Sawa Medical Journal
Reprint from
Vol.2 Issue.2 2026
ISSN : 3007-4738

Impact of Elevated Adrenocorticotropic Hormone Levels in Pregnant Women with Gestational Hypertension

Iman Sami AbdulAmeer, Noor Thamer Hamood , Roaa Waleed Dawood Hussein, Fatima M. A. Al-Kubaisi, Ruwaidah A.R. Abbas, Mohammed YI Al-Hamadani

Department of Pathological Analysis, College of Applied Science, University of Fallujah, Al-Anbar, Iraq

Article Information
Received: 11-2-2026
Accepted: 19-2-2026
Published: 1-4-2026

Abstract

Pregnancy-induced hypertension represents a significant public health issue due to its potential adverse effects on both maternal and fetal outcomes. Adrenocorticotropic hormone (ACTH), a key regulator of various physiological processes including blood pressure, has been proposed as a possible contributor to the development of gestational hypertension when present at elevated levels during pregnancy. This study explored the relationship between ACTH concentrations and blood pressure in pregnant women, with the aim of assessing its influence on maternal health. Thirty pregnant women were enrolled, from whom blood samples were obtained to determine ACTH levels, while blood pressure was monitored throughout pregnancy. The results demonstrated a significant association between elevated ACTH concentrations and increased systolic and diastolic blood pressure. Participants with higher ACTH levels consistently exhibited greater blood pressure values compared to those with normal levels. Additional factors such as age, body mass index, and gestational age were incorporated into the analysis to enhance reliability. Although elevated ACTH appears to be a potential contributor to gestational hypertension, no statistically significant differences were observed in liver function or other biochemical parameters between the comparison groups.

Keywords: *ACTH, Plasma biomarkers, Hormonal imbalance, Immunoassay analysis, Systolic variation*

Introduction

Adrenocorticotropic hormone (ACTH), also known as corticotropin, is a peptide hormone predominantly synthesized and secreted by the anterior pituitary gland. It is a major component of the hypothalamic-pituitary-adrenal (HPA) axis and an important mediator for stress responses, metabolism modulation, immune system homeostasis regulation and inflammatory pathway control [1, 2]. The immune system must change during pregnancy to accommodate and not reject the fetus. Immunomodulatory effects of ACTH, which participates in this immune tolerance. Together with cortisol, ACTH also has immunosuppressive effects via controlling cytokine expression and reducing the inflammatory response,

which serve to maintain pregnancy [3, 4]. In addition, ACTH has an indirect effect on fetal development. ACTH stimulates the production of cortisol, which goes through the placenta. Cortisol is involved in the maturation of the fetal HPA axis, organogenesis, and immune system functioning [5-7]. Changes in ACTH and cortisol levels are correlated with the beginning of HPA. High levels of ACTH and cortisol are found in women with pre-eclampsia in observational clinical trials [8]. Inadequate production of ACTH can result in hypocortisolemia, which is associated with underactive cortical hormone production in the body, particularly where the fetus is concerned, resulting in stunted growth and underdeveloped organs, especially the lungs [9-11]. The changes in ACTH concentration could also decline the immune function of the body, which may increase the risk of maternal and neonatal infections [12]. Therefore, while ACTH is important for the protective mechanism during the course of pregnancy, its dysregulation may in theory result in both positive and negative consequences at the same time, which could lead to excessive inflammation or immunosuppression resulting in consequential impact on the mother and fetus [13-15].
This study aims to investigate the effect of increased adrenocorticotropic hormone (ACTH) levels on blood pressure in pregnant women, examine the correlation between elevated ACTH levels and the development of gestational hypertension, and assess whether ACTH level monitoring can serve as a predictive marker for hypertensive complications during pregnancy.

Materials and Methods

2.1 Materials

The equipment and apparatus employed in this study are presented in Table 1, whereas the materials and kits used are outlined in Table 2.

Table 1: Equipment and apparatus used in the current study.

No.	Equipment & instrument	Company and Origin
1	Plastic Petri-dishes	Marienfeld (Germany)
2	Refrigerator	BIOMERIEUX (France)
3	Pipette and tubes	Almalak Company (Iraq)
4	Pipette tip	Almalak Company (Iraq)
5	Syringes and tourniquet	Novel(China)
6	Holder for tubes for freezing sample	Almalak Company (Iraq)
7	Centrifuge	Shanghai Cheer Instrument (China)
8	Sphygmomanometer Rossmax CH155F	Rossmax (Swiss)

Table 2: Materials and kits used in the current study.

No.	Materials and Kits	Company and Origin
1	A diagnostic kit for the quantification of ACTH in blood	NIPIGON Health corp (Canada)

2.2 Methodology

2.2.1 Data Collection

This study was conducted from July 21 to September 9, 2024, in Fallujah city, Al-Anbar, Iraq, involving 30 pregnant outpatient women at Fallujah Teaching Hospital for Maternity and Children and private laboratories. Participants were divided into two groups: 15 hypertensive pregnant women and 15

normotensive pregnant women without pregnancy complications. Data including age, symptoms, and gestational diabetes were collected via questionnaire. Blood pressure measurements were taken, and blood was collected into EDTA tubes which were centrifuged at 3800 rpm for 5 minutes to separate the plasma. In order to avoid stress related fluctuations in ACTH, plasma was stored at -20 degrees Celsius. ACTH in plasma was measured with a specific device, and results were produced after 30 minutes of incubation, which is the time required after thawing for 15 minutes. ACTH was measured during the periods of gestational hypertension, taking into account some external stressors which could artificially elevate the ACTH concentration because of gestational hypertension.

