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ARTICLE

Serum Catalase, Ceruloplasmin, and Advanced Oxidation Protein Products in Uterine Fibroids

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ABSTRACT

Background: Uterine fibroids are the most common benign pelvic tumors in women of reproductive age. Epidemiological and experimental evidence increasingly points to oxidative stress as a contributor to their onset and progression.

Objectives: This study aimed to measure serum catalase, ceruloplasmin, and advanced oxidation protein products (AOPP) in women with uterine fibroids.

Methods: This prospective hospital-based case-control study included 88 non-pregnant women of reproductive age recruited from hospitals in Mosul between 7th Jan. and 1st Dec. 2023. Fifty women who had myomectomy or hysterectomy for uterine fibroids formed the case group. Thirty-eight apparently healthy women with no fibroids on ultrasound formed the control group. Serum catalase, ceruloplasmin, and AOPP levels were measured in both groups, and the results were compared statistically.

Results: Participants' ages ranged from 26 to 50 years. Age did not differ significantly between the two groups. Serum AOPP correlated strongly and positively with ceruloplasmin in women with fibroids ($r = 0.501$; $p < 0.001$). Maximum fibroid diameter also correlated positively with ceruloplasmin ($r = 0.665$; $p < 0.001$) and with AOPP ($r = 0.774$; $p < 0.001$). **Conclusions:** The altered oxidant and antioxidant profile seen in women with fibroids suggested that oxidative stress may contribute to fibroid pathogenesis.

Introduction

The relationship between hypoxia, weakened antioxidant defenses, and fibroid tissue indicates that oxidative stress may be associated with the development and progression of uterine fibroids [1]. Fibroids are among the most common benign tumors of the female genital tract [2]. Oxidative stress arises when the generation of reactive species exceeds the ability of antioxidant systems to eliminate them, leading to lipid and DNA damage and disturbances in normal intracellular signaling [3]. Although reactive oxygen species and free radicals are continuously produced as by-products of aerobic metabolism, cellular damage typically develops only when their production overwhelms the mechanisms responsible for their removal. Several interconnected factors contribute to the maintenance of redox homeostasis, including angiogenesis, hypoxia-related signaling, nutritional status, and environmental exposures. When this balance is disturbed, changes may occur in genomic integrity, epigenetic regulation, and tissue fibrogenesis, processes that have been implicated in carcinogenesis [4] as well as in various gynecological disorders [5].

The present study considered three biomarkers that provide information about oxidant and antioxidant status. Catalase is a key antioxidant enzyme that contributes to cellular

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protection by converting hydrogen peroxide into water and oxygen, thereby limiting its accumulation [6]. Its activity is relatively low in erythrocytes and in organs such as the pancreas and heart [7]. Altered catalase activity has been reported in several pathological conditions, with reduced levels observed in depression, metabolic syndrome, and type 1 diabetes mellitus, while increased activity has been described in some malignant conditions [8]. Ceruloplasmin has an important role in copper homeostasis and serves as the major copper-carrying protein in plasma [9]. It binds approximately 70% of circulating copper, whereas albumin accounts for nearly 15% of copper transport [10]. Through its copper-dependent enzymatic activity, ceruloplasmin is also involved in iron metabolism under normal physiological conditions. Its serum concentration can change in response to different physiological and pathological states and has been reported to increase during inflammation, neoplastic disorders, pregnancy, oral contraceptive use, and rheumatoid arthritis [11]. In some pathological settings, however, ceruloplasmin may also contribute to oxidative processes and therefore does not act exclusively as an antioxidant [12]. AOPPs provide another indicator of oxidative injury, particularly oxidative modification of proteins, and may participate in inflammatory responses when produced by activated phagocytic cells [13]. Elevated AOPP concentrations have been associated with female reproductive disorders such as polycystic ovary syndrome, leiomyoma, and endometriosis [14], and higher levels have also been associated with advancing age and increased cardiovascular risk [15]. Taken together, catalase, ceruloplasmin, and AOPPs may provide complementary information regarding alterations in oxidant and antioxidant status in women with uterine fibroids. However, evidence concerning serum concentrations of these biomarkers in Iraqi women with uterine fibroids remains limited. Accordingly, the present study aimed to assess serum catalase, ceruloplasmin, and AOPP levels in women diagnosed with uterine fibroids.

