

## Original article

# Stage-specific treatment costs for cervical cancer in the Salah Azaiez Institute of cancer in Tunisia

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Cervical cancer (CC) is the fourth leading cause of cancer in women worldwide. The World Health Organization recommends performing country-specific economic assessments before the implementation of any national strategy. In Tunisia, studies about the cost of CC are rare. The latest study was in 2003, 20 years prior to our study. Our objective was to estimate the stage-specific costs associated with CC in the Salah Azaiez Institute of cancer in Tunisia. This was a cost study conducted at Salah Azaiez Institute in March 2023 consisting of two parts; collecting data about needed check-ups in every cervical cancer stage and estimating the financial cost of each procedure from the hospital's finance unit. The cost of cervical cancer diagnosis and treatment at Salah Azaiez Institute ranged from 550 to 2603 US\$ depending on the cancer stage and the treatment involved. The initial checkup of cervical cancer (including gynecological examination, biopsy, MRI, and laboratory checkups) cost 350\$. The diagnosis and treatments cost 550\$ for the IA stage and 585\$ for IB1 and IB2 stages. These costs were significantly lower than stages IB3, II, IIIA, IIIB, and IVA (2603\$). The diagnosis and treatment costs were of 1800\$ for stage IIIC and 750\$ for stage IVB. In conclusion, this study contributed in delivering essential data of the financial burdens associated to diagnosis and treatment of CC in Tunisia. This study would be an important tool to guide current strategy to fight against cervical cancer in Tunisia

**Keywords:** Cervical Cancer; Cost; Stage; Tunisia

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## 1. Introduction

Cervical cancer (CC) constitutes a global public health issue, ranking as the fourth most common cancer among women [1]. According to the Global Cancer Observatory (Globocan), in 2020, a total number of 604,127 new cases of CC occurred worldwide with a standardized incidence rate (SIR) of 13.3 per 100,000 inhabitants globally [1]. The mortality rates for CC were significantly lower than the incidence rates in 2020, with 341,831 deaths of CC estimated and a mortality-to-incidence ratio of 57% [1]. However, when examining regions and different countries; there is a disproportionate high burden of both CC incidence and mortality in low-middle income countries [2,3].

According to the World Health Organization (WHO) report, 90% of deaths occurred in low- and middle-income countries [1]. Globally, the SIR of CC, in 2020, was the highest among the WHO African region (AFRO) region (19.7 per 100,000 inhabitants). It was of 14.3 and 13.9 per 100,000 inhabitants in the American and the European WHO region (EURO) regions. The East Mediterranean region had the lowest estimated incidence rate of CC in 2020, 4.3 per 100,000 inhabitants [1]. In Tunisia, the SIR of CC was 5.7 per 100,000 inhabitants, considered as a low-to-middle incidence [1]. This rate places the country in the 6<sup>th</sup> position regarding incidence of CC in the WHO Eastern Mediterranean Region (EMRO) region.

Actually, in Tunisia, CC is ranked as the sixth most common cancer among Tunisian women with 216 CC cases accounted in 1994 and 342 cases in 2020 with a SIR of 5.74 per 100,000 people [4-7]. According to the North Cancer registry of Tunisia [7], there is a trend of a decrease of this incidence with an Annual percentage change of -2.3% ( $p < 0.05$ ). As we don't dispose of national data on deaths, an annual number of CC deaths of 185 was recorded in 2020 according to the Globocan corresponding to a mortality rate of 2.4 per 100,000 inhabitants [5-7].

In 2020, the Global strategy towards eliminating CC as a public health problem adopted by the WHO recommends a comprehensive approach to cervical cancer prevention and control [8]. At a national level, Tunisia has undertaken successive five-year cancer plans; the last one for the period 2021-2030 [9]. The current CC screening strategy is based on the cervico-vaginal smear test for women aged 35-64 every 5 years in primary care facilities and family planning with 15% of coverage. Human Papillomavirus vaccination has not yet been introduced to the national vaccination program. A comprehensive understanding of the economic impact of CC helps in developing national strategies. In fact, according to the WHO, before the implementation of a national strategy, it is necessary to perform country-specific economic assessments. Numerous recent studies from various countries have assessed the economic impact of CC, with the majority of reports focusing on estimating the direct costs of treatment [10-14]. In Tunisia, studies about the cost of CC are rare, the latest study estimating the cost of

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managing CC in Tunisia was carried out in 2003, 20 years prior to our study [15]. Thus, the objective of this present study was to estimate the stage-specific diagnosis, medical, surgical and paramedical treatment costs associated with CC in the Salah Azaiez Institute (SAI) of cancer in Tunisia.

