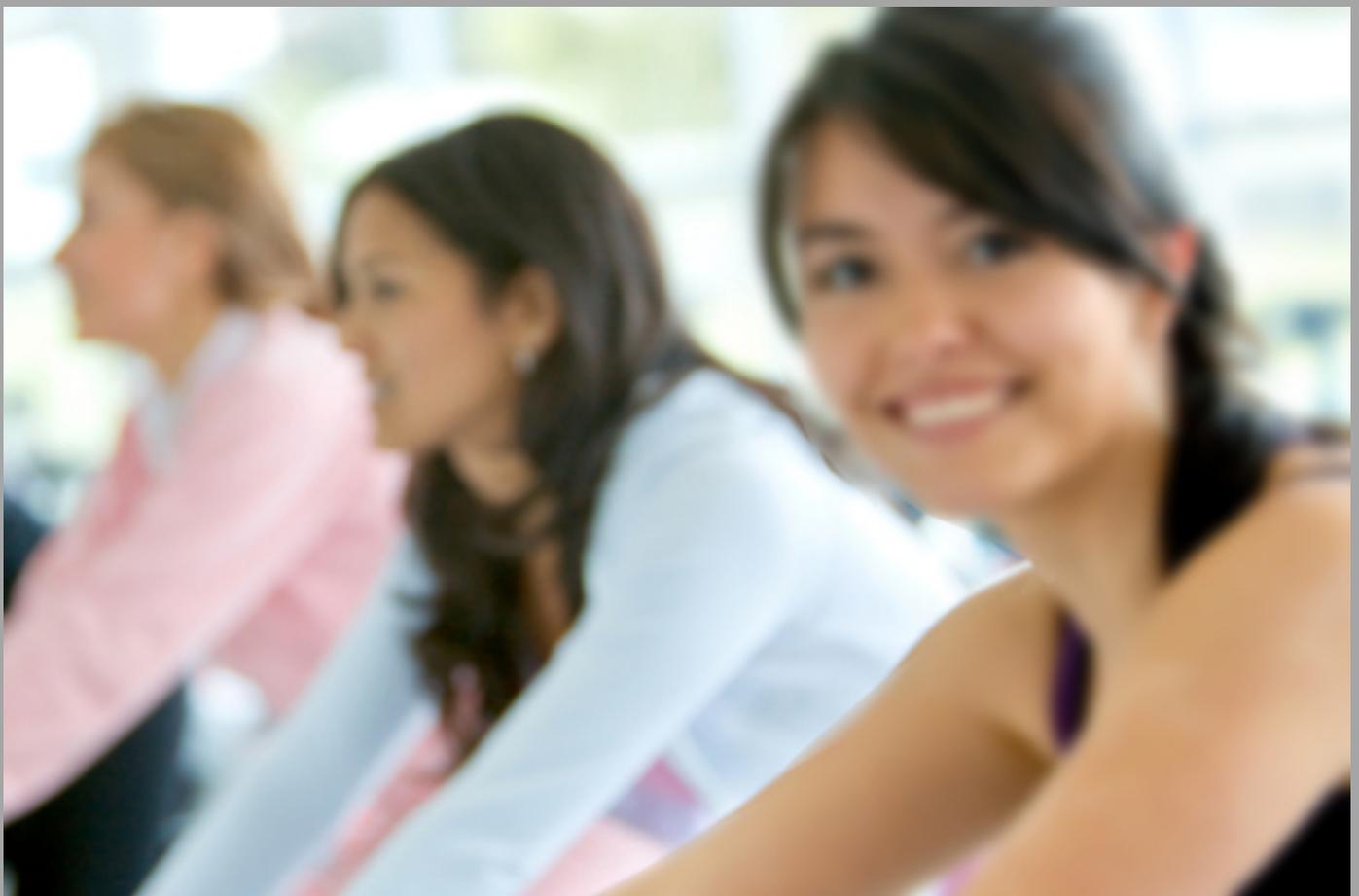


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Domestic Violence, Psychological Trauma and Mental Health of Women: A View from India

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With more than half a billion female population, India has the second largest population of females in the world. This immense resource needs to be provided safety, security and nurturance for society, and thereby the nation, to benefit in multitude ways. It goes without saying that at first the girl child has to be given a chance to be born and subsequently, not only accepted, but cherished. This requires an attitudinal shift in the way the girl child is perceived and treated in the patriarchal Indian society.

Several social ills that plague Indian society target the girl child and women. These include female feticide, neglect of the girl child, sexual abuse of the girl child, trafficking of girls and women, dowry harassment and domestic violence. Such violence against girls and women impairs their physical and psychological health which necessitates health professionals to be sensitive to such issues. Health professionals, including mental health professionals, need to be made aware of the underlying psychological trauma in order to ensure adequate and appropriate interventions. The government of India has passed legislations to punish abuse and violence against girls and women by treating them as crimes.

Domestic violence against women in India is especially significant in terms of prevalence and consequences. According to the Domestic Violence Act of India, domestic violence includes physical violence, emotional abuse and economic abuse.¹ The National Family Health Survey of India for the period 2005-2006 examined the prevalence of domestic violence among 83,703 women in the age range of 15 to 49 years. Results revealed that 34% of the women had experienced domestic violence and that domestic violence was higher among women who had low educational and economic status. Physical violence was more prevalent than sexual and emotional abuse with one third of the victimised women reporting cuts, bruises, burns, dislocations, deep wounds, broken teeth and bones. However, 75% of them did not seek help to end the violence and the data also suggested that neither education nor wealth implied a greater likelihood that women would seek help against violence.²

Domestic violence, especially physical violence, has been found to be strongly associated with poor mental health among women³ and it has also been implicated as an important factor in women seeking safety in shelter homes.⁴ In a review of studies on domestic violence in India,⁵ reported that sexual violence by husbands led to higher odds of women reporting gynaecologic symptoms like blood after intercourse, vaginal discharge, burning micturition, pain during intercourse, and symptoms suggestive of sexually transmitted infections. Further, the risk for infant mortality was 36% higher among mothers who experienced domestic violence compared with mothers who did not. In this context, it should be noted that alcohol abuse has been found to be a significant factor among men who indulge in domestic violence.^{6,4}

Interpersonal victimization of girls and women significantly impacts their ability to cope and can result in symptoms of psychological trauma such as dissociation, somatization, intru-

sive thoughts and images of the traumatic events, self-harm, and social withdrawal. Further, retraumatization and multiple traumatization contribute significantly to the risk of Post-Traumatic Stress Disorder (PTSD).⁷ However, Cook and Newman⁸ reported that mental health practitioners lack evidence based knowledge, assessment and psychotherapy skills to effectively treat trauma survivors. They recommended training for psychologists in 'Trauma Psychology' to obtain competencies in psychosocial trauma focused assessment, trauma focused psychosocial interventions and trauma informed professionalism apart from obtaining scientific knowledge and cross cutting competencies to understand trauma reactions.

A similar situation exists in India with little awareness about psychological trauma and its manifestations among counselors. Hence, it is important to train counsellors and other mental health professionals in trauma informed care. It was with this aim that a 'Trauma Recovery Clinic' was started in 2014 at NIMHANS urban well-being centre.⁹ The objectives of the clinic are to enable survivors to come to terms with the trauma and reclaim their lives by reducing emotional symptoms of trauma, enhancing self-esteem and resilience, improving social support and preventing re-traumatization. The clinic also conducts awareness and capacity building programmes for psychologists and counsellors. However, several such clinics are required in India to bring about a noticeable difference in the quality of life of girls and women in the country and ensure a life of freedom, empowerment and dignity for them.

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Editorial

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It is Time to Evaluate Human Chorionic Gonadotropin for the Treatment of Preterm Births

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Births between 20th to 37th completed gestational weeks are considered preterm. More births occur during late (34-36 weeks) than in early (before 34 weeks) preterm period. Preterm births account for more infant deaths than any other cause. The prematurely born infants have breathing problems, feeding difficulties, cerebral palsy, developmental delays, vision problems and hearing impairment. These complications are generally more severe in early than in late preterm born infants. Preterm infants require medical care in neonatal intensive care units for several weeks after birth. The surviving infants are at a greater risk for early death and life-long neurological and cognitive difficulties. All this medical care costs billions of US healthcare dollars. In addition, parents go through considerable amount of guilt and emotional trauma.

