

Multi-factorial Etiology of Gallbladder Cancer: A USA Case-Control **Population Study** Grace Hamadeh^{1,2}, Aishwarya Lanka³, Akram Shalaby MB BCh.³, Rikita Hatia M.P.H², Ahmed Shalaby, MB BCh.³, Adam Khalifa², Donghui Li, Ph.D.³, Milind Javle, M.D.³, Manal Hassan, MB BCh., M.P.H., Ph.D.² 1. Department of Biomedical Sciences, Texas A&M University 2. Department of Epidemiology, The University of Texas MD Anderson Cancer Center

Introduction & Objectives

Gallbladder Cancer (GBC) in USA

- Globally rare, asymptomatic, lethal cancer known for late diagnosis and poor prognosis^{1,2}
- Between 2007-2011, 3,700 GBC cases and 2,000 deaths (1.13 cases and 0.62 deaths per 100,000)¹
- 5-20% five-year survival rate and mean survival of 2-52 months ³
- Possible risk factors include: cholecystitis, gallstones, smoking, alcohol, female gender, race, and environmental toxins ^{3,4}

Research Question

- 1. Is GBC incidence dependent on specific demographic characteristics?
- What are the main environmental factors associated with GBC ris
- Which female factors contribute to the risk of GBC?
- What chronic conditions are associated with GBC?
- Is there an association between GBC and steatosis after adjustment for potential cofounders?

Methods

• Hospital-based case - control study conducted at UT MD Anderson Cancer (2017-2021).

Inclusion Criteria

- <u>Cases</u>: 79 patients with confirmed GBC diagnosis who reside in the US, without previous history of other cancers
- Controls: 660 healthy individuals without prior history of cancer, who are spouses of cancer patients (excluding GI or smokingrelated cancer)
- No restrictions by age, gender, or race
- All participants interviewed for prior history of GBC were reviewed for evidence of GBC and other GI Cancers (radiologically and clinically).

Statistical Analysis

- SPSS and STATA statistical softwares used to perform multivariable logistic regression to estimate odds ratios.
- Assess the independent effect and significance (p < 0.05) of multiple risk factors including cigarette smoking, alcohol drinking, diabetes, thyroid diseases, obesity, hormones, and family history of cancer
- Adjusted OR (AOR) and 95% Confidence Interval (95% CI) values calculated for each factor
- All AORs were adjusted for age, gender, race, educational level and marital status
- Analyses were performed in men and women separately and all populations.

Responsible Conduct of Research

Under IRB approval of MD Anderson, cases and controls were personally interviewed for different GBC risk factors. Protocol was strictly followed for data acquisition, management, ownership, and sharing to ensure patient privacy.

3. Department of Gastrointestinal Medical Oncology, The University of Texas MD Anderson Cancer Center

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 | Res | sults | | |

 | Resu | ilts
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Table 1: Demographic	

 | Characteris | stics of the S | tudy Populati | ons [79 cases | Table 3: Estimated Odd

 | ds Ratios (OF | R), 95% Con
 | ifidence Inter | val (CI) |
|

 | and 660 controls] | | | | of Female Factors: Multivariable Logistic Regression Analysis

