Clinical Evaluation:

Combined Visual Inspection and Pap for Cervical Cancer Prevention

Clínica Fara, Matagalpa, Nicaragua

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Dra. Oneyda Chavarria D, MD
Dr. Kay Edwards, Ph.D, Haverford College
Incidence of cervical cancer from estimates for 2008
## Cervical Cancer in Nicaragua 2008

<table>
<thead>
<tr>
<th>NICARAGUA</th>
<th>Rate age standardized</th>
<th>Ranking in South &amp; Central America &amp; the Caribbean</th>
<th>Ranking in the World</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>39.9</td>
<td># 3</td>
<td># 15</td>
</tr>
<tr>
<td>Mortality</td>
<td>20.9</td>
<td># 1</td>
<td># 27</td>
</tr>
</tbody>
</table>

Comparison of cancer rates -- data from 184 countries

*Based on crude rates standardized per 100,000.*

*Cumulative Risk [0-74] percent*


World Health Organization / International Agency for Cancer Research
Grafico 1: **NEOPLASIAS MAS FRECUENTES**

**CNR-"NORA ASTORGA" 2000 -2009**

- **T.M del Cervix**: 46%
- **T.M de Mamas**: 17%
- **T.M del Sistema Respiratorio (Orofaringe, Laringe, Pulmón)**: 9%
- **T.M Estómago-Colorectal**: 6%
- **T.M Sistema nervioso Central**: 6%
- **T.M Organos Linfaticos**: 5%
- **T.M Organos Urinarios**: 6%
- **T.M Organos Masculinos**: 2%
- **T.M Otras Neoplasias**: 2%

*Fuente: Estadísticas NCR.*
Figure 4: Incidence of cervical cancer compared to other cancers in women of all ages in Nicaragua

Annual crude incidence rate per 100,000
Nicaragua: Female (All ages)

Data sources:
IARC, Globocan 2002

WHO Summary Report, Nicaragua, 2010
Cervical cancer is one of the principal causes of death for women in Nicaragua over 30

Although maternal mortality is of concern in Nicaragua in 2008 there were 2 1/2 times more cervical cancer deaths than maternal deaths

<table>
<thead>
<tr>
<th>Maternal deaths</th>
<th>Deaths due to cervical cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>85</td>
<td>216</td>
</tr>
</tbody>
</table>

487 invasive cases treated in the National Radiation Center
Despite having a Pap program in place for over 30 years

- Low coverage
- Older women (Age >30) are missed
  - Focus on younger women coming for pre-natal control & family planning
  - Need for more health promotion/outreach
- Poor sensitivity
- Little quality control
- Results don’t get to patients
- Poor follow-up
What is Visual Inspection with Acetic Acid (VIAA)?

- Conduct pelvic exam with a speculum
  - Apply vinegar to the cervix
    (white vinegar -- 5%, no salt or spices)
- Wait 2 minutes
- Look for white spots or changes
Categories of results with VIAA

Negative

Positive

Suspicious for Cancer

Cervical Cancer

Photo source: JHPIEGO
• Private clinic for low income patients, subsidized by a local family foundation, the Fara Foundation

• Referral center that collaborates with Ministry of Health, NGOs, other community clinics & organizations

http://www.farafoundation.org/clinica-fara
Provides services hard to find in public health system

- Cancer prevention services
- Varicose vein treatment
- Dental services
- Education and counseling
- Other general medical services
Focus on women’s cancer

Clinic is developing a program of early cancer detection and prevention services in the north of Nicaragua

• Cervical Cancer
  • Early diagnosis and treatment (VIAA, Pap, Colpo, Biopsy, Cryotherapy & LEEP)
  • Diagnostic services needed prior to cancer treatment in Capital, in Managua (Cistoscopy)

• Breast Cancer
  • Early diagnosis (ultrasound and fine needle aspiration)
Why evaluate VIAA at Clínica Fara?