The incidence of preterm births is about 9% in US and higher in third world countries. Despite the basic science and clinical research advances to better understand and control preterm births, the rates are increasing. The current therapies include β -androgenic agonists, calcium channel blockers, non-steroidal anti-inflammatory compounds, nitric oxide donors, oxytocin antagonists, etc. Among them Magnesium sulfate ($MgSO_4$) is a popular first line therapy. Most of these drugs are only used for about 24-48 hours, so that the patients can be treated with corticosteroids to promote fetal lung maturity. The infants with relatively mature lungs have better survival chances. There is a clear unmet need to improve upon the current therapies to better control and treat preterm births.

The paradigm shift on human chorionic gonadotropin (hCG) actions revealed that it can act on human myometrium.¹ It contains hCG/luteinizing hormone receptors and their activation results in an inhibition of contractions.¹⁻⁵ These findings are consistent with the notion that hCG promotes myometrial quiescence, which is a prerequisite for pregnancy initiation and continuation.⁵ The quiescence declines as pregnancy advances, which permits myometrial stimulants to dominate so that they can facilitate normal labor progression.⁵ The maintenance of myometrial quiescence by hCG suggests, that it could be used for suppression of prematurely activated myometrial contractions, that are responsible for preterm births.^{5,6} In fact, hCG has been shown to be effective in preventing preterm birth in a mouse model.⁷

There are now five clinical studies testing hCG in the treatment of preterm births.⁸⁻¹² Four of them were on women with active labor and the fifth was on women with a previous history of preterm births.⁸⁻¹² The studies on women with active labor were compared with $MgSO_4$ treatment.⁸⁻¹¹ The results showed that while hCG was equally effective, it did not have the side effects of $MgSO_4$.⁸⁻¹¹ In the prophylactic study, hCG was found to be equally effective as vaginal micronized progesterone tablets with a better compliance rate than progesterone.¹²

Despite this encouraging data, there are no large scale clinical trials with hCG, like those conducted with 17-hydroxy-progesterone caproate (17-OHP-C) and progesterone.^{13,14} The US Food and Drug Administration approved 17-OHP-C use in women with previous his-

tory of at least one preterm birth with singleton pregnancies. It is effective, but it is not known how it works. For example, 17-OHP-C does not inhibit myometrial contractions, it is only a weak binder to PR-A and PR-B and is not converted to progesterone in the body.¹⁵ Finally, it is not cheap and the potential side effects have not yet been completely resolved. In contrast, hCG is an inhibitor of myometrial contractions, antagonizes the oxytocin actions and the mechanisms of action are rather fairly well defined.^{2,4,16} It has minor side effects that do not generally require medical attention. In addition, it is cheap and can be made even cheaper by scaling up the production of recombinant hormone. In third world countries, where access to medical care is minimal to non-existent in rural areas, inexpensive therapies, that have a minimal or no maternal or fetal side effects, are easy to adopt.

A large multicenter, randomized, double-blind clinical trials on women with active labor and those with a previous history of preterm births are needed for hCG on a comparable scale to the ones done with 17-OHP-C and progesterone. These trials require the support of governmental and non-governmental organizations, which are dedicated to improving maternal, neonatal and child health, which is heavily impacted by preterm births. Should hCG be proven useful, it is possible to develop long acting analogs, synthetic mimetics, lozenges, delivery by nanoparticles, improving intravenous infusion conditions, combination therapies to increase the treatment effectiveness, etc. As any therapy, hCG treatment may not work in every single patient. Finally, hCG therapy may not be a panacea, but it is likely to become an important part of an obstetricians tool box to treat preterm births.

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Research

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Assessing Geospatial Barriers in Refugee Resettlement Communities: A Descriptive Exploration about How to Identify the Health and Other Resource Needs of Recently Resettled Refugee Women

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ABSTRACT

Refugee women often arrive in the United States with extensive health care needs, yet significant barriers often prevent these women from accessing appropriate health care. Preliminary data suggests that refugee women living in Salt Lake County, Utah are largely immobile and experience great difficulty navigating outside their immediate neighbourhood. In addition, many refugee groups and individuals are resettled into communities where apartments are available without consideration of resource needs, i.e., access to public transportation, food and clothing retailers, schools, etc. This current research utilizes geographic information systems software to evaluate the geospatial barriers refugee women in a metropolitan areas face when seeking health and other resources. The analysis shows that, in addition to being spatially isolated from other refugees of their community of origin, these groups often reside in “resource deserts,” where resources are not in close proximity and significant barriers, such as multi-lane highways and reliable, timely public transportation prevent easy navigation. This study suggests that interventions seeking to improve refugee women’s health should evaluate the geographic barriers and seek to develop tools to expand the spatial mobility of these vulnerable populations.

KEYWORDS: Women’s health; Refugees; Barriers to services; Resource mapping; Resource deserts.

ABBREVIATIONS: RRH: Refugee Reproductive Health.

INTRODUCTION

The United States resettles more refugees than any other nation, accepting between 40,000 and 80,000 annually.¹ Frequently coming from dangerous, unsanitary conditions without consistent access to health care resources, these populations often arrives in desperate need of quality health care.²⁻⁶ Additionally, unlike many receiving nations, the United States prioritizes the admission of refugees with significant health concerns, further creating populations with pervasive and unique health care needs.⁵⁻⁷ While all refugees face significant barriers in resettlement, there is evidence to suggest that women may be particularly burdened by forced

migration.² According to a 2008 report by the United Nations High Commissioner for Refugees, the outbreak of conflict and subsequent displacement exacerbates already existing gender inequalities, resulting in a disproportionate strain on women's health.⁸

To address the health concerns of this vulnerable population and to ease transition into the American health care system, refugees are granted the same health care rights afforded to United States citizens and receive a brief period of public health insurance. However, research shows that despite such provisions, refugee women face significant barriers in understanding and accessing appropriate care for themselves and their families. Common barriers identified in recent studies include language barriers, difficulty finding the appropriate provider for specific needs, lack of awareness about health care services and their functions, financial restraints, concerns about confidentiality, the stigma of being diagnosed with certain diseases, and a lack of culturally competent care, including appropriateness of interpreters.^{3,5,9,10,11}

Of particular concern is the inability of many refugee women to overcome the geographic barrier of accessing health-care. As noted by Garfield, women view their geography in terms of landmarks and rely more on 3-D visualizations, such as buildings and/or natural structures.¹² Lack of familiarity with navigating by map and having access to only 2-D maps may hinder women's ability to identify methods for using the resources (e.g., transportation stops, clinics, major roads, etc.) they need for themselves and their families. Given that most maps are 2-D, with limited incorporation of 3-D structures, it is unclear how refugee women are able to incorporate their preferred geospatial understanding into a new environment. In a study of Cambodian refugees, researchers found that over 50% reported they were sometimes or always unable to see a doctor due to lack of transportation.¹³ Similar findings have been reported by researchers working with a variety of refugee populations.^{3,14,15} However, there is evidence to suggest that access to transportation is not the only geographic barrier refugees face in accessing care. Research has found that individual perception about the size of one's neighbourhood or "own" territory is often correlated with socio-demographic characteristics.^{16,17,18} In particular, recent migration and low income, characteristics of most refugees, are correlated with the perception of one's neighbourhood as a particularly small geographic area.¹⁷ There is also evidence to suggest that refugees may not feel comfortable leaving the boundaries of their familiar neighbourhoods, even when transportation options are available. For example, one study found that despite affordable and convenient public transportation, many refugees did not feel confident in their ability to use these resources and would rather miss their medical appointment than try to navigate the linguistic and cultural challenges of unfamiliar territory.¹⁸

Together, these studies suggest that refugees may have a limited geographic area they consider to be "their" territory

and that navigating outside those boundaries may be particularly difficult. Although it is clear that transportation is a central barrier to accessing healthcare, further research is needed to understand refugees' perception of their neighbourhood and to assess their mobility both within and outside of these boundaries.

In spring 2014, the Refugee Reproductive Health (RRH) Committee hosted a workshop for Congolese women refugees. The purpose of the workshop was to explore how the community defined "health" in the broadest possible sense.¹⁹ The RRH Committee had been working together for over two years with various refugee communities to provide workshops on topics of interest to these groups. The RRH Committee is composed of individuals from state government, refugee communities, and university. We spent three months planning the workshop topic and inviting presenters, as well as obtaining incentives for workshop participants. Members of the RRH Committee, including Congolese female community leaders, volunteered to transport participants from their homes or other locations so that they could participate in the workshop. The majority of refugee women from the Congolese community do not drive; therefore, transportation to/from events is always an issue. We discussed having the workshop participants take public transportation, but decided that in order to have individuals arrive in a timely manner we should provide transportation for these women. As volunteers set out to pick up the workshop participants, a number of problems arose. We identified three specific issues:

- We had thought that other members of the Congolese community could transport female participants; however, the female community leaders stated there were a number of cultural issues that prohibited that from happening;
- We had one set of volunteers picking up the participants for the workshop and a second set of volunteers taking people home after the workshop; and
- Volunteers, community leaders, and/or RRH Committee members had not communicated well enough about transportation needs and expectations, and refugee women were not familiar enough with their "new" communities to navigate their own neighbourhoods effectively.

