The Case of Fibroids as a Female-Specific Chronic Debilitating Condition

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Virtual Meeting
Disclosures

• Editor-in-Chief, Fertility & Sterility – Science
• Board Member, Division of Reproductive Endocrinology and Infertility, ABOG
• Women’s Healthcare Academy, Sponsored by Bayer

The views expressed in this presentation are the presenters, and do not represent the Uniformed Services University of the Health Sciences, the Department of Defense, or the Federal Government.
Defining Chronic Debilitating Disease

Chronic: Lasting over a year, require ongoing medical attention and/or limit activities of daily living.

Debilitating: Causing serious impairment of normal activity

Disease: Disruption of health that induces specific signs and/or symptoms


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# Chronic Debilitating Diseases

<table>
<thead>
<tr>
<th>Female Specific</th>
<th>Female Prevalent</th>
<th>Poorly Understood in Women</th>
<th>Morbid in Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gyn Cancers</td>
<td>Depression</td>
<td>Violence</td>
<td>Heart Disease</td>
</tr>
<tr>
<td>Menstrual abnormalities</td>
<td>Migraine</td>
<td>Dementia</td>
<td>Low back pain</td>
</tr>
<tr>
<td>Fibroids</td>
<td>Breast Cancer</td>
<td>Osteoarthritis</td>
<td>COPD</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>Autoimmune</td>
<td>Endocrine d/o</td>
<td>Drug use d/o</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>Rheumatoid Arthritis</td>
<td>Metabolic d/o</td>
<td>Stroke</td>
</tr>
<tr>
<td>Female Infertility</td>
<td>Multiple Sclerosis</td>
<td>Blood d/o</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>STIs</td>
<td>Immune d/o</td>
<td>Obesity</td>
</tr>
<tr>
<td>PCOS</td>
<td>Chronic Fatigue</td>
<td>Recurrent UTIs</td>
<td>Obesity</td>
</tr>
<tr>
<td>Pelvic Floor d/o</td>
<td>Fibromyalgia</td>
<td>HIV</td>
<td>Influenza</td>
</tr>
<tr>
<td>Menopause</td>
<td>Osteoporosis</td>
<td>Neuropathy</td>
<td>Pneumonia</td>
</tr>
<tr>
<td>PID</td>
<td>Candidiasis</td>
<td>Incalcntence</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td></td>
<td>Chronic pain</td>
<td></td>
</tr>
</tbody>
</table>

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Note: The list includes conditions that are more prevalent, poorly understood, or morbid in women.
### Impact vs Commitment to Female-Specific Health Issues, USA

<table>
<thead>
<tr>
<th>Health Issue</th>
<th>Est. Percent Symptomatic</th>
<th>Est. # Impacted (in Millions)</th>
<th>Est. NIH Funding (% 2020)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menopause</td>
<td>85%</td>
<td>140</td>
<td>&lt;0.00001%</td>
</tr>
<tr>
<td>Menstrual Disorders</td>
<td>50-60%</td>
<td>83</td>
<td>0.00004%</td>
</tr>
<tr>
<td>Fibroids</td>
<td>20-25%</td>
<td>33</td>
<td>0.001%</td>
</tr>
<tr>
<td>Pelvic Floor Disorder</td>
<td>17-19%</td>
<td>30</td>
<td>0.002%</td>
</tr>
<tr>
<td>Vulvodynia</td>
<td>16%</td>
<td>27</td>
<td>0.0008%</td>
</tr>
<tr>
<td>Infertility</td>
<td>15%</td>
<td>25</td>
<td>0.007%</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>10%</td>
<td>17</td>
<td>0.0009%</td>
</tr>
<tr>
<td>Invasive Breast Cancer</td>
<td>9.4%</td>
<td>16</td>
<td>0.3%</td>
</tr>
<tr>
<td>Polycystic Ovarian Syndrome</td>
<td>8%</td>
<td>13</td>
<td>&lt;0.00001%</td>
</tr>
<tr>
<td>Premenstrual Dysphoric Disorder</td>
<td>7.4%</td>
<td>12</td>
<td>&lt;0.00001%</td>
</tr>
<tr>
<td>Pelvic Inflammatory Disease</td>
<td>4.4%</td>
<td>7</td>
<td>0.002%</td>
</tr>
<tr>
<td>Endometrial Polyps</td>
<td>3-35%</td>
<td>6</td>
<td>&lt;0.00001%</td>
</tr>
<tr>
<td>Endometrial Cancer</td>
<td>2.8%</td>
<td>5</td>
<td>0.01%</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>2.5%</td>
<td>4</td>
<td>0.07%</td>
</tr>
</tbody>
</table>
# Chronic Debilitating Diseases