Methods

Study Design, Setting, and Data Collection Period

This prospective hospital-based case–control study included 88 women who underwent or were scheduled to undergo hysterectomy or myomectomy. Participants were recruited between 7th Jan. and 1st Dec. 2023 from Al-Khansaa Maternity and Childhood Teaching Hospital, Al-Batool Maternity Teaching Hospital, and a private hospital in Mosul, Iraq, using random sampling. The case group consisted of 50 women with symptomatic uterine fibroids or fibroids detected incidentally during infertility investigations. All 50 cases were surgical: 19 underwent myomectomy and 31 underwent hysterectomy. The control group consisted of 38 non-pregnant women of reproductive age. The controls were recruited from the outpatient gynecology clinics of the participating hospitals and from healthy volunteers, including hospital staff and relatives of patients, who attended for routine check-up. None had fibroid-related symptoms, and ultrasound confirmed a normal uterus in each. Clinical data and blood samples were collected from each participant shortly after enrollment. Venous blood was drawn from both groups to measure catalase, ceruloplasmin, and AOPP, along with routine biochemical tests. Eligible cases were women of reproductive age who were not pregnant. Each had at least one fibroid confirmed on ultrasound, either with related symptoms or detected incidentally during infertility investigations, and each underwent hysterectomy or myomectomy for fibroids.

Women were excluded if they were pregnant. Women with endometriosis, acute or chronic renal disease, or liver disease were also excluded. Further exclusion criteria included autoimmune or connective-tissue disorders such as rheumatoid arthritis, systemic lupus erythematosus, and inflammatory bowel disease. Women with chronic conditions such as diabetes, cardiovascular disease, cerebrovascular disease, or thyroid disease were excluded as well. Use of oral contraceptives, antioxidant supplements, lipid-lowering agents, or

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multivitamins was also an exclusion criterion. Smokers and alcohol users were excluded, as were women with malignancy and post-menopausal women. Finally, women with any sign of active inflammation, infection, or allergy were not included.

History and Examination

The study was approved by the Medical Research Ethics Committee, College of Medicine, University of Mosul (approval no. UOM/COM/MREC/23-24/SP8, dated 19th Sept. 2023). All participants were informed verbally and in writing about the study, and their consent was obtained before enrollment and blood sampling. Each participant was then assessed through a detailed medical history and clinical examination. The recorded demographic data included age, occupation, marital status, smoking status, and educational level. Obstetric and gynecological histories were obtained directly from the participants, while previous medical and surgical conditions were reviewed with particular attention to diabetes mellitus, hypertension, thyroid disorders, malignancy, previous surgery, and a family history of uterine fibroids. Current and previous medication use, as well as contraceptive methods, were also noted. The clinical presentation at the time of fibroid detection was documented, whether the finding was incidental or related to abnormal uterine bleeding, pelvic pain, pressure symptoms, subfertility, or other complaints. Physical assessment included measurement of vital signs and examination of the abdomen and pelvis for clinically detectable abnormalities or palpable masses. Pelvic ultrasonography was then performed to determine the presence and characteristics of uterine fibroids and to identify any associated abnormalities. For detected fibroids, anatomical location, dimensions, and echogenicity were assessed, with the latter classified as homogeneous, heterogeneous, or mixed; endometrial thickness was also measured. In women who underwent hysterectomy or myomectomy, the excised tissue was submitted for histopathological examination to confirm the diagnosis.

Biochemical Analysis of the Blood Samples

A blood sample was collected from every participant to measure catalase, ceruloplasmin, and AOPP. Venous blood was drawn at enrollment, before surgery. The skin was first cleansed with 70% alcohol. About 5 mL of blood was then withdrawn with a disposable plastic syringe into a sterile gel tube and left to clot at room temperature. The sera were separated by centrifugation for 5 minutes at 3000 rpm. They were transferred to sterile plain tubes and stored at -20 degrees Celsius. Once all samples had been collected, they were thawed to room temperature. Catalase, ceruloplasmin, and AOPP concentrations were then measured together in a single analytical run. Serum catalase, ceruloplasmin, and AOPP concentrations were quantified using commercially available ELISA kits (ELK Biotechnology), following the manufacturer's instructions. Catalase and ceruloplasmin were measured by the sandwich enzyme immunoassay, and AOPP by the competitive inhibition enzyme immunoassay. Absorbance was read at 450 nm ± 10 nm with a microplate reader, and concentrations were calculated from a standard curve.

