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Comparative Study between Pregnant and Non-Pregnant Women Regarding Variation of Liver Function Tests: Assessment of Health Literacy

Amina I. B. Othman[1], Dalia M. A. Elsherbini[2], Hayam F. A. Eittah[3], Manal S. Hakami[4], Badria M. A. Mohammed[5]

[1]Medical-Surgical Nursing, Faculty of Nursing, Menoufia University, Egypt.
e-mail: amina73737373@yahoo.com
[2]Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Jouf University, Sakaka, Saudi Arabia.
e-mail: delsherbini@yahoo.com
[3]Department of Anatomy, Faculty of Medicine, Mansoura University, Mansoura, Egypt.
e-mail: hfathi@yahoo.com
[4]Nursing Department, Faculty of Applied Medical Sciences, Al Baha University, Saudi Arabia.
e-mail: msalem@bu.edu.sa ORICD ID: https://orcid.org/0000-0002-4956-876X
[5]Medical-Surgical Nursing, Faculty of Nursing, Menoufia University, Egypt.
Nursing Department, Faculty of Applied Medical Sciences, Albaha University.
e-mail: d.badria@hotmail.com. ORICD ID: https://orcid.org/0000-0003-2121-6305

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ABSTRACT

Context: Pregnancy is associated with normal physiological adaptive changes. Biochemical parameters reflect these changes and are distinct from the non-pregnant state. Low levels of health literacy have been shown to result in less healthy choices, riskier behavior, poorer health, less self-management, and more hospitalization among that category of adult patients.

Aim: The study aimed to examine the effect of pregnancy on liver function tests among pregnant women during various trimesters of pregnancy and compare with non-pregnant and determine the patients' level of health literacy regarding the variation of liver function tests among those patients.

Methods: A descriptive cross-sectional design was used to achieve the study aim. A random sample of 65 women was selected from an outpatient clinic in the maternity hospital; 54 out of them were pregnant women. Three tools were used to collect data, socio-demographic and clinical data assessment sheet; assessment of liver function tests by Cobas c 311; and health literacy management scale.

Results: The sample's age range was between 20-40 years. This study revealed that; serum albumin levels decreased from the first trimester (3.7-4.7), and this decrease became progressively more accentuated as the pregnancy advanced (3.35-4.36 decreased significantly to 3.19-3.81). There was no significant decrease in serum AST between pregnant and non-pregnant women, but there was a significant decrease in ALT in pregnant women compared with non-pregnant women (11.90 Vs. 8.60 at p 0.017). In the current study, Serum alkaline phosphatase (ALP) was significantly higher (P<0.0001) during the third trimester (63-171) compared with the second trimester (33-137), and the first trimester (36-129), and with the control group (48-122). Finally, it was found that a significant decrease in total serum bilirubin concentrations during the second (0.11-0.38) and third trimesters (0.12-0.42) compared to control (0.11-1.57) and the first trimester (0.12-0.85). Moreover, most of the studied sample has a low level of health literacy for all subscales and the total scores.

***Conclusion*:** During normal pregnancy, most values of liver function tests remain below the normal upper limits compared to non-pregnant women. Any increase in serum ALT and AST activity levels and serum bilirubin should be considered pathologic and prompt for further evaluation. Moreover, most of the studied sample has a low level of health literacy for all subscales and the total scores. The study recommended that the liver function tests should be routinely investigated during pregnancy to outline any pathologic changes. Focusing on the nurse's role, she should emphasize increasing the patient's level of health literacy regarding the variation of liver function tests. So, it is a must for nurses to develop many skills to enable them to function for this category of patients with low health literacy levels. Also, those patients should be equipped with information-seeking behavior, decision-making abilities, and problem-solving approaches along their health and illness continuum.

Keywords: Pregnancy, nurse, liver function tests, health literacy assessment

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1. Introduction

During pregnancy, physiological changes happen to support the developing baby and equip mothers for labor. A portion of these progressions impacts ordinary laboratory values. It is critical to distinguish between typical physiological changes and pathological conditions *(Soma-Pillay et al., 2016).*

[1]*Correspondence author: Amina Ibrahim Badawy Othman*

The liver is the most valuable organ after the heart. It has profound functions, including metabolism, detoxification, and formation of important compounds such as blood clotting factors and albumin. Changes in liver laboratory profile are normal during pregnancy condition. Despite the rare incidence of severe liver disease during pregnancy, it must be recognized as early as possible to minimize morbidity and mortality among mothers and infants *(O'Grady et al., 2014).*

Maternal hormone concentrations, especially sex hormones, play a critical role in modulating the metabolic and immunologic changes required for a successful outcome in pregnancy. Steroids and peptides were produced by the fetus and placenta secreted into the maternal circulation, stimulating maternal hormone production *(Robinson & Klein, 2012).* The fetal and placental hormones change dramatically during the gestational course and progressively reach a maximum during the last trimester. These hormones have effects on metabolic, synthetic, and excretory hepatic functions. The other physiological changes on the liver are the hemodynamic changes caused by increased plasma volume during the gestational course, leading to hemodilution *(Murray & Hendley, 2020*; *Vishnyakova et al., 2021).*

