abstract

Building Oncofertility Core Competency in Developing Countries: Experience From Egypt, Tunisia, Brazil, Peru, and Panama

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PURPOSE Little is known about oncofertility practice in developing countries that usually suffer from a shortage of health services, especially those related to cancer care.

MATERIALS AND METHODS To learn more about oncofertility practice in developing countries, we generated a survey to explore the barriers and opportunities associated with oncofertility practice in five developing countries from Africa and Latin America within our Oncofertility Consortium Global Partners Network. Responses from Egypt, Tunisia, Brazil, Peru, and Panama were collected, reviewed, and discussed.

RESULTS Common barriers were identified by each country, including financial barriers (lack of insurance coverage and high out-of-pocket costs for patients), lack of awareness among providers and patients, cultural and religious constraints, and lack of funding to help to support oncofertility programs.

CONCLUSION Despite barriers to care, many opportunities exist to grow the field of oncofertility in these five developing countries. It is important to continue to engage stakeholders in developing countries and use powerful networks in the United States and other developed countries to aid in the acceptance of oncofertility on a global level.

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INTRODUCTION

MATERIALS AND METHODS

Because of advances in cancer diagnosis and treatment, the overall survival rates in most young women and men with cancer have significantly increased over the past four decades.¹⁻³ Consequently, the topic of how to prevent the chemotherapy- and radiotherapy-induced gonadotoxicity and subsequent fertility loss has gained attention. Oncofertility is a new interdisciplinary field at the intersection of oncology and reproductive medicine that expands fertility options for young cancer survivors.⁴⁻⁸ Throughout the past decade, international guidelines were published about oncofertility practice in developed countries.⁹⁻¹¹ However, little is known about oncofertility practice in developing countries that usually suffer from a shortage of health services, especially those related to cancer care. In this study, we investigated oncofertility practice in developing countries and explore the unique barriers and opportunities for growth and expansion.

A pilot survey was generated after the panel session

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to 3, 2016. To explore the various barriers and opportunities of oncofertility practice in developing countries, the survey questions were sent by e-mail to five centers from Africa and Latin America within the Oncofertility Consortium Global Partners Network (OCGPN).¹² The surveyed centers from Egypt, Tunisia, Brazil, Peru, and Panama are listed in Table 1. The survey questions were grouped into six categories: country profile, cancer care,

TABLE 1. Surveyed Centers From Five Developing Countries Country Surveyed Center

Africa	
Egypt	Reproductive Medicine Department, National Research Center, Cairo, Egypt
Tunisia	Aziza Othmana Hospital of Tunis, Tunis, Tunisia
Latin Amer	ica
Brazil	In Vitro Consultoria-Research and Development/ Clinical Embriology, Belo Horizonte, Minas Gerais, Brazil Department of Obstetrics and Gynecology, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil
Peru	Centro de Estudios e Investigaciones en Biología y Medicina Reproductiva, Lima, Peru
Panama	IVF Centro de Reproduccion (IVFPANAMA), Consultorios Hospital Punta Pacific, Panama City, Panama

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TABLE 2.	Pilot Survey Questions
Category	

Category	Question			
Country profile	Area			
	Location			
	Language			
	Population			
	Religion			
	Culture			
	Fertility rate (births per woman)			
	Economy			
	Gross domestic product			
	Global competitiveness index			
	Health system in global competitiveness index			
	Life expectancy			
	Total expenditure on health as percentage of gross domestic product			
	Total expenditure on health			
	State's health insurance			
Cancer care	Incidence rate per 100,000			
	Mortality rate per 100,000			
	Common cancers in women (%)			
	Common cancers in men (%)			
	Coverage of cancer treatment costs			
	Cancer treatments providers			
	Standard of cancer prevention and treatment			
Fertility treatments	Who can receive fertility treatments?			
	Available assisted reproductive techniques			
	Unavailable assisted reproductive techniques			
	Insurance coverage			
	Fertility treatment providers			
	Cost of a single cycle of in vitro fertilization/intracytoplasmic sperm injection			
	Success rates			
Fertility preservation treatments	Who can receive fertility preservation treatments?			
	Available fertility preservation treatments			
	Unavailable fertility preservation treatments			
	Insurance coverage			
	Fertility preservation treatment providers			
	Cost of a single frozen cycle of in vitro fertilization/intracytoplasmic sperm injection			
	Success rates			
Barriers to oncofertility	Medical			
	Economic			
	Social			
	Legal			
	Other			
Opportunities of oncofertility	What are the opportunities of oncofertility practice in your county?			

fertility treatments, fertility preservation treatments, barriers to oncofertility, and opportunities of oncofertility (Table 2). Responses from the surveyed centers were collected, reviewed, and discussed.

