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Pharmacotherapy for Infertility in Ghana: A Prospective Study on Prescription Patterns and Treatment Outcomes among Women undergoing Fertility Treatment

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ABSTRACT

Background: Pharmacotherapy remains a first-line and major treatment option for couples struggling with infertility, especially in sub-Saharan Africa, where other expensive alternatives are rarely available. Despite the reliance on pharmacotherapy for treating infertility in the subregion, especially for those diagnosed with unexplained infertility, little is known about the actual influence of drug therapies on conception.

Objectives: The study aimed to prospectively assess the prescription patterns and outcomes of pharmacotherapy for women undergoing fertility treatment in Ghana.

Methods: This prospective cohort study involved 482 infertile women presenting for fertility treatment in 4 fertility clinics in the Cape Coast Metropolis of Ghana between March 2019 and February 2021. A simple random sampling technique was used to recruit subjects for the study. The women were followed up for 12 months to assess the outcome of drug therapy on conception. Data analysis was done using Stata version 14. Logistic regression was used to assess the association between trends with dichotomous outcomes.

Results: The study identified that approximately 45.2% of the patients received monotherapy, whereas 24.1% received a combination of 2 drugs. Patients treated with a combination of 3 drugs were more likely to conceive (adjusted odds ratio = 4.10; 95% CI, 1.29–13.02; $P = 0.02$) than those without treatment.

Conclusions: Patients treated with combination therapies had higher chances of conception than those without medications. However, a combination of nutritional and herbal therapies were associated with improved outcomes compared with conventional and nutritional supplements. The study's outcome could provide fertility specialists and stakeholders insight into choosing appropriate treatment options for prospective couples seeking fertility care. Consequently, fertility patients can access specific treatment options to meet their desired needs.

Introduction

Infertility is a widespread health problem worldwide and childless couples seek care daily in many treatment centers.[1] It is defined as the inability of sexually active couples to achieve conception after at least 1 year of unprotected sexual intercourse.[2] In many parts of the world, especially sub-Saharan Africa, delayed

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childbearing is mostly blamed on women, thus placing a seemingly huge responsibility on them to seek medical care.[2,3]

In sub-Saharan Africa, infertile couples mostly rely on drug therapies due in part to their low socioeconomic status and the high cost of accessing assisted reproductive technologies. In Ghana, for instance, such couples may be subjected to different therapies ranging from conventional drugs like clomiphene citrate to nutritional and herbal formulation.[4] However, the selection of these therapies for treating infertile women is mostly not backed by evidence-based empirical data on how they influence conception. Although some drug therapies have gained popularity in infertility treatment,[5,6] little information is available to justify their selection and overall effect on conception, particularly in the sub-Saharan African population. Besides the orthodox (conventional) treatments, nutritional and herbal supplements have become a mainstay of treatment for infertile patients in Ghana. Therefore, it is common practice for patients seeking fertility care to be managed with these drug categories. However, little evidence exists on how these treatments (monotherapy or combination therapy) improve conception for patients desiring to conceive.

Considering the high preference for pharmacotherapy in managing infertility in the subregion, extensive and meticulous studies to ascertain the outcome of these treatments cannot be overemphasized.[7] Nonetheless, no study properly and convincingly evaluates the outcome of pharmacotherapy for infertility among women seeking fertility treatment in the subregion because data on conception rates remain scanty. Among the few related studies conducted in Southeast Nigeria focused only on conventional therapy, although other modes of treatment such as nutritional and herbal therapies form an integral treatment modality in sub-Saharan Africa.[1] Although our previous study assessed the outcome of conventional, nutritional, and herbal therapies among infertile couples, it relied on secondary data due to its retrospective nature.[4] As such, it was impossible to follow-up on the clients, thus resulting in our inability to know whether the patients adhered to the treatments or were noncompliant. However, compliance with fertility medications has been strongly associated with treatment outcomes.[8]

This current, prospective cohort study was conducted to follow-up with the patients and effectively monitor their compliance by frequently reminding them of the need for adherence to treatment protocols through telephone calls and ensuring regular hospital visits as scheduled. Therefore, the study's main objective was to assess the prescription patterns and conception rates among women undergoing infertility treatment in the Cape Coast metropolis, Ghana.

Methods

Study design

This prospective cohort study was conducted at 4 different fertility centers in the Cape Coast metropolis in the Central Region of Ghana for 2 years (March 2019 to February 2021) to assess the prescription pattern and outcome of pharmacotherapy for infertility.

