ISSN 2664-4169 (Print) & ISSN 2664-7923 (Online)
South Asian Research Journal of Biology and Applied Biosciences
Abbreviated Key Title: South Asian Res J Bio Appl Biosci

| Volume-7 | Issue-6 | Nov-Dec -2025 | **DOI: https://doi.org/10.36346/sarjbab.2025.v07i06.006**

Original Research Article

The Potential Effect of Physiological Disorder on the Formation of Gallstones in Iraqi Female Patients

Haylim N. Abud[1]*

[1]Department of Microbiology/ College of Science/ Al-Karkh University for Science, Baghdad-Iraq

***Corresponding Author:** Haylim N. Abud
Department of Microbiology/ College of Science/ Al-Karkh University for Science, Baghdad-Iraq

Article History
Received: 27.09.2025
Accepted: 21.11.2025
Published: 27.11.2025

Abstract: Gallstone disease (GD) is a common disorder worldwide. That Affecting variable age and gender categories, most of them are female gender (about 2-3 times higher than male). The influence of female sex hormones on the development of gallstones is well established. Therefore, the study focused on the extent of the relationship between gallstone disease and female hormones. The study included (100) Iraqi female patients with gallstone disease, aged (18±65) years. These female patients were referred to the Department of Immunology/ Medical City in Baghdad province/ Iraq during the time period (from Oct 2024 to Jan 2025). We concluded that the gallstone disease hormones tests in the included sample of female patients was high than the controls, Accordingly Incidence of gallstones disease was positively correlated to Gender and Sex hormones. Our aim to make a clear insight about the relationship between different female hormones and thyroxin to determine the dangerous factors associated with progression of gallstones.

Keywords: Gallstones, Female Hormones, Estrogen, Progesterone, Thyroxin.

INTRODUCTION

Gallstone disease, or gallbladder stones, is often considered a serious illness. This disease presents a global medical challenge, with geographical variations in the prevalence of gallstones (Njeze G 2013). The disease constitutes 10-15% of the population in the USA. (Stinton LM & Shaffer EA 2012) and is less frequent in India, Eastern Europeans, African Americans, and Japan. No accurate record of the prevalence of gallstones in Arab countries. Gallstones are becoming increasingly common, occurring in 7% of males and 15% of females. They are seen in all age groups (18–65 years, with an overall prevalence of 11%. In individuals under 40 years, there is a 3:1 female preponderance (Ralston SH *et al.*, 2018).

Gallstones are small, pebble-like substances that develop in the gallbladder. They are hardened, thickened, deposits of the olive-green or brownish-yellow fluid called Bile that can form and store within the gallbladder and help the body digest fats, is composed mainly of substances: water, cholesterol, bile salt, fats, protein and bilirubin. The liver produces up to 1 liter of bile per day (Singh VK *et al*., 2018). There are three types of gallstones. The first type is pure cholesterol stones, which are composed of at least 90% cholesterol. The second type is pigment stones, which can be either brown or black. The third type consists of cholesterol, bilirubin, and other substances such as calcium carbonate, calcium phosphate, and calcium palmitate. (Gillson Sh 2025).

Research has shown that 80% of patients most cases are asymptomatic. However, approximately 1-2% of individuals will develop symptoms each year that require surgery, making cholecystectomy one of the most commonly performed operations. The most common symptom of gallstones.is very uncomfortable, cramping pain in the upper abdomen (colic), and other symptoms include a feeling of extreme fullness, bloating, nausea, vomiting, and belching (Jones MW *et al*., 2025). Several factors influencing gallstone disease such as age progression, Female gender, Obesity, rapid weight loss, Diabetes (Yuan S *et al.*, 2022), Genetic, Drugs, Physical activity (Nam SY 2017).

Sex hormones (estrogens and progesterone) likely contribute to the increased risks associated with pregnancy, estrogen replacement therapy, oral contraceptive use, and obesity, and that`s why the gallstone disease is two to three times higher in females than in men (Heuman DM 2019).

Estrogen has been shown to increase cholesterol production in the liver, a key component in gallstone formation. Excess cholesterol is deposited in bile and leads to gallstone formation (Nam SY 2017). Progesterone has also been shown to reduce gallbladder motility, impeding bile flow and contributing to gallstone formation (Wong M 2023; Zakko SF 2024).

