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Contents:

THE ATLANTA CLASSIFICATION AND DEFINITIONS OF ACUTE PANCREATITIS HAVE BEEN REVISED AND ARE BASED ON WORLDWIDE CONSENSUS

(Review Articles)

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ABSTRACT
Background and Objective: In a complex disease such as acute pancreatitis, correct terminology and clear definitions are important. The clinically based Atlanta Classification was formulated in 1992, but in recent years it has been increasingly criticized. No formal evaluation of the use of the Atlanta definitions in the literature has ever been performed. Deficiencies identified and improved understanding of the disease make a revision necessary. Methods: A Medline literature search sought studies published after 1993. The guidelines, review articles, and their cross-references were reviewed to assess whether the Atlanta or alternative definitions were used. Revisions were made in response to comments. The consensus was reviewed, and only statements based on published evidence were retained. Results: The severity of the disease is classified as mild, moderate, or severe. Mild acute pancreatitis, the most common form, has no organ failure, local or systemic complications, and usually resolves in the first week. Moderately severe acute pancreatitis is defined by the presence of transient organ failure, local complications, or exacerbation of co-morbid disease. Severe acute pancreatitis is defined by persistent organ failure, that is, organ failure lasting more than 48 h. Local complications are peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocysts, and walled-off necrosis (sterile or infected). We present a standardized template for reporting CT images. There was a large variation in the interpretation of the Atlanta definitions of local complications, especially relating to the content of peripancreatic collections. Conclusion: The Atlanta definitions for acute pancreatitis are often used inappropriately, and alternative definitions are frequently applied. Such a lack of consensus illustrates the need for a revision of the Atlanta Classification. So, the consensus provides clear definitions to classify acute pancreatitis using easily identified clinical and radiological criteria.

Key words: Acute pancreatitis; Predictive severity scoring system; The Atlanta definitions; CECT imaging, Multi-organ failure; Necrosectomy; Pancreatic necrosis.

Introduction

Over the past 50 years, multidisciplinary symposia1-4 have produced a number of classification schemes for pancreatitis. The 1992 Atlanta Symposium, the most recent international conference on the subject, created a classification scheme with a clinical foundation.4.5 Acute pancreatitis was defined, along with its severity, organ failure, and local complications such "acute fluid collection," "pancreatic necrosis," "pseudocyst," and "pancreatic abscess." The Atlanta Classification made an effort to bring about consistency in the evaluation of clinical severity and the numerous illness consequences. The sole classification scheme utilised by radiologists and clinicians is this particular one.

Several writers have identified weaknesses in the Atlanta Classification due to growing understanding of the pathophysiology of pancreatitis and the creation of new interventional techniques.[6–13] Phlegmon and infected pseudocyst, for example, were terms dropped by the Atlanta symposium, but they are still commonly used in the literature. A recent analysis also showed that several new names, like "organised pancreatic necrosis" and "necroma," have been used since 1993.[14] There has never been a thorough analysis of how the Atlanta Classification is used in the literature.

Modern disease concepts were integrated into this revision in in order to clarify some points, improve clinical severity assessment, enable standardised reporting of data, aid in the objective assessment of new therapeutic treatments, and streamline communication between institutions and among treating physicians.

The current review analyses the level of diversity in these definitions' interpretations as well as the acceptance of the Atlanta Classification definitions in the literature. Consequently, this change is not meant to serve as a managerial directive.

Methods

The terms "acute pancreatitis and review" and "acute pancreatitis and guidelines" were used in a Medline search of literature published between 1993 and 2006 to find appropriate articles. Cross-references were collected from the found guidelines and reviews. All publications (reviews, recommendations, initial investigations, case reports, and editorials) were included in the search, however those not written in English were not included.

To determine if the following five elements of the Atlanta Classification were defined using the original Atlanta definitions from 1992 **(Table 1)** or another definition, one author (T.L.B.) did the selection and evaluated all full-text papers. Organ failure (determinants of specific failing organ systems, cut-off levels of determinants, distinction between single-organ failure and multi-organ failure), actual severity (difference between mild and severe pancreatitis, distinction between predicted and actual severity), local complications, and predicted severity (predictive scoring systems, predictive scoring systems, cut-off levels of scoring systems) (pancreatic necrosis and peripancreatic necrosis, infection of necrosis, morphological aspects and distinction of different types of collection).

One of the two other authors verified any instances where the components had differing definitions (H.C.v.S., M.G.B.). The authors discussed each issue to find a solution. Additionally, research findings that provided fresh perspectives and may have affected how the Atlanta Classification was interpreted

were noted and debated. Only the three most current publications for each element of the Atlanta Classification that was evaluated are cited here due to the vast number of references that were obtained.

Table 1 Summary of the 1992 Atlanta Classification

	Definition
Acute pancreatitis	An acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ systems Associated with raised pancreatic enzyme levels in blood and/or urine
Severity	Associated with minimal organ dysfunction and an uneventful
Mild acute pancreatitis	recovery; lacks the features of severe acute pancreatitis. Usually normal enhancement of pancreatic parenchyma on contrast-enhanced computed tomography
Predicted severity	Ranson score ≥ 3 or
APACHE II score ≥ 8 Organ failure and systemic complications	
Shock	Systolic blood pressure < 90 mmHg
Pulmonary insufficiency	Creatinine ≥ 177 □mol/l or ≤ 2 mg/dl after rehydration
Gastrointestinal bleeding	500 ml in 24 h
Disseminated intravascular coagulation	Platelets $\leq 100, 000/mm3$, fibrinogen $< 1{\cdot}0$ g/l and fibrin-split
products > 80 □g/l Severe metabolic disturbances	Calcium $\leq 1{\cdot}87$ mmol/l or $\leq 7{\cdot}5$ mg/dl
Local complications	
Acute fluid collections	Occur early in the course of acute pancreatitis, are located in or near the pancreas and always lack a wall of granulation of fibrous tissue. In about half of patients, spontaneous regression occurs. In the other half, an acute fluid collection develops into a pancreatic abscess or pseudocyst
Pancreatic necrosis	Diffuse or focal area(s) of non-viable pancreatic parenchyma, typically associated with peripancreatic fat necrosis Non-enhanced pancreatic parenchyma > 3 cm or involving more than 30% of the area of the pancreas
Acute pseudocyst	Collection of pancreatic juice enclosed by a wall of fibrous or granulation tissue, which arises as a result of acute pancreatitis, pancreatic trauma or chronic pancreatitis, occurring at least 4 weeks after onset of symptoms, is round or ovoid and most often sterile; when pus is present, lesion is termed a 'pancreatic abscess'
Pancreatic abscess	Circumscribed, intra-abdominal collection of pus, usually in proximity to the pancreas, containing little or no pancreatic necrosis, which arises as a consequence of acute pancreatitis or pancreatic trauma Often 4 weeks or more after onset Pancreatic abscess and infected pancreatic necrosis differ in clinical expression and extent of associated necrosis

Grades of severity

- ‣ Mild acute pancreatitis
  - ▪ No organ failure
  - ▪ No local or systemic complications
- ‣ Moderately severe acute pancreatitis
  - ▪ Organ failure that resolves within 48 h (transient organ failure) and/or
  - ▪ Local or systemic complications without persistent organ failure
- ‣ Severe acute pancreatitis
  - ▪ Persistent organ failure (>48 h)

- − Single organ failure
- − Multiple organ failure

Results

447 papers in all, including 82 reviews and 12 guidelines, were examined. These articles just used Atlanta definitions while reporting on research that weren't intended to evaluate the Atlanta Classification, such as a randomised trial comparing two treatment modalities with the result "pseudocyst." An evaluation of methodological quality was therefore ruled inappropriate. **Table 2** provides a summary of the papers by the article type and journal impact factor that they were published in. The most significant differences between the 12 guidelines and *the five components of the Atlanta Classification* are explored in order:

Diagnosis

Pancreatic enzyme levels have no cut-off value specified by the Atlanta Classification. A distinctive clinical history of stomach discomfort and an elevation of pancreatic enzyme levels to three or more times the upper limit of normal were necessary for the diagnosis of acute pancreatitis in 116 investigations. Although 31 studies utilised a variety of criteria, ranging from two or more[15-17] than four[18-20] and more than five[21-23] times the upper limit of normal, these thresholds were all within this range.

Predicted severity

A total of 283 articles included criteria for estimating acute pancreatitis severity. The severity rating schemes suggested by the Atlanta symposium were applied in about 86 reports.[16,17,23] However, 197 studies employed a different cut-off point to define severity, or they used extra or other scoring systems, such as the Sequential Organ Failure Assessment, Imrie (Glasgow) score, Imrie (CT) severity index, or severity predictors (such as C-reactive protein).[15,24,25] The severity stratification cut-off values varied widely between reports. The most well-known radiological grading system, the CT severity index, was created by Balthazar and colleagues in 1990. The cut-off value to distinguish between mild and severe disease ranged from three to eight points.[27-29]

Acute Physiology and Chronic Health Evaluation (APACHE) II threshold values (other than eight or more) varied between five and more in 32 studies, while the duration for calculating the score ranged from the day of admission to 24, and 48 h after admission.[30-32] Eleven studies, ranging in size from more than three to more than five, used various threshold values for the Ranson criteria (other than three or more).[32-34]

Since the Atlanta symposium in 1992, numerous researchers have discovered additional severity determinants, and these have been integrated into a number of guidelines. Obesity (body mass index greater than 30 kg/m2), age (above 55[6], over 70[35], or over 80[36] years), and [11, 24, 37]; left or bilateral pleural effusion on a chest radiograph;[38-40]; increased haematocrit;[6, 41, 42]; and a C-reactive protein level of more than 150 mg/dl after 48 hours.[43-45]

Table 2 Characteristics of retrieved articles (1993 – 2006) specified according to impact factor of journal

Total no. of studies ($n = 447$)	High ($> 5{\cdot}0$) ($n = 89$)	**Impact factor** Intermediate ($1{\cdot}5$–$4{\cdot}9$) ($n = 273$)	Low ($< 1{\cdot}5$) ($n = 85$)
Meta-analyses	3	2	1	0
Randomized controlled trials	34	13	18	3
Prospective series	144	28	99	17
Retrospective series	147	23	95	29
Reviews	82	10	44	28
Guidelines	12	5	5	2
Editorials	5	2	3	0
Other	20	6	8	6

Actual severity

Of the 297 articles that supplied definitions for severe acute pancreatitis, 195 did so in accordance with the Atlanta Classification, while 61 merely noted the adoption of the Atlanta criteria without giving further specifics.[46–48] The Atlanta Classification was not utilized to characterize serious disease in the remaining 102 articles. These definitions were based on various additional or undefined criteria, like intensive care unit admission, hospital stay length, complications requiring medical or surgical intervention, mortality, etc.[17,49,50] The authors of 45 publications used moderate acute pancreatitis and severe acute pancreatitis indiscriminately when talking to existence or absence of pancreatic necrosis.[47,51,52] However, several reports noted that individuals with the morphological diagnosis of interstitial pancreatitis can suffer clinically serious illness.[44,53,54]

It is unclear how the development of organ failure is impacted by pancreatic necrosis, a significant contributor to severe acute pancreatitis. Several studies found that only 51–55% of patients with pancreatic necrosis had organ failure.[55–57] In the study by Lankisch and colleagues, 53.5% of patients with acute edematous pancreatitis had organ failure. In a recent study, organ failure was discovered to be the main risk factor for mortality regardless of whether pancreatic necrosis was present or absent.[23] On the other hand, numerous studies showed a high correlation between organ failure and the severity of pancreatic necrosis.[16,58,59]

In 38 articles, which compared acute pancreatitis with both conditions, the distinction between "actual severe" disease (systemic or local complications) and "predicted severe" disease (Ranson, Imrie, or APACHE II score) was not readily apparent from the provided data.[17,28,60] The distinction is important because, according to recent studies, fewer than 50% of individuals who were expected to have severe disease really did so, according to the Atlanta criteria.[25,46] This lack of differentiation may account for the variation in incidence of severe acute pancreatitis between institutions.

Organ failure

149 articles contained organ failure criteria. The precise Atlanta definitions for organ failure were stated and used in 35 reports.[23,61,62] Seven publications limited organ failure to the respiratory and renal insufficiencies, two of the four Atlanta determinants for organ failure.[63–65] However, 107 articles used additional criteria for organ failure and systemic complications, including sepsis, leucocytosis, temperature, coagulopathy, nervous system failure, hepatic failure, and systemic inflammatory response syndrome, or they used different cutoffs or adjustments for the Atlanta definitions of organ failure.[52,66,67] The remaining articles either did not define organ failure at all or they only said that the Atlanta criteria were used without more explanation.

Multiorgan failure has been identified as an important predictor of mortality in recent years. Multiorgan failure, however most research did not define it, has been defined in 20 reports as the failure of two or more organ systems,[31,46,49] and eight reports as the failure of three or more organ systems.[23,68,69]

Numerous authors have distinguished between transitory and permanent organ failure, highlighting the dynamic process of organ malfunction.[70–72] Furthermore, numerous investigations revealed that while temporary organ failure typically had an easy course, early and progressive organ failure were associated with increased mortality.[72–74] According to the most recent UK guidelines on acute pancreatitis, organ failure in the first week that settles within 48 hours shouldn't be taken as a sign of a serious illness.[43]

The number of organ systems involved as well as the extent of each organ's dysfunction are taken into account by the Goris score, Marshall or multiple organ dysfunction score, Bernard score, Sequential Organ Failure Assessment, and logistic organ dysfunction syndrome score, all of which are developed since 1993. Some systems additionally require the use of mechanical ventilation, dialysis, and inotropic or vasopressor medications, which even the Atlanta symposium did not take into consideration.

Numerous studies have demonstrated that dynamic scoring systems, such as the delta APACHE II score, or scoring systems that take into account the physiological response to therapy, such as the delta organ failure score or cumulative Marshall score, are superior to static scoring systems as predictors of outcome.[31,32,71]

Local complications

Interobserver agreement was poor in a recent investigation on the Atlanta criteria for the various local complications; just three of the 70 collections visualized by contrast-enhanced CT (CECT) had five radiologists agree on the corresponding Atlanta classification.[8]

Acute fluid collection

In 64 articles, a definition was given for an "acute fluid collection'. The following terms were used to describe acute fluid collections: '(peri)pancreatic fluid collections",[75–77] "peripancreatic effusions",[78] "extra pancreatic fluid collections",[61,79,80] "immature pseudocyst",[81,82] and "exudates".[54] (Peri)pancreatic fluid collection was also used as an overall descriptive term for all types of collection related to acute pancreatitis.[83–85]

In most reports, the differentiation between acute fluid collection and pseudocysts was made after 4 weeks from the onset of disease (as proposed by the Atlanta Classification). In eight reports, however, a different time period was used as a criterion for this distinction, varying from 3 weeks[75, 86, 87] to 6[88, 89] and even 8[90] weeks. Moreover, they did not adequately describe whether acute fluid collections consisted of fluid alone or whether they may have contained necrotic debris.[85,91,92]

The authors of 17 articles regarded the occurrence of an acute fluid collection as a local complication and so a sign of 'severe disease'.[46,62,93] However, most others did not include acute fluid collection either in the definition of local complication or in that of severe disease.

Pancreatic necrosis

47 of the 152 articles *(Fig. 1)* that provided a comprehensive definition of "pancreatic necrosis" or "necrotizing pancreatitis" used the Atlanta criterion of more than 30% parenchymal necrosis to do so.[28,61,94] However, necrotizing pancreatitis was defined as any indication of pancreatic parenchymal necrosis, even if it was less than 30%.[47,95,96] The emergence of pancreatic necrosis, extra pancreatic necrosis, or both on CECT (along with a serum C-reactive protein value of more than 150 mg/dl) was a third definition of necrotizing pancreatitis that was cited in 20 studies.[52,86,97]

Pancreatic parenchymal non-enhancement on CECT is a requirement for pancreatic necrosis in the Atlanta Classification. [4] However, some healthcare professionals questioned if the absence of enhancement on CECT indicated necrosis and irreversible harm.[86,98,99] For instance, devitalized tissue discovered during surgery was classified as pancreatic necrosis by Traverso and Kozarek86. Takeda and colleagues,[100-102] who pointed out that pancreatic parenchymal perfusion was preserved during intra-arterial angiography whereas CECT revealed pancreatic non-enhancement, provided support for this. On the other hand, multiple investigations showed a strong association between the presence of pancreatic necrosis and parenchymal non-enhancement on CECT (confirmed at operation).[103–105]

a Normal enhancement of the pancreas
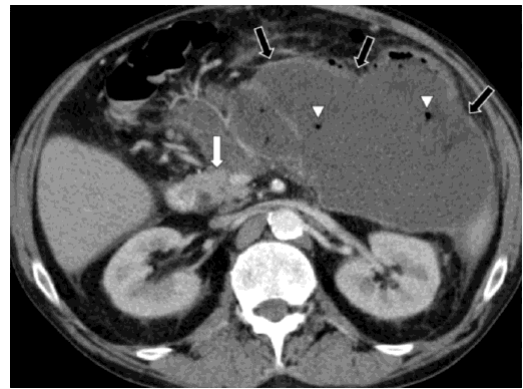
b Large fluid collection with gas bubbles
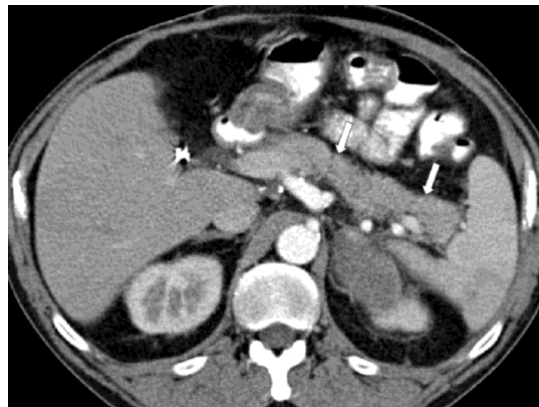
c Follow-up 6 months after operation

Fig. 1 Contrast-enhanced computed tomography (CT) of a patient with acute pancreatitis 22 days after onset of symptoms

    a with normal enhancement of the pancreas (white arrows) and

    b surrounded by a large heterogeneous and encapsulated fluid collection (black arrows) with gas bubbles (arrowheads) suggesting secondary infection. Some would call this 'necrotizing pancreatitis', but others would call it 'interstitial pancreatitis' because there is no evidence of pancreatic parenchymal necrosis (only peripancreatic necrosis). A large amount of fat necrosis was debrided during operation.

    c Follow-up CT 6 months after operation reveals a normal enhancing pancreatic parenchyma (white arrows)

Contradictory information exists on the diagnostic efficacy of CECT in extra-pancreatic or peripancreatic fat necrosis. Several investigations showed a strong association between extra pancreatic findings on CECT and the presence of fat necrosis at operation or autopsy, despite eight groups' claims that fat necrosis could not be consistently detected by CECT.[92,106,107,104,108,109]

According to the Atlanta Classification, "pancreatic necrosis" applies to both infected and sterile necrosis. 4 According to some organizations, pancreatic parenchymal necrosis without infection does not provide a significant morbidity risk.[110–112]

Studies demonstrating an uncomplicated course in the presence of necrosis without infection provided support for this.[23,55,56]

Beger and colleagues[81,113] were the first to point up necrosis as a potential nidus for secondary infection, which affects 40–70% of patients. This was supported by recent research, which showed that infected necrosis was the main reason for late mortality.[58,114,115] Definitions of "infected necrosis," though, varied widely. According to some writers, parenchymal necrosis, peri-pancreatic fat necrosis (in the absence of parenchymal necrosis), or both can be infectious.[67,76,119]

Pseudocyst

In 87 publications, the term "pseudocyst" had a particular definition that was similar to the Atlanta Classification. However, several issues continue to be controversial. The pseudocyst category comprised 38 articles that featured collections of both fluid and necrotic material (Fig. 2, 3).120–122 However, according to Baron123 and others85,124, pseudocysts should be free of substantial necrotic debris. According to the evidence, collections with fluid alone and those with fluid plus necrosis differed in their therapeutic approach and results.[84,125,126] The mistaken identity of (peri)pancreatic fluid collections as pseudocysts by CECT, in Bradley's [127] opinion, is a very frequent mistake in modern diagnostic radiography. This misinterpretation has two potentially harmful effects: *<u>first</u>*, by instrumentation of a sterile collection containing both fluid and necrosis, infection may be introduced6,[120,128]; *<u>second</u>*, a delay in appropriate intervention may occur.[33,120,129]

There were differences between acute and chronic pseudocysts in terms of incidence, natural history, and management choices. As a result of the lack of distinction made between pseudocysts and acute fluid collections, or between pseudocysts that complicated acute and chronic pancreatitis, several authors emphasized that the results of treatment for pancreatic fluid collections in the literature were challenging to interpret.[122,128,130] Only five of the 31 original studies on the topic of treating pseudocysts that were reviewed specifically addressed those that developed following an episode of acute pancreatitis.[89,120,131] The outcomes of treating pseudocysts that exacerbated acute and chronic pancreatitis were reported in the remaining 26 publications.[121,132,133]
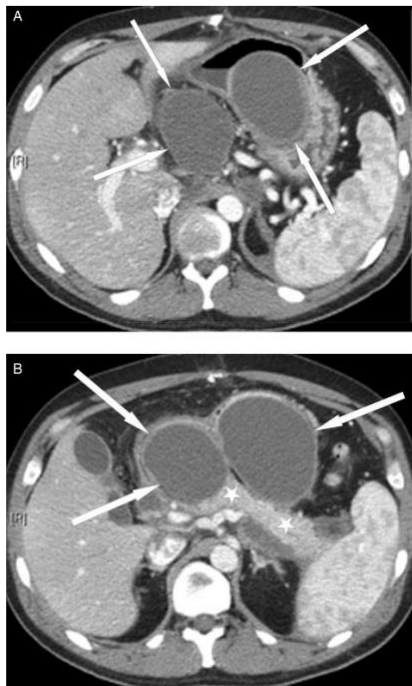
Figure 2 A 40-year-old man with two pseudocysts in the lesser sac 6 weeks after an episode of acute interstitial pancreatitis on CT (A, B). Note the round to oval, low-attenuated, homogeneous fluid collections with a well-defined enhancing rim (white arrows pointing at the borders of the pseudocysts), but absence of areas of greater attenuation indicative of non-liquid components. White stars denote normal enhancing pancreas.