Sampling

Four hundred eighty-two infertile women were recruited into the study using a simple random sampling technique. All recruited patients experienced infertility for a minimum of 12 months. The fertility centers conduct their clinic once or twice weekly, depending on the facility's protocol. Before booking an appointment with the specialist, the patients reported to the Antenatal Unit of the Out-Patients Department, where they were registered and given unique identity numbers. After the registration, the patients were given specific dates to report to the clinic to see the specialist. All patients who came for booking on the first day before seeing the doctor were informed about the purpose of the study, and those who consented to be part of it were recruited. The unique identification numbers for all patients required to see the doctor on a specific day were placed together in a container and uniformly mixed. Samples were randomly selected from the number already registered to see the doctor that day. This was repeated at all the study centers until the required sample size for each center was obtained. The selected patients were approached during the consultation with the doctor to obtain the information needed for the study. Finally, based on the total number of fertility patients who reported for treatment the previous year before the commencement of the study, the sample size for each center was calculated according to the formula deduced by Krejcie and Morgan.[9]

Evaluation of male partners

The male partners of the respective women were evaluated for any abnormalities. Semen analysis was performed using the World Health Organization protocol.[10] Men with semen abnormalities were treated with either conventional (Clomiphene citrate), herbal (Addyzoa; Charak Pharma, Mumbai, India), or nutritional supplements as prescribed by the health care provider for 3 months, after which semen analysis was performed for re-evaluation.

Inclusion and exclusion criteria

Included in the study were women, either single or married, diagnosed with infertility, and aged between 18 and 45 years. Excluded from the study were those with underlining conditions, such as blocked fallopian tubes and an existing uterine fibroid, which may require surgical intervention for correction.

Data collection

Data collection began in March 2019 and ended in February 2021, with an average of 12 months' follow-up. Trained personnel, including nurses and midwives, approached all recruited patients in the consulting rooms to obtain basic information after the doctor had seen them. Health care professionals (nurses and midwives) who were directly involved in the care of the patients were trained to collect the data. Four days of the orientation program, 1 at each treatment center was organized for the staff who collected the data. The data-capturing tool samples were given to the nurses and midwives during the training section to familiarize themselves with them. Detailed information on what to capture, including the names of drugs prescribed, the dosages, duration of treatment, and sociodemographic data, were specified on the instrument, which was made available in the consulting rooms. As a routine practice, each treatment center (the consulting rooms) had nurses or midwives stationed to assist the doctors during the consultation. After the doctor prescribes treatment for the patient, the nurse records exactly what the doctor prescribed from the patient's folder onto the data capture form. After documentation of the necessary information for a particular day, the nurse shows the information to the other trained nurse/midwife to check the accuracy of the information documented. Other details, such as the sociodemographic data, were obtained directly from the patients onto the data capture form. The patients did not have control over what was prescribed to them. Moreover, the doctors at the same or other treatment centers did not know what their colleagues prescribed for other patients. The doctors were not made aware of which of the patients were recruited into the study. All recruited patients were only made known to the nurses who assisted in the data collection.

