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Research Article

Possible Association between Self-Reported Medical Illnesses and Findings at Hysteroscopy Prior to Fertility Treatment Presented among Infertile Black African Women: A Predictive Probability Study

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Received: October 30, 2020; **Published:** January 27, 2021

Abstract

Objective: To determine possible association between medical conditions and hysteroscopic findings prior to IVF treatment.

Methodology: This was a retrospective study of 1631 infertile indigenous Nigerian women who consulted for IVF treatment. Stata 13 software was used for analysis.

Results: The relative risk of diabetes was higher among infertile women with submucous fibroid (SMF) ($\chi 2 = 0.07$, P-value = 0.79, RR = 1.31, 95% CI: 0.54, 3.19) than among women without fibroid and among those with intrauterine adhesions (IUA) ($\chi 2 = 0.88$, P-value = 0.35, RR = 1.36, 95% CI: 0.74, 2.51) than among those without IUA. Infertile women aged < 35 years with gastric ulcer (GU) had a higher probability of having SMF than older women (OR = 1.80, 95% CI; 0.42, 7.77) while those aged ≥ 35 years with GU had a higher probability of falling into the group that has IUA (OR = 1.21, 95% CI: 0.68, 2.17). Obese infertile women with diabetes had higher predictive probability of falling into SMF target group (SMFtg) (B = 19.27, $\chi 2 = 0.00$, OR = 234067446.6, 95% CI:0.00) than those with asthma, gastric ulcer or hypertension.

Conclusion: There may be some associations between medical conditions and findings at hysteroscopy prior to IVF. Women with fibroids, IUA or polyps should be further examined for asthma, gastric ulcer, hypertension, diabetes.

Keywords: *Medical conditions; Hysteroscopy; Infertility; Assisted Reproductive Treatment*

Introduction

Infertility, defined by the World Health Organization as a "disease of the reproductive system" which results in disability [1], is a global problem which, in 2010, was estimated to affect approximately 48.5 million infertile couples worldwide [2]. Infertility has also been defined as the failure to achieve a successful pregnancy (ultrasound evidence of pregnancy in the first trimester) after having appropriately timed unprotected intercourse over a period lasting 12 months or longer, for women of ages 20 - 34 years, or 6 months or longer for women aged 35 years or older [3]. Infertility, a disease of the reproductive system [now 4] may be a cardiovascular risk among women with unexplained infertility [5]. Female infertility is more widely known than male infertility [6], though the situation is changing. Infertile women in reproductive age, like any other patient, consult clinicians for a proper understanding of their condition and to resolve their main health problem - infertility. One of the cardinal duties of the attending health provider is to inquire about antecedent events such as

past family, social, medical, surgical and gynecological history of each patient, which provide a broad-based perspective on which to arrive at a definitive diagnosis and provide appropriate solution. Most studies focus on conditions that directly cause infertility, such as failure of an egg to mature properly [7], uterine fibroids [8], polyps [9] or structural problems of the reproductive system such as endometriosis [10], implantation failure [11], primary ovary insufficiency [12], among others. Very few studies have reported non-gynecologic illnesses as co-morbidities with infertility. These comorbidities are discerned when the clinician probes into past medical history of the patient and may have a bearing on her infertility. For example, among women in general but not specifically among infertile women, hypertension has been associated with uterine leiomyomata risk in circumstantial reports [13,14]. Research linking hypertension and hysterectomy may indirectly implicate fibroids. Farland., *et al*. [15] are among the few that however reported risk of hypertension among infertile women who consult for fertility treatment. Not much has been said about the risk of asthma or gastric ulcer among infertile women, though Gkioka., *et al*. [16] reported risk of uterine leiomyomata in relation to insulin-like growth factor-1. Almost all these studies were among women in general but not among those who were infertile, among Caucasians and African Americans but not among sub-Sahara black African women. These studies also did not segregate infertile women by age or by body mass index. To our knowledge, no study has examined the association of presenting medical illness and hysteroscopic findings prior to ART among infertile sub-Sahara black African women. This wide gap in knowledge has to be filled, hence the objective of this study was to investigate possible association of self-reported medical illnesses with findings at hysteroscopy before further management of infertility commenced.

Methodology

This study is part of another study and the methodology used for both are similar as earlier reported [17]. Briefly, between 2003 and 2018 there were 4,233 women in child-bearing age group (WCBA) who accessed the facilities provided by Nordica Fertility Center (NFC) for gynecological interventions. Of this number, medical records of 2857 (67.5%) clients for management of primary or secondary infertility were retrieved and relevant data were electronically re-documented by three newly recruited data recording officers who had been given a 2-day training exclusively to acquaint them with data extraction, electronic recording into excel spreadsheet, time schedule and order of reporting. An experienced IVF specialist and a member of the team (VDA) supervised these three trainees from June to December 2019. Specific data mined included age, body mass index (BMI), and socio-demographic characteristics, past medical and gynecological history. For the purpose of this study, those with previous history of recurrent failed IVF treatment in the form of three or more cycles; one or two attempts of IVF treatment at NFC; poor/non-distension of the endometrium at sonohysterogram; abnormal findings at Hysterosalpingogram (HSG) done within the previous one year were included in the study. Excluded were those with a history of pelvic inflammatory disease; (ii) pelvic cancer (iii) those whose infertility were mainly due to male factor infertility (iv) those with incomplete data and (v) those who did not sign consent form. In all, 1631 (57.1%) who met all the criteria were decisively included in the study. It is the norm in NFC that, at first point of contact, each patient should sign an informed consent form which entails their data, under strict anonymity is used for teaching and research purposes, though not all women signed the form and those who refused to sign were never considered for inclusion into any study. Detailed explanation of the procedure involved in IVF were given to all clients and their partner before the step-by-step process of the technique began. The instrumentation and procedures involved in hysteroscopy have been earlier reported [17]. In brief, a thin, flexible telescope-like instrument, known as a hysteroscope, is inserted in the vagina, to thoroughly inspect the cavity of the uterus when the patient is put under short general anesthesia. This process is a minimally invasive procedure used for medical diagnosis and corrective procedure.

