investigation on the prevalence of complication of bacterial meningitis and its related factors in children after the neonatal period- a retrospective study.

Mulham Almohamed (mulham.alm@gmail.com)
syrian private university

Bernard Khazem
syrian private university

Research Article

Keywords: bacterial meningitis, complications, children, pediatrics, syria

Posted Date: March 27th, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2739215/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

**Background:** Bacterial meningitis in children is a life-threatening condition, carrying a potentially large proportion of morbidity and mortality. Early reorganization of accurate diagnosis, and correct management are important in regard to avoiding complications and death. Others, such as the type of pathogen, also play an important role.

**Methods:** This retrospective cross-sectional study was conducted after obtaining ethical approval from the IRB, Faculty of Medicine, Syrian Private University. The study included a review of all cases of bacterial meningitis among children attending Damascus Hospital, during the period between the beginning of 2017 and the end of 2022.

**Results:** The number of cases of bacterial meningitis reached 122 patients, 56% of the sample were males, and infants were the most common age group. Crowded housing was found in 73% of patients. The percentage of positive bacterial cultures for CSF was 24.6% of the sample, while the percentage of positive cultures for Haemophilus influenzae, Streptococcus pneumoniae, and Neisseria meningitidis was few.

The incidence of complications was 32% of the sample, where the duration of the fever for more than 10 days was the most common complication, followed by organ failure accompanying trauma, inappropriate ADH secretion syndrome, and intracranial hypertension, respectively. Complications occurred more among females than males, and were also higher among infants than the rest of the age groups, and also higher among those with overcrowded housing. The occurrence of complication was statistically associated with hospital acquisition, hospitalization period, and bacterial type.

The death rate was 4% of the sample, 60% of whom were females. In 80% of the deceased, diagnosis and treatment were delayed for a week, and 80% of them were adult children. It was found statistically that the longer the hospitalization period is associated with a higher risk of death.

**Conclusion:** This study indicates the occurrence of both complications and death in pediatric patients with bacterial meningitis in Damascus Hospital. The disease itself carries a high risk of both morbidity and mortality, but the results of this study identify some factors whose correct control may avoid their occurrence as well as avoid long-term sequel.

Introduction

Bacterial meningitis is an inflammation of the three anatomical layers (meninges) that covers the brain and spinal cord (1). Over 1.2 million cases of meningitis are thought to occur globally each year, with the prevalence and causes varying by geographic region (2). In addition to an increasing economic burden, especially in development countries (3). The risk factors for the development of bacterial meningitis includes Anatomical lesions and adjacent infectious lesions predisposing to meningitis, such as Pneumonia, chronic sinusitis, and otitis media. It is a medical emergency associated with a high mortality
rate and as many as 50% of survivors develop neurological complications, such as Intracranial hypertension, subdural effusions, hydrocephalus, and neurological sequelae (4). Those early mentioned difficulties if left untreated carry high case-fatality rate of up to 30% differs between low- and high-income countries (4). This is the first study in Syria that aimed to determine the prevalence rates of complications caused by bacterial meningitis in children after the neonatal period, determine the factors associated with the occurrence of bacterial meningitis and link them with the complications, determine the death rate due to bacterial meningitis in children, Determine the factors associated with the occurrence of death.

Methods

Study design and participants:

This is a retrospective study composed of all children (from >1 month until 15 years old) who reviewed Damascus hospital between 1/1/2017 and 31/12/2022, and were diagnosed with Bacterial Meningitis.

This study included 122 patients diagnosed with BM. In this research meningitis caused by viral, tuberculous and parasitic meningitis were excluded. In addition, Neonates due to differences in inflammatory response and pathological agents were also excluded.

Variables addressed in this research:

Demographical information (age, sex and house nature), status of wellbeing through pregnancy and childbirth (history of PROM or PPROM, previous presence of genital or urinary mother’s infections, and the need for resuscitation or an incubator), type of any given vaccines before hospitalization period (such as BCG vaccine, Haemophilus influenzae type b vaccine, and Pneumococcal conjugate vaccine), Positive history of antibiotics and corticosteroids before hospitalization, and positive blood culture with identified pathogens. The presence of immunocompromised patients was investigated based on the rolling out diseases through verifying the absolute number of lymphocytes and neutrophils by a proven laboratory analyzes for each patient, the presence of a recurrence of major sepsis two or more times within one year, a proven diagnosis of one of the immunosuppressive disorders or positive history of immunosuppressive medication intake or corticosteroids for two weeks or more. In addition, we have documented the presence of a congenital or acquired anatomical connection between the cerebrospinal fluid and the mucocutaneous site, and have addressed the type of this connection, if any.