## 2. Patients and Methods

### *Study design and setting*

This was a hospital estimation cost study [16]. It was an observational descriptive study conducted at SAI in March 2023. This institute is a public healthcare establishment and the national reference center for the surveillance, diagnosis, and treatment of cancers. This study was based on the 2021 cervical cancer guidelines issued by a group of experts from the various cancer surgery, radiotherapy, pathology and medical oncology departments of the SAI Tunis [17]. These guidelines, which were based on the ethical principles of personal medical practice, were drawn up by a multi-disciplinary working group of oncology professionals practicing at the SAI, considering national recommendations and in accordance with the latest scientific data.

### *Data collection*

Our study consisted of two parts. The first one was the determination of the 2018 FIGO cervical cancer stages and collecting data about needed clinical and para-clinical procedure in every CC stage. These procedures include diagnosis, check-ups, hospitalization needs and treatments including laboratory, radiological, medical needs, and medicine/pharmaceutical drugs used. Our study did not include the procedures needed for follow up during the next years of monitoring the patient. These data were based on the CC therapeutic approach elaborated guidelines of SAI.

The second part consisted in estimating the financial cost of each needed procedure detailed above (clinical, para clinical and hospitalization) gathered from the finance unit of SAI. This second financial section has taken into account the minimum price requested in Tunisian dinars in this public institute for the minimum explorations required for each stage. The prices taken into consideration are the prices a full paying patient without health insurance would pay.

### *Clinical and Para-clinical needs for every stage*

Based on the 2021 CC guidelines of SAI, the initial examination confirming the existence of CC included a gynecological examination under general anesthesia with biopsy and/or abdominopelvic Magnetic Resonance Imaging (MRI) with other biological tests such as blood count, liver function tests and viral serology. The above biological tests were ordered as required and depending on the clinical situation. An average direct medical cost per 2018 FIGO stage was calculated for stages I (IA1 and IA2), I (IB1 and IB2), IIIC and IVB. Stages IB3, IIA, IIB, IIIA, IIIB and IVA were grouped together to ensure similarity in the investigations requested. Stage IA includes, apart from the initial examination, a laparoscopy under general anesthesia, with curettage and conization/hysterectomy depending on the patient's desire for fertility with or without

an inpatient stay and if necessary pre-operative tests (if they were not performed during the initial examination). Stages IB (1 + 2) of 2018 FIGO stages, include, apart from the initial examination, a laparoscopy under general anesthesia, with curettage and radical hysterectomy or trachelectomy if fertility desired. These procedures require days of hospitalization in a medical or post-surgical unit.

Based on the 2021 cervical cancer guidelines of SAI, FIGO Stages IB3, IIA, IIB, IIIA, IIIB, IVA include, apart from the initial examination, a PET SCAN, sessions of radiotherapy, chemotherapy, and check-ups before chemotherapy sessions, a minimum hospital stay of 5 weeks, brachytherapy. These stages also require an assessment at the 8th week of treatment, including a gynecological examination under general anesthesia followed by a pelvic MRI. In some cases, surgery may be advisable, requiring pre-operative check-ups and a minimum of two days' hospitalization. As for FIGO stage IIIC, it included, apart from the initial examination, laparoscopy, radiotherapy and chemotherapy. Chemotherapy sessions require biological tests prior to each session. A 3-week hospital stay in a medical unit is also required, with a clinical evaluation at the 3rd week of treatment, including a gynecological examination and an abdominopelvic MRI. Depending on the latter assessment, cycles of chemotherapy and surgery may be discussed, with a minimum stay of 2 days in hospital and the necessary tests before the operation. As for the FIGO Stage IVB, the patient would undergo, apart from the initial examination, chemotherapy and laboratory tests prior to each session and a hospitalization.

### *Data analysis*

Data were analyzed using MS Excel. The first column of the Excel table consisted of the investigations, examinations and surgeries required at each stage. The second column contained the costs of each procedure. The total minimum cost was calculated by adding up the costs of the various examinations required for each stage. The significance between the average costs of each stage was sought using Open Epi software.

