; FIGO III, 259; and FIGO IV, 185. Costs for the most frequent procedures were estimated as: €6,041 for radical hysterectomy or other surgery; € 4,901 for radio-chemotherapy; € 1,588 for brachytherapy; and €3,795 for palliative chemotherapy. Mean management costs for incident cases (including 10 years follow-up) were estimated at: FIGO I, € 6,024; FIGO II, € 10,572; FIGO III, € 11,367; FIGO IV, € 8707; and € 5,854 for the terminal phase (1 month). The total direct management cost was estimated at € 28.3 million per year. For the reason that the 34.64% of invasive cervical carcinoma has been diagnosed, in >65years old women it is necessary to consider the extension of screening programs after 65 years. With regard to screening histories of invasive cervical carcinoma, in Italy there are no published studies, of our knowledge, with exception of OrS programme of Friuli Venezia Giulia. In Italy, the complete screening history of women diagnosed with invasive cervical cancer has been performed only in Friuli Venezia Giulia – North-eastern Italy. In these regions, an OrS was initiated in 1999, targeting women aged 25 to 64 years, who are invited to have a pap-test every 3 years. The screening histories of Cervical Intraepithelial Neoplasia (CIN)3 - squamous cell carcinoma in >65 years-old women may be made with study of OpS, because the OrS offers a free-of-charge pap-test every 3 years to all women aged 25 to 64 years.

Zucchetto et al. (2010) have examined the screening histories of 438 women with invasive cervical cancer diagnosed in Friuli Venezia-Giulia between 1999 and 2005. 82 cases (49.7%) were found in >65 years-old women. 165 (37.7%) women were not screening. 69 (15.8%) women were not invited to OrS because of age >65 years old. Histological type and HPV detection of invasive cervical cancers has been reported. The study of Zucchetto et al. (2010) shows that the lack of screening among older women and of compliance with organized programs among women in the target population are the main limitation in cervical cancer secondary prevention. The results of Zucchetto et al. are in agreement with research conducted in northern Europe. Bos et al. (2006) analysed the screening history of 3.175 women with invasive cervical cancer diagnosed in the years 1994 to 1997 in the Netherland. 57% of 3175 women with invasive cervical cancer had no previous smears. Given to the high proportion of women with invasive cervical cancer older than 64 years at diagnosis, the possibility of inviting them to have at least one Pap smear in life after 64 years should be taken in consideration. In according to American Cancer Society Guidelines for the early detection of cancer and the guidelines of other national regional screening programme, women 70 years of age or older who have had 3 or more normal Pap-test in a know and no abnormal Pap-test results in the last 10 years may choose to stop having Pap-test. According to National Cervical Screening Program the current policy of screening women of

New Zealand is to continue organized regular screening until aged 69 years with pap-test every three years if the women have ever been sexually active remain in place. The National Cervical Screening Program of Australian Government believes that at age 70 women should consult with their doctor about whether they need to continue to have a regular Pap smear.

In conclusion, the present study support the screening policy to perform Pap test every 3 years until aged 69 years, independently to sexual activity because 34.64% of invasive cervical carcinoma has been diagnosed in > 65 years old women. Consequently, it is necessary to early diagnose to the decrease to mortality, morbidity and direct management costs of disease.

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Full Length Research Paper

Adolescent fertility in selected countries of Latin America and the Caribbean

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This article analyzes the advantages and disadvantages of different sources of quantitative data to measure teenage pregnancy in Latin American and the Caribbean countries. Previous studies discuss how low education, poverty, family background, low expectation of the girls about their future promote the increases in adolescent pregnancy observed in Latin American countries in the last decades. This study provides a comparison of descriptive data on socio-economic and demographic characteristics of girls 15 to 19 years old and specific fertility rate for this group in selected countries in the region, using descriptive analysis of data from demographic and health surveys and from censuses, with emphasis on differences in adolescent fertility and pregnancy and other related indicators by education level, ethnic characteristics, work and access to health services. Results highlight these differences among and inside countries. Internal inequalities and disadvantages in education, labor opportunities, access to health services and poverty are related to higher rates of adolescent motherhood. Differences among countries are linked to the structure of opportunities for youth in rural and urban areas. Finally, the study put emphasis in the importance of increasing the coverage of civil and health registration and health services in less developed countries, to integrate information from different sources, and to generate managerial information for local governments to implement policies to improve the access and quality of health services provided and the register of adolescent motherhood, preventing unwanted adolescent pregnancy and fertility, and to offer an adequate care and protection for teenage girls and their children.

Key words: Adolescent, fertility, pregnancy, reproductive health, census, surveys, civil, health registration.

INTRODUCTION

Adolescent fertility, development and welfare

The largest ever generation of adolescents in history is approaching adulthood in a rapidly changing world, aspiring to a better future. Educational attainment is one of the main policy levers available to lift people out of poverty (Kepinger et al., 1995; Gupta and Leite, 1999; Singh, 2000; Gokce, 2006). Delaying first births can improve the quality of life and educational and employment opportunities for young women, and it is a major long-term factor in reducing the total fertility rate, while social, emotional and economic costs associated with high adolescent pregnancy and fertility rates are considerable, particularly for families and youth, but also for the countries. In the case of adolescents, several studies identified support systems such us family, peers and school mediating the context and individual determinant factors to get pregnant early (Lipovsek et al., 2002; Pereira at al, 2005; Francisco, 2008).

However, some girls and their families who face limited life prospects may see early pregnancy or marriage as a cultural value, or as a form of economic and social security. Without education or employable skills, pregnant girls may be forced to drop out of school and are poorly prepared to take on the responsibilities of childrearing, while facing diminished income prospects.

In Latin America and the Caribbean, the most unequal region in the world, adolescent fertility rates remain constant or even have increased in some countries and periods, while fertility is consistently decreasing in all the other age groups of women. Moreover, early pregnancy is closely correlated with poverty (Baumgartner, 2009;

Gomes, 2007; Magnani et al., 2001). Improvements in data to analyze adolescent pregnancy and fertility are necessary, since data is insufficient, collected mainly from surveys, which sample sizes are insufficient to adequately know the situation of a scarce phenomena, prevalent in a small population group: Adolescent mothers. Moreover, civil registration is incomplete, and poorest adolescents are likely to deliver at home and without the support of trained personnel, and their children are likely not to be registered.

MATERIALS AND METHODS

The method used in this article is descriptive, using and analyzing data from demographic health surveys and censuses from selected countries of Latin America and the Caribbean region. The descriptive analysis on differences in adolescent fertility and pregnancy and other related indicators are presented through the proportions and levels of these events, and particularly the high rates of adolescent fertility by education level, ethnic characteristics, work, poverty and access to health services. Results highlight these differences among and inside countries. However, the discussion of the data presented and of their limitations to analyze events few frequents in smaller groups of the population sample, such as teenager pregnancies and intervals. For example, the number and proportions of adolescents in the total female population of the sample is small, and in surveys with a smaller number of cases, their classification in relevant variables such as a the proportion of pregnant adolescents by individual age, the distribution of married number of children ever born, and the birth interval do not have enough cases to be adequately analyzed. Surveys limitations, such as timing, cross-sectional data and the insufficient number of cases should be overcome with local, daily and integrated information, from censuses, school, health and register services, to integrate the set of information in managerial data bases.

RESULTS

Results from recent surveys in selected countries of Latin America and the Caribbean

Latin American population is very young, and the number of women in reproductive ages doubled between the 1990s and 2010. Although total fertility rate have decreased, the number and proportion of teenage births have been constant, due to the momentum of population growth.

Data from the most recent Demographic Household Surveys indicated that the highest rates of adolescent fertility in the region are observed in the youngest teenagers, in Nicaragua, Guatemala, Honduras, Venezuela, Dominican Republic and El Salvador.

At the time of most recent surveys in selected countries, mothers 15 to 19 varies from 28.0% of the total of teenage girls in Dominican Republic in 2007 (21.8% of adolescent mothers with one child and 6.2% with two children) to 16.1% in Colombia (2010), 14.4% in Bolivia (2008), 11.3% in Guyana (2007), and 10.7% in Peru (2010) (Table 1).

Taking into account only married adolescents, the wide majority of them were already mothers: In Dominican Republic, 66.5% of them had at least one child ever born (49.7% had one child and 16.8% had two children). In Bolivia, 67.9% of married teenagers were mothers (52% with one child and 15.9% with two); in Colombia 63.9% of married adolescents were mothers, and in Guyana they were 53.0%. Data from Table 1 show also the limits of health and fertility surveys to analyze trends in smaller groups, such as married adolescent mothers, who represent less than 40 cases in Guyana and Dominican Republic.