A list of complication was documented, Generalized or focal seizures, Nerve paralysis, Intracranial hypertension, Subdural effusion, Subdural abscess, hydrocephalus, coagulation disorders, Organ failure, Syndrome of inappropriate secretion of ADH, Prolonged fever more than 10 days, ataxia, Cerebral or cerebellar herniation, Symmetrical circumferential meridians, and death.

Furthermore, we have looked up for delay in diagnosis, delay in medications application, and hospitalization period. Delay in diagnosis was defined as the period between the first appearance of
symptoms until the diagnosis was confirmed by CSF puncture, and the diagnosis was considered late if it did not occur within less than 48 hours, whereas delay in medications application was defined as the period between the first appearance of symptoms until the application of treatment, and treatment was considered delayed if it did not occur within less than 48 hours.

Statistical Analysis:

The data were analyzed using the SPSS Statistical Package for Social Sciences version 25.0, showing numbers and percentages (for categorical variables), or averages and standard deviations, SD (for continuous variables). The Chi-Square independence test was used to test the independence of qualitative variables, and the T-test was used to assess the relationship between the complication occurrence and other variables. A p-value < 0.05 was adopted as statistical significance.

Results

Sample characteristics:

The number of cases of bacterial meningitis reviewed by Damascus Hospital during the period between 2017 and 2022, and after applying the exclusion criteria for the study, reached 122 patients, the number of males reached 69 patients, with a rate of 56.6%, and females 53 patients, with a rate of 43.4%, where the majority of patients were males. Regarding patients age, the number of infant patients was 44 children, with a rate of 36.1%, the young child was 41 children, with a rate of 33.6%, and those who were older children were 37 children, with a rate of 30.3%. The majority of children lived in a crowded type of housing, 89 children (73%), and the rest lived in a good type of housing, 33 children (27%).

In terms of pregnancy and birth conditions, out of 122 children, the number of children whose age was more than 3 months was 89 (73%), while those whose age was less than 3 months were 33 (27%). Conditions of pregnancy and childbirth in this latter category. Out of 33 children, most of them, 23 (69.7%) hadn't any special conditions of pregnancy and delivery, while six children (4.9%) needed incubators or resuscitation, and only four children (3.3%) whose mothers suffered from genital or urinary infections.

Studying the factors predisposing to the occurrence of bacterial meningitis and its complications:

Most of the children by 104 (85.2%) were previously vaccinated with at least one of the vaccines included in the national vaccination program, and only 18 children by 14.8% were not vaccinated with any specific vaccine.
101 children, 82.8%, were previously vaccinated with tuberculosis vaccine, and 98 children, 80.3%, were previously vaccinated with Haemophilus influenzae type b vaccine. No child was vaccinated with pneumococcal or Neisseria meningitidis vaccine. Four children, with a rate of 3.3%, were suffering from drug-induced immunodeficiency, and only one child (0.8%) was suffering from pathological immunodeficiency diagnosed with Leukocyte Adhesion Deficiency (LAD). Sixteen children with a rate of (13.1%) had anatomical connection between the cerebrospinal fluid and the mucocutaneous site, and the cerebral peritoneal shunt constituted the largest percentage of 7 children with a rate of (5.7%), followed by a skull fracture in 5 children with a rate of (4.1%), and finally meningocele in 4 children with a rate of (3.3%). In the study of the presence of a contiguous infectious disease, 36 patients (29.5%) suffered from at least one infectious disease as follows: 21 children (17.2%) had pneumonia, otitis media (9 patients) (7.4%), and chronic sinusitis (7 patients) (5.7%), mastoiditis patients with a rate of (1.6%). Out of 122 children, only 11 (9%) had acquired the disease during their hospital stay for another reason. 75 children (61.5%) received some type of antibiotic, and only 4 patients (3.3%) received corticosteroids.

In regard to the delay in diagnosis, only 13 children (10.7%) did not have delay in diagnosis, while for most children the diagnosis delayed for at least 48 hours as follows: 51 children (41.8%) were diagnosed with a delay of 48 hours, and 48 children with a rate of 39.3% had a delay in diagnosis for a week, while 10 children with a rate of 8.2% had a delay in diagnosis for more than a week.

Regarding the delay in starting treatment (Chart 6), only 13 children (10.7%) were not delayed in providing treatment, while most children were delayed at least for 48 hours as follows: 51 children (41.8%) were delayed in providing treatment for 48 hours and 39 children, 32%, were delayed for one week, while 19 children, 15.6%, delayed providing treatment for more than a week.

