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Research Paper

Survey to asses Iraqi pharmacists information about acetaminophen

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ABSTRACT

Background: Paracetamol/acetaminophen is sold over-the-counter in both mono- and multi-component formulations. It is among the most popular and widely used analgesic and antipyretic medications in the world. Those who cannot be treated with non-steroidal anti-inflammatory (NSAID). Medicines are advised to use it. The purpose of the current study was to examine and appraise pharmacists in Iraq's knowledge of the most popular medicine, acetaminophen.

Method: By posting a Google form on social media, whatsapp, and telegram and sending the link to all the medical groups of pharmacists, the survey research's data was gathered on October 29, 2021. We asked the Iraqi pharmacists 16 questions, 12 of which were regarding their knowledge of acetaminophen. Four of the questions concerned the pharmacists' characteristics (age, gender, degree, and government). On February 1, 2022, the survey research came to an end

Results: The researches received 145 surveys from different Iraqi Governorates. Twenty to thirty years old make up 97%. 56.6 percent of respondents thought acetaminophen placed future fetuses at risk for ADHD, whereas 43.4 percent actually thought it did. 34.5 percent agreed that chronic acetaminophen usage by pregnant women is safe for the fetus, compared to 65.5 percent who disagreed. While 16.6 percent of respondents disagreed, 83.4 percent of respondents said acetaminophen was safe for expectant mothers.

Conclusion: Most pharmacists had not good information about mechanism of acetaminophen action, while they knew that Acetaminophen active metabolite (APAP) cause liver damage. The study had been showed that most pharmacist were aware about OTC medication .However, about one-third of them had inadequate knowledge of how acetaminophen affects the fetus and may result in ADHD in addition to other acetaminophen indications.

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1. INTRODUCTION

A popular analgesic and antipyretic drug, mono- and multi-component versions of paracetamol/acetaminophen are available over-the-counter. People who cannot be treated with non-steroidal anti-inflammatory drugs (NSAIDs), such as those with bronchial asthma, peptic ulcer disease, hemophilia, or salicylate sensitivity, as well as those under the age of 12 and pregnant women, should take acetaminophen. Pain caused on by osteoarthritis is advised to use it as a first line therapy [1].

Its activity is comparable to that of nonsteroidal anti-inflammatory drugs (NSAIDs), with COX-2 selective inhibitors showing a particularly striking likeness. Although paracetamol tends to be a lesser pain reliever than NSAIDs and COX-2 selective inhibitors, these medications are frequently favored. The method by which paracetamol functions has been contested, despite the drug's similarity to NSAIDs and the idea that it inhibits COX-1 and COX-2 by lowering their peroxidase activity. As a result, the generation of phenoxyl radicals from a key tyrosine residue necessary for the activity of COX-1 and COX-2 cyclooxygenases as well as the synthesis of prostaglandin (PG) is prevented. Paracetamol preferentially prevents the synthesis of PGs and associated components when only trace amounts of arachidonic acid and peroxides are present, but it has little impact when these substances are present in high concentrations. Although paracetamol reduces the little inflammation caused by tooth extraction and works well in other inflammatory tests conducted on lab animals, it is ineffective to reduce the severe inflammation caused by rheumatoid arthritis and acute gout. Paracetamol seems to have a selectivity for COX-2. The apparent COX-2 selectivity of action of paracetamol is indicated by its little antiplatelet activity and well-tolerated gastrointestinal side effects. Myeloperoxidase and other peroxidase enzymes are both inhibited by paracetamol, in contrast to non-selective NSAIDs and selective COX-2 inhibitors. A number of inflammatory illnesses, including atherosclerosis and rheumatic disorders, are associated with suppressed myeloperoxidase, which results in reduced paracetamol oxidation and reduced generation of halogenating oxidants such hypochlorous and hypobromic acid. As a result, paracetamol could aid in slowing the course of some diseases. NSAIDs, COX-2 selective inhibitors, and paracetamol all have effects that are both central and peripheral. NSAIDs, especially selective COX-2 inhibitors, reduce the analgesic effects of paracetamol by inhibiting a number of endogenous neurotransmitter systems, such as the serotonergic, opioid, and cannabinoid systems. Paracetamol's hepatotoxicity at therapeutic doses is a hotly debated subject. The extensive use of paracetamol-opioid combinations in the United States may be to blame for most of the toxicity [2].

