Aflatoxin B1 Exposure Induced Obesity/Breast Cancer Based in Neighborhood Socioeconomic Status

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Running title: AFB1-induced Ob/BC in nSES.

Abstract—

Background: *Obesity (Ob) linked to Breast Cancer (BC) has reached epidemic proportions worldwide (WW) including Indonesia, Brazil, Bangladesh and also developed countries. To assess the prevalence and associated risk factors of central Ob and BC WW, are commonly linked with geography (wet and warm climate), race, immigrant, but not SES.*

Problem: *Low and middle-SES are associated with lower outcome affect late diagnosis, late hospitalization and treatment, but not with p53 mutation caused by AFB1 exposure.*

Objectives: *Low and middle-SES and neighborhood are linked to AFB1 exposure as the cause of Ob/BC prevalence.*

Method: *PRISMA design of Systematic Review using Science Direct and EBSCO data based with keywords Ob/BC AND SES. A Bayesian network of Ob (BMI, WC, WHR) and SES (neighborhood) are used. Mainly high AFB1 high guideline AFB1 exposures are recorded.*

Result: *One flowchart detected 152 references and one table or 30 references which included 153,099 subjects at least supported SES/AFB1-associated Ob/BC prevalence or almost related.*

Conclusion: *Low and middle-SES represent AFB1 exposure as the cause of Ob/BC beyond geography, race and ethnic.*

Keywords— Aflatoxin B1, Waist Circumference, Obesity, Breast cancer, socioeconomic status (SES), Neighborhood.

I. INTRODUCTION

Background/Aims: Prevalence Fat distribution due to Brown Adipose Tissue known as UCP2 abundant in Abdominal Adipose Tissue, UCP3 abundant in skeletal muscle, and UCP1 abundant in subscapular fat, is positively related with inflammation marker and the prevalence of Metabolic Syndrome (MS)-associated with pre diabetes, diabetes and its complication such as cardiovascular diseases.[1,2,3]Problem**:** Socioeconomic status (SES) are correlated with Ob-BC and Menopausal status (Estrogen),[4] neighborhood[5] and funding to early diagnostic,[6,7] treatment[8,9,10]and Physical Activity,[11,12]but Not AFB1 exposure are in the National government project. Socioeconomic change BC in Brazil in this 21 century.[13]Objective: AFB1 exposure marked by urine AFM1 sub ppb,[14,15,16,17] become the infrastructure of the cause and avoidance of SES problem positively related with Ob/BC high prevalence. AFB1 exposures are well known cause Liver Cancer, but almost never cause Ob/BC. Unlike that SES-associated better fund in early Ob/BC diagnosis, management, treatment project, a study SES-associated better management in AFB1 exposure in combatting Ob/BC. Abundance data of AFB1-Liver cancer will be useful for Ob/BC.

II. METHOD

Systematic Review design by PRISMA using Science Direct and EBSCO host data based and keyword Obesity/Breast Cancer (Ob/BC) AND socioeconomic status or SES. With a Bayesian network analysis Ob also marked by Waist Circumference (WC)/Waist Hip Ratio (WHR)/Metabolic Syndrome (MS)/diabetes mellitus (DM). Geography, race and minority are also use to be low and middle-SES which is broadly known as high AFB1 exposure (Brazil, Bangladesh, Hispanic, rural/urban etc).

III. RESULT

One flowchart to identified 152 references, which support Ob/BC AND SES/Aflatoxin exposure. Thirty References supported AFB1/SES-associated Ob/BC. Flowchart of the 30 identified Literatures on the association of SES and Ob/BC & SES and Aflatoxin are shown in Figure 1. Thirty References support Urine AFM1 sub ppb as a metabolite of AFB1 (SES) and Ob/BC high prevalence could be seen in Table 1. Not only in developed countries, Ob/BC and various risk factors are reported in Race/ethnic, SES and different geography area disparities.[18,19,20,21,22,23,24,25,26,27,28,29,30,31,32].