Fig. 3 Contrast-enhanced computed tomography (CT) of a patient with acute pancreatitis 30 days after onset of symptoms. The fluid collection seems to be homogeneous and encapsulated (white arrows) and could be interpreted as a 'pseudocyst' according to the Atlanta Classification. However, at operation the collection was found to contain large amounts of necrotic debris that CT had not show

Pancreatic abscess

A definition of "pancreatic abscess" was given in 68 papers, and it typically matched the original Atlanta definition. Three of the nine original publications published after 1993 that addressed the treatment of "pancreatic abscesses" strictly adhered to the Atlanta definition (collection of pus and almost little necrotic debris, more than 4 weeks after onset).[134–136] The others comprised specimens that were treated within 4 weeks after disease onset[140] or after surgery, or those contained solid necrotic material in addition to pus.[141,142] On CECT, the diagnosis of pancreatic abscess is similarly debatable. The "air bubble" phenomenon was deemed "diagnostic of a pancreatic abscess" in 10 articles.[93,143,144] Gas bubbles in a heterogeneous collection on a CT scan, however, were thought to be a strong indicator of infected pancreatic necrosis *(Fig. 4)*.[61,67,145] There are numerous theories as to the cause of pancreatic abscess. According to some authors, pancreatic abscesses and "post-acute pseudocysts" are late effects of necrotizing pancreatitis.[146–148] The interstitial pancreatitis with a normal augmenting pancreas on CECT, according to some, is the only condition in which pancreatic abscesses can develop.[117,149,150]

Several authors proposed that pancreatic abscesses arose from the gradual liquefaction of necrotic pancreatic and peripancreatic tissues, which eventually led to full liquefaction, in addition to the "infection of a pseudocyst".[76,123,151] Although some doctors detect "pancreatic abscesses" after 1[50,152],2[153,154] or 3[86,146,147] weeks, the Atlanta Classification states that the majority of pancreatic abscesses develop at least 4 weeks after the onset of symptoms.[4] Interestingly, variable degrees of liquefaction of necrotic tissue were seen during operational necrosectomy performed several months after the beginning of severe acute pancreatitis by Morgan and colleagues[10], Howard and Wagner[155], and others.[156] Given that they found both pus and necrotic material in these (infected) collections, several authors speculated that a collection would be a transitional form from (infected) pancreatic necrosis to a (infected) pseudocyst or pancreatic abscess.[7,12,139]

Fig. 4 Contrast-enhanced computed tomography of a patient with acute pancreatitis 36 days after onset of symptoms. The body and tail of the pancreas are largely non-enhancing. Adjacent to the pancreatic bed is a large collection with predominately fluid-like attenuation (white arrows). Because of the gas bubbles (arrowheads), some would call this a 'pancreatic abscess' but others would call it 'infected pancreatic necrosis'

Walled-off necrosis

WON consists of necrotic tissue contained within an enhancing wall of reactive tissue. This collection of pancreatic and/or peripancreatic necrosis is mature, encapsulated, and has a well-defined inflammatory wall (*figure 5)*; typically, this maturation takes place about 4 weeks following the commencement of necrotising pancreatitis. The term "organised pancreatic necrosis" as well as "necroma," "pancreatic sequestration," "pseudocyst associated with necrosis," and "subacute pancreatic necrosis" were previously proposed names for this condition.
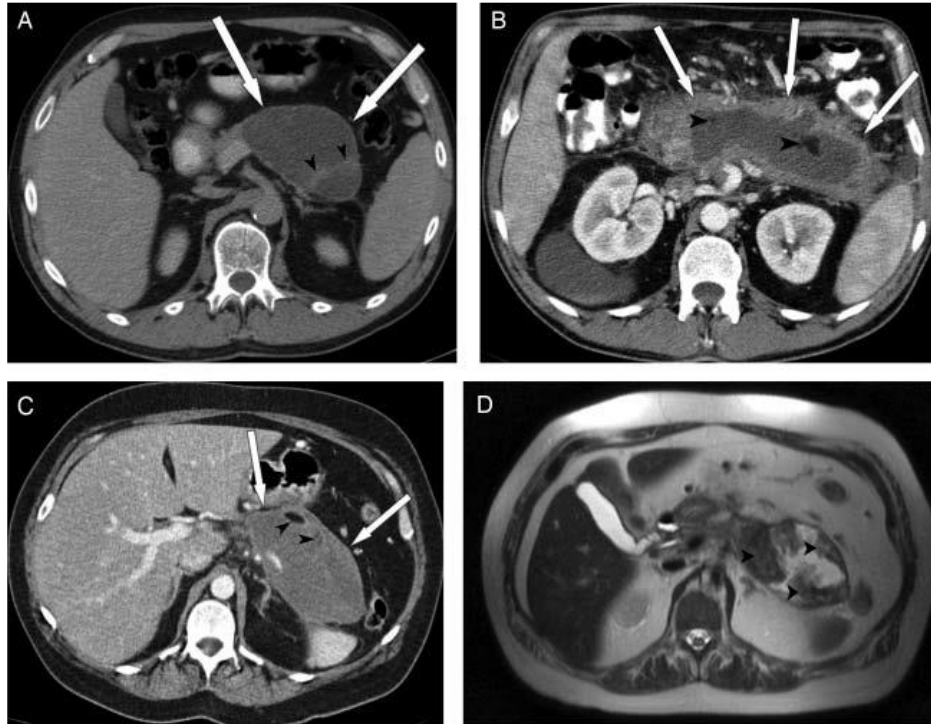

Figure 5 (A–C) Three different patients with walled-off necrosis (WON) after an acute attack of necrotising pancreatitis. In all three patients, a heterogeneous, fully encapsulated collection is noted in the pancreatic and peripancreatic area.

        (A) Non-liquid components of high attenuation (black arrowheads) in the collection ar noted. The collection has a thin, well defined, and enhancing wall (thick white arrows).

        (B, C) A largely liquefied collection in the bed of the pancreas is observed with non-liquid components representing areas of trapped fat (black arrowheads).

        (D) represents the corresponding T2-weighted MRI to (C), showing the tru heterogeneity of the collection. Black arrowheads denote areas of necrotic debris surrounded by fluid (white on T2-weighted image).

The most significant differences in the criteria of organ failure and those of projected severe disease were seen in the 12 guidelines[6,35,36,43,148,157-165] on acute pancreatitis. These are summarized in Table 3.

Table 3 Overview of definitions for organ failure and predicted severe acute pancreatitis in guidelines for acute pancreatitis published after **1993**

Guideline	Definitions for organ failure	Definitions for predicted severe acute pancreatitis
ACG 1997[157]	Refers to Atlanta Classification 1992	Ranson score ≥ 3 after 48 h APACHE II score > 8 after 48 h
UK 1998[158]	Refers to Atlanta Classification 1992	Ranson/Glasgow ≥ 3 CRP > 210 mg/l (first 4 days) or > 120 mg/l at 1 week APACHE II score ≥ 9 (severe acute pancreatitis) or ≥ 6 (includes all severe cases, but PPV of 50%)
SSAT 1998[159]	Not addressed	Not stated
Santorini 1999[160]	Not addressed	BMI > 30 kg/m^2 Pleural effusion APACHE II score ≥ 6 (at 24 h) APACHE (obesity) score ≥ 6 CRP > 150 mg/l

French 2000[36]	Renal failure: creatinine > 170 μmol/l
	Shock: systolic BP < 90 mmHg despite fluid replacement
	Pulmonary insufficiency: Pa_{O2} ≤ 60 mmHg on room air
	Glasgow Coma Score < 13
	Platelets < 80 g/l
		At admission Age
		  > 80 years
		  BMI > 30 kg/m^2
		Chronic renal failure
		  Pre-existing severe illnesses
		At 24–48 h
		  Presence of organ failure by using simple measures or use of scoring system (e.g. SOFA)
		  Ranson/Imrie score > 3
		  CECT: CT severity index ≥ 4 (48–72 h)
		  CRP > 150 mg/l
		Note: 'The non-specific scores (APACHE II, SAP II, etc) are not recommended by the Jury'

WCG 2002[35]	SIRS
	≥ 1 vital organ dysfunction
	ARDS
	Renal failure: increased serum creatinine > 0·5 mg/dl (44 μmol/l) or 50% above baseline or reduction in calculated creatinine clearance > 50% or need for dialysis
	Hypotension: mean arterial pressure < 60 mmHg
	DIC
	Acute adrenal insufficiency
	Acute hepatitis
	Metabolic encephalopathy
	Ileus
		At admission
		  Age > 70 years
		  Clinical assessment
		  BMI > 30 kg/m^2
		  Pleural effusion/infiltrates
		  CECT: > 30% non-enhancement of the pancreas
		  APACHE II score ≥ 8
		  Presence of organ failure
		At 24–48 h
		  Clinical assessment
		  Glasgow score (no cut-off value provided)
		  CRP > 150 mg/l
		  Presence of organ failure

IAP 2002[161]	Not addressed	Not stated: surgical guideline
JSAEM 2002[162]	Not addressed	Clinical signs CRP (48 h: no cut-off value provided) BMI (no value provided) CECT: necrosis Scoring system, like JMHW, APACHE II at 24 h or Ranson/Glasgow at 24–48 h: no cut-off values provided Japanese score ≥ 2
Nathens 2004[148]	Refers to the guidelines for intensive care unit admission, published in 1999[163]	Elderly (age not specified) BMI > 30 kg/m^2 Patients requiring ongoing volume resuscitation CECT: > 30% non-enhancement of the pancreas Clinical assessment *Note: 'Disease-specific scoring systems or severity scores are useful adjuncts to identify patients at high risk of a complication but should not replace serial clinical assessments. In addition, there is a recommendation against the use of markers such as CRP or procalcitonin to guide clinical decision making or predict clinical course of acute pancreatitis or to triage patients'*

Guideline	Definitions for organ failure	Definitions for predicted severe acute pancreatitis

UK 2005[43]	Refers to Atlanta Classification 1992	At admission
		  Clinical assessment
		  BMI > 30 kg/m²
		  Pleural effusion
		  APACHE score > 8
		At 24–48 h
		  Clinical assessment
		  Glasgow score ≥ 3
		  APACHE II score > 8
		  Persistent organ failure for 48 h (especially if multiple and progressive)
		  CRP > 150 mg/l
		Note: 'Organ failure present within 1 week, which resolves within 48 h, should not be considered an indicator of a severe attack of acute pancreatitis'

ACG 2006[6]	Refers to Atlanta classification 1992
	
	Note: 'Criteria of organ failure will change in the future: gastrointestinal bleeding will undoubtedly be deleted'
		At admission Age
		  > 55 years
		  BMI > 30 kg/m²
		  Presence of organ failure
		  Pleural effusion/infiltrates
		24–48 h
		  APACHE II score ≥ 8
		  Serum haematocrit ≥ 44%
		Note: 'Ranson signs are no longer advocated, due to a comprehensive evaluation of 110 studies that concluded that Ranson signs provided very poor predictive power of severity of acute pancreatitis'

JSAEM 2006[164,165]	Pulmonary insufficiency: dyspnoea Shock Central nervous system disorders Bleeding tendency Negative base excess failure: rise of blood urea nitrogen level and creatinine level	Japanese score ≥ 2

ACG, Practice Parameters Committee of the American College of Gastroenterology; APACHE, Acute Physiology And Chronic Health Evaluation; UK, Working Party of the British Society of Gastroenterology, Association of Surgeons of Great Britain and Ireland, Pancreatic Society of Great Britain and Ireland, and Association of Upper GI Surgeons of Great Britain and Ireland; CRP, C-reactive protein; PPV, positive predictive value; SSAT, Society for Surgery of the Alimentary Tract; Santorini, Santorini Consensus Conference; BMI, body mass index; French, French Consensus Conference on Acute Pancreatitis; BP, blood pressure; Pa_{O2}, arterial partial pressure of oxygen; SOFA, Sequential Organ Failure Assessment; CECT, contrast-enhanced computed tomography; SAP, Simplified Acute Physiology; WCG, World Congress of Gastroenterology; SIRS, systemic inflammatory response syndrome; ARDS, adult respiratory distress syndrome; DIC, disseminated intravascular coagulation; IAP, International Association of Pancreatology; JSAEM, Japanese Society of Emergency Abdominal Medicine; JMHW, Japanese Ministry of Health and Welfare; Nathens, Consensus Statement regarding the management of the critically ill patient with severe acute pancreatitis.

Discussion

The current review has revealed that the Atlanta definitions of acute pancreatitis severity and local complications are applied inconsistently and that various aspects of the classification have drawn a lot of criticism. The Atlanta conference improved the management of acute pancreatitis and clinical research pertaining to the condition by providing definitions, the outcome of consensus among more than 40 scientists based on the evidence available in 1992. The last 20 years, however, have seen advancements in imaging methods in addition to new understandings of pathophysiology and therapeutic approaches. It seems obvious that it is time to change how acute pancreatitis is categorised. Since the Atlanta symposium, the various predictive scoring systems have not much improved. When forecasting severe disease in a particular patient, they are only moderately accurate. Predictive systems were initially created to assign patients to clinical trials, not to determine the severity of an individual, as McKay and Imrie[166] have highlighted. There are additional drawbacks to determining severity based on the presence or absence of organ failure. The most significant predictor of morbidity and death, which are primarily correlated with the number of organ systems failing, the severity of the organs implicated, and the length of organ failure, is now widely acknowledged to be persistent organ failure (lasting longer than 48 hours). Because it includes both sterile and infectious necrosis, as well as pancreatic parenchymal necrosis and peripancreatic fat necrosis, the definition of necrotizing pancreatitis is questionable. Because the necrotic debris present in pseudo-cysts and pancreatic abscesses is frequently disregarded, interpretations of these collections differ considerably. This could be explained by CECT's inability to distinguish between sterile and infectious collections as well as its inability to detect necrotic material in collections predominately holding fluid.[7,10,12,92,167] Although endoscopic ultrasonography and magnetic resonance imaging (MRI) may be of further benefit in identifying these collections, their utility in critically unwell patients has been questioned.[168,169. 92,170]. The Atlanta Classification includes morphological and pathological descriptions of various local consequences, but it does not give precise radiological criteria for each. The necessity for new descriptive morphological terminology to describe CECT results is highlighted by the recently found low interobserver agreement on the Atlanta Classification of local complications.[8] The CT severity index, an existing radiological grading system, utilizes a numerical score system to quantify extra pancreatic alterations and the degree of pancreatic necrosis.[26] The CT severity score does not identify the regional consequences of acute pancreatitis, although having a clear predictive value in terms of morbidity and mortality.[26,171–174] The paucity of prospective evidence from extensive patient series is largely to blame for the ongoing discussion regarding the normal progression of (peri)pancreatic collections. Consequently, in order to better understand the etiology, natural history, and ideal care of (peri)pancreatic collections, the authors of this paper call for an international collaboration. The goal of the current review is to provide a summary of the controversies around the Atlanta Classification in the literature. The Atlanta Classification's recommended definitions have rarely been the subject of study. As a result, there are not many original data points on this subject that can be examined. Therefore, this analysis has only classified uses and readings of the Atlanta definitions. For effective communication in clinical settings and for comparing inter-institutional data for clinical research, correct terminology and standard definitions are crucial. The development of evidence-based recommendations has been impeded by the ongoing inability to employ standardised definitions for expected and actual severe acute pancreatitis, organ failure, local consequences, and patient inclusion criteria in clinical studies. Numerous research that have advanced understanding of the disease's natural course have been cited in this study. These fresh perceptions should be used to design new classification.

The author proposes the following recommendations for revision of the classification of acute pancreatitis:

First, two of the following four components must be present: upper abdominal pain, amylase and/or lipase levels that are at least three times above normal (this cut-off is most frequently used in the literature), and CT or MRI results that are compatible with acute pancreatitis.

Second, determining the severity of acute pancreatitis should take into account persistent organ failure (for at least 48 h).

Third, based on a thorough analysis of the information provided, it should be chosen which predictive scoring system(s), including cut-off value, should be used to characterise predicted severe acute pancreatitis.

Fourth, future research should always distinguish between anticipated severe and actual severe disease, with validation of the severity of the disease.

Fifth, a systematic review should show which organ failure scoring system should be utilised, and definitions for organ failure should take into account the number of failing organ systems, the length of time the organ has been failing (less than or greater than 48 hours), and the requirement for a particular therapy (such as inotropic or vasopressor agents, mechanical ventilation, and dialysis).

Sixth, necrotizing pancreatitis or peripancreatic fat necrosis should be considered if there is no pancreatic parenchymal necrosis.

Seventh, infected necrosis must be handled differently than other conditions. Moreover, infected necrosis needs to be treated as a distinct condition.

Eighth, enclosed collections that include both fluid and necrotic debris should be given a label.

Ninth, in order to rule out necrotic material in a collection that contains just fluid (such as a pseudocyst), MRI or (endoscopic) ultrasonography should be carried out first.

Tenth, to describe local problems on CECT, a new set of descriptive morphological terminology should be created.

Such a new classification system should be evaluated in high-quality interobserver and prospective clinical studies. Adjustments should be made every few years, based on new data. Most importantly, clinicians and radiologists worldwide should comply with the new classification in clinical practice and research. Progress in the field of acute pancreatitis is hampered greatly when various author groups use their own idiosyncratic definitions. When journal referees are requested to peer-review manuscripts, they should pay special attention to the correct use of definitions as defined by a new classification.

CONCLUSION

The definitions of acute pancreatitis from the Atlanta Classification have been revised and updated in this classification. The understanding that acute pancreatitis is a growing, dynamic condition and that the severity may evolve over the course of the disease is a crucial component. SIRS or organ failure at an early stage of the illness signal potentially serious illness.

- The condition is referred to as mild acute pancreatitis if the patient improves quickly during the early stages without experiencing organ failure or other local or systemic consequences.
- The condition is referred to as moderately severe acute pancreatitis if the patient experiences local or systemic consequences but does not have permanent organ failure.
- The condition is classified as severe acute pancreatitis and is linked to extremely high morbidity and mortality rates if the patient experiences prolonged organ failure.

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CLINICAL PROFILE OF ASTHMATIC CHILDREN AGED 6-14 YEARS: A RETROSPECTIVE STUDY IN AL-BAYDA MEDICAL CENTER

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Abstract

One of the most common chronic inflammatory pediatric disorders is bronchial asthma, it constitutes a major health problem affecting both genders, their prevalence worldwide varies, and different risk factors may predispose to develop of asthma in children. The present study aimed to evaluate the clinical profile of pediatric patients with chronic bronchial asthma. Patients and Methods: a retrospective study was carried out and analyzed the data of 118 children aged 6-14years who attended the Pediatric Allergy Clinic, at Al-Bayda medical center (AMC), Al-Bayda, Libya, who were clinically diagnosed with persistent asthma over one-year period. (2020) Results: A total of 118 children who were clinically diagnosed with asthma were enrolled: 25.4% mild persistent, 59.3 % moderate persistent and 15.3% severe persistent asthma of semi-equal sex distribution, most of them not exclusively breast feeding 54.2% and 51.7%had positive family history of asthma, the most commonly used medications were inhaled glucocorticosteroids and long acting b2-agonist(50%), overall cases the mean value of duration till disease control was 5.7±2.6 months, with longest duration till achievement of control is consumed by sever case. Loss of patient's adherence occurred in 20.3% of cases. No significance correlation between the age of patients, family history of atopy or breast-feeding history and the degree of asthma severity and duration till disease control. Conclusion: Moderate persistent asthma is the commonest pattern of severity, most of cases had positive family history of atopy and current asthma control was good with adjustment of a treatment according to the guidelines.

Keywords: Bronchial asthma, clinical profile, pediatric, Al-Bayda.

Introduction

Bronchial asthma is a major non communicable chronic disorder, represents the most common chronic illness in pediatric. (Pool J.A, 2014). Affecting more than 300 million individuals worldwide of different ages and ethnic groups. (Soriano JB et al,2017). It is more common in developed nations with greater rates seen in United Kingdom, Australia and New Zealand. (Masoli, M et al, 2004)

It is chronic inflammatory respiratory disorder of airways, which is characterized by hyperresponsiveness of airways, in form of narrowing of airways in response to various triggers such as allergens, respiratory viruses and exercise in susceptible peoples;(GINA, 2017) leading to attacks of wheeze, shortness of breath, chest tightness and or cough specially at early morning and night (Pinto Pereira, L. M. et al, 2010). Thus, detailed history and lung function test (spirometry for children $\geq$ 6 years) are cornerstone in the diagnosis of the asthma, the physical examination is often normal in cases of asthma, but the most recurrent finding is wheezing during auscultation. (GINA, 2022)

According to the National Asthma Education and Prevention Program Expert Panel Report 3(EPR3) the grade of asthma severity in patients while not taking medications is classified into intermittent and persistent type which is sub classified to (mild, moderate and sever), and the asthma control into: well, not well or very poor controlled.(Andrew H. Liu et al, 2019)

The present study was conducted in Pediatric Allergy Clinic /Al-Bayda Medical Center, at Al-Bayda city which is laying in the northeast part of Libya, it has Mediterranean weather. Our study aimed to evaluate the clinical profiles of asthmatic children in aspects of pattern of severity, medication usage and disease control.

