The Measurement of Delay in Diagnosis and Treatment among Moroccan Women with Cervical Cancer

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Abstract In Morocco, most of the cervical cancer patients have been reported diagnosed at advanced stage indicating delay in seeking diagnosis and treatment. The main purpose of this investigation was to measure the delay from the first symptom to treatment among Moroccan women with cervical cancer. **Methods:** We conducted a cross-sectional study at the National Institute of Oncology Sidi Mohammed Ben Abdellah in Rabat, Morocco. A consecutive series of patients with locally advanced cervical cancer or metastatic [stage II–IV] were recruited. We calculated delay by using two events dates of two periods in patient's pathway. Multivariate binary logistic regression analysis was performed to measure the association between all categories of delay and magnitude of total delay. **Results:** Four hundred and one patients were reached in this study. The median total delay was 183 days, the median patient delay was 120 days, the median diagnosis delay was 110 days, and the median Treatment delay was 57 days. Bivariate analysis showed that patients who did not have respectively patient and diagnosis delay were less likely to have total delay ($p < 0.001$, $p < 0.001$). **Conclusions:** Future studies are needed to better inform the scientific and healthcare system to effectively address a clear picture of delays.

Keywords Cervical Cancer, Delay, Morocco

1. Introduction

Cervical cancer is one of the most leading causes of women death in many countries despite the advancement in cancer treatment and diagnosis. It is the fourth most common cancer in women worldwide and it's responsible of 528,000 new cases and 266,000 deaths [1].

The underlying reasons who could explain this disappointing are the unavailability to routine screening, inadequate follow-up of abnormal Pap smears and possibly low awareness of women's population regarding the course of the disease [2].

Cervical cancer is the most curable form of any human cancer if detected early at the precancerous stage [3, 4]. One of the most important prognostic factors for cervical cancer is how early the disease is when detected and how far it has spread. Delay in diagnosis and treatment continues to be the greatest hurdle to be overcome in the fight to cure cancer [5, 6].

In Morocco, most of the cervical cancer patients have been reported diagnosed at advanced stage indicating the long duration between onset and final diagnosis of the disease [7].

Nearly 2258 cases of cervical cancer are diagnosed annually and 1076 die, with an age-standardized incidence rate of 14.3 per 100,000 per annum cervical cancer account for 12.8% of total female cancer [8].

Before 2010, organized cervical cancer screening was not available in Morocco. It was limited on an opportunistic screening based on Pap smear test provided in most of time by private clinic. In addition, Pap smear is not mandatory in Morocco. Some countries, such as France, recommend women aged between 25 and 65 to do Pap smear test every three years.

In 2010, the Ministry of Health, in partnership with the Lalla Salma Foundation for Cancer Prevention and Treatment, established a pilot project for cervical and breast cancer screening. After his evaluation a generalization of the program was launched, in primary health centers, by trained doctors, midwives, and nurses by using visual inspection with acetic acid (VIA) as the screening tool for cervical cancer. The eligible women are those aged between 30 and 49. Considerable efforts were made to prevent and control cancers in term of early detection, treatment and construction

of hospitals specializing in oncology. Until 2009, Morocco had only 2 public and 3 private hospitals of oncology. Currently, Morocco has 10 public and 9 private hospitals [9]. In term of budget, 7 % of the overall budget of the National Plan of Prevention and Control of Cancer from 2010 to 2019 is devoted to prevention, and more than 86% of the budget for early detection is intended to ensure access to early detection programs [10]

However, the evaluation of the screening program has detected many challenges, such as low compliance with the screening program, lack of knowledge among Moroccan women of cervical cancer, symptoms, causes and available treatments [11]

Delay in cancer has been an issue of concern within health services research for decades [12]. Pack and Gallo introduced the concept in 1938, and they defined it as 'an interval between the onset of symptoms and the start of treatment. Undue delay was arbitrarily defined as 4 months or more [13].

The time interval from first symptom to start of treatment is often labeled delay even if parts of this delay are unavoidable. Delay in cancer diagnosis is common and long delay is associated with significant mental strain and possibly a worsened prognosis [14].

Although the exact effect of delay on clinical outcomes remains unclear and varies between cancers, it is generally accepted that total delay should be as short as possible [15, 16, 17].

