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Abstract

Background: Identifying the causes of unexpected pediatric deaths is a clinical, medicolegal, and humanitarian requirement. This study included autopsied children aged < 18 years who suddenly died due to natural causes and excluded nonnatural deaths. The study was performed over 5 years in the Egyptian Forensic Medical Authority.

Results: The study included 244 cases, consisting of 51.6% of neonates (< 1 month), 18% of infants (1–12 months), and 30.3% of children (1–18 years). The cause of death in neonates and children was "explained natural diseases" in 73.8% and 91.9%, respectively, while it was only 45.5% in infants. Infection-related deaths account for 30.4% of all explained natural deaths. Infections were responsible for 11.8% of explained deaths in neonates, while 55% and 48.5% were in infants and children, respectively. Of the fatal infections, 60% occurred at the age of > 1 year. Pneumonia accounted for 61.8% of infection-related deaths, followed by myocarditis (12.7%) and septicemia (12.7%). Regarding systems that had fatal pathologies, respiratory causes were responsible for 64% of explained natural deaths, whereas cardiovascular and central nervous system diseases accounted for 11% and 7.7% of explained natural deaths, respectively. Considering prodromes, alarming symptoms were reported before death in 51.2% of cases, whereas death occurred without alarming manifestations in 29.9% of cases. The rest of the cases (18.9%) were abandoned children with unavailable antemortem data.

Conclusions: Present results serve as a valuable reference dataset for deaths in developmental stages in Egypt that quides forensic practitioners in managing child deaths.

Keywords: Pediatric deaths, Unexpected natural death, Explained, Unexplained, Undetermined, Egypt

Background

Unexpected pediatric deaths are events causing grief and concern faced by families and legal authorities. Sudden unexpected natural death means that the child is not considered at risk of death or had serious manifestations 24 h before the fatal outcome. Childhood is a long period that extends up to 18 years old, and every developmental stage in childhood has its characteristics that should

be considered while managing pediatric deaths (Byard, 2010; Byard, 2018; DiMaio and Molina, 2022).

Decedents' relatives and legal authorities usually have the need to clarify the cause of sudden deaths of children, as well as the chances of a sudden death in siblings. Exploring the fatal pathologies is crucial to initiate preventive measures to decrease future mortalities (Busuttil and Keeling, 2008; Rizzo et al. 2020).

Globally, increasing reported cases of child abuse and neglect led to the increased scrutiny of unexpected pediatric death investigations. Therefore, a significant number of sudden pediatric deaths are subjected to a medicolegal autopsy; however, most of the pediatric autopsy series were concerned with violent deaths rather than sudden natural deaths. Managing unexpected deaths

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during childhood necessitates adequate knowledge and experience regarding natural fatal pathologies that differ between children and adults (Rizivi and Herath, 2017; Grayaa et al. 2021; Feld et al. 2022).

Forensic medicine practice is well established decades ago in Egypt. Unexpected pediatric deaths that arouse criminal suspicions are referred to the Egyptian Forensic Medical Authority (EFMA) where forensic experts perform comprehensive postmortem examinations (Kharoshah et al. 2011).

The causes of death vary between nations and regions worldwide. A better data on the causes of death is necessary to realize the Sustainable Development Goals of the United Nations (United Nations, 2022). To date, no autopsy-based studies that investigate unexpected deaths due to natural causes during childhood in Egypt have been published. Therefore, this postmortem study has an in-depth look at unexpected natural pediatric deaths in Egypt.

Methods

The current study included all autopsied children aged < 18 years who suddenly died due to natural causes and were referred to the EFMA from January 2011 to December 2015. All cases with nonnatural deaths were excluded from this research. Ethical approval was obtained from the Research Ethics Committee, Faculty of Medicine, Cairo University.

In EFMA, experienced forensic medical examiners performed the autopsy procedures. The pathology samples from all Egyptian morgues are referred to the Forensic Pathology unit to be adequately examined by specialized forensic pathologists, where gross and histological examinations of preserved organs are performed. The procedures fulfill the requirement of international standards in post-mortem examination (Accredited [ISO/ICE 17020]) (State Information Service, 2021). Both forensic medical examiners and forensic pathologists receive initial training for 6 months before being allowed to practice under supervision. They handle a vast variety of cases each year, and strengthen their experience by completing postgraduate coursework (Kharoshah et al. 2011). Their postgraduate education programs comprised subspecialties supported by successful theses.