Clínica Fara:
• Uses a clear protocol for screening, diagnostic work-up and treatment
• Keeps good patient records
• Has reliable patient follow-up
• Maintains an electronic database available for analysis of all procedures & results
• Has an epidemiologist on-site

Objective of evaluation

• Monitor the Clinic’s protocol for ongoing program improvement
• Share the clinic’s experience to help implement and evaluate VIAA in Nicaragua
Clínica Fara VIAA & Pap protocol

**FIRST VISIT**
- VIAA Pos
  - Colpo
  - Biop
- Pap ?
  - Screen Result

**SECOND VISIT**
- VIAA Pos, CIN 2+
  - LEEP
- VIAA Pos, CIN 1
  - Cryo
- VIAA Pos, HPV
  - Cryo
- VIAA Pos, Neg
  - Cryo

**THIRD VISIT**
- VIAA Neg, CIN 2+
  - LEEP
- VIAA Neg, CIN 1
  - Cryo
- VIAA Neg, HPV
  - Cryo
- VIAA Neg, Neg
  - Cryo

**Follow-up**
- Pap Result
- Biopsy Result
Cervical cancer prevention program at Clínica Fara 2011-2013

379 (13%) patients were referred to the clinic for diagnostic work-up of abnormalities detected by other providers.

2438 (87%) patients were screened for cervical cancer using 3 different screening protocols:

1. VIAA + PAP: 817
2. Pap Only: 1,462
3. VIAA Only: 159

Total 2,438

The evaluation that follows is focused on the group that received both VIAA & Pap.
## Results of screening with VIAA & Pap

<table>
<thead>
<tr>
<th>VIAA</th>
<th>PAP</th>
<th>No</th>
<th>No Colpo</th>
<th>Colpo Performed</th>
<th>Biopsy</th>
<th>Bx. Normal</th>
<th>Low-grade (CIN 1/HPV)</th>
<th>High-grade (CIN2/CIN3/Ca in Situ-invasive)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pos</td>
<td>Pos</td>
<td>87</td>
<td>3</td>
<td>84</td>
<td>75</td>
<td>1</td>
<td>65</td>
<td>9</td>
</tr>
<tr>
<td>Pos</td>
<td>Neg</td>
<td>69</td>
<td>4</td>
<td>65</td>
<td>53</td>
<td>3</td>
<td>43</td>
<td>7</td>
</tr>
<tr>
<td>Neg</td>
<td>Pos</td>
<td>96</td>
<td>42</td>
<td>54</td>
<td>24</td>
<td>5</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>Neg</td>
<td>Neg</td>
<td>565</td>
<td>557</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>817</td>
<td>211</td>
<td>158</td>
<td>14</td>
<td>125</td>
<td>19</td>
<td>19</td>
</tr>
</tbody>
</table>

VIAA positive: 156 (19%)
- 108 Low-grade lesions (70%)
- 16 High-grade lesions (10%)
84% of High-grade lesions were detected by VIAA

Pap positive: 183 (22%)
- 81 Low-grade lesions (44%)
- 12 High-grade lesions (7%)
64% of High-grade lesions were detected by Pap
  - (32% by High-grade Pap)
  - (32% by Low-grade Pap)
How were high-grade (CIN2+) lesions detected?

<table>
<thead>
<tr>
<th>VIAA</th>
<th>Pap</th>
<th>Biopsy High-grade (CIN2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIAA Pos</td>
<td>Pap Pos</td>
<td>9</td>
</tr>
<tr>
<td>VIAA Pos</td>
<td>Pap Neg</td>
<td>7</td>
</tr>
<tr>
<td>VIAA Neg</td>
<td>Pap Pos</td>
<td>3</td>
</tr>
<tr>
<td>VIAA Neg</td>
<td>Pap Neg</td>
<td>0</td>
</tr>
</tbody>
</table>

Total 19

VIAA Pos 84%
VIAA Neg 16%
Pap Pos 64%
Pap Neg 36%
## High-grade (CIN 2+) lesions by grade of Pap