Good antenatal evaluation of pregnant mothers, especially biomedical liver tests, is crucial for early detection of hepatic disorders and eclampsia during pregnancy, resulting in HELP syndromes (hemolysis, elevated liver enzymes, and low platelets) *(Dacaj et al., 2016).* No single liver function test is available to quantify liver disease; the designation "Liver Function Tests LFTs" describes a panel of laboratory tests profiling discrete aspects of liver function. Liver cell injury or necrosis is measured by determining Glutamate Oxalacetate Transaminase (AST) and Glutamate Pyruvate Transaminase (ALT) levels *(Lee et al. 2012)* while the synthetic liver function is evaluated by determining albumin level. Biliary obstruction is evaluated by measuring alkaline phosphatase and bilirubin levels. The anatomic and physiological changes associated with pregnancy alter liver laboratory profile and physical findings. The identification of these physiological changes is crucial for the diagnosis of liver disease during pregnancy *(Sharma & John, 2020)*

About 3% of pregnancies are troublesome by some form of liver disorders and severe pregnancy-related liver diseases that can have fatal consequences for both mother and baby. The immediate diagnosis and management decision must be weighed up for both maternal and fetal effects. Rapid diagnosis is important for severe cases because immediate delivery is crucial for maternal and fetal outcomes *(Mikolasevic et al., 2018).*

Health literacy is defined as "the degree to which an individual can obtain, communicate, proceed and understand basic health information and services to proper health decision making." It is pertained to literacy and entails people's knowledge, motivation, and competencies to approach, comprehend, sum up and apply health information in order to make judgments and take decisions in everyday life concerning health care, disease prevention, and health promotion to maintain or improve quality of life during the life course *(World Health Organization, 2013).*

Health literacy is a stronger indicator of an individual's health status than income, educational level, employment status, and cultural and ethnic background. Literate individuals participate more actively in economic opulence, have higher income and employment, are more educated and informed, have more community activities participation, and relish a better quality of life *(Sørensen et al., 2015).*

Limited health literacy is correlated with less engagement in health-promoting and disease detection activities, unhealthy choices, more work accidents, poor chronic diseases management (such as diabetes, HIV infection, and asthma), poor medication regimen adherence, increased hospital length of stay and readmission, increased morbidity, and premature death *(Mitic & Rootman, 2012).*

Sørensen et al. (2012) mentioned that many conceptual approaches to health literacy had been developed during the past decade. The European Health Literacy Consortium developed a conceptual model for the European Health Literacy Survey (Fig. 1), which identifies 12 sub-dimensions of health literacy related to the main competencies of accessing, understanding, appraising, and applying health-related information within health care, disease prevention, and health promotion settings *(D'Eath et al., 2012).*

This integrated model of health literacy can serve as a basis for putting up interventions for consolidating health literacy and has provided a conceptual basis for developing and validating measurement tools, emerging the concept of health literacy within health care, disease prevention, and health promotion frameworks *(McPhail-Bell et al., 2013).*

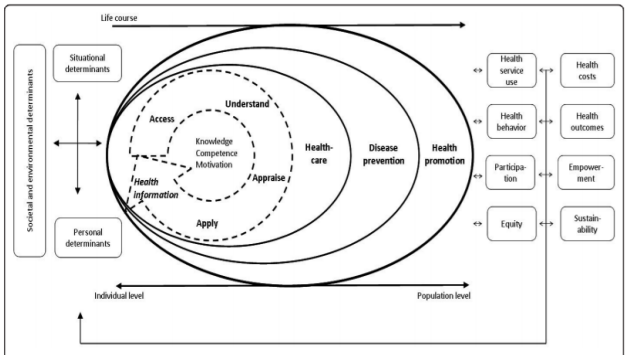


Figure (1): The European Health Literacy Consortium developed a conceptual model adopted from *Sørensen et al. (2012).*

Furthermore, other models including other relevant social dimensions of health and health literacy as independent variables have shown that health literacy influences self-assessed health. Thus, health literacy can be assumed to have a specific direct and independent effect on self-assessed health *(D'Eath et al., 2012).* Weak health literacy competencies have been shown to result in less healthy choices, inappropriate healthy behavior, poorer health, fewer self-care activities, and more length of

hospital stay *(Mitic & Rootman, 2012)*. It was significantly apparent that there was some draining of human and financial resources because of the poor health literacy competencies in the health care delivery system. Policy action to address the health literacy crisis has been slow to emerge at all levels. This publication aims to help to change this situation. The range of evidence supports a wider and relational concept of health literacy that considers both an individual's level of health literacy and the complexities of the contexts within which people act (Fig. 2). Both need to be measured and monitored *(McPhail-Bell et al., 2013)*.

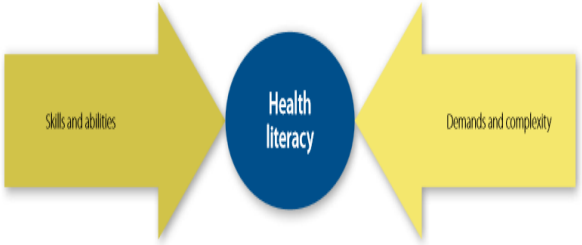


Fig. 2: Interactive health literacy framework.

The nurse has an outstanding role in increasing patients' health literacy with variations in liver function tests. He/she is responsible for providing nursing care that promotes a comfortable experience for pregnant women and provides a positive way to support women and enhance their acceptance of pregnancy. It may also help become a mother and influence a more comfortable delivery experience and better child-rearing. Additionally, the nurse is important in educating the mother regarding the dramatic changes that occur during pregnancy to different body systems and biochemical parameters *(Sharma & John, 2020; Mikolasevic et al., 2018)*.

