

Micropolycystic Ovary Syndrome: Phenotypes, Clinical and Ultrasound Profile of Infertile Patients in Butembo/Eastern DRC

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Abstract

Introduction: Micropolycystic ovary syndrome (MPCOS) is one of the most common endocrine disorders in women. The aim of the study was to determine the phenotypes and the clinical and ultrasound profile of MPCOS in infertile patients in Butembo. **Methods:** The study was a multicentre, cross-sectional, analytical study conducted in the city of Butembo. It included 89 married infertile patients with MPCOS, aged 20 to 45 years, without hyperprolactinaemia, selected according to the Rotterdam criteria of 2003; 89 infertile patients without MPCOS were matched. Data analysis was performed using R software version 4.4.1. **Results:** Phenotype A was the most common with 34.8% of patients, followed by phenotype C with 28.1%. Nulliparity (48.3%), oligomenorrhoea (42.7%), hirsutism (86.5%) and acne (61.8%) were significantly associated with MPCOS ($p < 0.001$). In multivariate logistic regression analysis of gynaecological characteristics, nulliparity (OR = 6.75 [95% CI = 2.24 - 22.5], $p < 0.001$) and oligomenorrhoea (OR = 189 [95% CI = 29.2 - 3984.0]) were significantly associated with MPCOS. Endovaginal ultrasound revealed microcysts distributed around the periphery, with a mean of 14.0 ± 5.4 for the right ovary and 13.8 ± 4.2 for the left ovary in all patients with MPCOS. The volumes of the ovaries of patients with MPCOS were greater than those of patients without MPCOS in 78.7% of cases for the left ovary and

in 76.4% of cases for the right ovary ($p < 0.001$). **Conclusion:** Phenotype A is the most common among infertile patients in the town of Butembo, followed by phenotype C, phenotype B and phenotype D. The clinical profile is dominated by oligomenorrhoea, hirsutism, acne and nulliparity. The ultrasound profile of patients with MPCOS is characterised by increased ovarian volume.

Keywords

Phenotypes, Clinic, Ultrasound, Profile, MPCOS, Infertility, Butembo

1. Introduction

Micropolycystic ovary syndrome (MPCOS) is the most common endocrinopathy in women of childbearing age [1].

Depending on the diagnostic criteria used, current estimates suggest that MPCOS affects 5 to 18% of women [2].

Its aetiopathogenesis is complex, multifactorial and heterogeneous, involving genetic, epigenetic and environmental factors, underlining the crucial importance of accurate diagnosis and treatment [3].

MPCOS encompasses gynaecological symptoms such as oligomenorrhoea, amenorrhoea and infertility; dermatological symptoms such as hirsutism, acne and alopecia; and metabolic complications such as type 2 diabetes [4].

Diagnosis is based on clinical and/or biochemical assessments of hyperandrogenism combined with ultrasound evaluation of polycystic ovaries and/or oligomenorrhoea as described by the Rotterdam criteria [5].

Based on the Rotterdam criteria, there are four main phenotypes: phenotype A (hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology); B (hyperandrogenism and ovulatory dysfunction); C (hyperandrogenism and polycystic ovarian morphology); D (ovulatory dysfunction and polycystic ovarian morphology) [6].

Despite significant progress in understanding the pathophysiology and diagnosis of the disease over the last twenty years, the disease remains under-diagnosed (70%) and poorly understood by many practitioners [7], requiring ongoing research.

Although several international studies have been carried out phenotypes, clinical and ultrasound characteristics, data on the subject are still scarce in the Democratic Republic of Congo and particularly in the town of Butembo.

The city of Butembo is an area with limited resources, characterised by a high number of patients who consult several health facilities for maternity. Diagnostic investigations are expensive compared with the general socio-economic level of the population; hence the determination of the most frequent phenotypes of MPCOS and knowledge of the clinical and ultrasound characteristics of this pathology would be very useful to clinicians in the management of female infertility in our area

The aim of this study is therefore to determine the phenotypes and the clinical

and ultrasound profile of MPCOS in infertile patients in Butembo.