RESULTS

All surveyed centers from the five developing countries (Egypt, Tunisia, Brazil, Peru, and Panama) responded to all questions. Responses are listed in detail in Tables 3 to 8 (developing country profile 2015/2016, cancer care, fertility treatments, fertility preservation treatments, barriers to oncofertility, and opportunities of oncofertility, respectively).

DISCUSSION

As survival rates continue to rise, the need for oncofertility services in developing countries has become increasingly

TABLE 3. Developing Country Profile 2015/2016

apparent. Although the mortality rate remains relatively higher in developing countries than in developed ones, quality of life matters for all patients, including future fertility of adult cancer survivors. Because approximately 50% of cancer in developing countries occurs in individuals younger than 65 years, many patients are of reproductive age, and their reproductive health, including endocrine health, should be considered before treatment starts. However, with limited resources, including significant financial burdens to patients and their families such as high out-of-pocket expenses and limited insurance coverage, oncofertility services are not viewed as a necessity and are disproportionally available to affluent patients with the means to pay for these additional services. Furthermore, many providers and patients are focused on eliminating cancer and do not consider that fertility can be an important quality-of-life concern later on.

Characteristic	Egypt ¹³⁻¹⁶	Tunisia ¹⁷⁻¹⁹	Brazil ²⁰⁻²²	Peru ²³⁻²⁷	Panama ²⁸
Area, million km ²	1	0.16	8.5	1.28	0.07
Location	Africa	Africa	South Americn	South America	Central America
Language	Arabic	Arabic	Portuguese	Spanish	Spanish
Population, million	92	11	206	31	4
Fertility rate, births per woman	2.8	1.98	1.9	2.26	2.4
Religion	90% Muslim 9% Christian 1% Other	98% Muslim 2% Christian and Jewish	65% Catholic 22% Protestant 8% No religion 5% Other	80% Catholic 20% Other	74% Catholic 19% Protestant 7% Other
Culture	Conservative	Conservative	Eclectic and syncretic	Conservative	Conservative
Economy	Lower-middle income	Lower-middle income	Upper-middle income	Upper-middle income	Upper-middle income
Nominal GDP total, billion USD	330	43	1,774	192	52
Nominal GDP per capita, USD	3,615	3,822	8,678	6,027	13,268
GCI	115	95	81	67	42
Health system world ranking in GCI	87	70	74	79	57
Female life expectancy, years	73	77.8	79	78	81
Male life expectancy, years	69	73	71	73	75
Total expenditure on health, % GDP	5	7	10	5	8
Expenditure on health, % (sources)	72 (out of pocket) 25 (state) 3 (other)	37 (out of pocket) 35 (CNAM) 28 (state)	52 (out of pocket) 48 (state)	35 (out of pocket) 30 (contribution of employers [tax expenses]) 31 (state) 4 (other)	73.2 (state) 22.3 (out of pocket) 4.5 (other)
Health insurance coverage, % population	40	80	100	62	37

Abbreviations: CNAM, National Health Insurance Company; GCI, global competitiveness index; GDP, gross domestic product; USD, US dollars.