Delays may occur at different stages of the cancer diagnostic journey and have been commonly defined as being either patient focused or healthcare provider focused [5,18]. Commonly, delay is found further categorized into different component delays such as patient delay, health care provider delay, referral delay and system delay [19]. Delays are calculated on the basis of dates provided by the patients and/or health care providers. Thus, delay in diagnosis and treatment of cancer patients may impact on poor prognosis and quality of life [20]. Various studies have been conducted to measure delay in diagnosis and treatment initiation. Previous studies differ with different definitions and different measurements of delay in total duration [21]. As a result, it has become difficult to draw meaningful information from these studies. Only few studies were carried out on more than one organ specific cancer that can provide similarity and differences about delays across different types of cancers in one study. There is a need of a study on different types of cancer to provide clear picture of delays so that results can be generalized [22].

Dividing total duration into two components has been clearly understood by the researchers. Primary delay is defined as duration between onsets of symptoms to first presentation to clinician. Next, clinician delay covers from first presentation to clinician until start of treatment [23].

This definition of primary delay has been found to be consistent in literatures. Primary delay has been referred to as patient delay since it is mainly influenced by the patients'

characteristics [24].

Clinician delay may not only influence by patient's characteristics but it may also associate with doctor and system related factors. Thus, clinician delay is clearly considered as a separate process from primary delay. Criteria for measuring clinician delay have been varying across the studies. Some studies measured clinician delay from first presentation to reaching secondary care center; some up to diagnosis; and some even up to starting treatment. Further, each of these considerations have either been addressed by different names or defined further in shorter durations [25, 26].

There is no consensus on an acceptable length of delay from diagnosis to the start of treatment in cancer patients. Studies often categorized delays to use simple regression models that obviously lose the information especially in absence of optimum time to define such delays [27, 28].

Due to different definitions of delay, their measurement and analytical procedures, it is more likely to get conflicting findings.

The main purpose of this investigation was to measure the delay from the first symptom to treatment among Moroccan women with cervical cancer. As such, no study exists from Morocco that provides measurement for various levels of delay.

2. Operational Definitions and Outcome Measures

In accordance with most other research we used the term delay when calculating the different time intervals from first symptom to treatment start, calculated from the dates entered in the questionnaires by the searcher. Delay was divided into three delay stages.

2.1. Patient Delay

The time period from patient's first becoming aware of symptoms till their first presentation to a health care provider (HCP): The duration of more than 90 days was defined as "long patient delay" and 90 days or less was defined as "short patient delay" [29, 30].

2.2. Diagnosis Delay

The time period from patient's first presentations to the health care provider (HCP) to Histological diagnosis: The period of fifteen days (2 weeks) or less was defined as "short diagnosis delay" and more than fifteen days was referred as "long diagnosis delay".

2.3. Treatment Delay

The time interval from the confirmations of the diagnosis by Histological investigations to treatment: The period of

fifteen days (2 weeks) or less was defined as “short treatment delay” and more than fifteen days was referred as “long treatment delay”.

2.4. Total Delay

The time period from onset of symptoms of cervical cancer and start of treatment: The period of more than 120 days was defined as “long total delay” and 120 days or less as “short total delay”. In this study, the term “delay” refers to the time interval between two specific events in patient’s pathway to treatment of cervical cancer.

3. Materials and Methods

We conducted a cross-sectional study at the National Institute of Oncology Sidi Mohammed Ben Abdellah in Rabat, Morocco. This Institute, which is part of the IbnSina University Hospital of Rabat, is dedicated exclusively to fighting cancer. It is the referral hospital for cancer care where most of the cases are diagnosed and treated.

A consecutive series of patients with locally advanced cervical cancer or metastatic [stage II–IV]. The data was collected between June 2014 and June 2015 using a face structured questionnaire. This tool was pre-tested and modified before final data collection was done. Data on clinical variables was extracted from hospital record of the patients under study.

Were included in the study, Moroccan women who had already started their treatment for cervical cancer, having a hospital record in the National Institute of Oncology, attending the hospital for processing or checking during the study period and who has signed a letter of informed consent to participate in the study. A consecutive series of eligible patients with locally advanced cervical cancer or metastatic (IIA–IVB) (International Federation of Gynecologists and Oncologists (FIGO) were carried [31]. All interviews were conducted by the searcher.

Were excluded of the study patients diagnosed with cervical cancer but who have not yet started treatment and patients with psychiatric disorders.

The sample size was calculated from a proportional of 54.5% cervical cancer patients who delayed in diagnosis and treatment [32] with 5% of precision and 95% for confidence interval. The minimum sample size $n=373$ was obtained using the formula developed by Schwartz [33]. All patients with locally advanced or metastatic cervical cancer (IIA–IVB) in a one year of the study that meet the inclusion criteria were involved and were able to reach a total of 401.

Written informed consent from each patient was obtained

after the improvement of the protocol of this study by Ethics Committee for Biomedical research, Mohammed V University, Faculty of Medicine and Pharmacy in Rabat.