Ethical approval

Each study subject signed a consent form for her data to be used for research purposes and that the data will be discreet, coded, and unnamed. The benefits of using data for teaching and research purposes were explained to the study subjects. This retrospective study was approved by a local Ethics Committee.

Statistical analysis

The cleaned and coded data was transferred from Excel spreadsheet into STATA 13 software which was used for further analysis. Age (years) was categorized into < 35 and ≥ 35, BMI (Kg/m^2) was stratified into the classical groups of underweight (< 18.5), normal (18.5 - 24.9), overweight (25.0 - 29.9), obese (≥ 30.0). Each finding at hysteroscopy was regarded as a target groups into which each disease entity falls or does not fall. Binary logistic regression analysis was performed to determine predictive probabilities of any of the diseases falling into a particular target group. Chi-square and Fisher exact test analysis with relative risks (RR) and 95% Confidence interval were used to evaluate the differences between two proportions or rates and to determine the risk of findings at hysteroscopy among those who reported or did not report a particular disease. Student's t-test was used to evaluate significant differences in means between two continuous variables. One-way analysis of variance (ANOVA) with Bonferroni adjustment or Kruskal-Wallis test was used to compare groups as appropriate. Data were presented as numbers and percentages for categorical variables, as mean with standard deviations for continuous variables and as tables and figures for all variables. A P-value < 0.05 was regarded statistically substantial. STATA version 13.0 (STATA Inc., Texas, USA) was used for statistical analysis.

Results

The mean (±) age of the 1631 study participants (462 [28.3%] aged < 35 years and 1169 [71.7%] aged ≥ 35 years) was 38.7 (6.4) and the mean BMI was 28.1 (5.5) Kg/m^2. Majority of the study subjects (n = 653, 40.0%) were overweight followed by obese (n = 561, 34.4%) and normal weight (n = 401, 24.6%) and underweight (n = 16, 1.0%). A total of 1256 (77.0%) of the women were nulliparous, 709 (43.5%) had experienced induced abortion and 463 (28.4%) had miscarriages (Table 1). In all, 52 (3.2%) of the infertile women were asthmatic, 103 (6.3%) were gastric ulcer patients, 95 (5.8%) were hypertensive and only 21 (1.3%) were diabetic. Majors findings at hysteroscopy revealed that 238 (14.6%), 401 (24.6%) and 225 (13.8%) of the study subjects had submucous fibroid (SMF), Intrauterine adhesion (IUA) and Uterine polyps (UP) respectively (Table 2); SMF was most prevalent (15.8%) among nulliparous subjects, IUA most prevalent (29.9%) among those with parity of 2 and UP was most prevalent (16.4%) also among those with parity of 2 (Figure 1). Distribution of uterine findings relative to age showed that IUA and SMF were more prevalent (28.7% and 16.9% respectively) in older women than among those < 35 years (14.4% and 9.0% respectively) (Figure 2a). The prevalence of SMF, IUA and UP were highest (44.1%, 43.4% and 37.3% respectively) prevalent among overweight women. Interestingly, SMF was commoner among those with normal body weight (29.8%) than among obese women (24.4%) though IUA and UP had higher prevalence (33.2% and 33.8%) among obese than among normal weight women (22.2%, and 27.6%) (Figure 2b).

Variable	Item	Freq	%	Mean	± sd	Minimum	Maximum
Age (years)	All	1631	100.0	38.7	6.4	20	61
	< 35	462	28.3	31.13	2.62	20	34
	≥ 35	1169	71.7	41.63	4.84	35	61
BMI (Kg/m^2)	All	1631	100.0	28.1	5.5	17.0	59
	< 18.5	16	0.98	17.44	0.51	17	18
	18.5 - 24.9	401	24.59	22.42	1.51	19	24
	25.0 - 29.9	653	40.04	26.96	1.36	25	29
	≥ 30	561	34.40	33.79	4.10	30	59
Parity	All	1631	100.0	0.32	0.68	0	4
	0	1256	77.01	0.0	0.0	0	0
	1	273	16.74	1.0	0.0	1	1
	2	67	4.11	2.0	0.0	2	2
	3	27	1.66	3.0	0.0	3	3
	4	8	0.49	4.0	0.0	4	4
Induced abortion	All	1631	100.0	0.80	1.17	0	7
	Yes	709	43.5	1.84	1.12	0	7
	No	922	56.5	0.0	0.0	0	0
Miscarriages	All	1631		0.49	1.00	0	8
	Yes	463	28.4	1.72	1.19	1	8
	No	1171	71.6	0.0	0.0	0	0