2. Significance of the study

Health literacy has gained considerable attention across the globe in recent years. Research from around the world is quickly deepening understanding of the vast potential that optimizing health literacy can have in improving health and wellbeing and reducing health inequities. Research studies concluded that low health literacy is associated with increased mortality, medication non-adherence, and readmissions. The relationship between health literacy and self-care is inconclusive. However, when aspects of health literacy, e.g., health system navigation, were also assessed, the impact of health literacy became statistically significant *(McEwing et al., 2017)*.

This area of research is one of the least studied topics among the adult population in general and specifically among pregnant and non-pregnant women. Especially, there was a continuous increase of liver disorders during pregnancy course in last years. Very few studies have been done to find out the direct relation between pregnancy and levels of liver enzymes and assess health literacy among this category of adult patients. So, this study is essential for examining the effect of pregnancy among those women by evaluating liver function tests as a biochemical indicator and determining the patients' level of health literacy regarding the variation of those tests. This research will be a preliminary step for upgrading patients' literacy, directly affecting their health and wellbeing.

3. Aims of the study

This study aimed to:

- Examine the effect of pregnancy on liver function in pregnant women during various trimesters of pregnancy and compare with non-pregnant women.
- Outline prevalence of disturbed liver enzymes during pregnancy as compared to control.
- Establish the reference range of liver function tests during various trimesters of pregnancy among pregnant women.
- Determine the patients' level of health literacy regarding the variation of liver function tests.

4. Subjects & Methods

4.1. Research Design

A descriptive cross-sectional study design was used to conduct this study. The primary goal of using this design was to assess a sample at one specific point in time without trying to make inferences or causal statements.

4.2. Study setting

The study was carried out in a Women's maternity and children hospital in Sakaka Governorate, Saudi Arabia. It is one of the government hospitals mainly concerned with providing care for women throughout their childbearing period and their children. It was under the Ministry of Health umbrella, Saudi Arabia.

4.3. Subjects

A simple random sampling technique was used to select 65 women (54 normal pregnant women and 11 non-pregnant women). The sample was selected from women who attended routine checkups during the study period.

Inclusion criteria

- Women between 20 to 40 years old.

Exclusion criteria

- Women with medical disorders like; hypertension, diabetes, and liver disease.
- Women with a previous history of receiving contraceptive pills or history of liver disease.
- Women with an abnormal pregnancy.

4.4. Tools of data collection

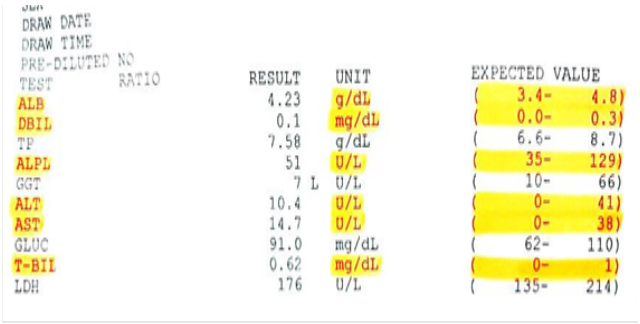
The following tools were used for data collection:

4.4.1. Socio-Demographic and Clinical Data Assessment Record

The researchers developed this tool to collect socio-demographic and clinical data such as personal data, history of medication, comorbid disease, operation, family history of liver disease, and any complaints during pregnancy. Physical examination and vital signs were taken.

4.4.2. COBAS C311 Assessment of Liver Function Tests

The test was conducted in reference to the COBAS C311 User Manual located in the laboratory (COBAS C311 User's Manual). The liver function tests, including Albumin, AST, ALT, ALP, and total bilirubin, were assessed by the clinical chemistry analyzer Cobas c 311.



DRAW DATE DRAW TIME PRE-DILUTED NO TEST RATIO	RESULT	UNIT	EXPECTED VALUE
ALB	4.23	g/dL	(3.4- 4.8)
DBIL	0.1	mg/dL	(0.0- 0.3)
TP	7.58	g/dL	(6.6- 8.7)
ALPL	51	U/L	(35- 129)
GGT	7 L	U/L	(10- 66)
ALT	10.4	U/L	(0- 41)
AST	14.7	U/L	(0- 38)
GLUC	91.0	mg/dL	(62- 110)
T-BIL	0.62	mg/dL	(0- 1)
LDH	176	U/L	(135- 214)

Figure (3): Example for liver function test results.

4.4.3. Health Literacy Management Scale (HeLMS)

It is used to assess health literacy among the studied sample. This tool was free access and used by many researchers. It assesses a range of health literacy constructs important to patients when seeking, understanding, and using health information within the healthcare system *(Jordan et al., 2013).*

Five of the eight domains focus on individual abilities: patient's attitude towards health (Items 2, 7, 13, 23), ability to understand health information (Items 9, 14, 20, 27), communication skills (Items 4, 17, 19), and pro-activeness (Items 3, 6, 25), and skills in using health information (Items 1, 5, 8, 26). The remaining three domains focus on broader factors that influence these abilities: The patient's level of social support (Items 11, 15, 21, 28), socioeconomic status (Items 16, 18, 24), and access to general practice healthcare (Items 10, 12, 22, 29). The HeLMS was chosen for this study because it has high-quality and high psychometric assessments *(Duell et al., 2015).* The HeLMS is an Australian-based tool. It also utilizes a framework informed by interviews with patients from primary care and other healthcare settings *(Joshi et al., 2014, Jayasinghe et al., 2016).* After testing the liver function tests, all women completed filling the HeLMS.