Once the workshop was completed, the RRH Committee met to discuss the various issues that impacted workshop implementation.

First, the cultural parameters for having non-family members provide transportation for workshop participants was a large problem. A number of women from the community mentioned that cultural expectations about "sexual favors" between men and women made them very uncomfortable. So having male community members (who might be more familiar with neighbourhood landmarks, etc.) volunteer to provide transportation was not a workable solution.

Second, it was unclear to volunteer drivers where the

refugee women lived. Community leaders had no address or phone list available so that it would be easy to determine where to collect the participants.

Third, there was no clear sense for the workshop participants that volunteers would be picking them up at a specific time and/or place for the afternoon workshop. As a consequence, volunteers drove around the city, locating participants and then made a number of trips back and forth so that participants not yet in attendance, but identified by attendees as they arrived, could attend the workshop.

Fourth, once the workshop was completed, participants could not tell the new set of volunteer drivers what their addresses were nor how to get back to their residences. Volunteers drove around attempting to locate familiar landmarks with the participants, which was very problematic because participants could not provide an idea of what was a familiar landmark.

The stress felt by all surrounding the workshop transportation issues led us to consider what could be done to ensure that these needs and expectations could be addressed more concretely for the next set of workshops for refugee women. Although having a listing of residence locations of refugee groups would have been helpful, we also needed a better understanding of where refugee women lived, what were the resources in their communities, and how refugee women viewed their neighbourhoods and community boundaries?

For this article, we identified critical resources that women from the refugee communities might have in their neighbourhoods. The purpose of the article is to describe our process in identifying these resources so that we can move to the next step of working with women in the communities to determine how they view their neighbourhoods and the resources therein.

METHODS

ArcGIS (version 10.2. Redlands CA: Environmental Systems Research Institute) mapping software was used to map the spatial distribution of refugee residences and basic resources across Salt Lake County. The Refugee Resources Manual provided addresses for seven apartment communities with significant resettled refugee populations.²⁰ Five additional apartment communities with refugee residents were identified by personnel from the refugee resettlement agencies and the Utah Department of Health. The addresses for these refugee residences were geocoded in ArcGIS, a process by which elements are assigned spatial coordinates based on street address, city, and zip code.

Shape files for roads, healthcare facilities, libraries, bus routes, and light rail routes were obtained from the Utah Automated Geographic Reference Center (<http://gis.utah.gov/data/>). These shape files were uploaded directly into ArcGIS with slight modification. The healthcare facilities shape file included ad-

resses for a broad variety of health-related resources that were deemed not relevant to this particular study (e.g., nursing homes, hospice centers, etc.). Authors RJ and LHG reviewed the list and limited the addresses to hospitals, emergency rooms, urgent care facilities and clinics where primary care services were offered. The bus route shape file was modified to exclude all inter-county express routes, as these were also deemed irrelevant to the current study. The shape file for libraries was modified to include public-access libraries only. Public libraries were included because they offer information on healthcare resources in Salt Lake County and serve as an important source for internet access for many refugees.

Addresses for grocery stores for six major chains located in the Salt Lake County area were identified from the respective corporate websites (www.dansfoods.com, www.freshmarketstores.com, www.harmonsgrocery.com, www.reamsfoods.com, www.smithsfoodanddrug.com, www.walmart.com). Halal markets, an important source of certain food items for Muslim refugees, were identified by a member of the Somali refugee community. The addresses for grocery stores and halal markets were geocoded in ArcGIS.

All shape files and geocoded addresses were combined to simultaneously map refugee residences, transportation routes, and resources. Distances from each residence to the nearest healthcare facility, library, grocery store, and halal market were measured in Arc Map as the shortest distance by road. Estimated travel times from each residence to the nearest resource of each type were calculated using the public transportation feature of Google Maps. The address of the residence and location of the resource were entered and the shortest travel time between 12:00 p.m. and 1:00 p.m. on a standard weekday was recorded.

One-way distance and travel time from residences to resources were graphed as box-and-whiskers plots using Stata (version 13.1, College Station, TX). The box represents the middle 50% of data points (either distance or travel time); the ends of the box correspond to the 25th and 75th percentiles and the line embedded in the box corresponds to the median. The ends of the whiskers generally represent the minimum and maximum observations. In cases where there are outliers in the data, the whisker represents the data point that does not exceed 1.5 times the box width and the outlier data points are marked with a dot beyond the whisker.

DISCUSSION

Based on these mapping data and resource elements, it is clear to us that spatial location presents barriers to the establishment of a refugee support network. Refugee housing is dispersed across a large geographic area (approximately 42 square miles) with substantial internal boundaries (e.g., Interstate 15 or I-15). A point of interest is that refugee groups are not housed

by community of origin. Members of one community could be housed up to 13 miles apart. In addition, many refugees do not speak English well enough to establish networks within their residential community with individuals or groups outside their community of origin. Many refugees reside in “resource deserts.” Four of the 12 residences had no resources within one mile. All of these issues lead to a very isolated existence in the Salt Lake Valley, and hinder attempts to gather community members for profession- and/or community-centered meetings.

Figure 1 illustrates the resources that are available near the refugee women’s residences (n=12). The following are clearly indicated on this map:

Most residences are on or near a public transportation route only one residence was not

- Five of the residences were near a public library resource
- Eight of the residences were near a clinic
- Two residences were near a hospital-in fact these two residen-

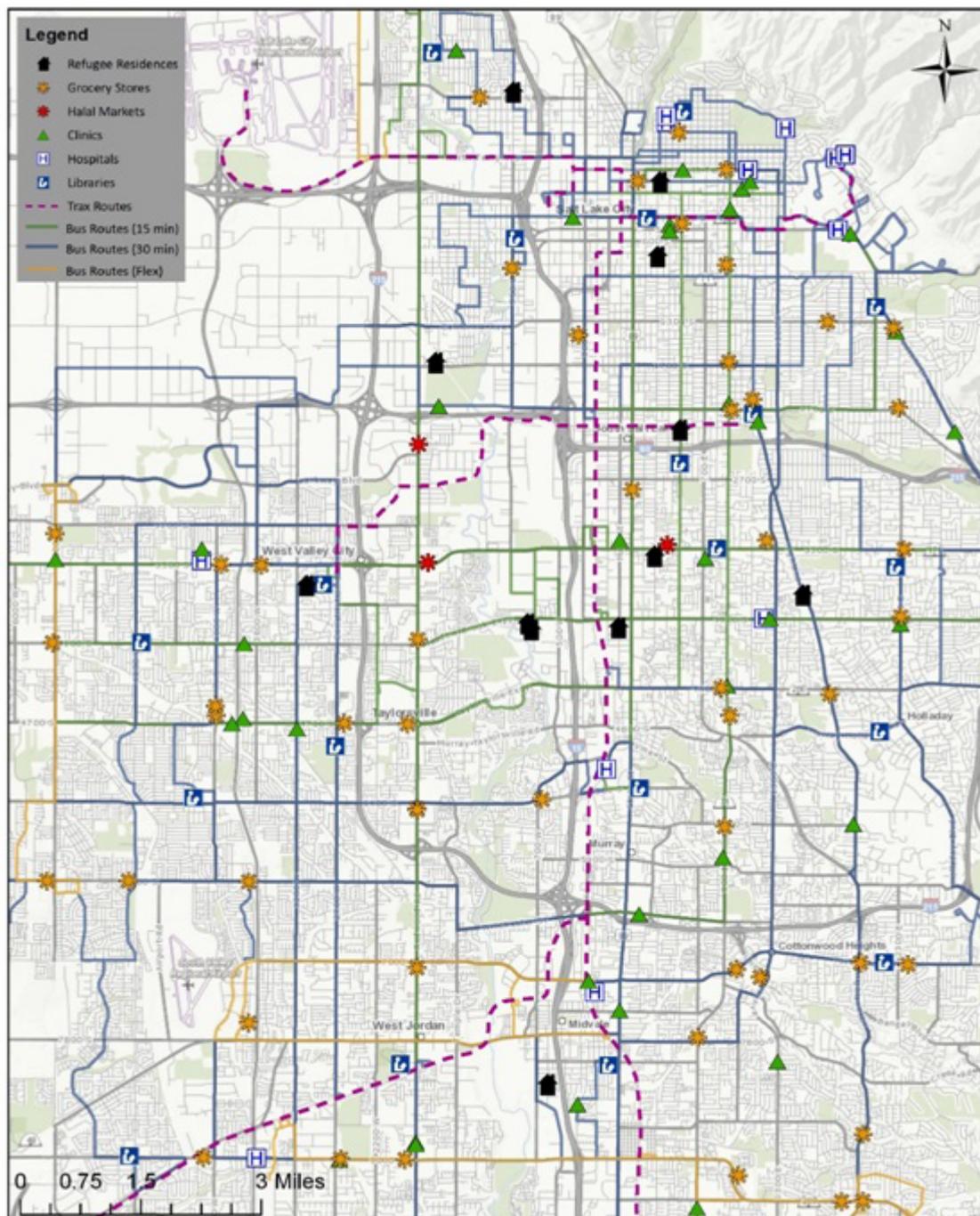


Figure 1: Location of refugee residences and health-related resources.