Table 1: *Social and gynecological characteristics of study subjects.*

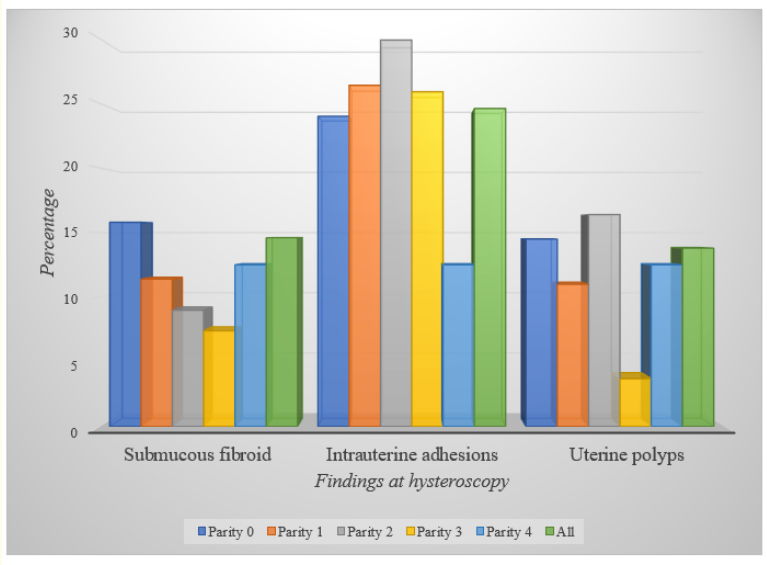

Figure 1: *Distribution of intrauterine findings at hysteroscopy relative to parity.*

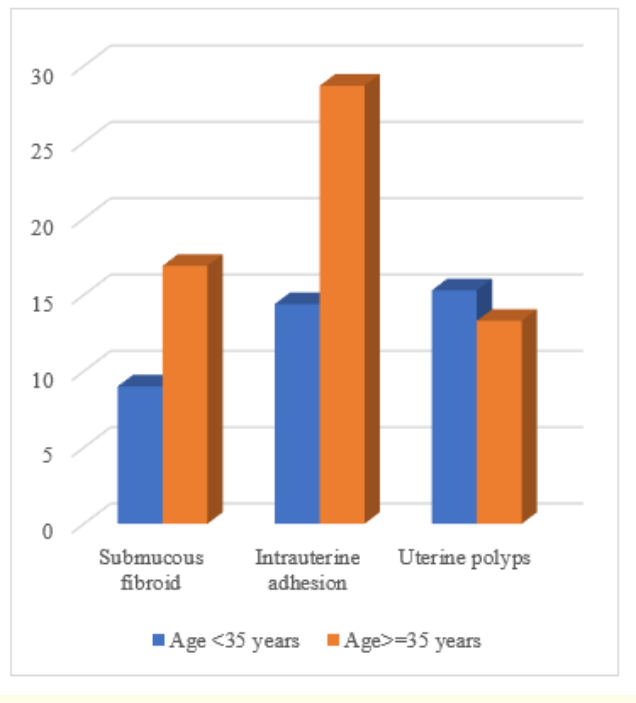

Figure 2a: *Distribution of uterine findings at hysteroscopy relative to age group.*

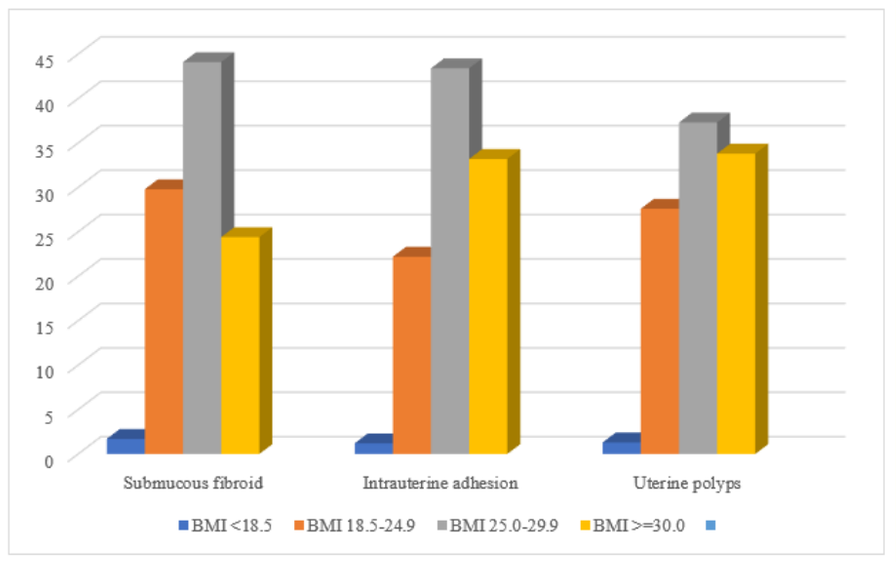

Figure 2b: *Distribution of uterine findings at hysteroscopy relative to BMI group.*

Figure 2: *Distribution of uterine findings at hysteroscopy relative to age groups and to BMI groups.*

Relative risk analysis

Table 2 also shows that those with diabetes had the highest relative risk (RR) of SMF (Fisher's χ^2 = 0.07, P-value = 0.79, RR = 1.31, 95% CI: 0.54, 3.19) than those with hypertension (χ^2 = 0.07, P-value = 0.80, RR = 0.93, 95% CI: 0.56, 1.57), asthma (χ^2 = 0.40, P-value = 0.53, RR = 0.79, 95% CI: 0.37, 1.68) or gastric ulcer (χ^2 = 2.10, P-value = 0.15, RR = 0.65, 95% CI: 0.36, 1.19). Likewise, those with diabetes had the highest RR of IUA (χ^2 = 0.88, P-value = 0.35, RR = 1.36, 95% CI: 0.74, 2.51) than those with hypertension (χ^2 = 0.80, P-value = 0.37, RR = 1.17, 95% CI: 0.83, 1.63), asthma (χ^2 = 0.01, P-value = 0.94, RR = 1.02, 95% CI: 0.63, 1.64) or gastric ulcer (χ^2 = 0.30, P-value = 0.58, RR = 0.92, 95% CI: 0.62, 1.31). However, those with gastric ulcer had the highest RR of UP (χ^2 = 2.92, P-value = 0.09, RR = 1.45, 95% CI: 0.96, 2.19) than those with hypertension (χ^2 = 0.42, P-value = 0.52, RR = 0.83, 95% CI: 0.47, 1.47), asthma (χ^2 = 0.23, P-value = 0.63, RR = 0.81, 95% CI: 0.34, 1.92) or diabetes (Fisher's χ^2 = 0.06, P-value = 0.80, RR = 0.69, 95% CI: 0.18, 2.58).