Pathological examination

The study was conducted in a central EFMA pathology unit that receives pathological samples from all Egyptian EFMA morgues. The lungs, heart, brain, kidneys, and liver were subjected to gross and histopathological examination in all autopsied cases. Additional organs were subjected to a histopathological assessment if relevant medical history or gross abnormalities were observed.

Hematoxylin and eosin staining was routinely used in the microscopic examination of all samples (Conran and Stocker, 2014; Delteila et al. 2018; Husain et al. 2021).

Classification of pediatric deaths

The World Health Organization (WHO) periodically updates the International Classification of Diseases (ICD); thus, the third International Congress on Sudden Infant and Child Death (Radcliffe Congress) was held in 2019 to address the coding nomenclature of sudden unexpected pediatric deaths. There is a consensus on using the terms unexpected, explained, unexplained, and undetermined (Goldstein et al. 2019).

- a. Explained death: deaths are described as "explained" when the circumstances, along with postmortem examination, identify the cause of death with a high degree of certainty. All explained nonnatural deaths were excluded from the current study. Thus, explained deaths are confined to explained natural deaths.
- b. Unexplained death: deaths are described as "unexplained" when thorough investigations could not prove the cause of death.
- c. Undetermined death: deaths are defined as "undetermined" when the required data for the management of the deaths is defective, such as in abandoned children. The term "abandoned children" refers to infants left in public restrooms, trash bins, or other locations where survival is not anticipated (Du Toit-Prinsloo et al. 2016).

Statistical methods

The recorded data were statistically analyzed using Statistical Package for the Social Sciences version 25 (IBM Corp., Armonk, NY, USA). Data were summarized using frequency (count) and relative frequency (percentage) for categorical data. A chi-square test was conducted to compare data. A statistical significance was considered when *P* values were < 0.05.

Results

In 5 years, the central pathology unit of EFMA received samples of 244 autopsied children aged < 18 years old, who met the inclusion criteria. The male-to-female ratio of these autopsied children was 1.5:1. Thus, unexpected natural fatalities were significantly higher in males than in females ($\chi^2 = 33.564$, p < 0.001).

Table 1 shows that 51.6% of cases were neonates (< 1 month), whereas 18% were infants (1–12 months). The rest of the cases (30.3%) were children (1–18 years).

Table 1 Classification of unexpected natural deaths in different pediatric age categories (n = 244)

Age	Classification of Death			χ²	P value	Total deaths
	Explained	Unexplained	Undetermined			
Neonates (< 1 month)	93	6	27	35.701*	< 0.001*	126
% within age category	73.8%	4.8%	21.4%			100%
% within cause of death	51.4%	17.6%	93.1%			51.6%
Infants (1 month-1 year)	20	22	2	58.513*	< 0.001*	44
% within age category	45.5%	50.0%	5.0%			100%
% within cause of death	11.0%	64.7%	6.9%			18.0%
Children (> 1 year)	68	6	0	19.703*	< 0.001*	74
% within age category	91.9%	8.1%	-			100%
% within cause of death	37.6%	17.6%	-			30.3%
Total	181 (74.2%)	34 (13.9%)	29 (11.9%)			244 (100%)

 $[\]chi^2$ Chi square test

Classification of deaths in different pediatric age categories (Table 1)

- Explained natural death: the etiology of unexpected death was explained in 181 cases (74.2% of all cases).
- Unexplained death: the cause of death remained unknown in 34 cases (13.9% of all cases).
- Undetermined death: the cause of death is undetermined in 29 abandoned children (11.9% of all cases) who lack antemortem data.

The cause of death in neonates and children was "explained" in 73.8% and 91.9% of cases, respectively, whereas it was only 45.5% of cases in infants.

Regarding unexplained deaths, approximately 64.7% of unexplained deaths occurred in infants. The cause of death was unexplained in half of the autopsied infants. These cases were assigned as an unexplained sudden unexpected death in infancy (SUDI) or sudden infant death syndrome (SIDS) because the cause of death remained unexplained after comprehensive investigations.