ces were near six hospitals of varying types

- Seven residences were near grocery stores; one was also near a halal market
- Three residences were near one another—although one residence was on the other side of I-15 (a major freeway)

As highlighted in Figure 2, the median distances from residence to resource suggest resources are often too far away to regularly reach by walking:

Grocery store: 1.05 miles

Halal market: 2.90 miles

Clinic: 1.00 miles

Hospital: 2.20 miles

Library: 1.50 miles

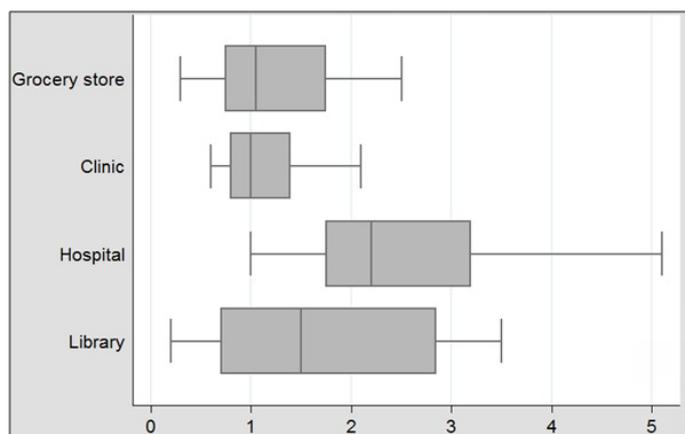


Figure 2: Distance to resources (one-way, in miles).

Since the majority of refugee women do not own a car of their own and do not drive, these women must rely on community members and/or public transportation when they need to access resources in their communities. However, as shown in Figure 3, using public transportation can take considerable time.

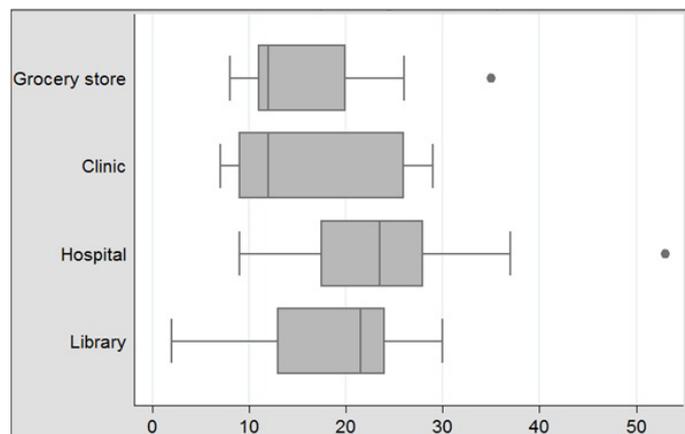


Figure 3: Public transportation travel times (one-way, in minutes)

Figures 2 and 3 should be considered within the context of other factors that may impact traveling to and from needed resources for refugee women. First, the duration of the time for traveling to and from resources were taken from the 12:00 p.m. hour on a week day. Early mornings and evenings may be more problematic because of higher traffic rates and increased numbers of travelers. In some cases, people may have to wait for a second train or bus before they can reach their destination. Along with the time issue, travelers will need to navigate the process of transferring to other routes to reach their destinations.

Second, Utah has winter weather where snow can halt a bus service and/or make public transportation run late. Thus, women need to travel in inclement weather, which may not be temperatures they are accustomed to if they have come from a more moderate or tropical climate. If a woman needs to travel in the snow and make a number of transfers to reach her location, she may decide not to travel at all and go without what she needs from the resource.

Third, public transportation in Utah runs more frequently and consistently during week days and daylight hours. If she has a job that is early in the morning, late in the evening, a graveyard shift, and/or a weekend shift, the woman may not be able to access public transportation to get to her job. Buses on the weekends, especially Sundays, run every 60 to 90 minutes beginning at 12:00 pm. until about 6:00 pm. on certain routes. Not all routes are available on weekends.

CONCLUSIONS

This descriptive article explores the impact of resource locations, geospatial settings, and public transportation on refugee women’s ability to access these services. It is clear from the geospatial discussion that refugee women are unclear about how to identify the landmarks in their neighbourhoods and how those landmarks connect to resources. In fact, some refugee women live in resource deserts and need to travel significant distances to obtain the resources they need.

The next steps for our work will be to establish perceived neighbourhood boundaries and navigation techniques among refugees of various communities of origin. We plan to utilize GoPro cameras to walk with refugee women as they navigate their neighbourhoods, travel to and from their jobs, and access health and other community resources. With these activities, we can determine the needs of refugee women in this arena. This information will be transferable in discussing resettlement issues for various refugee groups.

In addition, we will examine the differences in how refugee women and men navigate to resources across this Intermountain West city. We plan to obtain information from refugee groups about how they understand and “see” their neighbourhoods and communities as well as the resources in these

communities. Once we have a better understanding of these issues, we will work with providers and refugee women to develop a more comprehensive discussion about how to navigate to resources and how to obtain needed services.

IMPLICATIONS FOR HEALTH CARE PROVIDERS

In making treatment or referral recommendations for refugees, providers and clinical staff may need to consider geo-spatial issues. For example, is there a pharmacy in the neighbourhood setting where a prescription can easily be filled or will this patient have to travel outside his/her own neighbourhood to obtain the prescription? If the latter, then identifying contiguous neighbourhoods that can reasonably be accessed and/or identifying appropriate public transportation routes to a pharmacy could be important in empowering a refugee to adhere to a clinical recommendation.

In addition, providers should develop a sense of what resources are available for refugee communities given their addresses. Directions to resources should be provided in terms of landmarks with which clients would be familiar rather than street name or cardinal directions.

The overall take away message is that providers in all health and allied health fields need to be more aware of the types of resources and their locations so that information can be adequately provided for refugee client populations.

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Research

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Prevalence of Urogynaecological Symptoms in Survivors of Cervical Cancer in a Tertiary Care Gynaecologic Oncology Clinic of a Developing Country

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ABSTRACT

Background: A lot of research has focussed on bowel symptoms but data is relatively scarce on exact burden of urinary subset of urogynaecological symptoms in survivors of cervical cancer.

Aims and objectives: To find out the prevalence of urinary subset of urogynaecological symptoms, in women with advanced cervical carcinoma treated with surgery and/or radiotherapy and comparing same with a control group.

Methods: A questionnaire incorporating demographic and urogynaecological (urinary) symptoms (IUGA terminology) was prepared and used to interview over 400 women between October 2008 and June 2010 in a case control observational design; 200 patients (study group) with history of treated cervical cancer, attending gynaecological cancer clinic and 200 patients (control group) with benign conditions attending Gynaecology outpatient clinic were interviewed. The frequency of various urinary problems was correlated with the demographic data and cystoscopic findings wherever appropriate and available.

Results: Increased daytime frequency of urination (25% vs. 6%, p=0.0001), dysuria (25% vs. 3%, p= 0.0001) and hematuria (26% vs. 2%, p= 0.0001) were seen more in cervical cancer patients compared to the controls. Nocturia (30% vs. 6%, p=0.6) and urinary hesitancy (7% vs. 2%, p=0.09) did not show any statistically significant difference. Among urinary incontinence, 'any' urinary incontinence (38% vs. 3%, p=0.0001), urge incontinence was seen in 1% vs. 3%, stress incontinence in 28% vs. 8%, p=0.0001, "continuous (extra urethral origin)" incontinence was seen in 8% vs. 0% and "mixed" incontinence in 1% vs. 2% (all cancer versus control group).

Conclusions: There is a high burden of urogynaecological problems in women with carcinoma cervix treated with surgery and/or chemo-radiotherapy as compared to controls.