Variable	Egypt ²⁹⁻³¹	Tunisia ³²⁻³⁴	Brazil	Peru ^{35,36}	Panama ³⁷
Cancer incidence rate (per 100,000)	166.0	116.0	291.0	150.0	147.9
Cancer mortality rate (per 100,000)	95.0	66.7	92.0	92.0	70.6
Common cancers in women, %*	Breast (32.0) Liver (13.0) Brain (5.0) Ovarian (4.0) Non-Hodgkin lymphoma (4.0) Thyroid (3)	Breast (31.9) Skin (5.7) Colon (5.7) Cervical (4.3) Ovarian (4.1) Non-Hodgkin lymphoma (3.7)	Breast (28.0) Colon and rectum (9.0) Uterine cervical (8.0) Lung and respiratory system (5.0) Stomach (4.0)	Cervical (24.0) Breast (17.0) Stomach (9.0) Skin (6.0)	Breast (36.6) Cervical (26.6) Colon (13.4) Stomach (10.4) Lung (6.8) Ovarian (6.2)
Common cancers in men, %†	Liver (33.0) Bladder (10.0) Lung (6.0) Non-Hodgkin lymphoma (5.0) Brain (5.0) Prostate (4.0)	Lung (22.9) Bladder (9.9) Prostate (8.9) Skin (5.9) Colon (5.3) Stomach (4.5)	Prostate (29.0) Lung and respiratory system (8.0) Colon and rectal (8.0) Stomach (6.0) Mouth (5)	Prostate (15.0) Stomach (15.0) Skin (8.0) Hematopoietic system (7.0) Lung (6.0)	Prostate (54.7) Stomach (13.3) Lung (11.3) Colon (11.1) Oral (4.0) Liver (3.5) Esophageal (2.1)
Cancer treatment providers and coverage	National cancer institutes, university hospitals, specialized cancer hospitals, and public hospitals provide free services or are covered by insurance Some major private hospitals provide cancer treatment covered by insurance or out-of-pocket payment	The National Cancer Institute of Salah Azaiz covers 25% of cases; other patients with cancer are cared for either in the university hospitals of Sousse and Sfax or in private structures Cancer treatment costs are covered by households (50%), government (35%), and CNAM (15%)	Cancer institutes, university hospitals, and specialized public hospitals provide services covered by the national public health system Private hospitals provide cancer treatment covered by private insurance or out-of- pocket payment	Coverage of cancer treatments are possible through Fondo Intangible Solidario de Salud and an integrated health system (Sistema Integral de Salud) Cancer treatment providers include the National Cancer Institute, public hospitals, and private specialized cancer clinics	National Institute of Oncology is a large public hospital providing mostly free and public health insurance services Large public hospita also provide some cancer treatment for insured and uninsured patients Private hospitals and private providers and private health insurance or out-of pocket costs
National cancer registry	Under development	Three cancer registries: north, central, and south	Fully implemented	Under development	The Gorgas Memorial Institute for Health Studies/Geographic Information System Incidence and Mortality by Cancer

NOTE. ASCO recommendations on fertility preservation in patients of cancer.9,10

Abbreviation: CNAM, National Health Insurance Company.

*The most common cancers in young women and girls that may require aggressive gonadotoxic anticancer treatments and necessitate prior fertility preservation measures are breast, cervical, leukemia, lymphoma, CNS, renal, and bone.

†The most common cancers in young men and boys that may require aggressive gonadotoxic anticancer treatments and necessitate prior fertility preservation measures are testicular, leukemia, and lymphoma.

Respondents identified a number of barriers to oncofertility care in their countries. Common barriers are a lack of awareness among oncologists, lack of funds, high costs, and cultural and religious constraints that result in negative attitudes toward assisted reproduction technology and fertility preservation and oncofertility services. This general lack of awareness among providers may result in a reluctance to accept new technologies and practice.

Although survey respondents identified a number of barriers to care, these barriers can be positively viewed as opportunities for expansion, growth, and development. To facilitate collaborations and reduce duplicative efforts, the OCGPN was formed in 2012.⁸ The OCGPN works with reproductive specialists from 33 countries around the globe in an effort to better serve children, adolescents, young adults, and adults with cancer and other fertility-threatening diseases. It acts as an organizing center and fosters interaction among groups that can share resources, methodologies, and other experiences in the field. The establishment of a strong global network not only drives the

Treatment	Egypt ³⁸⁻⁴²	Tunisia	Brazil	Peru ⁴³⁻⁴⁵	Panama
Who can receive fertility treatments?	Married heterosexual couples only	Married heterosexual couples only	Married/stable union heterosexual and homosexual couples, single women	Married/unmarried couples/persons	Unregulated, provider dependent
ART					
IUI	Available	Available	Available	Available	Available
IVF	Available	Available	Available	Available	Available
ICSI	Available	Available	Available	Available	Available
PGD	Available	Not available	Available	Available	Available
Sex selection	Available	Not available	Available	Not available	Available
Cryopreservation					
Embryo freezing	Available	Available	Available	Available	Available
Egg freezing	Available	Available	Available	Available	Available
Social egg freezing	Not available	Not available	Available	Not available	Available
Ovarian tissue freezing	Not available	Will be available in 3 months	Available, under research projects	Recently available	Available
Sperm freezing	Available	Available	Available	Available	Available
Testicular tissue freezing	Not available	Not available	Available, under research projects	Not available	Available
Third-party reproduction					
Sperm donation	Prohibited	Prohibited	Allowed	Available but unregulated	Available but unregulated
Egg donation	Prohibited	Prohibited	Allowed Available but unregulated		Available but unregulated
Embryo donation	Prohibited	Prohibited	Allowed Available but unregulated		Available but unregulated
Surrogacy	Prohibited	Prohibited	Allowed	Available but unregulated	Available but unregulated
Adoption	Prohibited	Allowed	Allowed	Allowed	Allowed
Insurance coverage for fertility treatments	No	Fertility treatments are covered by insurance, which fully supports three stimulation cycles in women younger than 40 years and who have no children	Yes, but recently; majority No no coverage; sometimes		No
Fertility treatment providers, %		The centers of assisted medical procreation can do approximately 9,000 IVF cycles/year, 1,800 of which are provided in public centers		Mostly private centers, only one public hospital	
Private centers*	80		93		90
Public hospitals [†]	20		7		10
Average cost of a single cycle of IVF/ ICSI, USD	500-1,000	800-1,500	1,500-5,000	3,500-5,000	2,500-5,000
National registry	Not available	Not available	Available	Not available (but have a regional registry for Latin America)	Not available