Estrogen helps maintain the strength and thickness of the vaginal wall and urethral lining. Progesterone, which is another main female hormone, is sometimes called the "hormone of pregnancy "and is a derivative of cholesterol is commonly produced by the adrenal cortex as well as the gonads, which consist of the ovaries and the tests. Other hormones such as LH, FSH, prolactin, HCG, oxytocin, and vasopressin. That are involved in the functioning female reproductive systems. Any increase or decrease in the levels of these hormones is associated with many diseases such as certain cancers, heart diseases, PCOS and cholelithiasis. Both estrogen and progesterone have been shown to increase the risk of developing gallstones. Excess estrogen affects the gallbladder by increasing cholesterol absorption in bile. Bile salts help increase the saturation of bile with cholesterol, which can lead to the formation of cholesterol crystals. Estrogen alters bile acid composition, increasing the risk of gallstones. Progesterone may slow gallbladder emptying, allowing sludge to accumulate. (Liu T *et al*., 2018).

The patients who suffer from gallstones should know that the treatment of stones depends on their individual situation. So there are two general options: medical treatment, surgical treatment (Zakko SF *et al*., 2023) Ultrasound is the most effective method for diagnosing gallstones. Most stones are detected using trans-abdominal ultrasound, which has a sensitivity of over 92% and a specificity of 99% for gallstones. (Ralston S H *et al*., 2018). Also, complications may be detected using blood tests (Zakko SF *et al.*, 2023). Hormones are chemical messengers made up of either proteins or steroids. The endocrine glands release hormones into the bloodstream, which regulate various bodily processes, including appetite, sleep, and growth and maintain the body in a state of homeostasis. The female body produce and release a variety of hormones that are secreted by the adrenal gland and gonads (Gurarie M 2025). Estrogen is the major female hormone that produced of cholesterol by fat cells in addition to other estrogens (estradiol, estrone, estriol).

GD is the second most common non-gynecological condition that may require surgical intervention during pregnancy. Affecting as many as 12% of pregnant women (Portincasa P *et al*., 2023). A recent study indicated that as a woman's pregnancy progresses, her likelihood of developing gallstones increases. This can occur not only during pregnancy but also as a result of the changes experienced throughout each pregnancy. Frequent fluctuations in gallbladder volume, combined with the residual volume in the gallbladder and the cholesterol content of bile, may create conditions that promote gallstone formation. (Wiginton, K & Braverman, J 2023).

An increase in progesterone reduces gallbladder contractions. Estrogen also causes an increase in cholesterol in the bile and decreases the gallbladder's contraction. A study in 2017 found that gallbladder surgery and ERCP during pregnancy seem to be safe in terms of intra-and Postoperative complications must be managed safely for the expected child, regardless of trimester, previous bariatric surgery, indication, or the need for one or more ERCPs as an adjunct. (Van Erpecum K J 2006).

Pregnant patients often worry about their children and desire more information. Gallstones do not have any effect on the baby. However, the baby can be affected by the implications of the disease condition. Infection, nausea, and vomiting hamper the ability to nourish which can affect the development of the baby.

MATERIAL AND METHODS

Patients and Controls

The study was conducted on 30 female patients from Iraq with gallstone disease who were referred to the Department of Immunology/ Medical City during the time period (2023 Oct-2024 Jan). Their age range was (12-65) years. A questionnaire was created with various questions, including the duration of gallstone disease, family history, smoking habits, drug usage, duration of drug use, and a control group. The patient was first clinically examined for Gallstones (Kurtin WE *et al.*, 2000). After these evaluations, the consultant made the diagnosis. Sex hormone levels, including ES, Pro, and TT4, were assessed using an autoanalyzer (MiniVidas, Biomerieux, France). All procedures were completed according to the manufacturer's guidelines. Data was analyzed using the Statistical Package for Social Sciences (SPSS version 26). A normality test was conducted to examine the variables for normal distribution (Nam SY 2017). The Kruskal-Wallis Test The significance among the tested cytokines was determined. A statistical significance level was set at P-value < 0.05.

RESULTS AND DISCUSSION

Estrogen Hormone in Patients and Controls

Estrogen and progesterone hormones were a notable increase in the number of patients with gallstones compared to the control group, as shown in Table 1. The Estrogen levels were (457.66±56.9 ng/dl vs. 119.55±55.62 ng/dl). The progesterone hormone levels were increased in gallstone disease patients as compared to the controls (2.1±5.30 ng/dl vs. 46.30±7.8 ng/dl).

Progesterone hormone and Thyroxine hormone in Patients and Controls

Sera of Progesterone hormone and Thyroxine hormone in patients and controls were tested for both and Thyroxine were normal in patients compared to the control (81.1±18.0 vs. 160.33±7.4) mIU/ml, as in Table 1.

Table 1: Parameters in patients and controls

Parameters	Mean ± SD		P-Value
	Control (n=50)	Patients (n=50)	
ES.H (mIU/ml)	119.55±55.62	457.66±56.9	0.60
PRO.H (ng/dl)	2.1±5.30	46.30±7.8	0.0001
TT4 (mIU/ml)	81.1±18.0	160.33±7.4	0.001

This table is better understood when they were considered in terms of patients with gallstones. (Kurtin WE *et al.*, 2000). In this regard, the serum level of the test hormone were Estrogen, was significantly (p= 0.60) increased as compared to controls (119.55±55.62 mIU/ml vs. 457.66±56.9 mIU/ml). Singh *et al*., (2020), discovered in their study that female patients with gallstones had higher ES.H, PRO.H, and TT4.H levels than gallstone-negative controls, which agrees with our study.