Scoring system

HeLMS is a patient completed instrument containing a 5-point Likert scale assessing the level of 'difficulty' experienced with 29 items across eight domains, with a range from 1 "unable to perform at all" to 5 "experiencing no difficulty."

A mean score of <4 in any of the eight average domain scores of HeLMS was considered insufficient or low health literacy. The total score ranged from 29 to 145. It was classified as

- Low level: 29-67
- Average level: 67-105
- High level: 105-145

The mean total score of the whole tool was compared against these levels to conclude the level of health literacy among the study participants.

4.5. Procedures

The data were collected from February to May 2021. A total of 65 women attending the woman's maternity and children hospital in Sakaka Governorate were selected. The aim of the study was explained to the women. Each woman was interviewed to collect data about the socio-demographic characteristics as personal data, history of medication, comorbid disease, operation, family history of liver disease, and any complaints during pregnancy to assess for inclusion and exclusion criteria.

Each woman was asked to fast about 8 hours before taking the blood sample. About five ccs of blood were collected by venipuncture using disposable sterilized syringes in a dry and clean serum separating tube. Samples were centrifuged at 3000 rpm for five minutes to separate serum and then directly assayed. All women completed filling out the Health Literacy Management Scale (HeLMS) to assess their level of Health Literacy. It assesses a range of health literacy constructs important to patients when seeking, understanding, and using health information within the healthcare system.

Ethical consideration: The study proposal was submitted to the research ethics committee, faculty of applied medical sciences, Al-Jouf University for approval of all procedures for the study. Then a written letter was submitted to the head of maternity and children hospital to get approval for data collection. The agreement for participation of the women was taken after a full explanation of the study's aim to get their approval for participation in the study. Moreover, they were assured that the information was confidential and used only for the research purpose in addition to they could withdraw from the study at any time without giving any rationale.

4.6. Data analysis

The numerical data were collected and computerized using the SPSS (Statistical Package of Social Science) program, version 20. The data description was done using mean ± standard deviation (SD) for normally distributed quantitative data. The analysis of the data was done to test statistically significant differences between groups by

- A one-way ANOVA test was used to compare between more than two groups.
- The post Hoc test (least significant difference) was used to compare intergroup.

Significance was considered when the P-value was ≤0.05 at a confidence interval of 95 %.

5. Results

A total of 65 women were screened. Among the 54 healthy pregnant women, 14 were in the first trimester, 21 in the second, and 19 in the third; 11 non-pregnant women formed the controls. None of the women included had evidence of liver disease. The age range among the controls

and pregnant women was 20-40 years. The clinical data, which implies their history of medication, operation, comorbidities, family history, and pregnancy complaints, the results conveyed similarities between both groups where the majority of the sample in the study group had low educational level (63.7% versus 59.8%). Additionally, those women were unemployed (67.2%), overweight (73.4%), and had insufficient physical activity (78.1%).

Table 1 shows the results of LFTs values for pregnant (according to their trimester) and non-pregnant women. Serum albumin levels were significantly lower ($p \leq 0.05$) during the second trimester (3.67±0.24 g/dL) and third trimester (3.46±0.20 g/dL) when compared to controls (4.25±0.27 g/dL). There was a significant decrease in total protein during second and third trimesters (6.93±0.44 and 6.67±0.39g/dL respectively) as compared with control and first trimester (7.39±0.32 and 7.36±0.60 g/dL respectively). There was no significant change in serum AST between pregnant and non-pregnant women and among the three trimesters in pregnant women.

Serum ALT activity was significantly increased ($P \leq 0.05$) during the third trimester (8.63±4.26 IU/L) compared to the first trimester (12.86±6.27 IU/L) and controls (15.08±8.77IU/L). There was also a significant difference between the second trimester compared to the first trimester.

Serum alkaline phosphatase (ALP) was significantly increased ($P \leq 0.05$) during in the third trimester (110.95±29.01 IU/L) compared with the second trimester (75.38±23.61 IU/L) and the first trimester (73.79±26.96 IU/L) and with the control group (71.37±21.71 IU/L).

Total serum bilirubin concentrations were lower ($P \leq 0.05$) during second (0.20±0.07 mg/dL) and third trimester (0.26±0.12 mg/dL) compared to control (0.42±0.21 mg/dL) and first trimester (0.41±0.35 mg/dL). Means in a row followed by the same letters are not significantly different (ANOVA-post-hoc comparison, $P > 0.05$).

Figure 4 compares liver function tests among pregnant and non-pregnant women throughout the three trimesters. The figure illustrates the decrease in serum albumin, decrease in total protein, decrease in AST, and decrease in ALT.

Figure 5 illustrates the comparison of ALP in control and pregnant women in their three trimesters. There was a progressive increase in ALP of the pregnant women throughout the three trimesters and more than the controls.

Figure 6 elucidates the comparison of the total bilirubin level in non-pregnant and pregnant women. Total serum bilirubin concentrations were lower during the second and third trimesters compared to the first trimester and the controls.

Table 2 in terms of all study subjects, the prevalence rate for an abnormal albumin value (<3.4g/dL) was 12.31%. In non-pregnant, it was zero percentage, while it was 14.81% in pregnant women with a highly statistically significant difference between both groups.

Concerning individual groups, Table 3 shows the prevalence of abnormal albumin (<3.4 g/dl) in different studied groups. It was zero among the non-pregnant and the pregnant in the first trimester, while 9.52% and 31.58% in the second and third trimester, respectively.