 | |
 | | |
| Demographic Variables

 | Gallbladd
N=79 | | Controls
N=660 (%) | P value | Variable

 | Cases
N=44 (%) | Controls
N=253 (%)
 | OR (95% CI)* | P value |
| Sex

 | | | | 0.03 | Birth Control History

 | |
 | | 0.084 |
| Male

 | 35 (4 | 4.3) | 403 (61.1) | | No

 | 9 (20.9) | 63 (24.9)
 | 1 (reference) $2.00(0.07, 0.001)$ | |
| Female

 | 44 (5 | 55.7) | 257 (38.9) | | Yes
Hysterectomy History

 | 34 (79.1) | 190 (75.1)
 | 2.89(0.87-9.64) | 0.161 |
| Race

 | | | | <0.001 | No

 | 30 (68.2) | 123 (48.6)
 | 1 (reference) | 0.101 |
| White

 | 56 (7 | 70.9) | 596 (90.3) | | Yes

 | 14 (31.8) | 130 (51.4)
 | 0.45(0.15-1.37) | |
| African American

 | 8 (10 | 0.1) | 19 (2.9) | | History of ever Estrogen use

 | |
 | | <0.001 |
| Hispanics

 | 9 (1) | 1.4) | 41 (6.2) | | No
Vos

 | 37 (84.1) | 96 (37.4)
 | 1 (reference)
0.06(0.02, 0.22) | |
| Asian/Pacific Islander

 | 6 (7 | 7.6) | 4 (0.6) | | Yes $= < 2$ years of Estrogen use

 | 7 (15.9)
3 (6.8) | 161 (62.6)
29 (11.3)
 | 0.06(0.02-0.22)
0.15(0.04-0.66) | .012 |
| Age (Years)

 | | | | 0.849 | >2 years of Estrogen use

 | 4 (9.1) | 132 (51.4)
 | 0.04(0.01-0.15) | <0.001 |
| <=40

 | 3 (3 | , | 25 (3.8) | | History of ever Progesterone use

 | |
 | · · · · · · | |
| 41-50

 | 13 (1 | , | 101 (15.3) | | No

 | 39 (88.6) | 200 (77.8)
 | 1 (reference) | |
| 51-60

 | 20 (2 | , | 209 (31.7) | | Yes

 | drinking monopousal (| 57 (22.2)
 | 1.09(0.27-4.48) | d manifed at |
| 61-70

 | 30 (| | 224 (33.9) | | *ORs are adjusted for age, race, alcohol of

 | urmking, menopausal | age, gandiadder ston
 | ies or minammation, an | u marital sta |
| >70

 | 13 (1 | (6.5) | 101 (15.3) | | Summary Statics for Table

 | e 3: |
 | | |
| Education Level

 | | | | 0.150 | 94% decrease in the risk of

 | | nen who have h
 | and astronom aver | 201140 |
| <= High School

 | 22 (2 | , | 145 (22) | |

 | |
 | U 1 | |
| >High School

 | 57 (7 | 72.2) | 515 (78) | | • Females who used estrogen

 | a for less than or | equal to two ye
 | ears nave an 85% | uecrease |
| Marital Status

 | | | | <0.001 | risk of GBC

 | 1 |
 | | • • • • |
| Single

 | 17 (2 | , | 44 (6.7) | | • GBC protection increased w

 | Ŭ | •
 | | • |
| Married

 | 62 (7 | 78.5) | 616 (93.3) | | • Other female factors were 1

 | |
 | h GBC such as l | birth cont |
| Resident State

 | | | | <0.001 | history, hysterectomy history

 | y, and progestero | one use.
 | | |
| Texas & Adjacent States
Other States

 | 43 (5
36 (4 | , | 487 (73.8)
173 (26.2) | |

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| Table 2: Estimated Od

 | lds Ratios (O | | Confidence Inte | | Prevalence of Various Ch

 | aronic Medica | l Conditions
 | in Patients wit | th GBC |
| Table 2: Estimated Od different exposure Exposure

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s: Multivari
Case | OR), 95% C
iable Logist
Controls | Confidence Inte | | Prevalence of Various Ch
⁶⁰
⁵⁰
^(48.1)

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N=35
(44.3) | l Conditions
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| different exposure

 | lds Ratios ((
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P value | 60

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 | th GBC |
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N=660 (%) | Confidence Inte
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OR (95% CI) | Analysis | $\begin{array}{c} 60 \\ 50 \\ \hline \\ 50 \\ \hline \\ (48.1) \\ \hline \\ \\ \hline \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ $

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63 (79.7) | OR), 95% C
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534 (80.9) | Confidence Intended
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(44.3) | N=7
 | N=8 | |
| different exposure Exposure Age Above age of 50 Below age of 50

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| different exposure Exposure Age Above age of 50 Below age of 50 Race Non-white White Gender Male Female Cigarette Smoking

 | lds Ratios ((
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N=79 (%)
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23 (29.1)
56 (70.9)
35 (44.3)
44 (55.7) | OR), 95% C
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Controls
N=660 (%)
534 (80.9)
126 (19.1)
596 (90.3)
64 (9.7)
403 (61.1)
257 (38.9) | Confidence Inte
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OR (95% CI)
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| different exposureExposureAgeAbove age of 50Below age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokers

 | lds Ratios (
s: Multivari
Case
N=79 (%)
63 (79.7)
16 (20.3)
23 (29.1)
56 (70.9)
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iable Logist
Controls
N=660 (%)
534 (80.9)
126 (19.1)
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353 (53.5) | Confidence Intended Confid | Analysis
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| different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokers

 | Ids Ratios (Contraction of the set | $\begin{array}{l} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$ | Confidence Intended Confid | Analysis
P value
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| different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersSmokersMarital Status

 | Ids Ratios ((S: Multivariation Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ | $\begin{array}{l} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$ | Confidence Intended Confid | Analysis
P value
0.231
<0.001
0.005
0.151 | 60
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 | Ids Ratios (Contraction of the set | $\begin{array}{l} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$ | Confidence Intended Confid | Analysis
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$V^{aricose}$ V^{ains} D^{1} Multiple
$V^{aricose}$ D^{1} $Multiple V^{aricose} D^{1} Multiple D^{1} D^{1} Multiple D^{1} D^{1} Multiple D^{1} $ | r inflammation (5 ad polyps (30.4%)). | (1.9%), HB.
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| different exposureExposureAgeAbove age of 50Below age of 50BaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersSmokersMarital StatusNot MarriedMarriedAlcohol History