## Female Specific
- Gyn Cancers
- Menstrual abnormalities
- **Fibroids**
  - Endometriosis
  - Adenomyosis
  - Infertility
  - Miscarriage
  - PCOS
  - Pelvic Floor d/o
  - Menopause
  - PID

## Female Prevalent
- Depression
- Migraine
- Breast Cancer
- Autoimmune
- Rheumatoid Arthritis
- Multiple Sclerosis
- STIs
- Chronic Fatigue
- Fibromyalgia
- Osteoporosis
- Candidiasis

## Poorly Understood in Women
- Violence
- Dementia
- Osteoarthritis
- Endocrine d/o
- Metabolic d/o
- Blood d/o
- Immune d/o
- Recurrent UTIs
- HIV
- Neuropathy
- Incontinence
- Chronic pain

## Morbid in Women
- Heart Disease
- Low back pain
- COPD
- Drug use d/o
- Stroke
- Diabetes
- Obesity
- Influenza
- Pneumonia
Fibroids in Active Duty Women

"Incidence rates of uterine fibroids by age group and race/ethnicity, active component, U.S. Armed Forces, 2001-2010"

Cumulative Incidence of Fibroids over Reproductive Lifespan

![Graph showing cumulative incidence of fibroids over age for Blacks and Whites.](image)
Heavy Menstrual Bleeding

- Excessive menstrual blood loss that interferes with physical, emotional, social and material quality of life
- Impacts up to 30% of women in their lifetime
- Accounts for 18-30% of gynecologic visits
- Estimated annual direct costs = $1,000,000,000
- Estimated indirect costs = $12,000,000,000
  - Lost days of work and quality of life

Farquar and Brown Cochrane Database Syst Rev 2009;4:CD000154
Liu Value Health 2007;10:183-94
Pain

• Most common symptoms:
  • Menstrual pain 51-63%
  • Low back pain 58-65%
  • Pelvic pressure 16-33%
  • Abdominal pain 25%
  • Pain during sex 17-24%

1 in 4 find such symptoms extremely bothersome

Osuga Fertil Steril 2019;112:922
Fuldeore Int J Womens Health 2017;9:403
Soliman Curr Med Res Opin 2017;33:1971
Zimmerman BMC Womens Health 2012:12:6
Fibroids Increase Miscarriage Rate

Odds of miscarriage decreased with no myoma compared to myoma
Not Impacting the Cavity
OR = 0.737 [0.647, 0.840]

# Obstetric Complications of Fibroids

<table>
<thead>
<tr>
<th>Complication</th>
<th>Fibroid</th>
<th>No Fibroid</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal labor</td>
<td>49.6%</td>
<td>22.6%</td>
<td>2.2</td>
</tr>
<tr>
<td>Cesarean Section</td>
<td>46.2%</td>
<td>23.5%</td>
<td>2.0</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>13.8%</td>
<td>10.7%</td>
<td>1.5</td>
</tr>
<tr>
<td>Breech position</td>
<td>9.3%</td>
<td>4.0%</td>
<td>1.6</td>
</tr>
<tr>
<td>Postpartum Hemorrhage</td>
<td>8.3%</td>
<td>2.9%</td>
<td>2.2</td>
</tr>
<tr>
<td>Premature Rupture of Membranes</td>
<td>4.2%</td>
<td>2.5%</td>
<td>1.5</td>
</tr>
<tr>
<td>Placenta previa</td>
<td>1.7%</td>
<td>0.7%</td>
<td>2.0</td>
</tr>
<tr>
<td>Abruption</td>
<td>1.4%</td>
<td>0.7%</td>
<td>2.3</td>
</tr>
</tbody>
</table>