Another risk factor for mothers and children is the very early age of teenage mothers. In Dominican Republic, motherhood occurs in high proportions, at 15 years old; 7.8% of teenager were mothers, and this rate surpassed one out of five teenagers at age 17, when adolescent fertility rates increased considerably to 29.2% at 16 and 36.5% at 17 years old. Until this age, the Dominican girls have a similar pattern to the Guyanan girls. However, due to the shorter birth interval in Dominican Republic, at 18 years old more than a half of the girls were already mothers in this country, while in Guyana only 25% were already mothers at 18.

However, these data should be carefully analyzed, due to in most of the countries there are less than 20 cases of adolescent mothers with a second or more children or pregnancy (Table 1).

In Bolivia and Colombia, only girls aged 18 years have fertility rates above 20% (23.5 and 27.6%, respectively); and in Peru only at 18 years old 19.8% of the girls were mothers, and at 19, 33.5% of them had children.

Birth intervals

The length of time between two successive births is an important public health indicator, since short birth intervals indicate elevate risks of death and morbidity for mothers and children. The ideal length of time between two successive live births is at least 24 months. However, in these Latin American countries, about one out of five teenage mothers had another baby in less than 17 months after the previous child.

This very short and risky birth interval occurred in a significant proportion of births: 28.2% in Bolivia, 25.0% in Colombia, 19.2% in Dominican Republic and 16.1% in Guyana.

A particular and more worrying pattern occurs in Dominican Republic, where girls start early to have children with high rates and with a very short interval to have a second pregnancy and child before the age 19. The most similar pattern is Bolivia, but Bolivian girls started motherhood later than Dominican girls.

In the other extreme, Peruvian girls are mothers with less frequency and have more births within marriage, with longer intervals, and have fewer children before 19 years, suggesting that they adopt family planning.

Table 1. Distribution of teenage mothers, married teenage mothers, pregnant teens and birth intervals.

Parameter	Guyana 2007	Peru 2010	Bolivia 2008	Colombia 2010	Dominican Republic 2007
Percent distribution of women (15 to 19 years) by number of children					
N	***456***	***4278***	***3518***	***9100***	***378***
0	88.7	89.3	85.7	84.2	71.7
1	10.0	9.3	11.8	13.6	21.8
2 and above	1.3	1.4	2.6	2.2	6.2
Percent distribution of married women (15 to 19 years) by number of children					
N	***60***	***480***	***472***	***1249***	***110***
0	47.0	34.2	31.9	36.1	32.5
1	43.7	54.1	52.0	52.0	49.7
2 and above	9.3	11.6	15.9	11.9	16.8
Mean number of children ever born	0.6	0.8	0.9	0.8	0.9
Mean number of living children	0.6	0.8	0.8	0.8	0.8
Birth Intervals (months)					
N	***6***	***65***	***100***	***214***	***26***
7-17 month	-	16.1	28.2	20.5	(19.2)
18-23 month	-	30.6	37.0	33.4	(26.1)
24-35 month	-	38.0	24.7	34.2	(35.1)
36 month and above	-	15.4	10.2	11.9	(19.6)
% of women pregnant at ages between 15 and 19 years (years)					
N	***456***	***4278***	***3518***	***9100***	***378***
15	4.0	2.4	5.1	5.2	7.8
16	13.1	5.1	8.6	9.6	29.2
17	32.6	11.9	18.0	19.1	36.5
18	25.3	19.8	23.5	27.6	54.2
19	20.2	33.5	37.1	38.4	56.1

Source: DHS Measures.

Social inequalities and teenage motherhood

Important socio-economic differences are observed in the percentage of women who have begun childbearing early, according to their place of residence, education and income level.

In Colombia, Bolivia and Peru, the percent of adolescent mothers was much higher in rural areas (26.7, 24.7 and 19.3%, respectively), compared to urban (17.2, 14.4 and 11.2%, respectively). Guyana was a special case, since teenage fertility rates were very similar in the Capital, Georgetown, and in rural areas (13.4 and 14.0%, respectively) (Table 2).

Social differences were more impressive comparing levels of education and income. In Colombia and Dominican Republic, around a half of not educated teenage girls or those with primary education were already mothers; but after secondary teenage fertility rates decreased to 17.9% of girls with secondary and 10.6% of those with higher education in Colombia. In Dominican Republic, rates persisted high even among more educated adolescents: Around 40% of girls with secondary education and 18.5% of those with higher education were already mothers.

In Peru and Bolivia, one out of three adolescents with primary education was mothers. These percents were three times higher compared to mothers 15 to 19 with secondary education, and five times higher than those with the highest level of education. In these countries, inequalities are more impressive, in part due to the levels of teenage fertility deeply decreased among more educated girls, compared to those with completed primary; while in Colombia, education only makes difference to start motherhood for girls who completed secondary, and in Dominican Republic the rates of motherhood only reduce importantly after girls achieved more than secondary education.

A similar trend is observed according to poverty level: Among the poorest adolescent (lowest quintile of income), motherhood is four or five times more frequent,

Table 2. Social characteristics of adolescents who were already pregnant or Mothers.

Parameter	Peru 2010	Bolivia 2008	Colombia 2010	Dominican Republic 2007	Guyana 2007
Social characteristics- Adolescents, 15 to 19 years old who were already pregnant or mothers					
Area of residence					
N	***4278***	***3518***	***9100***	***378***	***456***
Urban	11.2	14.4	17.2	-	13.4
Rural	19.3	24.7	26.7	-	14.0
Total	13.0	28.6	19.5	-	13.8
Level of education					
No education	-	-	55.0	-	
Primary	33.8	32.0	46.5	50.7	
Secondary	11.5	12.6	17.9	40.0	
Higher	6.7	4.3	10.6	18.5	
Level of income					
Inferior quintile	22.4	31.2	29.5	48.3	
Second quintile	19.0	22.9	27.0	36.7	
Middle quintile	12.3	17.7	19.0	16.0	
Forth quintile	10.2	16.3	13.5	15.9	
Superior quintile	4.0	7.8	7.4	0.0	
Employment- Total of adolescents between 15 to 19 years old					
Employment					
n			**9100**		**456**
Currently employed	38.8	38.3	18.5	-	21.0
No currently employed	15.3	10.6	15.3	-	5.7
Not employed for the last 12 months	45.9	51.5	66.2	-	83.5
Studying	-	-	-	-	46.6
Housework, child care	-	-	-	-	18.7
Labor sector					
n			**3076**		**391**
Professional technical	4.5	2.2	2.5	-	16.9
Clerical	4.7	6.1	9.3	-	26.3
Sales and services	35.1	33.7	76.3	-	28.3
Skilled	5.1	9.5	5.0	-	-
Domestic elementary	19.1	15.7	-	-	18.1
Agriculture	28.5	32.0	5.4	-	3.6

Source: DHS Measures.

compared to those in the higher quintile. The highest inequality is observed in Dominican Republic and Colombia, where even the second quintile of income was riskier compared to the middle and further; while in Bolivia and Peru the most important gap is for girls between the inferior and second quintile of income.

Employment among teenagers 15 to 19 years old

Taking into account all the teenagers 15 to 19 years old, the Bolivians have the lowest level of education, compared to girls of the other selected countries. Bolivian and Peruvian girls have also higher rates of employment, 38.8% of them were employed, most of them were working in sales and services or in agriculture, and many are engaged in domestic work.

In the Caribbean countries, Dominican teenage girls have a very low level of education, compared to Guyana. In this last country, girls were more involved in professional labor sectors, such us sales and services, clerical and technical positions.

Table 3. Number of physicians and number of births attended by qualified personal.

Parameter	Doctor	Nurse technician	Midwife	Relatives	No attention	Health service	House	Other
Bolivia	69.8	5.4	3.0	21.2	0.4	72.1	27.4	0.5
Peru	79.4	4.5	9.9	5.7	0.5	84.4	15.2	0.4
Colombia	92.1	2.5	3.6	1.8	0.0	95.7	4.1	0.2
Dominican Republic	70.7	18.2	0.6	-	9.9	95.6	4.4	0

Source: DHS Measures.

In spite of these sub-regional differences, in Bolivia, Peru and Guyana, the percent of teenage girls involved in domestic work does not have large difference, since in all these countries, between 16 and 19% of them were engaged in household chores.

In Guyana, the survey provides additional information: 21.0% of teenage girls were working, but 46.6% were studying, and 18.7% were doing housework and child-care. Taking into account that in Guyana only 11.3% of the female adolescents are already mother or pregnant, this information indicate that adolescents were not dedicated only to care for their own children but also children of other.