Materials and Methods

This is a retrospective study was conductive to the files of children with persistent asthma, (Total No=118) aged 6-14 years, who attended to the Pediatric Allergy Clinic over one year period (From January to December 2020).

There were information's excluded in this study like; disease onset, intermittent cases of asthma, anthropometric measurement of patients, nationality/race, and address of the patients, information on diet, tobacco exposure and animal contact, because there was a lack of such information.

The data was examined and entered into the SPSS program version 19.0 for windows for analysis. The data were interpreted in tables and figures in mean and percentage, the Chi square test and Analysis of variance (ANOVA) test are used, and level of significance p value of 0.05 or less was considered statistically significant

Results

The study included 118 asthmatic children with age ranged from 6 to 14 years (mean: 9.4±2.5 years) and semi-equal sex distribution. Most of the children were not exclusively breastfeeding (54.2%). About 51.7% of the included children had positive family history for bronchial asthma, 7.6% for atopic dermatitis and 21.2% for allergic rhinitis (table 1).

Table (1): Baseline characteristics of the included patients

	Total cohort No. (%)
Age (years) mean±SD	9.4±2.5
Sex No. (%):	
Male	58 (49.2%)
Female	60 (50.8%)
Breastfeeding No. (%)	54 (45.8%)
Family history of asthma No. (%)	61 (51.7%)
Family history of other atopic diseases No. (%):	
Eczema	9 (7.6%)
Allergic Rhinitis	25 (21.2%)

The included patients (persistent severity) had variable degree of asthma as most of patients had moderate persistent disease (59.3%) while 25.4% had mild persistent disease and 15.3% had severe persistent disease. Mean value of volume ratio of peak flow meter was 65.98±8.11. Regarding maintenance medications, the most frequently used medication was inhaled Fluticasone/Salmeterol (50%), Montelukast granules or tablets was used for 31.4% of children, inhaled Fluticasone was used for 5.9%. About 11% of patients were maintained on combined inhaled Fluticasone/Salmeterol and Montelukast and 1.7% of inhaled Fluticasone and Montelukast.

A percent of 20.3% (24 out of 118 children) did not continue follow up while 94 children (79.7%) controlled and mean value of duration till control was 5.7±2.6 months (table 2).

Table (2): Disease characteristics and outcome

	Total cohort No. (%)
Degree of severity No. (%):	
Mild persistent	30 (25.4%)
Moderate persistent	70 (59.3%)
Severe persistent	18 (15.3%)
Peak flow meter mean±SD	65.98±8.11
Received medications No. (%):	
Fluticasone/Salmeterol	59 (50%)
Montelukast	37 (31.4%)
Fluticasone	7 (5.9%)
Fluticasone/Salmeterol+ Montelukast	13 (11%)
Fluticasone+ Montelukast	2 (1.7%)
Follow up No. (%):	
Missed	24 (20.3%)
Improved	94 (79.7%)
Duration for control(months) mean±SD	5.7±2.6

According to disease severity, patients were divided into 3 groups: mild persistent disease group included 30 children; moderate persistent disease group included 70 children and severe persistent disease group included 18 children. There was no statistically significant difference between the 3 groups regarding demographics including age, and family history or history of breastfeeding (table 3).

Table (3): Comparison between different grades of asthma regarding baseline characteristics

	Mild persistent (n= 30)	Moderate persistent (n= 70)	Severe persistent (n= 18)	Test of significance	P value
Age (years) mean±SD	8.4±2.3	9.7±2.4	9.7±2.9	F= 2.9	0.06
Sex No. (%):					
Male	15 (50%)	38(54.3%)	5 (27.8%)	X^2= 4.037	0.13
Female	15 (50%)	32 (45.7%)	13 (72.2%)		
Breastfeeding No. (%)	14 (46.7%)	33 (47.1%)	7 (38.9%)	X^2= 0.406	0.816
Family history of asthma No. (%)	14 (46.7%)	35 (50%)	12 (66.7%)	X^2= 2	0.37
Family history of other atopic diseases No. (%):					
Eczema	2 (6.7%)	5 (7.1%)	2 (11.1%)	X^2= 1.49	0.83
Allergic Rhinitis	7 (23.3%)	16 (22.9%)	2 (11.1%)		

X2: Chi square test; F= Analysis of variance (ANOVA) test; Level of significance<0.05

There were statistically significant differences between the 3 groups regarding peak flow meter (p<0.001) which had the highest values among mild persistent disease group and the lowest values among severe persistent disease group. Regarding maintenance medications, 93.3% of mild persistent disease children were maintained on Montelukast, 75.7% of moderate persistent disease children were maintained on inhaled Fluticasone/Salmeterol and 50% of severe persistent disease patients were maintained on combined regimen of inhaled Fluticasone/Salmetrol+ Montelukast with statistically significant difference (p<0.001). Mean values for duration till improvement were the highest among severe persistent disease group and the lowest among mild persistent disease group as severe persistent disease children needed longer duration to achieve improvement (p<0.001) (table 4).

Table (4): Comparison between different grades of asthma regarding disease characteristics

	Mild persistent (n= 30)	Moderate persistent (n= 70)	Severe persistent (n= 18)	Test of significance	P value
Peak flow meter mean±SD	75.6±3.2	64.8±4.5	54.56±6.9	F= 119.5	<0.001*
In between p value	Mild: moderate (P<0.001), Mild: Severe (p<0.001), Moderate: severe (p<0.001)				
Received medications No. (%):					
Fluticasone/Salmeterol	1 (3.3%)	53(75.7%)	5 (27.8%)		
Montelukast	28(93.3%)	7 (10%)	2 (11.1%)		
Fluticasone	0	6 (8.6%)	1 (5.6%)	X^2= 107.42	<0.001*
Fluticasone/Salmetrol+ Montelukast	1 (3.3%)	3 (4.3%)	9 (50%)		
Fluticasone+ Montelukast	0	1 (1.4%)	1 (5.6%)		
Follow up No. (%):					
Missed	8 (26.7%)	14 (20%)	2 (11.1%)	X^2= 36.4	<0.001*
controlleded	22(73.3%)	56 (80%)	16 (88.9%)		
Duration for control (months) mean±SD	3.95±1.7	5.7±2.4	8.1±3.6	F= 12.76	<0.001*
In between p value	Mild: moderate (P<0.001), Mild: Severe (p<0.001), Moderate: severe (p<0.001)				

X2: Chi square test; F= Analysis of variance (ANOVA) test; Level of significance<0.05

Sex, history of breastfeeding, family history of asthma or other atopic diseases did not influence significantly duration till disease control. Disease severity affected significantly duration till control (p<0.001) as longer duration till control was required for children with severe persistent disease. Maintenance medications also affected significantly duration till control as patients maintained on combined regiment of Fluticasone/Salmeterol and Montelukast required longer duration till control while patients maintained on montelukast required shorter duration with statistically significant difference (p<0.001) (table 5).

Table (5): Factors affecting duration for disease control

		Median (min, Max)	Test of Significance	P value
Sex	Male	5.3±2.4	t= -1.4	0.17
	Female	6.1±3.1		
Breastfeeding	Yes	5.7±2.8	t= 0.03	0.97
	No	5.6±2.6		
Family history of asthma	Yes	5.7±2.8	t= 0.04	0.96
	No	5.7±2.7		
Family history of atopic disease	Allergic rhinitis	5.5±2.4	t= 1.15	0.3
	Eczema	4.4±2.2		
Disease severity	Mild persistent	3.95±1.7	F= 12.76	<0.001*
	Moderate persistent	5.7±2.4		
	Severe persistent	8.1±3.6		
Received medications	Fluticasone/Salmeterol	5.7±2.3	F= 6.5	0.001*
	Montelukast	4.2±2.3		
	Fluticasone	6.8±2.9		
	Fluticasone/Salmeterol+ Montelukast	8.3±3.2		
	Fluticasone+Montelukast	9±2.8		

*Paired t test; F: Analysis of variance (ANOVA) test; *Level of significance<0.05*

All factors were entered 5 steps multivariate analysis to adjust variables for the confounders. Degree of severity (p= 0.016), PFV (p=0.006) and maintenance medications (p= 0.016) kept their statistically significance as factors affecting duration till control while age lost his statistically significant association with duration till control (p=0.09). Other factors did not show statistically significant effect of duration till disease control (table 6).

Table (6): Multivariate analysis for factors affecting duration of disease control

	B estimate	Beta coefficient	95% Confidence interval		Test of significance	P value
			Lower	Upper		
Age	0.179	0.155	-0.028	0.38	1.7	0.09
Sex	0.462	0.082	-0.517	1.44	0.939	0.35
Breastfeeding	-0.371	-0.066	-1.37	0.63	-0.736	0.46
Family history of asthma	-0.473	-0.084	-1.5	0.57	-0.897	0.37
Family history of atopic diseases	0.151	0.034	-1.17	1.48	0.226	0.82
Degree of severity	-1.023	-0.233	-1.85	-0.192	-2.7	0.016*
Peak flow meter	-0.151	-0.427	-0.256	-0.046	-2.8	0.006*
Medications	0.548	0.215	0.104	0.992	2.4	0.016*

Linear regression analysis; *Level of significance<0.05

There was statistically significant positive correlation between age and duration till control (r: 0.3; p= 0.012), Figure 1.
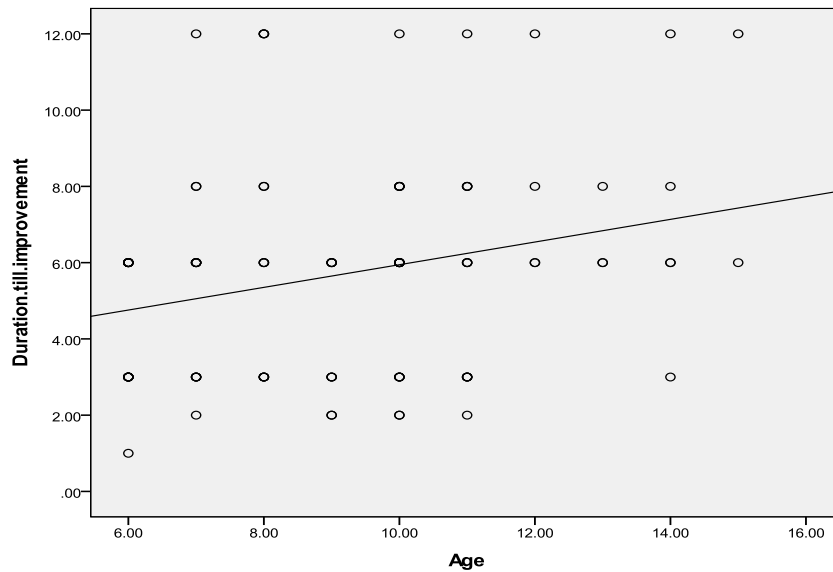

Figure (1): Pearson correlation between age and duration till improvement(control) showed significant positive correlation (r: 0.3; p= 0.012)

There was statistically significant positive correlation between Peak flow meter and duration till control (r: -0.56; p<0.001), Figure 2.

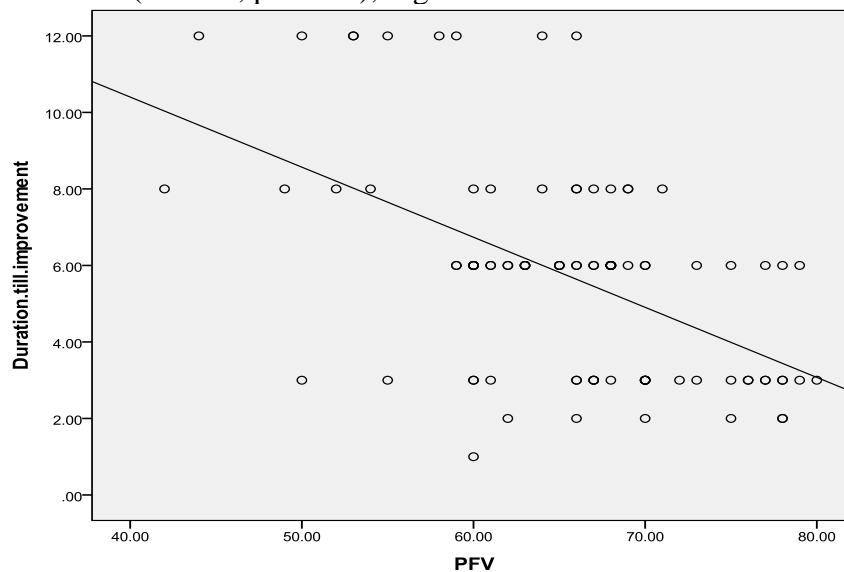
Figure (2): Pearson correlation between Peak Flow meter and duration till improvement (control) showed significant inverse correlation (r: -0.56; p<0.001)

Discussion

Asthma is global health problem; reported studies on asthmatic children in Libya are few. This study was undertaken in order to evaluate the clinical profiles of 118 asthmatic children in aspects of pattern of severity, medication usage and control of symptoms. However, there were no clear sex disparity among the studied children, and this agreed by previous study conducted by in Al-Bayda city by (Ali, M.T. et al, 2021) which showed same result. Different asthma phenotypes may be affected by breast feeding (Ek, W. E. et al,2018), this study showed that most of the asthmatic children were not exclusively breast feeding; this finding suggest that breastfeeding may have effect on asthma development.

In our study there was a relation between family history of asthma and studied group, it is consistent with other studies that show the same relation (Ali, M. S. et al, 2016) (Jain. A. et al, 2010). Overall, positive family history of other atopic disordered like atopic dermatitis and allergic rhinitis (7.6% and 21.2% respectively) is observed, but the percentage was less than observed by other study in Tripoli/Libya in which 92% have family history of atopy (Elzigallai O and Alrabty H, 2020). These may suggest a role of genetic predisposition for asthma development.

The grade of asthma severity among the studied cases had statistically significant difference, in which most of patients had moderate persistent disease followed by mild persistent disease then severe persistent disease, unlike other study done by (Tabbara, K. S. et al, 2010) in which mild persistent more frequent than moderate persistent and sever persistent types.

A stepwise algorithm is used for asthma treatment and control of symptom, which should be individualized foe each patient according to the disease severity, if child has recurrent symptoms step-up control therapy is planned, and if the child has a few symptoms a stepping down controller therapy is considered (GINA, 2022). In our study the frequently used medication was inhaled Salmeterol +Fluticasone, this result may be explained by the most of studied patients had moderate persistent disease, which they need step 3 or 4 for their management and may need adjustment of therapy according to control.

The preferred therapy for all persistent asthmatic patients is inhaled corticosteroid, as monotherapy or with adjunctive therapy. The treatment of choice for mild persistent type (step 2) is low dose ICS is therapy and Montelukast is used as alternative therapy (Andrew H. Liu et al, 2019), in our study 93.3% of mild persistent patients were maintained on montelukast, while 50% of severe persistent disease patients were maintained on combined regimen of Fluticasone/Salmeterol+ Montelukast with statistically significant difference (p<0.001) and this agreed with stepwise management of childhood asthma.

A percent of 20.3 did not continue follow up the allergic clinic, the adherence should be kept between patients and doctors, correction of wrong knowledge about controller medication and the patients must kept in contact by registering detailed address, telephone number to prevent poor adherence.

This study did not find a significant relation between the severity of asthma and family history of atopic disease, this consistent with the result of study done in Saudi Arabia (Al-Ghamdy, Y. S. et al, 2000). Moreover, no significant association between demographics including age and history of breast feeding among the different studied groups, the severity discrepancy may be due to other factors other than genetic factor like environmental factors (Allergens exposure, dust, air pollution or smoking exposure) or food allergy.

Peak flow meter results shows statistical significance between different studied groups, were the highest values among mild persistent disease group and the lowest values among severe persistent disease group, this supported the result of (Grad, R. et al, 2009) in which the peak flow readings tended to correspond to asthma disease activity.

Severe bronchial asthma is characterized by persistence of symptoms despite therapy with high doses of inhaled corticosteroids or oral corticosteroids thus longer duration as discussed by (Guilbert, T. W. et al, 2014), and this consistent with our result in which longest duration till achievement of control is consumed by sever case, this may explained by the effect of underlying sever inflammatory process on air ways and affection on lung function which consume longer time till improvement.

Conclusion

The present study concluded that moderate persistent asthma is the commonest pattern of severity, most of cases had positive family history of atopy, and current asthma control was good with adjustment of a treatment according to the guidelines.

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Effect of multi-phasic CTU on diagnostic confidence of radiologists. Are all three phases necessary?

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(Original Research Article)

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Abstract

Background: The availability of multidetector CT at medical centers has led to the routine use of CT Urography (CTU) in imaging of the urinary tract. The number of phases of CTU generally varies between two and four, and because of the high radiation dose of CTU, the number of phases should be kept to a minimum. There are not enough data available on how radiologists use the multiphasic nature of CTU in the diagnostic process of urological conditions. The purpose of this study was to determine the subjectively experienced usefulness of different CTU phases in urinary tract evaluation by measuring the level of diagnostic confidence at each phase. Methods: consecutive CTU examinations performed between February 2021 and November 2021 were retrospectively reviewed. Thirty-nine patients who underwent CTU examination on a 32-slice CT scanner were included. The standard protocol for CTU consisted of the following: unenhanced phase, enhanced corticomedullary phase, and in a subset of cases, an adjunct 10-min delayed excretory phase. All images were reconstructed with multi-planar reconstruction in three planes: axial, coronal and sagittal. During the reading sessions, the images of each phase were assessed individually for the presence of urinary tract abnormalities and the diagnostic confidence was estimated using a graded scale. Evaluation for incidental finding were also done on unenhanced and enhanced phase. Statistical analysis was performed using paired-sample t test. The limit for significance was set at p = 0.05. Results: a significantly higher diagnostic confidence scores were obtained in the enhanced corticomedullary phase for urinary tract pathologies (P = 0.0001) and incidental findings (P < 0.0001) when comparing the unenhanced phase to enhanced corticomedullary phase. The diagnostic confidence scores obtained in the corticomedullary phase for urinary tract pathologies were also higher than excretory phase, but the difference was not statistically significant. Conclusion: the enhanced corticomedullary phase had a significantly higher effect on diagnostic confidence when compared to the unenhanced phase. The analysis suggests that a corticomedullary phase CTU may be sufficient as a problem-solving imaging tool of urinary tract, especially in patients where radiation burden is of concern.

Key words: CT urography, diagnostic confidence, unenhanced phase, enhanced phase.

Introduction

Intravenous urography is the traditional Imaging technique of the upper urinary tract, but in recent years with the advances of multidetector CT (MDCT) enabling isotropic or near-isotropic high-quality multiplanar image reconstruction, CT urography (CTU) has become the modality of choice in imaging the urinary tract. [1,2] The problem in interpretation of the results of CTU is variability in the definitions of what CTU actually entails. [3] According to the definition suggested by the Working Group of the European Society of Urogenital Radiology, CTU is an examination optimized for imaging the kidneys, ureters and bladder, involves the use of MDCT with thin-slice imaging, intravenous administration of a contrast medium, and imaging in the excretory phase, however an unenhanced phase may be used. [2,4] The term CTU is often used in clinical practice for a multitude of MDCT techniques for evaluation of the urinary tract in which the clinical presentation will largely determine the protocol used. [2,5] In theory, the number of phases in CTU can be highly variable and suggestions for optimized use of CTU have been published by scientific societies, [5] 'true evidence-based guidelines were not formulated, but expert guidelines on indications and CTU examination technique were produced'. [2] The number of CTU phases generally varies between two and four, and because of the high radiation dose of CTU, the number of phases should be kept to a minimum. [2] Many variations of the standard CTU protocol of unenhanced, contrast-enhanced, and excretory phases have been investigated with the goal of reducing radiation exposure and optimizing imaging of the urinary tract. [4] As the availability of MDCT at medical centers has led to the routine use of this tool in the diagnostic process of urinary tract pathologies, there are not enough data available on how radiologists use the multiphasic nature of CTU in the diagnostic process of urological conditions. The aim of this study is to evaluate the subjectively experienced usefulness of different CTU phases in the radiologic diagnosis of the urinary tract by assessing the diagnostic confidence of the evaluating radiologist at each CTU phase.

Methods

This is a retrospective study; consecutive patients referred for a clinical CTU between 2021-02-20 and 2021-11-8 and examined on a 32-slice CT scanner (Aquilion, Toshiba Medical systems) at Omer Almukhtar hospital in the green-mountain area, Libya were included in the study. The following data obtained from a packed archive communicating system (PACS) were recorded for all patients: sex, age (measured in years), weight (measured in kilograms), effective dose volume CT Dose Index (CTDIvol, in mGy) and dose-length product (DLP, in mGy cm) as a measure of radiation dose output. Effective Doses were calculated with a CT patient dosimetry calculator.