2. Materials and Methods

2.1. Type and Scope of Study

This was a multicentre, cross-sectional, analytical study conducted over a 12-month period from 10/07/2023 to 10/07/2024 in the town of Butembo, in the province of North Kivu, in the Democratic Republic of Congo.

Six health facilities were used as research sites, including the Cliniques Universitaires du Graben, Matanda Hospital, Katwa General Referral Hospital, and the FEPSI, Mutiri and Wanamahika hospitals.

In fact, these health facilities are characterised by high attendance by infertile couples, the presence of at least one gynaecologist on the medical staff and a technical platform adapted to the exploration of infertility in the context of countries with limited resources.

2.2. Ethical Issues

The study was authorised by the North Kivu ethics committee (reference 07/TEN/CENK/2023), by the North Kivu provincial health division and by the heads of six facilities. In accordance with the HELSINKI Declaration of the World Medical Association, the patients who took part in the study gave and signed informed consent. Participation in the study was voluntary and anonymous. The refusal of to participate in this study had no impact on infertility patients' access to appropriate care.

2.2.1. Population Size and Sampling

The study population consisted of infertile patients who had consulted the six selected health facilities in the city of Butembo for an infertility problem during the study period. This population consisted of 518 infertile patients.

The sample size was calculated using Epi Info CDC 7.2.4.0 software in its STAT-CALC function adapted for minimum sample calculations in cross-sectional studies. Considering the MPCOS prevalence of 23.6%; the unexposed/exposed ratio of 0.38 as found by the Mbuyamba study conducted in Mbuji-Mayi, DRC in 2014 [8], at the power of 97%, we have a minimum sample size of 123 cases according to Fleiss. Thus, we increased this sample size to 178 cases including 89 patients with MPCOS and 89 patients without MPCOS.

2.2.2. Inclusion Criteria

All infertile, married patients aged between 20 and 45 who agreed to take part in the study, meeting at least two of the three Rotterdam criteria [9]: anovulation and/or hyper androgenism with polycystic ovaries were recruited for the study.

The group of patients without MPCOS was recruited sequentially at a ratio of one infertile patient without MPCOS for every case of MPCOS. Each MPCOS case was matched with a MPCOS-free patient, the first patient meeting the criteria de-

fined: infertile patient, aged between 20 and 45, in the same age group as the matched case, with normal ovaries on ultrasound and who agreed to take part in the study by signing an informed consent form.

Pregnant or breast-feeding women and patients with hyperprolactinaemia were excluded.

2.3. Data Collection

Data was collected progressively over the study period. It was based on interviews and documentary analysis. The data collection team consisted of 10 people: 6 obstetrician-gynaecologists (one per site), 2 medical biologists, a radio-imager and a supervisor who was the principal investigator. The entire team was trained for the study.

The data was collected using the data collection form prepared in advance.

Those who met the selection criteria were approached to take part in the study. After obtaining their agreement, they signed the informed consent form.

2.4. Study Variables

The following variables were sought in the history: age, parity, duration of infertility, length of menstrual cycle, patient's occupation, physical activity, alcohol consumption, use of cosmetics, consumption of imported food. The socio-economic level was assessed using the household economic well-being index as constructed by the second DRC demographic health survey conducted in 2014 (EDS-RDC II 2013-2014) [10]. This index takes into account households' possession of certain durable goods and certain housing characteristics.

The physical examination looked for oligomenorrhoea and acne (presence/absence); hirsutism was assessed according to the modified Ferriman and Gallwey score (taking as normal values those above 8) [11], and the body mass index (BMI) was calculated using the formula of weight divided by height squared.

In formula, $IMC = \frac{P}{T^2}$ in Kg/m².

Transvaginal ultrasound was performed using a SONOSCAPE model E1 2020 ultrasound scanner and a 7.5 MHz vaginal transducer.

