The Journal of Teachers Association

ISSN 1019-8555 (Print) & ISSN 2408-8854 (Online)
Frequency: Bi-Annual
DOI: https://doi.org/10.62469/taj.v037i02.038

OPEN ACCESS

Website: www.tajrmc.com
Email: editor@tajrmc.com
Volume-37 | Issue-2 | Jul-Dec 2024

Serum ALT and AST Among Combined Oral Contraceptive Pill Users Women in Rajshahi City

Shamima Nazneen Rupa[1*], Bedowra Begum[1], Shahin Mahmuda[1], Farjana Kabir[2], Sayeeda Sultana Jolly[3]

[1] Department of Physiology, Rajshahi Medical College, Rajshahi, Bangladesh
[2] Department of Physiology, Pabna Medical College, Pabna, Bangladesh
[3] Department of Physiology, Khulna City Medical College, Khulna, Bangladesh

Abstract: ***Background:*** Among all birth control methods, combined hormonal contraceptives are the most widely used. Previous studies have suggested that early oral contraceptive pills (OCPs) could be harmful to the liver. There was no research on how the more recent OCPs affected liver function, even though earlier OCPs had their dosage and content changed to reduce negative effects. ***Methods*****:** This cross-sectional analytical study was carried out on 184 healthy women aged 20-45 years. Among them 92 women were OCP users and 92 women were OCP non-users. BMI matched non-OCP users' women were recruited in the study for comparison of ALT and AST. Systematic sampling technique was applied to select each respondent. Having obtained ethical clearance from the Ethical Committee and informed consent from the respondents, data collection was commenced. ***Results*****:** The results showed that the mean ALT level was higher in OCP users women (52.65±16.96 U/L) compared to non OCP users (36.17±20.26 U/L) and it was statistically significant ($p < 0.05$). The mean AST level was also higher in OCP users women (48.15±12.94 U/L) compared to non OCP users (37.14±15.42 U/L) and it was also statistically significant ($p < 0.05$). ***Conclusions*****:** So, regular monitoring of liver function test should be done among OCP users women and adaptation of other suitable birth spacing method is necessary among them.

Keywords: Oral contraceptive pill, Aspartate aminotransferase and Alanine aminotransferase.

Original Research Article

Correspondence:
Dr. Shamima N. Rupa
Department of Physiology, Rajshahi Medical College, Rajshahi, Bangladesh
E-mail: shamimarupa43@gmail.com

How to cite this article:
Nazneen Rupa S, Begum B, Mahmuda S, Kabir F, Sultana Jolly S; Serum ALT and AST Among Combined Oral Contraceptive Pill Users Women in Rajshahi City. Taj 2024;37 (2): 289-295.

Article history:
Received: August 05, 2024
Revised: October 22, 2024
Accepted: November 12, 2024
Published: December 01, 2024

Article at a glance:

Study Purpose: *The purpose of this study was to investigate the effect of low dose OCP on ALT and AST, the most important two liver enzymes.*
Key findings: *Serum level of ALT and AST were increased with increased duration of OCP use.*
Newer findings: *Obesity was observed increase significantly with the duration of combined oral contraceptive use (p=0.001).*
Abbreviations: *ALT: Alanine Aminotransferase, AST: Aspartate aminotransferase and OCP: Oral contraceptive pill.*

INTRODUCTION

Contraceptives are procedures, medications, or devices that are used to avoid getting pregnant. Natural, barrier, and hormonal methods are the general categories into which contraceptive methods fall.[1] The most widely used and efficient reversible type of contraception is the combination oral steroidal contraceptive.[2] Nowadays, contraception is used by over 100 million women worldwide.[3] According to the BDHS from 2007, 55.8% of married women in the reproductive age group take contraception.[4] The first generation of pills gave way to the second generation, and now third generation pills with lower concentrations of the active hormones progestin and estrogen are available.[5] The third generation of pills has less side effects and is more economical, safe, and effective.[6] Yet, non-compliance has been found to be the reason for the failure rate of 9%.[4] The way that the tablets are

made determines how they work. The pituitary luteinizing hormone produced by the pills may prevent ovulation by making cervical mucus impermeable to sperm penetration.[7] Numerous employees have proposed that contraception has certain effects in addition to benefits. Due to the extensive use of hormonal contraceptives, there is a chance to evaluate the impact of progesterone and estrogen on a range of biochemical markers in users.[6] Almost all of the body's systems are impacted by combined hormonal contraception.[8] Burkman et al.[9] found that elevated serum liver enzymes could indicate hepatic dysfunction caused by the oral contraceptive pill's metabolism in OCP users.