KEYWORDS: Carcinoma cervix; Urogynaecological problems; Urinary incontinence.

ABBREVIATIONS: IUGA: International Urogynecological Association; ICS: International Continence Society; STROBE: Strengthening the Reporting of Observational studies in Epidemiology.

INTRODUCTION

Treatment of gynaecological cancer has its own unique sets of associated short- and long-term complications and morbidities. There is a lot of data available on the prevalence of bowel symptoms in patients treated and followed up for cancer of the cervix.^{1,2} These complications vary according to whether surgical or non-surgical treatment was used.^{2,3} Radiation

changes tissue pliability and vascularity, the latter by obliterating the small blood vessels as well as mucositis. This leads to vaginal atrophy, enteritis and cystitis. Cystitis is seen usually as radiation doses approach 3000 cGy to the bladder.¹⁻⁶ This presents as accompanied by suprapubic tenderness, dysuria, urinary frequency and urgency Incontinence. As doses to the bladder approach more than 6000 cGy, acute hemorrhagic cystitis, chronic cystitis, fibrosis with decreased bladder capacity, and fistula formation may ensue.¹⁻⁶ The treatment of urinary incontinence in patients with prior radiation exposure and history of radical hysterectomy is particularly complicated especially for continuous incontinence of extraurethral origin *viz* fistula as surgical treatments can be compromised by the poor vascular supply to the tissues after radiation therapy.⁴⁻⁷ Chemotherapy has widespread effects on various systems and specifically to lower urinary tract, can be a cause of haemorrhagic cystitis.²⁻⁴ While assessing the need for specialist urogynaecological input in our patients, we noticed that contemporary literature available on morbidity burden of urinary symptoms is restricted only to very few specific conditions/complications. Surgery in the form of radical hysterectomy has its own set of complications such as reduced/absent bladder sensation and ureteric fistulae (and the same has been adequately explored by researchers.^{3,4} Both Constipation and urinary dysfunction have been reported in earlier studies due to injury to the parasympathetic nerves during pelvic surgery.^{3,6-7} Women with cervical cancer frequently develop symptoms like hematuria and/or overactive bladder resulting from various causes including cystitis due to both direct and indirect effects of cancer and its treatments. The major syndromes encountered in these women are increased susceptibility to infections due to both physical and immunologic effects of treatment, haemorrhagic cystitis caused by chemotherapeutic urothelial toxins and urinary problems caused by both acute and chronic effects of radiation therapy. Radical hysterectomy also shortens vagina and affects coital function.⁵ The incidence of bladder sensory symptoms is one of the most common and debilitating long-term complications of radical pelvic surgery and/or radiation for the treatment of cervical cancer.⁴⁻⁶ Surgery involves inherent surgical complications, both general and specific, the latter including conditions like reduced/absent bladder sensation and ureteric damage with radical hysterectomy.⁸ The pathophysiology is believed to be related to the disruption of the innervation to the bladder during surgery and several groups advocate adoption of nerve sparing surgical techniques to avoid these.³⁻⁶ The number of women who report urinary symptoms may be the 'tip of the iceberg', and while the absolute prevalence of symptoms may be of academic interest, its impact on quality life will determine the need for health care services, specifically for the urogynaecologic subspecialty in the multidisciplinary set up of a tertiary care gynaecological cancer clinic.

The present study was conducted to find out the prevalence of a specific subset of urogynaecological problems in women with carcinoma cervix treated with surgery and/or radiation therapy. Determining the burden of such problems can

be used to provide urogynaecological/continence services in the community.

MATERIALS AND METHODS

This study is part of our larger project on prevalence of urinary and bowel morbidity in follow-up patients of gynaecologic malignancies approved by the Ethics Committee of the Hospital. In this present study, using a case-control observational design a total of 400 women 200 patients (study group) with history of cervical cancer, treated with surgery, chemotherapy, radiotherapy or varying combinations of same and attending a dedicated gynaecological cancer clinic and 200 patients (control group) with benign gynaecological conditions attending General Gynaecological outpatient clinic from October 2008 to June 2010 were randomly chosen and recruited using random number tables, and interrogated regarding various urinary problems following surgery and/or radio therapy as per the designed questionnaire. Both the clinics are part of a tertiary care research and referral hospital in urban northern India. A questionnaire to assess various urinary problems following surgery and/or radio therapy was specially designed to conduct the study in English and Hindi language versions and the same was used for interviewing the subjects after obtaining written informed consent. It included demographic data of the women like age, parity, socio-economic status, urinary symptoms. We adapted the questionnaire developed by Kelleher et al⁹ from Kings College Hospital London to develop the present questionnaire suiting our local needs. The symptoms were then reclassified from the data accrued as per the current definitions issued by the International Urogynecological Association (IUGA)/International Continence Society (ICS) Joint Report on the Terminology for Female Pelvic Floor Dysfunction,¹⁰ as these definitions came after the study was underway. The questionnaire elicited information on the increased daytime frequency (Complaint that micturition occurs more frequently during waking hours than previously deemed normal by the woman), nocturia (Complaint of interruption of sleep one or more times because of the need to micturate. Each void is preceded and followed by sleep), dysuria (burning micturition), urinary hesitancy (Complaint of a delay in initiating micturition), haematuria, urinary incontinence (Complaint of involuntary loss of urine). They were enquired about the stress incontinence (Complaint of involuntary loss of urine on effort or physical exertion), urgency incontinence (Complaint of involuntary loss of urine associated with urgency), both of them (mixed incontinence) and continuous incontinence (Complaint of continuous involuntary loss of urine).

A priori sample size was calculated. Using national and hospital estimates for cervical cancer, a sample size of 193 is required in each group for an intended power of 0.80 and alpha error of 0.05. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) recommendations for case-control observational studies have been followed as far as practicable. The frequency of various urinary problems was correlated

with the demographic data and cystoscopic findings wherever appropriate and available. Statistical analysis was performed using Statistical Package For Social Sciences 20.0.0 (SPSS Inc.) using Chi Square test and Fischer exact test taking P value <0.05 as significant. The study was adequately powered to tell the association between urinary symptoms and patient groups.

RESULTS

The demographic profile and general information of the respondents is shown in Table 1. At baseline, more women in the gynaecological cancer clinic group were post menopausal. The distribution of index conditions of patients recruited from the General gynaecological clinic as controls was: Fibroid uterus: 60(30%), Chronic cervicitis: 55(27.5%), Pelvic Inflammatory disease: 35(17.5%), Endometriosis: 25(12.5%), Prolapse uterus: 25(12.5%).

| Characteristics | Cases (Gynaecological Cancer clinic) (n=200) | Control (General Gynaecological Clinic) (n=200) | Total (n=400) | P value |
|------------------------------|--|---|---------------|---------|
| Age: Mean(yrs) | 50.87(10.7) | 48.7(10.7) | 49.77 | 0.05 |
| Range (yrs) | 35-68 | 32-56 | 32-68 | |
| Parity | 4(2-8) | 4(0-6) | 3.9 | 0.13 |
| Education | | | | |
| Illiterate | 48 | 38 | 86 | 0.22 |
| Literate | 152 | 162 | 314 | |
| Socio-economic status | | | | |
| Below poverty | 18 | 14 | 32 | 0.307 |
| Poor | 38 | 28 | 66 | |
| Middle class | 114 | 98 | 212 | |
| Upper Class | 30 | 40 | 70 | |
| Postmenopausal | 122 | 20 | 142 | 0.001 |
| Diabetes mellitus | 38 | 26 | 64 | 0.102 |

Table 1: Demographic Characteristics of patients.

There is high overall prevalence of urinary symptoms in patients treated for cancer cervix (104 out of 200; 52%, CI=44.8-59.1) compared to benign conditions (50 out of 200, 25%, CI=19.2-31.2); p=< 0.001. Various urinary symptoms in women treated for cervical carcinoma and benign conditions are shown in Table 2.

Frequency of urination (25% vs. 6%, p=0.0001), Dysuria (25% vs. 3%, p= 0.0001) and Hematuria (26% vs. 2%, p= 0.0001) are the symptoms that are seen more in cervical cancer patients compared to the benign conditions. Nocturia (30% vs.