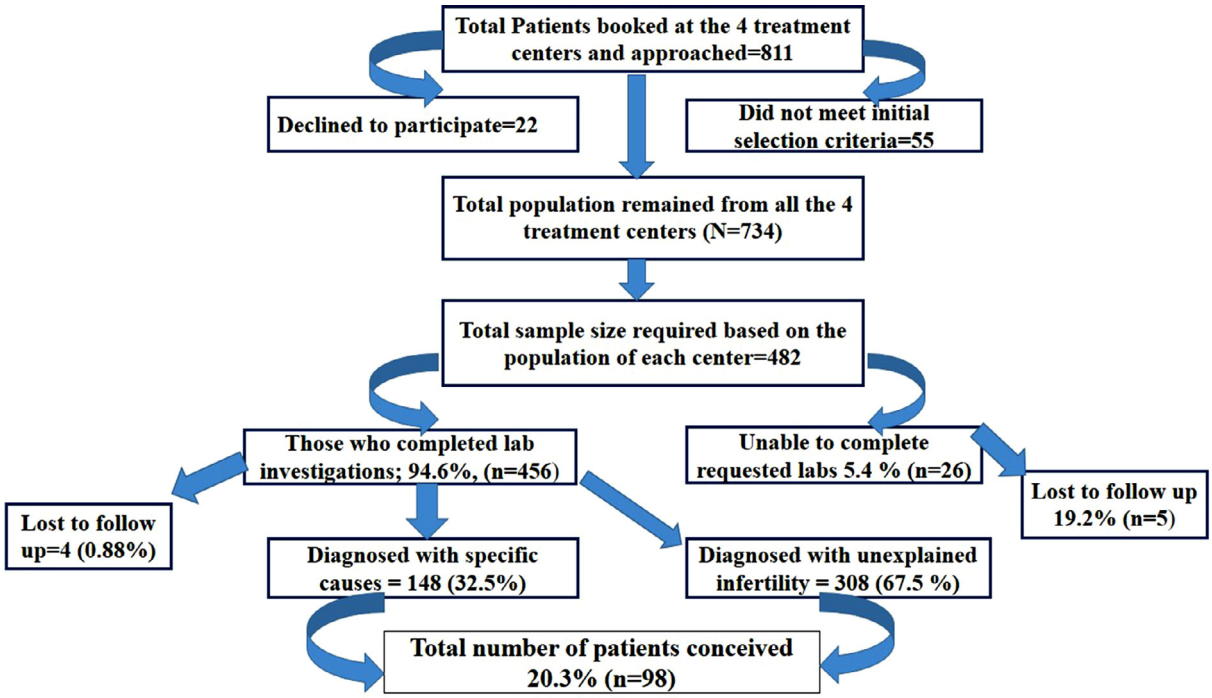

Figure 1. Flowchart showing the data collection process and general treatment outcome.

The principal outcome of treatment (pregnancy) was measured using standard laboratory procedures such that the participants' behavior could not influence the outcomes. Consequently, the possibility of observer bias was reduced. Semen analysis was performed for the male partners, and the outcome of the investigation was also documented on the data capture form of their respective female partners.

All the patients were followed-up via telephone to ensure compliance with treatment. After completion of treatment, the patients were asked to return to the clinic, where urine pregnancy tests were performed to know the treatment outcome and documented on the data capturing tool. For patients with positive pregnancy tests, pelvic scans were done after 6 weeks of testing positive for pregnancy.

Classification of drugs

The drugs used were classified based on their active constituents as conventional, nutritional, and herbal therapies. Nutritional supplements included drugs designed as food supplements containing major vitamins and minerals as active constituents. Herbal supplements included drugs designed as herbal formulations from India (oriental) and other Western countries with active ingredients like Ashoka Tree (*Ashoka*), which has potent estrogenic properties; lodh tree (*Lodhra*), which is known to improve fertility by regulating ovarian hormones; asparagus (*Shatavari*), which is known to restore hormonal balance in women; and malabar nut (*Vasaka*) with potent anti-inflammatory and analgesic properties. Conventional therapies included clomiphene citrate, metformin, and antibiotics (adjuncts). Male partners with abnormalities in their sperm were also treated alongside the women.

Follow-up

On the first day of patients' visits to the clinic, the researchers explained the purpose of the study to them, and those who agreed to participate were recruited. Follow-up began soon after the patient's first visit to the clinic. Patients were followed-up on their appointment dates during scheduled review visits to the hospital and through telephone calls. All patients were followed until they achieved conception or decided to discontinue fertility care.

Description of female participants

The description of the participants from the start of data collection to the total conception rate is detailed in the flowchart in Figure 1.

Ethical clearance

Permission to carry out this study was granted by the head of the 4 study centers, followed by ethical clearance issued by the Ethical Review Board of the Cape Coast Teaching Hospital (reference No.: CCTHERC/EC/2019), and the Institutional Review Board of the University of Cape Coast (reference No.: UCCIRB/EXT/2019). Permission from individual patients was sought before data were collected. The purpose of the study was explained to the participants in their preferred language after checking the eligibility criteria. Informed written consent was provided to all the study participants before study procedures took place. Patients' names were also excluded from the study to protect their confidentiality.

Statistical Analysis

Statistical analysis was done using a Microsoft Excel (Redmond, Washington) spreadsheet and Stata version 14 (StataCorp, College Station, Texas). A χ^2 test was used to determine trends in the case of ordered exposure categories. Logistic regression was used to assess the association between trends with dichotomous outcomes. A 95% CI was selected such that a P value < 0.05 was considered significant.