Therefore, various essential bodily systems are impacted by impaired liver function. While there are several tests used in LFT, liver enzyme testing is the most frequently performed.[1] Tests for liver function are performed to identify whether the liver is damaged or has impaired function.[2] In order to eliminate and digest a wide range of toxic substances, including prescription drugs and oral contraceptives, the liver filters the blood supply of the body. It may therefore be susceptible to several types of drug-induced liver damage. Many types of liver lesions can be brought on by oral contraceptives. They may be the direct cause of a liver disease or they may aggravate an underlying hepatic disorder.[10] The liver is essential to the metabolism of progestogens and estrogens.[11] It became clear that these chemicals might affect the liver either directly or indirectly, resulting in a wide range of biological effects that are significant from a physiological and pathological standpoint. Therefore, the purpose of this study was to ascertain how low doses of progestin and estrogen OCP affected the enzymes aspartate amino transferase (AST) and alanine amino transferase (ALT).[12] The activity of serum alanine amino transferase (ALT) and aspartate amino transferase (AST) were measured to assess liver integrity. The enzyme known as alanine amino transferase (ALT) is required for the synthesis of energy and is found in several tissues, such as the liver, heart, and skeletal muscles. It is concentrated in the liver.[3] Another enzyme that is essential for the synthesis of energy and is elevated in heart disease and the liver is aspartate amino transferase (AST). AST is not as elevated in liver disease as ALT is.[3]

Cholestatic jaundice, benign hepatic tumors, and hepatic dysfunction are the three main types of adverse hepatic effects that have been connected to the use of oral contraceptives. The development of jaundice is the most visible pathological modification in liver function that prompts the doctor to start the patient on oral contraceptives. The first documented side effect of oral contraceptives on the liver within the first six cycles was intrahepatic cholestatic jaundice.[10] Hepatic abnormalities associated with oral contraceptive use because of oestrogen's relative interference with the liver's ability to excrete different organic anions, such as bilirubin.[13] Hussein[3] found that serum ALT and AST level were higher in OCP users. He also found serum level of ALT and AST were elevated with increased duration of OCP use. Ekhator et al.[13] also observed that serum ALT and AST level were high in OCP users than the OCP non-users. Larsson-Cohn[14] observed that SGPT increased in 7% and SGOT in 6%. Jaundice subsides within four days inspite of continued medication. So, the present study had been designed to determine the effect of OCP on alanine amino transferase (ALT) and aspartate amino transferase (AST).

METHODS

This cross-sectional analytical study was done in the department of Physiology in collaboration with department of Biochemistry, Rajshahi medical college, Rajshahi from July 2017 to June 2018. Data were collected from Rajshahi model family planning clinic, Gynae outdoor of Rajshahi medical college hospital. Healthy married women aged 20-45 years in Rajshahi City were study population and among them 184 women were selected according to eligibility criteria. OCP users women were recruited in one group (n=92), while OCP non-users women were enrolled in another group (n=92). After taking informed consent, complete history was collected and physical examination were done and recorded in a preformed data sheet. Then-whole blood (about 5 ml) was collected from anterior cubital vein by venipuncture technique using 21-gauge hypodermic needle and collect in a sterile container. It was allowed to clot and there after centrifuged at 1200x 9 for 5 min at room temperature (29^0C-31^0C). Serum aspartate aminotransferase (AST) and alanine

aminotransferase (ALT) were estimated using Randox reagent kit using 2, 4-dinitrophenylhydrazine substrate, activity was determined far billiary integrity with Randox reagent kit using nithrophenyl phosphate substate. Data were analyzed by using SPSS software, version 20. The level of significance was set at 5% and p-value < 0.05 was considered statistically significant.

