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## ASSOCIATION BETWEEN BLOOD PRESSURE AND C-REACTIVE PROTEIN IN ACUTE ISCHEMIC STROKE

### العلاقة بين ضغط الدم والبروتين التفاعلي C في حالات السكتة الدماغية الإقفارية الحادة

Jasim Muhammed Taib, MRCP

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#### ملخص البحث

**هدف البحث:** على الرغم عدم وضوح السبب الكامن وراء ذلك حتى الآن، إلا أن هناك علاقة بين ارتفاع ضغط الدم والمستويات المرتفعة من البروتين التفاعلي C من ناحية والنتائج السيئة للحالة عند مرضى السكتة الدماغية الإقفارية الحادة من ناحية أخرى. هدفت هذه الدراسة إلى دراسة مستويات البروتين التفاعلي C عند مرضى السكتة الدماغية الإقفارية الحادة (التي تحدث للمرة الأولى) خلال الساعات 24 الأولى من حدوثها وتحديد ارتباطها بمكونات ضغط الدم.

**طرق البحث:** تم إجراء دراسة تحليلية مستقبلية شملت 60 مريضاً من مرضى السكتة الدماغية الإقفارية (التي تحدث لأول مرة) في مدينة الموصل. تم جمع البيانات السريرية للمرضى بما في ذلك العمر، الجنس، وجود ارتفاع في ضغط الدم الشرياني، وجود الداء السكري، مستوى الكولسترول، التدخين، أمراض القلب التاجية، تضخم البطين الأيسر، قياسات ضغط الدم، العلاجات الأخرى والأدوية الخافضة للضغط عند القبول. تم إجراء تخطيط القلب الكهربائي (12 مسرى)، تصوير مقطعي محوسب للدماغ CT لجميع المرضى. تم أخذ عينة دم (1 مل) من المرضى خلال الساعات 24 الأولى من بدء الأعراض السريرية. تم استبعاد مرضى آفات النسيج الضام، الأمراض الخبيثة، إنتان الدم والإنتانات المزمنة من الدراسة وذلك لارتباط هذه الحالات مع ارتفاع مستويات البروتين التفاعلي C.

**النتائج:** لوحظ خلال الساعات 24 الأولى من بدء السكتة الدماغية ارتفاع مستويات البروتين التفاعلي C عند 41 مريضاً (بنسبة 63.3%)، بينما كان البروتين التفاعلي C سلبياً عند 19 مريضاً (بنسبة 31.6%). لوحظ بتقييم العلاقة بين مكونات ضغط الدم ومستوى بروتين C التفاعلي أن ارتفاع ضغط الدم الانقباضي، ارتفاع ضغط الدم الانبساطي، ارتفاع ضغط الدم الوسطي أو الضغط النبضي ارتبطت ارتباطاً هاماً مع ارتفاع مستويات البروتين التفاعلي C بصورة مستقلة عن بقية العوامل التي شملتها الدراسة، حيث كانت قيمة p للارتباط ( $>0.001$ ،  $>0.001$ ،  $>0.001$  و  $>0.014$  على الترتيب)، وهي قيم تعكس وجود أهمية إحصائية كبيرة.

**الاستنتاجات:** إن ارتفاع مستوى البروتين التفاعلي C يعتبر شائعاً لدى مرضى السكتة الدماغية الإقفارية الحادة. كما نتجت هذه المستويات المرتفعة من البروتين التفاعلي C بشكل رئيسي عن زيادة ضغط الدم الشرياني لدى مرضى الدراسة. وفقاً لهذه النتائج، يمكن الاستنتاج بأن ارتفاع ضغط الدم الشرياني الحاد بعد السكتة الدماغية الإقفارية يمكن أن يكون له دور كحافز التهابي يؤدي إلى التهاب الدماغ الإقفاري.

**الكلمات المفتاحية:** ارتفاع التوتر الشرياني، السكتة الدماغية الإقفارية الحادة، الالتهاب، ارتفاع مستوى البروتين التفاعلي C.

#### ABSTRACT

**Objective:** Although the reason is yet not clear, there is a relationship between high blood pressure, and higher

levels of circulating C-reactive protein (CRP) on one hand and poor outcome among patients who suffer from acute stroke on the other hand. The aim of the study was to estimate the level of C-reactive protein in patient

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with a first events of acute ischemic stroke within 24 hours after its onset and to study its association with the blood pressure components.

**Methods:** Analytic prospective study involving 60 patients with first-ever ischemic stroke in Mosul city. Clinical data including age, sex, arterial hypertension, diabetes mellitus, cholesterol level, cigarette smoking, coronary heart disease, left ventricular hypertrophy, blood pressure measurement, concomitant treatments and antihypertensive drugs at admission. A standard 12 lead electrocardiographic tracing and brain computed scan (CT) were done for all the patients. A sample of blood of about 1 ml was taken from the patient within the first 24 hours of clinical symptoms. The study criteria exclude those with connective tissue disease, malignant disease, sepsis and chronic infections, as these conditions associated with elevated level of C-reactive protein.

**Results:** During the 24 hours after the start of the stroke, forty-one (63.3%) patients among the 60 participants of the study have elevated baseline CRP whereas 19 (31.6%) patients showed negative CRP. An increase in systolic, diastolic, mean blood pressure or pulse pressure was significantly associated with an increase in the odds of having an elevated CRP level, independent of other associated study factors with a p-value of <0.001, 0.001, <0.001 and 0.014 respectively, which is statistically highly significant.

**Conclusions:** Elevated CRP level is common among patients with acute ischemic stroke. Also, the high levels of circulated CRP were mainly due to increased blood pressure in the patients under study. According to these findings, we can conclude that acute hypertension after stroke can have a role as an inflammatory stimulus that leads to ischemic brain inflammation.

**Key words:** Hypertension, acute ischemic stroke, inflammation, CRP level.

## INTRODUCTION

Tillet and Francis were the first researchers who in 193 described the C-reactive protein. They demonstrated that the sera of those patients who suffered from acute infection precipitated with a non poetic pneumococcus.<sup>1</sup> C-reactive protein is the kind of protein that leads to this reaction. It has been recently found that CRP can

be seen in the sera of normal individuals though with very low concentrations whose levels are not more than 6 mg/l.<sup>2</sup> The liver makes the CRP as a reaction to the amplification of severe phase reaction cytokines, such as interleukin-1 (IL-1), interleukin 6 (IL-6), and tumor necrosis factor alpha (TNF-alpha), which can only be measured in specialized laboratories.<sup>3</sup>

CRP concentration is mainly dominant when there are inflammations, infections and neoplastic ailments. The following are specific illnesses: rheumatological diseases (e.g. rheumatoid arthritis and Sjogren's syndrome), vasculitis (e.g. Wegner's granulomatosis), and chronic infections (e.g. T.B endocarditis). Recently, it has been shown to be a strong predictor of cardiovascular events.<sup>4,5</sup>

Hypertension is considered to be the most recognized cause of ischemic stroke which also affects the treatment of BP lowering that can prevent the first stroke. However, the pathological and molecular mechanisms that are responsible for vascular disease due to high BP are still indefinite in spite of the fact that it is believed that hypertension could stimulate endothelial expression of cytokines<sup>6,7</sup> and arouse inflammation.<sup>8,9</sup> These records are very interesting taking into consideration that inflammation has a significant role in pathogenesis of atherosclerosis.<sup>10-12</sup> It has also been found that inflammation mainly CRP seems to give expectations on cardio-vascular happenings even among healthy individuals,<sup>13,14</sup> patients who suffer from high vascular risk,<sup>15,16</sup> patients who have either stable or unstable angina,<sup>17-19</sup> and finally with patients of stroke.<sup>20,22-26</sup>

Instances of evident severe inflammatory response are obvious in acute ischemic stroke.<sup>20-22,27,28</sup> The definite cause that develops inflammatory response responsible for ischemic stroke has not been completely explained. Furthermore, the BP response that happens after an ischemic response is inconstant.<sup>29</sup> It has been confirmed by almost all the studies that high BP in the severe phase of stroke has low results.<sup>30-32</sup>

No explanation was given to these results. However, if it is confirmed that that the relationship between BP and stroke outcome is due to inflammatory response, it

would be expected to clearly realize that there is positive links between BP and signs of systemic inflammation like CRP.<sup>33</sup> Researchers have declared that they are not certain if CRP levels are due to high BP that causes inflammation. However, those researchers believe they are very related as they are important for efforts that can prevent strokes due to the fact that high BP is considered the main reason.<sup>34</sup>

If it would be possible to prevent bad BP elevation within years or to reduce them by following anti-inflammatory means of treatments, a new development for early prevention could be introduced. The current study is an attempt to find out if BP levels could be due to inflammatory response in the severe phase among patients suffering from ischemic stroke.

The aim of the study was to estimate the level of C-reactive protein in acute ischemic stroke, and to become familiar with the nature of C-reactive protein and its relationship to cardiovascular disease. Finally, to clarify that an elevated blood pressure leads to increased inflammatory response after stroke.

## METHODS

This study was done in Ibn-Sina teaching hospital in Mosul. The study's protocol included 60 patients, 34 males and 26 females, all of them are hospitalized for a first event of acute cerebral infarction.

The criteria used in this study were to diagnose the first-ever ischemic stroke during 24 hours from the onset of symptoms through a combatable clinical symptoms and physical examination and confirmed by brain CT-scan. The patients excluded from the study included those, acute osteoarthritis or inflammatory disease, diseases that could significantly and noticeably has an effect on their levels of CRP (recent clinical infection within the last 4 weeks, concurrent major renal, hepatic or cancerous disease, recent surgery or major trauma in the previous month).

**C-reactive protein assay:** A sample of blood of about 1 ml taken from those patients within the first 24 hours. If it were not possible to perform the test on the same

day, the serum has to be stored at a temperature between 2 to 8°C, and for a period of not more than 8 days from the date of collection. The serum was examined by latex agglutination test where clear agglutination should appear (positive test) to differentiate it from uniform appearance of the control (negative test).

The dilution method was done as follows:

Dilution	1:1	1:2	1:4	1:8	11:16	11:32
mg/l	6	12	24	48	96	192

So CRP level <6 mg/l considered as normal level, where as a level of 6 mg/l considered as abnormal level.

**Blood pressure:** Blood pressure was measured at the entry of the patient to the hospital. Two measurements were taken on each arm. The lowest measurements on each arm were averaged to obtain the systolic blood pressure (SBP) and diastolic blood pressure (DBP) values.

**Other study variables:** The study also included the following factors: age and gender, other cerebrovascular risk factors (cigarette smoking status; alcohol abuse (>100 g/day); hypercholesterolemia from the history and/or fasting total cholesterol (>200 mg/dl), cardiovascular comorbidity including arrhythmia and impulse conduction disorders; left ventricular hypertrophy as documented by 12 leads ECG; coronary heart disease (angina pectoris or pervious myocardial infarction form the history and a chart review), neuroradiological findings which include leukoaraiosis; single/multiple infarcts; large/small infarcts. The researcher also collected information on the present use of antihypertensive medication

**Definitions:** Cerebral infraction is defined as “a focal neurological deficit of sudden onset that persisted beyond 24 hours in surviving patients, documented by a brain CT scan or an MRI indicating the presence of infarction or the absence of haemorrhage.