Health services

Access to health services is considered a potential element for prevention and attention of adolescent pregnancy and fertility. In Bolivia, 78.4% of women 15 to 19 years old are not affiliated in any contributive social security system; in Peru 48.1% of them are uncovered, as well as 12.9%in Colombia. However, governments provide public health services to unaffiliated population, which explains that the vast majority of births occur in health services and are attended by a doctor or a nurse.

In Colombia and Dominican Republic more than 95 percent of the births of adolescents 15-19 occur in health services and are attended by a trained personal. In Peru 84 percent of adolescent births occur in health services and are attended by trained personal, and in Bolivia these percents are 72.1 and 75.2, respectively. (Table 3)

Censuses and census surveys

Censuses are the primary source of data on population by age group, small areas and demographic changes over time, and for sampling or designing samples for rare events such as births and deaths. Censuses provide the number of adolescent girls, pregnancy and births, by age and sex at the micro, local, state and national levels. These data are also crucial for making estimates from inter-census surveys, for designing samples, for providing the adolescent population count for rate denominators, as well as for government and policies (Bulimic, 1998).

To take advantage of the census opportunities, Brazil has developed census samples with broader questionnaires focused on specific less frequent events in the population, such as adolescent pregnancy and fertility. Census samples estimated progressive and consistent increases in adolescent pregnancy rates, from 7.53 in 1970 to 7.87 in 1980, 8.84 in 1991 and 9.37 in 2000, and this proportion have been constant during the decade, and declined in 2010. In 2006 and 2007 adolescents under 20 years old were responsible for 20.5% of all the births, and rates are higher in the poorest regions of North (Amazonia) and Northeast, compared to other more developed regions. However, in Northeast and Southeast regions, fertility rates at age 15 are three times higher compared to the other regions (IBGE, 2010). Although the Southeast is the most developed region in the country, there were very poor populations concentrated in periphery areas of the metropolis and in the interior of these states.

These results are consistent due to the large size of the census sample. The biannual National Sample Survey of Households (PNAD) covers only 0.2% of the total population, with even weaker representation in rural areas. While the census sample cover 10% of Brazil's cities (more than 15,000 inhabitants) and 25% of the small localities, but is carried out only each for ten years (IBGE, 2000). The smaller surveys are more frequent, and useful to indicate some short-term changes in fertility, since they are carried out every two years (which allow to relate the phenomena to economic trends), while the census samples are implemented every 10 years and reflect more structural changes and provide more precise information at local level.

Information from the census sample has allowed government generating benchmarks to correct the underestimation of adolescent pregnancy and fertility for the entire population and geo-referenced benchmarks by micro, local and national levels, combining information from census samples and specific surveys, and contrasting it to civil and health services registration. In less developed areas, like the Amazonia, where services are scarce; it is assumed that the level of underreporting

is similar to other areas with similar level of development or is similar to similar social and local groups.

Civil registration in Latin American and the Caribbean countries

Improvements in civil and health registration are particularly facilitated in Latin America and the Caribbean countries where most of the births are attended by trained personal. That is the case of Argentina, Brazil, Chile, Colombia, Cuba, Dominican Republic, Panamá, Uruguay, Jamaica, St. Vincent and Grenadines, Antigua and Barbuda and Trinidad Tobago, where more than 95% of births take place in the health services, and data on adolescent pregnancy and fertility are available and reliable. In Brazil, for example, the number of births registered in health services is higher than in civil registration, and these data are used to correct national and sub-national information.

However, in Bolivia, Ecuador, Guatemala, Haiti, Honduras, Nicaragua, El Salvador, Paraguay and Peru, 20 to 40% of births take place at home and child register is not frequent, manly among uneducated, rural and indigenous women. While in the same countries, almost 100% of the more educated, non-poor and non-indigenous women have their births in health services. In these countries, improvements in health and civil registration, particularly at local level, would be very useful not only to generate better information, but mainly to reorient integral policies to prevent adolescent fertility, working with educational sector to promote female education, to care and protect teenage mothers and their children with inclusive policies. Although some of these countries have made efforts to improve civil and health services data such as training midwives to register births, and have promoted no-payment for children registration, results are not satisfactory yet. Therefore, census and surveys still have an important role in providing data to estimate adolescent pregnancy and fertility.

Even in countries with better information have internal inequalities in data coverage and quality. For example, although Brazil has increased the coverage and reliability of information from health services registrations, underestimation persists in rural areas.

All sources of information can be useful to achieve more accurate data on teenage pregnancy and fertility: The census and the census sample, specialized surveys and civil and health services registrations. The combination of different sources contributes to fix and correct the underestimation of adolescent pregnancy and fertility in rural and urban localities, and to provide managerial information to policy makers.

In countries where this combination is not available yet, surveys are reliable data sources to analyze adolescent pregnancy and fertility. The improvement of registration data can also promote results in preventing teenage pregnancy and fertility. For example, in Portugal teenage pregnancy rates have decreased since the mid-eighties after improving health service measures and, according to more accurate indicators and knowledge, reorienting family planning programs to reduce unwanted pregnancies among girls (Pereira et al., 2005).

DISCUSSION

In the selected Latin America and the Caribbean countries analyzed, the total fertility rate have decreased, but the number and proportion of teenage births have held constant or even increased, as was estimated during three decades in Brazil, with a recent decline in the first decade of the XXI Century. The highest rates of adolescent fertility in the region are observed in the youngest teenagers, mainly in the poorest countries, regions and population groups. Adolescent pregnancy occurs earlier in the Caribbean countries, compared to the Andeans, where adolescent motherhood is more frequent within marriage. Sub-regional differences are due to a combination of the culture and timing of early marriage among ethnic and rural populations, but are also related to modern patterns of adolescent behaviors in the Caribbean, without a correspondent level of information, expectations and empowerment in making decisions.

Social inequalities in rural areas, poorest and less educated girls in all the countries multiply the percent of adolescent motherhood in the region, related to the low access to health services. However, even in the countries where almost all births occur in health services, adolescent have had high fertility rates and increases on time.

These factors are beyond pregnancy and motherhood can surround the possibility of studies and to get a productive job among adolescent mothers, who start early their own domestic responsibilities.

Although in most of Latin American and Caribbean countries, the coverage of health services is almost universal, in the poorest countries and in poorest regions in Brazil, more than one out five births take place at home and child register is not frequent, manly among uneducated, rural and indigenous women, in contrast to almost all the births of richer and educated girls, who occur in health services. Even in emergent countries, where the coverage of health services has increased and almost all births occur in these services, disadvantages persist in rural areas and poorest regions. Health services could play a more important role in preventing adolescent pregnancy and in providing more accurate and complex information about the determinants, family and community context where teenage pregnancy occur, and their consequences, as well as in collaborating with education sector, civil registration and with poverty reduction programs to provide caring and attention to these girls and their children.

Health surveys have provided a larger set of questions

and factors that contribute to understand, explain, design and implement policies to prevent early pregnancies and fertility. As adolescent pregnancy and fertility represents few cases in the samples size, and the cost to achieve an adequate number of cases of the phenomena is very high, particularly in developing countries, surveys have been not very frequent in all the countries in the region, and they depend in any case on good census data for an appropriate sample frame.

Recent surveys have been useful to access teenage pregnancy and fertility, and to suggest the needs to generate more specific and relational information, closer to the real adolescent life, to completely understand the multiple determinants of the environment, school, peers and family contexts. Surveys limitations, such as timing, cross-sectional data and the insufficient number of cases should be overcome with local, daily and integrated information, from school, health and register services.

Although surveys and census surveys provide a wide set of variables to analyze individual, family and context factors related to adolescent pregnancy, the extent of coverage of sources and the quality of available data on teenage pregnancy and fertility varies enormously among countries, and efforts have being made by governments in Latin America and the Caribbean to improve the coverage and quality of different sources and thereby to contribute with reliable information to evidence-based policy-making.

Censuses remain an indispensable tool for estimating teenage fertility more accurately. Like most data sources in developing countries, there are significant limitations in using censuses as a basis for current estimates of adolescent fertility. The large period of ten years among censuses, the high cost to include more specific questions to smaller population groups and the need of specialized training to access controversial issues generate difficulties to produce more complex information on teenage pregnancy from census, and undercounting is a key issue limiting the quality of data on that infrequent and controversial event.

Beyond logistical concerns, adolescent pregnancy and fertility is likely to be undercounted due to cultural issues.

