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Predictive Value of Antimüllerian Hormone (AMH) and Other Predictors in the Diagnosis of Micropolycystic Ovary Syndrome in Infertile Patients from Butembo in the Democratic Republic of Congo

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Abstract

Introduction: Micropolycystic ovary syndrome (MPCOS) is one of the main causes of female infertility worldwide. The aim of the study is to determine the predictive value of AMH and other predictors in the diagnosis of MPCOS in the city of Butembo. **Material and methods:** This was a cross-sectional, analytical, multi-site study conducted in the town of Butembo on 89 infertile patients with MPCOS, married, aged 20 to 45, 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:** The area under the ROC curve was 0.845 with a sensitivity of 79.8%, a specificity of 76.4% and the best cut-off value for AMH to predict the diagnosis of MPCOS was 5.8 ng/l. In multivariate analysis, AMH (ORa = 1.30 [95% CI = 1.20 - 1.42], $p < 0.001$) was significantly associated with MPCOS. Other predictors of MPCOS detection were BMI in kg/m^2 (ORa = 1.17 [95% confidence interval = 1.06 - 1.30], $p = 0.002$) and testosterone in ng/l (OR = 2.02 [95% confidence interval = 1.25 - 4.00], $p = 0.012$). **Conclusion:** AMH proved to be a good predictor of MPCOS in our context, with satisfactory sensitivity, specificity, PPV and NPV. The best threshold value for AMH to

predict the diagnosis of MPCOS is 5.8 ng/l.

Keywords

Predictive Value, AMH, Other Predictors, MPCOS, Infertility, Butembo

1. Introduction

Micropolycystic ovary syndrome (MPCOS) affects between 5% and 15% of women of childbearing age worldwide [1]. This complex endocrine disorder is characterised by an excess of androgens, dysovulation and multifollicular ovaries visible on ultrasound.

There is now significant evidence of a correlation between AMH, oligoanovulation and hyperandrogenism [2].

In women, AMH (anti-mullerian hormone) inhibits the recruitment of primordial follicles from the pool of resting oocytes and can suppress the action of follicle-stimulating hormone (FSH), contributing to ovulation disorders [3] [4].

Several studies have shown that women with MPCOS have significantly higher AMH levels, suggesting a positive correlation between AMH elevation and the severity of the syndrome. However, despite its potential, its use as the sole diagnostic criterion remains controversial due to the absence of a universally validated threshold [5].

The latest published international guideline on MPCOS recommends including AMH in the assessment of anovulation and in the diagnostic criteria for MPCOS. However, no clear cut-off value for AMH has been established due to the lack of data on AMH values in people with MPCOS, as well as variations between tests and with age [6].

In Africa, the diagnosis of MPCOS is mainly based on the Rotterdam criteria (2003), but AMH is gradually being recognised as a complementary tool [7]. A study conducted in sub-Saharan Africa showed that African women with MPCOS had a mean AMH level of 6.3 ng/ml ± 3.2, which is significantly higher than in women without MPCOS [7].

Other studies in West and East Africa have shown that AMH is a reliable biomarker for MPCOS [8]. Furthermore, the correlation between AMH and female fertility is particularly important in African contexts where marriage and motherhood are major social issues.

In the Democratic Republic of Congo, studies on AMH and MPCOS are still limited, although some research is beginning to emerge.

A recent study in Kinshasa showed that 38% of infertile patients had confirmed MPCOS and that AMH was significantly higher in these patients [7]. The value of 5.8 ng/ml has been proposed as the reference value for the diagnosis of MPCOS in the DRC, although this threshold may vary according to the populations studied.

The local context of our environment (city of Butembo) is characterized by a

high number of patients who consult for maternity. As this is an area with limited resources, MPCOS diagnostic investigations are expensive compared to the average income of the population. Limited access to specialist hormone tests, the high cost of AMH assays and the lack of reproductive biology equipment remain major challenges. Consequently, the development of diagnostic protocols adapted to the Congolese context remains a priority for improving the management of infertile women with MPCOS.

The aim of this study is to determine the predictive value of antimüllerian hormone (AMH) and other predictors in the diagnosis of micropolycystic ovary syndrome in infertile patients in Butembo, in the east of the DRC.

2. Materials and Methods

2.1. Type and Scope of Study

This is 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 Cliniques Universitaires du Graben, Matanda Hospital, Katwa General Referral Hospital and FEPSI, Mutiri and Wanamahika Hospitals.