Figure 7 illustrates the prevalence of abnormal albumin in the studied groups. They were 9.52% in the second-trimester group and 31.58% in the third-trimester group compared to zero in the no-pregnant and first-trimester groups.

Table 4 demonstrates the present study's reference range of serum albumin, it was highly significant low in pregnant (3.19-4.73 g/dl) compared with non-pregnant (3.62- 4.73 g/dl), total protein is significantly low in pregnant (6.01-7.37g/dl) compared to (6.85-7.83) in the non-pregnant, ALT was significantly lower in pregnant mothers (1.80-26.80 IU/L) as compared with non-pregnant (5.70-34.10 IU/L), but total bilirubin was significantly high (0.12-0.85 mg/dl) in pregnant compared to non-pregnant subjects (0.11-1.57 mg/dL) respectively.

AST was also lower in pregnant mothers, but this difference was statistically non-significant. Also, ALP is higher in pregnant women but did not reach a significant level.

Table 5 illustrates the reference value range in the studied groups compared to the typical reference range adapted from *Girling et al. (1997); Walker et al. (2002). Lefkou, (2010); Walker et al. (2013).* It was observed an increase in the test range of albumin in pregnant women in the current study during different trimesters of pregnancy as compared with the typical reference range (2.8 - 3.7 g/dl), but it still lows as compared with non-pregnant (3.4-4.8 g/dl) especially during the second and third trimester (3.35-4.36 g/dl and 3.19-3.81 g/dl) respectively, the difference between groups was statistically highly significant ($P<.0001$). There was no significant difference in the reference range in serum AST in studied groups compared with the typical reference range.

In the present study, serum ALT reference value range was significantly low ($P \leq 0.05$) during the second trimester (2-22 IU/L) as compared with the typical reference range (6-32 IU/L) and other groups. Serum alkaline phosphatase (ALP) was significantly low ($P<0.0001$) during the third trimester (63-171 IU/L) as compared with the typical reference range (133-418 IU/L) but still high as compared with other groups Table.

The reference value range of the total serum bilirubin was significantly high ($P< 0.05$) during the first, second, and third trimesters compared with the typical reference range for the same groups but still lower than the control group.

Table 6 reveals that the largest percentage of the participants reported "unable to perform" all the health literacy subscales. The table also reveals a low mean score for total health literacy.

Table (1): Comparison of serum LFTs levels in non-pregnant and pregnant women according to trimesters of pregnancy.

Variables	Non-pregnant n=11	Pregnant		
		1st trimester 1,2,3 month n=14	2nd trimester 4,5,6 month n=21	3rd trimester 7,8,9 month n=19
Albumin (g/dl)	4.25±0.27 **a**	4.24±0.31 **a**	3.67±0.24 **b**	3.46±0.20 **c**
Total protein (g/dL)	7.39±0.32 **a**	7.36±0.60 **a**	6.93±0.44 **b**	6.67±0.39 **b**
AST (IU/L)	17.13±7.13 **a**	16.24±4.20 **a**	14.60±2.54 **a**	14.42±3.56 **a**
ALT (IU/L)	15.08±8.77 **a**	12.86±6.27 **ab**	10.12±4.95 **c**	8.63±4.26 **d**
ALP (IU/L)	71.37±21.71 **a**	73.79±26.96 **a**	75.38±23.61 **ab**	110.95±29.01 **c**
Total bilirubin (mg/dL)	0.42±0.21 **a**	0.41±0.35 **a**	0.20±0.07 **b**	0.26±0.12 **b**

**The values are the Mean ± Std. Deviation. **Means in a row followed by the same letters are not significantly different (ANOVA-post-hoc comparison, P > 0.05).*

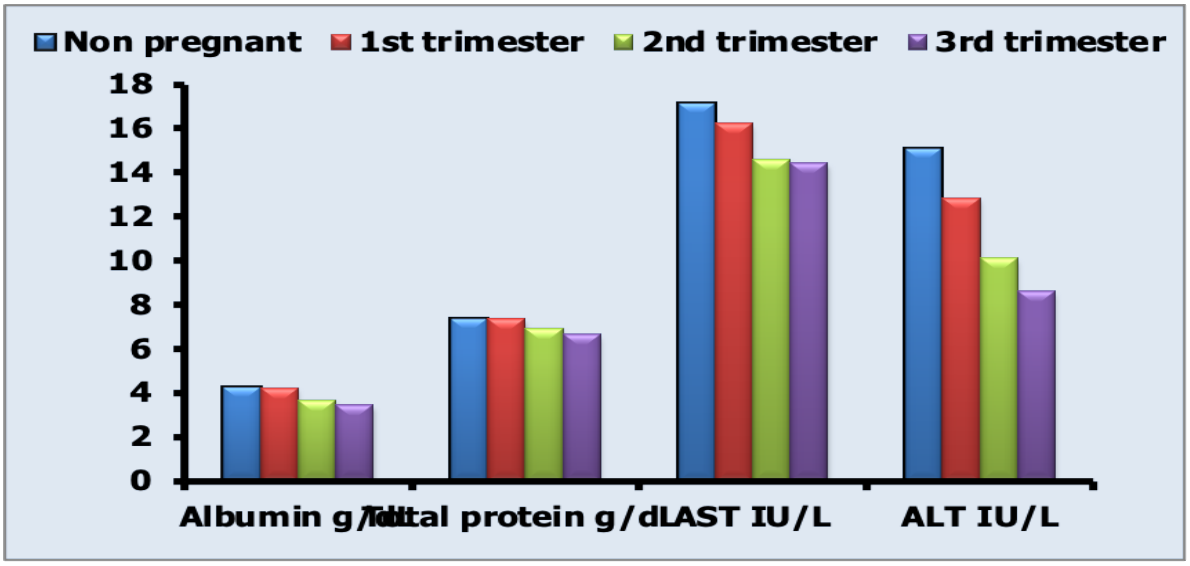


Figure (4): Comparison of serum LFTs (Albumin, total protein, AST, and ALT) levels in non-pregnant and pregnant women according to trimesters of pregnancy.