Almost half of the patients, 63 patients (51.6%) had a hospitalization period of 10 days, while 35 children, with a rate of 28.7%, had a hospitalization period of 14 days. The number of children who stayed in the hospital for 15-21 days was 24 children, with a rate of 19.7%.

*Studying the relationship between age and the duration of hospitalization:*

Most of the children whose hospitalization period reached 10 days were from the young child category with a percentage of 41.3%, followed by the infant category with a percentage of 30.2%, then the old child with a percentage of 28.6%.

Most of the children, whose hospitalization period reached 14 days, were from the category of infants with a rate of 42.9%, followed by the category of the old child with a rate of 40%, then the small child with a rate of 17.1%.
Most of the children, whose hospitalization period reached 15-21 days, were from the category of infants with a rate of 41.7% - this is explained by the fact that the category of infants is the most group of patients who had complications - followed by the two categories of the young child and the old child with a rate of 37.5% and 20.8%, respectively.

Regarding the bacterial type, 75.4% of the cultures were negative, while the rest were distributed as follows: Neisseria meningitidis for 0.8%, Streptococcus pneumoniae for 0.8%, Staphylococcus aureus negative coagulase with a rate of 7.4%, Staphylococcus aureus with a rate of 5.7%, Enterobacteriaceae 5.7%, Pseudomonas aeruginosa with a rate of 3.3%, and Beta-hemolytic streptococcus for 0.8%. no positive culture with Haemophilus influenzae type b were identified.

**Studying the correlation between the bacterial type and those who were infected during their stay in the hospital for other manner:**

Bacterial meningitis occurred in 11 children during their stay in the hospital for another reason, 7 of them could not identify the bacterial type. 3 children, 75% out of four infected with Pseudomonas aeruginosa, contracted the disease during their stay in the hospital, and only one child, 14.3%, out of 7 children infected with Enterobacter, had contracted meningitis during their stay in the hospital.

There was a statistically significant difference (P = 0.001). This indicates that infection with meningitis during hospital stay leads to infection with a certain bacterial type, which is mostly Pseudomonas aeruginosa in our findings.

**Studying the correlation of the bacterial type with the existence of an anatomical connection between the cerebrospinal fluid and a mucocutaneous site and recurrence:**

Approximately 19% of the children with bacterial meningitis who had an anatomical connection between the cerebrospinal fluid and the mucocutaneous site had coagulase-negative Staphylococcus, followed by Enterobacter at 12.5%. The distribution of infection by bacterial type for those with encephalomyelitis was as follows: 57.1% undefined, 14.3% with Enterobacter, 14.3% with Pseudomonas, and 14.3% with coagulase-negative Staphylococcus. The distribution of infection by bacterial type for those with a skull fracture was: 80% undefined, and 20% Enterobacter. While for those with meningocele, 50% had coagulase-negative staphylococci, and 25% had S. aureus, while 25% were undefined.

The recurrence of meningitis was studied in those who had some type of anatomical connection (N = 16), the recurrence rate was (37.5%) 6 patients, and the results were as follows: The presence of a skull fracture: the disease recurred in two children (40%) out of 5 children, Presence of Peritoneal cerebral shunt: the disease recurred in 3 children, at a rate of (42.9%) out of 7 children, Presence of meningocele: the disease recurred in one child by (25%) out of four children.

**Studying the incidence of complications and death in the studied sample:**
At least one complication occurred in 39 children, representing 32% of the entire studied sample, and most of the sample, 83 children, representing 68%, did not have any kind of complication. No cases of both symmetrical peripheral death and cerebral or cerebellar herniation were recorded.

The complication of prolonged fever for more than 10 days was the most common complication in the studied sample, as it constituted 9.8% of the sample. It was followed by organ failure associated with trauma, at 8.2%, and intracranial hypertension, as well as the syndrome of inappropriate ADH secretion, at 7.4% each. While ataxia and subdural empyema were the least common with 0.8% each of the sample. death occurred among five children, with a rate of 4.1%.

Studying the correlation between the occurrence of complication and the characteristics of the studied sample:

Of the children who had at least one complication (N=39), the percentage of females was higher than that of males, with 18 (46.2%) males and 21 (53.8%) females. As for age, the most complicated children were 17 infants (43.6%), and the number of young and old complicated children was equal to 11 children with a rate of 28.2% each. As for the type of housing, the majority of complicated children lived in crowded housing, with a rate of 71.8%.