This ultrasound examination was carried out by the gynaecologist between the 3rd and 5th day of the menstrual cycle (for women with regular periods) or at random (for women with oligomenorrhoea or amenorrhoea). This was used to calculate the volume of the ovaries, count the number of antral follicles and locate them. The results were validated by a radio-imager.

The laboratory samples for this study were taken and analysed by two medical biologists at the Centre Universitaire de Diagnostic du Graben (CUDG), a biomedical analysis laboratory at the Université Catholique du Graben in Butembo.

A total of 5 ml of blood was taken from each respondent to test for luteinising hormone (LH), total testosterone (TT), antimüllerian hormone (AMH) and pro-

lactin using an automated ELISA laboratory analyser: the Finecare IA Meter Plus (FS-113) immunochromatographic analyser according to the manufacturer's instructions.

Biochemical measurement of glycated haemoglobin (HbA1c) was carried out using a spectrophotometer based on the turbidimetric method.

Laboratory results are subject to quality control.

2.5. Statistical Analysis

The data collected using the collection sheets were entered and encoded on the Excel spreadsheet program (Microsoft, CDC, 2010). They were then exported for analysis using R software version 4.4.1.

The following analyses were carried out:

- Description of the sample: frequencies and proportions, averages and their standard deviations.
- Comparison of proportions between the two groups: we calculated Pearson's chi-square test, or Fisher's Exact test when the conditions for applying the chi-square test were not met. Student's t-test was applied to compare the means
- To measure the strength of association between two qualitative variables, we calculated the Odds ratio and its 95% confidence interval. To exclude confounding factors, factors associated with MPCOS were defined using multivariate logistic regression with determination of adjusted Odds ratios [12].
- The significance level was 5% (p -value < 0.05).

3. Results

3.1. MPCOS and Socio-Demographic Characteristics

Analysis of **Table 1** shows that the mean age of patients with MPCOS was 30.6 ± 5.7 years; secondary education was the most common level of education, with 57.3% of patients with MPCOS, and business occupation represented 37.1% of patients with MPCOS. Socioeconomic level was significantly associated with MPCOS, with wealthy patients accounting for 42.7%, including 56.2% of patients with MPCOS, compared with 29.2% of patients without MPCOS (p -value = 0.001) (**Table 1**).

3.2. MPCOS and Infertility-Related Characteristics and Phenotypes

Analysis of **Table 2** shows that 60.7% of patients with MPCOS had secondary infertility and 76.4% of them had infertility lasting less than 5 years.

In terms of phenotype type, phenotype A was the most common with 34.8% of patients, followed by phenotype C with 28.1% (**Table 2**).

3.3. MPCOS and Gynaecological Characteristics

Analysis of **Table 3** shows that nulliparity (48.3%), oligomenorrhoea (42.7%), hirsutism (86.5%) and acne (61.8%) were significantly associated with MPCOS ($p < 0.001$) (**Table 3**).

Table 1. Distribution of cases by socio-demographic characteristics.

Variables	Patients with MPCOS N = 89 ¹	Patients without MPCOS N = 89 ¹	Total N = 178 ¹	p-value
Age (years)				
Average	30.6 (5.7)	31.0 (6.0)	30.8 (5.8)	0.7
Age groups				>0.9
20 - 25	14 (15.7%)	14 (15.7%)	28 (15.7%)	
26 - 30	29 (32.6%)	26 (29.2%)	55 (30.9%)	
31 - 35	20 (22.5%)	23 (25.8%)	43 (24.2%)	
36 - 40	20 (22.5%)	18 (20.2%)	38 (21.3%)	
41 - 45	6 (6.7%)	8 (9.0%)	14 (7.9%)	
Level of education				0.3
Illiterate	2 (2.2%)	1 (1.1%)	3 (1.7%)	
Primary	3 (3.4%)	7 (7.9%)	10 (5.6%)	
Secondary	51 (57.3%)	57 (64.0%)	108 (60.7%)	
Superior	33 (37.1%)	24 (27.0%)	57 (32.0%)	
Profession				0.7
Retailer	33 (37.1%)	34 (38.2%)	67 (37.6%)	
Housekeeper	23 (25.8%)	17 (19.1%)	40 (22.5%)	
State agent	19 (21.3%)	19 (21.3%)	38 (21.3%)	
Grower	6 (6.7%)	11 (12.4%)	17 (9.6%)	
Liberal	8 (9.0%)	8 (9.0%)	16 (9.0%)	
Socio-economic level				0.001
Poor	21 (23.6%)	31 (34.8%)	52 (29.2%)	
Medium	18 (20.2%)	32 (36.0%)	50 (28.1%)	
Rich	50 (56.2%)	26 (29.2%)	76 (42.7%)	