The current study aimed to prove the extent of associated cholelithiasis with hormones in female patients in Baghdad province/Iraq. The average age of the patients included in the study was 65±12. We concluded that the gallstone disease hormone tests result (ES.H and PRO.H) in the included sample of female patients were higher than in the control. Risk factors were evaluated by taking a complete medical history, conducting a clinical examination, and performing an abdominal assessment. The incidence of cholelithiasis was positively associated with Sex hormones. As documented previously, Gallstones Disease is common gastrointestinal disorder over the world, This is attributed to one of several risk factors that influencing gallstone disease which is Gender, Female gender are more liable to cholelithiasis and this is contributed by sex hormones (Estrogen & progesterone), pregnancy hormones and HTR increase the incidence of Gallbladder stones formation9 (van Erpecum K J 2006). Increased levels of female sex hormones result in greater catabolism of cholesterol, which leads to higher cholesterol excretion in bile and an increased risk of gallbladder stone formation 1. This can be explained as follows: Estrogen is the main sex hormone in females. This hormone binds to multiple receptors it plays a crucial role in regulating mechanisms related to both health and disease. (Nam SY 2017). Basically, it regulates liver metabolism it helps prevent lipid accumulation in the liver by reducing fat production. (Biddinger SB *et al.*, 2008), lipid uptake, transport of HDL, and promoting lipolysis. Interestingly, Estrogen actively participates in regulating and increasing both cholesterol synthesis and secretion, maintaining cholesterol balance the text involves various receptors and their functions in the body. Specifically, through the action of ESR1 (Estrogen Receptor 1), SR-BI (Scavenger Receptor Class B Type 1), and ERα (Estrogen Receptor Alpha), ESR1 activates SREBP-2 (Sterol Regulatory Element Binding Protein 2) and cholesterol 7α-hydroxylase, which is a key enzyme involved in cholesterol and bile salt synthesis. Studies in female mice had established the liver's classical estrogen receptor α ER-α but not ER-β, plays a critical role in estrogen-induced gallstones in females. by augmenting it's functions in the liver and gallbladder, ER-α protects the liver from hypercholesterolemia; lack of it affects the whole body. Therefore, any defect affecting this receptor will lead to increased formation of gallstones (Kurtin WE *et al.* 2000).

The molecular mechanisms of estrogen's lithogenic effect on gallstone formation are complex, particularly due to the identification of G protein–coupled receptor 30 (GPR30), a newly discovered estrogen receptor associated with the gallstone gene lith18 (Patel H. & Jepsen J, 2024). Research has shown that estradiol (E2) can effectively attach to and stimulate both GPR30 and ER-α receptors. This leads to excessive cholesterol production and promotes greater Cholesterol production and increasing the likelihood of bile stone formation. (Maurer K. J *et al.*, 2009).

Other female sex hormones, particularly progesterone, contribute to gallstone formation by promoting biliary stasis. Increased levels of progesterone during pregnancy impair the gallbladder's response to cholecystokinin (CCK), a hormone responsible for stimulating fat digestion. (Shen HC *et al.*, 2014). Cholecystokinin causes the gallbladder muscle to contract, resulting in a decline in gallbladder size and the subsequent release of bile. (Van Erpecum K J 2006).

Many studies have indicated that people with hypothyroidism are at risk of developing gallstones, if the absence of TT4 affects cholesterol metabolism and hepatic biliary secretion. Therefore, this helps in the formation of gallstones. Our TT4. Hormone results appeared higher than control, and this confirms that the results reinforced that women developing gallstones were due to an imbalance in female hormones, and this is consistent with what our study discussed (Liu Z *et al*., 2018).

CONCLUSION

In this study, three hormones act as risk co-factors in Gallstone formation, including ES, PRO, and TT4. The text has demonstrated a causal relationship with cholelithiasis, suggesting potential new diagnostic and therapeutic strategies in clinical practice. However, the mechanisms underlying these causal connections are still unclear, indicating a need for further studies to investigate these mechanisms.

Acknowledgement

I want to thank the Department of Microbiology/ College of Science/ Al-Karkh University for Science, Baghdad-Iraq, for their support and help in completing this paper.