Histopathology

Following surgical intervention, histopathological examination confirmed the diagnosis of uterine fibroid in every operated participant.

Statistical Analysis

Data were entered and tabulated in Microsoft Excel 2010. Analysis was performed using the Statistical Package for Social Sciences, version 26. Continuous variables were expressed as mean plus or minus standard deviation. Categorical variables were expressed as frequencies and percentages. Group comparisons for categorical variables used the chi-square

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test. The independent-samples t-test was used to compare quantitative parameters between groups. Pearson's correlation coefficient was applied to examine associations between different parameters within each group. A p-value of 0.05 or less was considered statistically significant. Because stress markers were compared across multiple clinical and menstrual symptoms, a Bonferroni-corrected threshold was also calculated and applied to these specific comparisons to reduce the risk of false-positive findings from multiple testing.

Results

The mean age of women with uterine fibroids was 40.2 ± 7.01 years. The mean age of women without fibroids was 38.6 ± 5.20 years. This difference was not statistically significant (p = 0.222). Mean body weight was also similar between the case group (72.1 ± 10.03 kg) and the control group (68.6 ± 9.38 kg), with no significant difference. Mean body mass index, however, differed significantly between the two groups. It was 27.98 ± 4.24 kg/m² among cases and 26.22 ± 3.91 kg/m² among controls (p = 0.049).

A clear difference was also observed between the two groups in education and occupation, both reaching high statistical significance (p = 0.001). The control group showed higher educational attainment overall, and 84.2% of its members were in paid employment. Marital status did not differ significantly between the groups (p = 0.463). Passive cigarette smoking, however, differed significantly (p = 0.004) and was more frequent among the controls (81.6%) than among the cases (52.0%), as summarized in Table 1.

Table 1: Socio-demographic characteristics of the study sampled women.

Characteristics		Cases [n = 50]	Control [n = 38]	P-value**
Mean age, years		40.2 ± 7.01	38.6 ± 5.20	0.222
Median age, years		**41.0**	**39.0**	**---**
Mean weight (kg)		72.1 ± 10.03	68.6 ± 9.38	0.095
Mean BMI (kg/m²)		27.98 ± 4.24	26.22 ± 3.91	**0.049**
		No. (%)	No. (%)	
Education	Illiterate	20 (40.0)	4 (10.5)	**0.001**
	Primary	13 (26.0)	4 (10.5)	
	Secondary	4 (8.0)	3 (7.9)	
	University	13 (26.0)	27 (71.1)	
Occupation	Housewives	35 (70.0)	6 (15.8)	**0.001**
	Employers	15 (30.0)	32 (84.2)	
Marital status	Single	7 (14.0)	8 (21.1)	0.463
	Married*	41 (82.0)	27 (71.1)	
	Widow	2 (4.0)	3 (7.9)	
Passive cigarette smoking		26 (52.0)	31 (81.6)	**0.004**

*One divorced woman in the cases group was included in the married category; ** Independent t-test of two means was used for quantitative variables and the chi-square test for categorical variables.

Mean age at menarche was earlier in the case group (11.9 ± 1.01 years) than in the control group (12.9 ± 0.79 years). This difference was statistically significant (p = 0.001). Mean parity and mean number of abortions did not differ significantly between women with and without uterine fibroids. Nulliparity was more frequent among the cases (38.8% versus 23.7%), but the difference was not significant (p = 0.135), as shown in Table 2.

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Table 2: Comparison of gynecological and obstetric history between the two groups.

Parameters		Cases [n = 50]	Control [n = 38]	P-value*
Mean age of menarche/years		11.9 ± 1.01	12.9 ± 0.79	**0.001**
Mean parity		2.0 ± 1.14	2.3 ± 1.49	0.556
		No. (%)	No. (%)	
Parity	P0	19 (38.8)	9 (23.7)	0.135
	P ≥ 1	30 (61.2)	29 (76.3)	
Mean abortion		0.49 ± 1.16	0.16 ± 0.37	0.093

Mean catalase concentration was higher in the control group than in the case group (4.31 ± 3.68 versus 2.69 ± 1.39 u/mL). Ceruloplasmin, in contrast, was higher in the case group than in controls (35.62 ± 3.77 versus 29.19 ± 5.73 ng/mL). AOPP was likewise higher among cases (23.44 ± 5.95 versus 8.30 ± 1.384 ng/mL), as presented in Table 3.