1. Interviewers are sometimes afraid to ask about fertility and pregnancy, particularly to younger adolescents 10 to 13 years old and in front of relatives.
2. Younger adolescents may misunderstand or may be careful not to answer questions about pregnancy.
3. Some adults declare their grandchildren as their own children to hide the fact that their daughters are single, adolescent mothers.
4. Children may be under-declared for cultural reasons. Some rural, indigenous or less-educated people in Latin America and the Caribbean believe that small children are not “persons” still, in the way they understand the term, so when the interviewer asks “How many persons live in this household?” the respondents do not count small children.

In these poorest contexts, children are registered only after fulfilling one or two years old.

Specialized surveys use techniques to reduce undercounting of adolescent and fertility pregnancy. Interviewers are always women who receive special training to interview the adolescent directly and confidentially, avoiding the presence of relatives and other members of the household. They use sensitive questions and approaches, games with the interviewees and the like. Although these procedures do not guarantee the elimination of undercounting, they improve reporting and the quality of information in specialized surveys and can provide reliable data for adjusting census data on fertility by age.

Census undercounting can be estimated and reduced also combining data from demographic and health surveys, census samples, and also from civil registration and health services registration.

Census and surveys are complementary and invaluable tools for correcting data and detecting variations in less frequent events, such as adolescent fertility. And geo-referred and integrated data at local level are indispensable for orienting policies and focusing on higher risk population groups, to achieve best results in preventing adolescent pregnancy and fertility, to care and protect them and their children and to promote opportunities for youth.

Civil and health registration of births have low coverage and quality in less developed countries, due to limitations in access and training of officials and health professionnals, combined with cultural values among poorest, rural and indigenous groups. Therefore, some countries have adopted procedures and policies, as well as a combination of sources to know and contrast their underestimation, and to generate reliable data and estimates.

Improving adolescent fertility measures for evidence-based policy-making requires addressing both, logistical and cultural limitations to improve the availability, scope, coverage and quality of information from civil registration, health services data, surveys and censuses.

Conclusions

In Latin America and the Caribbean, teenage pregnancy and fertility persist and even is increasing in some countries, contributing to interrupt adolescent educational and labor development and expectancies, and exposes teen girls to risk conditions associated with abortion, delivery complications and maternal death – particularly poor, undernourished and indigenous adolescents, among them who live in rural areas, poor and less developed states, regions and countries.

Health services, with a large coverage in the region, provide access and registration of teenage and their

children, and represent an opportunity to refine the available information, to generate more complex, integrated and geo-referred information, to access the particular settlements, specific conditions, families, peers and the environment where teenage fertility is resilient and associated to persistent poverty, exclusion, poor education and low opportunities for these girls and their children, as well as to design and implement adequate policies for prevention and protection of these groups.

The integration of objective and subjective indicators, which consider also the perception of adolescents about their decisions and needs, should incorporate the spatial dimension. For it is essential to make improvements in information technology at local level, to organize the set of interrelated components and inputs, from the collection, processing and distribution of information for decision making in public health, education and social policies, to achieve potential impacts in human development, and to take advantages of the demographic bonus in Latin American and the Caribbean societies.

Geo-referenced data about institutional, family, peers, community and environment situations involving teenage pregnancy and fertility can contribute to generating detailed and integrated estimations of its rates and determinants at local level. Improving civil, health and school information to register some characteristics of adolescents, their families and peers, such as race-ethnic origin, family and peer relations, migration and girls decision making process and environment, to support focused prevention, education and protection for youth and their families.

Reconciling more detailed local and administrative data with census data allow governments to estimate sub-national rates to orient local, regional and national policies. Censuses and census samples provide the number of adolescents by age and sex and other socio-demographic characteristics, providing a reconciliation of micro census data with information from health services and civil registration at the local level. However, the production of more detailed institutional data at local level by civil and health services would give more precision to decision-making process.

It is also possible to estimate the probabilities of having an adolescent pregnancy according to geographical distribution, level of education, ethnic group, culture and religion, family structure and composition, income, poverty and other indicators of inequalities available in censuses.

Finally, another important advantage in integrating data from censuses, surveys and administrative registration is adopting a longitudinal and life-course approach, such as indicators on the timings and duration of transitions to adult life, combining data on changes in fertility, education, work and family life on time.

An integral analysis of teenage pregnancy and fertility should take into account socio-demographic, economic, cultural and institutional factors involved in adolescents' perceptions, decisions and practices at individual, family, and neighborhood and environment levels. This ideal approach is possible to achieve in the region, from a combination of available methods and sources of information to fully understanding the trends, timing and diversity of factors involved in the analysis, as well as to identify local needs for specific groups, and to reorient policies of prevention and care.

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Full Length Research Paper

Impact of human papillomavirus vaccination on anal cancer incidence in French women

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Human papillomavirus (HPV) 16 and 18 are found to be involved in 80% of anal cancers. Two vaccines against HPV infections are currently available, and vaccination policies aim to decrease mainly, incidence of cervical cancers. Moreover, an impact of HPV vaccination on the incidence of anal cancer can also be expected. Our aim was to assess the potential benefits of HPV vaccination on the occurrence of female anal cancer in France. We developed a dynamic model for the heterosexual transmission of HPV and its progression to anal cancer in women. The model was calibrated using French data of anal cancer incidence. Considering vaccine coverage observed at the launch of vaccination campaign in France, reductions of 55 and 85% in the incidence of anal cancers due to HPV 16/18 are to be expected in French women 30 and 50 years after vaccine introduction, respectively. In case of a significant decrease in vaccine coverage, a dramatic reduction in the impact of HPV vaccination on female anal cancers would be observed. The number of anal cancer cases in French women is therefore expected to decrease significantly in 30 years, assuming sustained HPV vaccine coverage.

Key words: Dynamic model, human papillomavirus, vaccine, anal cancer.

INTRODUCTION

Several western countries have recently developed vaccination policies against human papillomavirus (HPV) to prevent cervical cancer in women. It is expected that prevention against HPV can also dramatically decrease the risk of other male and female anogenital cancers. Therefore, the impact of HPV vaccination on non-cervical cancers must now be assessed. Some studies have considered non-cervical cancers including anal cancer (Elbasha and Dasbach, 2010; Jit et al., 2011). While epidemiological data of female anogenital non-cervical cancers remain sparse, some papers have reported on anal cancer incidence and its economic burden in France. For instance, the economic costs of anal cancer are close to that of cervical cancer, despite a lower incidence (Abramowitz et al., 2010b). In 2006, 2500 females with anal cancer were treated in French hospitals (Abramowitz et al., 2010b). The incidence of anal cancer is higher in women than in men; the French regional registers of cancers have published incidence rates varying from 0.2 to 0.7 per 100,000 in men and from 0.7 to 1.7 per 100,000 in women (IARC, 2007). An increase in anal cancer incidence has been reported in the past decades in Denmark, Scotland and Australia (Brewster and Bhatti, 2006; Jin et al., 2011; Nielsen et al., 2011). As with cervical cancer, epidemiological studies have established a causal relationship between human papillomavirus (HPV) infections and occurrence of anal cancer (Castor et al., 2011). HPV 16 and/or 18 are related to approximately 80% of anal cancers (Franceschi and De Vuyst, 2009; Abramowitz et al., 2010a).

Vaccination against HPV infections aims to decrease cervical cancer incidence and may reduce the occurrence of other cancers due to HPV infections (anogenital cancers and head and neck cancers). Two prophylactic

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vaccines against HPV infections are available in France and have been found to be highly effective in women who have never been infected with HPV (Paavonen et al., 2009; Munoz et al., 2009). The quadrivalent vaccine protects against HPV 6/11, which are responsible for genital warts, and against HPV 16/18, which are associated with 70% of cervical cancers. The bivalent vaccine protects against HPV 16/18 infection. The efficacy of the bivalent vaccine against anal HPV 16/18 infection has been found to be similar to vaccine efficacy against cervical HPV 16/18 infection in young women (Kreimer et al., 2011). The quadrivalent vaccine was found to be efficacious in prevention of anogenital lesions associated with HPV 16/18 in Men who have Sex with Men (MSM) (Giuliano et al., 2011) and in heterosexual men (Hillman et al., 2011). Thus a decrease in anal cancers due to HPV 16/18 could be expected after the initiation of HPV vaccination.

In France, the permanent Vaccines Advisory Committees ("Comité technique des vaccinations" and "Conseil supérieur d'hygiène publique de France") recommend vaccinating 14-year old females. Moreover, a catch-up program has been offered to women aged from 15 to 23. Females eligible for the catch-up program either have not been sexually active yet or may report a first sexual relationship that occurred in the year prior to vaccination (Haute Autorité de Santé).