RESULTS

Regarding BMI, out of 92 OCP users respondents 50.6% had normal BMI and 49.5% were overweight. On the other hands, out of 92 non OCP users women 49.4% had normal weight and 50.5% were overweight (Figure 1).

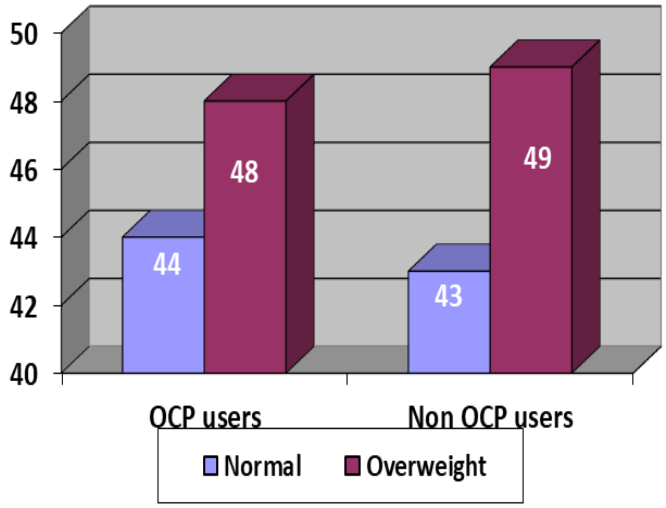

Figure 1: Body mass index of the respondents (n=92 in each group)

The mean ALT level was higher in OCP users women (52.65±16.96 U/L) compared to non OCP users (36.17±20.26 U/L) and it was statistically significant (p < 0.05) (Figure 2).

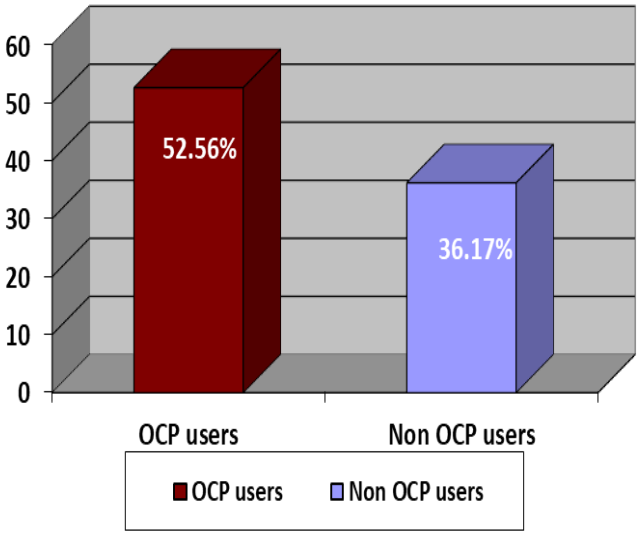

Figure 2: Serum alanine amino transferase (ALT) level between OCP users and non OCP users (n=184) (n=92 in each group).

The mean AST level was also higher in OCP users women (48.15±12.94 U/L) compared to non OCP users (37.14±15.42 U/L) and it was also statistically significant (p < 0.05) (Figure 3).

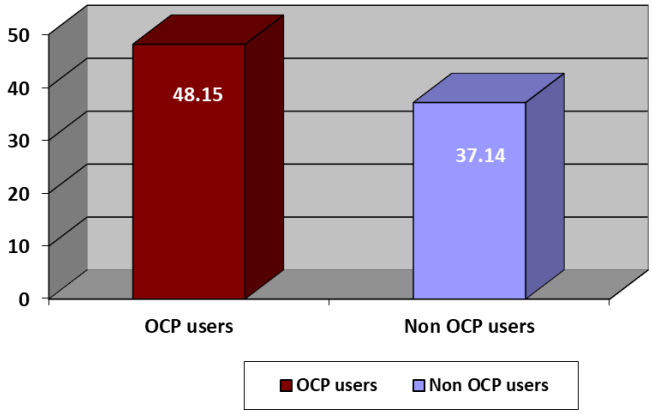

Figure 3: Serum aspartate amino transferase (AST) level between OCP users and non OCP users (n=184) (n=92 in each group)

Increased level of ALT and AST were 59.8% and 60.9% respectively in OCP users (Figure 4).