Medical Pathology		Statistics	All (n = 1631)						Total	%
			Submucous Fibroid		Intrauterine Adhesion		Uterine Polyps			
			Yes	No	Yes	No	Yes	No		
		n	238	1393	401	1230	225	1406	1631	100.0
		%	14.6	85.4	24.6	75.4	13.8	86.2	-	-
Asthma	Yes	Freq. (%)	6 (2.5)	46 (3.3)	13 (3.2)	39 (3.2)	6 (2.7)	46 (3.3)	52	3.2
	No	Freq. (%)	232 (97.5)	1347 (96.7)	388 (96.8)	1191 (96.8)	219 (97.3)	1360 (96.7)	1579	96.8
	χ^2 (P-value)		0.40 (0.53)		0.01 (0.94)		0.23 (0.63)		-	-
	RR (95% CI)		0.79 (0.37, 1.68)		1.02 (0.63, 1.64)		0.81 (0.34, 1.92)		-	-
Gastric Ulcer	Yes	Freq. (%)	10 (4.2)	93 (6.7)	23 (5.7)	80 (6.5)	20 (8.9)	83 (5.9)	103	6.3
	No	Freq. (%)	228 (95.8)	1300 (93.3)	378 (94.3)	1150 (93.5)	205 (91.1)	1323 (94.1)	1528	93.7
	χ^2 (P-value)		2.10 (0.15)		0.30 (0.58)		2.92 (0.09)		-	-
	RR (95% CI)		0.65 (0.36, 1.19)		0.92 (0.62, 1.31)		1.45 (0.96, 2.19)		-	-
Hypertension	Yes	Freq. (%)	13 (5.5)	82 (5.9)	27 (6.7)	68 (5.5)	11(4.9)	84 (6.0)	95	5.8
	No	Freq. (%)	225 (94.5)	1311 (94.1)	374 (93.3)	1162 (94.5)	214 (95.1)	1322 (94.0)	1536	94.2
	χ^2 (P-value)		0.07 (0.80)		0.80 (0.37)		0.42 (0.52)		-	-
	RR (95% CI)		0.93 (0.56, 1.57)		1.17 (0.83, 1.63)		0.83 (0.47, 1.47)		-	-
Diabetes	Yes	Freq. (%)	4 (1.7)	17 (1.2)	7 (1.7)	14 (1.1)	2 (0.9)	19 (1.4)	21	1.3
	No	Freq. (%)	234 (98.3)	1376 (98.8)	394 (98.3)	1216 (98.9)	223 (99.1)	1387 (98.6)	1610	98.7
	χ^2 (P-value)		*0.07 (0.79)		0.88 (0.35)		*0.06 (0.80)		-	-
	RR (95% CI)		1.31 (0.54, 3.19)		1.36 (0.74, 2.51)		0.69 (0.18, 2.58)		-	-

Table 2: *Relative risk analysis of medical conditions presented by patients at consultation relative to main findings (multiple) at hysteroscopy.*

Age related predictive probability analysis

Binary logistic regression was run with each major finding at hysteroscopy as dependent variable (target group) and medical conditions as independent variables (predictor variables) (Table 3). Age-related predictive probability was considered from the perspective of each predictor variable.

Predictor variable	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI
	Submucous fibroid target group (SMFtg)																	
	All						**<35 years**						**≥ 35 years**					
Asthma	0.25	0.44	0.32	0.57	1.28	0.54, 3.04	0.36	1.05	0.12	0.73	1.44	0.19, 11.19	0.20	0.49	0.17	0.68	1.22	0.47, 3.19
Gastric ulcer	0.49	0.34	2.06	0.15	1.63	0.84, 3.18	0.59	0.75	0.62	0.43	1.80	0.42, 7.77	0.36	0.39	0.84	0.36	1.43	0.67 3.05
Hyperten-sion	0.05	0.31	0.02	0.88	1.05	0.57, 1.92	-1.19	1.17	1.04	0.31	0.31	0.03, 3.00	0.28	0.32	0.74	0.39	1.32	0.70, 2.47
Diabetes	-0.23	0.56	0.17	0.58	0.79	0.27, 2.36	18.75	23100.58	0.00	1.00	138569429.3	0.00, 0.00	-0.22	0.57	0.16	0.69	0.80	0.26, 2.42
Constant	1.73	0.08	531.79	0.00	5.64	-	2.29	0.17	176.33	0.00	9.84	-	1.55	0.08	342.31	0.00	4.72	-
	Intrauterine adhesions target group (IUAtg)																	
Asthma	-0.03	0.33	0.01	0.92	0.97	0.51, 1.84	-1.02	0.56	3.38	0.07	0.36	0.12, 1.07	0.33	0.41	0.67	0.41	1.40	0.63, 3.10
Gastric ulcer	0.15	0.25	0.40	0.53	1.17	0.72, 1.88	-0.22	0.45	0.24	0.63	0.81	0.34, 1.93	0.19	0.30	0.42	0.52	1.21	0.68, 2.17
Hyperten-sion	-0.24	0.24	1.00	0.32	0.79	0.50, 1.26	19.36	20096.49	0.00	1.00	256455523.1	0.00, 0.00	-0.10	0.24	0.16	0.69	0.10	0.57, 1.46
Diabetes	-0.50	0.44	1.28	0.26	0.61	0.26, 1.44	-1.07	1.24	0.75	0.39	0.34	0.03, 3.88	-0.29	0.47	0.39	0.53	0.75	0.29, 1.89
Constant	1.13	0.06	329.30	0.00	3.10	-	1.84	0.14	166.66	0.00	6.30	-	0.91	0.070	166.18	0.00	2.47	-
	Uterine polyps target group (UPtg)																	
Asthma	0.25	0.44	0.32	0.57	1.29	0.54, 3.06	1.06	1.04	1.04	0.31	2.89	0.38, 22.33	-0.03	0.49	0.00	0.96	1.00	0.37, 2.56
Gastric ulcer	-0.45	0.26	3.02	0.08	0.64	0.38, 1.06	-0.54	0.41	1.74	0.19	0.58	0.26, 1.30	-0.34	0.35	1.00	0.33	0.71	0.36, 1.40
Hyperten-sion	0.20	0.33	0.37	0.55	1.22	0.64, 2.33	19.47	20096.49	0.00	1.00	286782040.4	0.00, 0.00	0.10	0.34	0.08	0.78	1.10	0.57, 2.12
Diabetes	1.11	0.63	0.03	0.86	1.11	0.33, 3.79	-0.85	1.25	0.46	0.50	0.43	0.04, 4.93	0.33	0.75	0.20	0.66	1.40	0.32, 6.09
Constant	1.84	0.08	560.26	0.00	6.32	-	1.73	0.14	154.64	0.00	5.63	-	1.89	0.09	404.66	0.00	6.63	-