REFERENCES

- Biddinger, S.B., Haas, J.T., Yu, B.B. & et al. (2008). Hepatic insulin resistance directly promotes formation of cholesterol gallstones. Nat Med.14,778-782
- Gillson, Sh. (2025). Gallstone (Cholelithiasis) Symptoms and Causes.verywellhealth.com
- Gurarie, M. (2025). 5 Signs and Symptoms of Gallstones. from: https://www.health.com/condition/digestive-health/gallstone-symptoms
- Heuman, D. M. (2019). Gallstones (Cholelithiasis). from. https://emedicine.medscape.com/article/175667-overview?form=fpf
- Jones, M.W., Weir, C.B., Marietta, M. (2025). Gallstones (Cholelithiasis). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. https://www.ncbi.nlm.nih.gov/books/NBK459370/
- Kurtin, W.E., Schwesinger, W.H.& Diehl, A.K. (2000). Age-related changes in the chemical composition of gallstones. Int J Surg Investig 2,299-307
- Lim, J., Wirth, J., Wu, K., Giovannucci, E., Kraft, P., Turman. C. & et al. (2021). Obesity, adiposity, and risk of symptomatic gallstone disease according to genetic susceptibility. Clin Gastroenterol Hepatol.2021,44. http://doi.org/10.1016/j.cgh.2021.06.044
- Liu, T., Wang, W, JY., Wang, Y, Liu, X., Cao, L. & et al. (2018). Association between different combination of measures for obesity and new-onset gallstone disease. PLoS One. 13, e0196457. http://doi.org/10.1371/journal.pone.0196457
- Liu, Z., Troy, J.,Yu-Tang, K. & et al. (2018). The Association of Circulating Inflammation Proteins and Gallstone Disease. http://doi.org/10.1111/jgh.14265
- Maurer, K.J., Carey, M.C.& Fox, J.G. (2009). Roles of infection, inflammation, and the immune system in cholesterol gallstone formation. Gastroenterology.136, 425–40.
- Nam, S. Y. (2017). Obesity-related digestive diseases and their pathophysiology. Gut Liver. 11,323–34. http://doi.org/10.5009/gnl15557
- Njeze, G.E. (2013). Department of Surgery, Enugu State University of Technology Teaching Hospital, Park Lane, Enugu, Nigeria. Gallstones,19(2), 49–55.
- Patel, H. & Jepsen, J. (2024). Gallstone Disease: Common Questions and Answers. Am Fam Physician. 109(6),518-524.
- Portincasa, P., Di Ciaula, A., Bonfrate, L., Stella, A., Garruti, G.& Lamont. J.T. (2023). Metabolic dysfunction-associated gallstone disease: expecting more from critical care manifestations. Intern Emerg Med.18(7),1897-1918. http://doi.org/10.1007/s11739-023-03355-z
- Ralston, S.H., Penman, I. D., Strachan, M.W.J. Hobson, R. P. (2018) Davidson's Principles and Practice of Medicine. 23rd Edition, Elsevier, Amsterdam.
- Shen, H.C., Hu, Y.C., Chen, Y.F. & Tung, T.H. (2014). Prevalence and associated metabolic factors of gallstone disease in the elderly agricultural and fishing population of taiwan. Gastroenterol Res Pract.2014,876918.
- Singh, V.K., Jaswal, B.S., Sharma, J.& Rai, P.K. (2020). Analysis of stones formed in the human gall bladder and kidney using advanced spectroscopic techniques. Biophys Rev.12(3),647-668. http://doi.org/10.1007/s12551-020-00697-2
- Stinton, L.M.& Shaffer, E.A. (2012). Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer. Published online 2012 Apr; 6(2): 172–187.
- van Erpecum, K.J., Wang, D.Q., Moschetta, A. & et al. (2006). Gallbladder histopathology during murine gallstone formation: relation to motility and concentrating function. J Lipid Res. 47, 32–41

- Wang,D.Q., Bren, A., Neuschwander-Tetri,& Portincasa, P. (2016). Colloquium Series on Integrated Systems Physiology, The Biliary System, Second Editionv.8(5), i-178. http://doi.org/10.4199/C00147ED2V01Y201611ISP071
- Wiginton, K.& Braverman,J. (2023). Gallstones (Cholelithiasis): What Are They? Ftom:https://www.webmd.com/digestive-disorders/gallstones
- Wong, M. (2023). Gallstones in Women: Understanding the Higher Risk and How to Minimise IT.
- Yuan, S., Gill, D., Giovannucci, E.L. & Larsson, S.C. (2022). Obesity, type 2 diabetes, lifestyle factors, and risk of gallstone disease: a mendelian randomization investigation. Clin Gastroenterol Hepatol. 20, e529–37. http://doi.org/10.1016/j.cgh.2020.12.034
- Zakko,S.F., Sanjiv Chopra,S. & Grover, Sh. (2024). Overview of gallstone disease in adults. From: https://www.passeidireto.com/arquivo/160882091/overview-of-gallstone-disease-in-adults-up-to-date