As anal cancers usually occur several decades after HPV infections, in France 75% of anal cancers are diagnosed in individuals aged more than 65 years (Fédération Nationale des Centres de Lutte Contre le Cancer, 1992), mathematical models are useful to assess any expected reductions in cancer cases. In these models, vaccine coverage in young women is taken into account.

Various dynamic models have been published to assess the potential impact of HPV vaccination in several countries focusing on cervical cancer (Dasbach et al., 2006). A cost-effectiveness evaluation has been done in France using a Markov model (Bergeron et al., 2008). Markov model do not take into account herd immunity effect. Another paper assessed the impact of HPV vaccination on cervical cancers in French women using a dynamic model (Ribassin-Majed et al., 2012). To estimate the cost-effectiveness of vaccination policies, other cancers due to HPV may be considered. In the US, the cost-effectiveness of HPV vaccination in Men who have Sex with Men (MSM) has been estimated considering anal cancers (Kim, 2010). Elbasha et al. (2007, 2010) developed several dynamic models to assess the economic impact of quadrivalent vaccine in the USA including a specific model for anal cancer (Elbasha and Dasbach, 2010). Jit et al. (2011) compared the effect and cost-effectiveness of bivalent and quadrivalent vaccines in UK considering a model of HPV transmission, progression to anal cancers was taken into account. To our knowledge, no dynamic model assessed specifically the impact of HPV vaccination on anal cancers in French females.

We estimated the potential impact of vaccination on the reduction of anal cancer incidence in French women. In this paper, we present a deterministic model for the heterosexual transmission of HPV and its progression to anal cancer in women. Several scenarios of vaccination were considered. Sensitivity analyses were conducted for all scenarios in order to assess the impact of vaccination considering variations in vaccine efficacy. We aimed to provide useful data to assess expected reductions of anal cancer incidence after vaccine introduction in France.

METHODOLOGY

Dynamic model structure

We used Scilab-5.1.1 software (http://www.scilab.org/fr) to design a deterministic model for heterosexual transmission of oncogenic HPV types 16 and 18. HPV types 16 and 18 are included in both vaccines (bivalent and quadrivalent). In our modeling, they are modeled jointly. We developed a system of 784 ordinary differential equations. We set the population size in the model to 100,000 individuals, equally divided into females and males. The epidemiologic model simulated heterosexual transmission of HPV-16/18 infections in males and females, and progression to anal cancer for females. Modeled natural history included compartments of precursor lesions of anal cancer AIN I, AIN II/III (Figure 1). After clearance of HPV 16/18 infection, infected individuals go back to susceptible compartments.

We assumed that individuals entered the sexually active population at 14 years old. This assumption was consistent with the sexual comportment of French population, 0.4% of women and 2.4% of men have had sexual intercourse before the age of 14 years old in 2006 (Bajos et al., 2008). Fourteen-year-old persons entered the model at a gender-specific and sexual activity-specific rate. Sexually active women could be infected with HPV 16/18 in the anal region if they had had sexual intercourse with men who were HPV infected in the anogenital region. HPV infections are transmitted by contact between mucosal in the anogenital region; we assumed that all sexual intercourse (anal or vaginal) between an infected man and a susceptible woman could induce HPV infection in female anal region. In fact, women are probably also infected in cervical region, potential synergy between anal and cervical infections have been studied (Goodman et al., 2010).

Individuals exited the model at death (age and gender specific using French data) or when they reached the age of 84. The heterosexually mixing population was divided into 14 age groups ([14 to 19], [20 to 24], [25 to 29], [30 to 34], [35 to 39], [40 to 44], [45 to 49], [50 to 54], [55 to 59], [60 to 64], [65 to 69], [70 to 74], [75 to 79], [80 to 84]). We developed a demographic model (Hethcote, 1997; Elbasha et al., 2007) which simulated the distribution of the French population. Details on the demographic model are described in Ribassin-Majed et al. (2012). Annual transition rates into age groups were defined by the demographic model.

Each age group was divided into 4 levels of sexual behavior. The level of sexual activity was defined by the number of sexual partners in the last 12 months (0 sexual partners-including non-sexually-active individuals-, 1 partner, between 2 and 3 partners and 4 partners or more in last year). Results from the French survey on sexual behavior were used to derive the distribution between groups of sexual behavior (Table A1, Appendix). Mixing between sexual activity groups was quantified by the mixing matrix as

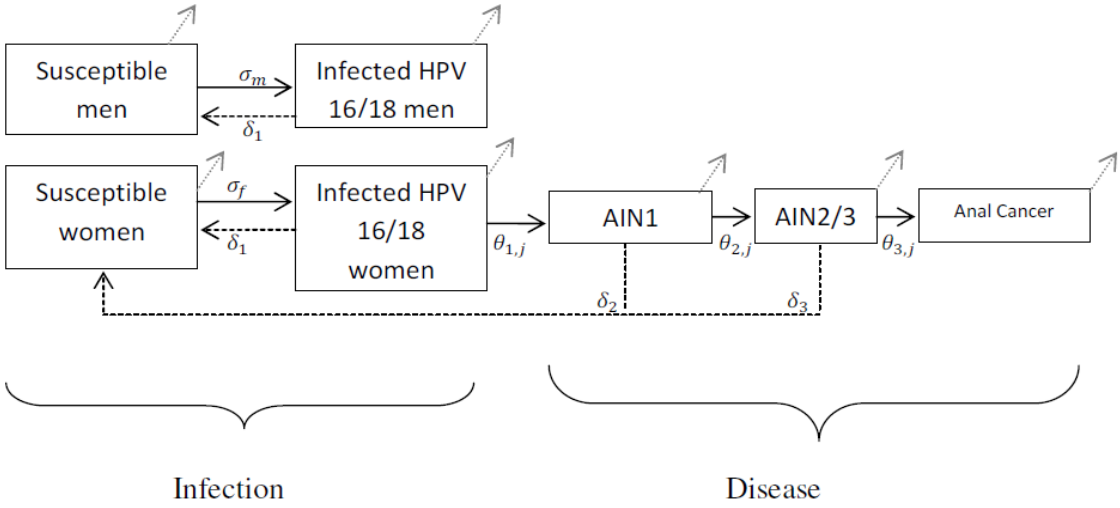

Figure 1. Flow diagram. Schematic representation of the dynamic model compartments corresponding to one age-group *i* (i = 1… 14) and one group of sexual activity *l* (i = 1… 4) in non-vaccinated population.

described by Garnett and Anderson (1993), details in Appendix. The parameter ε described the degree of mixing between sexual activity groups which may vary from fully assortative (ε = 0, when individuals have sexual partners in the same sexual activity class) to fully random (ε = 1). Mixing between sexual activity groups was assumed to be preferentially assortative (ε = 0.4).

Risk of infection

The risk of infection by gender depends on: probabilities of transmission from an infected individual to a susceptible one (σ_f and σ_m); the number of sex partners in last 12 months (C_l = 0, 1, 2 and 3, $\geq$4); the proportion of infected individuals in the pool of sexual partners according to their age-group and level of sexual behavior. We developed a mixing matrix $\rho_{g,i,k}$ appropriate for the sexually active population in France, which gives the proportion of individuals of gender *g*, in age-group *i* who have sexual partners in age-group *k* (Table A2, Appendix).

Transmission model data

In a fitting procedure, we derived the probabilities of HPV 16/18 transmission per partnership (from an infected individual to a susceptible one) for both sexes, the clearance rate (the same in males and females) and age-specific progression rates to AIN1, AIN 2/3 and anal cancer. To assess the probabilities of HPV transmission and the clearance rate, our criteria of best fitting was: the model reproduced HPV 16/18 female and male prevalence within 10%. As French data for male prevalence are not available, we used data from USA in both sexes in order to consider transmission of infection between the same population (Hernandez et al., 2005; Nielson et al., 2009). Several sets of the 3 parameters (200,000), probabilities of transmission in males, females and clearance rate, were tested. To assess age-specific rates for progression of the disease, we fit the model on female age-specific anal cancer incidence (IARC, 2007). As HPV types 16 and 18 are responsible for 80% of anal cancer (Abramowitz et al., 2010a), we multiplied the published French incidence rate of anal cancer by 0.8 to assess the incidence rate of anal cancer due to HPV types 16 and 18 (in French women).

Published data for regression rates from AIN 1 and AIN 2/3 compartments to susceptible compartments were used (Palefsky et al., 1998).