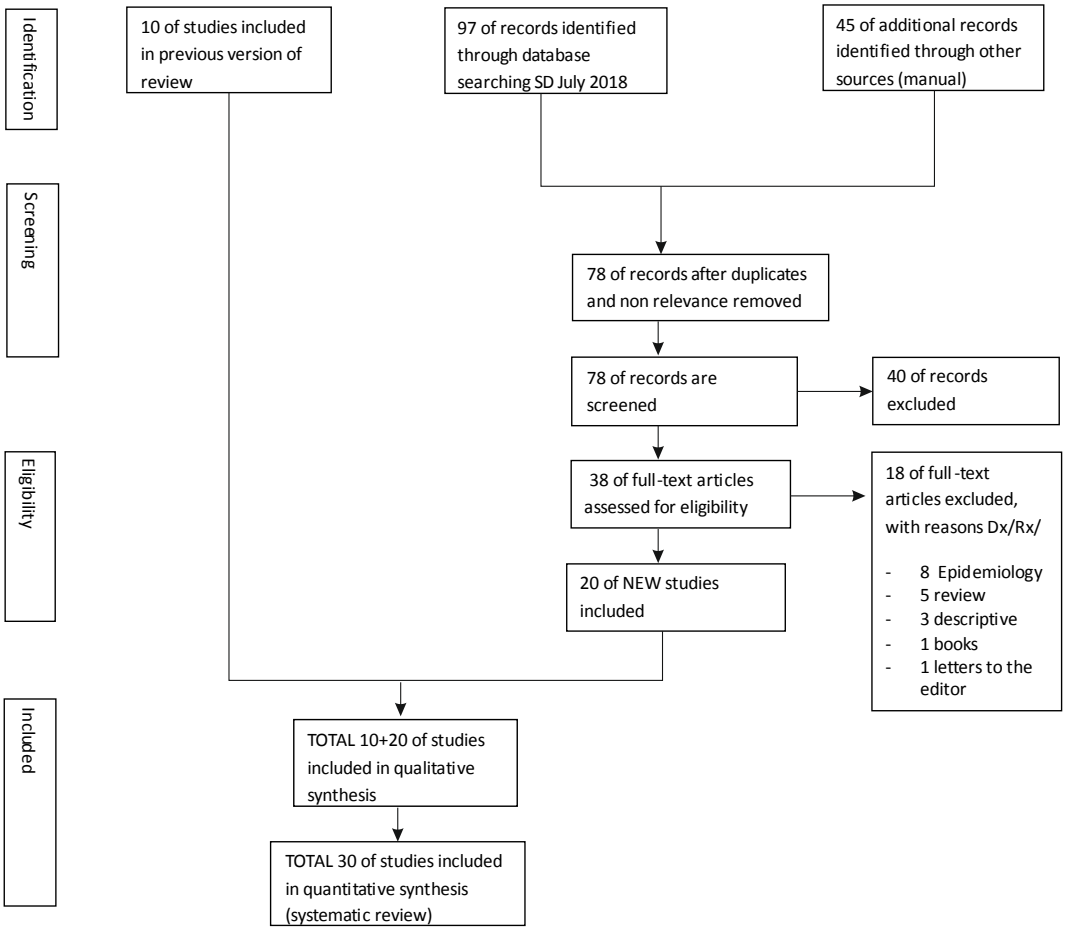

FIGURE 1. Flowchart of the 30 identified Literatures on the association of SES^Ob/BC and SES^Aflatoxin

TABLE 1
THIRTY REFERENCES SUPPORT URINE AFM1/ AFB1 (SES) AND OB-BC HIGH PREVALENCE

Study	Design	Population	Ob/BC	AFB1/*SES	Specific Definition
Shariff-Marko 2015	Descriptive	4347 SF Bay Area Dx/BC	WHR	Lower *SES, crowding	Social and built environment
Shariff-Marko 2017	Prospective Cohort	4,505 BC survivors N California	Ob/Ca	PA/diet	The Rich ##AA. US born Hispanic
Vigen 2016	Case control & survivor cohort	1,936 BC N California	BC	*SES or Education Multiethnic	DM, HT, MI, other heart diseases
Conroy 2017	Multiethnic cohort	48,247 postme-nopausal LA	Ob-BC risk	**nSES	Obesogenic
Conroy 2017	Case-control	1,838 cases 3,117control	BC risk	**nSES, Education	Race/Ethnic, urban, nativity
Padovani 2016	Descriptive Cross-sectional	40 Ob women	55% not aware of BC risk, None identify their own Ob	57,5 %made mammography annually	Unknown their Ob as a risk factor for BC
Espina 2017	Systematic Review	Low Africa High White	High mortality BC	Africa & Delays Dx/	Meta-analysis were not possible
Figueiredo 2018	Ecology study	Brazil 2004-2014	BC P Correlation, Linear Regression	Inequality income	Mortality, not the cause
Figueiredo 2018	Ecological study	Brazil 2004-2014	BC mortality increase Hospital adm rate increase	Socioeconomic development	Age-Hospi admission rates, mortality