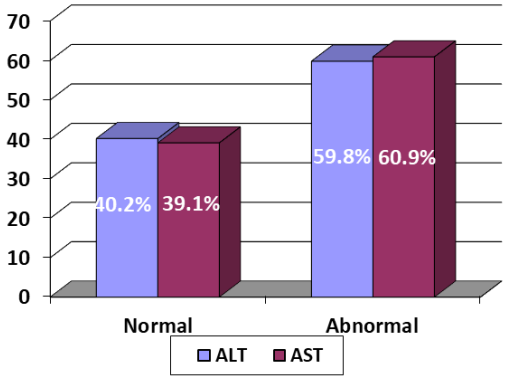

Figure 4: shows percentage of ALT and AST in OCP users (n=92 in each group)

OCP users women were categorized into 5 groups according to their duration of use i.e. 1-12 months, 13-24 months, 25-36 months, 37-48 months and 49-60 months. It showed changes in BMI with increase in the duration of combined oral contraceptive use (Table 1).

Table 1: Effect of duration of use of OCP on BMI (n=92 in each group)

BMI Kg/m²	1-12 months	13-24 months	25-36 months	37-48 months	49-60 months
	Frequency (%)				
<22.99	3(21.4%)	3(21.4%)	4(28.6%)	4(28.6%)	0
23-24.99	5(16.7%)	5(16.7%)	11(36.7%)	9(30.0%)	0
25-26.99	2(6.9%)	4(13.8%)	4(13.8%)	14(48.3%)	5(17.2%)
>27	0	2(10.5%)	2(10.5%)	5(26.3%)	10(52.6%)

Data were analyzed using Chi-square test and were presented as frequency and percentage. χ^2=35.406, df=12, p=0.001

Serum ALT and AST levels were also progressively increased with increase duration of OCP use (Table 2).

Table 2: Effect of duration of OCP use on Serum alanine amino transferase (ALT) and serum aspartate amino transferase (AST) (n=92 in each group)

Duration of OCP use (months)	No	Serum ALT (mean ± SD)	p value	Serum AST (mean ± SD)	p value
1-12	10	24.00±6.14	p=0.001	27.00±5.37	P=0.001

13-24	14	41.71±19.74	F=26.386	41.42±15.41	F=22.526
25-36	21	52.61±13.72		46.57±9.44	
37-48	32	60.15±7.92		54.09±6.92	
49-60	15	66.00±7.12		58.06±7.91	
Total	92	52.65±16.96		48.15±12.94	

Data were analyzed using ANOVA test and were presented as mean±SD.

DISCUSSION

The impact of second-generation monophasic combination oral contraceptives, which are widely used in Bangladesh, was the primary focus of this study. Two liver enzymes, ALT and AST, were measured as part of the study to see how the combination oral contraceptive pill affected liver function. This study also investigated the impact of OCP usage duration on BMI. Sukhi tablets, which contained 150 µg levonorgestrel and 30 µg ethinyl estradiol, were employed in this investigation. The users were divided into five groups based on how long they had been taking these medications.

In the present study serum ALT and AST level were significantly higher among OCP users in comparison to non OCP users. These findings were compatible with the study done by Hussein[4], Ekhator et al.[13], Larsson-Cohn et al.[14], Lindberg et al.[15], Dickerson et al.[16], Schaffner F. et al.[17], Hargreaves.[18]ALT and AST concentrations are known to be high in the liver and wide variety of tissues like muscles and neuronal cells[19]. The present findings in this regards reaffirms the fact that OCPs have effect to a number of metabolic and nutritional processes. The observed significant changes as shown in this study suggest that ingestion of OCPs can induce alterations in the serum liver proteins and concentrations of liver and billiary enzymes.[13] Injury to the liver is largely defined by the increase in the blood level of proteins that are liberated from the damaged hepatocytes like alanine amino transferase.[20] Some researcher found that serum ALT and AST level were within normal limit in spite of taking OCP. This finding is compatible with katz et al.[21] In this study the OCP users were categorized into 5 groups, according to their duration of OCP use. Minimum duration of use was 6 months. Highest duration of use was more than five years. Here serum level of ALT and AST were increased with duration of OCP use. These findings were coinciding with the study done by Hussein[3], Lindberg et al.[15]. However, ALT level was higher than the AST. This observation might be due to the half-life of the two enzymes. The half-life of ALT is longer than AST.[3]