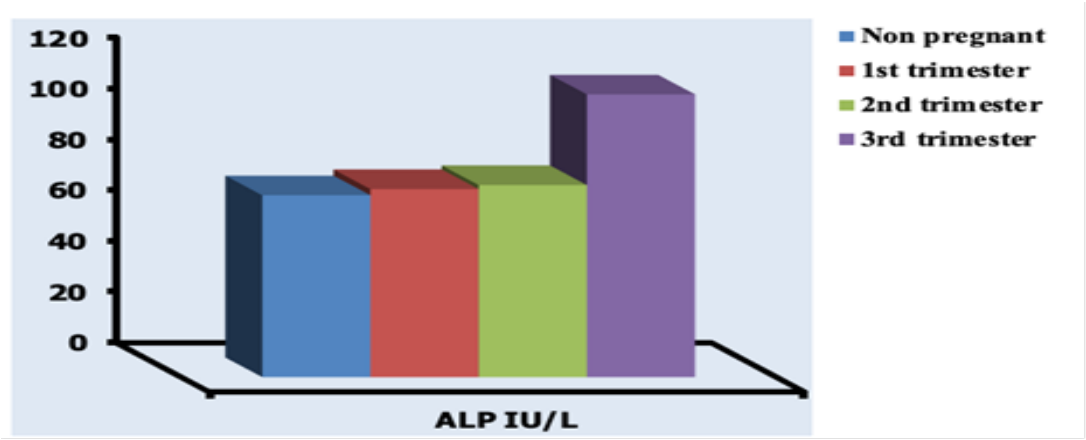


Figure (5): Comparison of serum alkaline phosphatase level in non-pregnant and pregnant women according to trimesters of pregnancy.

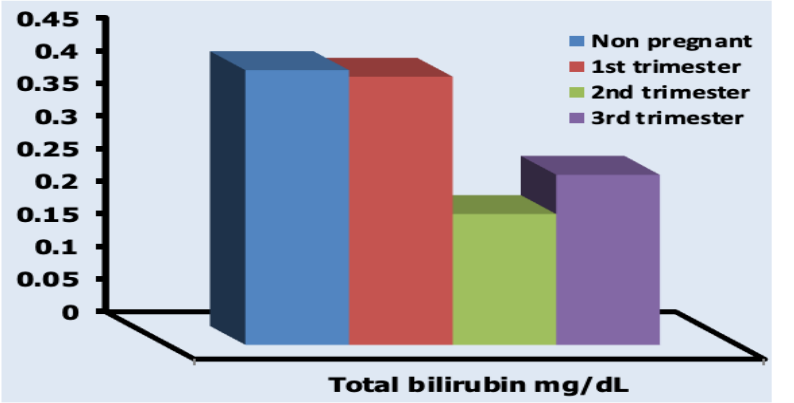


Figure (6): Comparison of serum total bilirubin level in non-pregnant and pregnant women according to trimesters of pregnancy.

Table 2: Comparison of prevalence of disturbed albumin in non-pregnant and pregnant women.

Variables	N. & %	Albumin < 3.4 g/dL	Albumin Normal Range (3.4-4.8 g/dL)	Total	P-value
Non-pregnant	N.	0.00	11	11	<0.000
	%	0.00	100	100	
Pregnant	N.	8	46	54	
	%	14.81	85.19	100	
Total	N.	8	57	65	
	%	12.31	87.69	100	

Table 3: Prevalence of disturbed albumin during various trimesters of pregnancy compared to control.

Variables	Non-pregnant n=11		Pregnant					
			1st trimester 1,2,3 month n=14		2nd trimester 4,5,6 month n=21		3rd trimester 7,8,9 month n=19	
	No.	%	No.	%	No.	%	No.	%
Albumin < 3.4 g/dL	0/11	0%	0/14	0%	2/21	9.52%	6/19	31.58%

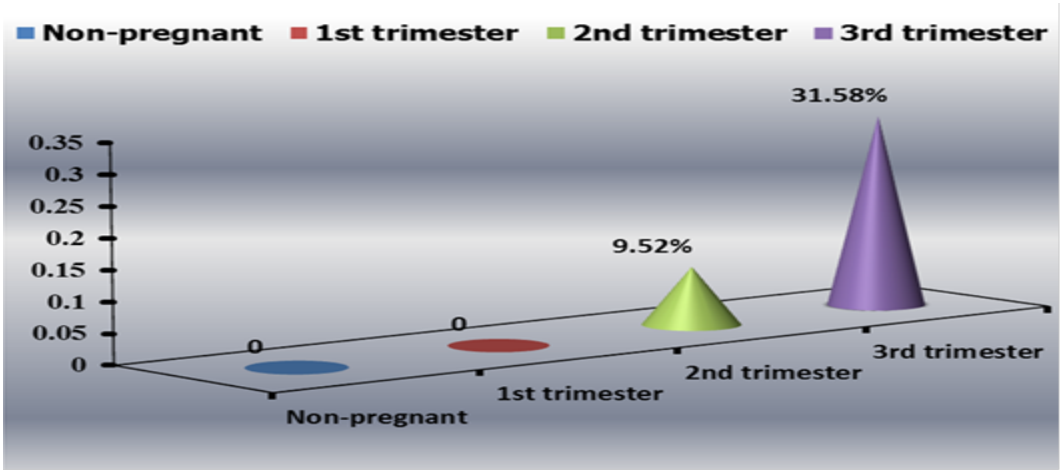


Figure (7): Prevalence of disturbed albumin during second and third trimesters of pregnancy.