Paracetamol is a safe pain medication when used in therapeutic dosages, but when used excessively, it can result in substantial liver damage. Following oral administration, it is easily absorbed from the digestive tract, with systemic bioavailability ranging from 70 to 90%. The pace of stomach emptying, which is sped up by metoclopramide and slowed down by food, propantheline, pethidine, and diamorphine, primarily determines the rate of oral absorption. The rectum is another area where paracetamol is efficiently absorbed. With a volume of distribution of roughly 0.9L/kg, it may disperse quickly and uniformly over the majority of tissues and fluids. Red blood cells bind 10%–20% of the drug. The primary and widespread metabolites of paracetamol are conjugated sulphate and glucuronides (mostly in the liver). A little amount of the medication is transformed into a highly reactive, alkylating metabolite, which glutathione inactivates and excretes in the urine as conjugates of cysteine and mercapturic acid. Excessive paracetamol usage that leads to severe liver necrosis can be avoided because of glutathione depletion and improved reactive metabolite binding to vital cell components [3].

N-acetylcysteine (NAC) is now used to avoid hepatotoxicity, but it also improves outcomes in patients with acute liver failure. NAC's major mechanism of action when taken soon after APAP administration is to preserve intracellular glutathione reserves in order to detoxify the electrophilic APAP metabolite, NAPQI. When taken intravenously, NAC is typically well tolerated, with anaphylactoid responses being the major concern. These responses are most common during loading dosages and can be managed by stopping the NAC infusion, taking antihistamines, and then repeating the loading dose at a slower rate. Current NAC dose is thought to be insufficient to treat massive APAP ingestions. Orthotopic liver transplantation may be an option for patients suffering from acute liver failure. According to a growing body of research, taking acetaminophen (paracetamol) regularly raises the risk of developing allergies in general, asthma in particular, and worsens other respiratory conditions; unwise use of over-the-counter acetaminophen can even cause allergies and asthma to develop in utero [4].

2. METHODOLOGY

By posting a Google form on social media, whatsapp, and telegram and sending the link to all the medical groups of pharmacists, the survey research's data was gathered on October 29, 2021. We asked the Iraqi pharmacists 16 questions, 12 of which were regarding their knowledge of acetaminophen. Four of the questions concerned the pharmacists' characteristics (age, gender, degree, and government). Survey study was completed on February 1st, 2022.

3. RESULTS AND DISCUSSION

The age of researchers received 145 surveys were 97% of them were 20-30 years old, 2% were 30-40 years old and 1% were 50-60 years old. Gender of the participants were 83% percent of them were females and 17% percent of them were males. A 78% of participant pharmacists had a bachelor's degree, 11% had a diploma, 1% had a master's degree and 10% have a PhD. Participant pharmacists were from different Iraqi Governorates and pharmacists from Nineveh had the highest percentage of Participations (20.7%) followed by pharmacist from Karbala (13.8%), Kirkuk (11.1%), Salahalddin (9%), Diyala (8.3%), Babil (7.6%).

3.1 Part Two: Knowledge about Acetaminophen

Do you think that acetaminophen mechanism is PG inhibitor work peripherally to block pain impulse generation?

A majority of pharmacists 68.3 % believed that acetaminophen works as a PG inhibitor to block the generation of pain impulses in the peripheral nervous system. A minority 29 % did not agree, 0.7% did not know, and others believed that it may instead block COX in the central nervous system rather than provide peripheral or central inhibition for PG.

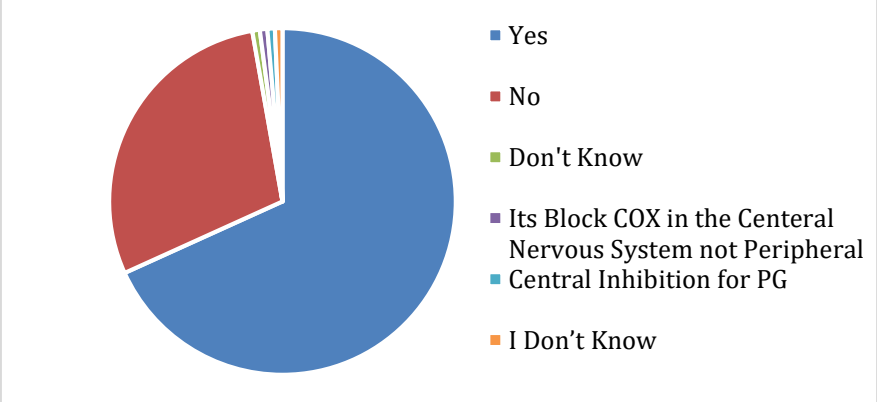

Figure 1. Percent of Participants According to their Information about Mechanism of Acetaminophen

Do you think that acetaminophen indication is (are)?