2.2.2 Measurement of ACTH Hormone

The evaluations of plasma levels of ACTH are useful in the assessment of the pituitary-adrenal axis functions and the tests were done using a device and a kit from Nipigon Company which does in vitro quantification of ACTH using enhanced chemiluminescence immunoassay (eCLIA).

2.2.3 Principles of the Testing Method (Sandwich Principle)

Employing a sandwich immunoassay format, the total time needed for the test is nine minutes. This procedure forms a sandwich complex using the sample, a biotinylated monoclonal antibody, and ruthenium conjugated monoclonal antibody around the target analyte. The biotin-streptavidin bond interaction subsequently enables the monoclonal antibody attached to the analyte to be adsorbed to the solid phase of the test by the addition of streptavidin-coated microparticles. After that, the reaction mixture is sucked into the measurement cell, where the microparticles are drawn to the electrode surface by magnetic attraction. Washing with the system reagent removes unbound materials. Chemiluminescent emission is activated and detected by a photomultiplier when a voltage is applied to the electrode. Quantitative results are obtained by referencing a calibration curve generated specifically by the instrument using a 20-point calibration and a master curve supplied via RFID.

2.2.4 Specimen Collection, Handling, and Storage

Human plasma anticoagulated with EDTA-K3 or EDTA-K2 is recommended for testing. Blood samples should be collected via standard venous puncture procedures. Following complete coagulation, the plasma component should be separated by centrifugation. Care must be taken to avoid bubble formation during testing. Any lipid layer floating on the surface of the sample should be carefully removed. Samples exhibiting severe hemolysis are not recommended. For storage, samples can be kept for up to 8 hours at 18°C–28°C, 3 days at 2°C–8°C, and up to 4 weeks at −15°C or below. Samples may be frozen once only. Prior to measurement, samples must be brought to room temperature (18°C–28°C). To minimize evaporation effects, samples and calibrators loaded onto the analyzer should be analyzed within 2 hours.

2.2.5 Testing Procedure

The ACTH test is initiated by setting up the assay according to the operational manual. The ACTH reagent pack is placed into the designated analyzer slot to allow automatic suspension of magnetic beads at least 30 minutes before testing. The recommended ambient conditions are 10°C–30°C temperature and 80% relative humidity. The kit is identified within the device, and sufficient buffers are confirmed to be available in the system. Pre-warmed serum samples brought to room temperature are loaded into the device using can tubes. Sample information is entered into the device, and the reaction is started by pressing “Start.” The test results are generated by the analyzer approximately 20 minutes after initiation.

2.2.6 Statistical Analysis

For statistical analysis, SPSS software (version 27) was used. Using mean ± standard deviation, the data were presented. Using one-way ANOVA and chi-square tests, comparative analyses were performed. Also used were receiver operating characteristic (ROC) curve analysis and regression analysis. Technically, statistical significance was determined at a significance level of $p < 0.05$ and $p < 0.01$.

Results And Discussion

3.1 Results

The first table presents the distribution of patients based on specific characteristics. Among the patients, 50.9% suffer from high blood pressure, while 36.8% have normal blood pressure; data for 12.3% were unavailable. Additionally, 12.3% of women had gestational diabetes, indicating that the majority of the sample (87.7%) had no history of this condition. Regarding swelling in the feet and the presence of albumin in the urine, 50.9% exhibited these symptoms, which may suggest kidney problems or pregnancy-related disorders. The most common age group was 25–35 years (52.6%), while the least represented group was those over 40 years old (1.7%), as shown in Table 3.

Table 3: Distribution of Patient Groups According to Study Characteristics.

Characteristics		**Frequency**	**Percent**
Hypertension	No data	7	12.3
	no	21	36.8
	yes	29	50.9
	Total	57	100.0
Gestational diabetes	Yes	7	12.3
	no	50	87.7
	Total	57	100.0
Albumin and feet swelling	No data	7	12.3
	no	21	36.8
	yes	29	50.9
	Total	57	100.0
Age group	No data	7	12.3
	< 25	18	31.6
	25-35	30	52.6
	>35	1	3.5
	Total	57	100.0

The average age of the patients was 26.38 ± 5.76 years, indicating that most of the sample belonged to a young age group. The mean gestational age was 7.65 ± 2.14 weeks. The average number of previous pregnancies was 2.42 ± 2.05, suggesting that most women were not experiencing their first pregnancy. The mean systolic blood pressure was 12.13 ± 1.52, while the diastolic pressure was constant at 8.00 ± 0.00, which may reflect missing data or uniform measurements for some patients. The average ACTH concentration was 14.82 ± 12.91, indicating substantial variability among the patients, as shown in Table 4.

Table 4: Means and Standard Deviations of Study Parameters in the Study Group.