 | Ids Ratios ((s: Multivaria Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$ | $\begin{array}{l} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$ | Confidence Intended Confid | Analysis
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 | $\sum_{\substack{N=38\\(51.9)}}^{N=38}$ (44.3) $\sum_{\substack{N=5\\(6.3)\\(1.3)}}^{N=7}$ $\sum_{\substack{N=5\\(6.3)\\(1.3)}}^{N=1}$ $\sum_{\substack{N=5\\(6.3)\\(1.3)}}^{N=1}$ $\sum_{\substack{N=5\\(6.3)\\(1.3)}}^{N=1}$ $\sum_{\substack{N=5\\(1.3)}}^{N=1}$ $\sum_{N=5$ | $\sum_{\substack{N=7\\8.9}}^{N=7\\(2.5)} \sum_{\substack{(2.5)\\2.5)}}^{N=2} \sum_{\substack{N=2\\(2.5)}}^{N=2} \sum_{\substack{(2.5)\\2.5)}}^{N=2} \sum_{\substack{N=2\\(2.5)}}^{N=2} \sum_{\substack{(2.5)\\2.5)}}^{N=2} \sum_{\substack{(2.5)\\2.5,}}^{N=2} \sum_{$ | ^{N=8}
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different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersSmokersMarital StatusNot MarriedAlcohol HistoryNon-drinkers	Ids Ratios (Case Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$ $34 (43)$	OR), 95% C iable Logist Controls N=660 (%) 534 (80.9) 126 (19.1) 596 (90.3) 64 (9.7) 403 (61.1) 257 (38.9) 353 (53.5) 307 (46.5) 44 (6.7) 616 (93.3) 295 (44.7)	Confidence Intended Confis	Analysis P value 0.231 <0.001 0.005 0.151 0.005	 60 50 60 60 60 60 60 60 60 61 61 61 62 63 64 74 74 75 76 7	$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ (44.3) $\sum_{\substack{N=5\\(44.3)}}^{N=5}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ (1.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ (1.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ (1.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=5\\(1.3)}}^{N=1}$ $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=5\\(1.3)}}^{N=1}$	$\sum_{\substack{N=7\\8.9\\(2.5)}}^{N=3} \sum_{\substack{N=2\\(2.5)}}^{N=2} \sum_{\substack{n=2\\(2.5)}}$	^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^N	(1.9%), HE betes histor (8.9%), ar (8.9%), ar
different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersSmokersMarital StatusNot MarriedAlcohol HistoryNon-drinkersDrinkers	Ids Ratios ((s: Multivaria Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$	$\begin{array}{l} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$	Confidence Intended Confid	Analysis P value 0.231 <0.001 0.005 0.151 0.005 0.027	 ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (3.8) <li< td=""><td>$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ $\sum_{\substack{(44.3)}}^{N=35}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{(1.3)}}^{N=1}$ $\sum_$</td><td>$\sum_{i=1}^{N=7} \sum_{\substack{n=2\\(2.5)}} \sum_{n=$</td><td>^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3)^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3)^N</td><td>(1.9%), HE betes histor (8.9%), ar (8.9%), ar</td></li<>	$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ $\sum_{\substack{(44.3)}}^{N=35}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{(1.3)}}^{N=1}$ $\sum_$	$\sum_{i=1}^{N=7} \sum_{\substack{n=2\\(2.5)}} \sum_{n=$	^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^N	(1.9%), HE betes histor (8.9%), ar (8.9%), ar
different exposureExposureAge Above age of 50 Below age of 50Race Non-white WhiteWon-white WhiteGender Male FemaleCigarette Smoking Nonsmokers SmokersMarital Status Not Married MarriedAlcohol History Non-drinkers DrinkersEducation	Ids Ratios ((s: Multivaria Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$ $34 (43)$ $45 (57)$	$\begin{array}{c} \textbf{OR}, 95\% \ \textbf{C}\\ \textbf{iable Logist}\\ \hline \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$	Confidence Intellic Regression A OR (95% CI) 1 (reference) 1.02 (0.99-1.05) 1 (reference) 0.21 (0.11-0.42) 1 (reference) 1.97 (1.23-3.16) 1 (reference) 0.70(0.44-1.14) 1 (reference) 0.26 (0.14- 0.48) 1 (reference) 1.97 (1.08-3.58)	Analysis P value 0.231 <0.001 0.005 0.151 0.005	 60 50 60 60 60 60 60 60 60 61 61 61 62 63 64 74 74 74 75 76 7	$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ $\sum_{\substack{(44.3)}}^{N=35}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{(1.3)}}^{N=1}$ $\sum_$	$\sum_{i=1}^{N=7} \sum_{\substack{n=2\\(2.5)}} \sum_{n=$	^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^N	(1.9%), HE betes histor (8.9%), ar (8.9%), ar
different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersSmokersMarital StatusNot MarriedMarriedAlcohol HistoryNon-drinkersDrinkersEducation>Highschool	Ids Ratios ((s: Multivari Case N=79 (%) $63 (79.7)$ $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$ $34 (43)$ $45 (57)$ $57 (72.2)$	$\begin{array}{c} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)}\\ \hline \\ 534 (80.9)\\ 126 (19.1)\\ \hline \\ 596 (90.3)\\ 64 (9.7)\\ \hline \\ 403 (61.1)\\ 257 (38.9)\\ \hline \\ 403 (61.1)\\ 257 (38.9)\\ \hline \\ 353 (53.5)\\ 307 (46.5)\\ \hline \\ 44 (6.7)\\ 616 (93.3)\\ \hline \\ 295 (44.7)\\ 365 (55.3)\\ \hline \\ \\ 515 (78)\\ \end{array}$	Confidence Intended ic Regression A OR (95% CI) 1 (reference) 1.02 (0.99-1.05) 1 (reference) 0.21 (0.11-0.42) 1 (reference) 1.97 (1.23-3.16) 1 (reference) 0.70(0.44-1.14) 1 (reference) 0.26 (0.14- 0.48) 1 (reference) 1.97 (1.08-3.58) 1 (reference) 1 (reference)	Analysis P value 0.231 <0.001 0.005 0.151 0.005 0.027	 ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (48.1) ⁶⁰/₅₀ (3.8) <li< td=""><td>$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ $\sum_{\substack{(44.3)}}^{N=35}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{(1.3)}}^{N=1}$ $\sum_$</td><td>$\sum_{i=1}^{N=7} \sum_{\substack{n=2\\(2.5)}} \sum_{n=$</td><td>^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3)^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3)^N</td><td>(1.9%), HE (1.9%), HE (1.9%), ar (8.9%), ar (8.9%), ar (8.9%), HE</td></li<>	$\sum_{\substack{N=38\\(51.9)}}^{N=38}$ $\sum_{\substack{(44.3)}}^{N=35}$ (44.3) $\sum_{\substack{N=5\\(6.3)}}^{N=1}$ $\sum_{\substack{N=1\\(1.3)}}^{N=1}$ $\sum_{\substack{(1.3)}}^{N=1}$ $\sum_$	$\sum_{i=1}^{N=7} \sum_{\substack{n=2\\(2.5)}} \sum_{n=$	^{N=8} (10.1) ^{N=3} N=4 N=5 (3.8) (5.1) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^{N=1} (1.3) ^N	(1.9%), HE (1.9%), HE (1.9%), ar (8.9%), ar (8.9%), ar (8.9%), HE
different exposureExposureAge Above age of 50 Below age of 50Bace Non-white WhiteWhiteGender Male FemaleCigarette Smoking Nonsmokers SmokersMarital Status Not Married MarriedAlcohol History Non-drinkers DrinkersDrinkersEducation >Highschool <=Highschool <=Highschool									