These health facilities are characterised by a high number of 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

We obtained authorisation from the North Kivu ethics committee, as well as from the North Kivu provincial health division and the heads of six facilities. In accordance with the World Medical Association's Declaration of HELSINKI, patients who participated in the study gave and signed informed consent. Participation in the study was voluntary and anonymous. Refusal to participate in the study had no impact on infertility patients' access to appropriate care.

2.3 Population Size and Sampling

The study population consisted of infertile patients who 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 the Epi Info CDC 7.2.4.0 software in its STATCALC function adapted to the calculation of the minimum sample in cross-sectional studies. Given 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 [9], at the power of 97%, we have a minimum sample size of 123 cases according to Fleiss. Therefore, we increased this sample size to 178 cases, including 89 patients with MPCOS and 89 patients without MPCOS.

2.4 Selection Criteria

2.4.1. Inclusion Criteria

Any infertile, married patient aged between 20 and 45 who agreed to take part in the study and met at least two of the three Rotterdam criteria [10]: anovulation and/or hyper androgenism with polycystic ovaries, was recruited for the study.

The group of patients without MPCOS was recruited sequentially at a ratio of one infertile patient without MPCOS to one with MPCOS. Each MPCOS case was matched with a MPCOS-free patient, the first patient meeting the criteria defined: an infertile patient aged between 20 and 45 years, in the same age range as the case, *i.e.* ± 5 years, with normal ovaries on ultrasound and who agreed to take part in the study by signing an informed consent form.

2.4.2. Exclusion Criteria

All pregnant or breastfeeding women and patients with hyperprolactinaemia were excluded.

2.5. Data Collection Procedure

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 whole team was trained for this study.

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

2.6. 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) [11]. 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 using the modified Ferriman and Gallwey score (taking as normal values those above 8) [12], 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/m^2.

Transvaginal ultrasound was performed using a SONOSCAPE model E1 2020 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 prolactin using an automated ELISA laboratory analyser: the Finecare IA Meter Plus immunochromatographic analyser (FS-113) 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.

2.7. Statistical Analysis

The data collected using the data collection forms were entered and encoded in an Excel spreadsheet (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 standard deviations.
- Comparison of proportions between the two groups: we calculated the Pearson chi-squared test, or the Fisher exact test when the conditions for applying the chi-squared test were not met. Student's t-test was used to compare means.
- To measure the strength of the association between two categorical variables, we calculated the odds ratio and its 95% confidence interval. To exclude confounders, factors associated with MPCOS were defined using multivariate logistic regression with adjusted odds ratios [13].
- The significance level was 5% (p-value < 0.05).

3. Results

3.1. Age and MPCOS

An analysis of Table 1 shows that the average age of MPCOS patients was 30.6 ± 5.7 years; secondary education was the most common, accounting for 57.3% of MPCOS patients, and business occupation accounted for 37.1% of MPCOS patients.

Socioeconomic status 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).

3.2 Comparison of Hormone Results

Analysing Table 2 of the hormonal and biochemical results of patients with MPCOS, we noted that only LH ($p < 0.001$) and AMH ($p < 0.001$) levels had a statistically significant difference.

Table 1. Breakdown of cases by socio-demographic factors.

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%)	

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

Table 2. Breakdown of patients according to hormonal and biochemical results.

Variables	Patients with MPCOS N = 89[1]	Patients without MPCOS N = 89[1]	Total N = 178[1]	*p*-value
Total testosterone				
Average	0.5 (0.9)	0.3 (0.6)	0.4 (0.8)	0.091
Rates				0.2
Top	15 (16.9%)	9 (10.1%)	24 (13.5%)	
Normal	74 (83.1%)	80 (89.9%)	154 (86.5%)	
LH				
Average	25.6 (25.4)	25.1 (41.2)	25.3 (34.1)	>0.9
Rates				**<0.001**
Top	67 (75.3%)	38 (42.7%)	105 (59.0%)	
Normal	22 (24.7%)	51 (57.3%)	73 (41.0%)	
AMH (ng/ml)				
Average	12.0 (8.1)	4.1 (4.6)	8.1 (7.6)	**<0.001**
Rates				**<0.001**
Top	58 (65.2%)	12 (13.5%)	70 (39.3%)	
Normal	31 (34.8%)	77 (86.5%)	108 (60.7%)	
Prolactin				
Average	21.0 (12.4)	25.1 (16.6)	23.1 (14.7)	0.063
Rates				0.059
Top	0 (0.0%)	5 (5.6%)	5 (2.8%)	
Normal	89 (100.0%)	84 (94.4%)	173 (97.2%)	