Table 3: Descriptive statistics for stress markers (catalase, ceruloplasmin, and AOPP) in the study sampled women.

Stress markers	Cases – Uterine fibroid [n = 50]			Control – No uterine fibroid [n = 38]		
	Mean±SD	Median	Range	Mean±SD	Median	Range
Catalase (u/mL)	2.69±1.39	2.50	0.10–6.50	4.31±3.68	3.30	1.50–9.70
Ceruloplasmin (ng/mL)	35.62±3.77	36.00	23.9–46.0	29.19±5.73	29.95	10.30–41.0
AOPP (ng/mL)	23.44±5.95	22.35	9.00–35.30	8.30±1.38	8.20	5.80–17.00

No significant differences in catalase, ceruloplasmin, or AOPP levels were found between women with a single fibroid and those with multiple fibroids, as shown in Table 4.

Table 4: Relationship between ultrasound features of uterine fibroids and stress markers in the study sampled cases.

Stress markers	Cases – Uterine fibroid		P-value
No. of fibroids	Single [n = 27]	Multiple [n = 23]	
Catalase (u/mL)	2.54 ± 1.31	2.87 ± 1.48	0.410
Ceruloplasmin (ng/mL)	34.82 ± 4.42	36.56 ± 2.61	0.105
AOPP (ng/mL)	22.33 ± 5.64	24.47 ± 6.15	0.146

* Independent t-test of two means was used.

Elevated catalase was associated with lower odds of uterine fibroid presence. The odds ratio was 0.25, with a 95% confidence interval of 0.095 to 0.641 (p = 0.004), as shown in Table 5. Because the study used a case-control design, this association did not establish a protective or causal effect. For ceruloplasmin, most women in both groups fell within the low or normal range: 94% of cases and 97% of controls. This categorical comparison was not significant, but the mean values differed significantly between the groups (p = 0.001). AOPP was elevated in 92% of cases, that is, 46 women, compared with only one control participant. This represented a highly significant difference in mean values between the two groups (p = 0.001).

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Catalase, ceruloplasmin, and AOPP levels did not differ significantly with backache, dyspareunia, dysmenorrhea, abdominal discomfort, abdominal bloating, or urinary symptoms. Catalase was the exception. It differed significantly according to the presence or absence of abdominal pain. AOPP and ceruloplasmin levels also differed significantly between women with fibroids who had infertility and those who did not, as shown in Table 6.

Table 5: Relationship between the presence of uterine fibroids and stress markers in the study sampled groups.

Catalase (u/mL)	Cases		Control		Odd ratio	95% C.I.	P-value
	No.	%	No.	%			
High [>2.51 u/mL]	24	48.0	30	79.0	0.25	0.095; 0.641	0.004*
Low and normal [0.10–2.51 u/mL].	26	52.0	8	21.0			
Ceruloplasmin (ng/mL)							
High [>40.00 ng/mL]	3	6.0	1	2.6	2.36	0.240; 23.650	0.452*
Low and normal [0.10–40.00 ng/mL]	47	94.0	37	97.4			
AOPP							
High [>16.31 ng/mL]	46	92.0	1	2.6	425.50	45.59; 1450.69	0.001*
Normal [0.687–16.31 ng/mL]	4	8.0	37	97.4			

*Chi-square test was used. f. = 1.

Table 6: Relationship between the presence of clinical symptoms and stress markers in the study's sampled cases.