¹n(%); ²Student's t test; chi-square test of independence; Fisher's exact test.

Table 2. Distribution of cases according to infertility-related characteristics and phenotypes.

Variables	N	N = 89 ¹
Infertility type	89	
Primary		35 (39.3%)
Secondary		54 (60.7%)
Duration of infertility (years)	89	
≤ 5		68 (76.4%)
> 5		21 (23.6%)
Type of phenotypes	89	
A		31 (34.8%)
B		21 (23.6%)
C		25 (28.1%)
D		12 (13.5%)

¹n(%).

Table 3. Distribution of cases by gynaecological characteristics.

Variables	Patients with MPCOS	Patients without MPCOS	Total	<i>p</i> -value
	N = 89 ¹	N = 89 ¹	N = 178 ¹	
Parity				<0.001
nulliparous	43 (48.3%)	7 (7.9%)	50 (28.1%)	
Paucipare	34 (38.2%)	44 (49.4%)	78 (43.8%)	
Multipare	12 (13.5%)	38 (42.7%)	50 (28.1%)	
Cycle time				<0.001
Amenorrhoea	14 (15.7%)	7 (7.9%)	21 (11.8%)	
Oligomenorrhoea	38 (42.7%)	1 (1.1%)	39 (21.9%)	
Short cycle	12 (13.5%)	2 (2.2%)	14 (7.9%)	
Normal cycle	25 (28.1%)	79 (88.8%)	104 (58.4%)	
Hirsutism				<0.001
Yes	77 (86.5%)	3 (3.4%)	80 (44.9%)	
No	12 (13.5%)	86 (96.6%)	98 (55.1%)	
Acne				<0.001
Yes	55 (61.8%)	16 (18.0%)	71 (39.9%)	
No	34 (38.2%)	73 (82.0%)	107 (60.1%)	

¹n(%); ²chi-square test of independence; Fisher's exact test.

3.4. Logistic Regression Analysis of Gynaecological Characteristics

Table 4 shows that in multivariate logistic regression analysis of gynaecological characteristics, nulliparity (OR = 6.75 [95% CI = 2.24 - 22.5], $p < 0.001$) and oligomenorrhoea (OR = 189 [95% CI = 29.2 - 3984.0] were significantly associated with MPCOS (**Table 4**).

Table 4. Multivariate analysis of gynaecological characteristics.

Variables	Univariate logistic regression			Multivariate logistic regression		
	OR ²	95% IC ²	<i>p</i>	OR ²	95% IC ²	<i>p</i>
Parity						
Paucipare	-	-		-	-	
nulliparous	7.95	3.34 - 21.3	<0.001	6.75	2.24 - 22.5	0.001
Multipare	0.41	0.18 - 0.88	0.026	0.14	0.03 - 0.47	0.003
Cycle time						
Normal cycle	-	-		-	-	
Short cycle	19.0	4.77 - 127	<0.001	45.9	7.72 - 449	<0.001
Oligomenorrhoea	120	24.1 - 2 186	<0.001	189	29.2 - 3 984	<0.001
Amenorrhoea	6.32	2.36 - 18.4	<0.001	10.0	3.11 - 37.4	<0.001

¹n(n/N); ²OR = odds ratio, CI = confidence interval.