The MDCT acquisition data were as follows: tube voltage of 120 kilovolts (kV); automatic current modulation, thickness of 1x16 (detectors), Helical pitch (HP) 1.5 and rotation time of 0.75 seconds, reconstruction slice thickness of 0.8 mm for the axial images. From the axial images, coronal images with a slice thickness and reconstruction interval of 3.0 mm were obtained. All scans were acquired from the diaphragm to the pubic symphysis.
Patients who had only undertaken a single unenhanced CT scan ($n = 90$ patients) were excluded; another four patients were not included due to differences in scan protocol. The standard CTU protocol was used with intravenous administration of contrast medium Iopromide (Ultravist 370 mgI/ml, Bayer, AG, Germany) or Iohexol (Omnipaque 350 mgI/ml, Bayer, AG, Germany); the dose tailored to patient body weight was given at 1ml/kg manually,

generally falling within volume of 80 to 100 ml.

The standard protocol for CTU consisted of the following phases: the native or unenhanced phase, an enhanced corticomedullary phase (degree of enhancement depending on patient weight, cardiac output, hydration state and renal function), and in a subset of cases an adjunct 10-min delayed excretory phase. All images were reconstructed with multi-planar reconstruction (MPR) in three planes: axial, coronal and sagittal.

During the reading sessions, the images were assessed for the presence of urinary tract abnormalities (the number, size and site of stones, signs of obstructive uropathy, hydronephrosis and hydroureter, congenital pelvi-ureteric junction obstruction, ureteric wall thickening and presence of neoplastic masses were evaluated). The radiologist documented the diagnosis and graded the diagnostic confidence after viewing each phase of CTU individually, evaluating non-contrast CT first then contrast enhanced CT. Grading of diagnostic confidence by the reader was on a 5-point scale: 1 (10% confidence, i.e. very unsure), 2 (30% confidence), 3 (50% confidence), 4 (70% confidence), and 5 (90% confidence, i.e. highly confident). The same process was done for assessment of incidental findings on unenhanced and enhanced phase.

For the purpose of analysis, the urinary tract was divided into renal parenchyma, renal calices and pelvis, upper ureter (pelvi-ureteric junction (PUJ) to iliac crest), middle ureter (ureter overlying iliac bone), lower ureter (ureter below iliac bone to the uretero-vesical junction (UVJ)), and bladder.

Statistical Analysis

Diagnostic confidence was assessed as mean ± standard deviation (SD) and range. Comparison of the diagnostic confidence scores acquired with unenhanced and enhanced (corticomedullary) phases was performed with the paired-sample t test. Comparisons of paired samples was used in the assessment for difference in diagnostic confidence scores between the unenhanced, enhanced and excretory phase in the subset group. P value equal to 0.05 value was considered significant. All analyses were performed with MedCalc Statistical Software version 20.027 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2022).

Results

After exclusion, there remained 39 cases all underwent an unenhanced and enhanced corticomedullary phase (21 males, 18 females and mean age of 52.2 years ± 18.3 (SD), range 25 to 90 years). The mean body weight of 88.61 kg (ranged from 70 to 100 kg).

Of the 39 patients included in the study, a subgroup of 23 cases underwent imaging in the excretory phase (11 males, 12 females, age range 25–80 years (mean 44.6 ± 17.5 (SD))

For the complete three-phase CTU examinations, the medians (25th and 75th percentiles) of CTDIvol, DLP and effective dose were 44 mGy (19.8–62.7 mGy), 2027.3 mGy·cm (925–3013.7 mGy·cm) and 30.4 mSv (13.8–45.1 mSv) respectively. The mean values, SD and ranges of DLP, CTDIvol, and effective dose for the unenhanced, corticomedullary and excretory phases are displayed in

Table 1. A summary of the number of urinary tract abnormalities that were detected is displayed in Table 2.

Table1. Means, standard deviation (SD) and ranges of dose length product (DLP), Computed Tomography Dose Index (CTDIvol) and effective dose

Phase	DLP mGy·cm	CTDIvol mGy	Effective dose mSv
Unenhanced			
Mean	790.1	16.5	11.8
SD	128	2.1	1.9
Range	539.9-1098.2	14.2-20.9	8-16.4
Enhanced			
Mean	763.6	16	11.4
SD	89.1	1.8	1.3
Range	596.9-952.1	14.2-20.9	8.9-14
Excretory			
Mean	753	16	11.2
SD	150.9	2.6	2.2
Range	406.6-1178.7	9.4-20.9	6-17.6

Table 2. Summarizes the number of urinary tract abnormalities that were detected.

	Findings	N
	Number of patients who had stones	21
	Number of detected stones	47
	Stone in kidney (calices and pelvis)	29
Urinary Stone	Stone in upper ureter including PUJ	6
	Stone in middle ureter	1
	Stone in lower ureter	8
	Stone in bladder	3
Congenital pelvi-ureteric junction [PUJ] obstruction		3
Neoplastic mass		8
Xanthogranuomatous pyelonephritis		1
Renal artery stenosis		1
Renal vein thrombosis		1
Medullary sponge kidneys		1
Ureteric wall thickening/stricture		3
Bladder diverticulum		3
Consequences of Obstructive Uropathy		
Hydronephrosis		18 (2 bilateral)
Hydroureter		14 (2 bilateral)
Ruptured calyces with perinephric urinoma		1

Table 3 shows the distribution of cases per each score of the 5-point scale for diagnostic confidence for urinary tract abnormalities on each phase of CTU.

The mean diagnostic confidence score obtained for urinary tract abnormalities was 4.48 ± 0.75 (range, 2–5) after viewing of the unenhanced images, 4.89 ± 0.3 (range 4–5) after viewing of the enhanced corticomedullary phase images. The diagnostic confidence was significantly

higher for the enhanced corticomedullary phase than for the unenhanced phase images (dependent-samples t test, t = 4.3, P = 0.0001). (Fig. 1).

The mean diagnostic confidence score was 4.82 ± 0.49 (range, 3–5) after viewing of the excretory phase images in the subgroup sample (n=23), (Fig. 1), the excretory phase was not significantly different from the corresponding unenhanced and enhanced corticomedullary phase. The diagnostic confidence was lower for the excretory phase than for the corticomedullary phase images (P = 0.49), and higher for excretory phase than for the unenhanced phase images (P = 0.17). Similar to the overall study sample, the diagnostic confidence was significantly higher for the enhanced corticomedullary phase than for the unenhanced phase images in the subset group (P= 0.0052).

Table 3. Summarizes the number and percentage of cases per every score on the 5-point scale.

CTU phase	No of cases (percentage) per each score					Total no of cases
	1	2	3	4	5	
Unenhanced phase	0	1 (2.5%)	3 (7.6%)	11 (28.2%)	24 (61.5%)	39
Enhanced phase	0	0	0	4 (10.2%)	35 (89.7%)	39
Excretory phase	0	0	1 (4.7%)	2 (9.5%)	20 (85.1%)	23
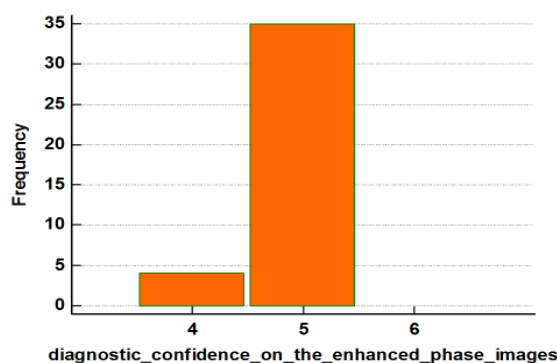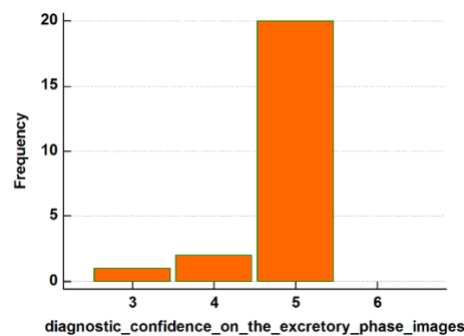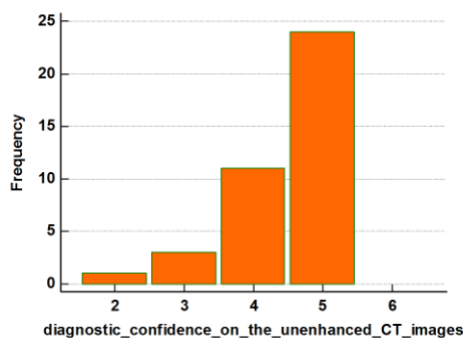
Histogram Figures show distribution of diagnostic confidence in imaging of patients with unenhanced, enhanced (corticomedullary), and excretory phase. Of the twelve patients with obstructive uropathy caused by urinary tract stones, the diagnostic confidence scores were neutral at unenhanced and enhanced corticomedullary phase images in nine patients, whereas the assessment of enhanced images increased the diagnostic confidence level in four patients. The diagnostic confidence scores were also higher at enhanced phase in all PUJ obstructions

(n=3), and in 2 out of 4 cases of obstructive uropathy due to neoplastic masses and in one case due to ureteric stricture. In cases with no obstructive uropathy, the diagnostic confidence scores were higher at the enhanced phase in two out of three cases of renal masses, confidence of presence of ureteral thickening, atrophied kidney due to renal artery stenosis and absence of urachal malignancy in three different cases was also higher at the contrast-enhanced scan. The diagnostic confidence scores were neutral at unenhanced and enhanced phase images in all patients with negative scan results (n=4), non-obstructing renal stones (n=5), non-obstructing ureteric stone (n=1), UB diverticulum (n=1), renal medullary calcinosis (n=1), and UB mass (n=1).

Figures 2, 3, 4 show examples of cases where the assessment of enhanced phase images has increased the diagnostic confidence score.
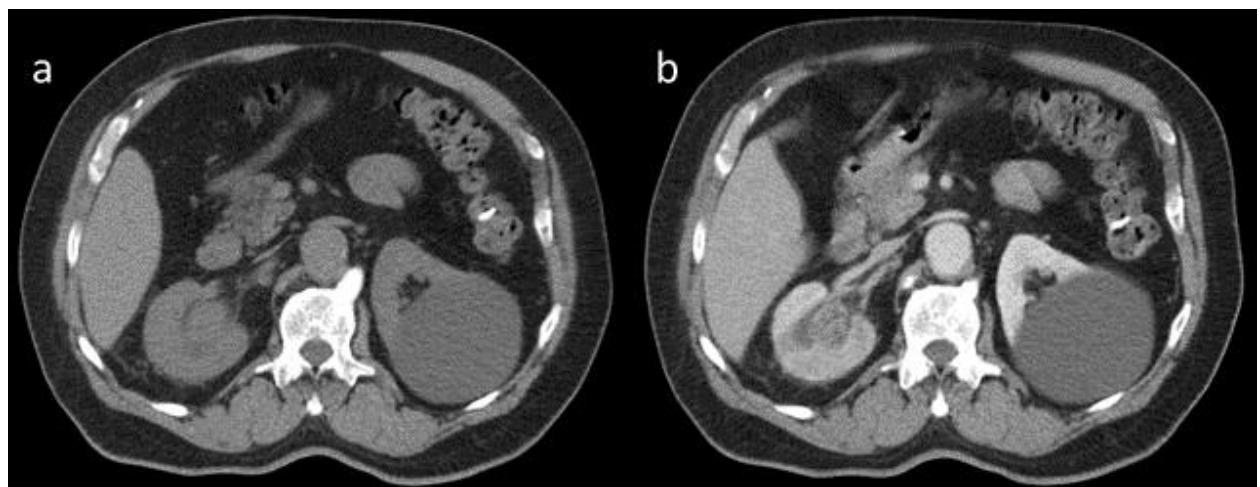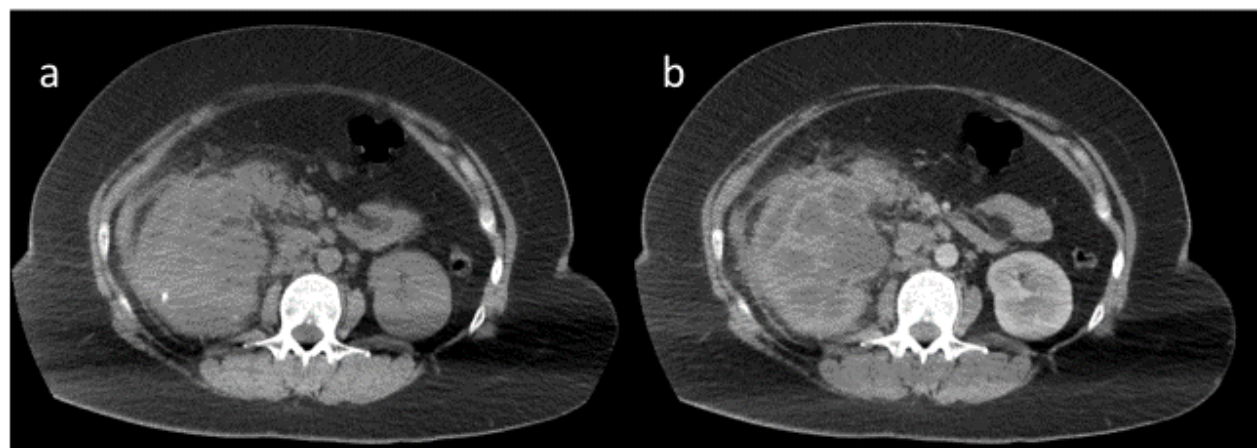

Fig. 2- A 66-year-old male with transitional (urothelial) cell carcinoma in the right renal collecting system. The presence of soft-tissue mass in right upper pole calyces was suspected on the unenhanced phase (a), at the enhanced phase (b) the mass became clearly conspicuous due to contrast enhancement.
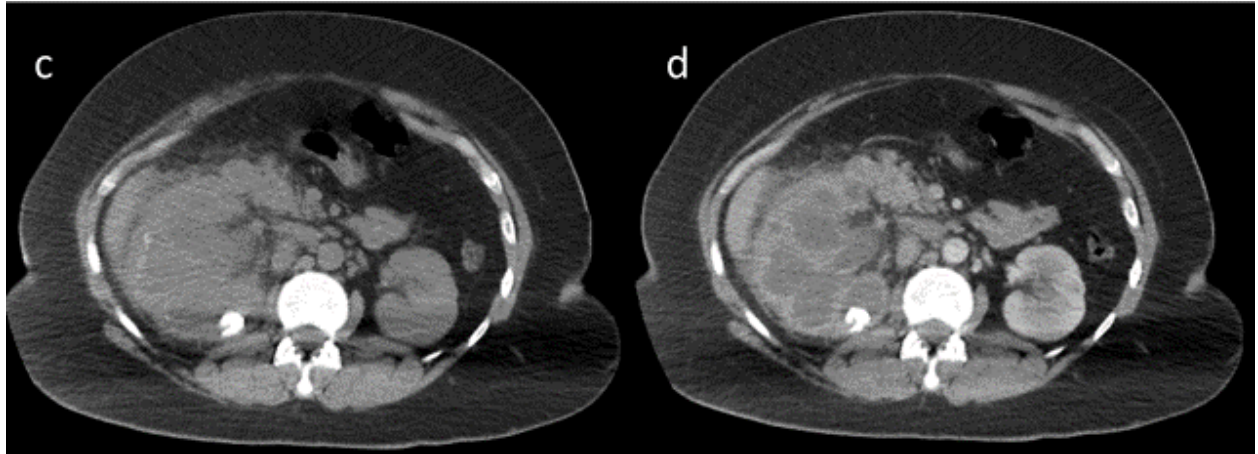
Fig. 3- A 33-year-old female with xanthogranulomatous pyelonephritis of right kidney as a sequel of upper ureteric stone obstruction. The appearance of the pear-paw sign of multiple low attenuation parenchymal areas is clearly depicted on the enhanced phase (b, d) compared to unenhanced phase images (a, c) significantly increasing the diagnostic confidence.
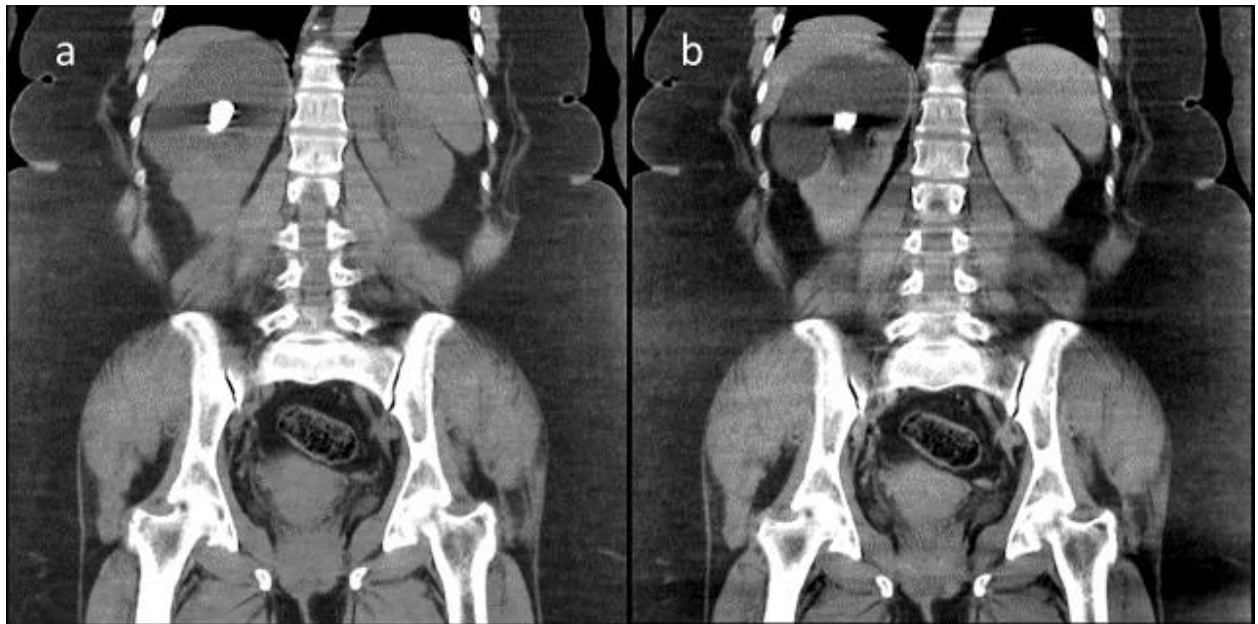

Fig. 4- A 52-year old female with 27 mm obstructing stone at right kidney with severe calectasis of the upper pole. The unenhanced phase (a) depicts a stone in right renal upper pole surrounded by large hypodense area; the contrast-enhanced phase (b) demonstrates the atrophic renal parenchyma surrounding a chronically dilated collecting system of the upper pole due to the obstructing stone. Significantly high confidence scores in favor of the contrast-enhanced phase are obtained for determination of incidental findings (P < 0.0001) when comparing unenhanced phase to enhanced corticomedullary phase images. Renal cysts were the urinary-tract-related incidental findings most commonly encountered; 10 patients (26%), double-moiety; two patients (5%), renal ectopia; one patient, unilateral absent kidney; one patient. For extra-urinary incidental findings, most of the incidental findings were related to the bowel; seven patients (18%), followed by the hepato-biliary system; six patients (15%), pancreas/spleen; four patients (10%), gynecological disorders; four patients, aortic aneurysm; one patient.

Discussion

'Changes in diagnostic confidence are used as a measure of a test's efficacy'. [6] This study evaluated how findings in different CTU phases influence the diagnostic certainty of the reviewing radiologist. The enhanced corticomedullary phase caused a statistically significant mean increase in the level of diagnostic confidence compared to the unenhanced phase.

As expected, the diagnostic certainty was higher after the administration of contrast material in cases of renal parenchymal diseases, neoplasm and renal vascular abnormalities. However, even in the presence of stones the diagnostic confidence was higher at the enhanced phase in some cases than the unenhanced phase. This is probably because the complications associated with urolithiasis such as calyceal rupture and xanthogranulomatous pyelonephritis as well as signs of obstruction such as ureteral thickening and renal tissue thinning of long-standing obstruction were better visualized on enhanced phase images without reduction in the detection of stones. The American college appropriateness criteria justifies the use of unenhanced CT when the diagnosis of urinary tract stone is clinically suspected, however, the results of this study shows that the lack of IV contrast is associated with a lower level of diagnostic confidence for other urinary tract diagnoses that could present with flank pain and hematuria mimicking urinary stone disease. For example, Neoplasm as urothelial cell carcinoma had a subtle appearance on unenhanced scan but were easily identified on the enhanced phase images, also pyelonephritis, non-urinary tract neoplasm invading the ureters, renal artery stenosis or occlusion and renal vein thrombosis were best evaluated on the enhanced CT. Even in cases of ureteric stones, ureters may be difficult to identify in the unenhanced phase, especially in the small pelvis. [3] The fear of using IV contrast resides in that parenchymal enhancement could mask the hyperdense renal stones. [7] However, there are no studies in the literature to support this claim while recent studies on renal stones detection on contrast-enhanced CT concluded that renal stones $\geq$ 2 mm can be depicted on contrast-enhanced CT with high sensitivity. [7,8] The present study confirms that renal stones can indeed be detected on the contrast-enhanced CT and that intravenous contrast will not hinder diagnosis of obstructive ureteral stone disease.

One of the strengths of this study was the inclusion of all consecutively referred patients for CTU imaging, all CTU studies with IV contrast but four patients were included. Therefore, no important selection bias is expected in the study results.