 | Ids Ratios ((s: Multivaria Case N=79 (%) $63 (79.7)$ $16 (20.3)$ $23 (29.1)$ $56 (70.9)$ $35 (44.3)$ $44 (55.7)$ $49 (62)$ $30 (38)$ $17 (21.5)$ $62 (78.5)$ $34 (43)$ $45 (57)$ | $\begin{array}{c} \textbf{OR}, 95\% \ \textbf{C}\\ \textbf{iable Logist}\\ \hline \textbf{Controls}\\ \textbf{N=660 (\%)} \end{array}$ | Confidence Intellic Regression A
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0.21 (0.11-0.42)
1 (reference)
1.97 (1.23-3.16)
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0.70(0.44-1.14)
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1.97 (1.08-3.58) | Analysis P value 0.231 <0.001 |
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Nonsmokers
SmokersMarital Status
Not Married
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Non-drinkers
DrinkersDrinkersEducation
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Below age of 50Aibove age of 50
Below age of 50 <b< td=""><td>Ids Ratios (Contraction of the set of the set</td><td>$\begin{array}{c} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)}\\ \hline \\ 534 (80.9)\\ 126 (19.1)\\ \hline \\ 596 (90.3)\\ 64 (9.7)\\ \hline \\ 403 (61.1)\\ 257 (38.9)\\ \hline \\ 403 (61.1)\\ 257 (38.9)\\ \hline \\ 353 (53.5)\\ 307 (46.5)\\ \hline \\ 44 (6.7)\\ 616 (93.3)\\ \hline \\ 295 (44.7)\\ 365 (55.3)\\ \hline \\ 515 (78)\\ 145 (22)\\ \end{array}$</td><td>Confidence Intended
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OR (95% CI)
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1.02 (0.99-1.05)
1 (reference)
0.21 (0.11-0.42)
1 (reference)
1.97 (1.23-3.16)
1 (reference)
0.70(0.44-1.14)
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0.26 (0.14- 0.48)
1 (reference)
1.97 (1.08-3.58)
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| different exposureExposureAgeAbove age of 50Below age of 50RaceNon-whiteWhiteGenderMaleFemaleCigarette SmokingNonsmokersSmokersMarital StatusNot MarriedMarriedAlcohol HistoryNon-drinkersDrinkersEducation>Highschool<=Highschool