3.5. MPCOS and Ultrasound Characteristics of the Ovaries

Analysis of **Table 5** shows that in all patients with MPCOS, endovaginal ultrasound revealed the existence of microcysts distributed around the periphery, with an average of 14.0 ± 5.4 for the right ovary and 13.8 ± 4.2 for the left ovary.

The ovarian volumes of patients with MPCOS were greater than those of patients without MPCOS in 78.7% of cases for the left ovary and in 76.4% of cases for the right ovary ($p < 0.001$) (**Table 5**).

Table 5. Distribution of cases according to ultrasound characteristics of the ovaries.

Variables	Patients with MPCOS N = 89 ¹	Patients without MPCOS N = 89 ¹	Total N = 178 ¹	p-value
Left ovary				
Volume (mm³)				
Average	13.9 (5.0)	5.5 (1.6)	9.7 (5.6)	<0.001
Measure				<0.001
Augmented	70 (78.7%)	0 (0.0%)	70 (39.3%)	
Normal	19 (21.3%)	89 (100.0%)	108 (60.7%)	
Follicles				
Average	13.8 (4.2)	3.8 (1.7)	8.8 (6.0)	<0.001
Number				<0.001
≤ 12	27 (30.3%)	89 (100.0%)	116 (65.2%)	
> 12	62 (69.7%)	0 (0.0%)	62 (34.8%)	
Location				
Central	0 (0.0%)	43 (48.3%)	43 (24.2%)	<0.001
Peripheral	89 (100.0%)	46 (51.7%)	135 (75.8%)	
Right ovary				
Volume (mm³)				
Average	14.0 (5.4)	5.9 (1.4)	9.9 (5.7)	<0.001
Measure				<0.001
Augmented	68 (76.4%)	0 (0.0%)	68 (38.2%)	
Normal	21 (23.6%)	89 (100.0%)	110 (61.8%)	
Follicles				
Average	14.8 (4.7)	4.2 (1.6)	9.5 (6.3)	<0.001
Number				<0.001
≤ 12	23 (25.8%)	89 (100.0%)	112 (62.9%)	
> 12	66 (74.2%)	0 (0.0%)	66 (37.1%)	
Location				
Central	0 (0.0%)	42 (47.2%)	42 (23.6%)	<0.001
Peripheral	89 (100.0%)	47 (52.8%)	136 (76.4%)	

¹Mean(SD); n (%); ²Student's t test; chi-square test of independence.

4. Discussion

The aim of this study was therefore to determine the phenotypes and the clinical and ultrasound profile of MPCOS in infertile patients in Butembo.

4.1. Phenotypes

Thus, phenotype A was the most common among infertile Congolese patients in Butembo, followed by phenotype C, phenotype B and phenotype D (**Table 2**).

With regard to MPCOS phenotypes, the results of our series converge with those found by Sachdeva *et al.* [13] who observed that phenotype A was the most frequent with 67.7%, followed by phenotype C with 17.7%, phenotype B with 11% and phenotype D with 3.6%.

The same was true for Espinosa *et al.* [14] in Ecuador where 61% of patients were phenotype A; 13% of patients phenotype B; 14% of patients phenotype C; and 12% of patients phenotype D. Tanuja *et al.* [15] in India found that largest phenotype group was phenotype A (41.17%), followed by B (26.47%), C (20.58%) and D (11.76%). In a study conducted in Iran by Leili *et al.* [16], 51.9% of the 160 women studied had phenotype A according to the Rotterdam criteria.

Vaggopoulos studied the phenotypes of 266 women in Greece and found that the prevalence of phenotype A was higher than that of the other phenotypes [6].

However, the results of our series differ from those of the series by Mohd *et al.* [17] in India where the MPCOS C phenotype was the most common (40.8%), followed by phenotypes D (24.6%), A (20.2%) and B (14.3%). Alawia *et al.* [18], in their study conducted in Sudan, found that phenotype D was the most common among Sudanese infertile women (51.6%), followed by phenotype B (22.6%), phenotype C (18.2%) and phenotype A (7.6%).