Items	Markers	Present	Absent	P-value
Backache	Catalase	2.53 ± 1.21	2.96 ± 1.66	0.301
	Ceruloplasmin	35.0 ± 3.47	36.8 ± 4.10	0.107
	AOPP	23.9 ± 5.72	22.6 ± 6.40	0.457
Abdominal pain	Catalase	2.50 ± 1.39	3.42 ± 1.33	0.048
	Ceruloplasmin	36.0 ± 3.01	34.4 ± 4.31	0.198
	AOPP	23.9 ± 6.00	21.5 ± 6.86	0.251
Dyspareunia	Catalase	2.54 ± 1.38	2.13 ± 1.45	0.189
	Ceruloplasmin	35.8 ± 3.41	35.7 ± 4.32	0.298
	AOPP	23.6 ± 5.76	21.9 ± 6.18	0.522
Dysmenorrhea	Catalase	2.90 ± 1.29	2.49 ± 1.29	0.367
	Ceruloplasmin	35.4 ± 4.01	35.9 ± 2.70	0.674
	AOPP	22.7 ± 5.40	24.4 ± 6.66	0.330
Abdominal discomfort	Catalase	2.64 ± 1.51	2.55 ± 1.15	0.932
	Ceruloplasmin	34.6 ± 3.47	36.7 ± 4.78	0.153
	AOPP	24.1 ± 5.33	22.2 ± 3.28	0.380
Abdominal bloating	Catalase	2.54 ± 1.38	2.73 ± 1.45	0.536
	Ceruloplasmin	35.1 ± 3.47	35.8 ± 4.68	0.566
	AOPP	22.6 ± 5.66	23.8 ± 6.70	0.567
Urinary symptoms	Catalase	2.74 ± 1.68	2.67 ± 1.45	0.867

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Items	Markers	Present	Absent	P-value
	Ceruloplasmin	36.0 ± 4.45	35.5 ± 3.72	0.655
	AOPP	26.9 ± 5.66	22.8 ± 5.78	0.106
Infertility	Catalase	2.72 ± 1.78	2.70 ± 1.28	0.974
	Ceruloplasmin	33.6 ± 4.55	36.3 ± 3.32	0.029
	AOPP	20.4 ± 5.65	24.6 ± 5.82	0.031

* Independent t-test of two means was used.

Stress marker levels did not differ significantly with the presence or absence of menstrual symptoms. Both AOPP and ceruloplasmin, however, differed significantly between women with and without anemia, as shown in Table 7. After applying a Bonferroni correction for the 42 comparisons performed across the clinical and menstrual symptoms in Tables 6 and 7, the corrected significance threshold was 0.0012. None of the associations reported in either table remained significant under this stricter threshold, and they should therefore be regarded as exploratory rather than confirmatory findings.

Table 7: Relationship between menstrual symptoms and stress markers in the study sampled cases.

Items	Markers	Present	Absent	P-value
Irregular cycle	Catalase	2.99 ± 1.47	2.47 ± 1.31	0.199
	Ceruloplasmin	35.9 ± 3.62	35.4 ± 4.14	0.638
	AOPP	24.1 ± 3.26	22.9 ± 5.92	0.502
Changes in duration vs. previous cycle	Catalase	2.71 ± 1.37	2.61 ± 1.50	0.833
	Ceruloplasmin	35.5 ± 3.47	36.0 ± 4.85	0.702
	AOPP	23.9 ± 5.62	21.9 ± 7.09	0.354
Menorrhagia	Catalase	2.74 ± 1.38	2.53 ± 1.45	0.662
	Ceruloplasmin	35.6 ± 3.47	35.7 ± 4.78	0.968
	AOPP	23.9 ± 5.66	21.8 ± 6.78	0.283
Intermenstrual bleeding	Catalase	2.82 ± 1.83	2.63 ± 1.15	0.652
	Ceruloplasmin	35.1 ± 4.63	35.9 ± 3.33	0.472
	AOPP	23.4 ± 5.88	23.5 ± 6.06	0.976
Post-coital bleeding	Catalase	3.00 ± 1.78	2.69 ± 1.33	0.608
	Ceruloplasmin	35.4 ± 5.01	35.4 ± 3.31	0.985
	AOPP	22.2 ± 6.00	23.5 ± 6.00	0.637
Anemia	Catalase	2.76 ± 1.52	2.60 ± 1.23	0.680
	Ceruloplasmin	36.9 ± 3.56	34.0 ± 3.48	0.007
	AOPP	25.1 ± 6.06	21.3 ± 5.20	0.025

* Independent t-test of two means was used. Bonferroni-corrected significance threshold for 42 comparisons across Tables 6 and 7: $p < 0.0012$.

Maximum fibroid diameter correlated positively with ceruloplasmin level in the case group. Ceruloplasmin rose as fibroid size increased (Figure 1A).

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Maximum fibroid diameter also correlated positively with AOPP. AOPP likewise increased as fibroid size increased (Figure 1B).