Cullberg et al.[22] mentioned that liver cell damage accords well with repeated observation of elevated transaminase during treatment with OCP. Shrikanth et al.[20] mentioned that oral contraceptives and anabolic steroids are associated with cholestasis, vascular lesions and hepatic neoplasm. Chronic use of oral contraceptives is associated with the development of hepatic adenoma, benign tumours typically observed only in women of childbearing age and these can be resolved completely with drug withdrawal and development of the risk factors depends upon the duration of the drug exposure. Both estrogen and progestin are metabolized in the liver and excreted in large part in the urine. Large doses of the estrogen and the progestin steroids must enter the liver so that adequate level may be achieved at the target tissues. The exposure of the liver to the high levels of sex steroids via the portal circulation puts this organ at risk for the adverse effects of these drugs.[23] OCPs induces alterations in liver cellular integrity as well as the billiary tract. This assertion is sequel to the significance of serum concentrations of hepatic enzymes and that these marker leak into the circulation when there is necrosis or damage to the hepatic cells.[13]

In fact, based on the results of this study, the remarkable result on the nature of the liver of OCP users seems to have challenged the normal physiological function and integrity of the liver. Thus, taking low doses of synthetic OCP may affect the function of the liver and cellular integrity and biliary systems in a dose dependent manner.[13] One of the strengths of our study was that sample size was relatively larger i.e. 184. This sample size could predict relatively accurate finding of our parameters. On the other hands we had collect the OCP user from the model family planning clinic of

Rajshahi medical college hospital. Here regular registration of OCP users were recorded. So, there was no chance of drop out of these sample. On the basis of our findings, we predict that OCP have significant effect on some liver function test. Our study suggest that estimation of liver enzyme should be done before starting OCP and regular monitoring is necessary to prevent liver damage.

CONCLUSION

In this study it is found that serum ALT and AST level were increased in OCP users. So, it is wise to avoid OCP use in patients suffering from liver problems and screening of every female before initiating OCP is necessary. It is also necessary to monitoring of liver function in female taking OCP for prolonged period.

Acknowledgements

Contribution of the women who participated in the study were acknowledged for their cordial co-operation in data collection.

Authors' contributions

SNR, BB, SM: Concept and design, data acquisition, interpretation and drafting. SNR, FK and SSJ: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Declarations

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Conflict of interest

Authors declared no conflict of interest.

Ethical approval

Ethical approval of the study was obtained from the Ethical Review Committee from Rajshahi Medical College, Rajshahi. Informed consent was taken from all women. All the study methodology was carried out following the relevant ethical guidelines and regulations.

Consent for publication: Taken.

REFERENCES

1. Onyesom, Osioma, Etagar, Ofili, I.d. Activities of some liver enzymes in serum of humans receiving DMPA and Cu- IUD contraceptives. Scholars Journal of Applied Medical Sciences. 2013; 1(2):62-64.
2. Datta D.C. Text Book of obstetrics. In: Konar H. editor. 7 th ed. Fundamentals of Reproduction and Abnormalities of placenta and cord. New central book agency, Calcutta, India. 2009 p. 30-220.
3. Hussein HJ. Physio-chemical study of some liver enzymes in the province of Najaf women s used low dose compound oral contraceptives pills (COCs). Int J Rec Sci Res. 2016; 7(6):11706-11709.
4. Chowdhury RI, Islam MA, Chakraborty N, Akhter HH. Determinants of antenatal morbidity: a multivariate analysis. World Health Popul. 2007;9(3):9–18.
5. Casey PM, Pruthi S. The latest contraceptive options: what you must know: proper counseling hinges on having the latest data at your fingertips. This review--and handy guide--will help. Journal of Family Practice. 2008; Dec;57(12):797-805.
6. Roumen FJME. The contraceptive vaginal ring compared with the combined oral contraceptive pill: a comprehensive review of randomized controlled trials. Contraception. 2007 Jun 1;75(6):420–429.
7. Sidd YH, Naz F, Jyoti S, Afzal M. Biochemical effects of oral contraceptives among users: a review. Int J Pharmacol. 2012; 8(5):314-320.
8. Malhotra N, Malhotra J, Saxena R, Bora NM. Jeffcoate's principles of gynaecology. Jaypee Brother's Medical Publishers, New Delhi, India. 2018 p. 250-252.
9. Burkman R, Schlesselman JJ, Zieman M. Safety concerns and health benefits associated with oral contraception. Am J Obstet Gynecol. 2004 Apr;190(4 Suppl):S5–22.
10. Valla D, Benhamou JP. Liver diseases related to oral contraceptives. Dig Dis. 1988;6(2):76–86.
11. Hall JE, Guyton AC. Pocket companion to Guyton & Hall textbook of medical physiology. Saunders Elsevier, Philadelphia, 2006 p. 132-135.
12. Ekhator CN, Osifo UC, Akpamu U. Effect of oral contraceptive pills (containing low doses