Patient characteristics	**N**	**Minimum**	**Maximum**	**Mean**	**Std. Deviation**
age	50	13	40	26.38	5.764
Gestational age	49	1	10	7.65	2.136
No. recent pregnancy	50	0	7	2.42	2.051
Systolic pressure	23	10	16	12.13	1.517
Diastolic pressure	23	8	8	8.00	.000
ACTH	30	0	53	14.82	12.909

Among the 57 patients with foot swelling and albumin in the urine, 22 had high blood pressure, a statistically significant association (P = 0.000), indicating that patients with hypertension are more likely to exhibit these symptoms. The age group of 25–35 years was the most common among patients with high blood pressure, while older age groups (>35 years) were underrepresented. Notably, none of the patients with gestational diabetes had high blood pressure, suggesting no direct correlation between the two conditions within this sample, as shown in Table 5.

Table 5: Distribution of Patient Characteristics According to the Presence of Hypertension.

Patient characteristics		**Hypertension**				
		No data	**No**	**yes**	**Total**	**P value**
Albumin in urine and feet swelling	No data	7	0	0	7	.000
	no	0	14	7	21	
	yes	0	7	22	29	
Total		7	21	29	57	
Age group	No data	7	0	1	8	.000
	< 25	0	10	8	18	
	25-35	0	11	19	30	
	>35			2	2	
Total		7	21	29	57	
Gestational diabetes	yes	7	0	0	7	.000
Total	no	0	21	29	50	
Total		7	21	29	57	

Patients with hypertension had greater ACTH concentrations (15.50 ± 9.19) than those without hypertension (5.88 ± 5.00); however, this difference was not statistically significant (P = 0.179), indicating that ADTH levels may be influenced by other variables, such as age. Patients with hypertension had a substantially higher mean age (28.10 ± 5.52) than those without (24.00 ± 5.34) (P = 0.01). Furthermore, there was a statistically significant difference (P = 0.016) in the average systolic blood pressure between individuals with and without hypertension, with the former having a substantially higher value (12.83) than the latter (11.36). Other variables, such as the number of prior pregnancies, did not show any significant variations. Table 6 presents these results, and Figure 1 shows them.

Table 6: Means and Standard Deviations of Study Parameters in the Study Group According to the Presence of Hypertension.

hypertension		**age**	**Gestational age**	**No. recent pregnancy**	**Systolic pressure**	**Diastolic pressure**	**ACTH**
No data	Mean						20.14
	Std. Deviation						22.954
	N						6
no	Mean	24.00	7.80	2.71	11.36	8.00	5.88
	Std. Deviation	5.339	1.765	1.901	.809	.000	5.004
	N	21	20	21	11	11	5
yes	Mean	28.10	7.55	2.21	12.83	8.00	15.50

	Std. Deviation	5.518	2.384	2.161	1.697	.000	9.191
	N	29	29	29	12	12	19
Total	Mean	26.38	7.65	2.42	12.13	8.00	14.82
	Std. Deviation	5.764	2.136	2.051	1.517	.000	12.909
	N	50	49	50	23	23	30
		0.011	0.694	0.394	0.016	-	0.179

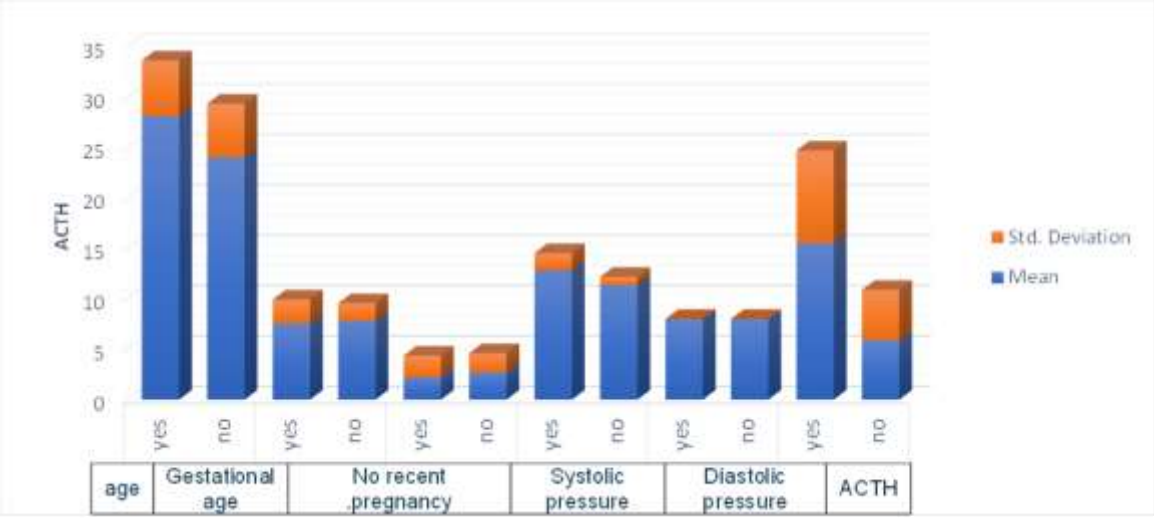

Figure 1: Means and Standard Deviations of Study Parameters in the Study Group According to the Presence of Hypertension.

Women in the 25–35 age group were 29.10 years old on average, compared to 20.56 years old in the <25 age group. There was no discernible variation in the mean gestational age across the various age groups. Although systolic blood pressure tended to be higher in the older age groups (>35 years), the difference was not statistically significant. The highest ACTH concentration was observed in the >40 years group, which may suggest a potential influence of age on this hormone, as shown in Table 7.