The most frequently used single contrast medium-bolus CTU protocol in most centers consists of unenhanced phase, nephrographic phase and excretory phase, [2] whereas the enhanced phase in this study was the corticomedullary phase. In research, the corticomedullary phase has been used in many previous studies most focusing on renal cell carcinoma, [9-12] and in studies that showed the urothelial cell carcinoma can be detected on corticomedullary phase. [13-16] There is also an argument that supports the use of corticomedullary phase over the nephrographic phase. [9,10,12]. In Dahlman et al [10] study in 2000, the corticomedullary phase was deemed the best phase in characterizing renal parenchymal tumors and the nephrographic phase was the least diagnostic phase. Dahlman et al 2009. [12] study was based on a total of 102 patients undergoing CTU due to suspected urinary tract malignancy with different versions of the CTU protocol between 1997 and 2008, the nephrographic phase was abolished from the four-phase CTU protocol since 1998 in efforts to reduce the effective radiation dose. The three-phase protocol including the corticomedullary phase was used instead. Furthermore, dynamic information is gained, and vessel anatomy is better evaluated in corticomedullary phase than nephrographic phase. [10] The value of excretory phase lies in the ability to detect urothelial cell carcinoma when the urinary tract is distended with contrast. Urothelial cell carcinoma becomes enhanced soon after IV contrast administration and if the urinary tract, including the bladder, is well

distended, it can therefore be easily detected on the corticomedullary phase. [9,13] The results of this study suggest that urothelial cell carcinoma can be diagnosed on the corticomedullary phase of CTU with greater confidence that was not increased on excretory phase.

To my knowledge, one study has previously compared pathology assessment between phases of CTU. [17] In Khataria et al. study, unlike this study, the unenhanced and excretory phases were of low dose CT (LDCT), and in addition to pathology assessment, image quality was compared between phases. The aim of their study was to explore if radiation burden can be reduced to younger patients, patients undergoing repetitive imaging or patients with negative outcomes. Similar to our study a 5-point scale was used in the analysis, but with different response alternatives, which indicated whether the examination was normal, probably normal, indecisive, probably pathological, and pathological examination. The responses then grouped together to calculate certainty scores. Their results showed a significantly high certainty scores in favor of nephrographic phase for renal pathology and incidental findings when comparing unenhanced phase to nephrographic phase. These findings are in keeping with the results of the present study as the diagnostic confidence scores for urinary tract abnormalities and incidental findings were also significantly higher on the enhanced phase of CTU compared to the unenhanced phase.

There are no international consensuses on how to perform a CTU, and as there are radiation dose considerations with CTU, each examination must be justified based on proper clinical indications, preliminary tests and patient categories, the CT scan protocol must be optimized according to the ALARA principle. [18] A number of ways are used to achieve dose reduction, such as, limiting scan lengths, the use of lower exposure settings and MDCT features such as automatic dose modulation and iterative reconstruction. [17] A split-bolus protocol, where the corticomedullary or nephrographic phase is combined with the excretory phase, can be used to reduce radiation dose by reducing the number of scans. The effective dose is reported to be significantly reduced in the split-bolus technique compared to the single-bolus triple scan. [19] Nevertheless, there are advantages in separating the corticomedullary phase from the excretory phase in the single-bolus protocol as urothelial carcinoma enhances with contrast and can be evaluated in the corticomedullary phase. However, if corticomedullary and excretory phases are combined, blooming artifacts from the concentrated contrast material in the urinary tract may mask smaller lesions. [9] Moreover, Evaluation for urothelial carcinoma on the corticomedullary phase and again in the excretory phase would probably increase the likelihood of identifying the malignancy more than a single combined phase. Recent advancements show a trend towards use of low-dose CT (LDCT) in unenhanced and excretory phases in order to reduce radiation dose of CTU examination. There are studies that have evaluated the effect of LDCT on dose reduction, image quality and pathology assessment of CTU. [9,17] A dose-escalation study by Dahlman et al. [9] in 2012 showed that the Low-dose unenhanced and excretory phase series might be sufficient despite the low image quality associated with LDCT, as long as the images are systemically reviewed alongside the normal-dose corticomedullary phase images. Similar to the present study, they assessed the change in the diagnostic confidence in their analysis and used a 5-point scale for scoring. The diagnostic confidence in the low-dose images was found to be equal to that in the normal-dose images when the low-dose unenhanced and excretory phase images were read alongside the normal-dose corticomedullary phase images.

In the current study, the corticomedullary phase had significantly increased the level of diagnostic confidence, and therefore was considered the most important phase of CTU in the diagnostic process. These results support the algorithm suggested by the Netherlands society

of Urology in the work-up of patients with haematuria. In general, when CTU is used for the evaluation of hematuria, the primary goal is urothelial-cell cancer tumor detection. The algorithm suggested by the Netherlands society of Urology is that the three-phase CTU should be used as a first-line imaging test only for patients with a high-risk probability of malignancy, i.e. patients older than 50 years and patients with known or suspected urothelial carcinoma. For all other risk categories such as patients younger than 50 years or patients with microscopic haematuria, a single corticomedullary phase CTU is a problem-solving modality if initial test results remain inconclusive and symptoms persist. [3,9] As such, each CTU examination should be adapted according to the question from the referring clinician and according to the age and history of the patient, and the number of previous CT examinations must be considered especially in younger patients. [18]

It should be emphasized that the patients who undergo multiphase CTU because of suspected malignancy are generally older patients and therefore less sensitive to radiation. [18] Radiation doses should be taken into close consideration in younger individuals and patients with suspected urinary calculi, these patients should not undergo the standard three-phase CTU. Instead, they should undergo tailored CTU protocols consisting of one or two phases. [9,18] This however requires continuous collaboration between the technician and the radiologist, which can sometimes be difficult to achieve in daily practice especially in busy departments dealing with many emergency cases.

The present study is not without limitations. No comment could be made on the influence of experience on measure and change of diagnostic confidence level, as the study did not involve more than one reviewer. The level of diagnostic confidence would differ between experienced and inexperienced radiologists. Despite this limitation, since the diagnostic confidence was significantly increased by the administration of contrast material, the effect is expected to be more pronounced for the unexperienced radiologist. Another limitation, which was due to the retrospective design of the study, is that not all of the CTU examinations included an excretory phase. However, this limitation did not hinder the analysis, as the number of examinations that included an excretory phase was satisfactory for comparison.

In conclusion, this study demonstrates that the enhanced (corticomedullary) phase has a significantly higher effect on diagnostic confidence than the unenhanced phase, while the excretory phase was not significantly different. This suggests that a corticomedullary CTU can be sufficient in the diagnosis of urinary tract abnormalities, which is helpful in reducing the number of CTU phases especially in patients where radiation burden is of concern and the risk of malignancy is low.

Acknowledgements

Declarations

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Myo-Inositol: The New Challenge in Treatment of Polycystic Ovary with Infertility

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Abstract

Introduction: Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age, affecting approximately 6–15% of them associated with chronic anovulation. Myo-inisitol is insulin-sensitizing agent ingested with food and actively synthetized in liver and brain. Aim of the work: To study the effect of Myo-inositol and Metformin in treatment of PCOS with infertility in Tobruk-Libya. Methods: The study group included 800 selected cases of PCOS with infertility and insulin resistance, diagnosed and treated in Gynecology and Obstetrics department of Tobruk Medical Center, Libya, from January 2018 to January 2022. Patients then were randomly distributed into two groups; Group 1 (n = 400) in which Myo-inositol 2000 mg daily by taking two tablets (2x500 mg) after breakfast and another tow tablets after dinner and take Metformin 850 mg during lunch. Group 2 (n = 400) in which they take Metformin 850 mg during lunch only. All patients were followed up by ultrasound to see the progress of ovulation. Results: The mean age of the patients at group 1 is 29 years (range, 18–40 years) and at group 2 is 32 years (range, 22–42 years). Mean pre-study serum glucose level is 193 mg/dl in group 1 and 208 mg/dl in group 2. Mean pre-study Insulin level is 284 mIU/L in group 1 and 295 mIU/L in group 2. There are highly significant relationship between treatment with Myo-inisitol and Metformin (Group-1) with serum glucose level, serum insulin level, acne, hirsutism, body weight, menstrual cycle regularity, follicles diameter and pregnancy. Conclusion: Our results shows that use of Myo-inositol and Metformin is a useful treatment of polycystic ovary with infertility with improvement of laboratory, clinical and ovulation with subsequent pregnancy.

Keywords: PCOS; Infertility; Myo-inisitol

Introduction

Polycystic ovary syndrome (PCOS) is a common reproductive condition associated with chronic anovulation. It commonly shows oligomenorrhea, irregular menstrual cycle, and increase androgen level, with typical ovarian ultrasound features [1]. It is the most prevalent cause of disorder of ovulation and subfertility in females and affects approximately 6-10% of childbearing women in population [2]. Although its pathogenesis is poorly understood, the role of insulin in the pathogenesis of hyperandrogenemia in PCOS is central. Insulin resistance in association with luteinizing hormone (LH) increases the production of androgen in theca cells [3]. Therefore, treatment with insulin-sensitizing agent like inositol, troglitazone, or metformin in women with PCOS may lead to continuation of spontaneous ovulation [4-8]. Inositols are chemically identified as hexahydroxycyclohexanes and include a family of nine stereoisomers [9]. Myo-inositol (MI) is the most widely distributed in nature, including animals and mammals [10]. MI is ingested with food mostly from fruits, beans, grains, and nuts. Daily intake of MI from phytate-rich food does not exceed 500–700 mg/day.

MI can also be actively synthetized (up to 4 g/day) in human body (especially the liver and brain) [11]. The cellular precursor of MI is glucose-6-phosphate, which is isomerized to inositol-3-phosphate (IP3) by D-3-myo-inositol-phosphate synthase. IP3 is then dephosphorylated to free MI by inositol monophosphatase-1.

Free inositol may also be obtained by recycling inositol-1,4,5-trisphosphate and inositol1,4-bisphosphate. MI biosynthesis varies among tissues depending on changing functional requirements [9]. There is a complex relationship between glucose and MI metabolism. On the one hand MI inhibits duodenal glucose absorption and reduces blood glucose rise, suggesting the existence of a competitive affinity for the same transporter system [9,12]. On the other hand, glucose significantly counteracts cellular uptake of inositol and may induce MI depletion by the activation of the glucose-sorbitol pathway. Inhibiting aldose reductase in cultured cells restores MI levels counteracting the depleting effect of sorbitol [13].

Metformin is an insulin sensitizer that lowers fasting levels of plasma insulin, C-peptide, and proinsulin-like molecules, increases binding of insulin to its receptor, increases peripheral utilization of glucose, and decreases hepatic glucose production. It also lowers theca cell androgen synthesis in vitro [14]. Metformin has a positive effect on metabolic disturbances and bleeding disorders in women with PCOS [15]. Due to increased incidence of Polycystic ovary syndrome (PCOS) in Tobruk, Libya, we were able to collect a cohort of 800 Polycystic ovary syndrome patients with follow up information. In this project we utilized this patient collection for treatment of PCOS and anovulation by using myo-inositol and metformin.

Methods

It was a randomized controlled trial conducted at Gynecology and Obstetrics department of Tobruk Medical Center, Libya, from January 2018 to January 2022. A total of 800 female patients between the age of 18-42 years - who have Polycystic ovary syndrome (PCOS) - were included in the study. Patients gave written informed consent before sharing in the study. After we took the consent, we started our research. All patients are investigated for insulin and glucose levels to confirm the insulin resistance by increasing both insulin and glucose levels. So, we take the patients with insulin resistance in our study. All patients informed about the possible result in our study and half of them refuse using myo-inositol for financial causes. Patients then were randomly distributed into two groups; Group 1 (n = 400) in which Myo-inositol 2000 mg daily by taking two tablets (2x500 mg) after breakfast and another tow tablets after dinner and take Metformin 850 mg during lunch. Group 2 (n = 400) in which they take Metformin 850 mg during lunch only. All patients were followed up by ultrasound to see the progress of ovulation.

Statistical Analysis

The collected data were coded then entered and analyzed using the SPSS version 22 (Statistical package for social science). Descriptive statistics was done for categorical variables by frequency and percentage, and for numerical variables in the form of mean and standard deviation (mean ± SD). Suitable statistical tests of significance were used, Chi-Square ($\chi2$) test for categorical data, P-values equal to or less than 0.05 were considered statistically significant.

Results

The details of 800 patients selected for analyses are as follows. The mean age of the patients at group 1 is 29 years (range, 18–40 years) and at group 2 is 32 years (range, 22–42 years). Mean pre-study serum glucose level is 193 mg/dl in group 1 and 208 mg/dl in group 2. Mean pre-study Insulin level is 284 mIU/L in group 1 and 295 mIU/L in group 2. (Table 1).

Variables	Group 1 (Mean)	Group 2 (Mean)
Age (years)	29	32
Pre-study glucose mg/dl	193	208
Pre- study insulin mIU/L	284	295

Table (1): Mean age and pre-study serum glucose and insulin levels in group 1 and group 2.

Relation of Myo-inositol and Metformin effects with respect to laboratory, clinical and radiological findings and pregnancy in group 1 and group 2 is shown in Table 2.

Variables	Group 1 (n:400) Use of Myo-inositol and Metformin	Group 2 (n:400) Use of Metformin only	*Chi*-square test
Serum glucose level			
Improved (642 cases)	372	270	*P*=0.00001*
Not (158 cases)	28	130	
Serum insulin level			
Improved (702 cases)	368	334	*P*=0.000246*
Not (98 cases)	32	66	
Acne			
Improved (503 cases)	302	201	*P*=0.00001*
Not (297 cases)	98	199	
Hirsutism			
Improved (582 cases)	343	239	*P*=0.00001*
Not (218 cases)	57	161	
Body weight			
Decreased (312 cases)	193	119	*P*=0.00001*
Not (488 cases)	207	281	
Menstrual cycle regularity			
Improved (678 cases)	371	307	*P*=0.00001*
No (122 cases)	29	93	
Follicles diameter (Folliculometry)			
Improved (532 cases)	321	211	*P*=0.00001*
No (268 cases)	79	189	
Pregnancy			
Yes (561 cases)	347	214	*P*=0.00001*
No (239 cases)	53	186	

*p-value <0.05 was considered to be statistically significant.

Table 2: Relation of Myo-inositol and Metformin effects with respect to laboratory, clinical and radiological findings and pregnancy.

Discussion

Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine disorder in women of reproductive age, affecting approximately 6–15% of them [16–18]. It is a major cause of menstrual disturbances, hirsutism, and female anovulatory infertility [19]. However women with PCOS may also have other comorbidities including psychological (anxiety, depression, body image) [17,20,21], metabolic (obesity, insulin resistance, metabolic syndrome, prediabetes, type 2 diabetes, cardiovascular risk factors (hypertension, dyslipidemia), and increased risk for sleep apnea, endometrial carcinoma, and pregnancy-related complications (gestational diabetes, preeclampsia, pregnancy-induced hypertension, postpartum hemorrhage and infection, preterm delivery, meconium aspiration, stillbirth, operative deliveries, and shoulder dystocia) [22]. Thus PCOS negatively affects not only reproduction, but also general health, sexual health, and quality of life [18].

In our study, combination of Myo-inositol and Metformin shows significant improvement of serum insulin and glucose levels with decrease body weight. That is in agree with Nestler et al., [4] the first to report the efficacy of inositol in the treatment of obese PCOS women, demonstrating increased insulin action, improved ovulatory function, and decreased serum androgen concentrations, blood pressure, and plasma triglyceride concentrations. Few years later the same effects were demonstrated in lean PCOS women [23].Donà et al. studies show that treatment with MI proved its effectiveness in reducing hormonal, metabolic, and oxidative abnormalities in PCOS patients by improving insulin resistance [24]. Genazzani et al. [25] demonstrated the same effect in overweight PCOS women. A recent meta-analysis by Unfer et al. [26] evaluated the efficacy of treatments with MI, showed significant reductions in fasting insulin. In Shokrpour et al. study, the effect of MI on fasting plasma glucose serum, insulin levels, serum triglyceride, and VLDL-cholesterol levels and quantitative insulin sensitivity check index was significantly higher compared with metformin [27]. MI and metformin in combination could act in an additive or synergistic way allowing the use of reduced doses of metformin in patients intolerant to the normal therapeutic administration of metformin [28].

In our study, combination of Myo-inositol and Metformin shows significant improvement of acne and hirsutism. That is in agree with Minozzi et al. that shows patients with mild and moderate hirsutism with administration of 2g Myo-inositol twice daily for 6 months led to significant decrease in the severity of hirsutism and the levels of total androgens, FSH, LH, and LDL cholesterol [29].

We showed a significance improvement of menstrual cycle regularity and ovulation by measurement of follicles diameter with subsequent pregnancy. The same results were obtained in some studies that have demonstrated that Myo-inositol treatment in patients with PCOS improved ovarian function and fertility [30,31], decreased the severity of hyperandrogenism, acne and hirsutism [32-33], and positively affected metabolic parameters and modulated various hormonal parameters deeply involved in the reproductive axis function and ovulation [34,35] and thus it became a novel method to improve spontaneous ovulation [5] or ovulation induction [36,37].

In a study by Papaleo [38] there was a beneficial effect on restoration and maintenance of normal menstrual cycle during 6 months of Myo-inositol treatment. Similar results were shown in another study that demonstrated significantly higher ovulation frequency in the MI-treated group (25%) with shorter time to first ovulation compared with the placebo (15%) [39].

Raffone reported that 65% of Myo-inositol treated patients restored spontaneous ovulation activity, compared to 50% of metformin treated patients [40]. The combination of MI and metformin showed better effect on menstrual cycle than metformin alone despite the similar effect of both treatments on weight, body mass index (BMI), waist and hip circumferences [41].

Conclusion

Our results shown that use of Myo-inositol and Metformin is a useful treatment of polycystic ovary with infertility with improvement of laboratory, clinical and ovulation with subsequent pregnancy. We are attentive that further, larger researches are compulsory as meta-analysis in Libya.

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Brown tumor in patients with secondary hyperparathyroidism due to chronic renal failure: a case series study

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(Original Research Article)

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Abstract

Brown tumor (BT) is an un-common benign bone lesion caused by hyperparathyroidism. Occurrence of BT in sitting of chronic renal failure is considered as sever form of renal-osteodystrophy. Prevalence of BT is (1.5-13%) among dialysis patient. The definite diagnosis of BT is by histopathology. However, BT can be diagnosed noninvasively by using lab and imaging-based criteria. The most frequent sites: ribs, clavicles, extremities, pelvis and facial bones. Although no malignant potential for BT, it can result in catastrophic complications if not treated. Unfortunately, no universal guideline management for BT. This necessitates recognition of clinical manifestation and imaging patterns of BT to be detected and managed properly. Aim of study: Describe the clinical features and the imaging patterns of BT among the studied population. A descriptive case series study was conducted in the central hospital of Al-Baida city /Libya from December 2021 to the end of March 2022, involved 3 hemodialysis male patients. The age ranges from 32-42 years. Parathyroid hormone level measured, Digital x-rays and Non-contrast CT-scan (chest, abdomen and pelvic) performed to all patients. All cases exhibited multifocal lesions located in spine, ribs, pelvic bone. Expansile lytic lesions found in 100% of cases. Some showed mixed solid and lytic lesions. None of studied cases received a proper pharmacological treatment, one case underwent decompressive surgery. This humble case series shed light on the pattern of BT aiming for early discovering and proper management. The findings of this study can be used as baseline for further research in future.

Introduction

Brown tumor (BT) is an un-common benign lesion of the bone caused by increase osteoclast activity and deposition of hemosidrin as consequence of uncontrolled hyperparathyroidism HPT. It can be primary or secondary to other disease (Nago et al, 2021). The secondary hyperparathyroidism usually due to end stage renal failure (ESRF) and appearance of BT in such patients is considered as severe form renal osteodystrophy (ben fatama, 2010). The prevalence of BT is (1.5-13%) among dialysis patients and the incidence increase with chronicity of renal failure (Resic, 2011). The definite diagnosis of brown tumor is by histopathology. However, BT can be diagnosed noninvasively by using the diagnostic criteria of Balon & Kalavar (1998) and Chew et al (1993) that is a lytic lesion with Hounsfield units equal to blood and fibrous tissue in end stage renal failure, patient on hemodialysis therapy with secondary hyper-parathyroidism (HPT). The most frequent sites of BT are in ribs, clavicles, upper and lower limbs, pelvis and facial bones. Clinical presentation can vary from asymptomatic swelling to diffuse bony pain and pathological fracture (Kamal et al). It could be invasive in a number of patients; however, it does not have a malignant potential (Pinto et al, 2010). The radiological features of BT can be a single or multiple and the lesions resemble the appearance of lucent bone tumors like aneurysmal bone cyst, gaint cell tumor, metastatic carcinoma and myeloma (Kamal et al, 2020). Although there is no universal guideline management for BT, according to literatures, the main treatment is control HPT effectively either by pharmacological or surgical means, and bone curettage or decompression when it necessarily (Kamal, 2020; Wiederkehr, 2020). Giving the above-mentioned knowledge, it emphasizes the significance of think about BT in patients on hemodialysis, with single or multiple lytic lesions and bone symptoms. Therefore, this case series study of three patients with secondary HPT due to renal failure in hemodialysis department in Albida Medical Center is carried out. Aiming for analyze the clinical and radiological pattern of brown tumors among the studied population. Hoping to be a nucleus for further comprehensive studies and to draw more attention for this disease as there is no screening, prevention programs or even national guideline to follow and manage this preventable disease in order to avoid the catastrophic out comes.

 Methods

This descriptive case series designed according to definition of case series of Gordis epidemiology text book (Celentano & Szklo 2019) and Hennekens and their colleagues (abu-Zaidan et al. 2012). The study was conducted from 11 December 2021 to the end of February 2022. The ethical form approval to conduct the study was obtained from the radiology department\ Al-Baida Medical Centre\ Al-Baida-city. The number of studied cases is 3, all were males. Their ages range from 32-42 years. The average period for hemodialysis was 10 years (9-12years).