The differences observed in these results compared with the results of our study can be attributed to genetic factors, lifestyles, dietary habits, differences in the size of the sample of participants and the model of ultrasound scanner used.

Knowledge of the most frequent phenotypes in our environment is very useful to clinicians in diagnosing the most likely causes of female infertility

4.2. Clinical Profile

With regard to the clinical profile, the results of the bivariate analysis showed that nulliparity (48.3%), oligomenorrhoea (42.7%), hirsutism (86.5%) and acne (61.8%) were significantly associated with MPCOS ($p < 0.001$). (**Table 3** and **Table 4**). In multivariate analysis, nulliparity increased the risk of having MPCOS 6.75 times [95% C.I. = 2.24 - 22.5], and oligomenorrhoea increased this risk 189 times [95% C.I. = 29.2 - 3984.0] (**Table 4**).

The results of our series differ from those of Jacob *et al.* [19] in Washington, USA, who showed that nulliparous women accounted for 70.9% of MPCOS cases compared with cases without MPCOS.

In our country, a previous study by Mbuyamba *et al.* [8] showed that the risk of developing MPCOS was 1.61 times higher when the patient was nulliparous (RR

= 1.61; 95% CI: 1.39 - 1.88).

These differences can be linked to ethnic and geographical factors, as well as eating habits.

With regard to oligomenorrhoea, the results of our series converge with those of Ligia *et al.* [20] in Brazil, where 54.7% of MPCOS cases had oligomenorrhoea.

As for clinical hyperandrogenism, mainly hirsutism and acne, the results of our series converge with those of other researchers. The prevalence of hirsutism in MPCOS varies from 70% to 80%, compared with 4% to 11% in women in the general population [21].

Sanad, in Egypt, found a prevalence of hirsutism of 60.4% in infertile women with MPCOS [22]. Ligia *et al.* [20] in their study conducted in Brazil found that 59.7% of patients with MPCOS had hirsutism.

Alawia *et al.* [18] in their study carried out in Sudan found that 46.5% of women with MPCOS had acne.

Finally, the expression of hirsutism varies according to geographical region, ethnic origin and genetics.

4.3. Ultrasound Profile

Pelvic ultrasound revealed that in all patients with MPCOS, the microcysts were distributed around the periphery with an average size of 14.0 ± 5.4 for the right ovary and 13.8 ± 4.2 for the left ovary. The volumes of the ovaries of patients with MPCOS were greater than those of patients without MPCOS in 78.7% of cases for the left ovary and in 76.4% of cases for the right ovary (p -value < 0.001). Around three quarters of the women in this study had ultrasound diagnostic features of micropolycystic ovaries. (Table 5).

It has been documented that micropolycystic ovary on ultrasound is the most common feature of MPCOS [23].

The results of our series converge with those of Zhang *et al.* [24] who found that 94.2% of MPCOS cases had micropolycystic ovaries on ultrasound in their study carried out in China.

However, these results differ from those of Lauritsen *et al.* [25] in Denmark where 53.5% met the criteria for micropolycystic ovaries.

5. Conclusion

Phenotype A is most common in infertile patients in the town of Butembo, followed by phenotype C, phenotype B and phenotype D. The clinical profile is dominated by oligomenorrhoea, hirsutism, acne and nulliparity. The ultrasound profile of patients with MPCOS is characterised by increased ovarian volume.

6. Limits of Work

Given that this study was carried out in an urban population, the results cannot be generalised to the entire population of the DRC. In addition, not all cases of infertility were seen, as some people do not consult a doctor for lack of funds or

lack of information

Other relevant hormonal parameters such as FSH, SHBG, free androgen index or insulin resistance were not investigated due to the rarity of these markers in our environment.

Conflict of Interest

The authors declare that they have no direct or indirect interest in the subject matter.

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