Large infarcts: Designated when the sum of largest two diameters divided by two was >1.5 cm.<sup>18</sup> Small infarcts: Designate when the sum is <1.5 cm.<sup>18</sup>

**Statistical analysis:** The following statistical tests were used: X<sub>o</sub> analysis to evaluate the difference in proportions, Fisher's exact test whenever it was fit and t-test for continuous normally distributed variables. The association of blood pressure components (SBP, MAP, PP) were assessed. The variables were both dependent and independent; the independent variables included the blood pressure components among other study factors. On the other hand, the dependent variable was CRP. The CRP was analyzed as dichotomous outcome (CRP ≤ 6 mg/l, i.e. negative or CRP > 6 mg/l, i.e. positive) in logistic regression models. Individual blood pressure component models assessed the effect of a single blood pressure component on CRP.

## RESULTS

Acute ischemic stroke in the study group was found to be higher among the age between 60-69 years for both sexes and over 71.7% are >60 years old.

**Table 1.** shows the age distribution according to the CRP level. The distribution was significant with a p-value <0.01. The mean (mean±SD) age was relatively old (63±9.4) years. Table 2. shows the mean age of the study group in both sexes.

Age (years)	Positive CRP		Negative CRP		Total	
	No.	%	No.	%	No.	%
30-39	0	0	1	100	1	1.7
40-49	1	50	1	50	2	3.3
50-59	8	57	6	43	14	23.3
60-69	19	70.3	8	29.7	27	45
>70	13	81.3	3	18.7	16	26.7

Fisher's exact test, p-value <0.01

**Table 1. Distribution of acute ischemic stroke according to the age.**

Table 3. shows the number and frequency of both genders among the study group. Thirty four (56.6%) patients were males and twenty six (43.4%) were females. The distribution not reach statistical significance.

Approximately 68.3% (n=41) of the patients had a CRP level of 6 ml/l or higher (positive) within 24

hours of the onset of stroke. The rest 31.7% (n=19) had negative result. The average SBP, DBP, MAP, and PP at admission according to CRP level are shown in Table 4. Using t-test for the equality of means in both groups, p-value was <0.001, 0.001, <0.001, and 0.001 respectively, which is statistically highly significant.

Sex	Positive CRP	Negative CRP	Total
Male	61±10.8	62.1±8.8	61.4±1
Female	66.4±7.9	62.8±8.3	65.4±8
Total	63.5±9.9	62.4±8.4	63.2±9.4

**Table 2. The mean (mean±SD) age among the study group in years in both sexes.**

Sex	Positive CRP		Negative CRP		Total	
	No.	%	No.	%	No.	%
Male	22	64.7	12	35.3	34	56.6
Female	19	73.1	7	26.9	26	43.4

Not significant

**Table 3. The number and frequency of both genders among the study group.**

BP	Positive CRP	Negative CRP	p-value
SBP	161.1±26.5	128.4±14.6	<0.001
DBP	92.1±17.1	78.2±5.2	0.001
MAP	115.2±18.4	94.9±6.8	<0.001
PP	69±20.4	50.3±13.8	0.001

**Table 4. The average BP components (USD) at admission among the study group in mmHg.**

Table 5. presents the results of multivariable-adjusted logistic regression models assessing the association of single blood pressure component with elevated CRP level. Model 1 shows that, after adjustment for other study variables, an increase in SBP was significantly associated with an increase in the odds of having an elevated CRP level (OR 9.9, CI 2.8-35.7, p<001). Models 2, 3 and 4 show that, similarly to SBP, an increase in DBP, MAP and PP was significantly associated with an increase in the odds of having an elevated CRP level (OR=38.8, CI 4.7-332.4, p=0.001), (OR=63.9, CI 7.5-546.6, p<0.001), and (OR=7.34, CI 1.49-35.9, p=0.014) respectively, which is statically highly independent of other study variables.

Models	OR	95% CI	p-value
Model 1 SBP	9.99	2.80-35.68	<0.001
Model 2 DBP	38.76	4.66-322.4	0.001
Model 3 MAP	63.99	7.49-546.6	<0.001
Model 4 PP	7.34	1.49-35.9	0.014

Table 5. Logistic regression models assessing the association between single blood pressure components and the odds of having an elevated CRP level.

Table 6 shows the cerebrovascular risk factors in our study group according to the CRP level.

**Cigarette smoking:** Thirty-seven patients (61.7%) never smoked, 26.7% (n=16) was current smokers, and 11.7% (n=7) was previous smokers. The distribution was significant with a p-value <0.05.

**Hypercholesterolemia:** Twenty-seven (45%) patients of the study group had hypercholesterolemia, and the remaining 55% (n=33) hadn't. The Ten distribution was significant with a p-value of 0.025.

**Hypertension:** History of hypertension was positive

Risk factor		Positive CRP		Negative CRP		Total		p-value
		No.	%	No.	%	No.	%	
Cigarette smoking	Never	23	62.2	14	37.8	37	61.7	<0.05
	Current	14	87.5	2	12.5	16	26.7	
	Previous	5	71.4	2	28.6	7	11.7	
Hypercholesterolemia	Positive	23	85.2	4	14.8	27	45	0.025
	Negative	18	54.5	15	45.5	33	55	
Hypertension	Positive	28	80	7	20	35	58.3	0.025
	Negative	13	52	12	48	25	41.7	
Diabetes mellitus	Positive	22	64.7	12	35.3	34	56.7	NS
	Negative	19	73.1	7	26.9	26	43.3	

Table 6. The frequency of cerebrovascular risk factors among study group.

Cardiovascular co-morbidity		Positive CRP		Negative CRP		Total		p-value
		No.	%	No.	%	No.	%	
AICD	Positive	10	90.9	1	9.1	11	18.3	NS
	Negative	31	63.3	18	36.7	49	81.7	
LVH	Positive	6	66.7	3	33.3	9	15	NS
	Negative	35	68.6	16	21.4	51	85	
CHD	Positive	21	95.4	1	4.6	22	36.7	0.001
	Negative	20	52.6	18	47.4	38	63.3	

Table 7. Number and frequency of cardiovascular co-morbidities among study group.

in 58.3% (n=35), and negative in 41.7% (n=25) of the patients. The distribution was significant with a p-value of 0.025.

**Diabetes mellitus:** Thirty-four (56.7%) patients were diabetics, and the rest twenty-six (43.3%) were not diabetic. The distribution not reach statistical significance.

**Cardiovascular comorbidities:** The cardiovascular comorbidities are shown in Table 7.

**Arrhythmias and impulse conduction disorders:** Eleven (18.3%) patients had arrhythmia and impulse conduction disorders and 49 (81.7%) hadn't. The distribution was not significant.

**Left ventricular hypertrophy:** Nine (15%) patients had LVH according to the ECG criteria, and 51 (85%) hadn't. The distribution is not significant.

**Coronary heart disease:** The distribution of CHD among the study group was highly significant was a

p-value of 0.001. The number of patients with CHD was 22 (36.7%), while those with no CHD was 38 (63.3%).

**Neuroradiological findings:** Table 8 shows the neuroradiological findings in the study group.

**Large/small lesions:** Two (3.3%) patients had normal brain CT-scan. Forty-two (70%) patients had large lesions, and sixteen (27.7%) had small lesions. The distribution was significant with a p-value of <0.05.

**Single/multiple lesions:** Forty-four (73.3%) patients had single lesion, fourteen (23.3%) patients had multiple lesions, while 2 patients (3.3%) had normal radiological

finding. The distribution is statistically significant with p-value of <0.05.

**Cortical involvement:** Thirty-six (60%) patients had cortical involvement, and twenty-four (40%) hadn't. The distribution was not significant.

**Leukoaraiosis:** It was positive in thirty-five (58.3%) patients, and negative in twenty-five (41.7%). The distribution was highly significant with a p-value of <0.01.

**Concomitant drugs and antihypertensives used at admission:** These are shown in Table 9. Among six drugs

Neuroradiological findings		Positive CRP		Negative CRP		Total		p-value
		No.	%	No.	%	No.	%	
Infarction size	None	1	50	1	50	2	100	<0.05
	Large	33	78.6	9	21.4	42	70	
	Small	7	43.7	9	56.3	16	27.7	
Infarction number	None	1	50	1	50	2	100	<0.05
	Single	34	77.3	10	22.7	44	73.3	
	Multiple	6	42.8	8	57.2	14	23.3	
Cortical involvement	Positive	26	72.2	10	27.8	36	60	NS
	Negative	15	62.5	9	37.5	24	40	
Leukoaraiosis	Positive	30	85.7	5	14.3	35	58.3	<0.01
	Negative	11	44	14	56	25	41.7	

Table 8. The neuroradiological findings among study group.

Drug		Positive CRP		Negative CRP		Total		p-value
		No.	%	No.	%	No.	%	
Aspirin	Positive	13	61.9	8	38.1	21	35	NS
	Negative	28	71.8	11	28.2	39	65	
Statins	Positive	5	62.5	3	37.5	8	13.3	NS
	Negative	36	69.2	16	30.8	52	86.7	
CCB	Positive	2	28.6	5	71.4	7	11.7	<0.01
	Negative	39	53.6	14	26.4	53	88.3	
ACE-I	Positive	9	52.9	8	47.1	17	28.3	NS
	Negative	32	74.4	11	25.6	43	71.7	
Diuretics	Positive	7	70	3	30	10	16.7	NS
	Negative	34	68	16	32	50	83.3	
B-blockers	Positive	16	61.5	10	38.5	26	43.3	NS
	Negative	25	73.5	9	26.5	34	56.7	

Table 9. The concomitant drugs and antihypertensive used by the patients at admission

used by the patients in the study group (Aspirin, Statins, Calcium channel blockers, ACE Inhibitors, Diuretics, and B-blockers), those taking calcium channel blockers had low levels of CRP in comparison to those not taking the drug. The result was significant statistically with a p-value of <0.01.

## DISCUSSION

The current study has first come up with the finding that shows an increase in BP levels was associated with increased odds of having an elevated CRP level among first-ever ischemic stroke patients. Our study addresses the possible relationship between BP levels and CRP in ischemic stroke. Patients with high CRP level had higher mean SBP, DBP, MAP, and PP, with a p-value of <0.001, 0.001, <0.001, 0.001 respectively, which is statistically highly significant. These findings come in agreement with other studies.<sup>33,35-37</sup>

This study tries to find out whether there was any association between BP levels and CRP in ischemic stroke. The mean age of the study group was 63±9.4 years, while in Mario Di Napoli study<sup>33</sup> it was 72±9.1 years. This difference may be due to shorter life expectancy in our society. Thirty-four (56.6%) patients were males versus 42.2% in Mario Di Napoli study.<sup>33</sup>

High CRP levels were found among old smoker patients who also had coronary heart disease, hypertension, and hypercholesterolemia. They had single large lesions with leukoaraiosis, and they were less likely to take calcium channel blockers. All these findings are consistent with Mario Di Napoli study.<sup>33</sup>

There was no significant difference between the CRP level in those patients taking ACE-I and those who not. This result, in contrast to that in Mario Di Napoli study,<sup>33</sup> (which showed significantly low levels of CRP level in patients taking ACE-I), may be due non-compliance of our patients with the treatment.

Increased risk of stroke and of cardiovascular disease are associated with high BP levels.<sup>38</sup> It has been confirmed that vascular inflammation is the risk for the development of atherosclerosis.<sup>39</sup> In addition to that it

would be possible to predict the risk of an ischemic stroke that might happen later in the future when there is a low-grade inflammation as assisted by CRP.