6%, p=0.6) and urinary hesitancy (7% vs. 2%, p=0.09) did not show any statistical significance between the study and the control groups. Although various types of urinary Incontinence are seen in both the groups (Table 3), Overall urinary incontinence (38% vs. 3%, p=0.0001) and specifically stress incontinence (28% vs. 8%, p= 0.0001) and continuous (extraurethral i.e. fistula) incontinence 16% versus 0% (p=0.007) were more commonly noted in cervical cancer group compared to controls.

| Urinary symptoms | Cervical cancer (cases) patients n=200 (%) | General Gynaecology (control) patients n=200 (%) | P Value |
|------------------------|--|--|---------|
| Frequency of urination | 50(25) | 12(6) | 0.0001* |
| Nocturia | 60(30) | 12(6) | 0.623 |
| Burning micturition | 50(25) | 6(3) | 0.0001* |
| Urinary hesitancy | 14(7) | 4(2) | 0.092 |
| Hematuria | 52(26) | 4(2) | 0.0001* |

*Statistically significant

Table 2: Comparison of urinary symptoms between Cases and Controls

| | Cervical cancer (Cases) n=200 (%) | Benign conditions (Control) n=200 (%) | P value |
|-----------------------------------|-----------------------------------|---------------------------------------|---------|
| Urinary Incontinence | 76(38) | 6(3) | 0.0001* |
| Stress incontinence | 56(28) | 16(8) | 0.0001* |
| Urge Incontinence | 2(1) | 6(3) | 0.623 |
| Mixed Incontinence | 2(1) | 4(2) | 1.000 |
| Continuous incontinence (fistula) | 16(8) | 0(0) | 0.007 |

*Statistically significant

Table 3: Urinary Incontinence in cervical cancer and benign conditions.

We retrospectively analysed the cystoscopic findings in all the cervical cancer patients prior to radiotherapy (Table 4). In 65% of cases, there was no positive finding and even post-radiotherapy, it did not correlate significantly with regard to symptoms. Mean time to onset of urinary symptoms from completion of cervical cancer treatment was 14.14 weeks.

| Findings | Percentage |
|----------------|------------|
| Normal | 65 |
| Cystitis | 17.5 |
| Bullous Oedema | 10 |
| Growth | 7.5 |

Table 4: Cystoscopy findings (%) in patients with cervical cancer prior to radiotherapy.

DISCUSSION

The treatment of cervical cancer may be surgical or using chemotherapy or radiation or a combination of either depending mainly on the stage mainly and secondarily on behaviour of the disease and patient characteristics.

All modalities may lead to pelvic pain and altered self body image leading to sexual dysfunction.^{1-6,11} Thus there myriad

of ways how treatment of cervical cancer affects woman's health and generates several subsets of symptoms including pelvic floor dysfunction/urogynaecological symptoms.⁵ Yet it is surprising that often pelvic floor care givers such as urogynaecologists, physiotherapists and continence nurses are missing as regular components of the multidisciplinary fabric expected of a gynaecological cancer clinic setup especially in developing countries like India where emergency obstetrics and gynaecological cancer are priority areas and urogynaecology is yet to arrive as a separate subspecialty. Amongst urogynaecological symptoms, most of the studies from gynaecological cancer groups focus on bowel/faecal symptoms and some on sexual function.^{1-7,11} The relative dearth of data regarding the set of lower urinary tract symptoms explored by us may also point towards lack of holistic approach towards gynaecological cancer patients in many set-ups and the fact that often these symptoms stay unattended unless adequately probed for and hence they continue to impair quality of life as these may be perceived both by the patients and care-givers as less important in the context of the primary condition, that is cervical cancer. Nonetheless they are widely prevalent as seen in our study and may be indirectly contributing to the low quality of life scores in cancer patients and addressing them may be a useful adjunctive tool to increase positive perception of gynaecological cancer treatment strategies.^{5,11} In the study of the quality of life of cervical cancer survivors compared with the quality of life of a sample of the general Korean female population,⁵ the survivors reported more impaired social functioning and, as in earlier studies more severe constipation and diarrhoea, urinary symptoms, and chronic leg lymphedema. More studies to explore this premise would be needed to make recommendations for care givers in such setting.^{5,11} As more women survive gynecologic cancer, they will encounter the long-term effects of treatment on their pelvic floor function. It may be noted in our results that while the age was not statistically different in the cases and control groups, many more women in the cases group were post menopausal. This is because of treatment related menopause, whether surgical/radiation/chemotherapy/chemoradiation. The urinary symptoms may partly be contributed by the urogenital atrophy induced by the iatrogenic menopause over and above other direct and indirect effects on the local tissues.

While the overall prevalence of urinary incontinence symptoms in gynaecologic oncology patients¹² has been reported by Del Priore et al to be 60%, with 23% reporting severe symptoms, how these statistics compare to the prevalence of pelvic floor disorders experienced by woman without gynaecologic cancer remains to be described. The incidence of long-term bladder dysfunction was reported by Benedetti et al in a case-control study of 76 patients undergoing neoadjuvant chemotherapy and type 3-4 radical hysterectomy for the treatment of locally advanced cervical cancer.⁶ Detailed urogynecologic assessments were higher than expected based on previous reports, at 76%; the main disturbances were detrusor over activity (21%), mixed urinary incontinence (24%), and de novo stress incontinence (21%). Despite these high rates of abnormal urodynamic func-

tions, only 20 patients (26%) complained of urinary symptoms (sensory loss, difficult micturition, severe urinary incontinence.⁶ How these statistics compare to the prevalence of pelvic floor disorders experienced by woman without gynecologic cancer remains to be described. This is one novel aspect of our study where we have used a random and substantially large control group from general gynaecology clinic to assess the prevalence. In our study, urinary symptoms were experienced by 52 % of patients following radiotherapy with the mean period of 14.14 weeks which was similar to studies done by Covens et al (1993),¹³ Anderson et al (1997),¹⁴ Klee et al (2000),¹⁵ and Zola et al (2000).¹⁶

CONCLUSION

Our study confirms the high prevalence of urogynaecological problems in survivors of cervical cancer patients compared to controls.

CONFLICT OF INTEREST: None.

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Review

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Women and Heart Disease: Understanding Risk Factors for Coronary Artery Disease

Ahmad Alsarrah^{1*}, Osama Alsara¹ and Heather S. Laird-Fick²¹Department of Internal Medicine, Michigan State University, East Lansing, MI, USA²Associate Professor, Department of Internal Medicine, Michigan State University, East Lansing, MI, USA**ABSTRACT**

Cardiovascular disease (CVD) is the leading cause of death in women in the US. Although the overall death rate due to CVD has decreased recently, it has actually increased in young women. Coronary Artery Disease (CAD), which may lead to myocardial infarction, congestive heart failure, and death, is an important focus for preventive efforts. The impact of traditional cardiovascular risk factors such as family history, diabetes mellitus, hypertension, hyperlipidemia, and smoking differs with gender. Women face unique risks related to pregnancy, menopause, and exogenous estrogen, and are more likely to develop other diseases (e.g autoimmune diseases, breast cancer) whose course or treatment may be complicated by CAD. This article will review CAD risk factors in women, tools to quantify that risk, and interventions to decrease it.

KEYWORDS: Women; Cardiovascular disease; Coronary Artery Disease; Risk factors.**ABBREVIATIONS:** CAD: Coronary Artery Disease; CV: Cardiovascular; CVD: Cardiovascular disease; CAC: Coronary Artery Calcium; DM: Diabetes Mellitus; HDL: High Density Lipoproteins; hs-CRP: high sensitivity C-reactive protein; LDL: Low Density Lipoprotein; MI: Myocardial Infarction; OSA: Obstructive Sleep Apnea; PCOS: Polycystic ovarian syndrome.**INTRODUCTION**

Cardiovascular disease (CVD), which includes structural and functional disorders of the heart and blood vessels, is the leading cause of death in both men and women in the United States. It causes 25% of overall mortality in women.¹ The number of CVD deaths in the last three decades was higher in women than in men,² and the mortality rate attributable to Coronary Artery Disease (CAD) in young women actually increased despite decreased mortality in the general population.³ Reasons for these trends are complex. Typical symptoms of CAD are sometimes absent or subtle in women. Studies have shown that nearly two-thirds of women who die suddenly of CAD had no previous symptoms that might have triggered treatment.⁴ Many CVD risk factors, such as Diabetes Mellitus (DM), High Density Lipoproteins (HDL) and triglyceride levels have greater impact on women than men.⁵ Women face unique risks related to pregnancy, menopause, and use of exogenous estrogen for hormone replacement therapy or contraception.⁶ Use and efficacy of primary prevention measures may vary in women.⁷ Finally, women continue to receive less-aggressive therapy for established CVD despite evidence that they benefit from the same therapies as men.⁸ This article will review the risk factors for CAD in women, and interventions to decrease that risk.