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

3.3. Diagnostic Value of AMH in the Detection of MPCOS

To assess the predictive value of antimüllerian hormone (AMH) as a biomarker of micropolycystic ovary syndrome (MPCOS) and to determine the optimal diag-

nostic threshold for AMH in our setting, we used the ROC curve. The area under the ROC curve was 0.845 with a sensitivity of 79.8%, a specificity of 76.4% and the best threshold value for AMH to predict the diagnosis of MPCOS was 5.8 ng/l (Figure 1 and Table 3).

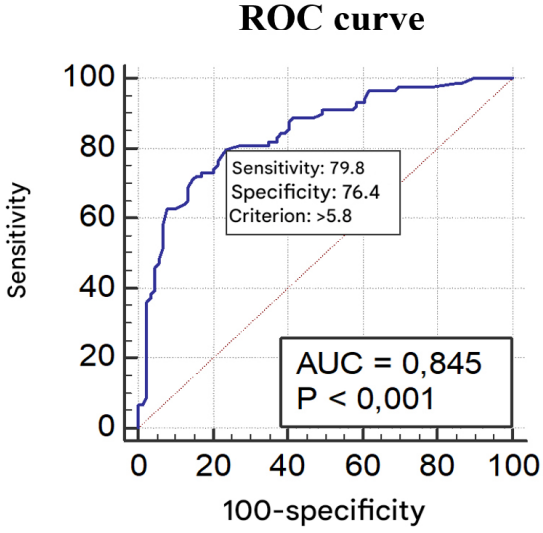

Figure 1. ROC curve (Receiver operating characteristic).

Table 3. Specificity and sensitivity of AMH.

Variables	Sensitivity (IC)	Specificity (IC)	PPV (CI)	VPN (IC)
AMH (5.8 ng/ml)	79.78 (69.9 - 87.6)	76.4 (66.2 - 84.8)	77.2 (69.6 - 83.3)	79.1 (71.1 - 85.3)

AMH = Antimüllérien Hormone;
CI = 95% confidence interval;
PPV = Positive predictive value (%);
NPV = Negative predictive value (%).

3.4. Other Factors Predictive of MPCOS Detection

Table 4 shows the distribution of patients with MPCOS according to the results of other predictive factors in the detection of MPCOS.

In multivariate analysis, BMI in kg/m² (ORa = 1.17 [95% C.I. = 1.06 - 1.30], p = 0.002), AMH in ng/l (OR = 1.30 [95% C.C at 95% = 1.20 - 1.42], $p < 0.001$) and testosterone in ng/l (OR = 2.02 [I.C at 95% = 1.25 - 4.00], $p = 0.012$) were significantly associated with MPCOS.

Table 4. Distribution of cases according to other predictive factors in the detection of MPCOS.

Variables	Univariate logistic regression			Multivariate logistic regression		
	OR[2]	95% IC[2]	p	OR[2]	95% IC[2]	p
Age	0.99	0.94 - 1.04	0.7	1.00	0.93 - 1.08	>0.9
BMI	1.16	1.08 - 1.26	**<0.001**	1.17	1.06 - 1.30	**0.002**
AMH	1.28	1.19 - 1.40	**<0.001**	1.30	1.20 - 1.42	**<0.001**

Continued

LH	1.00	0.99 - 1.01	>0.9	1.00	0.99 - 1.02	0.4
Testosterone	1.50	0.96 - 2.74	0.12	2.02	1.25 - 4.00	**0.012**
Prolactin	0.98	0.96 - 1.00	0.066	0.97	0.94 - 1.00	0.065

[1]Average (TE);
[2]OR = odds ratio, CI = confidence interval.

4. Discussion

MPCOS and Socio-Demographic Factors

The results of our study show that the average age of patients with MPCOS was 30.6 ± 5.7 years; secondary education was the most common 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).

Our results are comparable to those reported in other studies in Africa and other developing countries.

In our country, the Democratic Republic of Congo, Kabengele *et al.* (2024) reported a similar mean age of 31.2 years for patients with MPCOS, with a higher prevalence among women of intermediate to high socio-economic status [7].

In other Third World countries, trends vary slightly.