Table 3: *Predictive probability of any of the predictor variables (asthma, gastric ulcer, hypertension, diabetes) falling or not falling into the target groups relative to age group.*

B: Regression coefficient.

Asthma

In general, there was a low probability that those with asthma would fall into the SMFtg (B = 0.25, χ^2 = 0.32, OR = 1.28, 95% CI:0.54, 3.04) but when segregated by age, younger infertile women had a higher predictive probability (B = 0.36, χ^2 = 0.12, OR = 1.44, 95% CI:0.19, 11.19) of falling into the SMFtg than older infertile women (B = 0.20, χ^2 = 0.17, OR = 1.22, 95% CI:0.47, 3.19). The expressed negative coefficient indicates that younger infertile women with asthma (B = -1.02, χ^2 = 3.38, OR = 0.36, 95% CI: 0.12, 1.07) were unlikely to fall into IUAtg while with positive coefficient, older infertile women with asthma (B = 0.33, χ^2 = 0.67, OR = 1.40, 95% CI: 0.63, 3.10) were more prone to fall into the IUAtg. On the contrary, with positive predictive coefficient (B = 1.06, χ^2 = 1.04, OR = 2.89, 95% CI: 0.38, 22.33), younger infertile women with asthma were more likely to fall into the UPtg. Negative predictive coefficient recorded for older (B = -0.03, χ^2 = 0.00, OR = 1.00, 95% CI: 0.37, 2.56) indicated that they were not likely to fall into the UPtg.

Gastric ulcer (GU)

Overall, there was a high predictive probability that infertile women with gastric ulcer were more likely to fall into the SMFtg (B = 0.49, χ^2 = 2.06, OR = 1.63, 95% CI: 0.84, 3.18). However, this probability was higher among women aged < 35 years (B = 0.59, χ^2 = 0.62, OR = 1.80, 95% CI: 0.42, 7.77) than among those aged ≥ 35 years (B = 0.36, χ^2 = 0.84, OR = 1.43, 95% CI: 0.67, 3.05). While younger infertile women with GU (B = -0.22, χ^2 = 0.24, OR = 0.81, 95% CI: 0.34, 1.93) were less likely to fall into the IUAtg, older infertile women (B = 0.19, χ^2 = 0.42, OR = 1.21, 95% CI: 0.68, 2.17) were more prone to fall into the IUAtg.

Hypertension

Younger women with hypertension had very high predictive probability (B = 19.36, χ^2 = 0.00, OR = 256455523.1, 95% CI: 0.00, 0.00) of falling into the IUAtg while older women were not likely to fall into that group (B = -0.10, χ^2 = 0.16, OR = 0.10, 95% CI: 0.57, 1.46). Younger women with hypertension also had a very high predictive probability (B = 19.47, χ^2 = 20096.49, OR = 286782020.4, 95% CI: 0.00, 0.00) of falling into UPtg than older women (B = 0.10, χ^2 = 0.08, OR = 1.10, 95% CI: 0.57, 2.12).

Diabetes

With a negative predictive probability (B = -0.23, χ^2 = 0.17, OR = 0.79, 95% CI: 0.27, 2.36), infertile women with diabetes were unlikely to belong to SMFtg. However, on segregating them by age, younger diabetic infertile women, with positive predictive probability, (B = 18.75, χ^2 = 0.00, OR = 138569429.3, 95% CI: 0.00, 0.00) were more likely to fall into the SMFtg while older diabetic women were unlikely to fall into that target group (B = -0.22, χ^2 = 0.16, OR = 0.80, 95% CI: 0.26, 2.42). With positive predictive probability (B = 0.33, χ^2 = 0.20, OR = 1.40, 95% CI: 0.32, 6.09), older women with diabetes were more likely to fall into the UPtg while, with negative predictive probability, (B = -0.885, χ^2 = 0.46, OR = 0.43, 95% CI: 0.04, 4.93) younger women with diabetes were unlikely to fall into that group.

BMI related Predictive probability analysis (Table 4a-4c).