Gomez 2015	Distribution	Northern California BC pts.	Lowest and highest SES	Academic medical center vs. integrated medical center	Suburban metropolitan area
Cheng 2015	Cross-sectional	B,995 BC California	BMI/Ob/BC	**nSES), Race/ethnic	PA, healthy eating
Figueiredo 2017	Secondary analysis	Brazil 2004-2014	BC	BC cost Regression	Health policy Bi implicative
Ali 2017	Descriptive & Cohort	218 Urine AFM1 rural-urban Bangladesh	AFB1 high risk exposure	HPLC-FD for Urine AFM1	Hot and Humid Climate: 1
Ali 2016	Descriptive	43 Urban-52 Rural Urine AFM1 Bangladesh	Food & Feed	Rural 99, Urban 54 pg/ML	Metabolite/ biomarker 31-348 pg/mL
Ali 2016	Descriptive	24 AFs spices in market Malaysia	Spices common ingredients in Asian	AFs 8,38 ng/g AFB1 7,31ng/g (>5 ng/g)	HPLC-FD LOD 0,01 ng/g
Gerding 2015	Descriptive	Bangladesh Germany Haiti	References; Ob/BC prevalence and risk	Urine AFM1 only in Bangladesh and Haiti	LC-MS/MS Tandem Individual Detection
Alam 2016	Exploratory study	1243 Undiagnosed/vs. Neverdiagnosed/ Bangladesh	Similar to WHR	Low-income settings	T2D and pre-diabetes
Sposto 2016	Cohort	12.098 BC	54% BC ##NHW	Lifestyle	Race/ethnic disparity
Wu 2015	Multiethnic Cohort	8,952 BC California	Body size/DM mortality	Race/ethnic similarity	Ca-spec mortality
Wee 2016	Cross-sectional	963 LSES 1060 control Singapore	Cardiovascular Ca screening	Low *SES rental flat	Breast Ca Ca Cervix
Wee 2000	Population-based Survey	11,435 Singapore	OvW/Ob/Mortality rate BC	Less screen	Social & Psychological
Sabran 2012	Descriptive	160 Urine AFM1 Malaysia	Milk & Dairy > median 67,79 g/day: significant high level of urine AFM1	Ref. permissive AFs Malaysia (>5ng/g)	61,3% n 0,0234 ng/mL urine AFM1
Sabran 2016	RCT Probiotic Cross-over	71 Employee Univ Malaysia	Ref.: Ob/BC risk	Reduce AFB1 serum & urine AFM1	Yellow & Blue group longer warranty
Sabran 2013	A Mini review	Peanuts, cereal, spices Malaysia	AFs greater than the permissible limit, postulated moderate	AFs exposure recorded in Malaysia since 1960,	Foodstuffs and human AFs detected
Rachmi 2016	Cross-sectional	4101 2-4,9 y Indonesian, 13 of 27 prov.	Overweight or Obesity BMI	Risk factors Low and middle-income	Z-score uW, stunted Doubleburden
Mitchell 2016	Cohort & Observation	Nepal age 15, 24, 36 month	Childhood stunting	AFB1-lysine	g-mean 3,62 pg/mg alb
Moss 2017	Surveillance, Epidemiology, End Result	#NHW 2009-2013 UR	Cancer incidence Urban BC >& CC<	Ecological analysis SES	Weighted at least Sq-Reg
Owusu 2018	Cohort	60 Older ##AA, NHW (66-87y)	Survivor BC	*SES	Physical Activity> Race
Rutherford 2015	Cohort	England Wales BC pts.	Relative survival	*SES	Life expectancy
Kweon 2017	Surveillance, Epid, End R	10,528 pts Korea incl. BC	Ca Dx/incl. BC	*SES	Stage at Ca Dx/

SES: Socioeconomic Status; **nSES: neighborhood SES;#NHW: Non Hispanic White;##AA: African America

IV. DISCUSSION

AFB1/ inflammation induce UCP2/Ob-associated BC and MS/Pre-MS is associated with BC. Education and SES is recorded to be AFB1 exposure. Geography, Race, rural/urban should not be the infrastructure fighting undiagnosed DM, pre-DM, Ob-associated BC. Obesity-BC were associated with neighborhood SES.[4,5]Not only WHRas a marker of Ob-BC associated with low income,[18] but also middle income-associated BMI,WC, Cardiovascular risk[34] also a marker of Ob/BC. Breast Cancer cases in integrated health care[10]also associated with SES[10]and survival BC[12]but not the prevalence BC is related to SES which is associated with recreational Physical Activity.