Table 7: Means and Standard Deviations of Study Parameters in the Study Group According to Age Groups.

Age group		**Age**	**Gestational age**	**No. recent pregnancy**	**Systolic pressure**	**Diastolic pressure**	**ACTH**
No data	Mean	40.00	8.00	6.00			20.09
	Std. Deviation	.	.	.			20.955
	N	1	1	1			7
< 25	Mean	20.56	7.00	1.44	11.29	8.00	14.01
	Std. Deviation	2.895	2.716	1.199	.756	.000	11.612
	N	18	17	18	7	7	7
>35	Mean	36.00	8.00	.00			15.43
	Std. Deviation	.	.	.			.
	N	1	1	1			1
25-35	Mean	29.10	8.00	2.97	12.50	8.00	12.70
	Std. Deviation	3.595	1.762	2.173	1.633	.000	8.954

	N	30	30	30	16	16	15
> 40	Mean	40.00	8.00	6.00			19.81
	Std. Deviation	.	.	.			.
	N	1	1	1			1
Total	Mean	26.38	7.65	2.42	12.13	8.00	14.82
	Std. Deviation	5.764	2.136	2.051	1.517	.000	12.909
	N	50	49	50	23	23	30
		.000	.500	.010	.076	.	.681

The average age of patients with foot edema and albumin in their urine did not differ statistically significantly from that of individuals without these symptoms (P = 0.063). However, systolic blood pressure was significantly higher in patients exhibiting these symptoms (13.08 vs. 11.09; P = 0.000), indicating a strong association with elevated blood pressure. There was no discernible variation in the two groups' ACTH concentrations. Table 8 presents these results, and Figure 2 provides illustrations.

Table 8: Means and Standard Deviations of Study Parameters in the Study Group According to the Presence of Foot Swelling and Albumin in Urine.

Study characteristics		**N**	**Mean**	**Std. Deviation**	**Minimum**	**Maximum**	**P value**
Age	yes	27	28.00	6.361	13	40	.063
	no	19	24.74	4.605	17	34	
	Total	46	26.65	5.874	13	40	
gestational.age	yes	26	7.85	2.130	1	10	.306
	no	19	7.16	2.292	3	9	
	Total	45	7.56	2.201	1	10	
no.recent.pregnancy	yes	27	2.67	2.075	0	6	.886
	no	19	2.58	1.953	0	7	
	Total	46	2.63	2.004	0	7	
syst.pressure	yes	12	13.08	1.379	11	16	.000
	no	11	11.09	.831	10	12	
	Total	23	12.13	1.517	10	16	
diast.pressure	yes	12	8.00	.000	8	8	-
	no	11	8.00	.000	8	8	
	Total	23	8.00	.000	8	8	
ACTH	yes	16	12.92	10.995	0	37	.844
	no	4	11.79	2.977	7	14	
	Total	20	12.70	9.852	0	37	

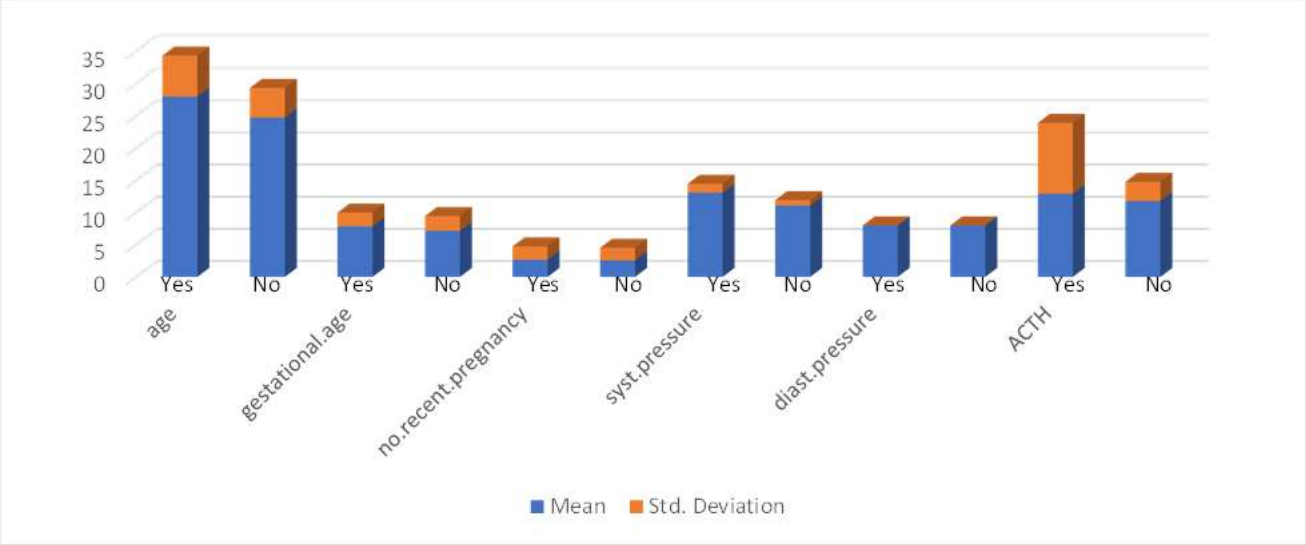

Figure 2: Means and Standard Deviations of Study Parameters in the Study Group According to the Presence of Foot Swelling and Albumin in Urine.