RISK OF CVD RELATED TO SOCIAL FACTORS AND FAMILY HISTORY**Family History**

Clinicians routinely enquire about family history of premature CAD (younger than 50

years in male first degree relatives or 65 years in female first degree relatives).⁹ Yet in a multivariate analysis of traditional risk factors, family history was predictive only in women. Analysis of two large cohorts in the Physician's Health Study and Women's Health Study showed complex relationships. History of maternal Myocardial Infarction (MI) was associated with increased risk for men and women. Paternal MI at any age was associated with increased risk in men, but only premature paternal MI increased risk for women.^{10,11}

Smoking

Smoking tobacco significantly increases Cardiovascular (CV) risk, even in those who smoke fewer than five cigarettes a day.¹² The effect of smoking may be greater in women due to the interactions between components of tobacco smoke and hormonal factors.¹³ Since the risk in second hand smokers increases by 25-30%,¹⁴ history of smoking should include these exposures as well. Some markers such as toenail nicotine levels can be used as an objective tool to estimate the average nicotine exposure. One study showed that toenail nicotine levels are predictive of CVD among women, independent of other risk factors.¹⁵

Alcohol Consumption

Although moderate consumption of alcohol (no more than one drink a day in women) may be beneficial for the heart health, heavy drinkers are at increased risk of DM, elevated triglycerides, weight gain, hypertension, stroke, heart failure and other cardiovascular diseases. Thus, the American Heart Association recommends against initiating or increasing alcohol consumption to lower CV risk.¹⁶

Physical Activity

Sedentary life is associated with increased risk of CVD in women. The Women's Health Initiative study showed that postmenopausal women who sit 10 hours or more a day have a greater incidence of CVD compared with women who sit 5 hours a day or less, regardless of leisure-time physical activity. This risk is significantly augmented in women with both low levels of physical activity and prolonged sitting.¹⁷

RISK OF CAD RELATED TO OTHER MEDICAL CONDITIONS

Hyperlipidemia

Hyperlipidemia is very important risk factor for CAD in both men and women. Higher levels of HDL are associated with lower risk of CAD, but the protective effect varies with gender. Women need higher levels of HDL to have the same level of protection; their threshold is 50 mg/dL, compared with 40 mg/dL in men.¹⁸ While the role of triglycerides in CVD is more controversial, studies have shown that elevated triglycerides and low HDL levels were independent predictors of CVD mortality

in elderly women, and that risk quadrupled in women with both conditions.¹⁹

Hypertension

The prevalence of hypertension increases with age, particularly for women. In young adults, hypertension is more common in men, but the prevalence equalizes during middle age (45-65 years). After age 65 years, it is more common in women.^{20,21} Elderly women also have the lowest rates of hypertension control.²² Bearing in mind that women live longer than men on average, more attention should be paid to this risk factor to prevent MI, stroke, and heart failure.

Obstructive Sleep Apnea (OSA)

Obstructive Sleep Apnea (OSA) is defined as recurrent episodes of apnea (lack of breaths) or hypopnea (smaller breaths) during sleep because of soft tissue obstruction of the upper airway. Most frequently this is related to increased neck circumference, but tonsil enlargement and other maxillofacial factors may contribute as well. OSA has been linked to hypertension and arrhythmias, particularly with more frequent and prolonged episodes of apnea.²³ Research has linked OSA to endothelial dysfunction,²⁴ which can occur with even moderate OSA in women.²⁵ Severe OSA has been linked with higher mortality from CVD in women.²⁶

Autoimmune Disease

Rheumatoid arthritis and systemic lupus erythematosus, which are more common in women, are associated with increased risk of CVD. In turn, CVD is an important cause of morbidity (e.g. myocardial infarctions) and death in these patients, even controlling for other risk factors.²⁷ The reasons for these associations are not well understood.

Obesity

It is estimated that about 64% of American women are now either overweight or obese.¹⁷ For many years, the relationship between obesity and CVD was thought to be due to higher rates of hypertension and DM. However, a 26 year follow-up of participants in the Framingham Heart Study indicated that obesity was a significant independent predictor of CVD, particularly among women.²⁸

There are many measures to identify obesity. The most commonly used is the Body Mass Index (BMI), which is calculated using measurements of weight and height. However, other measures that reflect intra-abdominal obesity, such as waist/height ratio and waist/hip ratio, have been found to be better predictors of CVD among middle-aged and older women.²⁹ Current joint guidelines issued by the American College of Cardiology, American Heart Association, and The Obesity Society recommend that waist circumference and BMI should be obtained at

least annually. Women with BMI 25 or greater or waist circumference greater than 35 inches (88 cm) should be counseled regarding their elevated CVD risk.³⁰

Diabetes Mellitus

DM affects about 11% of women in the US.³¹ It is considered a “coronary equivalent” – that is, individuals with established diabetes have risk for CAD approaching that of people who have already had an MI. Among people with DM, the risk of CVD is greater for women than men.³² Furthermore, diabetic women have higher mortality from MI compared to non-diabetic women and men with or without diabetes.³³

Metabolic Syndrome

The metabolic syndrome is a clinical entity defined by the presence of at least three of the following: elevated systolic blood pressure (or treatment for hypertension), elevated blood glucose (or treatment for DM), low HDL cholesterol, high triglycerides, and increased waist circumference.³³ Metabolic syndrome is common, and prevalence increases in women after menopause.³⁴ A meta-analysis of 37 studies found that metabolic syndrome increases CV risk beyond that associated with its component risk factors, and that CV events and death were higher among women with metabolic syndrome than men.³⁵

Polycystic ovarian syndrome (PCOS)

PCOS is a clinical syndrome defined by presence of two or more of the following: ovulatory dysfunction, hyperandrogenism, and polycystic ovaries. Between 6-20% of reproductive aged females are affected.³⁶ Women with PCOS may also meet diagnostic criteria for DM or metabolic syndrome. Controlling for BMI, PCOS has been linked to two-fold higher risk of CVD.³⁷

Depression

There is a complex relationship between depression, stress, and heart disease that appears to be independent of self-care and adherence to medical therapy. A higher burden of stressors has been associated with worsening atherosclerosis, the underlying pathologic change in CAD.³⁸ Major depression is associated with changes in the hypothalamic-pituitary-adrenal axis, resulting in elevations of cortisol, a stress hormone that antagonizes insulin, influences fat distribution, and may affect fluid retention.³⁹ Studies have shown that major depression is a risk factor for congestive heart failure in older women, but not men.⁴⁰ Depression is also more common after MI in women than in men.⁴¹

Complications of Pregnancy

A history of certain complications during pregnancy confers long term CV risk. Women with pre-eclampsia and ec-

lampsia may continue to have marked elevations in blood pressure even years after delivery.⁴² They have a four-fold higher risk of hypertension and two-fold higher risk of CVD.⁴² Similarly, roughly half of women with gestational diabetes develop DM in the future.⁴³ The placenta is a highly vascular structure; abruption and infarction of it predict future vascular disease like hypertension.⁴⁴

Exogenous Estrogen and Progesterone

Use of exogenous estrogen has been linked to elevations in diastolic and systolic blood pressure, particularly at higher doses, and can be prothrombotic.^{45,46} Estrogen-containing oral contraceptives should generally be avoided in women with known hypertension, and should not be used in women aged 35 years and older who smoke, as they increase the risk of MI in this population.⁴⁷ On the other hand, post-menopausal hormone replacement with estrogen, at doses lower than in oral contraceptives, was once thought to lower the risk for CAD.⁴⁸ The Women's Health Initiative, however, found a small increase in the absolute risk for CVD with combined therapy.⁴⁹ Due to the side effects associated with using hormonal replacement therapy, the harm of combined therapy, and the small overall net benefit of estrogen alone, the American Heart Association (AHA) has recommended against using hormonal replacement therapy for CVD prevention.¹⁸

Left Chest Wall Irradiation

Breast cancer is the most common cancer in women and localized disease is routinely treated with excision and chest wall irradiation. Other neoplastic conditions, such as esophageal cancer, lung cancer, and lymphoma, can also be treated with thoracic irradiation. Unfortunately, radiation to the left chest wall has been associated with increased risk of cardiac complications because of resulting fibrotic changes within the coronary arteries and other structures. Risk is related to cumulative radiation doses, and is further modified by the presence of other cardiovascular risk factors.⁵⁰

PREDICTIVE VALUE OF SCREENING TESTS

Exercise Stress Testing

Exercise stress testing can provide significant prognostic information in men and women.⁵¹ Two specific abnormalities – reduced exercise capacity and poor heart rate recovery – have been shown to be independent predictors of death in asymptomatic women.^{52,53} At this time, however, there is insufficient evidence to support routine screening for asymptomatic or low-risk patients.⁵⁴