Predictor variable	B	SE	Wald χ^2 test	P-val-ue	OR	95% CI	B	SE	Wald χ^2 test	P-val-ue	OR	95% CI	B	SE	Wald χ^2 test	P-val-ue	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI
	Submucous fibroid target group																							
	BMI <18.5						BMI 18.5-24.9						BMI 25.0-29.9						BMI ≥ 30					
Asthma	-22.50	40192	0.00	1.00	5923409921	0.000	0.60	0.69	0.75	0.39	1.81	0.47, 6.98	-0.94	1.04	0.82	0.37	0.39	0.05, 3.00	-19.22	8755.77	0.00	1.00	0.00	0.00
Gastric ulcer	19.90	28420.7	0.00	1.00	440584054.4	0.000	0.59	0.63	0.89	0.35	1.80	0.53, 6.16	0.92	0.61	2.27	0.13	2.52	0.76, 8.35	-0.37	0.57	0.42	0.52	0.69	0.23, 2.10
Hyperten-sion	-	-	-	-	-	-	-0.50	0.68	0.53	0.46	0.61	0.16, 2.32	-0.67	0.47	0.02	0.88	0.93	0.38, 2.32	0.28	0.55	0.26	0.61	1.33	0.45, 3.88
Diabetes	-	-	-	-	-	-	-0.96	1.23	0.61	0.43	0.38	0.03, 4.27	-1.03	0.72	2.02	0.16	0.36	0.09,1.47	19.27	12092.48	0.00	1.00	234067446.6	0.00
Constant	1.30	0.65	3.98	-	-	-	1.06	0.68	2.44	0.12	2.89	-	2.58	1.04	6.21	0.01	13.25	-	21.21	8755.77	0.00	1.00	1621646564	

Table 4a: *Predictive probability of any of the predictor variables (asthma, gastric ulcer, hypertension, diabetes) falling or not falling into the Submucous fibroid target groups relative to BMI cluster.*

Predictor variable	B	SE	Wald χ^2 test	P-val-ue	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-val-ue	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI
	Intrauterine adhesions target group																							
	BMI <18.5						BMI 18.5-24.9						BMI 25.0-29.9						BMI≥30					
Asthma	-20.29	40192.96	0.00	1.00	0.00	0.00	0.27	0.68	0.15	0.70	1.31	0.34, 4.96	0.55	0.53	1.10	0.29	1.74	0.62, 4.88	-0.39	0.57	0.47	050	0.6	0.22, 2.07
Gastric ulcer	-0.92	1.53	0.36	0.55	0.40	0.02, 8.07	-0.17	0.45	0.14	0.71	0.85	0.35, 2.05	0.07	0.37	0.04	0.84	1.08	0.53, 2.21	0.86	0.55	2.43	0.12	2.37	0.80, 6.99
Hyperten-sion	-	-	-	-	-	-	0.26	0.79	0.11	0.74	1.30	0.28, 6.06	-0.21	0.38	0.32	0.57	0.81	0.39, 1.69	-0.33	0.34	0.92	0.34	0.72	0.37, 1.41
Diabetes	-	-	-	-	-	-	19.83	23205.42	0.00	1.00	408892005.2	-	-0.81	0.68	1.43	2.32	0.44	0.12, 1.68	-0.60	0.65	0.85	0.36	0.55	0.16, 1.96
Constant	21.20	40192.96	0.00	1.00	1615474518	-	1.11	0.68	2.69	0.10	3.03	-	0.50	0.52	0.91	0.34	1.64	-	1.44	0.56	6.53	0.01	4.21	-

Table 4b: *Predictive probability of any of the predictor variables (asthma, gastric ulcer, hypertension, diabetes) falling or not falling into the Intrauterine adhesions target group relative to BMI cluster.*

Predictor variable	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI	B	SE	Wald χ^2 test	P-value	OR	95% CI
	Intrauterine polyps target group																							
	BMI <18.5						BMI 18.5-24.9						BMI 25.0-29.9						BMI≥30					
Asthma	-19.41	40192.99	0.00	1.00	0.00	0.00	0.66	0.69	0.91	0.34	1.94	0.50, 7.56	-0.08	0.77	010	0.92	0.93	0.21, 4.18	-19.49	8762.93	0.00	1.00	0.00	0.00
Gastric ulcer	-1.79	1.61	1.24	0.27	0.17	0.01, 3.89	-0.82	0.44	3.45	0.06	0.44	0.19, 1.05	-0.22	0.46	0.23	0.63	0.82	0.32, 1.98	-0.18	0.52	0.12	0.73	0.84	0.30, 2.30
Hyper-tension	-				-	-	0.59	1.06	0.31	0.58	1.80	0.23, 14.35	0.92	0.74	1.55	0.21	2.51	0.59, 10.67	-0.29	0.42	0.47	0.49	0.75	0.33, 1.70
Diabe-tes	-				-	-	19.32	23205.42	0.00	1.00	246365231.0	0.00	19.24	13334.26	0.00	1.00	227155827.5	0.00	-0.73	0.69	1.11	0.29	0.48	0.12, 1.88
Con-stant	21.20	40192.99	0.00	1.00	1615475412		1.22	0.69	3.15	0.08	3.38		1.99	0.76	6.81	0.01	7.32	-	21.27	8762.93	0.00	1.00	1718969804	

Table 4c: *Predictive probability of any of the predictor variables (asthma, gastric ulcer, hypertension, diabetes) falling or not falling into the intrauterine polyps target group relative to BMI cluster.*

Underweight infertile women

Underweight women with gastric ulcer had higher predictive probability of falling into SMFtg (B = 19.90, χ^2 = 0.00, OR = 440584054.4, 95% CI:0.00) than those with other medical conditions. No underweight infertile woman presented with hypertension or diabetes.