If the BP is increased the possibility of inflammation is promoted due to the modulation of the biochemical stimuli.<sup>40</sup> It has also been found that the cyclic strain increased soluble adhesion molecule-1 (expression and mRNA expression and secretion of monocyte chemoattractant protein 1 (MCP-1)).<sup>41-44</sup> Furthermore, it has been shown that ischemia in both vivo and vitro helps regulate the expression of Ig-families of adhesion molecules in cerebral endothelial cells and facilitates leukocyte adhesion and transmigration into the brain.<sup>45</sup> Inflammatory activation with dose dependent in expression and release of IL-6 leads to stimulation of human vascular smooth muscle cells by angiotensin\ (Ang) II.<sup>8,9</sup> Moreover, the major cause of IL-6 in stroke appears to be related to cerebral ischemia that induces the expression of IL-6 in neurons and astrocytes, and an ischemic brain tissue.<sup>27,28,46,47</sup>

## CONCLUSIONS

We found that elevated CRP level is common among patients with acute ischemic stroke. Also, the high levels of circulated CRP were mainly due to increased BP in the patients under study. According to these findings, we can conclude that acute hypertension after stroke can have a role as an inflammatory stimulus that leads to ischemic brain inflammation.

## RECOMMENDATIONS

Patient with established acute stroke and high CRP levels should be followed closely and other risk factors in those patients should be treated accordingly. BP seems to be related high levels of CRP. Accordingly it is important to revise the existing approach of treating of acute hypertension after stroke.

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## CONTRIBUTIONS OF ACQUIRED ANATOMICAL ABNORMALITIES OF FALLOPIAN TUBES IN SOME GYNECOLOGICAL DISORDERS IN MOSUL PROVINCE/IRAQ: A SINGLE CENTER STUDY

دور الشذوذات التشريحية المكتسبة في قناتي فالوب  
في بعض الاضطرابات النسائية في محافظة الموصل في العراق: دراسة وحيدة المركز  
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### ملخص البحث

**هدف البحث:** يعتبر انقطاع الطمث والعقم من المشاكل الصحية ذات التأثيرات السلبية في المجتمع، والتي ولسوء الحظ تعاني من قلة التقييم رغم أهميتها وخاصة في الدول النامية. توجد عدة عوامل تشريحية كذلك المتعلقة بقناتي فالوب تؤدي إلى قلة أو انقطاع الطمث، قلة الخصوبة، فقدان الحمل وإلى مضاعفاتٍ توليدية أخرى. لا تزال المعلومات المتوافرة حول دور الشذوذات التشريحية في قناتي فالوب في هذه الاعتلالات في محافظة نينوى/العراق قليلة. تهدف هذه الدراسة إلى تحديد حدوث مختلف الشذوذات في قناتي فالوب لدى الإناث اللواتي يعانين من العقم مع/أو بدون انقطاع الطمث في محافظة نينوى.

**طرق البحث:** تمت الدراسة في مستشفى البتول التعليمي للأمهات غربي محافظة نينوى في شمال العراق. شملت الدراسة تحليل بيانات أخذت من تقارير 1682 مريضة أدخلن إلى مستشفى البتول التعليمي للأمهات إلى وحدة العقم بسبب معاناتهن من العقم أو انقطاع الطمث. خضعت جميع الحالات المشمولة في هذا العمل إلى الفحص بتنظير البطن، أما حالات العقم سواءً مع أو بدون انقطاع الطمث فقد تم فيها أيضاً إجراء تصوير الرحم والأنابيب الظليل.

**النتائج:** تم تقسيم البيانات حسب الحالات إلى أربع مجموعات. شملت المجموعة الأولى النساء اللواتي يعانين من انقطاع الطمث البدئي وعددهن 81، كانت قنوات فالوب طبيعية في 51 (بنسبة 62.9%) من أصل 81 حالة، بينما أظهر تنظير البطن وجود شذوذات خلقية في قنوات فالوب في 30 حالة (بنسبة 37%). أما في المجموعة الثانية التي شملت النساء بحالات العقم البدئي وعددهن 1069 فقد لوحظ وجود قنوات فالوب طبيعية في 714 من أصل 1069 حالة (بنسبة 66.7%)، وشذوذات مختلفة في قنوات فالوب في 26.8% من أصل 1069 حالة عقم، حيث شملت هذه الشذوذات انسداد الأنابيب في 148 حالة (بنسبة 13.7%)، استسقاء وتوسع الأنابيب في 44 حالة (بنسبة 4%) من 1069 حالة، كما لوحظت مظاهر التدرن في 5 حالات (بنسبة 0.4%)، والتهاب الأنابيب في 30 حالة (بنسبة 2.8%) من حالات العقم (1069 حالة)، في حين ظهرت التغييرات المكتسبة المختلطة في 60 حالة (بنسبة 5.6%). من جهة أخرى شهدت 68 حالة (بنسبة 6.3%) وجود شذوذات خلقية مختلفة في الأنابيب، كما لوحظت شذوذات مكتسبة في الرحم لدى 123 حالة (بنسبة 5.11%) من 1069 حالة. شملت المجموعة الثالثة 9 نساء يعانين من انقطاع الطمث البدئي والعقم البدئي، كانت قنوات فالوب طبيعية في حالة واحدة (بنسبة 11%)، وتبين وجود شذوذات خلقية في قنوات فالوب في 8 حالات (بنسبة 88%). أما المجموعة الرابعة فشملت 523 من النساء بحالات العقم الثانوي، وهنا كانت قنوات فالوب طبيعية في 336 حالة (بنسبة 64%)، بينما لوحظت شذوذات مكتسبة في قنوات فالوب في 179 حالة (بنسبة 34%)، في حين وجدت تشوهات خلقية في الأنابيب في 8 حالات (بنسبة 1.5%) في هذه المجموعة. من ناحية أخرى لوحظت شذوذات مكتسبة في الرحم في 64 من أصل 523 حالة (بنسبة 12%).

**الاستنتاجات:** كانت العوامل المكتسبة في الأنابيب هي السبب الأكثر شيوعاً لحالات العقم. يجب على الأطباء السريريين الأخذ بالاعتبار العوامل المؤدية إلى أمراض الأنابيب المختلفة (وخاصةً الإنتانات التي قد تؤدي إلى انسداد الأنابيب)، الأمر الذي سيساعد في الحد من معدلات العقم.

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## ABSTRACT

**Objective:** Amenorrhea and infertility are health problems that adversely affect the society, however; for unfortunate reasons; they are underappreciated especially in developing countries. Several anatomical factors as the tubal factors can lead to hypomenorrhea or amenorrhea, infertility, pregnancy loss, and other obstetric sequels. Little is known about the contributions and frequencies of the anatomical fallopian tubal factors in such disorders in Nineveh Province/Iraq. The aim of this study was to determine the frequencies of different fallopian tubes abnormalities in females who presented with infertility and/or amenorrhea in Nineveh province.

**Methods:** This work was done in Al-Batool Maternity Teaching hospital in the west of Nineveh Province in Northern Iraq. It included analysis of data which were obtained from the reports of 1682 women who were admitted to Al-Batool Maternity Teaching Hospital as they were referred to the infertility institute either as they are complaining from infertility and or amenorrhea. All cases that enrolled in the present work had undergone laparoscopy, while laparoscopic examination was done beside hysterosalpingography in women who had history of infertility and amenorrhea.

**Results:** Data of the present work were grouped according to the complaints of cases into 4 groups: Group 1 includes cases presented with history of primary amenorrhea (n=81). Normal fallopian tubes were noticed in 51 (62.9%) out of 81 cases, while laparoscopic examination of 30 (37%) out of 81 cases showed different congenital tubal abnormalities. Group 2 included women who suffer from primary infertility (n=1069). Normal fallopian tubes were noticed in 714 (66.7%) out of 1069 cases. Different tubal abnormalities were noticed in 26.8% of 1069 infertile patient, including tubal occlusion in 148 (13.8%) out of 1069 women, hydrosalpinx in 44 (4%) out of 1069 cases. Features of tuberculosis were detected in 5 (0.4%) out of 1069 women. Tubal inflammation was shown in 30 (2.8%) out of 1069 cases, while 60 (5.6%) out of 1069 women revealed mixed acquired findings. Sixty-eight (6.3%) out of cases showed different congenital tubal abnormalities. Acquired uterine abnormalities were shown in 123 (11.5%) out of 1069 cases. Group

3 includes cases presented with history of primary amenorrhea and primary infertility (n=9). Normal tubes were shown in 1 (11%) out of 9 women, 8 (88.8%) out of 9 women presented with congenital anatomical tubal abnormalities. Group 4 included 523 women with secondary infertility. Normal tubes found in 336 (64%) out of 523 women, while 179 (34%) showed different tubal acquired abnormalities. Different congenital tubal abnormalities were noticed in 8 (1.5%) out of 523 women in this group. On the other hand, acquired uterine abnormalities were shown in 64 (12%) out of 523 cases.

**Conclusions:** Acquired tubal factors are the most frequent cause of infertility. The clinicians should take in considerations the factors that lead to different tubal diseases (especially the infectious one that result in tubal occlusion), and that may help to achieve a decrease in rates of infertility.

## INTRODUCTION

Several anatomical factors can lead to amenorrhea, hypomenorrhea, fertility problems, pregnancy loss, and other obstetric sequels.<sup>1,2</sup> Infertility involves about 15% of the population. One couple approximately from six couples searching for the clinicians' advices at some time in their lives to solve this health problem.<sup>3</sup> In addition, amenorrhea, either primary or secondary, is manifested frequently in primary care centers and infertility units.

The fallopian tubes allowing passage of the ova from the ovary to the uterine cavity also they allow passage of sperm to ampulla of the tube to fertilize the ova. They developed from the cranial part of the paramesonephric ducts. In fact, tubal factors represent one of the important female anatomical causes of infertility.<sup>4</sup> About 25% to 35% of women that are looking for infertility treatment are diagnosed with tubo-peritoneal disorders.<sup>5,6</sup>

Beyond history taking, clinical examination, seminal fluid analysis and ovulatory status assessment, patency of fallopian tubes must be the next step urgently. A globally accepted test to check if tubes patent or not have not been reached. A spectrum of investigation techniques is utilized. Hysterosalpingography (HSG), laparoscopic dye hydrotubation are of them.<sup>7,8</sup>

The tubal anatomical causes of infertility include congenital and acquired anomalies. Pelvic inflammatory disease found to be one of the frequent factors for fallopian tubes damage.<sup>4</sup> On the other hand, these tubes can be influenced and injured by uterine myoma, postoperative adhesive lesions or endometriosis and indirectly contribute in infertility and amenorrhea. Infertility may result from direct anatomical uterine causes including endometriosis, and congenital/acquired uterine anomalies (as myomas disrupting the uterine cavity).<sup>9-11</sup>

In certain cases, although there are trials to find the exact etiology of infertility, the causes of this common health problem still not known. In general, hysterosalpingography and laparoscopy with dye are useful to diagnose the tubal lesions.

Al-Batool Maternity Teaching Hospital is the site where most of females in Nineveh Province presented with infertility and or amenorrhea and seeking for diagnosis and treatment of their conditions.

The contributions of tubal factors in cases suffering from infertility and amenorrhea have not been fully studied in our locality, so this study aims to identify the frequency of tubal abnormalities in females suffering from these problems in Nineveh Province/Iraq using laparoscope.

## METHODS

This work reviewed patient medical records of 1682 women who were admitted to Al-Batool Maternity Teaching Hospital in Nineveh Province in Iraq. These women were referred to the infertility institute either by their specialists or they came from the outpatient clinic or from the consultatory clinic as they are complaining from infertility and or amenorrhea.