Biderman-Madar Arch Gynecol Obstet 2005;272:218
Coronado Obstet Gynecol 2000;95:764
Navid Ayub Med Coll Abbottabad 2012;24:90
Stout Obstet Gynecol 2010;116:1056
Ciavattini J Matern Fetal Neonatal Med 2015;28:484-8
Sheiner J Reprod Med 2004;49:182
Qidwai Obstet Gynecol 2006;107:376
What are Fibroids, and What Can We Do?
What are Uterine Fibroids?

- Hormonally sensitive benign tumors that produce an abundance of fibrosis

- Account for 50% of all hysterectomy procedures

- Grow in the presence of estrogen and progesterone
Fibroids Throughout History

5,000 year old calcified mass from human skeletal remains

Kramar M Arch Pathol Lab Med 1983;107:91-93
Fibroids are Predominantly Scar Tissue

Uterus with Fibroid

Fibroid

Normal Uterus
TREATMENT CONCEPT 1: Fibroids Need Blood

- Hysterectomy
- Myomectomy
- Uterine artery embolization
- Uterine artery occlusion
- MRI guided HIFU
- Radiofrequency ablation
TREATMENT CONCEPT 2: Ovarian Hormones Stimulate Fibroid Growth

- Gonadotropin releasing hormone analogues
- Aromatase inhibitors
- Selective progesterone receptor modulators
## Treatment options for Uterine Leiomyomas

<table>
<thead>
<tr>
<th>Surgical</th>
<th>Radiologic / Minimally Invasive</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysterectomy</td>
<td>Uterine Artery Embolization</td>
<td>Oral Contraceptive</td>
</tr>
<tr>
<td>Open</td>
<td>MRI-Guided HiFU</td>
<td>Pills NSAIDs</td>
</tr>
<tr>
<td>Myomectomy L/S</td>
<td>Endometrial Ablation</td>
<td>GnRH Analogues</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>L/S Radiofrequency</td>
<td>Aromatase Inhibitors</td>
</tr>
<tr>
<td>Robotic Myomectomy</td>
<td>Ablation Uterine Artery Occlusion</td>
<td>SPRMs</td>
</tr>
<tr>
<td>H/S Myomectomy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Damages uterus
- Starves uterus
- Hormonal regulation Pain control
Why Such Poor Options After 150 Years of Study?

• The disrespected uterus
• Symptom taboo
• Poor models
• Poor focus
Remaining Gaps in Fibroid Knowledge to Improve Women’s Care

- Increased Public Awareness
- Diversify Study Populations
- Improved Understanding of Fibroid Growth
- Improved Understanding of Fibroid Impact on Pregnancy
- Identification of Novel Therapies
- Improved Fibroid Classification
- Identification of Environmental Exposures
- Identification of Different Fibroid Phenotypes
- Large-Scale Cohort Studies
- Mechanism of Hormonal and anti-hormonal Regulation

Awarded Fibroids RCDC applications
FY2018-2021

Ad hoc review (SEP) 62%
Study Section 38%
Need for Focused Research in Women’s Health

• Adding women to a study is not the same as studying women
• Intermittent research in women’s health insufficient
• Diseases unique to women result in life-long disability

• Recommendations
  o Development of a National Institute of Women’s Health
  o Specifically address diseases unique or more common in women
  o Collaborate with other institutes regarding diseases that also impact women, with an effort to design trials directly related to the disease experience in women
Societal Benefits for the Investment

• Decreased death
• Decreased disability
• Decreased suffering
• Improved quality of life
• Improved productivity
• Improved care of children
• Improved care of the elderly
Thank You!