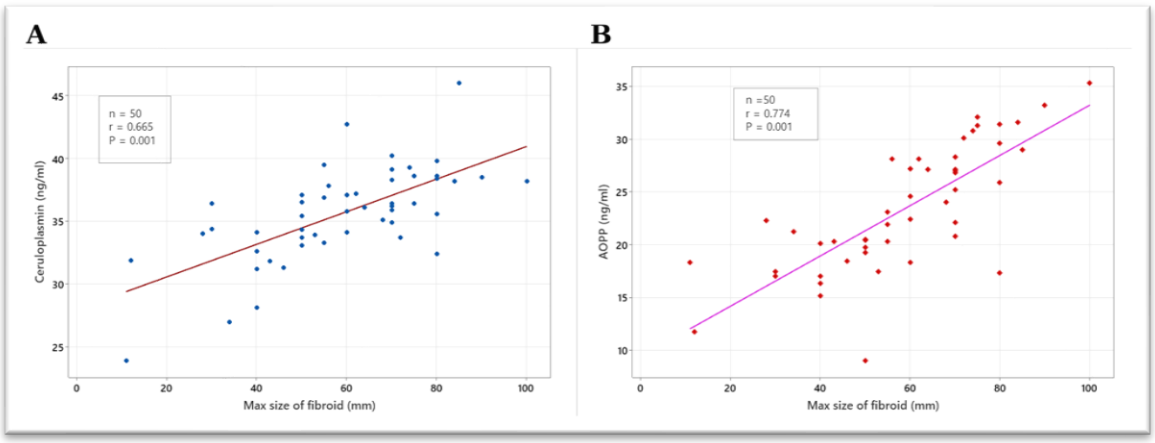


Figure 1: Correlation between maximum fibroid diameter and (A) ceruloplasmin and (B) AOPP.

Discussion

Uterine fibroids have been widely studied, and the present findings supported a possible relationship between oxidative stress and fibroid development. No significant difference in age was observed between the case and control groups. This may partly reflect the relatively restricted age range of the participants, which was 25 to 50 years, and agrees with the findings of previous research [16]. Body mass index, on the other hand, differed significantly between the two groups, similar to the results reported by Cetinkaya et al. [17]. Differences were also observed in educational level and occupational status. Recruiting healthy women as controls proved relatively difficult, and most participants who agreed to provide blood samples had a relatively higher educational level. This characteristic of the control group may have contributed to the observed difference. Previous studies have also described a higher prevalence of uterine fibroids among women with lower educational attainment and unemployed women [18]. Differences in lifestyle and access to healthcare services may partly explain this observation. Marital status was comparable between the two groups, in accordance with Adaiah et al. [19]. Passive exposure to cigarette smoke was significantly more common among the controls (81.6%) than among women with fibroids (52.0%). This direction was unexpected, because tobacco exposure has been examined among the potential risk factors for fibroid subtypes [20]. It probably reflected the sociodemographic differences between the two groups rather than a true protective effect, and it should be interpreted with caution. Among the reproductive characteristics, an earlier age at menarche was found in women with fibroids. This finding is consistent with previous evidence linking early menarche with an increased risk of uterine fibroids [21]. Parity did not show a significant difference between the groups, which agrees with the Santulli et al. study [16] but differs from the findings of Arinkan et al. [22]. The latter difference may be explained by the fact that many women with fibroids had completed their families before hysterectomy. Abortion history was also comparable between the groups, in agreement with the Hartmann et al. study [23], although Song et al. [24] reported a different finding.

The biomarker findings point to differences in oxidant and antioxidant status among women with uterine fibroids. Serum catalase was detected at elevated levels in 48% of the case group and 79% of the controls. Women with higher catalase concentrations had lower odds of

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having uterine fibroids, with an odds ratio of 0.25 and a 95% confidence interval of 0.095 to 0.641. A similar association was reported by Adaiah et al. [19] and by other investigators [25]. The interpretation of this association requires caution because the case control design cannot establish whether altered catalase levels precede fibroid development. Reverse causation is also possible. The hypoxic environment within fibroid tissue could influence catalase activity, meaning that reduced activity may occur as part of the disease process rather than contribute to its initiation. Ceruloplasmin behaved differently, with higher concentrations among women with fibroids despite its established antioxidant role. One possible explanation is related to the copper-dependent pro-oxidant activity of ceruloplasmin. Under certain conditions, it may enhance lipid oxidation, affect nitric oxide activity, and promote apoptosis through increased generation of reactive oxygen species [26]. Excess reactive oxygen species may also modify copper binding within the ceruloplasmin molecule, with a consequent reduction in its ferroxidase and protective functions. At the same time, greater availability of free copper could increase oxidative injury. The higher ceruloplasmin levels observed in the present study were comparable with those reported by Cetinkaya et al. [17] and Vural et al. [27].