In India, Génard *et al.* (2023) observed a lower mean age (28.7 years) in patients with MPCOS, but a similar correlation with high socio-economic status, indicating that better-off women consulted more frequently for infertility and were diagnosed more often [14].

In Indonesia, Kicińska *et al.* (2023) had reported that patients with MPCOS had a higher income level, which could be linked to a diet richer in carbohydrates and fats, factors often incriminated in the development of the syndrome [15].

These results suggest that MPCOS may be influenced by socio-economic factors, due to increased access to medical care and a more sedentary lifestyle in patients from more affluent backgrounds. However, further studies are needed to better understand these associations and establish management strategies tailored to each context.

4.1. Comparison of Hormonal Results

The hormonal results for patients with MPCOS showed that only LH ($p < 0.001$) and AMH ($p < 0.001$) levels were statistically significantly different.

The area under the ROC curve for AMH was 0.845, with a sensitivity of 79.8% and a specificity of 76.4%. The best cut-off value for AMH to predict the diagnosis of MPCOS was 5.8 ng/l.

The results of our series are consistent with several previous studies.

Kabengele *et al.* (2024) reported that AMH was a good predictor of MPCOS [7].

Similar trends have been observed in other Third World countries.

In India, Le *et al.* (2021) found an area under the ROC curve of 0.787; with a sensitivity of 61% and an optimal threshold of 5.2 ng/ml, indicating that AMH can be a complementary criterion to clinical and ultrasound diagnosis [16].

In the Philippines, Yu *et al.* (2024) determined that AMH had an excellent diagnostic performance with an optimal threshold of 3.86 ng/ml, a sensitivity of 72% and a specificity of 78%, which is slightly lower than our results [17].

These results confirm that AMH can be an effective diagnostic tool for MPCOS, although the optimal threshold varies slightly depending on the populations studied. The combined use of AMH with other diagnostic criteria (ovarian ultrasound, hyperandrogenism) could improve the accuracy and universality of diagnosis in developing countries.

4.2. Other Factors Predictive of MPCOS Detection

In multivariate analysis, BMI in kg/m^2 (ORa = 1.17 [95% C.I. = 1.06 - 1.30], p = 0.002), AMH in ng/l (OR = 1.30 [95% C.C at 95% = 1.20 - 1.42], $p < 0.001$) and testosterone in ng/l (OR = 2.02 [I.C at 95% = 1.25 - 4.00], $p = 0.012$) were significantly associated with MPCOS.

In Africa, Dube *et al.* (2024) found that BMI was significantly associated with MPCOS (OR = 1.21; $p = 0.001$), with an increased risk in obese women [18].

In addition, their study confirmed that AMH was a major predictive factor (OR = 1.28; $p < 0.001$), with an optimal threshold of 6.0 ng/ml.

Another study conducted in North Africa by Sikiru *et al.* (2023) also showed an association between high testosterone levels and MPCOS (OR = 2.05; $p = 0.010$), confirming that hyperandrogenism plays a key role in the diagnosis of the syndrome [19].

In other Third World countries, the results are similar.

In India, Zad *et al.* (2024) reported a strong association between BMI and MPCOS (OR = 1.15; $p = 0.005$), with a dose-response effect: the higher the BMI, the greater the risk of MPCOS [20].

In Indonesia, Prieto-Huecas *et al.* (2023) observed that patients with MPCOS had a significant increase in AMH (OR = 1.32; $p < 0.001$) and testosterone (OR = 1.98; $p = 0.015$), results that are virtually identical to our own [21].

These results confirm that AMH, testosterone and BMI are robust predictors of MPCOS in different populations. However, AMH thresholds vary slightly from region to region, requiring studies tailored to local populations to refine diagnostic criteria and optimise the management of PCOS in developing countries.

5. Conclusion

AMH proved to be a good predictive marker of MPCOS in our context compared with the other predictors studied, with an OR greater than 1 and significant in both multivariate and univariate logistic regression. In addition, its sensitivity, specificity, PPV and NPV are all satisfactory (well above 50%). However, as the literature points out, its optimal threshold varies slightly from one region to an-

other, requiring studies tailored to local populations in order to refine diagnostic criteria and optimise the management of MPCOS in developing countries.

6. Limits of Work

As this study was carried out on an urban population, the results cannot be generalised to the entire population of the DRC.

What's more, not all cases of infertility were observed, as some people do not consult a doctor for lack of money or information.

Conflict of Interest

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

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