3.1. Statistical Analysis

The concept of delay in diagnostic and treatment of cervical cancer is elaborated in Figure 1.

We calculated patient delay by using two dates, date of first symptoms and date of first consultation with HCP. If the patients were unable to recall the date of first symptoms and date of first consultation with HCP, we use an approximated date by asking the patient about the time between onset of symptoms and first medical consultation, as we tried to come back with the patient to remember some events in the same period to find the month and the year.

Diagnosis delay was calculated between two dates: date of the first consultation with HCP and date of the confirmation of diagnosis. Treatment delay was calculated between two dates: date of diagnosis confirmation and date of treatment starting. Date of diagnosis and date of treatment were extracted from medical records. Total delay was calculated by the addition [Total delay = patient delay + diagnosis delay + treatment delay].

Delays were divided into two groups “short and long day” using Chi-square tests. Multivariate binary logistic regression analysis was performed to measure the association between all categories of delay and magnitude of total delay. Adjusted odds ratio (OR) with its corresponding 95% confidence interval (CI) were calculated. Significance was when $p < 0.05$. All the calculations were performed in computer software the Statistical Package for Social Sciences (SPSS) 18.0 version.

4. Results

Four hundred and one patients were reached in this study. According to the socio-demographic and clinical data which are presented in table 1, of the all patients identified 53.4% were aged above 50 years. Age ranged from 28 to 83 years, the mean age was 52.4 years ($SD=11.48$). 53.6% were illiterate, 63.3% married. More than half of patients were urban inhabitants (68.6%). In 78.6% of the patients, the first consultation place from the residence was at a distance of less than 3km. For 57% of patients the diagnosis center was at more than 3km far from the place of residence. The distance to the treatment center was at more than 3km for 89.3% of patients.

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Figure 1. Categorization of delays in cervical cancer [34]

Table 1. Socio-demographic characteristics of the study population (n=401)

Characteristics	n	%
Age(Years)		
≤50	187	46.6
>50	214	53.4
Marital status		
Married	254	63.3
Unmarried	147	36.7
Education status		
Illiterate	215	53.6
Primary level	93	23.2
Secondary and higher level	93	23.2
Education status of husband (n=254)		
Illiterate	54	21.2
Primary level	85	33.5
Secondary and higher level	115	45.3
Residence		
Urban	275	68.6
Rural	126	31.4
Occupation		
Employed	77	19.2
Unemployed	324	80.8
Occupation of husband (n=254)		
Employed	168	66.1
Unemployed	86	33.9
Socio economic status		
Low	325	81.0
Moderate and high	76	19.0
Social security		
Yes	391	97.5
No	10	2.5
Distance to the first consultation (Km)		
≤3	315	78.6
[3-10[	17	4.2

[10-50[	36	9.0
≥50	33	8.2
Distance to the Diagnostic center (km)		
≤3	173	43.1
[3-10[	44	11.0
[10-50[	141	35.2
[50-100[	26	6.5
>100	17	4.2
Distance to the treatment center (km)		
≤3	43	10.7
[3-10[	64	16.0
[10-50[	79	19.7
[50-100[	117	29.2
>100	98	24.4
Patient delay (days)		
≤90	179	44.6
>90	222	55.4
Diagnosis delay (days)		
≤15	103	25.7
>15	298	74.3
Treatment delay (days)		
≤15	51	12.7
>15	350	87.3
Total delay (days)		
≤120	143	35.7
>120	258	64.3

Of all patients 81% were poor and 80.8% were unemployed. The majority of patients had a social security (97.5%). For 55.4% of cases were found having patient delay, 74.3% having diagnosis delay, 87.3% having treatment delay and 64.3% having total delay.

Table 2. Clinical characteristics of the study population (n=401)

Characteristics	n	%
Medical history		
Yes	104	25.9
No	297	74.1
Surgical history		
Yes	56	14
No	345	86
Obstetric Gynecologic history		
Abortion		
Yes	149	37.2
No	252	62.8
Menopause		
Yes	203	50.6
No	198	49.4
Sexually transmitted infection		
Yes	139	34.7
No	262	65.3
Contraception		
Yes	228	56.9
No	173	43.1
Multiparity		
Yes	144	35.9
No	257	64.1
Personal history of cancer		