In our study, we used the conversion rates of the Tunisian Dinar into US Dollar mentioned on the website of the Tunisian Central Bank during March 2023 [18].

### *Ethical considerations*

Our study was not based on patients' medical records; neither included personal data of patients. It consisted of calculation of the mean fees of the CC diagnosis and treatment based on guidelines. Thus, we did not need consent or information of any patient. This study was approved by the Institutional Review Board of the Epidemiology, Statistics and Medical Informatics Department in the Salah Azaiez Institute.

## 3. Results

Based on the 2021 CC guidelines issued by SAI experts, and on the finance's unit at the same public institute, the total minimum direct medical cost of CC diagnosis, check-ups and treatment in the reference institute in Tunis (Tunisia) ranged from 1700 to 8030 Tunisian dinars corresponding to 550 to 2603 US\$, depending on the cancer stage and the

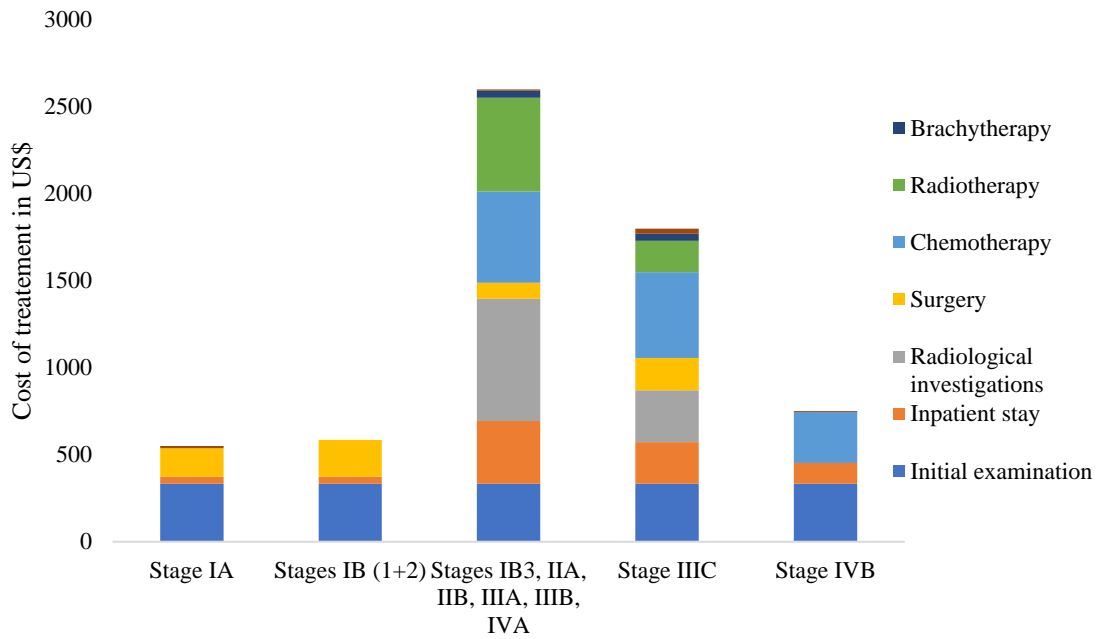


Fig.1. FIGO stage specific treatment cost of cervical cancer in US\$ - Salah Azaiez Institute, Tunisia, 2023

treatment involved. The initial medical visit confirming the existence of CC among women, and staging their cancer including a gynecological examination under general anesthesia with biopsy and/or abdominopelvic MRI and other biological tests, cost a minimal mean of 1080 Tunisian Dinars corresponding to 350 US\$. This corresponds to the direct financial cost of diagnosis of CC in a public health care in Tunisia.

After staging the cancer of the patient, each stage of the classification required different and various medical interventions including clinical, biological, radiological, and pharmaceutical resources. FIGO stage IA laparoscopy under general anesthesia, curettage, conization/ hysterectomy, inpatient stay and necessary pre-operative tests were needed for diagnosis and treatment of this stage depending on the multidisciplinary medical staff and the patient’s desire for fertility. This IA stage of CC among women cost at SAI in Tunis, Tunisia, a mean direct financial cost of 1700 Tunisian Dinars corresponding to 550 US\$. FIGO Stage IB1 and IB2, the necessary tools for diagnosis and treatment, including laparoscopy under general anesthesia, curettage, radical hysterectomy or trachelectomy, and possible hospital stays at a medical or post-surgical unit, cost a mean price of 1800 Tunisian dinars corresponding to 585 US\$ (Fig.1).