72% of respondents believed that acetaminophen is used as an antipyretic, 16% as an anti-inflammatory, and 79.3% believed that it is used as an analgesic.

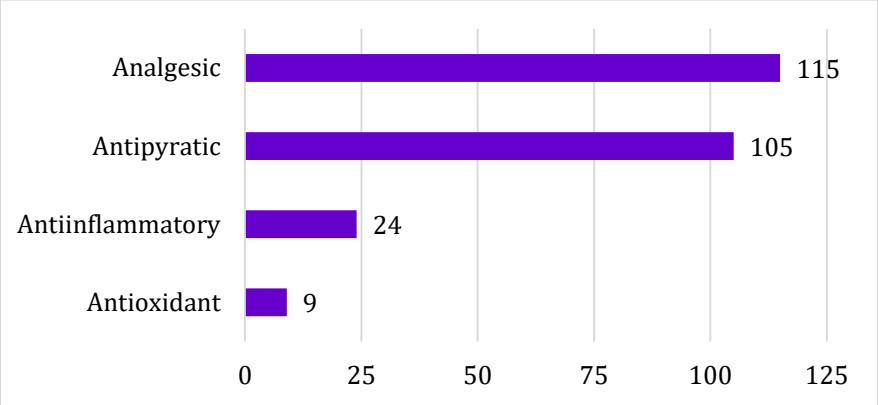

Figure 2. Percent of Participants According to their Information about Acetaminophen Indications

What do you think about acetaminophen acceptable? Dose 82% thought that acetaminophen acceptable dose is 4g, 16% thought it is 8g, 9% thought it is 10g, and 2% said it is 12g.

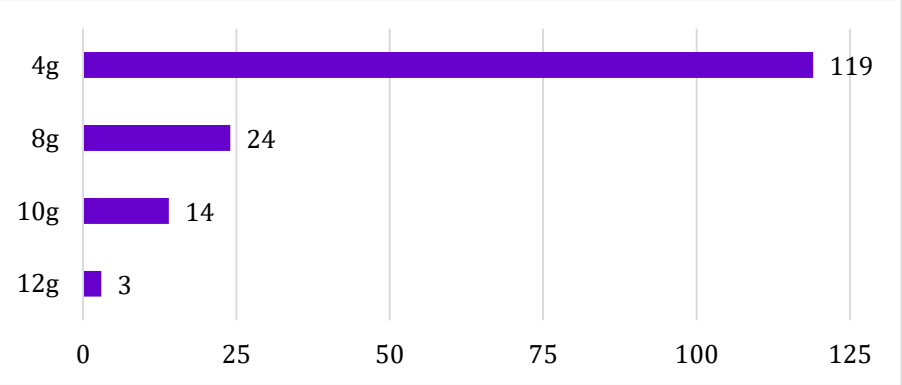

Figure 3. Percent of Participants According to their Information about Acetaminophen Doses

Do you think that acetaminophen has adverse effect on?85 % of pharmacists thought that acetaminophen has adverse effect on the liver, 34% voted on the renal, 11% on the heart and 7.6% voted to the brain.

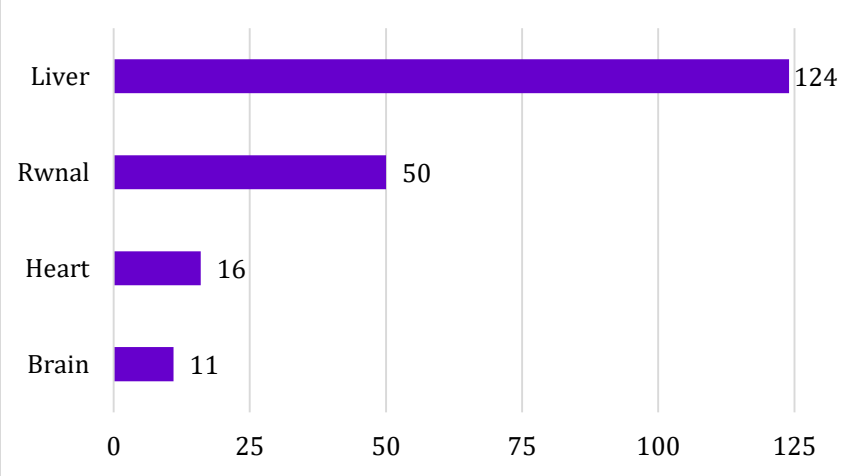

Figure 4. Percent of Participants According to their Information about Acetaminophen Adverse Effects

Do you think that acetaminophen need dose adjustment in renal failure? 58.6% of pharmacists thought that acetaminophen need dose adjustment in renal failure and 41.4 % did not.