Data regarding demography, symptoms, reason for imaging, types of medications were collected directly from patients and medical records during the scan. Data filled manually in special paper forms, A blood samples were collected from all patients, and parathyroid hormone level analyzed at the main lab of Baida Medical Centre. The inclusion criteria followed Balon & Kaleva (1998) and Chew et al (1993), that means all patients with end stage renal failure on hemodialysis therapy, secondary hyper parathyroidism, and CT lytic lesions with Hounsfield units equal to blood and fibrous tissue, were included. The x-ray of site of interest and CT scans were performed using a FCT Speedia HD, Fujifilm, 64-MDCT scanner.

The following parameters were used; 80-120 kV, 5mm beam collimation, 1.58 pitch, 0 gantry tilt, and the FOV (347-500) depending on patient's size. The scans covered the extremities bony deformity, Chest, spine and pelvis. No intravenous contrast had been administered. Following acquisition, the images reported by two radiologists.

Results

The number of studied cases is 3, all were males. Their ages range from 32-42 years. The average period for hemodialysis was 10 years (9-12years).

The reasons for imaging were as following: for first patient, neurological deficient for which CT spine requested; the second patient, acquired bony deformities in hands, the third patient accidently discovered in Chest X ray as a part of covid-19 work up as seen in (table 1) and (figure: 1).

Table-1: The main clinical and radiological patterns among the studied population

| Patient age	Duration of hemodialysis	Reason of imaging	Other symptoms	Site of lesions
32	11	Cough/accidently discovered lesion during Chest x ray examination	Bone pain	Ribs, pelvis, femur, thoracic vertebral of spine.
40	9	Quadri-paresis	Bone pain	Multiple lesion spine with Compression lesion in cervical spine,
42	10	Bony deformity hands	Bone pain	Both hands, right scaphoid, ribs, pelvis, spine, humeri
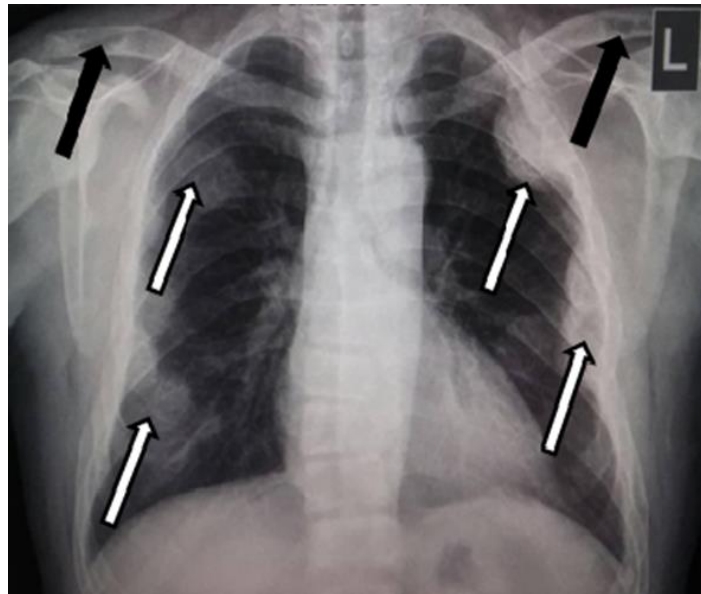
Figure (1): PA chest x ray; showing multiple expansile bony lesions along the ribs (white arrows), multiple lytic lesions clavicles (black arrows).

The most common CT patterns among the studied cases were lytic in 100% with some lesions exhibit mixed solid and lytic lesions (figure 2, 3b). The HU of lesions ranges from 25-80. Most of lesions are asymptomatic or exhibit mild bony pain. However, the spinal lesion in one patient was large enough to cause compression on cervical spinal cord leading to quadriparesis. All cases exhibited multifocal lesions located in spine, ribs, and scapulae. Pelvic bones (figure 4). One case showed brown tumors involving the carpal bones in addition to above mentioned sites (figure 3A). Although all patients were on calcium, none of them were on regular one alpha (VIT D analogue). None of them underwent parathyroidectomy. Only one patient underwent decompression surgery as a part of treatment.
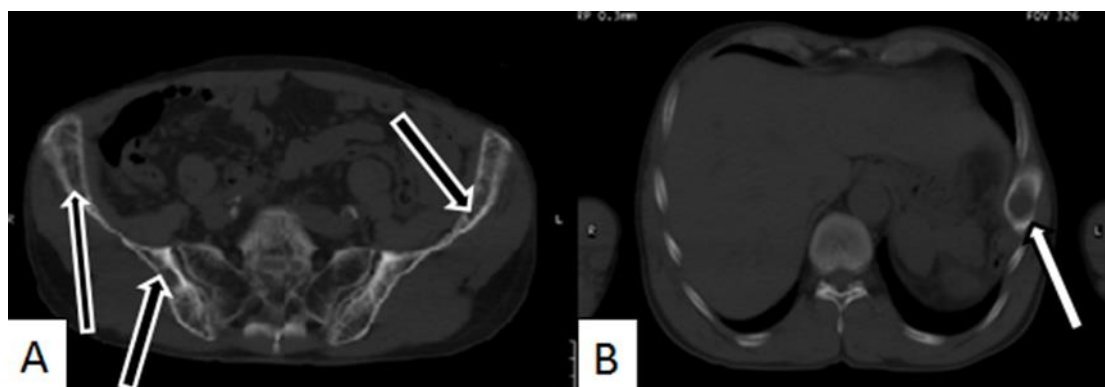

Figure (2): CT axial views; (A) multiple lytic lesions in pelvic bones (black arrows). In (B) ; expansile bony lesions along the left 9th rib (white arrow)
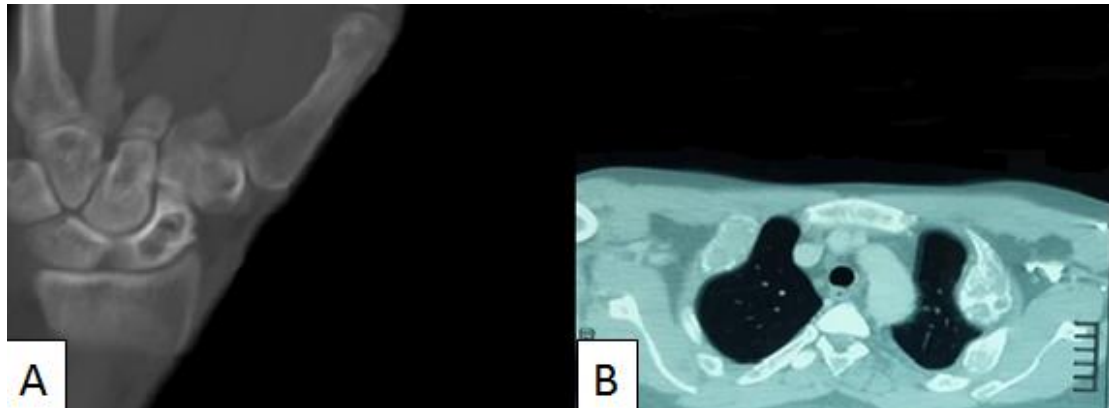
Figure (3): (A) CT for carpal bones showing lytic lesion in right scaphoid (black arrow). In (B); CT chest axial view showing expansile mixed solid\lytic bony lesions involving left 3ird ribs (white arrow.)
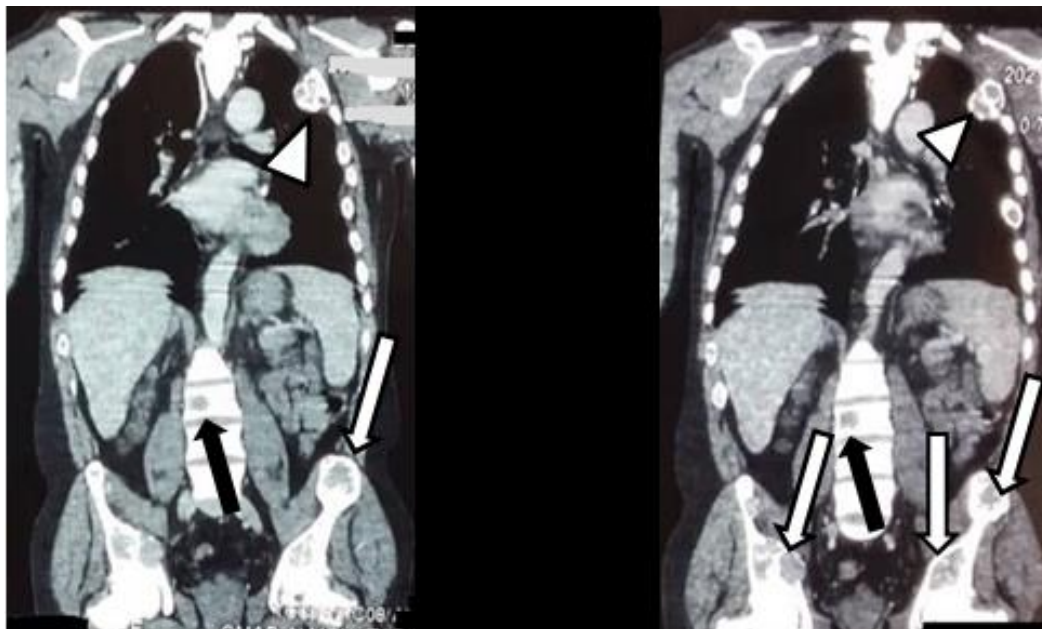

Figure (4): CT coronal reconstructions views; multiple lytic / mixed expansile bony lesions in pelvic (white arrow), lytic lesion in vertebrae (black arrow), and mixed expansile lesion in ribs (white arrow head).

Discussion

Brown tumors are a type of cystic fibrous osteitis, even though, BT are found in primary hyperparathyroidism, cases with secondary hyperparathyroidism as a result of chronic renal failure are documented with raising rate (pinto et al). Its rate is increasing due to increase survival rates in patients with chronic renal failure (pinto et al, 2010; Ben Fatma et al,2010). The incidence of BT in secondary HPT due to chronic renal disease vary from 1.5% to 13 % (Ben Fatma et al, 2010). BT in end stage renal disease occurs in patients with very elevated PTH level and over a long interval of time (WiederKehr, 2020). Increase PTH secretion changes the ratio of extra – and intra- cellular calcium, leading to increase resorption of bone thus decrease bone density and deposition of calcium in soft tissue, lesions are found in places of sever bone resorption (pinto et al, 2010). BT can be found in any bone, nevertheless, published articles are mainly in maxillofacial and dental journals because of high frequency for maxilla, mandible and hard palate, they are occurred also in ribs, femur and pelvis, and less frequently in spine (WiederKehr 2020). In our study all cases showed multifocal lesions placed in spine, ribs, scapulae and pelvic bone, one case, carpal bones are involved in addition to above mentioned places. The clinical presentation of BT is differed according to its location; they are mainly asymptomatic, although it can lead to swelling or dis-configuration, particularly in the face (WiederKehr 2020). Pain is due to the tumor itself or due to the sequel of the disease such as pain because of pathological fracture, tumor in vertebral column may cause paraesthesis, radicualar pain, more critical manifestations such as Para paresis, cauda equine syndrome and paraplegia represents a neurological emergency (WiederKehr 2020). In this study there was three patients, the lesions are mainly asymptomatic or show mild bony pain, one of the patients has spinal lesion that was large and causing compression on cervical spinal cord leading to quadriparesis. BT do not have particular laboratory or radiographic findings, most frequently cases have significant increase of PTH, phosphorus and calcium (WiederKehr, 2020). Radiographic imaging could be showed an osteolytic lesion with well—circumscribed margins with bone expansion and thinning of cortex. This may mimic bone metastasis, anurysmal bone cyst, osteosarcoma, giant cell tumor, multiple myeloma or chondroma (Kamal et al, 2020). The CT patterns amongst the studied patients were mainly lytic lesions in 100% with a few lesions display mixed lytic and solid lesions. The proper management of BT is often not easy and there is no common reference to guide the management. There is no refer to BT in published guidelines, also there is no talk on BT in standard textbooks of nephrology (WiederKehr, 2020). Management including partial or complete removal of parathyroid gland and when there is fracture or severe deformity orthopedic surgical procedures is considered (Kamal et al). Complete remission and regression of the tumor has been well reported after parathyroidectomy in both primary and secondary HPT (Pinto et al, 2010; and WiederKehr 2020). In addition, Vit D and phosphate binders are helpful preventive treatment of secondary HPT and BT (Ben Fatma et al, 2010). All of the studied cases in this study received calcium, no one of the studied patients were on regular one alpha (VIT D analogue), none of them underwent parathyroidectomy. Decompression surgery was done to one patient as a part of treatment. We should consider BT due to secondary hyperparathyroidism in patients with chronic renal disease if there is osteolytic lesions, we suppose that BT are under-reported, and its diagnosis is not simple thing to do, clinical history and examination, lab investigation and medical imaging should be correlated together to reach diagnosis.

In this study the number of cases is small, none of them underwent parathyroidectomy or received proper medical treatment, other studies with large number, receiving proper management and follow-up to monitor the effect of management is recommended.

Conclusion

Brown tumor is one of the complications of secondary Hyperparathyroidism due to chronic renal disease; however, it may become asymptomatic until cause severe destruction. Therefore, screening for secondary HPT in patients with chronic renal disease is recommended, with considering BT in differential diagnosis of any single or multiple lytic lesion(s). Multi displinary view is necessary in management cases with osteolytic lesions.

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THE SIGNIFICANCE OF PAIN IN LEIOMYOMA WITH ADENOMYOSIS AND LIOMYOMA WITHOUT ADENOMYSIS

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(Original Research Article)

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Abstract:

The pain represented as dysmenorrhea, dyspareunia and pelvic pain, which are common symptoms to leiomyoma and adenomyosis since these two disorders frequently occur concurrently. The study aimed to compare women undergoing hysterectomy with a pathological finding of both leiomyoma and adenomyosis to women with leiomyoma alone in relation to the clinical symptom of pain. identifying adenomyosis in women with leiomyoma will allow improved clinical decision-making regarding alternative to hysterectomy and likely a decreased risk of treatment failure. Methods: A retrospective study done at Salesi-hospital ANCONA (ITALY), The data collected from the patient files from January -2012 to December -2012. All operated patients for leiomyoma by hysterectomy was included. Result Our study sample comprised of 97 cases operated for leiomyoma by hysterectomy. From the 97 cases, there were 90 cases of leiomyoma without adenomyosis and 7 cases of leiomyoma with adenomyosis. Conclusion the pain is an important symptom of both leiomyoma uterus alone or leiomyoma with adenomyosis but present more in leiomyoma with adenomyosis in women undergoing hysterectomy, the pain commonly present more in patient with adenomyosis with leiomyoma and correlate in high percentage to the presence of adenomyosis on histopathological examination of specimen, so in cases of leiomyoma uterus adenomyosis must be expected as this affect the line of treatment.

Key words: Hysterectomy**,** Leiomyoma**,** Adenomyosis**,** Pain.

Introduction

At least 25% of premenopausal women have uterine fibroids, which are a very common type of non-cancerous growth. The two most prevalent gynecologic conditions in women of reproductive age are leiomyoma or fibroid and adenomyosis. Uterine leiomyomas are benign monoclonal tumors that primarily develop as a result of myometrial smooth muscle cell proliferation. Adenomyosis is a benign condition marked by invasion of the myometrium by the endometrium, which means the presence of ectopic endometrium outside of its usual location lining the endometrial cavity. It is linked to uterine enlargement and histological examination reveals ectopic, non-neoplastic endometrial glands and stroma surrounded by hypertrophic myometrium [1]. In premenopausal women, uterine leiomyoma and adenomyosis are both prevalent gynecological conditions that may necessitate hysterectomy. Uterine leiomyomas can either be asymptomatic or show symptoms. If they are large enough, they can push on the urinary tract and result in a variety of symptoms, including abnormal uterine bleeding, persistent pelvic pain, and urinary problems [2]. Since leiomyoma and adenomyosis frequently coexist, they cannot be clearly separated by symptoms alone. Adenomyosis, which typically affects multiparous women, can cause discomfort that is expressed as dysmenorrhea, dyspareunia, pelvic pain, or menorrhagia [3]. which are typical symptoms of leiomyoma and adenomyosis because these two conditions frequently coexist, it is difficult to tell them apart by their symptoms alone [4,5]. Despite the fact that the symptoms of leiomyoma and adenomyosis have been largely identified, comparative research on the symptoms of these conditions when present separately and concurrently have been done very infrequently. Accordingly, this study aimed to examine clinical characteristics and symptoms by dividing hysterectomy patients into two groups based on histology outcomes: concurrent leiomyoma and adenomyosis group and leiomyoma only group. According to Walker & Stewart (2005) [6], uterine leiomyomas (fibroid or myoma) are the main reason for hysterectomy in the United States. They are benign myometrial neoplasms. Adenomyosis is a myometrial lesion characterized by the presence of ectopic endometrium with or without hyperplasia of surrounding myometrium. Furthermore, Adenomyosis and leiomyomas frequently coexist; the percentage of women with simultaneous adenomyosis in hysterectomy specimens with leiomyomas ranged from 15 to 57% [7].

Age, multiparity, surgical endometrial and myometrial border disturbances, high FSH and prolactin levels, smoking, and a history of depression are risk factors for adenomyosis (Parazzini et al., 1997, 2009; Taran et al., 2009) [8]. Leiomyomas have been linked to a number of symptoms, including painful or heavy periods, pelvic discomfort, bowel and urinary system issues, and heavy menstruation. Similar to menstrual pain, chronic pelvic pain, and abnormal uterine bleeding, symptoms of adenomyosis are frequently reported. However, since both conditions frequently coexist in the same uterus, it can be difficult to attribute symptoms to either condition. In addition, since adenomyosis is typically diagnosed only at the time of hysterectomy, the disease's contribution to the symptoms can only be understood retrospectively (Weiss et al, 2009) [9].The (MRIGFus) magnetic resonance guided - focused ultra sound and uterine artery embolization are reported as safe and effective minimally invasive therapies for symptomatic uterine leiomyoma [10].The likelihood of both treatments failing appears to be higher when concurrent adenomyosis is present [11].

The design of the current study aims to compare women undergoing hysterectomy with a pathological finding of both leiomyoma and adenomyosis to women with leiomyoma alone in relation to the clinical symptom of pain identifying adenomyosis in women with leiomyoma will allow improved clinical decision-making regarding alternative to hysterectomy and likely a decreased risk of treatment failure.

Methods

A retrospective study done at Salesi-hospital ANCONA (ITALY) review of records from the files of the patients which operated for leiomyoma uterus by hysterectomy. The study was approved by the Ethical Committee at the hospital.

The data collected from the patient files from January -2012 to December -2012
All operated patients for leiomyoma by hysterectomy in this year was included, review of the pain symptoms and the histopathological examination of uterus specimen after hysterectomy for presence of adenomyosis was done. The cases divided into two groups: cases of leiomyoma alone, cases of leiomyoma with adenomyosis by the histopathological examination. Comparison of pain in both groups was done as a presence of any type of pain dysmenorrhoea, pelvic pain, and dyspareunia.

Results

Our study sample comprised of 97 cases operated for leiomyoma by hysterectomy. The symptom of pain searched for from every patient's file for all the 97 cases. The histopathology report for every patient's file also reviewed for the presence of adenomyosis in each specimen. The cases divided into 2 groups, cases of leiomyoma only and cases of leiomyoma with adenomyosis, and the pain studied in both groups.Pain either as pelvic pain, dysmenorrhoea or dyspareunia.
From the 97 cases, there were 90 cases of leiomyoma without adenomyosis and 7 cases of leiomyoma with adenomyosis.
The symptom of pain reviewed in every case from the patient's file there were 38 cases from the 90 cases of the first group which is the group of leiomyoma without adenomyosis have pain which represent 36.86% from the all cases and 42.2% from the first group which 90 cases of the leiomyoma only group.
There were 7 cases of the second group which is leiomyoma with adenomyosis 4 of which have pain which represent 57% of cases and of the second group.
The results are plotted in tables as shown

Table (1): This table shows the total number of cases in the year of study 2012 and number of cases in each group.

Total number of leiomyoma operated by hysterectomy	only leiomyoma (G-I)	leiomyoma with adenomyosis (G-II)
97 cases	90 cases	7 cases

Table (2): show percentage of the cases in two studied groups from the total cases.

Cases of leiomyoma only (group I)	Percentage from total cases	Leiomyoma with adenomyosis (group II)	Percentage from total cases
90 cases	92.8%	7 cases	7.2%

The first group (G-I) which is leiomyoma only are 90 cases of the total 97 cases represent 92.8%. The second group (G-II) which is leiomyoma with adenomyosis which 7 cases from the 97 cases were which represent 7.2% of the total cases.

Table (3): show the percentage of pain in both groups.

Cases of leiomyoma only which had pain (G-I)	Percentage %	Cases of leiomyoma with adenomyosis which had pain (G-II)	Percentage %
38 cases from 90 cases	42.2%	4 cases from 7 cases	57.1%

The pain Present in percentage of 42.2% in cases of leiomyoma only and in 57.1% in cases of leiomyoma with adenomyosis.