All cases that enrolled in the present work had undergone laparoscopy while laparoscopy with dye test examination was done beside HCG in women who had history of infertility alone or with amenorrhea. Laparoscopy was performed in the Infertility institute at Al-Batool Maternity Teaching Hospital in order to gain

the panoramic visualization of the peritoneal cavity, right ovary and left ovary, outside of the tubes and the uterus.<sup>13</sup> During the laparoscopy, inspection of pelvis for any adhesions or endometriotic spots. Any structural abnormalities of uterus and tubes were noted. Fallopian tubes patency was checked via injecting a dilute solution of methylene blue through cervix by Rubin's Canula. Reviewing of reports were for the findings in tubes, myometrium, or endometrial and for any variations in anatomy. Tubal acquired abnormalities were classified into: tubal occlusion, hydrosalpinx, features of tuberculosis, inflammation and mixed acquired abnormalities<sup>14</sup> while uterine acquired abnormalities were recorded (adenomyosis or fibroids).

**Procedure of laparoscopy:**<sup>13,14</sup> After receiving anesthesia, a needle was inserted into the abdomen. Then to facilitate the viewing of organs and structures, a gas was injection into the abdomen. After that, removing of the needle was done and insertion of a small camera on a laparoscope via a small incision, then a second incision was done to insert a probe (which help in moving or lifting any structure). Using the camera, examination of abdominal structures was performed by the gynecologist. According to the view that is shown by the examiner, additional steps may be done, as injection of a dye through the uterine tubes to assure their patency (with an attempt to open the blocked tube(s)), scar removing or adhesion removing, and correcting abnormalities may be done via a third in the abdomen to insert instruments to conduct these additional procedures. Finally, removing of the used tools and equipment by the gynecologist with stitching up the incisions. Females were remained under observation for a few hours to be sure that there is a full recovery and that there are no complications.

The frequency of detection of each abnormality was calculated.<sup>14,15</sup> Microsoft Excel for Windows was used for setting up the database file for facilitating data entry and retrieval. Performing of statistical analysis was done via SPSS version sixteen for Windows. Comparison between the frequency of congenital and acquired uterine anomalies were measured using the Pearson 2 test, when  $p < 0.05$  so statistical significance was considered.<sup>15</sup>

**RESULTS**

The laparoscopic reports of 1682 women who were suffering from infertility and or amenorrhea were retrospectively analyzed in this work. The data of the present work were grouped according to the complaints of cases and were categorized into 4 groups:

**Group 1** included cases presented with history of primary amenorrhea (n=81). Their mean age was 19.3 years (range 15-23 years) with mean duration of their complaint 2.30±1.4 years (range 1 to 5.8 years). Normal fallopian tubes were noticed in 51 (62.9%) out of 81 cases, while laparoscopic examination of 30 (37%) out of 81 cases showed different congenital tubal abnormalities. No any case of acquired tubal or uterine abnormalities was detected in this group.

**Group 2** included women who suffer from primary infertility (n=1069). They aged from 14-44 years with mean of 27 years. They had primary infertility ranging from 1-19 years. Normal fallopian tubes were noticed in 714 (66.7%) out of 1069 cases (**Figure 1**). Different acquired tubal abnormalities were noticed in 26.8% of 1069 infertile patient, including tubal occlusion in 148 (13.8%) out of 1069 women, while hydrosalpinx in 44 (4%) out of 1069 cases (**Figure 2**). In addition, features of tuberculosis were detected in 5 (0.4%) out of 1069 women which was determined when there is beaded appearance of fallopian tubes. On the other hand, tubal inflammation was shown in 30 (2.8%) out of 1069 cases, while laparoscopic examination of 60 (5.6%) out of 1069 women revealed mixed acquired findings. On the other hand, laparoscopic examination of 68 (6.3%) out of

cases showed different congenital tubal abnormalities. In addition, acquired uterine abnormalities were shown in 123 (11.5%) out of 1069 cases.

**Group 3** included women who were presented with primary infertility and primary amenorrhea (n=9). Mean age was 19.5 years with range 18-21 years. The duration of their primary infertility and primary amenorrhea was ranged from 1-15 years with mean of 3 years. Normal tubes were shown in 1 (11%) out of 9 women, while the laparoscopic assessment revealed 8 (88.8%) out of 9 women presented with congenital anatomical tubal abnormalities. On the other hand, no any acquired uterine or tubal abnormalities were detected.

**Group 4** included 523 women with secondary infertility. Their ages range between 18 to 45 years (mean 29.23±5.1 years). The mean of duration was 5.19±2.35 years (range from 2 years to 17 years). The laparoscopic examination revealed normal tubes in 336 (64%) out of 523 women, while 179 (34%) showed different tubal acquired abnormalities including tubal occlusion in 101 (19%) out of 523 of women, hydrosalpinx in 20 (3.8%) out of 523 cases. In addition, features of tuberculosis were detected in 3 (0.5%) out of 523 women, inflamed tubes were seen in 26(4.9%) out of 523 and finally more than one lesions are noticed in 29(5.5%) out of 523 women. In addition, different congenital tubal abnormalities were noticed in 8 (1.5%) out of 523 women in this group. On the other hand, acquired uterine abnormalities were shown in 64 (12%) out of 523 cases. The frequencies of different tubal and uterine abnormalities in different study groups were shown in Tables 1, 2 and 3.

Fallopian tubes abnormalities	Primary amenorrhea (N=81)	Primary infertility (N=1069)	Primary infertility and primary amenorrhea (N=9)	Secondary infertility (N=523)
Tubal occlusion	0 (%)	148 (13.8%)*	0 (0%)	101 (19%)*
Hydrosalpinx	0(%)	44 (4%)	0 (0%)	20 (3.8%)
Features of tuberculosis	0 (%)	5 (0.4%)	0 (0%)	3 (0.5%)
Inflammation	0 (%)	30 (2.8%)	0 (0%)	26 (4.9%)
Mixed acquired abnormalities	0 (%)	60 (5.6%)	0 (0%)	29 (5.5%)
Total	0 (0%)	287 (26.8%)*	0 (%)	179 (34%)*

\*p≤0.5 is considered as significant.

**Table 1. The frequencies of various acquired anatomical abnormalities in fallopian tubes of the four study groups.**

## DISCUSSION

Infertility and childlessness represent one of the frequent underestimated health problems in developing countries and it adversely affect their society.<sup>16</sup> Normal fertility can be affected by spectrum of factors like age, anatomy, ovulation, and sperms' quality. Potentially the causes of infertility are categorized into male and female causative class including anatomic, endocrine, genetic beside the behavioral category.<sup>17</sup>

There are multifactorial etiologies of female infertility that need comprehensive assessment as clinical examination, hormonal testing, besides imaging.<sup>14</sup> There is a need of organized and serial evaluation as the infertility represents a tragedy for many populations. Particularly, assessment of the woman seeking for conceiving necessitates evaluation of her uterus, endometrium, and uterine tubes for the potential abnormalities that prevent her to achieve normal

pregnancy. The best strategy for assessment of these regions in usual is the involvement of some combinational method of HSG and hysteroscopy, transvaginal sonography, or laparoscopy with or without dye test.<sup>18</sup> This study aims to identify the contributions of tubal factors in some gynecological disorders including infertility and amenorrhea by laparoscopy (with or without dye test) as this procedure is frequently used in many clinical articles on tubal cause of infertility as the reference standard. Some studies questioningly discussed the using of laparoscope with dye test as a golden standardized method.<sup>14</sup>

Laparoscopic assessment of 1592 infertile women revealed that acquired tubal findings shown in 466 (29%) of these cases, while acquired uterine abnormalities reported in 17.7% of these infertile women. These findings are consistent with those of others who revealed that tubo-peritoneal lesion was shown in 25-35% of cases presented with infertility.<sup>5,6</sup>

Fallopian tubes findings	Primary amenorrhea (N=81)	Primary infertility (N=1069)	Primary infertility and primary amenorrhea (N=9)	Secondary infertility (N=523)
Combined agenesis (Mayer-Rokitansky-Kauster syndrome)	8 (9.8%)	0 (0%)	4 (44%)*	0 (0%)
Tubal agenesis	2 (2.4%)	8 (0.7%)	3 (33%)*	5 (0.9%)
Tubal dysgenesis	0 (0%)	4 (0.3%)	0 (0%)	3 (0.5%)
Short tubes	10 (12%)	19 (1.7%)	1 (11%)	0 (0%)
Rudimentary tubes	10 (12%)	35 (3%)	0 (0%)	0 (0%)
Tubal cyst	0 (0%)	2 (0.1%)	0 (0%)	0 (0%)
Total	30 (37%)*	68 (6.3%)	8 (88.8%)*	8 (1.5%)

\*p<0.5 is considered as significant.

Table 2. The frequencies of different congenital anatomical abnormalities in fallopian tubes of in the various study groups.

Uterine findings	Primary amenorrhea (N=81)	Primary infertility (N=1069)	Primary infertility and primary amenorrhea (N=9)	Secondary infertility (N=523)
Endometriosis	0 (0%)	45 (4%)	0 (0%)	23 (4%)
Fibroid	0 (0%)	71 (6.6%)	0 (0%)	30 (5.7%)
Uterine adhesion	0 (0%)	0 (0%)	0 (0%)	2 (0.3%)
More than one subtype	0 (0%)	7 (0.6%)	0 (0%)	9 (1.7%)
Total	0 (0%)	123 (11.5%)	0 (0%)	64 (12%)

Table 3. The frequencies of different acquired uterine abnormalities among various study groups.

In addition, this study revealed that tubal occlusion was reported in 249 (15.6%) out of 1592 infertile women. These findings are in agreement of those of others.<sup>14,19</sup> The pathological occlusion resulting from post-infectious fibrosis; or technical problem. Sometimes, thick endometrium may act as a valve.<sup>20</sup> A higher rate of occlusion was found in a study of Aslam *et al* who attributed that to high incidence of PID due to lack of trained health professionals and defect in sterilization, besides the low socioeconomic state and incorrect use of antibiotics.<sup>21</sup>

Sixty-four (64%) out of 1592 infertile patient revealed features of tubal inflammation and infections, these findings are consistent with those of others who revealed that PID-pelvic inflammatory disease represents a cause of damaged tube (4). However; another study showed a higher frequency of inflammation which may attributed to the small sample size.<sup>21</sup>

In general, the frequency of acquired tubal findings in the present work was more in patients with 2ndry-secondary infertility in comparison with those presented



Figure 1. A Photograph of hysterosalpingograph of a female presented with infertility. Bicornuate uterus is seen with patent tubes.



Figure 2. A Photograph of hysterosalpingograph of a female presented with infertility with features of bicornuate uterus is seen, both tubes look dilated and positive spillage is noticed.

with Iry-primary category and that may be due the fact the repeated infection results in more complications.<sup>21,22</sup>

Congenital diseases of the uterus may lead to infertility and or amenorrhea. It was reported that the frequency of congenital diseases of the uterus in infertile women and in amenorrhea in Nineveh Province was 5.9% and 54.8% respectively, which is comparable with that of others,<sup>23,24</sup> while it is higher that of others and that may be due to the war conditions in Iraq.<sup>21</sup>

This work revealed that 68 (4%) out of 1592 infertile patients had got features of endometrioses which is characterized by the extra uterine endometrial glands and stroma.<sup>25</sup> The cause of infertility related with this lesion is still elusive, there is a multifactorial factor including immunological, genetic, and environmental one. It is frequent lesion but the precise pathogenesis is unknown and it clearly diagnosed by laparoscope.<sup>26</sup> The frequency of this lesion in other studies was higher than the present work and that may be due to the high experience of diagnoses, the small sample size used, the differences in genetics, and environmental factors.<sup>21</sup> In fact, this lesion may lead to anatomical disruption, adhesive lesion of adnexa and ovarian distortion. Another lesion, uterine fibroid may affect fertility,<sup>12,27</sup> while intrauterine adhesive lesions could distort the cavity of uterus, leading to amenorrhea and infertility with hypomenorrhea.