 | Ids Ratios (Contraction of the set | $\begin{array}{c} \textbf{OR}, 95\% \text{ C}\\ \textbf{iable Logist}\\ \textbf{Controls}\\ \textbf{N=660 (\%)}\\ \hline \\ & 534 (80.9)\\ 126 (19.1)\\ \hline \\ & 596 (90.3)\\ 64 (9.7)\\ \hline \\ & 403 (61.1)\\ 257 (38.9)\\ \hline \\ & 403 (61.1)\\ 257 (38.9)\\ \hline \\ & 353 (53.5)\\ 307 (46.5)\\ \hline \\ & 44 (6.7)\\ 616 (93.3)\\ \hline \\ & 295 (44.7)\\ 365 (55.3)\\ \hline \\ & 515 (78)\\ 145 (22)\\ \hline \\ & 581 (88)\\ \end{array}$ | Confidence Intended
ic Regression A
OR (95% CI)
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1.02 (0.99-1.05)
1 (reference)
0.21 (0.11-0.42)
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1.97 (1.23-3.16)
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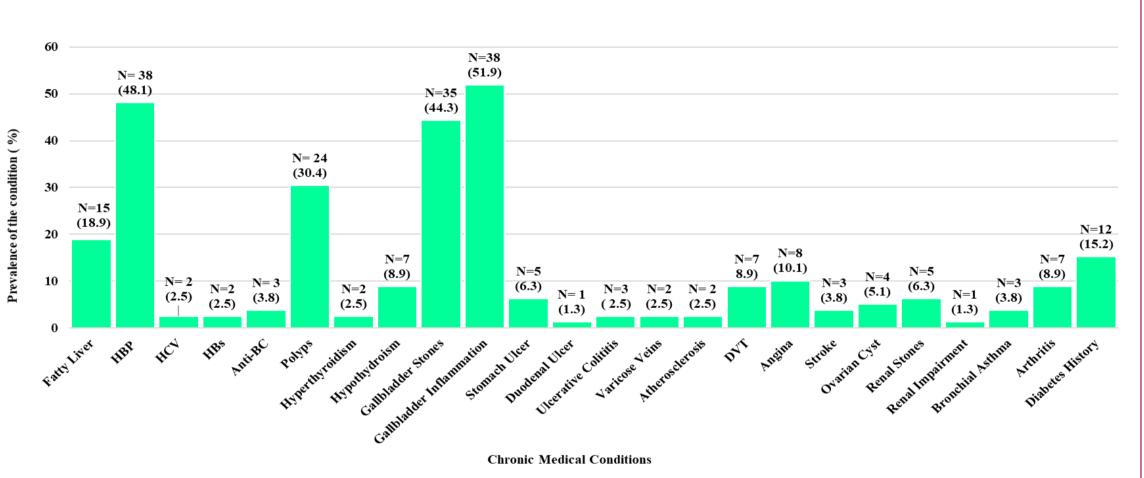
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59 (74.7)	432 (65.5)	1.53(0.85-2.77)	
			0.533
72 (91.1)	600 (90.9)	1 (reference)	
7 (8.9)	60 (9.1)	0.74(0.29-1.88)	
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Summary Statistics for Tables 1 & 2:

Table 1: Significance variation was observed in race, gender, marital status, and the resident state of Texas and its adjacent states.

Table 2: Increase of GBC risk was observed in the female-gender, non-white race, non-married marital status, alcohol history, and gallstone history.