Table (4): show types of pain that present and its percentage in each group

	Leiomyoma without adenomyosis (G-I)	**Leiomyoma with adenomyosis (G-II)**
Painful menses dysmenorrhea	10 (11.1%)	4 (57%)
Dyspareunia	10 (11.1%)	4 (57%)
pelvic pain	18 (20%)	4 (57%)

Pain in cases of leiomyoma with adenomyosis is dysmenorrhoea and dyspareunia in leiomyoma cases
 without adenomyosis also pain is present but more as pelvic pain.

Discussion

Uterine leiomyomas are often Asymptomatic, but may cause abnormal uterine bleeding including menorrhagia, chronic pelvic pain and urinary symptoms such as urinary frequency, urinary urgency or nocturia and others [13]. The symptoms depend on site, size of leiomyoma and any degeneration changes in it. The diagnosis of leiomyoma is usually determined by pelvic examination and imaging tests, such as pelvic U.S.S and magnetic resonance imaging. A symptomatic leiomyoma are typically observed with serial follow up, while symptomatic leiomyomas can be managed by drug therapy using a hormone- releasing intra uterine device, interventions such as uterine artery embolization, and surgical modalities such as myomectomy or hysterectomy [14]. the most common symptoms of adenomyosis are dysmenorrhoea, dyspareunia, chronic pelvic pain and abnormal uterine bleeding. Patients of these symptoms can be suspected of having adenomyosis and often undergo hysterectomy. Drugs, interventional or surgical management can be attempted for patients with adenomyosis even though sex hormones, progestins, danazol, and gonadotropin releasing hormone can help alleviate dysmenorrhoea. Several controlled studies have shown that no drug has inhibit the development of adenomyosis [15,16]. In the current study the pain was Present more in the group of leiomyoma with adenomyosis(G2) 57.1% Dysmenorrhoea and dyspareunia and pelvic pain are also present more in the second group , this suggests that presence of adenomyosis with leiomyoma is a contributing to symptomatology which leads to hysterectomy consequently in women with symptoms that seem disproportionate to the level of leiomyoma disease, F. Andrei Taran et-al found that a Women undergoing hysterectomy with both adenomyosis and leiomyomas have a number of different clinical features compared with women with only leiomyomas at the time of hysterectomy, Women with substantial pain despite a smaller fibroid burden may be more likely to have concomitant adenomyosis[17]. UAE studies reported pelvic pain in up to 20% of the participants (Pron et al., 2003; Edwards et al., 2007) [18,19]. Furthermore, a previous population-based study showed that pelvic pain and dyspareunia increased in severity in women with leiomyomas compared with women without leiomyomas; however, consistent with these reports, we found, in the group of women with only leiomyomas, approximately one-fifth of women reporting non-cyclical pain. The proportion is, however, doubled in the group with adenomyosis and leiomyomas and the difference is significant in the multivariable model. These findings suggest that chronic pain is present in some women with leiomyomas but enlarged in women with both diseases.

Conclusion

Co-existence of the two diseases exhibits mixed symptoms of each disease but show different tendency. The pain is an important symptom of both leiomyoma uterus alone or leiomyoma with adenomyosis but present more in leiomyoma with adenomyosis women undergoing hysterectomy. the pain commonly present more in patient with adenomyosis with leiomyoma and correlate in high percentage to the presence of adenomyosis on histopathological examination of specimen, so in cases of leiomyoma uterus adenomyosis must be expected as this affect line of treatment, further study on large cohort, prospective study is needed.

Acknowledgments

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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Knowledge and Perception of the Medical and Health Science Students Regarding COVID-19 in Tobruk University, Libya

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Abstract

Background: A coronavirus is a highly contagious virus causing severe acute respiratory diseases in human beings. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is a highly pathogenic virus. The virus emerged in China's Wuhan state in December 2019., The aim of our study to assessing the knowledge and perceptions about COVID-19 among medical and allied health science students. Methods: A web-based observational cross-sectional descriptive study was conducted using a "Google Form" to obtain responses from medical and allied health science students during Aguste and September 2021. Results: Out of 221 participants that filled out the web-based survey, 221 participants gave their consent for voluntary participation and completed the questionnaire. The mean age of the study participants was 22 years. The majority of students were from pharmacy (40.7%), medical technology (30.8%), medicine (24.9%) and dentistry (3.6%). Conclusion: The current Study Showed that the students from different institutions have adequate awareness of COVID-19. Also, it has been observed that the majority of participants acquired the information from social media, which is an unauthenticated resource for obtaining evidence about diseases.

Key words: coronavirus, respiratory diseases, knowledge, Perception, Libya.

Introduction

A coronavirus is a highly contagious virus causing severe acute respiratory diseases in human beings. It is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is a highly pathogenic virus (1). The virus emerged in China's Wuhan state in December 2019(2). The novel coronavirus (CoV) named "2019-nCoV" or "2019 novel coronavirus" or "COVID-19" by the World Health Organization (WHO) is in charge of the current outbreak of pneumonia that began December 2019 in Wuhan City, Hubei province, China (3-4). Knowledge, attitude, and practices (KAP) are important in controlling the spread of the disease. Knowing the cause of the disease, the signs and symptoms, the possible methods of prevention can facilitate the proactive application of preventive measures (5-6). The signs and symptoms of the disease may range from asymptomatic to mild (such as fever, dry cough, fatigue, myalgia, dyspnea, and shortness of breath) to severe (such as pneumonia, SARS, kidney failure, cardiac injury, respiratory failure, and acute respiratory distress syndrome) (7-8–9). The elderly and patients who have chronic medical illnesses such as hypertension, cardiac disease, lung disease, cancer, and diabetes are more vulnerable to COVID-19 infection.

Early recognition of symptoms and seeking supportive care is very important for recovery due to the absence of an effective cure (10). The transmission of COVID-19 was very high among university students due to the presence of different contributing factors (11). They live away from their families, who give them an opportunity to make judgments on their own. Furthermore, they may participate in different activities like sports clubs and part-time work, which makes them a good opportunity to contact the COVID-19 pandemic (12). Furthermore, different prevention measures, such as provision of handwashing facilities, face masks on free, alcohol-based hand sanitizer, reducing the number of students by half in dormitories and classes, and temperature measurement, are implemented to divert the transmission of the disease. Prevention and control of the disease requires knowledge, attitude, and prevention practices (KAP) (13).

The virus is spread by small droplets discharged from the cases during coughing, sneezing, and talking. It is also transmittable by contaminating the nose and mouth with contaminated hands or contaminated surfaces containing the virus. The virus has an incubation period that may range from 2 to 14 days with the main clinical manifestations of fever, cough, and shortness of breath. There is no cured antiviral treatment for the virus, so reducing transmission remains the mainstay of prevention (14). Hand hygiene, covering the mouth and nose when coughing or sneezing, avoiding close contact with anyone showing symptoms of respiratory illness, and avoiding unprotected contact with farm or wild animals are all standard recommendations to prevent infection spread (15-16).

Current treatment guidelines of the Center for Disease Control and Prevention (CDC) as well as WHO majorly focus on symptomatic management and the application of infection prevention measures (17). The students from medical and allied health sciences are not directly involved in managing COVID-19 patients, they can serve as information providers. They can sensitize community people about maintaining personal hygiene, symptoms of COVID-19 and how to prevent its spread. Students must possess basic knowledge about novel coronaviruses and be able to clear the myths pertaining to COVID-19. With this background, the aim of our study to assessing the knowledge and perceptions about COVID-19 among medical and allied health science students.

Methods

A web-based observational cross-sectional descriptive study was conducted using a "Google Form" to obtain responses from medical and allied health science students during Aguste and September 2021.

Creating, validating, and distributing a survey questionnaire

A survey with 24 questions (in English language) was formulated by KH Gohel *et al*. (18)The survey covered the domains of student demographics, general awareness, information sources, knowledge, and perceptions related to COVID-19. The survey link was distributed among the students in the form of a "Google Form" via various media platforms such as WhatsApp, Gmail, and Facebook. Ethical approval was obtained from Tobruk University's Research Ethics Committee, ref. No.221102-03.

Data analysis

All the collected data was entered into Microsoft Excel and cross checked for the presence of any errors to maintain its accuracy. Descriptive statistics were applied to calculate proportions and frequencies. Statistical analysis was performed using IBM SPSS software for Windows version 27 (NY, USA).

Results

Out of 221 participants that filled out the web-based survey, 221 participants gave their consent for voluntary participation and completed the questionnaire. The mean age of the study participants was 22 years. The majority of students were from pharmacy (40.7%), medical technology (30.8%), medicine (24.9%) and dentistry (3.6%). The demographic characteristics of participants are detailed in Table 1.

Table 1 Demographic characteristics of study participants (n = 221, 100%).

Characteristics	Participants(n)	Percentage (%)
Gender		
Male	35	15.8
Female	186	84.2
Age		
Mean age = 22.0362		
Std. Deviation = 1.99512		
Collage of study		
Medicine	55	24.9
Dentist	8	3.6
Pharmacy	90	40.7
Medical technology	68	30.8

Sources of information

Participants were also asked about the source of valid and reliable information about COVID-19. The main sources of information were social media (Facebook, WhatsApp, YouTube, and Instagram) (62.4%), followed by news media (TV/video) (28.1%) and college (4.5%). The remaining participants reported that they got the information through print media (magazines, newspapers), and other sources. Few students obtained information from their resources, such as newsletters, posters, and guest lectures. Details of the above-mentioned sources of information are represented in Fig 1.
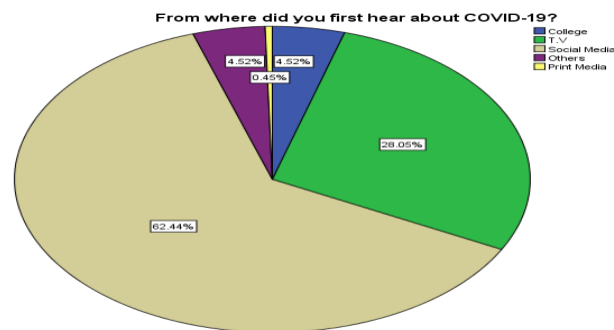

Fig. 1. Sources of information about COVID-19.

Knowledge about novel coronaviruses

The subsequent table (Table 2) illustrates the knowledge of novel coronavirus among the students. The majority of the study participants (61.1%) correctly identified a novel coronavirus, i.e., COVID-19. A high proportion of study participants (98.2%) provided the correct response, while 1.8% did not have any idea of whether COVID-19 is contagious or not. Furthermore, more than half of the participants were not aware of the origin of COVID-19, as many of them gave incorrect answers or had no knowledge of it. More than two-thirds of the participants know about the incubation period of COVID-19. Additionally, more than one third of study participants knew that elderly people or people with comorbidities are more prone to acquiring COVID-19. More than one-third of students were aware that a person infected with COVID-19 can remain asymptomatic, but 15.4% were incorrect. The majority of participants had partial knowledge (those who selected either respiratory symptoms or neurological symptoms) regarding the symptoms of severe COVID-19 cases, while only 0.5 percent had no knowledge about the symptoms. About half of the participants (15.4%) correctly identified the modes of COVID19 transmission. About 44.8% of participants correctly identified that RT-PCR (Reverse Transcriptase Polymerase Chain Reaction) and Immunofluroscent antigen detection assay are the diagnostic tests for COVID-19, while 39.8% had partial knowledge (selected either RT-PCR or Immunofluroscent antigen detection assay).

Table 2. Knowledge about novel Coronavirus among study participants (n = 221).

Question	Correct Response (%)	Incorrect Response (%)	No Knowledge (%)
1. Which of the following is novel Coronavirus?	61.1	38.9	-
2. Is COVID-19 contagious?	98.2	1.2	-
3. What is the origin of COVID-19?	94.6	5.4	-
4. What is the incubation period of COVID-19?	41.2	49.7	9.0
5. Is there any similarity between COVID-19, SARS-CoV and MERS-CoV?	53.8	10	36.2
6. Who are more prone to COVID-19?	51.6	48	0.5
7. Do you know the fatality rate of a person infected with COVID-19?	16.3	41.1	42.5
8. Do you think a person infected with COVID-19 can remain asymptomatic?	81.0	15.4	3.6

Question	Correct Response (%)	Partial Knowledge (%)	No Knowledge (%)
9. What are the symptoms of Severe COVID-19?	23.1	76.5	0.5
10. How does the COVID-19 spread?	15.4	0.9	83.9
11. What are the diagnostic tests for COVID-19?	44.8	39.8	15.4

Prevention of COVID-19

Students were also asked to rate their attitudes toward COVID-19 prevention. The majority of all the students (95.9%) positively agreed to the ways of preventing COVID-19 as prescribed by WHO. These precautionary measures are: cleaning hands with an alcohol-based sanitizer; avoiding personal contact; and maintaining at least 1meter distance (social distancing).

Perception about novel coronavirus

A high majority of the participants (81.4%) believe that wearing a surgical mask is a significant approach to prevent COVID-19, while some (13.6%) of the participants do not agree with the statement. A participant (44.3%) incorrectly believes that it is not safe to receive a package from areas where a case of COVID-19 has been reported. Of the students, 33.5%) were found to have a correct perception that antibiotics are not effective in COVID-19 treatment, as well as 50.7% rightly agreed that vaccines are not sufficient to prevent COVID-19 transmission at present. Notably, the participants did not know that a thermal scanner could help to detect fever in a person infected with COVID-19. Furthermore, participants (48.4%) rightly believed that COVID-19 can primarily occur year-round and the infection is not bound to any specific climatic condition. The rest of the information about the perception of students about COVID-19 is detailed in Table 3.

Table 3. Perception about novel Coronavirus among study participants (n = 221).

Question	Correct Response (%)	Incorrect Response (%)	No Knowledge (%)
1. Do you think wearing a Surgical mask can protect people from COVID-19?	81.4	13.6	5.0
2. Is it safe to receive a package from any areas where a case of COVID-19 has been reported?	38.5	44.3	17.2
3. At present, do you think antibiotics are effective in preventing or treating COVID-19?	33.5	57	9.5
4. At present, do you think vaccines are effective in preventing COVID-19?	62.4	27.1	10.4
5. Are traditional herbal medicines effective for COVID-19?	50.7	29.4	19.9
6. Are hand dryers effective in killing new Coronavirus?	23.1	44.3	32.6
7. Can an Ultraviolet (UV) disinfection lamp kill the new Coronavirus?	13.6	28.1	58.4
8. Are thermal scanners helpful in detecting FEVER in people infected with new Coronavirus?	61.5	15.8	22.6
9. Can spraying Alcohol or Chlorine all over your body kill the new Coronavirus?	38.9	45.7	15.4
10. In your opinion, can eating garlic help prevent infection with the new Coronavirus?	48.4	25.3	26.2
11. In which climatic condition COVID-19 infection can PRIMARILY occur?	41.2	53.8	5.0

Discussion

The current study was designed to assess the knowledge and perceptions of COVID-19 among medical and allied health science students in university of Tobruk, in light of the global burden and media attention surrounding the virus. Our study discovered that the majority of students obtained knowledge about COVID-19 from social media, 62.4%. Another survey conducted in Pakistan reported that social media (87.68%) remained the primary source of information among healthcare professionals (19). Similarly, a study carried out by Bhagavathula AS et al. revealed that the participants' main source of information was official government websites (33%) followed by social media (30%) (20). Presently, a wide range of information is available on the internet, including unverified, biased, and deceptive information, which can easily misguide the public. The emphasis should be on educating and providing authentic information to students so that the appropriate information can be communicated to the community.

A large proportion of study participants were aware and had general knowledge about COVID-19 except for symptoms of severe conditions and the category of people more prone to COVID-19. About 94.6% of participants correctly identified the novel coronavirus and gave the correct answer about its incubation period. whereas a study conducted among health care workers showed that only 36.4% correctly identified the incubation period of COVID-19, i.e., 2–14 days. (19) Other cross-sectional surveys conducted in Pakistan, China, and Iran reported 96.38%, 66.40%, and 85.4% correct responses about the incubation period, respectively (18,20). Information about the incubation period would be useful to identify the suspected cases and provide medical care at an early stage. In this study, (53.71%) of the students knew about the modes of transmission of COVID-19. In contrast to that, studies carried out by Zhong BL et al., Abdelhafiz AS et al., and Bhagavathula AS et al. stated that 98.85%, 95.9%, and 39% of respondents correctly recognized the transmission modes of novel Coronavirus (19,21,23). In our study, nearly 51.4% of participants believed that the elderly or those with co-morbidities were more vulnerable to COVID-19. a study conducted among the Egyptian public also demonstrated that around 95% of study participants believe that COVID-19 is more dangerous for the elderly and patients with chronic diseases (22). According to a summary of a large survey conducted among the general public in the United States (US) and the United Kingdom (UK), 96.3% and 97.5% of people believe that older adults are the most likely to die from the novel coronavirus infection, respectively (24). The majority of participants (76.5%) in our study had partial knowledge (either selected only respiratory, enteric or neurological symptoms) about the symptoms of severe COVID-19 cases. On the other hand, 98.63% and around 90% of respondents of a Chinese and Egyptian survey accurately identified the symptoms of COVID-19, which is higher than our study results (21,23). It is very necessary that people be informed about the most common as well as severe symptoms of COVID-19 infection through validated sources to avoid this misconception. At present, there is no clear evidence about the origin of COVID-19. Recently, a study conducted in Bangladesh reported that 37.22% of participants gave an incorrect response about the COVID-19 origin (25). In contrast to that, 41.2% of participants from our study gave correct responses and were found to have good knowledge of the origin, which is yet unknown as stated by WHO. Considering the asymptomatic behavior of COVID-19, about 81.0% of students in our study rightly believed that a person infected with a novel coronavirus can remain asymptomatic. Also, 81.8% of participants in a survey conducted in Egypt correctly responded that COVID-19 could be transmitted from asymptomatic person to asymptomatic person as well as agreed with our study (23).

Almost all our study participants (95.9%) knew about the measures that should be adopted for the prevention of COVID-19, such as maintaining a 1 m distance, cleaning hands with soap and water, using an alcohol-based sanitizer, and avoiding personal contact. This finding is in line with the reported rates in studies conducted among healthcare workers (85.6% and 98.31%) (17,18) and students (98.6% and 93.8%) (21, 22). A majority of participants (81.4%) believe that wearing a surgical or face mask can protect people from getting infected with COVID-19. Contrary to our results, only 37.8% and 29.7% of people from the US and UK agree with the statement (24). About half of the students rightly stated that, at present, antibiotics (57.0%) and vaccines (27.1%) are not effective in preventing or treating COVID-19 but roughly 84% of the respondents also thought that antibiotics or vaccines might be useful, which is a wrong perception. Likewise, in a survey conducted among healthcare workers, around 90% believed that flu vaccination is not sufficient in preventing COVID-19.17 A cross-sectional study conducted among medical and non-medical students in Jordan reported that 89% and 78.9% of respondents knew that there was no vaccine or specific treatment available

for COVID-19(26). A few discrepancies were also noted in the perception of our study participants. As an example, around 50.7% of students believed that the use of herbal medicines and eating garlic could protect against COVID-19 infection, 33.1% of the Egyptian public also incorrectly stated that eating garlic could prevent the spread of disease (23). Considering the association of climatic conditions and COVID-19 infection, more than half of participants (51.1%) believe that it either occurs in winter or spring/fall, which is an incorrect perception as it could occur round the year as per available evidence.

Conclusion

The current global pandemic situation demands substantial awareness about the clinical presentation, spread, preventive measures, and management of COVID-19. The present study showed that the students from different institutions have adequate awareness of COVID-19. Also, it has been observed that majority of participants acquired the information from social media, which is an unauthenticated resource for obtaining evidence about diseases. Students should be informed about the authentic sources of information as provided by global health authorities and the health ministries of respective countries. Our study findings also highlight specific aspects of knowledge and perception where partial or incorrect responses were observed, and these areas should be addressed in the future through webinars, leaflets, and educational campaigns to improve understanding and dispel COVID-19 myths.

Declaration of competing interests
The authors declare that they have no conflict of interest.

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Polycystic ovarian syndrome (PCOS) awareness among young women in Tobruk, Libya

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Abstract

Background: Polycystic Ovarian Syndrome (PCOs) is a common chronic multisystem endocrine disorder in young reproductive aged women, PCOS is often associated with chronic anovulation, obesity and impairs reproductive health, it increased risk of adverse pregnancy and birth outcomes, and it's one of the leading causes of infertility, if it's not treated can develop serious health problems, especially if they are overweight: As type 2 DM, Heart disease, endometrial carcinoma and psychological features and worsened quality of life. Not all women who have PCOS receive a formal diagnosis or if they do, it may take years and several different doctors before diagnosis is made. This may be attributable to both a lack of awareness and educational material available at the correct level for individuals and healthcare providers so, this study was aiming to assess the level of awareness regarding Polycystic Ovarian Syndrome among young women of age group between 18-30 years in Tobruk , Libya. Methods: cross sectional research analysis, using an online link of the web-based multiple-choice questionnaire "Google Forms", the questionnaire link was distributed randomly mainly using the social media and messengers. The study was conducted on the month of September 2021 after ethical clearance from the Research Ethics Committee of Tobruk University. Results: We had a total of 373 sample size for analysis, the distribution of the samples on demographic characteristics revealed that about 50% of the sample were in the age group between 25-30 years, 92.8% of the studied females were university graduates, 327(87.7%) had moderately adequate knowledge and there is a strong relation between the level of education and level of knowledge about PCOS, also there is a statistical significant between the age and the level of knowledge where the age group between 20-24 had a moderately adequate knowledge. 58% of them received information's about PCOS from Health Personal, and There is a large number of participants have a poor life style where 84.7% of participant like junk foods which is a risk factor for obesity and other metabolic issues related to PCOS. Conclusion: There is a good level of awareness of PCOS among majority of young women in Tobruk. The Health Personal and Social Media were the prevalent source of information.