Vaccine characteristics

We divided the population into vaccinated and unvaccinated categories. Individuals entered the model at 14 years old (being vaccinated or not) in susceptible compartments. Individuals in the youngest age groups ([14 to 19] and [20 to 24]) could be vaccinated after entrance into the model in accordance with the French vaccine program and then moved to vaccinated categories. We considered several vaccination scenarios. Immunity from the vaccine was assumed to be sustained lifelong and vaccine efficacy was assumed to be 90% in the base case. Thus, vaccinated individuals could experiment breakthrough HPV infections and may progress to disease (anal cancer in females). Efficacy of 90% means that vaccination avoids 90% of HPV infections in vaccinated individuals compared to non-vaccinated individuals.

Vaccination scenarios

First, we studied the vaccine coverage observed in France at the beginning of the vaccination campaign in 2007 to assess vaccine efficacy (scenario 1). Then, we assessed vaccine efficacy in different hypothetical situations; in scenario 2, we considered a lower vaccine coverage, as observed in France a few years after the initiation of the vaccination campaign (Fagot et al., 2011). Finally, in the last scenario (scenario 3), we considered a very pessimistic vaccine coverage.

In the scenarios considered, vaccine coverage was assumed to be constant in time. We considered only individuals who received the 3 doses of vaccine. In the first scenario, coverage of vaccination (using 3 doses of vaccines) was set to that observed in France in 2007 (Fagot et al., 2011): 30% of women aged 14 to 19 and 10% of women aged 20 to 24 (Table 1). Please note that these vaccine coverages are annual rates in the model (e.g. each year, 30% of women aged 14 to 19 years receive the 3 doses of vaccine), the corresponding cumulative rates for scenario 1 are presented in

Table 1. Scenarios of vaccination considered in simulations. Vaccine coverages are annual rates.

Vaccine coverage for women	Scenario 1 (%)	Scenario 2 (%)	Scenario 3 (%)
14-19	30*	20	5
20-24	10	10	5

*E.g.: each year, 30% of women in the age-group [14 to 19] receive the 3 doses of vaccine.

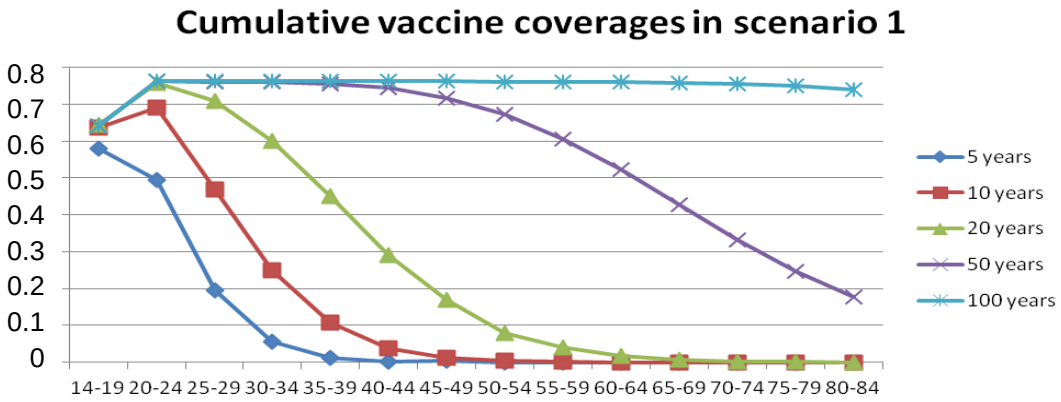

Figure 2. Cumulative vaccine coverages in scenario 1: 5, 10, 20, 50 and 100 years after introduction of vaccination assuming constant vaccine coverage.

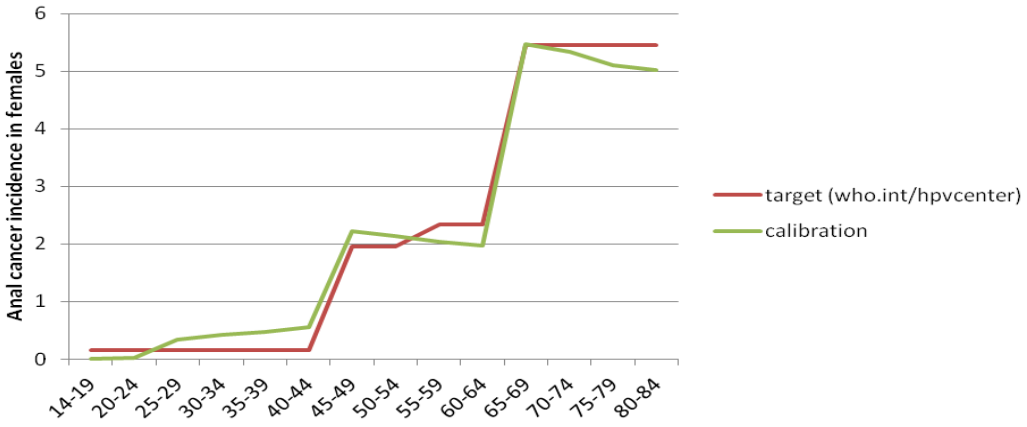

Figure 3. Anal cancer incidence in females estimated in calibration step (model without vaccination) (number of new cases of female anal cancer per 100,000 women).

Figure 2. For instance, a few years after vaccination launch, almost 60% of women aged 14 to 19 years could be vaccinated (3 doses), assuming constant vaccine coverage (Figure 2). In the second scenario, we considered a lower vaccine coverage in women: 20% of women aged 14 to 19 and 10% of women age 20 to 24 as observed a few years after initiation of vaccination (Fagot et al., 2011). In the last scenario, only 5% of women aged 14 to 24 were completely vaccinated (with 3 doses of vaccine).

Model validation

To validate the model, we considered the epidemiological data before vaccination introduction and compared it with the steady-state estimates of the deterministic model for non-vaccinated individuals. Probabilities of transmission of HPV 16/18 (from an infected individual to a susceptible one) have been estimated in our fitting procedure to 0.21 (female) and 0.16 (male) and the clearance rate has been estimated to 0.83.

Among infected females, the rates of progression to anal cancer were estimated for each age-group. We compared the age-specific incidence of anal cancer predicted by the model with published data (Human Papillomavirus and Related Cancers in France; Summary Report, 2010; available at who.int/hpvcenter). Each age-specific incidence rate of anal cancer predicted by the model was similar to the age-specific incidence rate of anal cancer due to HPV 16/18 in France within a precision of 10% (Figure 3).

Table 2. Anal prevalence of HPV 16/18 in women in each scenario: 20, 30 and 50 years after initiation of vaccination (t = 0). Vaccine coverage was supposed constant in each scenario. Percentage of reduction in HPV prevalence compared to the case without vaccination.

Anal prevalence of HPV 16/18 for women	20 years (%)	30 years (%)	50 years (%)
Scenario 1	-58	-75	-91
Scenario 2	-53	-70	-86
Scenario 3	-29	-42	-58

Table 3. Prevalence of HPV 16/18 in men in anogenital site in each scenario: 20, 30 and 50 years after initiation of vaccination (t = 0). Vaccine coverage was supposed constant in each scenario. Percentage of reduction in HPV prevalence compared to the case without vaccination.

Prevalence of HPV 16/18 for men	20 years (%)	30 years (%)	50 years (%)
Scenario 1	-52	-69	-87
Scenario 2	-47	-64	-82
Scenario 3	-24	-37	-52

Sensitivity analysis

Sensitivity analyses were conducted to assess the effect of parameter variations on model results. Although, vaccine efficacy was initially set to 90%, we set vaccine efficacy in sensitivity analyses to 60 and 40%. Thus, we studied the impact of vaccination on HPV prevalence and anal cancer incidence using low (60 and 40%) vaccine efficacies. Another sensitivity analysis corresponding to a variation in the sexual mixing parameter is described elsewhere (Ribassin-Majed et al., 2012).

RESULTS

HPV infection prevalence

Both vaccination strategies considered in scenarios 1 and 2 led to a sizeable decrease in HPV prevalence in the anal region among females 20, 30 and 50 years after vaccination introduction (Table 2). At the horizon of 20 years after launch of vaccination, reductions in anal HPV prevalence (females) of 58 and 53% will be expected considering respectively scenario 1 and 2. Five decades after introduction of vaccination, anal HPV 16/18 prevalence in females could be approximately divided by 10 in both scenarios 1 and 2.

The deterministic model that we developed takes into account the reduction of male HPV 16/18 prevalence in the anogenital region due to female vaccination. Table 3 shows the expected reduction in male prevalence for each scenario.