Latin America)

Abbreviations: ART, assisted reproductive technology; ICSI, intracytoplasmic sperm injection; IUI, intrauterine insemination; IVF, in vitro fertilization; PGD, preimplantationgenetic diagnosis; USD, US dollars.

*Private centers include private hospitals and clinics.

†Public hospitals include university and governmental hospitals.

Treatment	Egypt ³⁸⁻⁴²	Tunisia	Brazil ⁴⁶	Peru	Panama
Who can receive fertility preservation treatments?	Married heterosexual couples more than patients with cancer	Patients who are planned to receive any gonadotoxic treatments	Married/stable union heterosexual and homosexual couples, single women, patients with cancer	Married/unmarried couples and persons, more than patients with cancer	Unregulated, provider dependent
Cryopreservation					
Embryo freezing	Available	Available	Available	Available	Available
Egg freezing	Available	Available	Available	Available	Available
Social egg freezing	Not available	Not available	Available	Not available	Available
Ovarian tissue freezing	Not available	Available	Available under research projects	research Recently available	
Sperm freezing	Available	Available	Available	Available	Available
Testicular tissue freezing	Not available	Not available	Available, under research projects	Not available	Available
Insurance coverage for fertility preservation treatments	No	No	Yes, but recently; majority No not covered; sometimes only by request of justice		No
Fertility treatments providers, %				Private centers	
Private centers*	80		93		
Public hospitals†	20	100	7		100
Average cost of a single frozen cycle of IVF/ ICSI, USD	500-1,000	800-1,500	2,000-5,500 3,500-5,000		1,500-3,500
National registry	Not available	Not available	Available (not fully implemented, does not consider patients with cancer alone)	Not available	Not available

Abbreviations: ICSI, intracytoplasmic sperm injection; IVF, in vitro fertilization; USD, US dollars.

*Private centers include private hospitals and clinics.

†Public hospitals include university and governmental hospitals.

collaborative nature of the consortium but also helps global partners to build their own programs and fertility preservation networks, as with the Brazilian Oncofertility Consortium, the Peruvian Oncofertility Network, and the Latin American Oncofertility Network. These networks were born out of the work of the OCGPN and are now models of success for future networks.

The OCGPN assists these developing countries as their programs develop and grow. All the survey respondents are current members of the consortium (Table 1), and members from both Brazil and Tunisia have adapted existing oncofertility materials to their native languages for their communities. For example, Brazil, one of the first countries to join the OCGPN, translated materials from Northwestern University's Save My Fertility online fertility preservation toolkit⁴⁷ to Portuguese so that their providers receive information in the native language. Furthermore, the group published an oncofertility textbook in Portuguese: *Preservação da Fertilidade: Uma Nova Fronteira Entre Medicina Reprodutiva e Oncologia.*⁴⁸ This book is intended for health professionals to increase their understanding of fertility

preservation in patients with cancer. Members from Aziza Othmana Hospital of Tunis, Tunisia, also translated Save My Fertility materials to French. These translation projects engage partners in consortium-wide activities, but more importantly, they bring utility to providers, patients, other health professionals in their home countries. Members of the OCGPN have hosted a number of conferences, meetings, and seminars in their home countries to educate their communities about oncofertility and fertility preservation in patients with cancer. Furthermore, the group has worked collectively on three publications that assist developing programs with justifying their program with local governmental or clinical governing bodies and with increasing awareness about oncofertility throughout their home institutions, countries, and regions.^{8,49,50} The goal is to reduce duplicative efforts and ease the burden of setting up an oncofertility practice in a country that may have limited resources.