Causes of pediatric deaths

Infection and noninfection-related deaths

Table 2 shows that infections account for 30.4% of explained deaths. Infections were responsible for 11.8% of explained deaths in neonates, whereas it was 55% and 48.5% in infants and children, respectively. Nearly 60% of infection-related deaths occurred in children aged ≥ 1 year.

Table 3 illustrates the types of fatal infections in autopsied cases. Pneumonia accounted for 61.8% of infection-related deaths. Figures 1 and 2 revealed the pathological features of bacterial bronchopneumonia and viral pneumonia, respectively. Myocarditis accounted for 12.7% of fatal infections while septicemia accounted for 12.7%. Figures 3 and 4 illustrated pathological features of myocarditis and septicemia, respectively.

Noninfectious diseases that led to sudden deaths were prematurity, congenital anomalies, anaphylactic shock, amniotic fluid aspiration syndrome, malignancies, cardiomyopathies, pulmonary embolism, cord or placental disorders, status asthmaticus, status epilepticus, coronaries insufficiency, intussusception, and disseminated intravascular coagulation (DIC).

Fatal pathologies in different systems

Table 4 demonstrates different systems with fatal pathologies in explained deaths. Pulmonary-related causes were responsible for 64.1% of explained deaths. Cardiovascular and central nervous system diseases accounted for 11% and 7.7% of explained deaths, respectively.

Prodromes before sudden deaths

The prodromes were alarming symptoms occurring in minutes or hours before death that differ from antecedent symptoms that appear days, months, or years before death. Prodromes were reported before death in 125 cases, representing 51.2% of the studied cases. No prodromes were observed in 73 (29.9%) cases, and death was their first presentation. Moreover, the

^{*}Statistically significant at $p \le 0.05$

Table 2 Infection and noninfection-related deaths in different pediatric age categories (n = 181)

Age	Infection-related deaths	Noninfection-related deaths	χ²	P value	Total deaths
Neonates (< 1 month)	11	82	31.146*	< 0.001*	93
% within age category	11.8%	88.2%			100%
% within cause of death	20.0%	65.1%			51.4%
Infants (1 month–1 year)	11	9	6.439*	0.011*	20
% within age category	55.0%	45.0%			100%
% within cause of death	20.0%	7.1%			11.0%
Children (> 1 year)	33	35	16.949*	< 0.001*	68
% within age category	48.5%	51.5%			100%
% within cause of death	60.0%	27.8%			37.6%
Total	55 (30.4%)	126 (69.6%)			181 (100%)

 $[\]chi^2$ Chi square test

Table 3 Pathological types of fatal infections in the autopsied cases (n = 55)

Types of fatal infections	Number	Percentage
Pneumonia	34	61.8%
Myocarditis	7	12.7%
Septicemia	7	12.7%
Meningitis	3	5.5%
Gastroenteritis	1	1.7%
Bronchitis	1	1.7%
Encephalitis	1	1.7%
Peritonitis	1	1.7%
Total	55	100%

current study included 46 (18.9%) abandoned children with unavailable medical history data.

The reported prodromes in 125 cases were as follows:

- Respiratory difficulties in 58 cases constituted 46.4% of 125 symptomatic cases, as follows: (i) 50 cases were premature, (ii) 4 cases had amniotic fluid syndrome, and (iii) 4 cases had congenital anomalies (2 cases of cystic lung disease, 1 case of persistent pulmonary hypertension, and 1 case of Fallot tetralogy).
- Fever and malaise were reported in 53 (42.4%) infection cases.
- Fever and severe diarrhea were reported in 4 (3.2%)
 DIC cases.
- Recurrent bronchial asthma attacks were reported in 4 (3.2%) asthma and anaphylaxis cases.
- Seizures were reported in 2 (1.6%) cases; 1 had focal gliosis and 1 had an arachnoid cyst.
- Fatigue and bone aches in 2 (1.6%) leukemia cases.
- Abdominal pain in 2 (1.6%) cases; one had hepatoblastoma and another had intussusception.