Uterine fibroids were reported in 101 (6%) of infertile women in the present study. A finding which are in accordance with those of Philips *et al.*<sup>14</sup> This lesion can displace the cervix, distorts the uterine cavity, and damaged tubes.<sup>27,28</sup>

The prevalence of intrauterine adhesive lesions in infertile women of this work is about 1.5% which was lower than that of other studies,<sup>21,29</sup> and that may be due to differences in sample size and methods used for the diagnosis and also due to the high prevalence of PID.<sup>30,31</sup> Laparoscopy and chromo-tubation test must be seriously performed as an initial step in investigation of females presented with infertility prior to doing any treatments including high costs and or potential harms.<sup>21,32</sup>

In fact, this work represents the first study that included a huge number of study sample size, as it enrolled 1682 females and that adding strength to it besides the factor that the infertility Unit in Al-Batool Teaching Maternity Hospital is the site where huge number of females referred to it for management of their complaint.

## CONCLUSIONS

The present study revealed that acquired tubal factors are the most frequent cause of infertility in Mosul/Iraq, while the uterine acquired lesions represented the second one. The clinicians should take in considerations the factors that lead to different tubal diseases (especially the infectious one that result in tubal occlusion) and that may help to achieve a decrease in rates of infertility. Education and counseling by gynecologists must be performed to follow the proper methods of evaluation of these gynecological problems which facilitate the decision making regarding their management. More researches are needed to highlight the risk factors of fibroid and endometriosis in our locality.

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## MANAGEMENT OF PATIENTS WITH ACUTE PANCREATITIS IN AL-KARAMA TEACHING HOSPITAL

### تدبير مرضى التهاب البنكرياس الحاد في مستشفى الكرامة التعليمي

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#### ملخص البحث

**هدف البحث:** لا يعتبر التهاب البنكرياس الحاد -وهو حالة التهابية حادة- مرضاً غير شائع في البلدان المتقدمة والنامية على حد سواء، حيث يسبب معدلات مراضة ووفيات عالية، وينطوي على عبء اقتصادي ثقيل. يلاحظ التهاب البنكرياس الحاد الشديد عند 25% من مجمل مرضى التهاب البنكرياس الحاد، مع تميزه بوفيات كبيرة. ساهمت التغييرات في تدبير حالات التهاب البنكرياس الحاد خلال العقدين الماضيين في خفض معدلات الوفيات. تهدف هذه الدراسة إلى مراجعة تشخيص وتدبير مرضى التهاب البنكرياس الحاد، والمعالجة المطبقة سواءً المحافظة أو الجراحية، ونتائج العلاج عند مرضى التهاب البنكرياس الحاد في مستشفى الكرامة التعليمي.

**طرق البحث:** شملت هذه الدراسة المستقبلية 63 مريضاً من مرضى التهاب البنكرياس الحاد في الأجنحة الجراحية والباطنية في مستشفى الكرامة التعليمي خلال الفترة بين من 1 تشرين الأول 2014 وحتى 30 أيلول 2017.

**النتائج:** تم إدراج 63 مريضاً يعانون من التهاب البنكرياس الحاد (35 ذكور و28 إناث)، أما المرضى الذين يعانون من آلام في الجزء العلوي من البطن والتي لم يتم تأكيد التشخيص فيها من خلال التصوير المقطعي CT أو مستوى الأميلاز في مصل الدم أو البروتين التفاعلي CRP فقد تم استبعادهم من الدراسة. لم يكن للعمر والجنس أي علاقة مهمة بالنتائج. كان العلاج الطبي هو حجر الأساس في المعالجة مع العلاج الداعم الذي يتكون من تعويض السوائل والتغذية المعوية. إن التفجير قليل الغزو والتضيق يلعبان دوراً هاماً في تدبير حالات تخر البنكرياس الإلتاني، ولكن عموماً يجب عدم استخدامهما إلا بعد 4 أسابيع على الأقل من الحالة الحادة.

**الاستنتاجات:** التهاب البنكرياس الحاد هو اضطراب سليم في البطن في 85% من الحالات. أما في الحالات 10-15% المتبقية فيكون هذا الاضطراب مهدداً للحياة، حيث يتطلب تدبيره القبول في وحدة العناية المركزة مع مراقبة قلبية، تنفسية وكلوية مع معالجة داعمة.

#### ABSTRACT

**Objective:** Acute pancreatitis is an acute inflammatory condition. It's not an uncommon disease, in both the developed and developing countries, causes high morbidity and mortality, and inflicts a heavy economic burden. Severe acute pancreatitis is present in up to 25% of patients with acute pancreatitis, with

considerable mortality. Changes in the management of acute pancreatitis in the last 2 decades contributed to reduce the mortality. The aim of this work was to review the diagnosis and management of patients with acute pancreatitis, and the treatment whether conservative or surgical, and outcome of management of patients with acute pancreatitis in Al-Karama Teaching Hospital.

**Methods:** This prospective study included 63 patients

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*with acute pancreatitis in surgical and medical wards in Al-Karma Teaching Hospital from the 1st October 2014 to 30 September 2017.*

**Results:** *Sixty-three patients with acute pancreatitis were included, 35 males and 28 females, patients with upper abdominal pain in which the diagnosis was not confirmed by CT or serum amylase or by CRP are not included in this study. Age and gender had no significant relations to outcome. Medical therapy is the mainstay, with supportive therapy consisting of controlled volume resuscitation and enteral feeding. Minimally invasive drainage and debridement play a role in managing infective pancreatic necrosis, but in general should not be used until at least 4 weeks after the acute illness.*

**Conclusions:** *Acute pancreatitis is a benign abdominal disorder in up to 85% of cases. In the remaining 10-15% of cases the disorder is life threatening with management of the disorder requiring admission to an intensive care unit with cardiovascular, respiratory, and renal monitoring and support.*

## INTRODUCTION

Acute pancreatitis is an acute inflammatory disorder of the pancreas caused by an intracellular activation of pancreatic digestive enzymes. The destruction of pancreatic parenchyma induces a systemic activation of coagulation, kinin, complement and fibrinolytic cascades with liberation of cytokines and reactive oxygen metabolites which, if severe and overwhelming, can lead to shock, acute renal failure and the acute respiratory distress syndrome.

Acute pancreatitis (AP) is one of the most common diseases of the gastrointestinal tract, leading to tremendous emotional, physical, and financial human burden,<sup>1,2</sup> with high morbidity and mortality.

In 85-90% of patients, acute pancreatitis is self-limiting and subsides spontaneously within 4-7 days. Specific treatment for acute pancreatitis currently does not exist and management is still supportive, with therapy aimed at reducing pancreatic secretion, replacing fluid and electrolytes losses and analgesia. All patients with severe acute pancreatitis who have one (or more) organ failures (e.g. circulatory, pulmonary or renal) should

be managed in an intensive care unit with mechanical ventilation, inotropic agents and renal replacement therapy being used to manage organ failure.

Intense pancreatitis is an incendiary malady of the organ that is connected with minimal or no fibrosis of pancreas. Patients with intense pancreatitis create extra difficulties such that sepsis, shock, and respiratory and renal failure, bringing resulting in considerable morbidity and mortality.<sup>3</sup>

Acute pancreatitis is the most common gastrointestinal discharge diagnosis in the United States (274,119 patients in 2009), an incidence which has increased 30% since 2000, the annual incidence of acute pancreatitis in Native Americans is 4 per 100,000, in whites is 5.7 per 100,000 while in blacks is 20.7 per 100,000.<sup>4</sup> The risk for African-Americans aged 35-64 years is 10 times higher than for any other group. About 300,000 cases happen in the USA yearly, 10-20% of which are severe, leading to more than 3000 deaths, and poses a big economic burden, accounting for more than \$2 billion health costs every year.<sup>4</sup> The crude mortality rate of 1.0/100,000 ranks it as the 14th most fatal illness overall and the ninth most common noncancer gastrointestinal death. Worldwide the incidence of acute pancreatitis ranges from 5 to 80/100,000 population, with the highest incidence recorded in Finland and United States.<sup>3</sup>

Etiologies of acute pancreatitis include cholelithiasis-associated pancreatitis accounts for approximately 45% of cases of acute pancreatitis and ethanol abuse accounts for 35%; other causes account for 10%, and in up to 10% no cause may be found (i.e. idiopathic pancreatitis).<sup>5,6</sup> Alcoholic pancreatitis often occurs in patients less than 40 years of age and is predominantly a male disease. Acute pancreatitis associated with cholelithiasis usually occurs in patients aged from 50-60 years, and females predominate in a ratio of 3:1. While hypercalcaemia is commonly included in the list of causes of pancreatitis, the incidence of pancreatitis in patients with hyperparathyroidism or hypercalcaemia in one study approximated that of the general population.<sup>5</sup> On the other hand, calcium administration was closely associated with the occurrence of pancreatic injury in a study of risk factors for pancreatic injury after

cardiopulmonary bypass.<sup>7</sup> It is now believed that corticosteroids and H<sub>2</sub>-blockers probably do not cause acute pancreatitis.<sup>5</sup>

Clinical presentation of acute pancreatitis; epigastric abdominal pain, which may radiate through to the back, chest, flanks or lower abdomen, is the predominant symptom of acute pancreatitis. It is usually gradual in onset, constant and boring in nature and may be mild or severe. The pain may be relieved if the patient sits forward or the legs are drawn up. Nausea and vomiting occur in 90% of cases.

The signs include tachycardia, tachypnoea, fever, hypotension and diaphoresis as well as the abdominal signs of tenderness, rigidity, guarding and distension. Respiratory signs of pleural effusions, basal collapse (characteristically on the left), wheezing, and basal crepitations are found in 10-20% of patients. A faint blue discolouration around the umbilicus (Cullen's sign) due to haemoperitoneum, and a blue red purple or brown discolouration of the flanks (Grey-Turner's sign), due to retroperitoneal haemorrhage, may be observed after 48 hr. Occasionally, erythematous skin nodules due to subcutaneous fat necrosis are found.