Normal weight infertile women

Normal weight infertile women with asthma had higher predictive probability of falling into SMFtg (B = 0.60, χ^2 = 0.39, OR = 1.81, 95% CI: 0.47, 6.98) than those with gastric ulcer, hypertension, or diabetes. Normal weight infertile women with diabetes had higher predictive probability of falling into the IUAtg (B = 19.83, χ^2 = 0.00, OR = 408892005.2, 95% CI: 0.00) than those with asthma, hypertension, or gastric ulcer in that order. Normal weight infertile women with diabetes had higher predictive probability of falling into the UPtg (B = 19.32, χ^2 = 0.00, OR = 246365231.0, 95% CI: 0.00) than those with asthma, hypertension, or gastric ulcer in that order.

Overweight infertile women

Overweight infertile women with gastric ulcer had higher predictive probability of falling into SMFtg (B = 0.92, χ^2 = 0.13, OR = 2.52, 95% CI: 0.76, 8.35) than those with asthma, hypertension, or diabetes. Overweight infertile women with asthma had the highest predictive probability of belong to the IUAtg (B = 0.55, χ^2 = 1.10, OR = 1.74, 95% CI: 0.62, 4.88) than those with gastric ulcer, Overweight infertile women with hypertension or diabetes were unlikely to fall into the IUAtg. Likewise, overweight infertile women with diabetes were most likely to fall into the UPtg (B = 19.24, χ^2 = 0.00, OR = 227155827.5, 95% CI: 0.00) than overweight infertile women with hypertension.

Obese infertile women

Obese infertile women with diabetes had higher predictive probability of falling into SMFtg (B = 19.27, χ^2 = 0.00, OR = 234067446.6, 95% CI: 0.00) than those with asthma, gastric ulcer, or hypertension. Obese infertile women with gastric ulcer were the only group had positive predictive probability (B = 0.86, χ^2 = 0.12, OR = 2.37, 95% CI: 0.80, 6.99) of falling into IUAtg while those with asthma, hypertension, gastric ulcer and diabetes were unlikely to fall into the IUAtg. All obese infertile women with asthma, gastric ulcer, hypertension, and diabetes recorded negative predictive values and most likely belonged to the group with no uterine polyps.

Discussion and Conclusion

Limited former studies have reported medical conditions of infertile women seeking ART, much less any association between such medical illness and findings at hysteroscopy prior to IVF treatment. Part of the reason may be lack of cooperation between clinicians and specialists in fertility treatment such as gynecologists and embryologists. More fundamentally however, this dearth of attention probably reflects the assumption that medical conditions are not related to gynecological problems that affect fertility. Yet, there may just as well be such relationship, albeit not that of course and effect.

There are certain key findings in this study. Firstly, the commonest medical illnesses among infertile women consulting for IVF in Nigeria were gastric ulcer, hypertension, asthma, and diabetes, in that order. The relatively high prevalence of gastric ulcer patients among infertile Nigerian women was most likely due to stress of being infertile. This finding agrees with what Rooney., *et al*. [18] reported that clearly, infertility causes stress. Long-standing, elevated levels of stress may cause waning of the immune system, which can prompt other diseases such as high blood pressure, fatigue, anxiety and depression and possibly heart disease [19]. The relationship between stress and infertility has been a long-standing topic of debate [19]. Gastric ulcer may arise due to inappropriate eating habit of the infertile woman, susceptibility to Helicobacter pylori and medications consumed for other ailments.

The relative risk of having uterine polyps was highest among infertile women presenting with gastric ulcer, especially among obese infertile women who had the weakest negative probability of falling into the uterine polyp group. The relationship of gastric ulcer with uterine polyps among obese infertile women is not clear. Probably, this is due disruption of hormonal pathways brought about by stress or increased concentration of estrogen receptors and decreased concentration of progesterone receptors. Further studies on this is of high essence.

Another key finding is that infertile women with hypertension had a higher relative risk of IUA than those with asthma or gastric ulcer and higher predictive probability of having submucous fibroid (SMF), especially older patients, as well as intrauterine adhesions (IUA) and uterine polyps (UP), especially younger women. This agrees with the finding of Haan., *et al*. [13] that elevated blood pressure may increase fibroid risk through uterine smooth muscle injury, similar to atherosclerosis. Armanini., *et al*. [14] suggested a possible role of the renin-angiotensin-aldosterone system in the development of uterine fibroids in women with hypertension. Raised blood pressure is probably a risk factor for smooth muscle cell injury whereby certain cytokines are freed to trigger the evolution of uterine fibroid onset in a manner similar to the development of atherosclerosis. How hypertensive infertile women develop uterine fibroid may be through a similar mechanism. Again, intensive studies are needed to throw more light into this phenomenon.

This study also found that the relative risk of SMF and IUA were similar for infertile women with diabetes than the relative risk of uterine polyps. This finding is in line with the report of Chelsea., *et al*. [20] that numerous factors that are likely to increase the risk of IUA include "genetic polymorphisms activator inhibitor-1 and thrombin activatable fibrinolysis inhibitor, diabetes mellitus and obesity", among others. Another novel finding is that younger diabetic women had higher predictive probability of developing submucous fibroid group. Many factors may be responsible for this, including oral hormone therapy, binge alcohol consumption and medication. Also, obese diabetic women had a higher predictive probability of falling into submucous fibroid target group. Although no study that we are aware of has analytically demonstrated whether any of these medical diseases among infertile black African women is associated with findings at hysteroscopy prior to IVF treatment, our observation that these diseases statistically relate to submucous fibroid, intrauterine adhesions or uterine polyps appear to constitute the first empirical attempt at an exploration of possible association between uterine aberrations and previous medical conditions.