Collaborations are imperative to the success of oncofertility centers in developing countries. However, networking is only one of the characteristics of a successful program. Persistence is key. With limited resources and lack of

Barrier	Egypt	Tunisia	Brazil	Peru	Panama
Medical barriers					
Lack of awareness among oncologists, gynecologists, and patients	Yes	Yes	Yes	Yes	Yes
Lack of advances in early diagnosis and treatment of cancer	Yes	Yes	No	Yes	Yes
Lack of interinstitutional communications	Yes	Yes	Yes	Yes	Yes
Lack of referrals from oncologists	Yes	Yes	Yes	Yes	Yes
Lack of some fertility preservation options	Yes	Yes	Yes	Yes	No
Lack of oncofertility specialists	Yes	Yes	No	Yes	No
Economic barriers					
Lack of health insurance coverage for fertility services	Yes	Yes	Yes, coverage recent; few insurance companies; sometimes only by request of justice	Yes	Yes
Most of fertility services are provided in private centers	Yes	No	Yes	Yes	Yes
Lack of institutional and research funds	Yes	Yes	Yes	Yes	Yes
Social barriers					
Sperm donation	Not accepted	Not accepted	Accepted	Not accepted	Accepted
Egg donation	Not accepted	Not accepted	Accepted	Not accepted	Accepted
Embryo donation	Not accepted	Not accepted	Accepted	Not accepted	Accepted
Surrogacy	Not accepted	Not accepted	Accepted	Not accepted	Not Accepte
Adoption	Accepted	Accepted	Accepted	Accepted	Accepted
Legal barriers					
Sperm donation	Prohibited	Prohibited	Allowed	Unregulated	Unregulated
Egg donation	Prohibited	Prohibited	Allowed	Unregulated	Unregulated
Embryo donation	Prohibited	Prohibited	Allowed	Unregulated	Unregulated
Surrogacy	Prohibited	Prohibited	Allowed	Unregulated	Unregulated
Adoption	Prohibited	Allowed	Allowed	Allowed	Allowed

institutional support, oncofertility advocates easily could become discouraged with the process of setting up their own practice. These challenges are faced even in developed nations, and many people in the oncofertility community experience similar barriers. Even in a challenging environment, oncofertility champions must continue their work to increase awareness and advocate for increased access to fertility preservation services for cancer survivors.

Success is not defined by 100% of patients with cancer pursuing oncofertility services; success is defined simply as increased awareness among both patients and providers. Even in the United States and other developed nations, not all patients choose to pursue fertility preservation options, but the goal of the oncofertility community is to ensure that these conversations take place and that providers are empowered to navigate the complex fertility issues patients with cancer face.

This study had some limitations, including a lack of data on pediatric and adolescent and young adult cancer incidence in these countries. This patient population and their parents, guardians, and providers should be aware of the effects of cancer and cancer treatments on future fertility, reproductive health, and quality of life throughout survivorship. In the future, a similar study could examine the state of pediatric and adolescent and young adult oncofertility services in developing countries and implement strategies for increasing awareness.

Even with structural and financial limitations, there are many opportunities to expand oncofertility in developing countries. An increase of awareness about available fertility preservation options is the collective goal of the community. Continued tenacity, network building, and advocacy can accomplish this goal. The use of the services offered by the existing OCGPN will reduce duplicative efforts in developing countries. As a consequence

TABLE 8.	Opportunities	of Oncofertility
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Opportunity	Egypt	Tunisia	Brazil	Peru	Panama
Chance to overcome medical barriers	Yes	Yes	Yes	Yes	Yes
Chance to overcome economic barriers	Yes	Yes	Yes	Yes	Yes
Chance to overcome social barriers	No	No	Yes	Yes	Yes
Chance to overcome legal barriers	No	No	Yes	Yes	No

of the unmet needs identified by survey respondents, the OCGPNC will use this survey as a baseline for developing countries to evaluate their own programs within the context of their country profile. This exercise will not only force sites to provide thorough self-evaluations, but also

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Provision of study materials or patients: All authors Collection and assembly of data: All authors help them to identify shortcomings and opportunities for future development and success.

In conclusion, common barriers were identified by each country that responded to this survey. These barriers were lack of insurance coverage and high out-of-pocket costs for patients, lack of awareness among providers and patients, cultural and religious constraints, and lack of funding to help to support oncofertility programs. Despite these barriers, many opportunities exist to grow the field of oncofertility in these five developing countries. Continuing to engage stakeholders in developing countries and the use of powerful networks in the United States and other developed countries will aid in the acceptance of oncofertility on a global level.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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