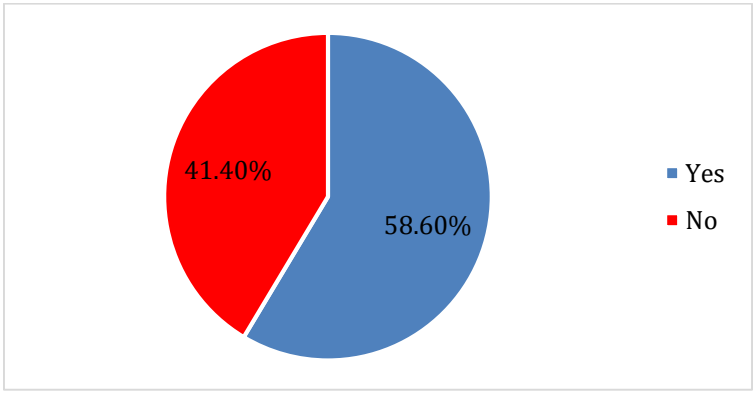

Figure 5. Percent of Participants According to their Information about Acetaminophen Adjustment in Renal Failure

Do you think that acetaminophen need dose adjustment in liver disease? 85.5% of pharmacists thought that acetaminophen need dose adjustment in liver disease and 14.5% did not

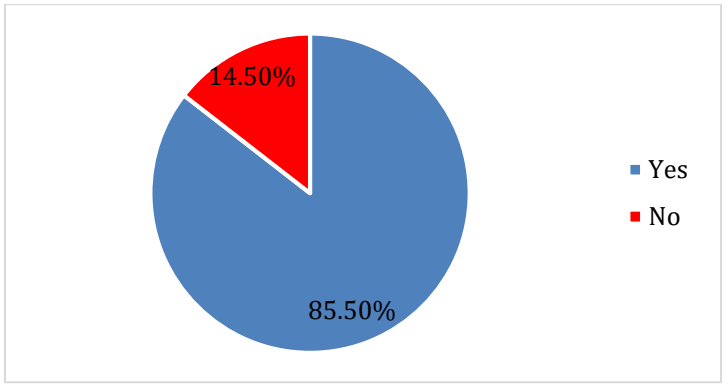

Figure 6. Percent of Participants According to their Information about Acetaminophen Adjustment in Liver Failure

Do you think that acetaminophen itself cause toxicity? 64.8% thought that acetaminophen itself cause toxicity, and 35.2% said the opposite

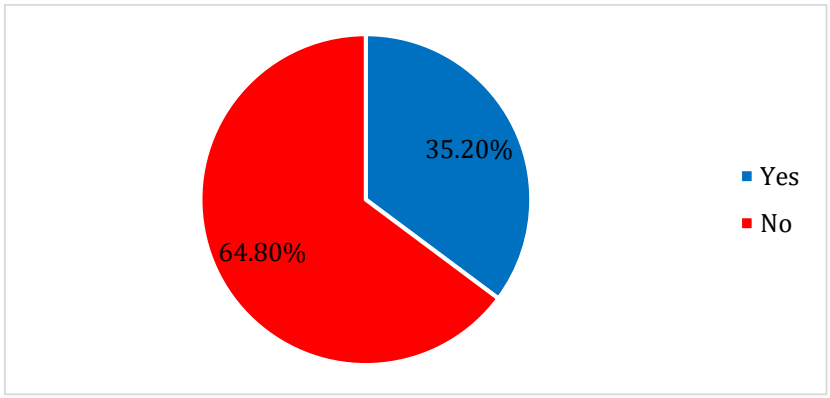

Figure 7. Percent of Participants According to their Information about Acetaminophen Toxicity

Do you think that acetaminophen active metabolite cause toxicity? 74.5% thought that acetaminophen active metabolite cause toxicity, 25.5% did not think that.