Results

Sociodemographic data of the women and their effect on conception

The results presented in Table 1 show the sociodemographic characteristics of respondents and their effect on conception. The mean (SD) age of respondents was 32 (5.4) years (range = 22–45 years). Approximately one-half of the respondents had experienced infertility for 1 to 3 years. The most dominant educational background among the respondents was tertiary education (33.2%). Regarding the respondents' employment status, the majority (51.8%) had an informal occupation (eg, trading, farming, and tailoring), whereas 7.1% were unemployed. Concerning the religious affiliations of the respondents, it was established that most of the respondents were Pentecostal Christians (41.9%).

In terms of the effect of sociodemographic factors on conception, it was found that increasing age was inversely associated with the conception rate. Hence, 75.5% of conceptions occurred among respondents younger than age 35 years. Furthermore, the conception rate decreased with the increasing duration of infertility. Unsurprisingly, those infertile for 1 to 3 years had a 23.6% chance of conception, whereas those infertile for more than 7 years had only a 14.3% conception rate, although this was not statistically significant. Moreover, respondents' employment status and education level did not significantly influence the conception rate. Among the religious groups, Pentecostal Christians had the least chance of conceiving during pharmacotherapy (adjusted odds ratio [aOR] = 0.36; 95% CI, 0.17-0.76; $P = 0.007$) compared with Catholics, Mainline Protestants, and Muslims.

Effects of various diagnosis on conception

Table 1 describes the effect of various diagnoses on conception. Respondents with polycystic ovarian syndrome (PCOS) diagnosis alone had the highest conception rates with pharmacotherapy. Respondents diagnosed concurrently with PCOS and ovulatory dysfunction had significantly lower conception rates compared with respondents diagnosed with only PCOS (ie, 22.4% vs 68.8%; aOR = 0.06; 95% CI, 0.01–0.63; $P < 0.019$). Respondents diagnosed with only ovulatory dysfunction had 25.0% conception rates (aOR = 0.25; 95% CI, 0.05-1.24; $P \leq 0.09$), as shown in the regression analysis. respondents with unexplained infertility had higher conception rates (19.8%; aOR = 0.18; 95% CI, 0.04–0.75; $P < 0.018$) than those who were diagnosed with pelvic inflammatory disease (10%; aOR = 0.15; 95% CI; 0.03–0.73; $P = 0.018$).

Prescription pattern and drug classifications

Results presented in Table 1 describe the prescription pattern and classification of drugs used to manage infertile women. It was evident that 45.2% of the respondents received single-drug treatment, followed by a combination of 2 drugs (24.1%) and 3 combinations (7.1%). Approximately 23.7% of the patients received no treatment for various reasons, including relatively shorter periods of infertility (1 year on average) with no definitive cause, and were therefore not given any medication. On drug classifications, nutritional supplements remained the single most prescribed drug therapy for the respondents (30.1%), followed by conventional drugs (14.5%). Approximately 1 out of every 3 respondents (31.1%) received combination therapy.

Treatment combinations and their effect on conception

Table 1 describes the effect of the combination of drugs on conception. Pharmacotherapy for infertile women resulted in higher conception rates (15.9%–45.5%) than those without medications. Generally, increasing the number of therapeutic agents also increased conception rates. Treatment with single therapies (aOR = 2.49; 95% CI, 0.27–16.48; $P = 0.35$) or double therapies (aOR = 1.77; 95% CI, 0.76–4.10; $P = 0.18$) resulted in a higher probability of pregnancy compared with those without any treatment, although no significant difference was observed. However, clients treated predominantly with 3 combinations (aOR = 4.1; 95% CI, 1.29–13.02; $P = 0.02$), were associated with statistically greater chances of conceiving than the control group.

The effect of drug classes on conception.

Table 1 shows the effect of various classes of drugs on conception using binary logistic regression. Clients treated with only nutritional supplements had lower conception rates (13.5%) than those who received only conventional therapies (20%).

However, conception rates increased when nutrition therapy was added to conventional (28.8%; aOR = 2.06; 95% CI, 0.84-0.501; $P = 0.0.11$), although no statistically significant difference was observed. Also, the combination of nutritional and herbal therapies was associated with a significant increase in conception rates (31.7%; aOR = 2.91; 95% CI, 1.25–6.75; $P = 0.01$). A combination of 3 therapies was associated with higher conception rates (50%; aOR = 6.0; 95% CI, 2.31–15.58; $P < 0.001$).