Anal cancer in females

In the base-case analysis, we assumed a 90% efficacy for the vaccines. In scenario 1 which considers the vaccine coverage observed in France at the initiation of the vaccination campaign, a 55% reduction of anal cancer incidence in females due to HPV 16/18 may be expected 30 years after the introduction of the vaccine. Scenario 1 predicted a 85% reduction of anal cancer cases due to HPV 16/18 50 years after vaccination launch, assuming constant vaccine coverage (Table 4 and Figure 4).

In scenario 2, which considers a lower vaccination coverage (20 and 10% respectively in women aged 14 to 19 and 20 to 24), 50 and 80% reductions in the numbers of new anal cancers would be expected respectively 30 and 50 years after vaccine introduction.

Considering the pessimistic scenario in which 5% of females aged 14 to 24 years were vaccinated (scenario 3), a 26% reduction of anal cancer incidence would be expected in a horizon of 30 years after initiation of vaccination, this reduction reached 52% in a horizon of 50 years if vaccine coverage is constant.

Sensitivity analyses

As efficacy of vaccine was initially set to 90% in the base-case, we considered the effect of lower vaccine efficacies on the incidence of anal cancer in sensitivity analyses (Table 4). A lower efficacy of vaccine (60%) reduced the impact of vaccination on anal cancer incidence. Considering scenario 1 with an efficacy of 60%, our model predicted lower reduction in anal cancer incidence compared to a 90% efficacy 50 years after introduction of the vaccine (reductions of 63 and 85%, respectively). In case of an efficacy of 40%, impact of vaccination would dramatically decrease. A 45% reduction of anal cancer incidence would be expected 50 years after initiation of vaccination whereas a 85% reduction would be reached with an efficacy of 90% in scenario 1 (assuming constant vaccine coverage).

Table 4. Expected reductions in incidence of anal cancer (annual number of new cases per 100,000 individuals) due to HPV 16/18 in French women in each scenario 20, 30 and 50 years after initiation of vaccination (t = 0) and considering efficacy of vaccine of 90% in base-case, 60 and 40% in sensitivity analyses.

Time since introduction of vaccination (years)	Vaccine efficacy (%)	Scenario 1 (%)	Scenario 2 (%)	Scenario 3 (%)
20	90	-28	-24	-8
	60	-16	-13	-3
	40	-9	-7	-0
30	90	-55	-50	-26
	60	-37	-33	-16
	40	-24	-22	-10
50	90	-85	-80	-52
	60	-63	-59	-35
	40	-45	-42	-23

Vaccine coverage was assumed constant in each scenario.

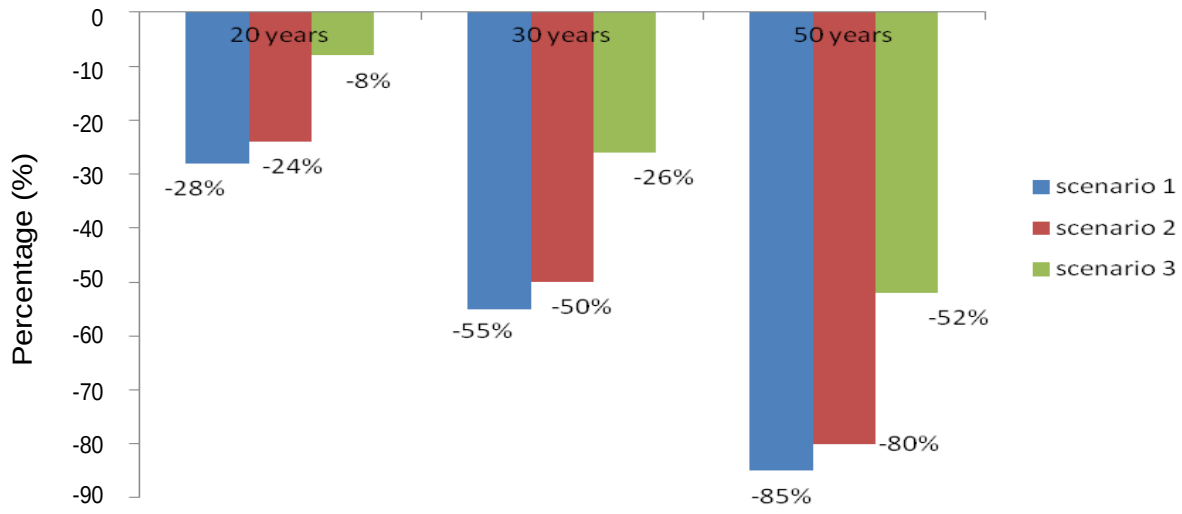

Figure 4. Expected reductions in female anal cancer incidence (due to HPV 16/18): 20, 30 and 50 years after launch of vaccination campaign in France (compared to anal cancer incidence prior to vaccination).

DISCUSSION

We have developed a dynamic model to assess the impact of HPV vaccination on the incidence of anal cancer in French women using observed coverage of vaccination. Using deterministic modeling, we have estimated the potential impact of vaccination against HPV to prevent anal cancers. Considering the vaccine coverage reached at the initiation of vaccination in France (30% of women aged 14 to 19 years and 10% of women aged 20 to 24 years) are vaccinated every year, the incidence of anal cancer in women could be reduced by 55% in the horizon of 30 years and by 85% in the horizon of 50 years compared to anal cancer incidence prior to vaccination. We compared several scenarios of vaccination coverage. The first scenario corresponded to the vaccination coverage observed in France at the initiation of the vaccination campaign (Fagot et al., 2011). To understand the impact of vaccination, cumulative vaccine coverages have to be considered. In modeling, annual rates are used.

The second scenario corresponded to a lower vaccine coverage, as described by Fagot et al. (2011) in France a few years after the introduction of HPV vaccines. Finally, in the third scenario, we considered a very low vaccine coverage. In all scenarios, vaccine coverage in the age-

group targeted for ongoing vaccination was assumed to be constant in time. In the base-case, we assumed a 90% efficacy of vaccine, and in the sensitivity analysis we assessed the impact of vaccination considering lower efficacies of vaccine: 60 and 40%. Efficacy of HPV vaccination to prevent anal cancers in females decreased dramatically when vaccination coverage was very low. In addition to cervical cancer preclusion, HPV vaccination can also prevent anal cancer in women. Our results supports maintaining the vaccination coverage at a level no lower than that observed after vaccination introduction.

Nonetheless, our findings depend on the assumptions made in our modeling. We considered that individuals entered into the sexually active population when they are 14 years old. This assumption is consistent with the survey on the sexual behavior in France (Bajos et al., 2008). Only 0.5% of the interviewed women (aged from 18 to 69 years) declared having their first sexual intercourse before the age of 14 years.

In the deterministic model that we developed, we used a Susceptible-Infected-Susceptible (S-I-S) structure. We did not assume that individuals who cleared HPV infection developed natural immunity against HPV. This approach of natural history for HPV infections has been used in other HPV models (Myers et al., 2000; Goldie et al., 2003; Kulasingam and Myers, 2003; Sanders and Taira, 2003; Goldie et al., 2004; Taira et al., 2004; Ribassin-Majed et al., 2012), whereas some other published models assumed natural immunity against HPV using Susceptible-Infected-Removed (S-I-R) structure (Elbasha et al., 2010). Existence and length of natural immunity after HPV clearance is uncertain and not biologically proved. The way that natural history is modeled has an impact on predictions (Van de Velde et al., 2010). Dynamic models which used SIS structure predict higher effectiveness of vaccine (Van de Velde et al., 2010).

The model assumed constant vaccine coverage whereas a decrease was observed in France between 2007 and 2009. Efficacy of vaccination was assumed to last lifelong. Consequently, we did not include the need for vaccine booster shots in our model. The protective effect of vaccines is known to last at least several years and the need for boosters is currently unknown (Paavonen et al., 2009; Castellsague et al., 2011).

Using deterministic modeling, our model took into account the “herd immunity” effect corresponding to a decrease in HPV 16/18 infections and anal cancers in non-vaccinated subpopulations of females due to vaccination coverage of other individuals.

One of the strengths of our modeling is that we considered the actual vaccine coverage observed in France. In France, vaccine coverage has been reported to be low and decreasing: while 33.3% of girls aged 14 in 2007 were vaccinated with 3 doses of the vaccine, only 23.7 and 5.4% of girls aged 14 were vaccinated, respectively in 2008 and 2009 (Fagot et al., 2011). However, cumulative rates have to be considered.