This entity has been classified by the 1992 Atlanta international symposium on acute pancreatitis into: Acute oedematous pancreatitis (EP), Necrotizing pancreatitis (NP), haemorrhagic pancreatitis (HP).<sup>7</sup> The 2012 revised Atlanta classification is an update of the original 1992 Atlanta classification, a standardized clinical and radiologic nomenclature for acute pancreatitis and associated complications based on research advances made over the past 2 decades. Acute pancreatitis is now divided into two distinct subtypes, necrotizing pancreatitis (NP) and interstitial edematous pancreatitis (IEP), based on the presence or absence of necrosis, respectively. The revised classification system also updates confusing and sometimes inaccurate terminology that was previously used to describe pancreatic and peripancreatic collections. As such, use of the terms *acute pseudocyst* and *pancreatic abscess* is now discouraged. Instead, four distinct collection subtypes are identified on the basis of the presence of pancreatic necrosis and time elapsed since the onset

of pancreatitis. Acute peripancreatic fluid collections (APFCs) and pseudocysts occur in IEP and contain fluid only. Acute necrotic collections (ANCs) and walled-off necrosis (WON) occur only in patients with necrotizing pancreatitis and contain variable amounts of fluid and necrotic debris. APFCs and ANCs occur within 4 weeks of disease onset. After this time, APFCs or ANCs may either resolve or persist, developing a mature wall to become a pseudocyst or a WON, respectively. Any collection subtype may become infected and manifest as internal gas, though this occurs most commonly in necrotic collections. In this review, the authors present a practical image-rich guide to the revised Atlanta classification system, with the goal of fostering implementation of the revised system into radiology practice, thereby facilitating accurate communication among clinicians and reinforcing the radiologist's role as a key member of a multidisciplinary team in treating patients with acute pancreatitis.<sup>8</sup>

The revised Atlanta classification of acute pancreatitis is an international multidisciplinary classification of the severity of acute pancreatitis, updating the 1992 Atlanta classification. It was initially revised in 2012 and then further updated in 2016.<sup>8</sup>

The classification system is based on both local and systemic determinants of severity with:

- Local determinants related to the presence or absence of (peri) pancreatic necrosis (sterile or infected).
- Systemic determinants related to presence or absence of organ failure (transient or persistent).

The grade of severity (mild, moderate, severe, and critical) is based on combinations of these determinants.

**Radiographic features:** The Atlanta classification divides acute pancreatitis into two basic types:

- Interstitial edematous pancreatitis (IEP)
- Necrotising pancreatitis (NP) which is further subdivided into:
  - parenchymal necrosis
  - peripancreatic necrosis
  - combined type (peripancreatic and parenchymal necrosis): most common

All types of necrotising pancreatitis may be sterile or infected; gas formation is the best imaging feature to suggest infection.

The management of acute pancreatitis covers a wide spectrum of severity. Patients with suspected acute pancreatitis should be admitted to hospital. Those with mild acute pancreatitis usually remain in hospital for less than a week, while those with severe and critical acute pancreatitis may require many weeks or months of intensive treatment.<sup>3</sup>

The risk of mortality reflects this spectrum of severity. The risk is less than 1% for those with mild disease, increasing to around 10% for those with moderate disease, but for severe and critical disease the mortality risk is much higher (20% to 40% and greater than 50%, respectively).<sup>3</sup> The earlier identification of these high-risk categories and the transfer of these patients to specialized centers is an important priority of management. Scoring systems such as Ranson's Criteria identify these high-risk patients. The management of acute pancreatitis should be multidisciplinary and it is important that a coordinated care plan is carefully supervised.<sup>3</sup>

## METHODS

Between the 1st October 2014 till 30th September 2017, 63 successive patients with intense pancreatitis were gathered prospectively starting with the branch from claiming surgery during. The criteria to patient's gathering were dependent upon information sheet at Al-Karama Teaching Hospital numerous information's in light of clinical picture (history and examination) and examination (U/S, a rise for S. amylase will be more than 3 times the upper typical limit, frequently serum lipase, CT examine). In all cases, a plain abdominal film an erect chest X-ray were taken to exclude other respiratory and acute abdominal conditions.

### *Criteria for acute pancreatitis*

- Characteristic abdominal pain.
- Elevated level of serum amylase or lipase level 3 or more times.
- Changes consistent with acute pancreatitis on imaging.

On patient's admission, data involved age, gender, time, delay from pain onset until admission, APACHE-II score and or Ranson's score. On discharge, data were collected by inspection of hospital's records including severity stratification, aetiology, outcome, staying duration in the hospital and in the intensive care unit (ITU), endoscopy and imaging as well as operative findings. In accordance with the Atlanta criteria, severe outcomes were defined as organ failures and/or local complications.

In an abdominal ultrasonography ought to further bolster to make to performed on record those vicinity of cholelithiasis for alternately without ductal dilatation.

Necrotizing pancreatitis (NP) might have been characterized similarly as those manifestation for extreme kind of intense pancreatitis with pancreatic alternately additional pancreatic corruption once contrast-enhanced figured tomography (CT) or a serum C-reactive protein quality of more than 150 mg/L.

Acute edematous pancreatitis (EP) was defined as less severe type of pancreatitis in which just pancreatic swelling on contrast-enhanced computed tomography (CT) & clinical picture of acute pancreatitis. Those patients who have been treated conservatively in accordance with the generally accepted principles consisting of withholding oral intake, providing pain relief, and restoring fluid and electrolyte losses, vomiting had been a prominent part of the clinical picture, a nasogastric tube was inserted. A proton pump inhibitor was given to prevent stress ulcers, and the low-molecular weight heparin (3,000 Unit per day) was administrated to prevent thrombosis, unless he has contraindication.

Pain treatment included using of intravenous narcotics except morphine and analgesics. Clinical severity staging of acute pancreatitis has been performed by applying Ranson prognostic signs & the APACHE II scoring systems, but in case of organ failure, patients were referred to intensive care units. In NP patients, prophylactic antibiotic treatment was administrated in less than one day after necrosis detection by CT scanning. We used imipenem/ (Ig three time/day,

intravenously) for 14 days metronidazole (500 mg three time/day, intravenously) for 14 days according to the study protocol if imipenem was not available 3rd generation cephalosporin + metronidazole for 14 days.

**Two types of ERCP were performed:** In biliary cholestasis cases, early endoscopic retrograde cholangiography was done (within the first 24-48 hrs.) as confirmed by laboratory findings and ultrasonography of cholestasis such as high levels of serum aspartate aminotransferases, alkaline phosphatase or bilirubin. While late endoscopic retrograde cholangiopancreatography has been performed prior to hospital discharge on 3 patients with unknown etiology and to exclude tumor-induced acute pancreatitis. Ultrasonography guided-needle aspiration (FNA), consecutive Gram stains and bacteriologic cultures were done to 8 patients with NP. (The decision to intervene is based on the clinical status and trajectory of the patient and the poor response to maximal intensive care support. This means close monitoring of the patient by serial examination, supplemented by regular measurement of inflammatory markers (e.g., C reactive protein) and a pancreatic protocol CT scan if a local complication is suspected and intervention considered warranted. In practice, intervention is delayed in order to allow demarcation of necrosis, and a reduced the risk of bleeding, disseminated infection and collateral damage to adjacent organs by an intervention. Appreciation of this has resulted in a notable trend toward delayed intervention, now uncommon before 3 to 4 weeks from the onset of symptoms.<sup>3</sup> An important emerging approach is the increasing use of percutaneous catheter drainage in patients with suspected infected complications. Fine needle aspiration is now rarely used to confirm infection, because the insertion of a needle at the time of planned drainage allows confirmation of the suspected infection.<sup>3</sup> In which other differential diagnosis was suspected including in haemodynamically unstable patient like perforated DU, mesenteric ischemia and a gangrenous small bowel obstruction and the diagnosis of Fat necrosis was confirmed intra-operatively.

**RESULTS**

In this prospective study 63 patients were collected

between October 2014 and September 2017 in whom acute pancreatitis was identified. Patients’ characteristics are summarized in Table (1). There were 35 (55.6%) men and 28 (44.4%) women. Mean age was 53.2 years (range 25-78). Mean age of EP was 50 (25-78) and of NP was 56.5 (35-78).

Hemorrhagic pancreatitis removed from new classification (the Revised Atlanta classification of acute pancreatitis); therefore, did not mentioned.

No. (%)	dematous pancreatitis No. (%)	Necrotizing pancreatitis No. (%)
Female	16 (25.4%)	12 (19%)
Male	13 (20.6%)	22 (35%)
Mean age (range)	50 (25-78)	56.5 (35-78)
Mean Ranson score (range)	1.9 (0-7)	3.9 (0-8)
Mean APACHE II score (range)	6.3 (1-16)	12.6 (5-28)
Mean hospital stay in days (range)	15 (2-18)	17.1 (11-20)
Hospital death	0	11 (1.7%)

Table 1. Summarized patients’ characteristics with acute pancreatitis.

Distribution of patients with acute pancreatitis in both types of acute pancreatitis was higher in the last year but this increase is more prominent in (NP) than in (EP).

Distribution of patients with edematous pancreatitis (EP) according to age group and gender. It was found that highest no. of patients in the age group (50-59) years for both male and female, as shows in the Table 2.

Age-Group	Male	Female
20-29	1	0
30-39	0	0
40-49	3	5
50-59	6	5
60-69	2	4
70-79	1	2
Total	13	16

Table 2. Distribution of edematous pancreatitis patients (EP) according to age-group and sex.

Distribution of patients with necrotizing pancreatitis (NP) according to age group and gender. It was found that highest no. of patients in the age group (40-49) years for both male and female, Table (3).

Age-Group	Male	Female
20-29	0	0
30-39	2	2
40-49	7	4
50-59	5	3
60-69	6	1
70-79	2	2
Total	22	12

Table 3. Distribution of patients with necrotizing pancreatitis (NP) according to age-group.

Regarding the association between age groups and gender in both NP & EP; the highest age group affected by AP were (40-49) & (50-59), the association was statistically not significant ( $\chi^2=1.60$ ,  $df=5$ ,  $p\text{-value} = 0.901$ ), as shows in the Table 4.

Age - Gender association			
Age	Male	Female	Total
20-25	1	0	1
30-39	2	2	4
40-49	10	9	19
50-59	11	8	19
60-69	8	5	13
70-79	3	4	7
Total	35	28	63

Table 4. Association between age group & gender.

Distribution of patients with edematous pancreatitis (EP) and necrotizing pancreatitis (NP) according to causes. The causes of acute pancreatitis in our study were biliary in 31 patients (49%) patients, alcohol overindulgence in 7 patients (11%), blunt trauma in 3 patients (4.8%). Post-endoscopic retrograde cholangiopancreatography (ERCP) 2 patients (3%) and other or undefined in 20 patients (32%) in spite of the ultrasound scan (U/S) and/or the computed tomography (CT) scan.

Pain was found in all patients 100%, followed by nausea and vomiting which were found in 63% of

patients, while the lowest symptom was jaundice which was found in only 2% of patients, as shows in Table 5.

Cause	EP (No.)	%	NP (No.)	Total (No.)
Biliary	17	58%	14	31 (49%)
Alcohol	2	7%	5	7 (11%)
Undefined	6	21%	14	20 (32%)
Post ERCP	2	7%	0	2 (3%)
Trauma	2	7%	1	3 (4.8%)

Table 5. Distribution of patients with edematous pancreatitis (EP) and necrotizing pancreatitis (NP) according to causes.

It seems that biliary cause was the most common cause in both types. There significant association between type of management and the prognosis  $X^2=59.19$ ,  $df=6$ ,  $p\text{-value}<0.05$ , showed among the 18 patients those who were treated conservatively without cholecystectomy<sup>11</sup> improved an eventually, while 4 patients had complication but improved after 4 weeks and 3 patient died from organs failure.

Those who were treated conservatively but underwent laparoscopic cholecystectomy were 14 patients improved un eventually in less than four weeks, 2 patients develop complication but improved after 4 weeks, while 5 patients treated conservatively needed open cholecystectomy; and only 1 patient have complication but improved after 4 weeks and 1 patient die after 2 months due to diabetic-ketoacidosis in the medical wards.

Surgical intervention was indicated in 22 patients (35%). Different techniques were applied “open packing”, “planned relaparotomies”, “closed over drains”, and the pancreatic cavity irrigation”. Out of 22 patients who treated surgically, 8 patients improved within two weeks, 7 patients complicated by (fistula and bleeding) but improved after 4 weeks and 7 patients died from multiple organs failure, as shows in Table 6.