Outcome of evaluation of the male partners

Among the 482 men expected to do semen analysis, approximately 71.6% made themselves available for the initial test. For those who performed the first semen test, normal semen parameters were obtained among 54.8% of them, whereas 45.2% of the respondents had some form of abnormalities. Among those with semen abnormalities, more than one-half of them (55.1%) had abnormalities in all the 3 key semen parameters measured. Following treatment of the men with semen abnormalities, most of them (50.6%) received herbal therapies (Addyzoa) as first-line treatments, followed by nutritional supplements (30.8%), as shown in Table 2.

Initiation and compliance with treatment reviews by couple pair

As shown in Table 3, it was revealed that among the couple, more than two-thirds of the women (72%) took the first step in seeking treatment at the various treatment centers. Regarding the compliance status of the couple, it was identified that approximately 40.7% of them did not comply with treatment at some point during the period. Patients who skipped review appointments, including failure to perform investigations and discontinuation of treatment before conception, were classified as noncompliant when this was exhibited.

Outcome of semen analysis for the male partners

Figure 2 shows the outcome of the semen analysis for the male partners before and 3 months after treatment. It was revealed that all semen parameters saw significant improvement from the baseline following treatment.

Discussion

The study assessed drug treatment outcomes of women seeking care at 4 fertility clinics. The current study established important and notable associations between demographic factors and treatment outcomes. Our previous study estimated the rate of infertility

Table 1
Sociodemographic factors, diagnosis, treatment classification, and their effect on conception.

Variable	*f*	%	% conceived	χ^2 *P* value	COR (95% CI)	*P* value	AOR (95%CI)	*P* value	Model 1*	
									AOR (95% CI)	*P* value
Age group, y			**0.004**							
21-25	6	1.2	33.3		1		1		1	
26-30	122	25.3	22.9		0.6 (0.10-3.42)	0.56	0.32 (0.31-3.20)	0.33	0.32 (0.02-4.71)	0.4
31-35	162	33.6	27.2		0.75 (0.13-4.22)	0.74	0.37 (0.04-3.38)	0.4	0.36 (0.03-5.27)	0.46
36-40	120	24.9	15		0.35 (0.06-2.07)	0.25	0.30 (0.03-3.19)	0.32	0.21 (0.01-3.36)	0.27
45-45	72	14.9	8.3		0.18 (0.03-1.20)	0.08	0.17 (0.01-1.90)	0.15	0.16 (0.01-2.63)	0.2
Total	**482**	**100**	**20.3**		NA	NA	NA	NA		
Duration of infertility, y		0.15								
1-3	242	50.2	23.6		1		-	-	-	-
4- 6	156	32.4	18.6		0.74 (0.45-1.22)	0.24	-			
≥7	84	17.4	14.3		0.54 (0.27-1.07)	0.08	-	-	-	-
Total	**482**	**100**	**20.3**		NA	NA				
Education level			**0.03**							
No formal education	16	3.3	25		1		1		1	