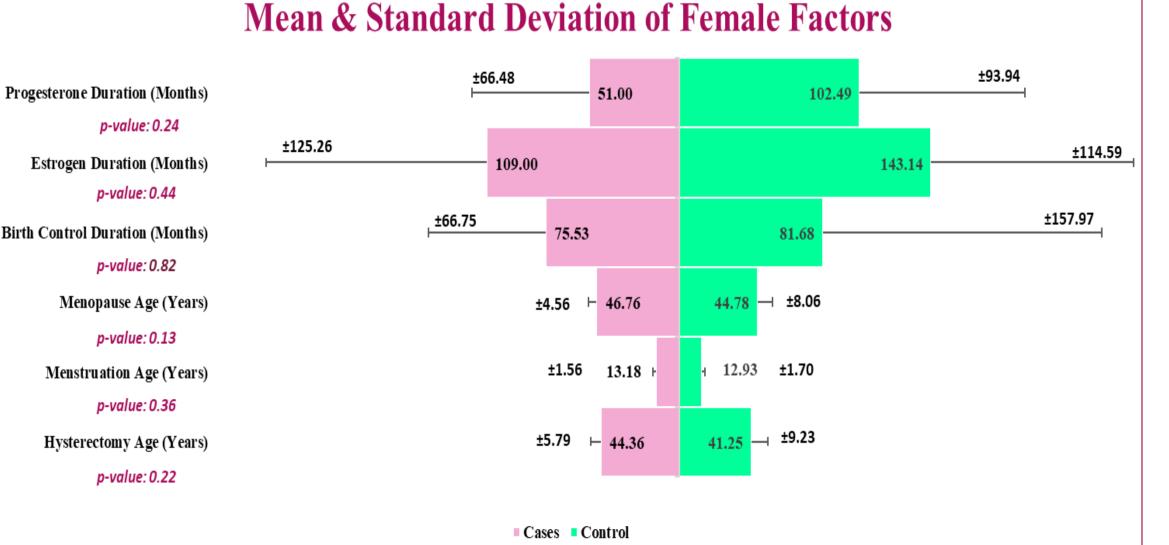


Figure 2 Summary:

• No significant variation between cases and controls in terms of duration of female factors such as the duration of progesterone, estrogen, birth control, menopause age, menstruation age, and hysterectomy age.



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Making Cancer History[®]

Results

• GBC was more common in females, non-white races, and non-married individuals. The geographical variation observed was most likely due to the referral pattern of patients.

• Gallbladder inflammation was related to 8 times higher risk for GBC.

• Alcohol users had approximately two-fold higher risk for GBC.

• Restricted analysis among 44 women cases and 257 women controls yielded 94% reduction in GBC risk among estrogen users (the reduction was associated with the duration of estrogen intake).

• Despite that 19% of the GBC patients had pathological evidence of steatosis, obesity and diabetes was not significantly related to GBC risk.

• The most prevalent chronic medical conditions in patients with GBC were high blood pressure, polyps, gallbladder stones, gallbladder inflammation, and fatty liver. (Note: Prevalence of chronic medical conditions was not studied in *control group*)

Conclusions & Future Implications

• GBC is multi-factorial in origin

• Control of environmental exposures (alcohol use) may reduce GBC susceptibility and promote primary prevention

• Patients with high risk factors such as GBD and cholecystitis should be considered for early GBC prevention and screening programs • Mechanistic pathway for GBC with GBD and cholecystitis needs to be further explored

• Limitation of this study was small sample size due to GBC rarity • Further validation of GBC risk factors is necessary as it will help confirm findings and develop diagnostic markers and early treatments of GBC.

• Strategic planning of prevention and management of GBC should be further investigated and developed by healthcare providers.

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Contact Information

Grace Hamadeh Department of Epidemiology GWHamadeh@mdanderon.org The University of Texas MD Anderson Texas A&M University | grace18024@tamu.edu