The ACTH test demonstrated low discrimination between cases of hypertensive pregnancy and normal blood pressure, with a low area under the curve (AUC = 0.224), which was not statistically significant (P = 0.055), as shown in Figure 3.

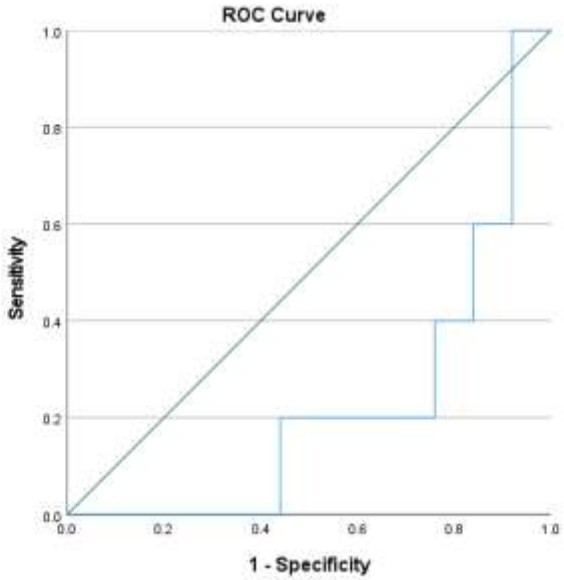

Figure 3: ROC Curve Analysis of ACTH for Hypertension (Area Under the Curve = 0.224; P = 0.055).
However, as Figure 4 illustrates, the area under the curve was modest (AUC = 0.490) and the difference was not statistically significant (P = 0.951), despite the fact that the ACTH test demonstrated greater discriminating between subjects with albumin in urine and foot edema during pregnancy and normal cases.

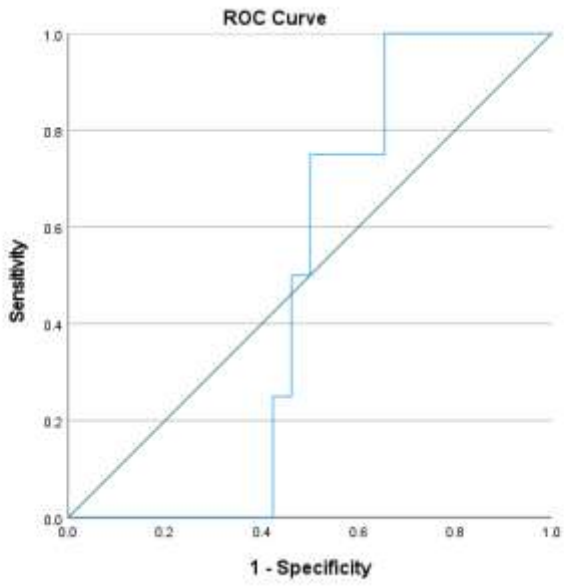

Figure 4: ROC Curve Analysis of ACTH for Albumin in Urine and Foot Swelling (Area Under the Curve = 0.490; P = 0.951).

A linear correlation with a P-value of 0.983 showed that there was no significant relationship between age and ACTH levels. Gestational age and ACTH levels showed a positive but non-significant association (P = 0.555). Regression analysis also revealed a positive, non-significant association between ACTH values and systolic blood pressure (P = 0.677) and a negative, non-significant association between ACTH values and the number of recent pregnancies (P = 0.626). Figure 5 provides an illustration of these interactions.