Primary	78	16.2	10.3		0.34 (0.09-1.32)	0.12	1.33 (0.23-7.55)	0.75	1.72 (0.33-9.09)	0.52
JHS	128	26.6	15.6		0.56 (0.16-1.90)	0.35	0.95(0.0.20-4.35)	0.93	0.83 (0.19-3.61)	0.8
SHS	58	12	20.7		0.78 (0.21-2.87)	0.71	1.55 (0.29-8.44)	0.61	1.05 (0.20-5.35)	0.96
Tertiary	160	33.2	26.3		1.07 (0.33-3.49)	0.91	5.59 (0.82-37.97)	0.08	5.74 (0.86-38.22	0.07
Subtotal	**440**	**91.3**	**19.5**		NA	NA	NA	NA	NA	
Unavailable	42	**8.7**								
Total	**482**	**100**								
Occupation			**0.04**							
Informal	280	58.1	16.4		1		1		1	
Formal	124	26.6	26.6		1.83 (0.80-4.18)	0.15	1.37 (0.440-4.21)	0.58	2.18 (0.61-7.78)	0.23
Unemployed	34	7.1	26.5		1.84 (1.11-3.07)	0.02	0.45 (0.13-1.54)	0.21	0.3 (0.08-1.18)	0.09
Subtotal	**438**	91.8	20.1		NA	NA	NA	NA		
Unavailable	44	9.1								
Total	**482**	**100**								
Religion				**0.04**						
Catholic	84	17.4	26.2		1		1		1	
Pentecostal	202	41.9	14.4		0.47 (0.23-0.88)	0.02	0.36 (0.17-0.76)	0.007	0.27 (0.12-0.61)	0.002
Protestant	130	27	20.8		0.74 (0.39-1.41)	0.36	0.69 (0.32-1.48)	0.35	0.9 (0.39-2.08)	0.81
Muslim	34	7.1	29.4		1.17 (0.49-2.84)	0.72	2.35 (0.69-8.04)	0.17	4.53 (1.21-16.92)	0.03
Subtotal	**450**	**93.4**	**19.6**		NA	NA	NA	NA		
Unavailable	32	6.6								
Total	**482**	**100**								
Type of diagnosis			**0.002**							
Polycystic ovary syndrome†	16	3.3	68.8		1		1		1	
Ovulation dysfunction	40	8.3	25		0.15 (0.04-0.54)	0.004	0.25 (0.05-1.24)	0.09	0.49 (0.10-2.51)	0.39
Pelvic inflammatory disease	60	12.4	10		0.09 (0.03-0.32)	< 0.001	0.15 (0.03-0.73)	0.018	0.14 (0.03-0.69)	0.016
NAD (unexplained)	308	63.9	19.8		0.11 (0.04-0.34)	< 0.001	0.18 (0.04-0.75)	0.018	0.20 (0.05-0.85)	0.029
Polycystic ovary syndrome + ovulation dysfunction	18	3.7	22.4		0.13 (0.03-0.60)	0.009	0.06 (0.01-0.63)	0.019	0.06 (0.004-1.01)	0.05
Ovulation dysfunction + pelvic inflammatory disease	14	2.9	14.3		0.08 (0.01-0.47)	0.006	1		1	
No. of treatments		**< 0.001**								
No treatment†	114	23.7	10.4		1		1		1	
Single treatment	218	45.2	15.9		1.57 (0.78-3.17)	0.21	0.72 (0.31-1.67)	0.44	0.77 (0.31-1.89)	0.56
Double treatment	116	24.1	33.9		3.67 (1.80-7.52)	< 0.001	1.77 (0.76-4.10)	0.18	1.80 (0.73-4.42)	0.2
3 treatments	34	7.1	45.5		8.5 (3.45-20.90)	< 0.001	4.10 (1.29-13.02)	0.02	4.63 (1.31-16.67)	0.018
Treatment classification		**< 0.001**								
No treatment†	114	23.7	10.5						1	
Conventional‡	70	14.5	20		2.1 (0.82-4.90)	0.08	–	–	1.28 (0.53-3.06)	0.59
Nutritional§	148	30.1	13.5		1.33 (0.62-2.84)	0.47	–	–	0.94 (0.42-2.08)	0.87
	53	11	28.3		3.36 (1.44-7.81)	0.005	–	–	2.06 (0.84-5.01)	0.11
Conventional + nutritional										
Nutritional + herbal‖,¶	63	13.1	31.7		3.95 (1.77-8.79)	< 0.001	–	–	2.91 (1.25-6.75)	0.01
Conventional + nutritional + herbal#	34	7.1	50		8.5 (3.34-20.90)	< 0.001	–	–	6.0 (2.31-15.58)	< 0.001