FIGO Stage IB1 and IB2, the necessary tools for diagnosis and treatment, including laparoscopy under general anesthesia, curettage, radical hysterectomy or trachelectomy, and possible hospital stays at a medical or post-surgical unit, cost a mean price of 1800 Tunisian dinars corresponding to 585 US\$ (Fig.1) IB3, IIA, IIB, IIIA, IIIB, and IVA for cervical cancer among women in the oncology institute, included a PET SCAN, sessions of radiotherapy, chemotherapy, brachytherapy, hospital stays and an assessment at the 8th week of treatment. Considering all the mentioned interventions, these stages cost a mean price of 8050 Tunisian dinars corresponding to 2603 US\$ (Fig.1). This median minimum cost was significantly higher than costs of stages IA and IB (1+2). Stage IIIC of CC included laparoscopy, radiotherapy, chemotherapy followed by a medical assessment after 3 weeks of inpatient, and potential

surgery. This stage cost a mean price of 5555 Tunisian dinars corresponding to 1800 US\$ (Fig.1).

Concerning stage IVB of CC among women, it requires chemotherapy, its laboratory tests pre-chemotherapy sessions, and its needed hospitalization days. At this stage, diagnosis and treatment mean cost is 2315 Tunisian dinars corresponding to 750 US\$ (Fig.1).

#### 4. Discussion

This study investigated the cost of treatment of CC among Tunisian females in the SAI in Tunisia. The economic direct cost of treating the various stages of CC in Tunisia in 2023 ranged between 532\$ and 2603\$, depending on the stage of the disease. In our study, as in all countries, the cost of CC care varied according to the stage. In 2003, a Tunisian study by Ben Gobrane et al. at SAI of Tunis, demonstrated that CC treatment varied between 777 to 7 458 Tunisian Dinars corresponding nowadays to 253\$ to 2420\$ [15,19]. Although the cost of cancer did not vary between the two studies throughout a 20-year-gap, it is crucial to note that the data collection methodologies differed considerably, to consistent and permanent screening and treatment practices, and a decreasing trend of CC rates [4,6,20]. The first study was based on the precise compilation of cervical cancer records over a one-year period, thus offering a more specific and detailed approach. In contrast, the present study opted for a procedure-based method of cost collection, interacting directly with the finance department in 2023. This approach may lead to variations in the results, as it takes into account the specific costs associated with each medical procedure, rather than focusing on a more global assessment over a longer period. Therefore, despite the apparent stability of costs, the difference in methodology highlights the importance of critically analyzing the data and understanding the specific nuances of each study. It is necessary to mention that Tunisia is classified by the World Bank as lower-middle income country.

Our result were compared to those from other lower-middle countries, such as Morocco, India, and Vietnam [2]. In Morocco, the average cost of treatment in the National



Public Institute of Oncology in Rabat was US\$ 2,599±US\$ 839 [10]. This average cost, estimated in 2015, is higher than the cost of the present study. This comparison might be biased, underlining the need to consider methodological differences. The Moroccan study adopted a more case-specific approach by saving data from cervical cancer records. This difference can also be explained by the time-gap between the two studies, making them incomparable due variation in the economic situations of the countries. In India, a lower middle income country, the cost to the healthcare system for different treatment modalities for CC ranged from \$291 to \$617 [11]. This result is much lower than the direct cost of the current study. This variety, indeed, may reflect cultural and financial differences between the two countries, as well as variations in the availability and quality of treatment. In Vietnam, as a third example from a lower-middle income country, the cost of treatment of CC ranged from 368\$ to 11400\$, depending on the type of institution and treatment provided [12,21]. For the minimum threshold, this approximated the minimum direct financial cost in Tunisia for stage IA cancer. This was explained by the fact that our study only considered the public sector, whereas the Vietnamese study rather took into account the public and private sectors, which explained the maximum cost limit. In fact, private facilities tend to raise prices and increase the number of necessary and non-necessary investigations in the interests of the patient's physical and psychological comfort.