To conclude, the most prevalent illnesses presented by infertile women consulting for IVF treatment were asthma, gastric ulcer, hypertension, and diabetes mellitus. This retrospective study has shown that there may be possible association between these diseases and findings at hysteroscopy such as submucous fibroid, intrauterine adhesion, and uterine polyps. Younger women with diabetes may be more predisposed to submucous fibroid than older women and overweight infertile women with asthma may be more predisposed to intrauterine adhesions. Clinicians and gynecologists should take this information into consideration when seeing infertile women. In addition, more data collection from multiple study sites and further extensive research are needed on the relationship between medical conditions and findings at hysteroscopy before infertile women commence IVF treatment. Ameliorating such medical conditions might improve the outcome of IVF.

This study however has certain limitations that need clarification. First and most importantly, cause-effect relationship has not been established thus the study cannot ascribe causality to the findings therein, probably accentuated by the fact that the proportion of clients with medical illnesses was low. Secondly, medical illnesses were self-reported by the patients though in some cases, previous medical reports were documented as "known asthmatic", "known hypertensive", "known diabetic" and "known ulcer patient". However, there was no reason to doubt those who self-reported and showed or mentioned the prescribed drugs by their physicians. Although some patients were known hypertensive, the systolic and diastolic blood pressure of each patient was taken and recorded but not all patients had their blood sugar or insulin level measured. In the same vein, lung function test or barium meal test was not done for asthmatic or ulcer patients. Next, this was a facility-based study and the result may not necessarily be extrapolated to a community-based study which would have demanded more material and financial resources. Also, the patients in this study were mainly urban women and the data from them may

not reflect data from rural or semi-urban women. Finally, geographical location may render the result of this study, which was conducted in the south, rain-forest region of Nigeria, to be different, had the study been conducted in the north arid or the mountainous middle-belt part of the country.

Authors' Contribution

ABA, BMA, VDA and AA conceived and designed the study: ABA, VDA and IOO performed the hysteroscopy: BMA, AA and VDA analyzed the data: BMA, VDA and AA wrote the paper.

Declaration

The authors declare no conflict of interest.

Acknowledgment

The authors are very grateful to the patients who participated in this study, to the Nurses at Nordica Fertility Center who meticulously screened all the patients and collected various vital statistics, to the clinicians who examined the patients and to the Surgeons who performed all the necessary procedures.

Bibliography

1. Wakefield Research. "Trends in Infertility 2016 Survey and Report". *Reproductive Medicine Associates of New Jersey* (2016).
2. Mascarenhas MN., *et al*. "National, regional, and global trends in infertility prevalence since 1990: a systematic analysis of 277 health surveys". *PLOS Medicine* 9 (2012): e1001356.
3. Practice Committee of American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion". *Fertility and Sterility's* 99.1 (2013): 63.
4. Mascarenhas MN., *et al*. "Measuring infertility in populations: constructing a standard definition for use with demographic and reproductive health surveys". *Population Health Metrics* 10.1 (2012): 17.
5. Verit FF., *et al*. "Cardiovascular risk may be increased in women with unexplained infertility". *Clinical and Experimental Reproductive Medicine* 44.1 (2017): 28-32.
6. Ajayi A., *et al*. "Awareness, knowledge and perception of in-vitro fertilization among final-year medical students in South-West Nigeria". *International Journal of Pregnancy and Child Birth* 2.1 (2017): 5-12.
7. Beall S., *et al*. "Ooocyte maturation failure: a syndrome of bad eggs". *Fertility and Sterility's* 94.7 (2010): 2507-2513.
8. Guo XC and Segars JH. "The impact and management of fibroids for fertility: an evidence-based approach". *Obstetrics and Gynecology Clinics of North America* 39.4 (2012): 521-533.
9. Chami AA and Saridogan E. "Endometrial polyps and subfertility". *The Journal of Obstetrics and Gynecology of India* 67.1 (2017): 9-14.
10. Bulletti C., *et al*. "Endometriosis and Infertility". *The Journal of Assisted Reproduction and Genetics* 27.8 (2010): 441-447.
11. Mojarrad M., *et al*. "Polymorphism of genes and implantation failure". *International Journal of Molecular and Cellular Medicine* 2.1 (2013): 1-8.

12. Cox L and Liu JH. "Primary ovarian insufficiency: An update". *International Journal of Women's Health* 6 (2014): 235-243.

13. Haan YC., *et al*. "The risk of hypertension and cardiovascular disease in women with uterine fibroids". *Journal of Clinical Hypertension* 20.4 (2018): 718-726.

14. Armanini D., *et al*. "Uterine fibroids and risk of hypertension: Implication of inflammation and a possible role of the renin-angiotensin-aldosterone system". *Journal of Clinical Hypertension* 20.4 (2018): 727-729.

15. Farland LV., *et al*. "Infertility, Fertility treatment and risk of hypertension". *Fertility and Sterility* 104.2 (2015): 391-397.

16. Gkioka E., *et al*. "The Role of Insulin-like Growth Factor-1 Signaling Pathways in Uterine Leiomyoma". *In Vivo* 29.6 (2015): 637-649.

17. Ajayi AB., *et al*. "Detection of Intrauterine Lesions by Hysteroscopy among Women with Fertility Challenges in an In-Vitro Fertilization Center in Lagos, Nigeria". *Critical Care Obstetrics and Gynecology* 1.1 (2015): 8.

18. Rooney KL. "The relationship between stress and infertility". *Dialogues in Clinical Neuroscience* 20.1 (2018): 41-47.

19. Howley EK. "Does stress cause stomach ulcers?". health.usnews.com.

20. Chelsea F., *et al*. "Predisposing factors to post-operative adhesion development". *Human Reproduction* 21 (2015): 536-551.

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