Key words: PCOS, obesity, endocrine disorder, young women, reproductive age, Infertility, Libya.

Introduction

Polycystic Ovarian Syndrome (PCOS) is a common chronic multisystem endocrine disorder, it is increase among adolescent girls and young women, with prevalence of 5%-10% in different ethnic populations and as much as 22% of women in general population, It is a problem in which a woman's hormones are out of balance leading to menstrual disturbance as well as multiple abnormal cysts in enlarged ovaries, the real causes of the syndrome have not been yet identified exactly and clinical presentation of it with a wide range of symptoms including: Irregular menstrual cycle, obesity, infertility, hirsutism, insulin resistance, and it can develop serious health problems, especially if they are overweight: Such as type ll DM, Heart disease, endometrial carcinoma and psychological features such as depression and worsened quality of life[1,2,3,4,5]. PCOS should be diagnosed according to the Rotterdam consensus criteria, with two out of three of the following: 1.polycystic ovaries, 2.oligo-ovulation or anovulation, 3.clinical and/or biochemical signs of hyperandrogenism. [5] Globally, PCOS prevalence estimates range between 2.2% and 26%. [6] The high prevalence was attributed to PCOS association with obesity, sedentary lifestyle, and genetic predisposing factors. [7] Lack of awareness regarding PCOS leads to delayed diagnosis and delayed treatment which causes many problems as PCOS increases the risk of adverse pregnancy and birth outcomes As increased risk of gestational diabetes, increased prevalence of early pregnancy loss (EPL), strongly associated with pre-eclampsia, preterm birth and birth of small-for-gestational-age (SGA) babies [8,9] also, PCOs is one of the leading causes of infertility, and many women with PCOS are also overweight or obese, and Obesity is responsible for an increased risk of sub-fecundity and infertility[10] moreover, women with PCOS have a 3 times more risk than other women to develop endometrial cancer[11] therefore, early detection and therapy of this disorder would decrease it's associated long-term adverse effects. Although is no cure for PCOS, but there are several ways to treat and manage the condition, therefore education of women with PCOS about food habits, exercise and weight loss all of these can restore hormones level to normal, and because hyperinsulinemia and insulin resistance play an important role in the pathogenesis of PCOS therefore, Insulin-sensitising agents such as, Metformin has been widely used to improve ovarian function, glucose metabolism and hyperinsulinemia in women with PCOS, as well as metformin decrease the hyperandrogenism, and significantly decreased abdominal obesity[12], moreover use of metformin combined with thiazolidinediones appear superior to metformin alone in improving insulin resistance and decreasing total testosterone, also use of Myo-inositol combined with d-chiro-inositol is particularly efficacious in menstrual recovery[13]. Studies had been carried out on PCOS which emphasizes only on the diagnostic modalities and clinical categorization but studies focusing on awareness of the condition is very sparse which subsequently results in increase in case load. The studies that had been conducted to analyze the problem of PCOS, states that only one-third of affected females has gained some awareness of the condition and its complications and rest of the study population are unaware of either sequelae or morbidities.[14] Another Studies have found that there was a gap in the knowledge of students about PCOS and its symptoms and signs, and that lifestyle preferences may predispose to PCOS. [15] Not all women who have PCOS receive a formal diagnosis or if they do, it may take years and several different doctors before diagnosis is made. This may be attributable to both a lack of awareness and educational material available at the correct level for individuals and healthcare providers. A recent study showed that over one-third of women with PCOS had to wait over 2 years and visit with at least three different health professionals before their diagnosis was established.[16]

Furthermore, when these women were finally diagnosed, they receive little information regarding long term complications for PCOS, treatment options, or emotional support and counseling. Instead, women reported seeking information about PCOS from online resources, where the information quality is variable.[16]

Healthy lifestyle and adequate reproductive health knowledge are important for maintenance of physical and mental well-being of women to avoid major fertility problems so, there is a need to increase awareness of PCOS symptoms and complications for early treatment and to prevent further serious complications of it, so that our study aiming to assess the level of awareness regarding Polycystic Ovarian Syndrome, clinical presentation, risk factors and complications among young women in Tobruk in age group between 18-30 years, and its relation to some common socio-demographic factors.

Methods

Study Design and sitting

An observational cross-sectional descriptive study was carried out using a self-administered structured online multiple-choice questionnaire was developed using "Google Forms" used for data collection during September 2021. The data collected included the demographic variables as age, marital status, educational level and type of work, life style characteristics, some clinical parameters and Source of Informations and knowledge regarding Polycystic Ovarian Syndrome. The questionnaire was posted in Arabic language with minor modifications to Anjana Devi, G. questions. Ethical approval was obtained from Research ethical Committee of Tobruk University. The questionnaire link was distributed randomly mainly using the social media and messengers. The Participation in this study was not restricted to PCOS patients; it is for all females within the age group consistent with the pre-defined criteria.

Study population

The inclusion criteria were all individuals who agreed to participate in the study, young women in Tobruk of age group 18-30 years who are willing to participate in the study and who able to read and write, there were no restrictions on educational level, occupation, or socioeconomic level of the participants. The exclusion criteria were women of age group of less than 18 years and more than 30 years or those who refused to take part in the study.
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Statistical analysis

We had a total of 373 sample size for analysis. Data were entered using (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp2015.). Quantitative data were expressed as the mean $\pm$ SD & (range), and qualitative data were expressed as absolute frequencies (number) & relative frequencies (percentage). Percent of categorical variables were compared using Chi-square test. All tests were two sided, p-value < 0.05 was considered statistically significant (S), p-value < 0.001 was considered highly statistically significant (HS), and p-value ≥ 0.05 was considered statistically insignificant (NS).

Results

This study was conducted on 373 Young females, scanning the period during September 2021. Table (1) shows the distribution of females' demographic characteristics. Out of   373 respondents, about 50% were over 24 years old while 43.4% and 6.2% were between 20-24 years old and 18-19 years old, respectively. The mean age was 24.75±3.49, with range from 18 to 30 years. Regarding to marital status, 60.3% were single, and 36.7% were married. Concerning the educational level, 92.8 % were Post Graduate, and 5.6% were graduated from Secondary school. Health care provider represented 60.6%.

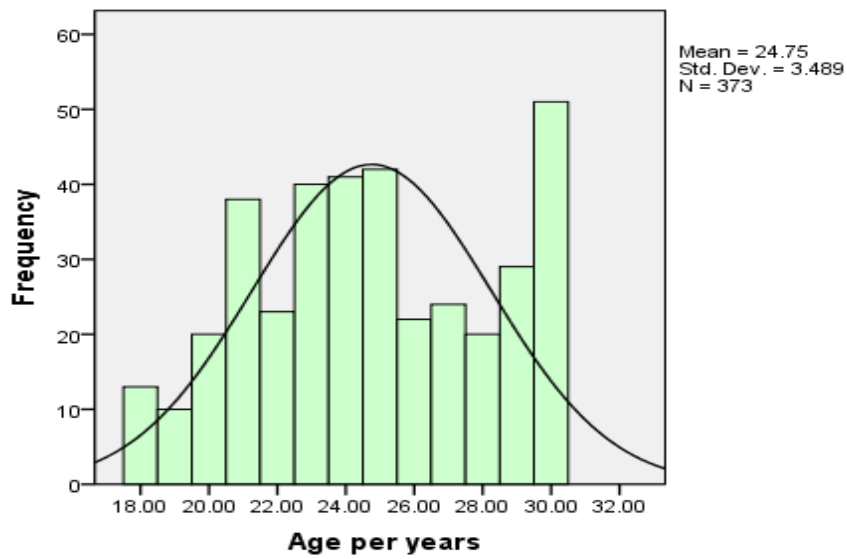|	Variables	n.	percent
Age	18-19 years	23	6.2
	20-24 years	162	43.4
	>24 years	188	50.4
	Mean± SD	24.75±3.49	
	range	18-30	
Marital Status	Divorced	10	2.7
	Married	137	36.7
	Single	225	60.3
	Widow	1	0.3
Educational Status	No Formal Education		0.3
	Primary Education		1.3
	Secondary Education		5.6
	Graduate		92.8
health care provider	No	147	39.4
	Yes	226	60.6

Figure 1: Histogram define age frequency per years of studied females
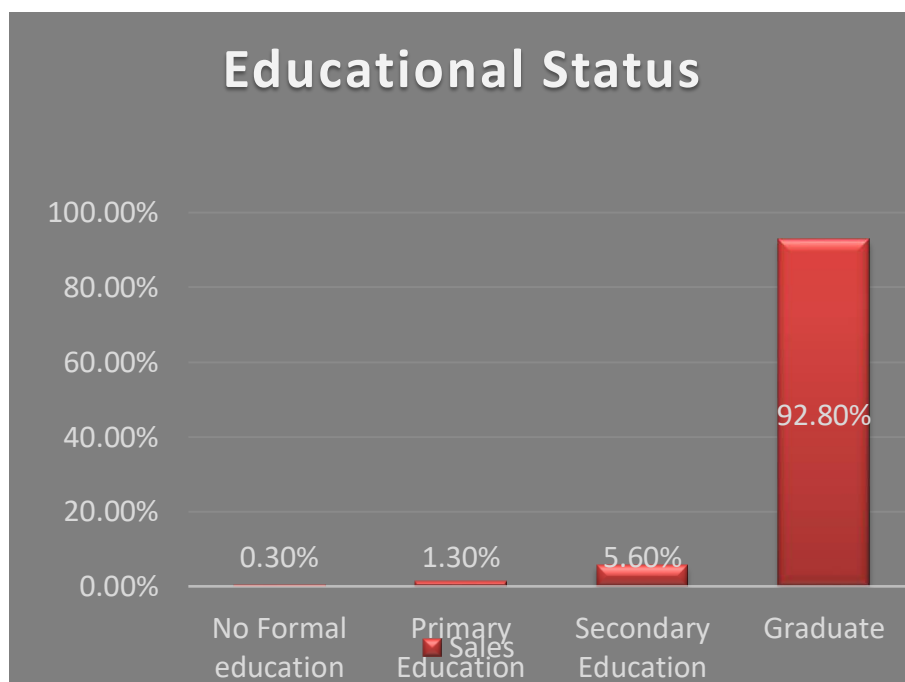
Figure2: Education level of studied females

Variables		n.	percent
Dietary Pattern	Non-Vegetarian	350	93.8
	Vegetarian	23	6.2
Do you like junk foods	No	57	15.3
	Yes	316	84.7
Amount of water intake per day	> 2000 ml	30	8.0
	1000 – 2000 ml	124	33.3
	500 – 1000 ml	219	58.7
BMI	underweight	43	11.5
	Normal weight	179	48.0
	overweight	92	24.7
	obese	59	15.8
Number of Children	No Children	251	67.3
	One	44	11.8
	Two	31	8.3
	Above Two	47	12.6
Do you have any associated disease	No	339	90.9
	Yes	34	9.1
Menstrual Cycle	Irregular	120	32.2
	Regular	253	67.8
Do you have any menstrual disorder?	No	219	58.7
	Yes	154	41.3
Have you ever heard of PCOS?	No	53	14.2
	Yes	320	85.8

Table 2: Lifestyle characteristics and Clinical parameters of studied females (n=373)

About 98.3% of females are Non-Vegetarian, 84.7 % like junk foods. Concerning Amount of water intake per day, 33.3 % were drink one – two liter per days while 58.7% drink between 500-1000 ml. Normal weight females represented 48% while 24.7% were overweight. Regarding associated diseases, it revealed that only 9.1% of them had chronic diseases. More than 50% of participants have regular cycle 67.8%, and irregular menses complaint of 32.2 % females, and menstrual disorder mention by 41.3% of them. Majority of studied females heard about PCOS.

	Frequency/373	%
Source of information		
Health Personal	215	58%
Social Media (Facebook, what's app ...etc	183	49%
Friends, family, neighbors	94	25%

Table3: Frequency of Source of Information's about polycystic ovaries Syndrome on Selection by studied females

Regarding the source of knowledge 58% of participant received information from Health Personal while 49% by social media.
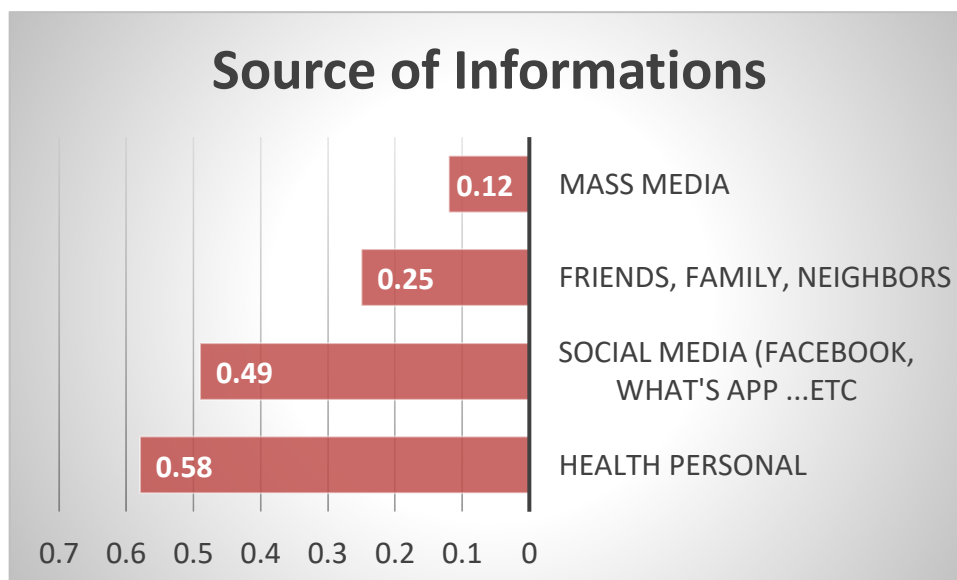

Figure3: This Pie chart showing Source of Information's about polycystic ovaries Syndrome of studied females

Young women knowledge level about polycystic ovaries syndrome	Frequency	Percent
Adequate knowledge	25	6.7
moderately adequate knowledge	327	87.7
Inadequate knowledge	21	5.6
Mean± SD range	16.44± 3.19 6-23	

Table 4: Frequency of knowledge level about polycystic ovarian syndrome

Table 4 reveals that among 373 young women, most of them 327(87.7%) had moderately adequate knowledge, 25 (6.7%) had adequate knowledge and only 21 (5.6%) had Inadequate Knowledge. with mean± SD (16.44± 3.19) and range from 6 to 23.
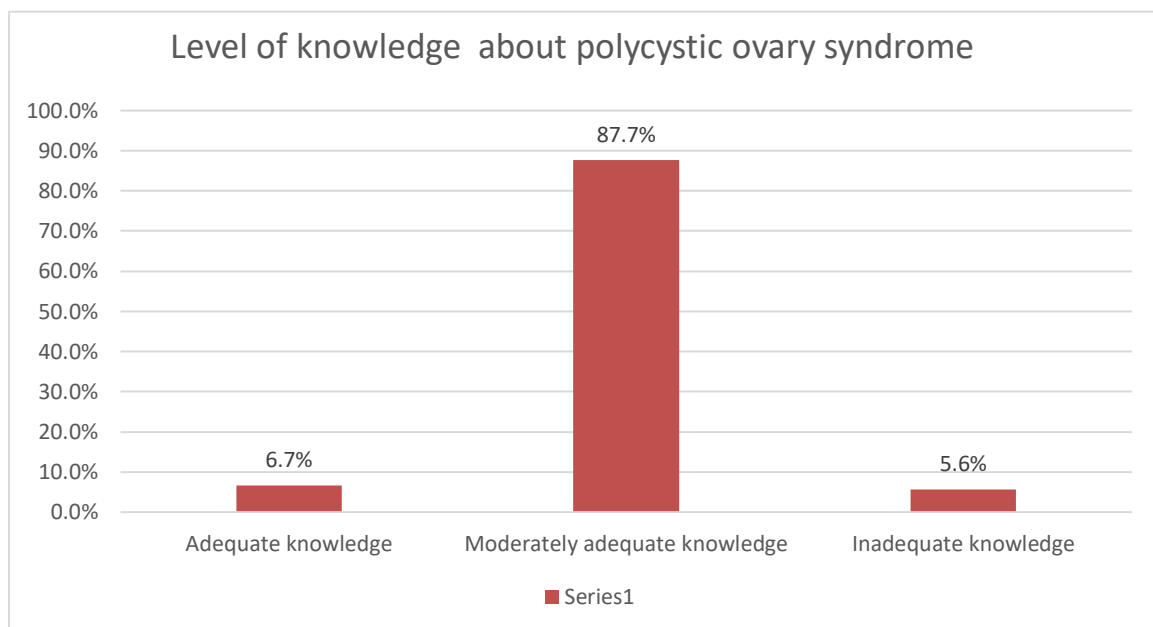

Figure 4: Pie chart illustrated young Libyan women knowledge level about polycystic ovaries syndrome

Variables	Women Knowledge level about polycystic ovary						n.	χ^2	P. value
	Adequate knowledge		moderately adequate knowledge		Inadequate knowledge				
	No.	%	No.	%	No.	%			
18-19 years	2	8.7	17	73.9	4	17.4	23	14.92	0.005
20-24 years	4	2.5	149	92.0	9	5.6	162		(S)
>24 years	19	10.1	161	85.6	8	4.3	188		
Primary Education	0	.0	0	.0	1	100.0	1		
Secondary Education	0	.0	2	40.0	3	60.0	5	50.58	0.0001
Higher Education	0	.0	18	85.7	3	14.3	21		(HS)
Post Graduate	25	7.2	307	88.7	14	4.0	346		
No	6	4.1	131	89.1	10	6.8	147	1.14	0.21
Yes	19	8.4	196	86.7	11	4.9	226		

Table5: Relation between young women Knowledge level about polycystic ovary and their age, Education level, job (n= 373)

There were significant relation between the age of participants and the level of knowledge especially in the age groups between 20-24 years and >24 years where the level of knowledge was moderately adequate with 92% and 85.6% respectively, also there was statistically highly significant relation between Knowledge level about PCOS with educational level (p<0.0001) where the post graduate and participant with higher education have moderately adequate knowledge with 88.7% and 85.7% respectively. The type of work between participant either a health care provider or not have no statistically significant.

Discussion

This study is the first study to evaluate the level of awareness of PCOS among females in Tobruk, Libya. The source of knowledge was mostly from Health Personal, followed by Social Media and Friends, family, neighbors, these results is similar to study done in Sudan which revealed that the main source of information was medical professionals (gynecologists)[17], and also complies with another study was done in Saudi Arabia where women did get information from medical doctors [18,] the source of knowledge is important to gives us an impression about preferred method of gaining knowledge in Libyan community. The present study revealed that (87.7%) of the studied women had moderately adequate knowledge level and (5.6%) had inadequate knowledge. This result was higher than result of similar study was conducted in India (2017) which revealed that (13.3%) had moderate knowledge, (86.7%) had inadequate knowledge, and no one had adequate knowledge [10], this is can be explained by that: the Indian study was done on adolescent girls aged between (18-20 years) while the age group in present study was between (18-30 years), in addition to the women more than 24 years old are more likely to have adequate knowledge level than younger women like in previous Indian study, this explanation is supported with the another Indian study in 2016 conducted on higher age group between (21-25 years) , showed that (76.0%) had moderate knowledge, (13.3%) had inadequate knowledge, and (10.7%) had adequate knowledge [1] , also supported by another study conducted in Jordan which revealed that age groups differed significantly in their PCOS awareness scores (p < 0.001), and the highest scoring group was among those aged between 22 and 23 years old [19], the study concluded that there was lack of knowledge of teenage girls regarding PCOS, it could be due to a lack of education and discussions regarding reproductive health in their schools and families, the administration of information booklet, or information through social media may have help the teenage girls to understand more about PCOS.

One of objectives of this study was to determine the relation between educational level and knowledge level regarding PCOS, the current study showed statistically highly significant relation between young women knowledge level about PCOS with education level (p<0.0001) , It is obvious that females who are university graduates are more likely to have adequate knowledge level, these results were similar to results of study was done in Saudi Arabia (2017) which revealed that the level of awareness of PCOS was significantly related to educational levels, it increased with higher education level (P < 0.001) [20], also similar to results of Jordanian study which showed significant associations between the level of knowledge and education level [19] , this may be explained by the fact that women with higher educational levels have better access to information, this makes us direct our interest in educating people to raise awareness among them.
This study also found that, the large number of participants have poor life style such as the majority of females (84.7%) were preference junk (fast) foods, and (58.7%) were inadequate water intake per day, these results were similar to results of study done in Emirates which revealed that 85.4% of students reported consuming fast food at least 1-5 times a week, and nearly 12% consumed fast food 5-10 times a week [21] these poor life style habits increase risk factors such as obesity, cardiovascular diseases , type 2 diabetes and aggravated PCOS and other metabolic issues, also our study reveals nearly 25% of participants were overweight, and 16% were obese that's could be due to majority of them preferred fast food, and usually fast food consumption associated with high BMI (Body Mass Index) Therefore, spreading awareness and knowledge among young women about the dangers of these bad habits will help them adopt a healthy lifestyle.

Conclusion

There is a good level of awareness of PCOS among majority of young Libyan women in Tobruk and the higher educational level was associated with higher level of awareness, the health personal and social media were the prevalent source of information. It would be desired to increase knowledge about PCOS among Libyan women to increase awareness and promote health seeking behavior for early treatment to avoid complications.

Declaration of competing interests

The authors declare that they have no conflict of interest.

Acknowledgement

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