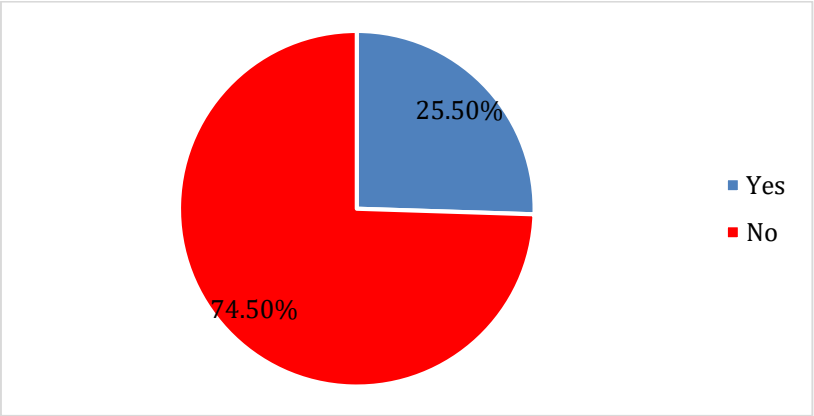

Figure 8. Percent of Participants According to their Information about Acetaminophen Metabolism and Toxicity

Do you think that acetaminophen toxicity can be reverse by antidote? 77.9% thought that acetaminophen toxicity can be reverse by antidote, and 22.1% did not.

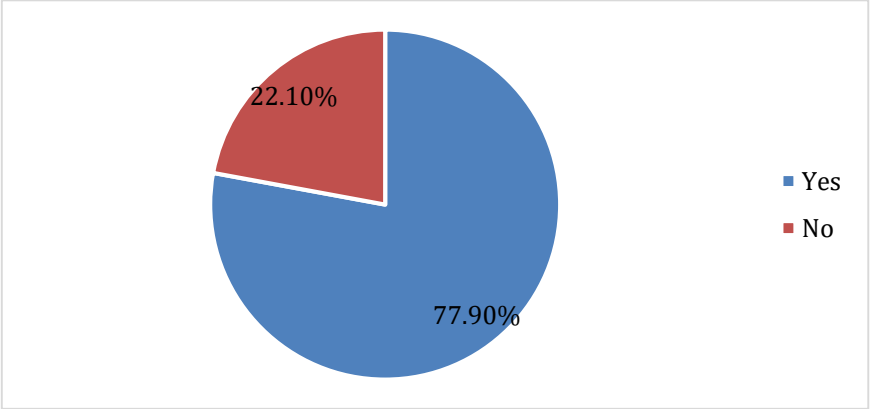

Figure 9. Percent of Participants According to their Information about Acetaminophen Antidote

Do you think that acetaminophen is safe to pregnant woman? 83.4% thought that acetaminophen is safe to pregnant woman, and 16.6% did not.

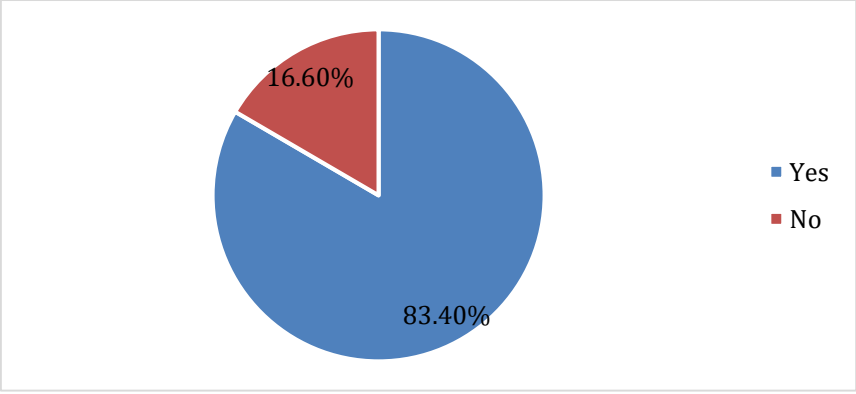

Figure 10. Percent of Participants According to their Information about Safety of Acetaminophen Pregnant Woman

Do you think that acetaminophen is safe to the fetus when pregnant woman taking its chronically? 34.5% thought that acetaminophen is safe to the fetus when pregnant woman taking it chronically, and 65.5% did not.