4.1 AFB1 exposure induce Ob-BC

AFB1 is inflammation stuff induce UCP2 function as antioxidant present central Ob which associated with BC. Central Ob, UCP2, BMI that represent Adipose Tissue distribution positively related with CRP and other inflammation marker.[35,36,37]Abdominal fat (represented by WC) as antioxidant of inflammation in Diabetes and Pre Diabetes,[38] is in high prevalence in rural Bangladesh[39] was widely known as central Obese. Central Ob is associated also with Metabolic Syndrome (MS) and pre MS in health professional in Brazil,[35] also in wet and warm climate area such in rural Bangladesh. Urine AFM1 as a metabolite of AFB1 exposure are also in high prevalence in Brazil,[20,40,41,42,43] and Bangladesh.[17,15]

4.2 Specific of General Knowledge bring to controversies which still not clear

Latin America and China export maize all over the world. There are paired of nations (developing-developing, developed-developed countries) trading large amounts of maize. Paired countries have very similar aflatoxin regulations: nations with strict standards tend to trade maize with each other, while nations with more relaxed standards tend to trade maize with each other. Rarely among the top pairs of maize-trading nations do total aflatoxin standards (standards based on the sum of the levels of aflatoxins B1 etc.), more than 5 μg/kg.[44] So, it is reported that globally, countries with the same standard level has separate maize trading communities. These nations tend to trade with other nations that have very similar food safety standards. These evidence based report failed to proof that Developed countries still have Ob-BC are due to AFB1 exposure came from developing countries maize export merchandise shipment network.[44] Socioeconomic status positively correlated with Ob/BC but related to late diagnostic and late therapy not with AFB1 exposure.[13] Metabolic Syndrome and pre MS in health professional means middle SES also have AFB1 exposure, and urine AFM1 support that the middle socioeconomic income people still not aware of AFB1 exposure. So do Hispanic vs. non Hispanic White women which still significant higher prevalence in Ob, BMI and WC which is associated with ER negative, not associated AFB1 exposure.[45] In Latin America, also where AFB1 could be associated with BC high prevalence.[46] Aflatoxin regulation in a Network of Global Maize Trade has fail to proven the AFB1 exposure in low- and middle-socioeconomic class in developed countries.[20] Epidemiology is inconsistent to prove Ob/BC, but WC are associated with BC and menstrual status,[47,48] which Estrogen and fat distribution control AFB1 exposure.[49] The conclusion of the lost of weight not the avoiding of AFB1 exposure once again need the urine AFM1 sub ppb to convince people the AFB1 exposure.[11,48]

4.3 AFB1-induced Ob/BC

While Ob is well-understood to increase BC risk, high prevalence in AFB1 exposure which induce central Ob and TNBC in wet and warm area or low and middle socioeconomic status are proven. Geography, race/ethnic are positively related with neighborhood, such as in Hispanic American,[45] Latin America,[46] and population who has large WC in association with high BC prevalence masked by Menstrual status,[47,48] low and middle SES neighborhood bring us to the risk of Ob/BC expose by AFB1. Central Ob marked by WC is in high prevalence in rural Bangladesh.[39] are parallel with urine AFM1 high prevalence in Brazil.[41,42,43] Further the role of AFB1-Neighborhood SES/crowded that influence body size and adipose tissue distribution should account for obesogenic environment,[4] independent of racial/ethnic.[5] Targeted prevention effort of BC could be use that potentially be averted if all women attained a BMI less than overweight and obese.[50]

V. LIMITATION

Study design Meta-analysis could not be trapped to build this Systematic Review. Simple characterized low and middle-SES as AFB1 exposure are bridged by WC and/ or Ob/BC need furtherAFB1 exposure intervention. We need prevention of AFB1 exposure through urine AFM1 sub ppb marker to convince people without awareness in their not healthy food.[14,15,41,42,43] Confuse definition of exposure AFB1 and other mycotoxin and different outcome variable such as survival, surveillance, mortality rate but not the prevalence of BC, spread the focus of AFB1 exposure as the cause of Ob/BC in fighting it.[33-40]

VI. CONCLUSION

Not only in wet and warm known as developing countries, but also low and middle SES population in developed (dry and cold) countries, the food and feeds have AFB1 exposure high risk, and this inflammation stuff is the cause of Ob/BC has been masked by estrogen in premenstrual age.

CONFLICT OF INTEREST

No Conflict of Interest till the date.

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