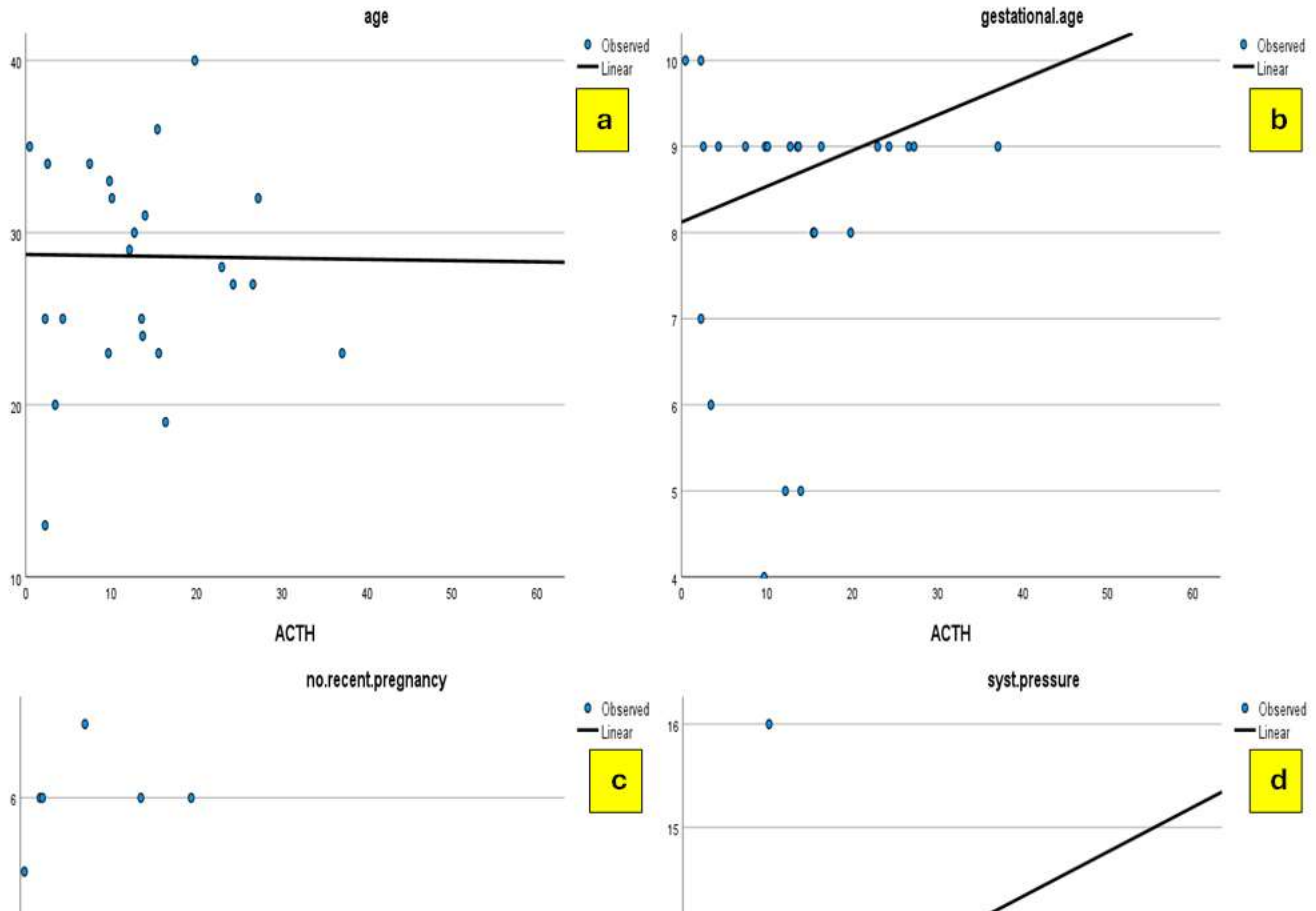

Figure 5: Regression analysis of the correlation between ACTH values and: (a) age (P = 0.983), (b) gestational age (P = 0.555), (c) number of recent pregnancies (P = 0.626), and (d) systolic blood pressure (P = 0.677).

Discussion

This study identified a positive correlation between elevated adrenocorticotropic hormone (ACTH) levels and increased blood pressure in pregnant women. Blood pressure measurements were noticeably higher in those with greater ACTH concentrations than in those with normal levels, indicating that ACTH may be important for controlling blood pressure during pregnancy. These results emphasize the necessity for more investigation to clarify the physiological effects and underlying processes of ACTH in this situation. The findings align with what has been published by [1] reviewing the pathophysiology of adrenal insufficiency and noting the roles of ACTH with cortisol secretion, as well as blood pressure via sodium and water retention. During pregnancy, CRH and ACTH levels were noted as elevated [16], which likely influences blood pressure as well. Our results also align with those of [17] where increased cortisol and plasma ACTH levels were noted in both fetal and maternal blood, suggesting the possibility of hormonal influences on the mother's blood pressure.

Nevertheless, [18] pointed out the need for further research regarding the interplay CRH has, and the blood pressure during pregnancy, which seems to be multifaceted. On the other hand, we differ from the findings of [19] who noted the absence of a relationship between ACTH and blood pressure control during pregnancy. This difference could stem from study design, sample size, or other factors that were controlled for in the analyses.

The correlation that has been noted with blood pressure and ACTH levels might be because of the ACTH's role in cortisol synthesis, which increases blood pressure by causing the retention of sodium and water in the kidneys, as shown in [19]. As noted in [20] and [3], maternal anxiety and the HPA axis activation during pregnancy may elevate cortisol which can, in turn, elevate blood pressure. Moreover, it has been suggested that HPA axis activation during pregnancy might exacerbate hypertension by the stress response causing vasoconstriction and increased blood pressure from the sympathetic nervous system.

This study employed accurate and standardized measurement techniques for both ACTH and blood pressure, enhancing the reliability and validity of the results. The inclusion of a comparison group with normal ACTH levels provided a more robust assessment of ACTH’s effect on blood pressure. The results' applicability to broader groups, however, could be constrained by the very small sample size. Moreover, external factors such as maternal diet, physical activity, and psychological stress were not fully controlled, which may have influenced blood pressure outcomes. Additionally, the study did not assess the long-term effects of elevated ACTH levels on blood pressure in the postpartum period.

The effect of ACTH on albuminuria in pregnant women has been examined indirectly through studies involving related conditions such as hypertensive disorders, diabetic nephropathy, and Cushing’s syndrome. In our study, a non-significant elevation in ACTH levels was observed among patients presenting with albuminuria and peripheral edema (feet swelling), indicating a possible but inconclusive link.

The study by [21], although not involving pregnant women, explored ACTH’s potential role in modulating glomerular permeability a pathway relevant to albuminuria in pregnancy by suggesting podocyte repair mechanisms through melanocortin receptor activation.