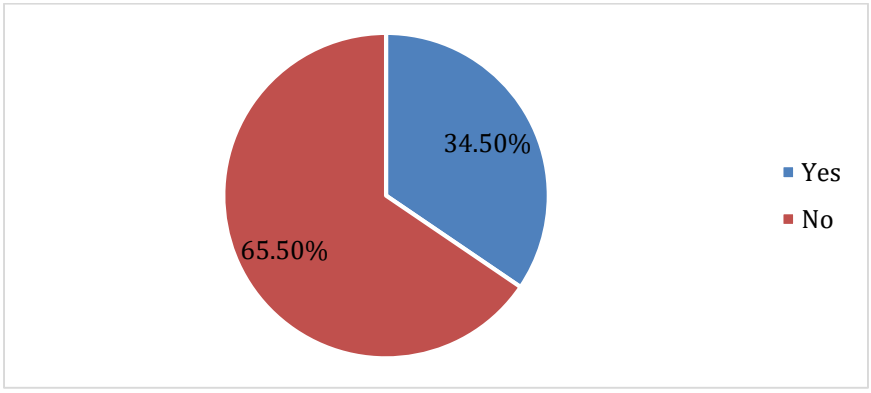

Figure 11. Percent of Participants According to their Information about Safety of Acetaminophen to Fetus

Do you think that acetaminophen increase risk of ADHD to fetus in future? 56.6% thought that acetaminophen increase risk of ADHD to fetus in future and 43.4% did not think that it is increase risk of ADHD.

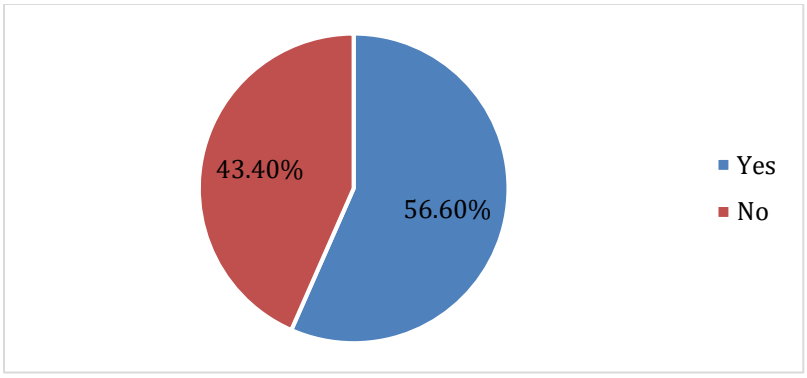

Figure 12. Percent of Participants According to their Information about Acetaminophen Increase Risk of ADHD to Fetus

3.2 Discussion

Acetaminophen suppresses prostaglandin production in the central nervous system, producing analgesic and antipyretic effects, as stated by KarenW. 2019 Show. Acetaminophen is a drug that reduces pain and treats fever. Its modest anti-inflammatory effects are explained by its less significant effects on cyclooxygenase in peripheral tissues (as a result of peripheral inactivation). .68.3 percent of Iraqi pharmacists believed that Acetaminophen mechanism is PG. [5] According to EivindYstrom's 2017 research, short-term maternal usage of acetaminophen during pregnancy was inversely related with ADHD in kids. While 56.6 percent of Iraqi pharmacists believe that acetaminophen increases risk of ADHD, 43.4 percent disagree. Long-term maternal acetaminophen use during pregnancy was strongly associated to ADHD, even after adjusting for use factors. [6] 74.5 percent of Iraqi pharmacists felt that the active metabolite of acetaminophen causes toxicity, contrary to C J McClain's 1999 study, which demonstrated that the medicine itself does not cause acetaminophen-induced liver damage but rather the formation of a toxic metabolite. [7] According to Wei-Xing Zhao in 2017, through processes including its antioxidant and anti-inflammatory characteristics, acetaminophen may provide neuroprotective advantages against LPS-induced cognitive impairment as well as inflammatory and oxidative stress. Acetaminophen was believed to be used as an analgesic by 79.3 percent of pharmacists in Iraq, an antipyretic by 72.4%, an anti-

inflammatory by 16.6 percent, and an antiocxidant by 6.2 percent. [8] The antidote known as N acetyl cysteine, which has been used to treat acetaminophen overdose for almost 50 years, can cure acetaminophen poisoning, according to Kennon Heard's 2012 study. The remedy for acetaminophen intoxication cannot be reversed, according to 22.1% of Iraqi pharmacists. Acetylcysteine is regarded as an effective therapy for avoiding liver damage when administered quickly after an acetaminophen overdose [9].

4. CONCLUSION

The majority of pharmacists were unaware of the mechanism of acetaminophen action, although being aware that its active metabolite, APAP, causes liver damage. The study had been showed that most pharmacist were aware about OTC medication, but nearly one third of them had poor information about the effect of acetaminophen on fetus and may cause ADHD as well as acetaminophen indications.

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Author Contributions Statement

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Zainab Mustafa Mahdi	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓

C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

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

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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