<table>
<thead>
<tr>
<th>VIAA</th>
<th>Pap</th>
<th>Biopsy High-grade Lesion (CIN2+)</th>
<th>% of Total (CIN2+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIAA Pos</td>
<td>Pap HG</td>
<td>4</td>
<td>21%</td>
</tr>
<tr>
<td></td>
<td>Pap LG</td>
<td>5</td>
<td>26%</td>
</tr>
<tr>
<td></td>
<td>Pap Neg</td>
<td>7</td>
<td>36%</td>
</tr>
<tr>
<td>VIAA Neg</td>
<td>Pap HG</td>
<td>2</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>Pap LG</td>
<td>1</td>
<td>5%</td>
</tr>
<tr>
<td></td>
<td>Pap Neg</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Total:** 19

<table>
<thead>
<tr>
<th>VIAA</th>
<th>Pap</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIAA Pos</td>
<td>84%</td>
</tr>
<tr>
<td>Pap HG</td>
<td>32%</td>
</tr>
<tr>
<td>Pap LG</td>
<td>32%</td>
</tr>
<tr>
<td>Pap Neg</td>
<td>36%</td>
</tr>
<tr>
<td>VIAA Neg</td>
<td>16%</td>
</tr>
</tbody>
</table>
High-grade lesions (CIN 2+) by results of screen

- Pap HG VIAA Neg 11%
- Pap HG VIAA Pos 21%
- Pap LG VIAA Neg 5%
- Pap LG VIAA Pos 26%
- Pap Neg VIAA Pos 36%

 Chrysler Products

- VIAA+ Pap HG
- VIAA+ Pap LG
- VIAA+ Pap Neg
- VIAA- Pap HG
- VIAA- Pap LG
- VIAA- Pap Neg
Rate of detection of high-grade lesions

Detection rate depends primarily on two major factors

1. Sensitivity of the screening test

2. Proportion of high-risk women reached

High-risk = More than 30 years old &
            More than 3 years from last screen
Rate of detection of high-grade lesions (CIN2+) at Clinica Fara

<table>
<thead>
<tr>
<th>VIAA &amp; Pap (N=817)</th>
<th>Rate of detection of high-grade lesions</th>
<th>2.3%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% of high-risk* women</td>
<td>44%</td>
</tr>
</tbody>
</table>

* High-risk = >30 years old & >3 years since last screen
Performance of the acetic acid test when used in field conditions as a screening test for cervical cancer

P. Claesys¹, H. De Vuyst¹, C. Gonzalez², A. Garcia², R. E. Bello³ and M. Temmerman¹

1 International Centre for Reproductive Health, Ghent University, Ghent, Belgium
2 Universidad Nacional Autónoma de Nicaragua, Managua, Nicaragua
3 Servicios Médicos Comunales, San Juan del Sur, Nicaragua

Table 2 Distribution of histological results by outcome of screening tests

<table>
<thead>
<tr>
<th>VIA</th>
<th>PAP</th>
<th>N</th>
<th>Did not attend colposcopy</th>
<th>Colpo performed</th>
<th>Colpo normal</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No dysplasia</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>47</td>
<td>4 (8.5%)</td>
<td>43</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>+</td>
<td>−</td>
<td>275*</td>
<td>52 (18.9%)</td>
<td>223</td>
<td>112</td>
<td>33</td>
</tr>
<tr>
<td>−</td>
<td>+</td>
<td>30</td>
<td>6 (20.0%)</td>
<td>24</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>−</td>
<td>−</td>
<td>724†</td>
<td>−</td>
<td>17‡</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1076</td>
<td>62§</td>
<td>307</td>
<td>131</td>
<td>48</td>
</tr>
</tbody>
</table>
# Comparison with other programs in Nicaragua