CT scanning with IV contrast has become the gold standard for detecting and assessing the severity of pancreatitis. In our study CT-scan had been done for 48 patients with acute pancreatitis, there were 22 patients

Management	Prognosis			
	Improved an eventfully	Complicated but improved after 4 weeks	Died	Total
Conservative without cholecystectomy	11	4	3	18
Conservative with lap. cholecystectomy	14	2	0	16
Conservative with open cholecystectomy	5	1	1	7
Surgical	8	7	7	22
Total	38	14	11	63

$\chi^2=59.19$ ,  $df=6$ ,  $p\text{-value}<0.05$

**Table 6. The outcome of management with acute pancreatitis. There was significant association between type of management and the prognosis**

(35%) with edematous pancreatitis (EP) and 26 patients (41%) with necrotizing pancreatitis (NP), fifteen patients developed organ failure (23.8%), but mechanical ventilation was required by only eight patients of them.

There were eleven patients (17.5%) with acute pancreatitis; died 10 patients of them died after the surgical management for severe cases. The median staying days in hospital was 16 days (range 2-25), and 6 patients (9.5%) were treated in ICU, with a median staying of eight days (range 1-22); while the median staying days in mild cases was 6 days (range 4-8). Multiple organ failure was not found in patients with edematous pancreatitis, but only one patient (1.6%) with single organ failure showed pulmonary insufficiency.

## DISCUSSION

In this cohort study we collected 63 patients with acute pancreatitis (28 female and 35 male). Hospital stay was more in (NP) than (EP) and this is because it is more severe and more complications developed in (NP) than (EP), anyhow these complications include only short-term complications (develop within 8 weeks of admission).

In our hospital, the estimation of diagnosis was similar to that in UK that delayed diagnosis is considered as an indication of under diagnosis, the high diagnosis rate within 48 hours in Wessex indicates that under diagnosis is perhaps less common such as that S. amylase result is currently a part of the routine abdominal pain evaluation. However, in our hospital, we do not have such facility

yet, so our diagnosis may be an underestimate one. BANK et al<sup>9</sup> in their review stated that in the last 20 years, the causes of mortality rate decrease were: the early identification of severity with prompt treatment, nutritional support improvement, angiography, ERCP and antibiotics use.

In their prospective observational study, BUTER et al<sup>10</sup> revealed that in the mortality rate was about (50%) in organ failure patients that persisted for over than 48 hours. By contrast, patients with organ failures treated in the R.C.U. that resolved within two days had zero mortality rate.

In this study the mortality rate was 11 patients (17.5%) in comparable to the mortality rate of Biichler P, Reber et al<sup>11</sup>) (mortality rates of about 15% was reported), but it is much different from mortality rate of Glaus Niederau et al<sup>12</sup> who reported mortality rate of (0.7%) in his study on 145 patients; while Tercio De CAMPOS et al. in Brazil reported a mortality rate of 25% in his study.

In our study the mortality rate was high as compared to international studies. Because large no. of patients are referred patients from other hospital due to disease severity, and the limited no. of R.C.U. bed available; while Wessex Hospital used to refer critically ill patients to more specialized center.

Recently we have noticed a raise in the diagnosis of acute pancreatitis in our hospital especially in the last year, this is may be due to increase in the incidence of

gallstones and biliary diseases (which is believed to be the main causes of acute pancreatitis), and change in pattern of gallstones diseases to affect male and young age group also may be due to the improvement in the community general condition as well as the advanced diagnostic facilities.

The attack of acute pancreatitis (EP) in both male and female are more common among patients in their forties, but it also peaks in fifties specially in male patients, this peak may be due to the peak of gall stones incidence in patients in their forty and fifty, or the raise of acute pancreatitis in male patients in their forties may be due to alcohol consumption.

The causes of acute pancreatitis in our study were biliary in 31 patients (49.2%), alcohol overindulgence in 8 patients (12.6%), trauma in 3 patients (3.2%), endoscopic retrograde cholangiopancreatography (ERCP) 2 (3%) and other or undefined in 20 patients (30.2%) in spite of the ultrasound scan (U/S) and/or the computed tomography (CT) scanning. Gallstones is the commonest cause of both types of acute pancreatitis in our study as well as to a study done in KSA by Professor Ravi Kant et al.

While alcohol is less common cause in our study as compared to Ravi Kant et al. But alcohol was found to be more common in NP than EP. This may be because alcoholism is less common problem in our community than in the west. Glaus Niederau et al.<sup>13</sup> (in Germany) found that alcoholic pancreatitis represents (54.5%) and biliary in (26.2%) of patients (other causes, 18.6%), which is believed to be a cause of the highly prevalence of men's acute pancreatitis. In 2003, Lankisch et al<sup>14</sup> reported that alcoholic AP patients were more severe than the other people, particularly those who arrive to the hospital in less than 24 hour-period because of severe pain.

Diagnosis of these alcoholic patients may be difficult due to an abnormal baseline serum amylase at time of admission. Serum lipase, which is more specific than S. amylase, is the key for AP diagnosis in these patients. Lipase is usually increased in alcoholic patients and the diagnosis is confirmed despite normal

amylase results. In such conditions, CT scan can be necessary.<sup>14</sup>

Acute pancreatitis without prominent cause is present in 21% in EP and 38% in NP, according to Lankisch et al.<sup>14</sup> While in our study its (30.2%) and this may be because of lack of some particular investigation, as DNA analysis or toxicology screening study.

Also, it has been found that trauma and post ERCP acute pancreatitis causes only mild type of pancreatitis, anyhow this much depends on the severity of trauma itself and on the operator.

Upper abdominal pain is the main symptom of presentation, it was present in all patients in our study and represents the 1st clue for diagnosis, anyhow the severity and pattern of pain greatly vary between patient and another. Nausea and vomiting are also common in patients with acute pancreatitis.

There is a significant association between type of management and the prognosis ( $X^2=59.19$ ,  $df=6$ ,  $p\text{-value}<0.05$ ).

The treatment of acute pancreatitis is either conservative or surgically.

In our study, we found that morbidity and mortality were higher among surgically treated patients. Kelly and Wagner<sup>15</sup> selected 165 acute gallstone-associated pancreatitis patients to early surgery (within 48 hours after their admission) or delayed surgery (over 48 hours after their admission). Their results showed that the early surgery was correlated with a much greater morbidity (83 vs 48% respectively) and mortality rate (18 vs 12% respectively) in severe pancreatitis patients compared to the delayed surgery.

In their research, Company et al studied 67 patients AP patients and recorded (31.3%) mortality rate. They demonstrated that the majority of systemic complications after surgical treatment of acute pancreatitis were related to mortality. The high mortality rate could be attributed to the high mean age of 69 years and the high necrosis number of patients (55.2%).

Kong et al retrospectively studied surgically-treated (94) severe acute pancreatitis patients and found 54% with necrosis and (23.4%) of deaths. They have found that fatal outcome was anticipated by cardiovascular, respiratory and renal failure, that is increased after surgical treatment. Thus, the development of systemic complications in surgically-treated patients with necrosis can result in worst prognosis. So both of those studies agreed with our result. Surgical intervention was indicated in 22 patients (35%) due different indication, and different techniques were applied “open packing”, “planned relaparotomies”, “closed over drains”, “closed over drains and the pancreatic cavity irrigated”.

It looks that, “closed over drains” is the most popular technique which 14 patients has undergo this technique, although it has a high mortality rate (29%). Anyhow “planned relaparotomies” has less mortality rates.

In the U.K, (30-50%) of acute pancreatitis cases are associated with gallstones, while (15-29%) with alcohol. In our audit, 950%) were gallstone-related, whereas (12%) were alcohol-related. It is greatly differed in alcoholic pancreatitis this may be because of the difference in dietary habits and prohibition of alcohol in our society.

However, the greater percentage (32%) was in idiopathic cases in these series, and this percentage is greater than the standard (20-25%).

## CONCLUSIONS

The current study again emphasizes the importance of early assessment of severity and intensive care administration in acute pancreatitis depends on clinical, laboratory assessment, ultrasound and contrast-enhanced CT imaging. Lab markers with high values of lipase, CRP associated with the mortality and morbidity.

Numeric systems (APACHE II, RANSON) are often applied nowadays to help organ failure detection, and the acquired information are employed as evidence of the severity of disease, with a high specificity and sensitivity. CT-scan with I.V contrast enhancement appeared to early detect (90%) with nearly (100%)

sensitivity after 4 days for acute pancreatitis. The CT severity index showed an excellent association with the development of local complications and death incidence.

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## SEASONALITY OF INTUSSUSCEPTION IN IRAQI CHILDREN

### فصلية انغلاف الأمعاء لدى الأطفال في العراق

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#### ملخص البحث

**هدف البحث:** يعد انغلاف الأمعاء سبباً هاماً للانسداد المعوي لدى الأطفال وخاصةً الرضع الصغار. أظهرت الدراسات المنشورة وجود علاقة متباينة بين الموسم وحدوث انغلاف الأمعاء. هدفت هذه الدراسة إلى تحديد موسمية انغلاف الأمعاء لدى الأطفال العراقيين إن وجدت، واختبار التأثير الهام للعمر والجنس على تلك الموسمية ومقارنة النتائج مع الدراسات المنشورة سابقاً.

**طرق البحث:** أجريت دراسة راجعة شملت 285 طفلاً من المصابين بانغلاف الأمعاء في مشفى حماية الأطفال التعليمي في بغداد للفترة بين عامي 2013 و2018. تم أخذ بيانات العمر، الجنس، التوزيع الشهري والموسمي للحالات من السجلات الطبية للمرضى. تم تطبيق الإحصائيات الوصفية واختبار كاي مربع لعرض وتحليل البيانات على التوالي.

**النتائج:** سجل موسم الصيف أعلى نسبة لحالات انغلاف الأمعاء (بنسبة 30.8%)، بينما سجلت نسب أقل في مواسم الخريف والربيع والشتاء (بنسبة 25.3%، 22.1% و21.8% على التوالي). كانت الموسمية مرتبطة إحصائياً بالجنس (قيمة p تساوي 0.048)، دون وجود ارتباط مع العمر (قيمة p تساوي 0.678).

**الاستنتاجات:** أظهرت نتائج الدراسة موسمية انغلاف الأمعاء في الصيف لدى مجموعة الدراسة. يجب على أطباء الأطفال وجراحي الأطفال الأخذ بعين الاعتبار الموسمية أثناء تقييم الأطفال بحالات الشك بانغلاف الأمعاء. هناك حاجة لدراسات متعددة المراكز وكبيرة الحجم للتحقق من نتائج الدراسة.

#### ABSTRACT

**Objective:** Intussusception is an important cause of intestinal obstruction in children, particularly young infants. Anecdotal published studies have disclosed variable correlation of seasonality with pediatric intussusception. The aims of the study were to determine intussusception seasonality in Iraqi children, if any, test the significant influence of age and gender on that seasonality, and compare the results with those reported previously elsewhere.

**Methods:** We carried out a retrospective study on 285 pediatric intussusceptions admitted to the Children's Welfare Teaching Hospital in Baghdad between 2013 and 2018. Data on age, gender, and monthly and seasonal distribution were taken from medical records of the patients. Descriptive statistics and Chi-square test were applied to address and analyze the data respectively.