In a case report by Xu et al. (2023) [22], a 26-year-old pregnant woman was diagnosed with ACTH-independent Cushing’s syndrome due to an adrenal adenoma. The patient presented with severe albuminuria (24-hour urinary cortisol: 1,190.5 μg/24 h), hypertension, and hypokalemia. Surgical resection of the adenoma effectively resolved hypercortisolism and its associated complications, resulting

in a successful pregnancy outcome. This case highlights that excessive cortisol independent of ACTH elevation can contribute to albuminuria and preeclampsia-like symptoms during pregnancy.

Additionally, the study by [23] on hypertensive pregnancies noted that ACTH stimulates aldosterone secretion, which may exacerbate hypertension and renal stress. Although albuminuria was not directly measured, this mechanism suggests that ACTH-induced aldosterone production may indirectly contribute to endothelial dysfunction and glomerular damage, potentially increasing albuminuria in hypertensive pregnancies.

A significant correlation between the incidence of hypertension and the presence of albuminuria observed in our study is consistent with findings by [24], which reviewed 26 studies and concluded that elevated albuminuria in early pregnancy (measured via the urine albumin-to-creatinine ratio) is strongly associated with preeclampsia risk. Although ACTH was not evaluated in that study, it reinforces the clinical importance of albuminuria as a biomarker for pregnancy complications and provides a context for exploring hormonal influences, such as ACTH.

Additionally, according to the Centers for Disease Control and Prevention (CDC), albuminuria is closely associated with hypertensive disorders of pregnancy (HDPs), which include preeclampsia and impact around 15.9% of births in the US. While ACTH was not investigated in the CDC report, it underscores the urgent need for reliable biomarkers and interventions targeting endothelial dysfunction a physiological pathway potentially influenced by ACTH [25].

Conclusion

This study demonstrates a positive correlation between elevated ACTH levels and increased blood pressure in pregnant women, suggesting a significant role of ACTH in blood pressure regulation during pregnancy. The effect of rising ACTH levels was more pronounced with advancing maternal age. Hypertension was found to be significantly associated with albuminuria; however, despite this association, ACTH levels did not differ significantly between patients with positive and negative albuminuria. Furthermore, the ACTH test showed poor discriminatory ability in distinguishing pregnant women with hypertension and albuminuria from those with normal blood pressure and urine findings.

Statements and Declarations

Declaration of Authorship

According to the authors, this study is unique and hasn't been published anywhere else. All information sources and other researchers' contributions have been properly referenced.

Competing Interests

The authors declare no conflict of interest.

Author Contributions

Iman Sami Abdul-Ameer was responsible for drafting the main manuscript text and contributed to the preparation of figures 1–5 and tables 1–8.

Statement of Usage of Artificial Intelligence

The authors confirm that they did not use artificial intelligence (AI) techniques or software in any part of the study or in the writing of their article.

Data Availability

University of Fallujah digital Repository

Funding Information
No particular grant from a governmental, private, or nonprofit funding organization was obtained for this study.

Acknowledgments
We sincerely thank the University of Fallujah for providing the opportunity to conduct this research and for their support in facilitating the publication of our findings in this esteemed journal.

References

1. Hahner, S., Ross, R.J., Arlt, W., Bancos, I., Burger-Stritt, S., Torpy, D.J., ... & Quinkler, M. (2021). Adrenal insufficiency. Nature Reviews Disease Primers, 7(1), 19. https://doi.org/10.1038/s41572-021-00252-7
2. Rhodes, M.E. (2007). Adrenocorticotropic hormone (ACTH). Encyclopedia of Stress, 1, 69–72.
3. Briffa, J.F., Hosseini, S.S., Tran, M., Moritz, K.M., Cuffe, J.S., & Wlodek, M.E. (2017). Maternal growth restriction and stress exposure in rats differentially alters expression of components of the placental glucocorticoid barrier and nutrient transporters. Placenta, 59, 30–38. https://doi.org/10.1016/j.placenta.2017.09.006
4. Bhaumik, S., Lockett, J., Cuffe, J., & Clifton, V.L. (2023). Glucocorticoids and their receptor isoforms: roles in female reproduction, pregnancy, and foetal development. Biology, 12(8), 1104. https://doi.org/10.3390/biology12081104
5. Fink, G. (Ed.). (2016). Stress: Neuroendocrinology and Neurobiology: Handbook of Stress Series, Volume 2 (Vol. 2). Academic Press.
6. Sheng, J.A., Bales, N.J., Myers, S.A., Bautista, A.I., Roueinfar, M., Hale, T.M., & Handa, R.J. (2021). The hypothalamic-pituitary-adrenal axis: development, programming actions of hormones, and maternal-fetal interactions. Frontiers in Behavioral Neuroscience, 14, 601939. https://doi.org/10.3389/fnbeh.2020.601939
7. Howland, M.A., Sandman, C.A., & Glynn, L.M. (2017). Developmental origins of the human hypothalamic-pituitary-adrenal axis. Expert Review of Endocrinology & Metabolism, 12(5), 321–339. https://doi.org/10.1080/17446651.2017.1356222
8. Wood, C.E., & Walker, C.D. (2016). Fetal and neonatal HPA axis. Comprehensive Physiology, 6(1), 33–62. https://doi.org/10.1002/j.2040-4603.2016.tb00676.x
9. Pelizzo, G., Calcaterra, V., Baldassarre, P., Marinaro, M., Taranto, S., Ceresola, M., ... & Zuccotti, G. (2024). The impact of hormones on lung development and function: an overlooked aspect to consider from early childhood. Frontiers in Endocrinology, 15, 1425149. https://doi.org/10.3389/fendo.2024.1425149
10. Fandiño, J., Toba, L., González-Matías, L.C., Diz-Chaves, Y., & Mallo, F. (2019). Perinatal undernutrition, metabolic hormones, and lung development. Nutrients, 11(12), 2870. https://doi.org/10.3390/nu11122870
11. Makrigiannakis, A., Semmler, M., Briese, V., Eckerle, H., Minas, V., Mylonas, I., ... & Jeschke, U. (2007). Maternal serum corticotropin-releasing hormone and ACTH levels as predictive markers of premature labor. International Journal of Gynecology & Obstetrics, 97(2), 115–119. https://doi.org/10.1016/j.ijgo.2007.01.007
12. Zawadzka, A., Cieślik, M., & Adamczyk, A. (2021). The role of maternal immune activation in the pathogenesis of autism: a review of the evidence, proposed mechanisms and implications for treatment. International Journal of Molecular Sciences, 22(21), 11516. https://doi.org/10.3390/ijms222111516