<table>
<thead>
<tr>
<th></th>
<th>Clínca Fara</th>
<th>Rivas / MINSA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># Examined</strong></td>
<td>(817)</td>
<td>(1076)</td>
</tr>
<tr>
<td><strong>Rate of Detection</strong></td>
<td>2.3%</td>
<td>4.7%</td>
</tr>
<tr>
<td><strong>% High Risk</strong></td>
<td>44%</td>
<td>75%</td>
</tr>
<tr>
<td><strong>Detection by VIAA</strong></td>
<td>2.0%</td>
<td>4.2%</td>
</tr>
<tr>
<td><strong>Detection by Pap</strong></td>
<td>1.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td><strong>High-grade Pap</strong></td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Low-grade Pap</strong></td>
<td>0.7%</td>
<td></td>
</tr>
</tbody>
</table>
Conclusions: What have we learned?

Clinica Fara should:

• Continue combined VIAA and Pap protocol
  – Work up all VIAA positives and high-grade Pap results
  – Follow up (6-month rescreening) low-grade Pap results

• Expand the VIAA and Pap protocol
  – Cover all patients receiving cervical cancer screening
  – Train other clinic providers in VIAA

• Share these findings with:
  – Other organizations (NGOs) working in cervical cancer prevention in Nicaragua, and
  – Ministry of Health, as it evaluates its own VIAA screening protocols
Diagnostic work-up versus “Screen and Treat”

- What is “Screen & Treat”?
  - Treat VIAA positives with cryotherapy at the same first screening visit (if adequate for cryotherapy)
  - Advantages:
    - Immediate counseling & treatment while woman is at health center
    - Reduced loss to follow-up
  - Challenges:
    - Post treatment follow-up necessary due to (10-15% failure rate on high-grade lesions)
    - Overtreatment of low-grades (70%) and normals (20%)
WHO recomends “Screen and Treat” for low-resources settings

WHO guidelines
WHO guidelines for screening and treatment of precancerous lesions for cervical cancer prevention

• Use a strategy of screen with an HPV test and treat, over a strategy of screen with VIA and treat.

• In resource constrained settings, where screening with an HPV test is not feasible, the panel suggests a strategy of screen with VIA and treat.

• Use a strategy of screen with VIA and treat, over a strategy of screen with cytology followed by colposcopy (with or without biopsy) and treat.

• The recommendation for VIA over cytology followed by colposcopy can be applied in countries that are currently considering either programme or countries that currently have both programmes available.
Advantages of VIAA

- More sensitive
- Immediate results
- No laboratory required
- Can treat at the same visit “Screen and Treat”

Disadvantages of VIAA

- High rate of positives
  - Some overtreatment if “Screen and Treat” used
  - More patients referred if referral used

Advantages of Pap

- High-grade is more specific (fewer referrals)

Disadvantages of Pap

- Not very sensitive (<40%)
- Problems with results
  - Lengthy delay
  - Patients don’t receive results
- Barriers to follow-up
  - Find the patient, appointment, transport & lodging
Suggestions to support & expand VIAA screening

- Train more providers in VIAA & cryotherapy
- Equip more health centers with cryotherapy
- Develop system to maintain gas supplies for cryotherapy equipment
- Develop maintenance system for cryotherapy equipment
- Strengthen outreach to high-risk women through community health networks
Natural history / life cycle of HPV infection
Decline of cervical cancer mortality rates in United States

MEASURING THE IMPACT

The Pap smear is credited with significantly decreasing the death rate from cervical cancer. Mortality rates for this disease alone are not available for all years, but the combined rates for this carcinoma along with uterine cancer went down by 82% from 1931 to 2004.

1941: Dr. George N. Papanicolaou and Herbert F. Traut, MD, publish “Diagnostic value of vaginal smears in carcinoma of the uterus” in the American Journal of Obstetrics and Gynecology

1945: American Cancer Society promotes the test as part of its campaign, “Every Doctor’s Office a Cancer Detection Center”

1954: Dr. Papanicolaou publishes his extensive treatise, The Atlas of Exfoliative Cytology, which specifies the criteria for cancer

1962: Dr. Papanicolaou dies.

2000: Food and Drug Administration approves HPV DNA test