COR = crude odds ratio; AOR = adjusted odds ratio; NAD = xxxxxx; NA = missing responses (%).

* Model 1 analysis adjusted for treatment of the male partner, male diagnosis, and treatment adherence. Treatment classification analysis was run separately by adjusting for the confounders listed under Model 1 due to collinearity.

† Reference category.

‡ Conventional therapies active constituents: clomiphene citrate, with or without antibiotics.

§ Nutritional supplements active ingredients: folic acid, vitamins D and C, selenium, zinc, iron, magnesium, B vitamins, vitamin E, coenzyme Q10, and N-acetyl cysteine, inositol, and L-arginine.

‖ Herbal therapies active ingredients: ashoka (*Saraca indica*), iodhra (*Symplocos racemose*), shatavari (*Asparagus racemosus*), ashwagandha (*Withania somnifera*).

¶ Includes a few samples with only herbal treatment.

Includes a few categories excluding nutritional supplements.

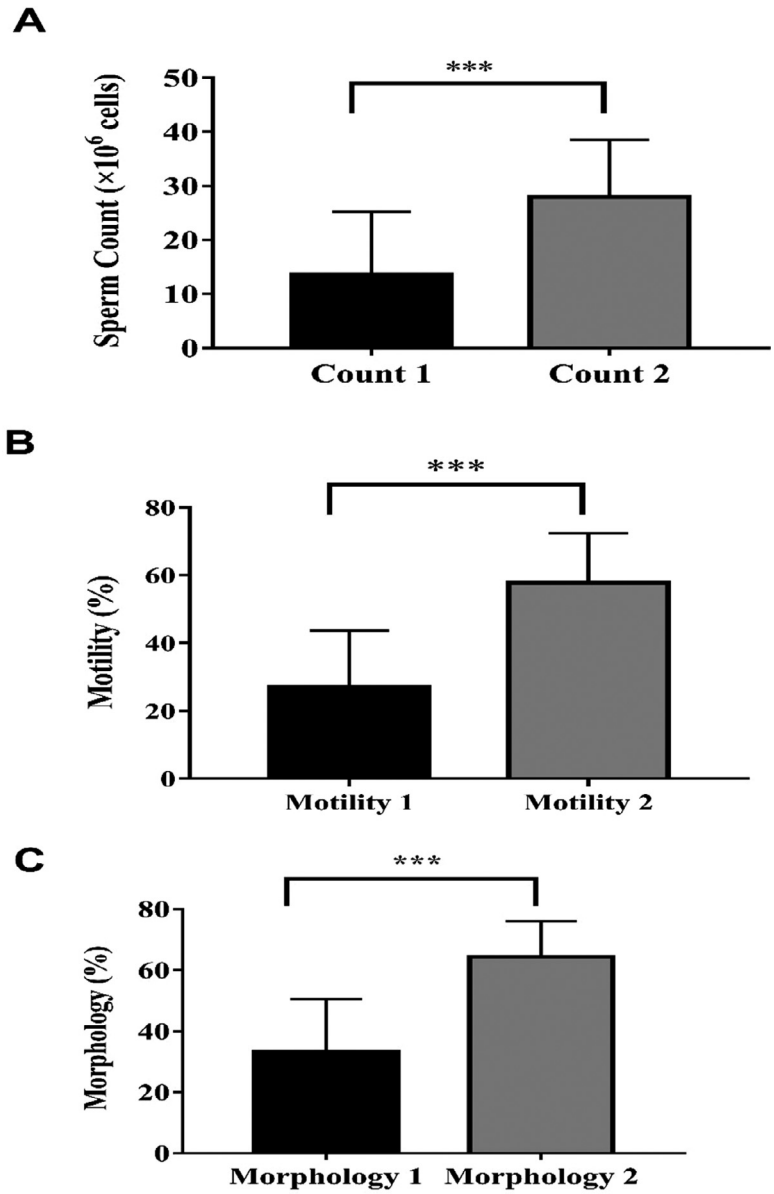

Figure 2. Comparison of semen analysis outcome; count (A), motility (B), and morphology (C) respectively, for men with semen abnormalities irrespective of the type of treatment. Sperm samples were taken before and three months after treatment. Values are Mean±SD (n=100). *** means $p<0.001$. (Paired sample t-test was used).

to be 12.3% at the Cape Coast Teaching Hospital, among the major study centers where the present research was conducted.[4] In the current study, although infertility cases were reported among women aged 21 to 45 years, more than half of the respondents were younger than age 35 years and experienced infertility between 1 and 3 years. This suggests that patients were more eager and determined to seek prompt treatment to avoid the condition's perceived worsening, which is consistent with other studies.[1,11,12] Although some form of noncompliance was observed among the couples, women mostly took the first step in seeking treatment at the fertility centers. This is probably because infertile women in our subregion are highly stigmatized and become abused by their spouses and in-laws.[2,3]

The study also established that infertile women seeking fertility treatment were exposed to different drug therapies, as determined by the health care provider. However, such a trend is not in isolation; similar patterns have been reported in existing studies.[13–15] Although specific therapies exist for a few known causes of infertility,[16–19] related studies have established an association between idiopathic infertility and nonspecific therapies.[20–24] An overall 20.3% conception rate was achieved among the women recruited in the current study. Conception rates were higher among women diagnosed with polycystic ovarian syndrome and ovulation dysfunction, due to the availability of specific therapies for treating such conditions. Pelvic inflammatory diseases, as a single form of diagnosis, although a known cause of infertility, recorded a lower pregnancy rate because they can leave lesions that may interfere with the fertilization process.[22,25]

The various fertility drugs explored in the current study provide interesting insights regarding their relationship to conception. In this present study, drug combination therapy was associated with an enhanced outcome compared with monotherapy or no treatment. The enhanced conception rate of the combination therapies might be due to the possible synergistic effect produced by the drugs. Again, whereas many fertility specialists rely on nutritional supplements to manage infertility cases of unknown origin, conventional therapies such as clomiphene citrate are frequently used to manage hormonal imbalances.[17,26] This might account for their

Table 2
Outcome of evaluation and treatment strategies for male partners with semen abnormalities.