of synthetic hormones) on liver function in adult female rabbits. 2014; 6(1):15-20.
13. Lockhat D, Katz SS, Lisbona R. Oral contraceptives and liver disease. Can Med Assoc J.1981 Apr 15;124(8):993-9.
14. Larsson-Cohn U. Oral contraception and liver-function tests. Br Med J. 1965; May 29; 1(5447): 1414–1415.
15. Lindberg MC. Hepatobiliary complications of oral contraceptives. Journal of general internal medicine. 1992; Mar-Apr;7(2):199-209.
16. Dickerson J, Bressler R, Christian CD. Liver function tests and low-dose estrogen oral contraceptives. Contraception. 1980 Dec;22(6):597–603.
17. Schaffner F. The effect of oral contraceptives on the liver. JAMA. 1966 Nov;198(9):10-19.
18. Hargreaves T. Oral contraceptives and liver function. J Clin Pathol. 1969; 3:1-10.
19. Dial SM. Clinicopathologic evaluation of the liver. Veterinary Clinics: Small Animal Practice.Vet Clin North Am Small Anim Pract.1995 Mar;25(2):257-73.
20. Srikanth BA, Manisree V. Oral contraceptives induced hepatotoxicity. International Journal of Basic & Clinical Science. 2013;2(1):90-93.
21. Katz R, Tushman M. An investigation into the managerial roles and career paths of gatekeepers and project supervisors in a major R & D facility. R & D Management. 1981;11(3):103-110.
22. Cullberg G, Lundstroem R, Stenram U. Jaundice during treatment with an oral contraceptive, Lyndiol. Br Med J. 1965 Mar 13;1(5436):695–697.
23. Hossain, Q., Hossain, A., Nizum, M. Z., & Naser, S. B. (2024). Influence of Artificial Intelligence on Customer Relationship Management (CRM). International Journal of Communication Networks and Information Security, 16(3), 653-663.
24. Haque, M. A., Islam, M. I., & Hasan, H. (2024). Successful Surgical Creation and Management of an Arteriovenous Fistula: A Case Report. Asia Pacific Journal of Surgical Advances, 1(1), 34-38.
25. Hasan, H., Rahman, M. H. ., Haque, M. A., Rahman, M. S. ., Ali, M. S. ., & Sultana, S. . (2024). Nutritional Management in Patients with Chronic Kidney Disease: A Focus on Renal Diet. Asia Pacific Journal of Medical Innovations, 1(1), 34-40.
26. Azad, A. K., Rahman, M. M., & Beg, M. O. (2024). Comparative Analysis of Open vs Minimally Invasive Approaches in Lumbar Spine Surgery A Multi Center Study. IAR Journal of Medicine and Surgery Research, 5(6), 91-99.
27. Tazri, S. A., & Anam, K. (2024). Prevalence of low back pain in post menopausal women in the peripheral community of Bangladesh. IAR Journal of Medicine and Surgery Research, 5(6), 73-82.
28. Lindberg MC. Hepatobiliary complications of oral contraceptives. J Gen Intern Med. 1992 Apr;7(2):199–209.

The Journal of Teachers Association
Abbreviated Key Title: TAJ
Official Journal of Teachers Association Rajshahi Medical College