13. Solano, M.E., & Arck, P.C. (2020). Steroids, pregnancy and fetal development. Frontiers in Immunology, 10, 3017. https://doi.org/10.3389/fimmu.2019.03017
14. Sic, A., Cvetkovic, K., Manchanda, E., & Knezevic, N.N. (2024). Neurobiological implications of chronic stress and metabolic dysregulation in inflammatory bowel diseases. Diseases, 12(9), 220. https://doi.org/10.3390/diseases12090220
15. Gitau, R., Cameron, A., Fisk, N.M., & Glover, V. (1998). Fetal exposure to maternal cortisol. The Lancet, 352(9129), 707–708. https://doi.org/10.1016/S0140-6736(05)60824-0
16. McLean, M., & Smith, R. (1999). Corticotropin-releasing hormone in human pregnancy and parturition. Trends in Endocrinology & Metabolism, 10(5), 174–178. https://doi.org/10.1016/s1043-2760(98)00146-5
17. Thomson, M. (2013). The physiological roles of placental corticotropin releasing hormone in pregnancy and childbirth. Journal of Physiology and Biochemistry, 69(3), 559–573. https://doi.org/10.1007/s13105-012-0227-2
18. Kassotaki, I., Valsamakis, G., Mastorakos, G., & Grammatopoulos, D.K. (2021). Placental CRH as a signal of pregnancy adversity and impact on fetal neurodevelopment. Frontiers in Endocrinology, 12, 714214. https://doi.org/10.3389/fendo.2021.714214
19. Mastorakos, G., & Ilias, I. (2003). Maternal and fetal hypothalamic-pituitary-adrenal axes during pregnancy and postpartum. Annals of the New York Academy of Sciences, 997(1), 136–149. https://doi.org/10.1196/annals.1290.016
20. Wadhwa, P.D., Culhane, J.F., Rauh, V., Barve, S.S., Hogan, V., Sandman, C.A., ... & Glynn, L.M. (2001). Stress, infection and preterm birth: a biobehavioural perspective. Paediatric and Perinatal Epidemiology, 15, 17–29. https://doi.org/10.1046/j.1365-3016.2001.00005.x
21. Tumlin, J.A., Galphin, C.M., & Rovin, B.H. (2013). Advanced diabetic nephropathy with nephrotic range proteinuria: a pilot study of the long-term efficacy of subcutaneous ACTH gel on proteinuria, progression of CKD, and urinary levels of VEGF and MCP-1. Journal of Diabetes Research, 2013(1), 489869. https://doi.org/10.1155/2013/489869
22. Xu, S., Liu, M., Xu, J., Che, B., Zhang, W., Li, W., ... & Tang, K. (2023). Pregnancy complicated with adrenal adenoma causing ACTH-independent Cushing's syndrome, accompanied by obstetric antiphospholipid syndrome and severe pre-eclampsia: case report and literature review. Frontiers in Endocrinology, 14, 1147316. https://doi.org/10.3389/fendo.2023.1147316
23. Brown, M.A., Thou, S.T., & Whitworth, J.A. (1995). Stimulation of aldosterone by ACTH in normal and hypertensive pregnancy. American Journal of Hypertension, 8(3), 260–267. https://doi.org/10.1016/0895-7061(94)00213-U
24. Rashidian, P., Parsaei, M., Hantoushzadeh, S., & Salmanian, B. (2025). Investigating the association of albuminuria with the incidence of preeclampsia and its predictive capabilities: a systematic review and meta-analysis. BMC Pregnancy and Childbirth, 25(1), 322. https://doi.org/10.1186/s12884-025-07444-z
25. Ford, N.D. (2022). Hypertensive disorders in pregnancy and mortality at delivery hospitalization—United States, 2017–2019. MMWR. Morbidity and Mortality Weekly Report, 71, 585–591. http://dx.doi.org/10.15585/mmwr.mm7117a1