**Results:** Summer had the highest rate (30.8%); while fall, spring, and winter had the lower rates (25.3%, 22.1%, and 21.8%, respectively). Seasonality was

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statistically correlated with the gender ( $p=0.048$ ), but not with the age ( $p=0.678$ ).

**Conclusions:** The study results showed summer seasonality of intussusception in the studied cohort. Astute pediatricians and pediatric surgeons should consider the seasonality during evaluating children with the clinical picture suggestive of intussusception. Large size multicenter studies are needed to verify the study results.

## INTRODUCTION

Intussusception is one of the most common causes of intestinal obstruction in children, particularly young infants. It involves the invagination of one segment of the bowel into an adjacent segment. The most common form of intussusception in children is idiopathic typically managed with non-operative reduction through pneumatic and/or hydrostatic enemas.<sup>1</sup> Secondary intussusception, seen in 0.3-20% of cases, is often associated with various pathological leading points, including Meckel's diverticulum, intestinal duplication, polyp, mesenteric cyst, heterotopic pancreas, mesenteric purpura, and neoplasm.<sup>2</sup> The classical cases of intussusception are readily diagnosed clinically, and despite recent improvements in radiological techniques, the diagnosis of intussusception and success in its non-operative reduction has been suboptimal, thus making operative management a veritable backup.<sup>3</sup> Delayed presentation is associated with increased hospital cost, morbidity, and risk of bowel resection.<sup>3,4</sup> Therefore, a high index of suspicion is needed and effort should be geared to make early diagnosis and referral to improve the outcome.

Seasonal rhythm of pediatric intussusception has been studied worldwide and the results disclosed variable correlation of the seasonality with intussusception.<sup>5-9</sup> However, this issue is not yet studied in Iraqi children. We, therefore, attempted in this study to define the intussusception seasonality in Iraqi children, study the significant influence of age and gender on that seasonality, and compare the results with those reported elsewhere.

## METHODS

Regrettably, the national registry data on the

pediatric intussusception are not yet present in Iraq. We, therefore, reviewed the medical records of patients with intussusception admitted to the Children's Welfare Teaching Hospital in Baghdad during the period from the 1<sup>st</sup> January 2013 to 31<sup>st</sup> December 2018. The retrieved data included the age, gender, and month of admission. The seasonal distribution of the patients was nominated as the following: winter (December-February); spring (March-May); summer (June-August); and fall (September-November). The diagnosis of intussusception was established on the suggestive clinical presentation and ultrasonography /or barium studies. Chest X-ray was taken whenever necessary to rule out other causes of abdominal pain like basal pneumonia and as a part of the routine preoperative assessment for surgical treatment. The treatment of the intussusception was individualized utilizing the hydrostatic/pneumatic reduction or surgical intervention. The statistical Package for the Social Sciences version 17 software (SPSS Inc., Chicago IL, USA) was used to analyze the data. The data were presented using descriptive statistics. Chi-square was employed to test the significant effect of the variables of age and gender on the intussusception seasonality. The statistical significance was set at  $p<0.05$ . The study proposal was approved by the Scientific and Ethical Committee at Al-Kindy College of Medicine, University of Baghdad.

## RESULTS

During the six-year study period (2013-2018), 285 patients with intussusception were enrolled. The studied population included 186 (65.3%) males and 99 (34.7%) females with a male to female ratio of 1.9:1. The mean age of patients was  $11.9\pm 4.9$  months. The age distribution involved 212 (74.3%) cases below one year of age, 40 (14.1%) cases within the age group of 1-3 years, and 33 (11.6%) cases above the age of three years. Table 1 revealed the annual and monthly distributions of the studied patients. The highest number of patients in the annual distribution was in 2018 [65 (22.8%)] followed by 2017 [48 (16.8%)] while the least was in 2015 [39 (13.7%)]. The highest number of patients in the monthly distribution was in August [38 (13.3%)] followed by July [28 (9.8%)], while the least was in April [14 (4.9%)]. Figure 1 showed the seasonal distribution of the patients

where the highest rate was in summer 88 (30.8%), while the lower rates were in fall 72 (25.3%), spring 63 (22.1%), and winter 62 (21.8%). Table 2 demonstrated a statistically significant correlation between the intussusception seasonality and gender (p=0.048), but not with the age (p=0.678). Table 3 addressed the comparison between the pattern of intussusception seasonality in our study and others reported elsewhere.

## DISCUSSION

Studying the seasonality of a particular illness in a given pediatric population is crucial in setting up the diagnostic, therapeutic, educational, and preventive interventions to confront that illness. In Iraq, few studies on the seasonality of certain pediatric illnesses have been published, notably diarrheal disease,<sup>10</sup> cholera,<sup>11</sup> chicken pox,<sup>12</sup> Guillain-Barré syndrome,<sup>13</sup> and acute appendicitis.<sup>14</sup> To broaden the list of the seasonality-

associated illnesses in Iraqi pediatric literature, we attempted in the current work to study the seasonality of pediatric intussusceptions, if any.

The seasonal distribution of intussusception cases in the current study showed the highest rate in summer (30.8%) compared to the season of fall (25.3%), spring (22.1%), and winter (21.8%), (Figure 1). Summer seasonality could be partly related to the antecedent gastrointestinal infections. This could be concluded from retrieving data from the latest annual statistical report published by the Ministry of Health/ Environment in Iraq where gastroenteritis rate was the predominant illness in summer among children visiting health care centers.<sup>15</sup> Various viral infections could play a pivotal role in the intussusception development as the virus detection rate was found to be high (63%) in the stools of intussusception patients. The intussusception seasonality occurrence rate was noticed to be parallel with seasonal

Variable		Season				Total No. %	p-value
		Winter No. %	Spring No. %	Summer No. %	Fall No. %		
Age (years)	<1	47(16.5)	45(15.8)	68(23.8)	52(18.2)	212(74.3)	0.678
	1-3	8(2.8)	8(2.8)	10(3.5)	14(4.9)	40(14.1)	
	>3	7(2.5)	10(3.5)	10(3.5)	6(2.1)	33(11.6)	
	Total	62(21.8)	63(22.1)	88(30.8)	72(25.2)	285(100)	
Gender	Male	41(14.4)	32(11.2)	62(21.8)	51(17.9)	186(65.3)	0.048
	Female	21(7.4)	31(10.9)	26(9.0)	21(7.4)	99(34.7)	
	Total	62(21.8)	63(22.1)	88(30.8)	72(25.2)	285(100)	

Table 2. Statistical correlation between the season and age and gender in the studied patients.

Researchers	Country	No. of cases	Period of the study	Seasonality
Gadisa et al <sup>5</sup>	Ethiopia	130	4 years	Wet season
Carneiro and Kisusi <sup>6</sup>	Tanzania	26	4 years	Dry season
Serayssol et al <sup>7</sup>	France	306	10 years	No seasonality
Giak et al <sup>8</sup>	Malaysia	62	3 years	No seasonality
Jiang et al <sup>9</sup>	World literature (from North America, Asia, Europe, Oceania, Africa, Eastern Mediterranean, and Central and South America)	44,454	10 years	No seasonality
Al-Mendalawi et al (Current study)	Iraq	285	6 years	Summer season

Table 3. Comparison of the intussusception seasonality between the current study and worldwide studies.

these viral detection rate in the stool samples.<sup>16</sup> The intussusception seasonality in the current study appears interesting on comparing it with other published studies worldwide (Table 3). For instance, Gadisa et al<sup>5</sup> pointed out to the intussusception predominance in wet season in their four-years retrospective study on 130 Ethiopian children with intussusception. Carneiro and Kisusi<sup>6</sup> studied 26 children with intussusception at Muhimbili National Hospital, Dar es Salaam, Tanzania through a four-year period and demonstrated that intussusception seasonal variation was seen, most cases (78.6%) presenting in the dry season when there was shortage of water in the city. However, Serayssol et al<sup>7</sup> in their evaluation of 306 idiopathic ileocolic intussusceptions (280 patients) in France over a 10-year period found no seasonal pattern of intussusception or fall/winter predominance ( $p=0.6$ ) in the cumulative number of monthly cases: 24% of the intussusceptions occurred during fall, 29% during spring, 27% during summer, and 21% during winter. Similarly, Giak et al (8) found no distinct intussusception seasonality during the three-year study period on 62 Malaysian children hospitalized due to intussusception. Interestingly, Jiang et al<sup>9</sup> conducted a literature review on 82 studies recruiting 44,454 cases of intussusception from North America, Asia, Europe, Oceania, Africa, Eastern Mediterranean, and Central and South America revealed no particular intussusception seasonality. The difference between our observation in the current study and the above-mentioned studies could be attributed to the variations in the number of the studied patients and study period.

Although the majority of our studied patients

(74.3%) were under the age of one year, no statistically significant correlation was noticed between intussusception seasonality and age ( $p=0.678$ ), Table 2. This looks interesting with the notion that children with intussusception might be misdiagnosed or diagnosed late because they often present with a wide range of non-specific systemic symptoms, with less than one quarter presenting with the classic triad of, abdominal pain, vomiting, and bloody stools.<sup>17</sup> Importantly, intussusception should be considered in the differential diagnosis in infants and young children presenting as a pediatric emergency with hypotonia, lethargy, paroxysmal events, and/or altered mental status, particularly when none of the classical signs and symptoms of intussusception are present.<sup>18-19</sup>

In the current study, males outnumbered females (65.3% vs. 34.7%). Statistical analysis revealed a significant correlation between intussusception seasonality and gender ( $p=0.048$ ) (Table 2). In Iraq, medical care is equally offered to all patients irrespective of gender. However, some sort of gender discrimination in seeking early medical consultation for sick children is traditionally followed by many parents in Iraqi community. Males are culturally preferred at the expense of females. This might possibly explain the preponderance of male patients in the studied cohort.

The current study has two limitations. First, it was a single center experience. Second, it was retrospective with the inherited biases from this kind of study. Better idea on intussusception seasonality could have been obtained if a national registry was already established

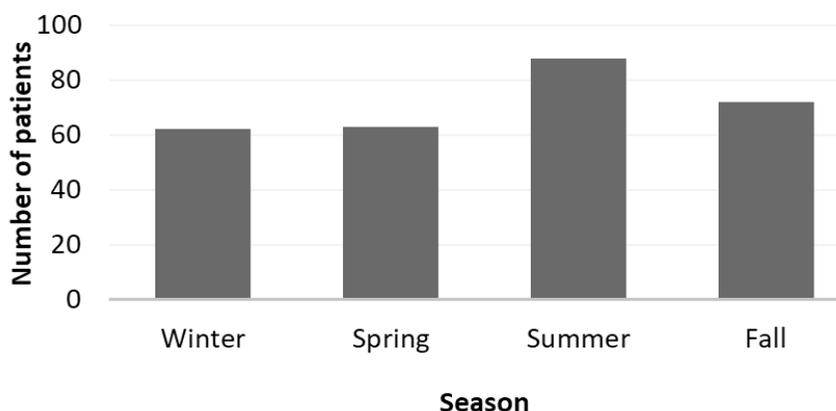


Figure 1. Seasonal distribution of the studied patients.

and data were collected across the country. Regrettably, the absence of national registry on intussusception in Iraq has hampered our attempt to precisely study the intussusception seasonality at the national level.

## CONCLUSIONS

The study results pointed out to summer seasonality of the intussusception in the studied population. Pediatric surgeons and pediatricians should consider seasonality on evaluating children with the clinical presentation suggestive of intussusception. Conducting large size, multi-center, prospective studies encompassing different regions across the country is suggested to verify our results.

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