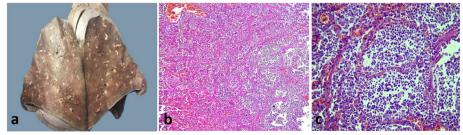


Fig. 1 Bacterial bronchopneumonia. **a** A Lung with multiple yellowish foci, **b** histopathological picture of septic bronchopneumonia showing the pulmonary alveoli and bronchi densely infiltrated by polymorphonuclear leukocytes in (H&E × 40), **c** dense polymorphonuclear leukocytes are collecting inside the alveoli (H&E × 400)

^{*}Statistically significant at $p \le 0.05$

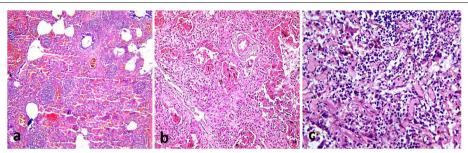


Fig. 2 Histopathological picture of viral pneumonia. **a** Pronounced and dense interstitial lymphomonocytic inflammatory infiltrate (H&E \times 100). **b** Interstitial mononuclear inflammatory infiltrate and giant cells in the alveolar lumina (H&E \times 200). **c** Interstitial mononuclear inflammatory infiltrate and giant cells in the alveolar lumina with polymorphic hyperchromatic cell nuclei (H&E \times 400)

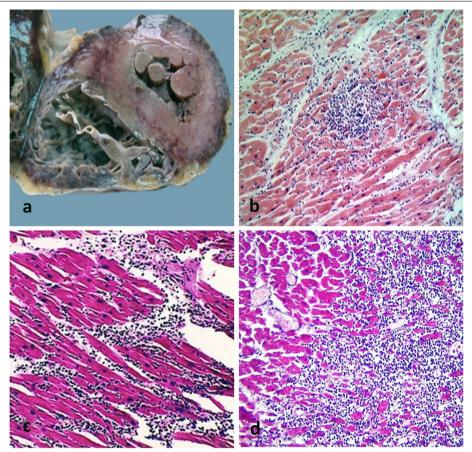


Fig. 3 Myocarditis. **a**, **b** Neutrophilic myocarditis. **a** A heart with yellowish areas in the myocardium and red foci of congestion; **b** histopathological picture of myocarditis showing neutrophilic inflammatory cells infiltrating the myocardium with myocyte necrosis and abscess formation in (H&E × 100); **c**, **d** histopathological pictures of lymphocytic myocarditis showing lymphocytic inflammatory cells infiltrating the cardiomyocytes with myocyte necrosis (H&E × 100)

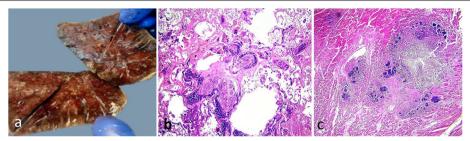


Fig. 4 Septicemia. **a** A cross-section of the lung with multiple yellowish foci and dark areas of hemorrhages denote septic pneumonia; **b** histopathological picture of neutrophilic bronchopneumonia with multiple abscesses containing germ colonies and septic emboli at the interstitial blood vessels (H&E × 40); **c** histopathological picture of neutrophilic myocarditis with multiple abscesses containing germ colonies and septic emboli at the interstitial blood vessels (H&E × 40)

Table 4 Different body systems with fatal pathologies in explained deaths (n = 181)

Systems with fatal pathologies	Number	Percentage			
Respiratory system	116	64.1%			
Cardiovascular system	20	11%			
Central nervous system	14	7.7%			
Gastrointestinal tract	9	5.0%			
Cord and placenta	6	3.3%			
Others	16	8.8%			
Total	181	100%			

Table 5 Cause of explained death in autopsied children who died suddenly without any prodrome (n = 37)

Cause of unexpected death without prodroma	Number	Percentage	
Congenital anomalies	11	29.7%	
Anaphylactic shock	10	27%	
Cord and placental anomalies	6	16.2%	
Cardiomyopathies	5	13.5%	
Thromboembolism	3	8.1%	
Coronary atherosclerosis	1	2.7%	
Medulloblastoma	1	2.7%	
Total	37	100%	

The cause of death could not be explained in nearly half (49.3%) of the 73 cases who suddenly died without any prodrome. The diagnosed causes of death without alarming prodromes were congenital anomalies, anaphylactic shock, cord/placental abnormalities, cardiomyopathies, thromboembolism, coronary atherosclerosis, and medulloblastoma (Table 5).

Deaths of abandoned children

The current study included 46 abandoned children with no available data on their identity, medical history, and death circumstances. The causes of death in these cases were as follows: (i) undetermined in 29 (63%), (ii) prematurity in 15 (32.6%), and (iii) infection in 2 (4.4%) cases.