Yes	3	0.7
No	398	99.3
Family history of cancer		
Yes	41	10.2
No	360	89.8
Histopathology		
Squamous cell	349	87.0
Adenocarcinoma	52	13.0
Stage at diagnosis		
IIA-IIB	241	60.1
IIIA-IIIB	145	36.2
IVA-IVB	15	3.7
Type of earlier symptoms		
<i>Abnormal vaginal bleeding(between periods, after sex, postmenopausal)</i>		
Yes	264	65.8
No	137	34.2
<i>Vaginal discharge</i>		
yes	69	17.2
no	332	82.8
<i>Pain (painful sex, pelvic pain, dysuria) (n=309)</i>		
Yes	139	45
No	170	55
Misinterpretation of symptoms by patients		
Yes	347	86.5
No	54	13.5
Type of first contact health facilities		
Health center	53	13.2
Public Hopital	136	33.9
Private medical shops	212	52.9
Consulted by		
Generalist	91	22.7
Gynecologic	262	65.3
Midwife	48	12.0
Per-Speculum examination in initial consultation		
Yes	311	77.6
No	90	22.4
Misinterpretation of symptoms during the first consultation		
Yes	90	22.4
No	311	77.6
Medical prescription		
Symptomatic treatment	66	16.4
Pap Smear	22	5.5
Cervical biopsy	230	57.4
Reference to a higher level	83	20.7
Number of consultation before diagnosis		
1	276	68.8
[2-3]	120	29.9
>3	5	1.3

Table 3. Measurement of delay from the symptom onset to treatment

Delays measurement	Median	Range [IQ]
First symptoms to first contacting health-care provider	120	[15-210]
First contact with health care provider to Histological diagnosis	110	[27-246]
Histological diagnosis to treatment	57	[40-82]
First symptom to treatment	183	[84-312]

Table 4. Associations between total delay reporting different delays

Categorical variables	Total delay							
	≤120 days n=401	>120 days n=401	Univariate analysis			Multivariate analysis		
	n (%)	n (%)	OR	95% CI	P	OR	95% CI	P
Patient delay								
≤90 days	141(78.8)	38(21.2)	0.002	[0.001-0.010]	0.001**	0.004	[0.001-0.017]	0.001*
>90days	2(0.9)	220(99.1)						
Diagnosis delay								
≤ 15 days	59(96.7)	2(3.3)	0.011	[0.003-0.047]	0.001**	0.078	[0.018-0.335]	0.001*
>15 days	84(24.7)	256(75.3)						
Treatment delay								
≤ 15 days	2(40)	3(60)	0.829	[0.137-5.023]	0.839	0.241	[0.003-21.401]	0.534*
>15 days	141(35.6)	255(64.4)						

*Model included variables that were significant on univariate analyses at the p(0.20 level).

**significant at p value<0.05

Regarding clinical data presented in table 2. Patients used contraception in 56.9 % of cases, and 50.6% were menopausal. Only 10.2% of patients had a family history of cancer. Greater proportion (87%) had squamous cell tumor type and 60.1% of total patients were diagnosed at stage II. As earlier symptom, abnormal vaginal Bleeding was identified for 65.8% patients. In 86.5% of cases patients misinterpreted symptoms, about half (52.9%) of patients made their first visit at a private medical center, and 65.3% of patients underwent the first consultation with a gynecologist. Greater proportion (77.6%) had a per-Speculum examination in initial consultation. In 22.4 % of cases we identified a misinterpretation of symptoms by the (HCP) during the first consultation. Cervical biopsy was in 57.4 % of cases as a medical prescription and 68.8% had one consultation before diagnosis.

4.1. Estimates of Delays in Diagnosis and Treatment

Table 3 shows the different delays in study population. Overall, among patients, the median total delay was 183 days (IQI 84 to 312) with a minimum of 22 days and a maximum of 1234 days, the median patient delay was 120 days (IQI 15 to 210), the shorter delay was 1 day and the longer delay was 1080 days. The median diagnosis delay was 110 days (IQI 27 to 246) with a minimum 5 days and a maximum of 1140 days. The median Treatment delay was 57

days (IQI 40 to 82), with a minimum of 7 days and a maximum of 516 days.

The association of all categories of delays with the total delay is summarized in table 4. Bivariate analysis showed that patients without patient delay were less likely to have total delay (Adjusted OR=0.002, CI: 0.001-0.010, p<0.001), the same findings were found for diagnosis delay (Adjusted OR=0.011, CI: 0.003-0.047, p<0.001). But for treatment delay any association was found with total delay (Adjusted OR=0.829, CI: 0.137-5.023, p=0.839).

5. Discussion

The delay in diagnosis and treatment refers to the total period of time between symptom onset and when the diagnosis is established, from then until the start of the treatment. There is no standardized definition of delay; the studies on delays have several common themes regarding the length of delay based on dates of important events in diagnostic journey of the patients. Variation can be found in the point of dichotomization of each type of delay into long and short delay but it is very contextual [18, 35].