Considering scenario 1 and assuming constant vaccine coverage, at the horizon of 10 years after introduction of vaccination, more than 60% of females aged 14 to 19 years will have received the 3 doses of vaccine. Fifty years after vaccination launch, more than 70% of women aged 14 to 44 years will be vaccinated. In our modeling, vaccination rates are constant, therefore variations in vaccine coverage over the time could not be considered. The trend observed (decrease of vaccine coverage) could be balanced with an increase in a long term perspective. Controversies in HPV vaccines and others vaccines (e.g. Influenza H1N1 vaccine or Hepatitis B Vaccine) could explain the mistrust of vaccines in French individuals. Campaigns of information for the targeted population (females and their mothers) and for gynecologist and pediatricians may have an impact on the acceptance of HPV vaccination (Blödt et al., 2011; Hughes et al., 2011; Lutringer-Magnin et al., 2011).

We considered 3 vaccination scenarios and confirmed a dramatic decrease of HPV vaccination efficacy to prevent anal cancer. We assumed that only individuals who received 3 doses of vaccine were protected against HPV infection. Our modeling also considered different values regarding the efficacy of vaccines. In the base-case, we considered a high efficacy as observed in clinical trials which conducted statistical analyses in “per protocol” cohorts. The efficacy of vaccines in girls and young women who have never been infected with HPV is close to 100%, whereas efficacy drops significantly in “intention to treat” analyses (full cohort) (Rambout et al., 2007; Paavonen et al., 2009; Munoz et al., 2010; Castellsague et al., 2011). We therefore considered HPV vaccination with different levels of efficacy in sensitivity analyses. In France, populations targeted by HPV vaccines are represented by girls aged 14 years while young women aged 15 to 23 years can be vaccinated in a catch-up program. We may assume that some of the targeted populations, particularly in the catch-up program, could have been infected with HPV prior to vaccination. In this case, efficacy of vaccine is expected to be lower than 100%. We aimed in our paper to assess the impact of HPV vaccination in the presence of a decreased vaccination efficacy due to HPV infections prior to vaccination. For instance, Hernandez et al. (2005) observed a prevalence of anal HPV infections of 12% in young females (age 18 to 24 years old). Some countries have chosen to target younger females of 9 to 12 years old (ECCA).

In conclusion, to our knowledge, this analysis is the first to explore the potential impact of HPV vaccination on anal cancer incidence in France. The findings suggest that a 85% reduction in anal cancer incidence due to HPV 16/18 is expected in French women in the horizon of 50 years assuming sustained HPV vaccine coverage (which corresponds to a cumulative vaccine coverage of 60% in women aged 14 to 19 years a few years after vaccination launch) and full (90%) vaccine efficacy.

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APPENDIX

Table A1. Distribution in the model in the 4 sexual-activity groups.

Group of sexual behavior	Female				Male			
	0 (%)	1 (%)	2 – 3 (%)	≥ 4 (%)	0 (%)	1 (%)	2 - 3 (%)	≥4 (%)
Distribution	15	75*	9	1	15	75	9	1

E.g. * 75% of women declared having one sexual partner in last 12 months.

Table A2. Mixing matrix between age-group. Proportion of individuals who have sexual contact with partners in youngest age-group (<), the same age-group (=) or older age group (>). e.g. *56% of women in [20 to 24] age-group have contact with men of the same age-group.

Age group	% Female			% Male		
	<	$\rho_{f,s,t}$	>	<	$\rho_{m,s,t}$	>
14 to 19	to	35	65	to	86	14
20 to 24	5	56*	39	25	62	13
25 to 29	7	46	47	38	46	16
30 to 34	8	46	46	42	44	14
35 to 39	15	41	44	45	40	15
40 to 44	16	44	40	46	44	10
45 to 49	16	39	45	50	35	15
50 to 54	13	42	45	45	41	14
55 to 59	19	42	39	46	46	8
60 to 64	22	40	38	56	50	7
65 to 69	17	47	36	53	39	8
70 to 74	17	47	36	53	39	8
75 to 79	17	47	36	53	39	8
80 to 84	17	83		53	47	to

Mixing between sexual activity groups was quantified by the mixing matrix as described by Garnett and Anderson (1993). The probability for someone from the sexual-behavior group *l* to form a partnership with someone from the sexual-behavior group *o* is defined by:

$$w_{lo} = \varepsilon \frac{N_o C_o}{\sum_{s=1}^{4} N_s C_s} + (1-\varepsilon)\delta_{lo}$$

with N_o being the proportion of individuals in sexual-activity group *o*, c_o representing the average number of annual partners in group *o*, δ_{lo} is the Kronecker delta (δ_{lo} = 1 if *l* = *o* and δ_{lo} = 0 if *l* ≠ *o*), the parameter ε described the degree of mixing between sexual activity groups which may vary from fully assortative (ε = 0, when individuals have sexual partners in the same sexual activity class) to fully random (ε = 1). Mixing between sexual activity groups was assumed to be preferentially assortative (ε = 0.4).

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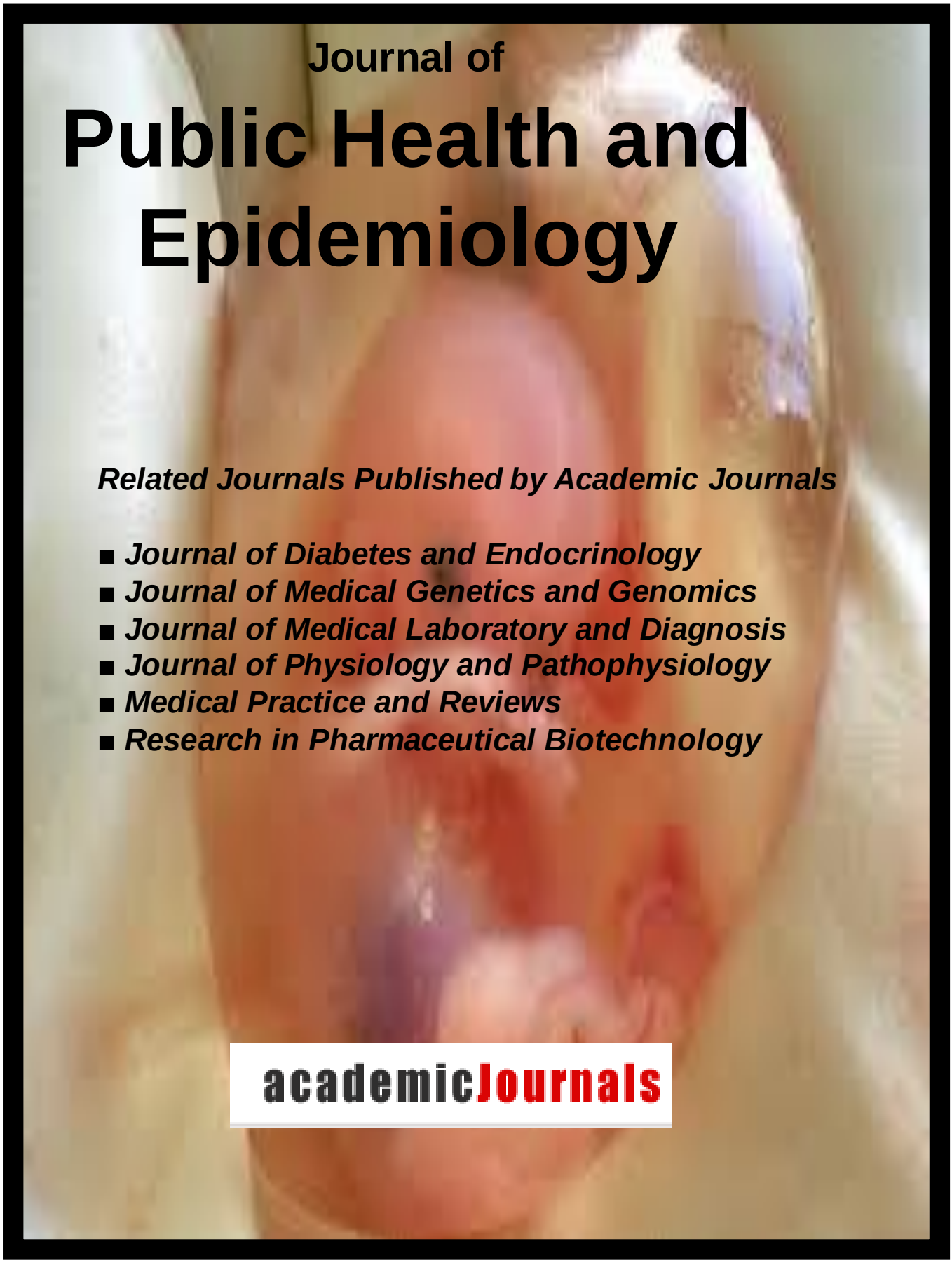

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