Discussion

Thus, this 5-year study included 244 autopsied children who suddenly died due to natural causes in Egypt. Globally, the autopsy series that are concerned with unexpected natural pediatric deaths are scarce (Winkel et al. 2014; Bryant et al. 2022). Additionally, childhood is a long period that extends up to 18 years old. Childhood consists of developmental stages and each has its characteristics. Most autopsy-based studies are either restricted to certain pediatric age categories, such as neonates and infants (Weber et al. 2008; Özkara et al. 2009). Others included all pediatric deaths from birth to adulthood as a single group (Parham et al. 2003).

The current study included the full spectrum of natural unexpected pediatric deaths along with the categorization of cases into 3 age groups including neonates, infants, and children, which is in agreement with the study design of Tumer et al. (2005) who conducted their study in the Council of Forensic Medicine, Ankara for 5 years.

More than half of the cases in the present research constituted neonates. Considering that the neonates, who died within days of their birth, often did not have confirmed antemortem diagnoses of their serious disorders, especially in developing countries, such as Egypt (Pugliese-Garcia et al. 2020). Inadequate perinatal care with a subsequent defective diagnosis of fatal pathologies could explain the high percentage of autopsied neonates in the current study.

Conversely, in Turkey, Tumer et al. (2005) stated that neonates constituted only 25.77% of the cases. The relatively small proportion of medicolegal autopsies in neonates could be attributed to advances in perinatal health care in Turkey that identify potentially fatal diseases during life (Alparslan and Demirel, 2013). Thus, enhancing maternal sanitation, increasing awareness of the risks of preterm labor, and providing improved health and neonatal care are necessary in Egypt.

The current study revealed male dominance with a male-to-female ratio of 1.5:1. Similarly, Tumer et al. (2005) and Kaenjua and Srettabunjong (2012) reported a male-to-female ratio of 1.48:1 and 1.3:1, respectively.

A lot of classifications were adopted for sudden deaths during childhood. The current study followed an updated classification adopted by the WHO in ICD-11 that assigned unexpected deaths to "explained," "unexplained," and "undetermined" (Goldstein et al. 2019). "Explained" cases are referred to as explained natural deaths, which constituted 74.2% of cases because nonnatural deaths were excluded from the current study. The cause of death remained unknown in 25.8% (13.9% unexplained death and 11.9% undetermined death). Similarly, Bryant et al. (2022) who conducted their autopsy-based study in hospitals of the UK for 20 years explained the cause of death in 74% of pediatric deaths. Nevertheless, Wren et al. (2000) and Tumer et al. (2005) explained the cause of death in 85% and 80.42% of autopsied children, respectively.

Regarding unexplained deaths, the present study revealed that half of the infant deaths were unexplained, which could be described as unexplained SUDI or SIDS. The current result is congruent with the autopsy-based study findings conducted by Weber et al. (2008) who assigned 63% of infancy deaths as unexplained SUDI. Conversely, Parks et al. (2021) conducted a population-based survey and assigned 82% as unexplained infant deaths. A high percentage of unexplained deaths is an inevitable limitation to the nonconduction of the autopsy. Thus, pathologies that are diagnosed only during autopsy could be missed. Therefore, unexplained SUDI or SIDS should not be diagnosed in the absence of a comprehensive autopsy.

Unfortunately, to date, SIDS results in a significant proportion of deaths during infancy worldwide despite the improvement in healthcare and medical research. The etiology of SIDS is unknown, but it is considered a multifactorial disorder (DiMaio and Molina, 2022; Tan and Byard, 2022).

Infection is one of the leading causes of death during childhood considering explained deaths. Thus, the current study analyzed infection-related deaths that were responsible for nearly one-third of explained natural deaths. Of infection-related deaths, 60% occurred above

the age of 1 year. Recently, Bryant et al. (2022) demonstrated infection as the most common cause of death in children aged > 1 year, accounting for 46% of all deaths and 62.2% of explained deaths that coincide with the current results. This research suggests that reforms in public health are needed, including improved sanitation and immunization programs, to reduce the infection problem. Another example of a shift that relates to a general improvement in housing and standards of living, nutrition, and improved health care is the accessibility of antibiotics for infectious disease treatment (Ferreras-Antolín et al. 2020).