Table (4): Reference range of liver function tests between non-pregnant and pregnant women.

Variables	Non-pregnant (n=11)	Pregnant (n=54)	P
Albumin(g/dl)	4.25 (3.62- 4.73)	3.66 (3.19-4.73)	<0.0001
Total protein (g/dl)	7.40 (6.85-7.83)	6.93 (6.01-7.37)	0.011
AST (IU/L)	14.70 (10.70-33.80)	14.25 (9.30-27.30)	>0.05
ALT (IU/L)	11.90 (5.70-34.10)	8.60 (1.80-26.80)	0.017
ALP (IU/L)	66.00 (48.00-122.00)	75.50 (33.00-171.00)	>0.05
Total bilirubin (mg/dl)	0.24 (0.11-1.57)	0.42 (0.12-0.85)	0.046

**Values as median (range).*

Table (5): Reference ranges for liver enzymes by pregnancy and trimester compared to typical reference range*.

Variables	Non-pregnant n=11		Pregnant						P (between groups)
			1st trimester (n=14)		2nd trimester (n=21)		3rd trimester (n=19)		
	Reference range	Test range	Reference range	Test range	Reference range	Test range	Reference range	Test range	
Albumin (g/dl)	3.4-4.8	3.62-4.73	2.8-3.7	3.7-4.7	2.8-3.7	3.35-4.36	2.8-3.7	3.19-3.81	<0.0001
AST (IU/L)	0-38	11-34	10-28	10 -25	11-29	10-28	11-30	10-21	>0.05
ALT (IU/L)	0--41	6-35	6-32	6-25	6-32	2-22	6-32	6-27	0.019
ALP (IU/L)	35-129	48-122	32-100	36-129	43-135	33-137	133-418	63-171	<0.0001
Total bilirubin (mg/dl)	0-1	0.11-1.57	0.05-0.18	0.12-0.85	0.03-0.15	0.11-0.38	0.03-0.16	0.12-0.42	0.004

**Values as range ** Typical reference range is adapted from Girling et al. (1997); Walker et al. (2002), Lefkou (2010), Walker et al. (2013) ***Non-pregnant reference ranges is specified locally to the laboratory reference range.*

Table (6): Number and percentage distribution of the participants' level of health literacy (HeLMS) regarding the variation of liver function tests (N=65).

HeLMS subscales and total scores	Unable to perform at all		Slightly difficulty		Mild difficulty		Moderate difficulty		Experiencing no difficulty	
	No.	%	No.	%	No.	%	No.	%	No.	%
Patient's attitude towards health	41	63.1	6	9.2	5	7.7	6	9.2	7	10.8
Ability to understand health information	44	67.7	3	4.6	4	6.2	8	12.3	6	9.2
Communication skills	50	76.9	5	7.7	2	3.1	4	6.2	4	6.2
Pro-activeness	43	66.2	4	6.2	3	4.6	7	10.8	8	12.3
Skills in using health information.	47	72.3	3	4.6	6	9.2	4	6.2	5	7.7
Patient's level of social support	51	78.5	2	3.1	5	7.7	3	4.6	4	6.2
Socioeconomic status	45	69.2	7	10.8	6	9.2	5	7.7	2	3.1
Access to general practice healthcare.	42	64.6	5	7.7	9	13.8	6	9.2	3	4.6
Total mean score	60.6±6.2									

6. Discussion

Pregnant women experience some physiological changes to sustain fetal growth and development. Both progesterone and estradiol levels increase progressively throughout pregnancy. Hepatic metabolic, synthesis and excretory functions were affected by sex hormones. Away from pregnancy as an adult person, serum liver function tests are essential in managing liver diseases. Routine liver function tests usually include albumin, total protein, AST, ALT, alkaline phosphatase, and total bilirubin *(Mutua et al., 2018; Soma-Pillay et al., 2016)*. This study aimed to examine the effect of pregnancy on liver function in pregnant women during various trimesters of pregnancy and compare with non-pregnant women, outline the prevalence of disturbed liver enzymes during pregnancy as compared to control, the establishment of the reference range of liver function tests during various trimesters of pregnancy among pregnant women and determine the patients' level of health literacy regarding the variation of liver function tests.

The current study measured LFTs in fifty-four healthy pregnant women and eleven controls not receiving oral contraception. None of the women included had evidence of liver disease. In this study, serum albumin levels decreased from the first trimester, and this decrease became progressively more accentuated as the pregnancy advanced (P<0.001), Moreover the prevalence of disturbed albumin levels was more obvious in pregnant as compared with non-pregnant especially during the third trimester (31.58%). This result was supported by previous studies conducted by

Jarvis and Nelson-Piercy, (2020); Goel et al. (2014); Walker et al. (2013).