Evaluation or treatment strategy	*f*	%
General diagnostic outcome		
Specific causes	156	45.2
Normal semen analysis	189	71.6
Total	345	100
Specific semen diagnosis		
Oligoathenoteratozoospermia	86	55.13
Oligospermia	23	14.74
Azoospermia	14	8.79
Asthenoteratozoospermia	14	8.79
Asthenozoospermia	10	6.4
Teratozoospermia	4	2.56
Oligoasthenozoospermia	4	2.56
Oligoteratozoospermia	2	1.28
Subtotal	156	100
Treatment category		
Conventional*	18	11.5
Nutritional†	48	30.8
Herbal‡	79	50.6
Nutritional +herbal	11	7.1
Total	156	100

* Clomiphene Citrate, Antibiotics.
† Vitamins B-12, C, and E, selenium, zinc, Co-enzyme Q10, arginine, and carnitine.
‡ Addyzoa (Charak Pharma, Mumbai, India.

Table 3
Initiation and compliance with treatment reviews by couple pair.

Variable	*f*	%
Initiation of Rx		
Female partne	347	72
Male partner	48	10
Both partners	87	18
Total	482	100
Compliance with Rx		
Complied	286	59.3
Did not comply*	196	40.7
Total	482	100

Rx = prescription.
* Includes skipping review orders, failing to perform investigations, discontinuation of treatment before conception; patients who exhibited at least 1 of the above-listed behaviors were considered noncompliant.

improved outcome over the nutritional supplements, as identified in the current study.

The commonly prescribed herbal therapies such as Evecare (Himalay Wellness, Bangalore, India) and M2Tone (Charak Pharma) have functional properties, including stimulation of the immune system, improvement in ovulation, and protection of eggs from oxidative damage, among others.[27–29] On the other hand, most nutritional supplements are measured by their antioxidant properties and ability to boost the immune system. Although the antioxidant properties of nutritional supplements can protect eggs from oxidative damage, they provide very little ovulation stimulation. These factors might account for the better outcome of herbal and conventional drugs over nutritional supplements regarding conception, as observed in this study.

It is important to note that all combination therapies were associated with higher chances of conception than single conventional therapy. Although nutritional supplements as monotherapy were associated with a minimal conception rate, better conceptions were achieved when combined with conventional or herbal supplements. This finding may guide fertility specialists in treating infertility in health facilities while assuring the patients seeking treatment. For example, our recent report revealed that prolonged pharmacotherapy of infertility without the desired outcome might lead to apathy, increased financial burden, psychological distress, and subsequent withdrawal from treatment.[7] Therefore, increasing the expected outcome of pharmacotherapy for infertility by employing evidence-based treatment protocols may significantly reduce treatment discontinuation and its associated psychological distress.

A major limitation of the current study is that the investigators did not have control over respondents' diets and other socioeconomic factors, which could affect treatment outcomes. It was also impossible to determine whether or not the women used what was prescribed or something else. Additionally, the baseline fertility rates of the selected facilities could not be obtained, although it could provide a good picture of what is happening on the grounds. However, according to the Ghana Health Services report, the fertility rate within the metropolis was 2.2, and the general fertility rate of 59.2 births per 1000 women aged between 15 and 49 years.[30,31] Also, although a sufficiently big sample size was used in this study, it is not large enough to conclude for all persons in diverse geographical locations. Therefore, to generalize the findings of this study, it is recommended that larger sample sizes in randomized control trials may be needed. The study provides novel findings concerning the pharmacotherapy of infertility in a resource-limited setting. Finally, the findings provide a new perspective to drive research in this field while informing policies and practices in the research area.

Conclusions

Monotherapy with nutritional supplements was the most prescribed fertility treatment regimen, although it was the least associated with improving the conception rate. However, combination therapy was strongly associated with conception rate compared with monotherapy. Therefore, conventional and herbal combination therapies should be given preeminence in fertility treatment with or without nutritional supplements. However, due to the small sample size and the fact that the study design was observational, a multicenter randomized controlled trial with a larger sample size is recommended to confirm the observation in the current study.

Declaration of Competing Interest

The authors have indicated that there is no conflict of interest regarding the content of this article.

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