Comparing our results to a low income country, this cost, as in a recent 2021 Senegalese study, varied from 1495\$ to 10662\$[13]. This direct cost in Institute Joliot Curie in Dakar varied according to the type of treatment undergone. In other words, it calculated the cost of, simultaneously, all possible treatments and not the minimal needed as we did. That is why the range in financial costs is higher than those found in our study. This cost was also higher among other low-income countries studies [22].

The cost of CC differs from one country to another depending on the diagnostic and therapeutic resources available and the cost of care but also social and health cover. As for High-Income countries, the United States of America (USA) as an example, the average cost of cervical-cancer treatment was \$29,649 in 2008 [23]. This difference between cervical-cancer treatment costs in Tunisia and the USA might be explained by the American liberal health care system where the government does not fund healthcare and where its intervention is reduced to Medicare and Medicaid; health insurance is not mandatory and the private sector covers all the healthcare system. In Sweden, the direct medical costs of treatment varied between 12317 and 31352 depending on the FIGO cervical cancer stage [14,24]. In fact, the CC direct treatment costs in high-income countries were higher than low middle income countries as highlighted in a systematic review in 2016 [24].

All the studies that were included in this discussion, even ours, used the payer perspective, where only direct financial costs were calculated. Indirect costs, within the societal perspective, were not included. Yet, it appears that the societal perspective have a stronger justification for comparison between studies [25]. In fact, the real cost of any cancer is the moral cost to the patient and his family, psychological impact, loss of quality of life, absenteeism, and the loss of productivity. This guides us to the limits of our study that only included direct financial costs of CC among Tunisian women.

### *Implication for Healthcare system*

Measuring the direct economic and financial costs of CC in this study encouraged us to not overlook the preventive aspect of the matter, which can contribute to the decrease of the economic burden.

Studies all over the globe, and in Tunisia, tried to study the cost-effectiveness analysis of CC screening strategies especially those related to the introduction of Human Papillomavirus vaccination [9,14,19,21]. This would encourage policymakers and public health actors to introduce and reinforce the strategies of prevention from CC. In fact, in Tunisia, until the date of our study, the anti-papillomavirus vaccination is not introduced in the country yet.

The present study constitutes the first one since 2003 to determine the direct cost of cervical cancer in Tunisia, which is crucial for cost effectiveness analysis of CC screening strategies in Tunisia. Further research in cost-effectiveness domain about cancer and prevention campaigns can offer valuable insights into the economic implications of CC and its prevention methods, especially that this specific cancer is preventable by a worldwide available vaccination. Indeed, health care interventions in Tunisia could be influenced by such further research. These would be evidence-based decision-making and would enhance the overall societal response.

### *Study limitation*

The principal limitation of this study is that cost of CC was determined in terms of unitary cost. It is important to mention that patients turn to the private sector for several investigations and treatments because of the great distances involved in public-sector appointments, so this is the minimum theoretical cost for patients who are covered by health insurance in the public health sector.

This study did not include data from the medical records of hospitalized patients and/or receiving healthcare in our institution (SAI). This was due to missing data from both paper and computer-based medical records on the hospital server. These problems were identified in previous attempts to carry out the same study using patient data. In fact, several patients were trying to shorten the waiting time for their treatment by carrying out their explorations in the private sector without any proof of cost in their records.

In conclusion, cervical cancer is the fourth most common malignant neoplasia in women worldwide. Despite progress in detection and treatment, CC remains a health concern on a global scale. It is also a real burden on the economy of every health care system. This study contributed in delivering essential data of the financial burdens associated to diagnosis and treatment of CC in Tunisia. Its impact resumes in guiding researchers, policymakers, and healthcare professionals in devising effective strategies to allocate resources, design cost-efficient interventions, and improve overall cancer care. CC is a preventable form of cancer. Prior to the introduction of a new action to the actual program in Tunisia for CC, our study would act as an important tool.

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## Authors' contributions

Study concept and design were done by EM and HK. Data were acquired by EM and HK. The data were analyzed and interpreted by EM and HK. Drafting of the manuscript was done by EM and HK. All authors read and approved the final manuscript.

## Conflict of interest disclosures

The authors declare no competing interest.

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