The cause of decreased albumin level in pregnancy, especially during the third trimester, might pertain to hemodilution following mechanisms because of the increased plasma volume and decreased serum protein concentration *(Soma-Pillay et al., 2016; Costantine, 2014).* Plasma volume was increased by approximately 50% from the 6th to the 36th week of gestation**.** Red cells volume also increased to a lesser extent and more gradually than plasma volume about (20%) *(Chandra et al., 2012).*

Additionally, *Bacq (2013)* reported that the hematocrit decreased by the 24th week and became stable. Consequently, the total blood volume increases with plasma, and red cell volume decreases rapidly after delivery, aided by the blood loss at delivery. This phenomenon of hemodilution should be kept in mind during the interpretation of all serum concentrations during pregnancy *(Soma-Pillay et al., 2016).*

Liver cell injury or necrosis is measured by determining the activity of ALT and AST *(Contreras-Zentella & Hernández-Muñoz, 2016).* The current study demonstrates that; there was no significant decrease in serum AST between pregnant and non-pregnant women, but there was a significant decrease in ALT in pregnant as compared with non-pregnant women. The effects of pregnancy in serum ALT and AST activity levels are somewhat controversial.

This finding was similar *to Bacq's (2013)* study, which stated that ALT and AST values remained below the normal upper limit during pregnancy. In contrast to this finding, *(Mutua et al. 2018)* reported that a slight increase in ALT and/or AST activity has been found during the third trimester. However, in most published studies, serum ALT and AST activity levels do not change during pregnancy or remain within the normal limits compared to non-pregnant women *(Sharma & John 2020).* Thus, it should be emphasized that serum AST or ALT activity values above the normal upper limit during pregnancy should be considered pathologic and lead to further investigations *(Bacq, 2013).*

Regarding the serum alkaline phosphatase (ALP), the current study reveals no significant elevation during the first and second trimesters of pregnant women compared with non-pregnant women. This finding was parallel to earlier findings conducted by *Walker et al. (2013),* who stated that alkaline phosphatase normally increases during pregnancy because of the production of the placental isoenzyme and, by term, may reach three times the normal adult upper reference value.

The present study demonstrates a significant decrease in total serum bilirubin concentrations during the second and third trimesters of pregnant women in the study group compared to non-pregnant women in the control group. These findings were in agreement with previous studies conducted by *Lata (2013),* who reported that free bilirubin concentrations are lower in pregnant women than in non-pregnant controls during all three trimesters, and explained that by the hypothesis that hemodilution could at least partly be responsible for the decrease in bilirubin concentration because albumin is the protein that transports bilirubin.

The current study shows an increment in the reference range of albumin and serum bilirubin in the study group (pregnant women) during different trimesters of pregnancy compared with the typical reference range. However, it is still low compared with the typical reference range of non-pregnant with statistically highly significant (P<0.0001). However, there is no significant difference in AST in the reference range in the study group compared with the typical reference range during the three trimesters. Serum ALT reference range was significantly low during the second trimester compared with the typical reference range to the control group. Additionally, Serum alkaline phosphatase (ALP) was significantly low (P<0.0001) during the third trimester compared with the typical reference range. This finding was supported by *Lefkou (2010); Walker et al. (2013).*

The current study findings reveal that most of the studied sample has a low level of health literacy for all subscales and the total mean scores. Their low educational level can explain it. These results followed *Jayasinghe et al. (2016),* who investigated the impact of health literacy on HRQoL after simultaneous adjustment for both patient demographics and lifestyle risk factors in adults without chronic vascular disease or diabetes. They reported that among low health literacy patients, those who were female, older, not well-educated, unemployed, a smoker, overweight, or had insufficient physical activity were likely to have lower physical health.

In addition, patients with lower health literacy may have difficulties with complex health tasks and ability to seek and understand health information, have limited access to health care *(Schoenthaler et al., 2014),* have a lack engagement with health care providers*,* and have poorer uptake of preventive health care *(Jordan et al., 2013).* Those patients tend to have difficulties with communication, which prevents them from asking questions, clearly expressing their concerns, emotions, and needs to health care providers, and seeking additional services such as support for mental health *(Schoenthaler, 2014).*

These explanations were evidenced in the current study as the highest percentage of participants were "unable to perform at all" concerning their attitude toward heath, unable to understand health information, had not proper communication skills, not proactive, missing skills in using health information, lacking access to general health care services. As a nurse, recognizing low health literacy is important in general practice as there is good evidence to tailoring health-related communication to those patients, which in turn can improve health outcomes *(Schoenthaler et al., 2014).*

7. Conclusion

During normal pregnancy, except for alkaline phosphatase, most values of serum liver function tests that

are done routinely remain below the normal upper limits established in non-pregnant women. Thus, when liver disease is clinically suspected in a pregnant woman, any increase in serum ALT and AST activity levels and serum bilirubin should be considered a pathologic condition and prompt further evaluation. Moreover, most of the studied sample has a low level of health literacy for all subscales and the total mean scores.

8. Recommendations

Liver function tests were important biomedical indicators that reflect any changes in an adult person, and they should be routinely investigated during pregnancy to outline any pathologic changes. Focusing on the nurse's role, she should emphasize increasing the patient's level of health literacy regarding the variation of liver function tests. So, it is a must for nurses to develop many skills to enable them to function for this category of patients with low health literacy levels. So, those patients will be equipped with information-seeking behavior, decision-making abilities, and problem-solving approaches along their health and illness continuum.

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