In the current study, respiratory tract infections represented 61.8% of infection-related deaths and respiratory system affection was responsible for 64% of explained deaths. Similarly, Weber et al. (2008) revealed that infections, particularly pneumonia, was responsible for 58% of the explained pediatric deaths. Additionally, Du Toit-Prinsloo et al. (2011) pointed pneumonia as one of the most common causes of unexpected death during childhood.

The current study included 46 cases of death in abandoned children with no available data. The cause of death is undetermined in nearly two-thirds of cases. Similarly, Li et al. (2012) reported death in 27 abandoned babies in a 5-year retrospective study in Shanghai, China, with a significant difficulty in determining the cause of death.

In the present study, the prodromes before death were reported in more than half (51.2%) of unexpected natural pediatric deaths. History of respiratory difficulties and fever were the most common alarming signs. The high incidence of respiratory distress and fever is related to many cases of fatal infections, particularly pneumonia.

In this study, alarming manifestations were absent in nearly a third (29.9%) of unexpected natural deaths. Moreover, the cause of death of nearly half of them was unexplained. The most commonly identified causes that led to death without prodromes were congenital anomalies and anaphylactic shock. Studies reported that congenital malformations, especially in the heart, are not usually manifested during life and were diagnosed for the first time during autopsy (Sheppard, 2020; Fnon et al. 2021). Anaphylactic shock has an abrupt onset and rapidly progressive course; thus, prodromes are not usually reported in cases of fatal anaphylaxis (Greenberger et al. 2007).

This research shed light on forensic medicine practice in Egypt as autopsy procedures are done by forensic medical examiners, whereas pathological examination of retained samples is conducted with forensic pathologists. All forensic experts in EFMA are well-trained and work harmoniously to conduct post-mortem examinations adequately (Kharoshah et al. 2011; State Information Service, 2021). It is worth mentioning that in jurisdictions in

developed Western countries, the forensic practice is different as forensic pathologists always carry out the entire procedure, starting with the external examination (Al-Waheeb et al. 2015).

The current study was restricted to the sudden natural pediatric deaths referred to the pathology unit of EFMA. However, the present results serve as a valuable reference dataset for deaths in different developmental stages in Egypt. From a forensic perspective, the present study guides forensic practitioners in managing child deaths. Clinically, early diagnosis of potentially fatal diseases might decrease the possibility of death.

Conclusions

The current study investigated the causes of sudden natural deaths in autopsied children in Egypt for 5 years. The included cases were subdivided into neonates, infants, and children. The deaths were assigned as explained, unexplained, and undetermined. Neonates accounted for more than half of included cases. The cause of death is mostly explained in neonates and children, whereas mostly unexplained in infants. Infection-related deaths are more prevalent among children as 60% of infection-related deaths occurred above the age of 1 year. Pneumonia was responsible for nearly two-thirds of infection-related deaths. Regarding body systems, respiratory pathologies accounted for approximately two-thirds of explained deaths.

Considering prodromes before death, alarming symptoms were reported in only 51.2% of cases. Congenital anomalies and anaphylactic shock were the most common explained pathologies that presented with sudden death without prodromes. The present study could assist forensic practitioners in managing pediatric deaths. However, similar autopsy-based studies that analyze a wide range of age categories in different populations are recommended.

Abbreviations

DIC: Disseminated intravascular coagulation; EFMA: Egyptian Forensic Medical Authority; ICD: International Classification of Diseases; SIDS: Sudden infant death syndrome; SUDI: Sudden unexpected death in infancy; WHO: World Health Organization.

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Authors' contributions

NF, NI, HH, and SE contributed to the conception of the study, analysis of data, and interpretation of results. NF and HH examined and diagnosed all studied cases. ZS contributed to the analysis of data, reviewing of literature; and drafting of the manuscript. All authors approved the final manuscript.

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Availability of data and materials

Tables and figures were attached to the submission files. The raw data of the current study are available and could be provided upon reasonable request.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the Research Ethics Committee of the Faculty of Medicine, Cairo University. The Ethics Committee is constituted and operates according to ICH GCP Guidelines and applicable local and institutional regulations and guidelines that govern ethics Committees operation.

Consent for publication

Not applicable as the research did not include any individual person's data in any form.

Competing interests

All authors declare that they have no competing interests.

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