AOPP concentrations were significantly higher in women with uterine fibroids than in the control group, a finding that agrees with the results of Adaiah et al. [19]. The increased AOPP levels may indicate greater oxidative protein modification among women with uterine fibroids and provide additional support for the presence of an altered oxidant and antioxidant balance in these patients. Taken together, the findings related to catalase, ceruloplasmin, and AOPPs suggest that oxidative imbalance may be associated with uterine fibroids. However, these findings should be interpreted in consideration of the case control nature of the study, which limits conclusions regarding causality. The relationship between these markers and specific clinical symptoms was more limited than the overall case-control comparison. No significant associations were found between catalase, ceruloplasmin, or AOPP and irregular bleeding, changes in cycle pattern, menorrhagia, intermenstrual bleeding, or postcoital bleeding, comparisons for which no directly relevant prior data could be identified. Anemia stood out as an exception: catalase did not differ significantly by anemia status, but both ceruloplasmin and AOPP did, likely reflecting ceruloplasmin's ferroxidase role in iron metabolism [28] and the broader role of multicopper ferroxidases in iron homeostasis [29], together with the fact that anemia itself increases oxidative stress, since erythrocytes contribute substantially to the antioxidant capacity of blood and their reduction weakens overall antioxidant defenses [30]. A similar pattern of largely null associations held for pain and discomfort symptoms; catalase, ceruloplasmin, and AOPP did not differ significantly with backache, dyspareunia, dysmenorrhea, abdominal discomfort, abdominal bloating, or urinary symptoms, again without directly comparable prior research, though catalase did differ significantly with the presence of abdominal pain, and AOPP showed no significant variation with these symptoms, consistent with Santulli et al. [16]. Infertility, however, was associated with significantly elevated ceruloplasmin and AOPP, consistent with Santulli et al. [16] and with an Iraqi study specifically examining ceruloplasmin in infertile women [31], suggesting that infertile women experience greater oxidative stress.

Beyond these group based comparisons, maximum fibroid diameter was positively and significantly associated with both ceruloplasmin and AOPP. This finding is consistent with Santulli et al. [16] and Adaiah et al. [19], who similarly observed that larger fibroids were associated with higher oxidant-marker levels and lower antioxidant levels. Collectively, these findings support a link between oxidative stress and fibroid size. In the broader correlation analysis, catalase was not associated with age, consistent with Bolzán et al. [32], or with BMI, in agreement with Amirkhizi et al. [33]. Likewise, ceruloplasmin showed no significant relationship with either age, as reported by Denko et al. [34], or BMI, as reported by Cox [35]. No comparable studies examining the associations of either marker with age at menarche or

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parity were identified. Clinically, these findings suggest that serum ceruloplasmin and AOPP might eventually complement ultrasound in monitoring fibroid activity or growth. However, this potential application must first be confirmed in larger prospective cohorts before clinical use can be recommended.

Limitations

Women with uterine fibroids had significantly lower catalase concentrations and higher levels of ceruloplasmin and AOPP than women without fibroids. However, because the study used a case-control design, it could not determine whether higher catalase levels in the control group had a protective effect or played a causal role in fibroid development. Among women with fibroids, AOPP levels were inversely related to catalase and directly related to ceruloplasmin, supporting the possibility that ceruloplasmin may exert pro-oxidant effects when present at elevated concentrations. Both ceruloplasmin and AOPP also increased with fibroid size. Overall, these results indicate that ceruloplasmin and AOPP may contribute to the pathogenesis of uterine fibroids, although this hypothesis requires confirmation through larger, prospective studies that account for potential confounding factors.

Declaration

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Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this manuscript.

Credit Authorship Contribution Statement

Thekra Ali Mohammed: Conceptualization, Investigation, Data curation, Formal analysis, Writing (original draft). Raida Muhammed Norri: Supervision, Methodology, Validation, Writing (review and editing).

Declaration of Artificial Intelligence (AI) Use

The authors used an AI tool (Claude) to improve grammar and sentence.

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