Coronary Computed Tomography Angiography (CTA)

Coronary CTA is a newer non-invasive test that detects calcium deposition within coronary arteries. The Coronary

Artery Calcium (CAC) score predicts adverse cardiovascular events,⁵⁵ improving assessment of women otherwise classified as low or intermediate risk using traditional risk calculators. It can be used to target statin therapy to those individuals most likely to benefit for primary prevention of CAD, which may have economic benefits.⁵⁶ There is also an association between high sensitivity C-reactive protein (hs-CRP) and CAC score in women, but not men.⁵⁷

hs-CRP

hs-CRP is a marker of inflammation. Elevated hs-CRP levels are associated with increased cardiac risk in older men and women, and higher CV mortality in men but not women.⁵⁸ The American Heart Association (AHA) does not endorse its routine use, however, since reducing hs-CRP has not been shown to improve clinical outcomes.¹⁸

Uric Acid Level

Uric acid is another biomarker may be useful in identifying women at high risk of CV events. Elevated uric acid levels may negatively affect endothelial function and oxidative metabolism.⁵⁹ In a cross-sectional retrospective study of 607 premenopausal women who had undergone coronary angiography, serum uric acid levels were associated with the presence of CAD.⁶⁰ This finding was confirmed in patients with transient ischemic attacks or stroke; an elevated uric acid level independently predicted long-term CAD in women but not men.⁶¹ It is as yet unclear whether lowering uric acid levels reduces CVD risk.⁶²

RISK CALCULATORS

It is difficult for busy clinicians to quantify the cumulative risk of multiple predisposing factors in individual patients. Therefore, algorithms have been developed to do so. Overall risk has then guided the use of preventive measures like statin and aspirin therapy in individuals.

The Framingham and American Heart Association (AHA) Risk Scores are the best known and most widely used in the United States. The Framingham score incorporates age, hypertension, hyperlipidemia, diabetes, smoking, and aspects of lifestyle like unhealthy diet and sedentary lifestyle. It does not account for menopausal status or pregnancy.⁶³ Old American Heart Association guidelines classified women into three risk categories based on the presence of comorbidities (e.g chronic kidney disease, diabetes, hypertension, hyperlipidemia, metabolic syndrome, subclinical atherosclerosis, and systemic autoimmune disease), central adiposity, lifestyle factors (e.g diet, physical inactivity, and exercise tolerance), family history of premature CAD, and history of pregnancy complications (Table 1).¹⁸

| |
|--|
| <p>High risk (>=1 high-risk states)</p> <ul style="list-style-type: none"> • Clinically manifest CVD • Clinically manifest cerebrovascular disease • Clinically manifest peripheral arterial disease • Abdominal aortic aneurysm • End-stage or chronic kidney disease • Diabetes mellitus • 10-y Predicted CVD risk 10% |
| <p>At risk (>=1 major risk factor[s])</p> <ul style="list-style-type: none"> • Cigarette smoking • SBP>120 mm Hg, DBP>80 mm Hg, or treated hypertension • Total cholesterol >200 mg/dL, HDL-C<50 mg/dL, or treated for dyslipidemia • Obesity, particularly central adiposity • Poor diet • Physical inactivity • Family history of premature CVD occurring in first-degree relatives in men <55 y of age or in women<65 y of age • Metabolic syndrome • Evidence of advanced subclinical atherosclerosis (e.g coronary calcification, carotid plaque, or thickened IMT) • Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise • Systemic autoimmune collagen-vascular disease (e.g lupus or rheumatoid arthritis) • History of preeclampsia, gestational diabetes, or pregnancy-induced hypertension |
| <p>Ideal cardiovascular health (all of these)</p> <ul style="list-style-type: none"> • Total cholesterol <200 mg/dL (untreated) • BP <120/80 mm Hg (untreated) • Fasting blood glucose <100 mg/dL (untreated) • Body mass index <25 kg/m2 • Abstinence from smoking • Physical activity at goal for adults >20 y of age: 150 min/wk moderate intensity,75 min/wk vigorous intensity, or combination • Healthy (DASH-like) diet |

Table 1: AHA Classification of CVD Risk in Women.

The new American Heart Association CV risk calculator was introduced in 2014, and includes only age, gender, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, and DM.⁶⁴ Its use has been validated only for whites and blacks, not other ethnic and racial groups.

The Reynolds Risk Score (RRS), unlike the others, was developed using data specifically for women. It adds hs-CRP and parental history of MI before age 60 years to the variables used in the Framingham risk score in an attempt to better risk stratify women.⁶⁵

Unfortunately, none of these tools is perfect. A recent analysis found that Framingham and American Heart Association scores overestimate CV risk in women, while the Reynolds score underestimates it.⁶⁶ These scores may help clinicians initiate discussions about CV risk, but their limitations should be acknowledged as part of shared decision making.

PREVENTION OF CVD IN WOMEN

Some risk factors are clearly modifiable. Smoking cessation and avoidance of environmental tobacco smoke are well-accepted approaches for preventing MI.¹⁸ Developing healthy lifestyles among young women and maintaining these behaviours through mid life may substantially lower the incidence of CVD.⁶⁷ Management of hypertension also lowers CVD risk, although the newest guidelines for blood pressure targets are controversial (Table 2).⁶⁸

High-risk women

- Aspirin therapy (75–325 mg/d) should be used in women with CVD unless contraindicated (Class I; Level of Evidence A).
- Aspirin therapy (75–325 mg/d) is reasonable in women with diabetes mellitus unless contraindicated (Class IIa; Level of Evidence B).
- If a high-risk woman has an indication but is intolerant of aspirin therapy, clopidogrel should be substituted (Class I; Level of Evidence B).

Other at-risk or healthy women

- Aspirin therapy can be useful in women >65 y of age (81 mg daily or 100 mg every other day) if blood pressure is controlled and benefit for ischemic stroke and MI prevention is likely to outweigh risk of gastrointestinal bleeding and hemorrhagic stroke (Class IIa; Level of Evidence B)
- Routine use of aspirin in healthy women <65 years of age is not recommended to prevent MI. (Class III, Level of Evidence B)

Table 2: Use of Aspirin in prevention of CVD in women.

Aspirin has been the cornerstone of prevention for atherosclerotic diseases like MI and stroke for many years, but comes at a price. While aspirin at doses of 81 mg daily or 325 mg every other day⁶⁹ lowers risk of MI in men, in women it only lowers risk of thrombotic stroke.⁷⁰ Benefits of therapy are partially offset by an increased risk for bleeding.⁷¹

LDL cholesterol has been a target for CV prevention for several decades. Statin therapy lowers the incidence of CV events, even in people with normal LDL cholesterol levels.⁷² Research suggests that this class of medications has beneficial actions that extend beyond its lipid-lowering effects.⁷³

Interventions for other metabolic risk factors are variably effective. Tight glycemic control in patients with DM has not been associated with CVD risk reduction.⁷⁴ On the other hand, early lifestyle interventions aimed at treating obesity and hyperlipidemia in women with PCOS impact the development and progression of atherosclerosis.⁷⁵ For patients with autoimmune disorders, disease modifying agents are preferred over corticosteroids, which have been linked to development of metabolic syndrome and premature atherosclerosis.⁷⁶ Biologics such as tumor necrosis factor antagonists and anti-CD40 agents are associated with lower rates of CVD.⁷⁷

CONCLUSION

The prevention and diagnosis of CVD in women are clinically challenging. Women have unique risk factors that are often underappreciated, including polycystic ovarian syndrome and connective tissue diseases. Other traditional risk factors, such as family history and comorbid conditions, have different predictive values in women. Existing risk calculators can under or overestimate the risk of individual women. Of these, the Reynolds Risk Score (RRS) appears to be the most accurate, but requires an additional laboratory test (hs-CRP). Additional research to refine our risk calculators is needed.

Women at risk for CVD derive benefit from some standard preventive therapies, like statins. Current evidence does not support use of aspirin for primary prevention of myocardial infarction in women, and the benefits for ischemic stroke are counter balanced by an increased risk in hemorrhagic stroke.

Women with CAD events may have subtle or atypical symptoms; the majority present with sudden cardiac death as their first event. This finding highlights the need for better primary prevention efforts and for public health outreach and education directed specifically at women.

In summary, CVD is an increasingly important cause of morbidity and mortality in women. Clinical and public health approaches to women at risk for and with CAD should be informed by the known differences of risk, clinical presentation, and response to preventive therapies of women compared to men. Additional research is needed that includes women of child bearing age and the elderly, if we are going to effectively improve health care and outcomes.

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