In the present series, we identified that patient delay accounted for 99.1% in total delay, diagnosis delay for 75.3%, and treatment delay for 64.4 %. The results of this study found a median total delay of 183 days. The median

time of symptom onset to medical consultation was 120 days, 110 days as a median for the time between the first consultation and the confirmation of diagnosis and 57 days for the time between diagnosis and treatment. Patient and diagnosis delays accounted for most of the total delay. Also, we found an association between those delays and the total delay. Our findings accord with those of Allgar and Neal who conducted a study in United Kingdom for six cancer types in a large population and found that the main problem was patient and diagnosis delay [5].

As a major delay, Moroccan women had suffered longer patient delay with the wide range of 15 to 210 days. The present findings are consistent with a research conducted in Morocco showing that 60% of women had a patient delay [34]. The longer patient delay in Morocco can be explained by the influence of patient's characteristics such as education status, failure to recognize or to interpret causes and earlier symptoms by patients [36].

Other studies demonstrated that the manner in which individuals interpret their symptoms has been shown to influence help-seeking behavior in a wide range of illnesses including cancer. It has been suggested that symptom recognition accounts for at least 60% of the total delay in cancer treatment in women with gynecological cancer [33]. However, well recognized specific symptoms are more likely to lead to prompt recognition of serious illness [37].

Time at diagnosis is an important level in diagnosis delay that may change the process of subsequent delay [38]. Our findings showed that the diagnosis delay was another major delay in cervical cancer and established its association with the total delay. Longer diagnosis delay has been observed in previous studies conducted in Morocco and in Denmark [34, 19]. This result can be explained by health facilities such as the remoteness to the place of diagnosis. Note that, 81% of our study population are poor and suffer for financial problems due mainly to the costs of transport, biological and radiological investigations in private clinic, even they have social security called RAMEL (Health insurance scheme for the economically disadvantaged) they must wait long time for appointment.

Some women do not have access to gynecologists for their symptoms. As well some patients had more than one consultation before diagnosis [16]. Also, some (HCP) failed to recognize some symptoms. Those arguments are in line with the findings found in a study conducted by Gyenwali et al in Nepal [39].

In a systematic review by Mitchell et al, diagnosis delay related to initial misdiagnosis and insufficient examination by the practitioner, was the most commonly occurring theme responsible for delay [40].

The median time to the start of treatment was 57 days. This time includes the scheduling of the treatment planning. There are many problems involving delay in diagnosis, especially in the public health care system. A prompt initiation of an indicated treatment is needed because. Many shortcomings impact the difficulty in treating cervical cancer.

But this delay was found to be shorter than the patient and diagnosis delays that are obvious at the National Institute of Oncology with a new department specialized in gynecologic cancer in partnership with "Lalla Salma Fondation- Cancers Prevention and Treatment". Many efforts have been taken in terms of infrastructure, Investigation, medication and follow up. Furthermore, Lalla Salma Foundation to support and encourage patients to access to treatment created "Houses of life" dedicate to house poor women who live far from treatment centers [41, 42].

6. Limitations

The measurement of delay times presents a number of problems. The difficulty of obtaining reliable information is one such problem, since the responses provided by patients cannot be validated against a gold standard. As well, this study is a cross sectional design planned at tertiary level in the country capital. As obvious, the patients coming to this setup are expected to have peculiar characteristics mainly because of dealing referred patients. The findings under this study may not be easily generalizable.

7. Conclusions

Most cervical cancer is diagnosed at advanced stages. Delay occurred in all periods in patient's pathway. Methodological of measurement on diagnostic and therapeutic delay in cervical cancer are still under development and lack standardization. Future studies are needed to better inform the scientific and healthcare system to comprehensively understand and effectively address a clear picture of delays so that results can be generalized.

Abbreviations

HCP: health care provider; FIGO: International Federation of Gynecologists and Oncologists; SPSS: Statistical Package for Social Sciences; SD: Standard deviation; OR: Odds ratio; CI: Confidence interval; IQ: Interquartile.

Declarations

Ethics Approval and Consent to Participate

The Ethics Committee for Biomedical research, Mohammed V University, Faculty of Medicine and Pharmacy in Rabat is registered with the Office for Human Research Protections of the U.S. Department of Health and Human Services under the number (IOG0006594) (<http://ohrp.cit.nih.gov/search/search.aspx>).

Consent for Publication

Not applicable.

Availability of Data and Materials

Please contact author for data requests.

Competing Interests

Ouasmani F, Hanchi Z, HaddouRahou B, Bekkali R, Benazzouz B and Abdelhalem Mesfiouideclare, they have no competing interests.

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