Studying the correlation between the occurrence of complications and the conditions of pregnancy and childbirth:

The relationship between the occurrence of at least one complication and the conditions of pregnancy and delivery was studied in children whose age was less than three months, and the percentage of those who had a complication was 36.4% of them. 8 children, at a rate of 34.8%, who had normal conditions of pregnancy and childbirth, had a complication out of 15 children whose circumstances were similar, and half of the children who needed incubators or resuscitation had at least one complication, and only one child complicated at a rate of 25% out of four children whom Their mothers had genital or urinary infections.

Studying the correlation between the occurrence of complications and predisposing factors:

Of the 104 children who received at least one vaccine, only 31 children (29.8%) had a complication, but most of them 73 children (70.2%) did not have any complication. While among the 18 children who did not receive any kind of vaccination, 8 of them had at least one complication with a rate of 44.4%. The incidence of at least one complication among those who had anatomic lesions was 50% of them, compared to 29.2% of patients who did not have anatomic lesions.
Most of the patients who had drug-immunosuppression immunity had a complication rate of 75% of them, while patients without any form of immunosuppression had a complication rate of 30.8% of them. The percentage of patients who had a complication of children with an adjacent infectious disease was 41.7% of them, while the percentage was 27.9% for those who did not suffer from any adjacent infectious disease. 2.8% of patients with a complication had chronic sinusitis with a statistically significant difference ($P = 0.01$). This indicates that chronic sinusitis is more likely to develop at least one complication in the sample studied, and approximately 18% of patients who had a complication had pneumonia, 10% of patients had otitis media, and 5% of patients had mastoiditis. The results showed that 63.6% of children who acquired their illness in the hospital had a complication, with a statistically significant difference ($P = 0.01$), indicating that hospital acquisition is more dangerous for developing at least one complication in the studied sample.

Among the children who had a complication, approximately 72% of them were diagnosed with a delay of 48 hours and up to a week, 10.3% of them were diagnosed with a delay of more than a week and only 17.9% were not diagnosed with a delay.

Among the children who also had a complication, approximately 70% of them had a delay in starting treatment for them by 48 hours and up to a week, 12.8% of them had a delay in starting treatment for them for more than a week and only 17.9% starting treatment did not delay for them.

43.6% of the patients who had a complication had a hospitalization period of 15-21 days, followed by those with a duration of 14 days at a rate of 30.8%, followed by 25% whose hospitalization was 10 days, with a statistically significant difference ($P = 0.000$), which indicates increasing the duration of hospitalization increased the risk of happening at least one complication. Finally, most of the patients who had a complication of 24 children (61.5%) had taken antibiotics, and 3 out of 4 who had taken corticosteroids had a complication.

**Studying the correlation between the occurrence of seizures and the presence of thromboembolic complications:**

28.6% of the patients who had a complication of generalized seizures had one of the thrombotic complications (DIC), with a statistically significant difference ($P = 0.04$), and half of the patients with focal seizures also had They suffer from one of the thrombotic complications, with a statistically significant difference ($P = 0.002$). This indicates that the presence of thromboembolic complications is associated with the occurrence of both types of seizures.

**Studying the correlation between the occurrence of death and other variables:**
60% of the patients who died were female, and 40% were male. Most of the children who died were old children, 4 (80%), and only one child was from the category of young children, while death did not occur among infants. 4 out of 5 children who died had a diagnosis delay of a week. 4 out of 5 children who died had treatment delayed for more than a week. 3 children out of 5 who died had a hospitalization period of 15-21 days, with a statistically significant difference (P = 0.05), meaning that the length of hospitalization reflects the presence of complications and this was associated with a higher risk of death, the other two children reached the hospitalization period 10 days.

**Discussion**

Despite the continuous progress in the field of antibiotics, the burden of complications and death is still high for bacterial meningitis in children, as this is related to several factors. Bacterial meningitis is a major challenge, especially in low- and middle-income countries (5). This retrospective study aims to investigate the prevalence of complications caused by bacterial meningitis and its associated factors in children and infants’ post-neonatal period, admitted to Damascus Hospital. The number of cases of bacterial meningitis hospitalized from 2017-2022, whose ages ranged from one month to fifteen years, was 122 patients.

In this study, the number of male patients is greater and their percentage is 56.6% of the studied sample, compared to a study that was conducted in the University Children's Hospital in Damascus, the percentage of males was 61.8% (6). In this study, the category of infants was the most infected with the disease by (36.1%), and compared to a study issued by the World Health Organization, the category of infants was also the most affected by the disease (8), as well as in a study in the University Children's Hospital in Damascus (6).

The percentage of Haemophilus influenzae type b vaccination was 80.3% of the studied sample, compared to Italy at a rate of 93% (9), and Afghanistan at a rate of 24% (8). Children included in this study are not vaccinated against both Streptococcus pneumoniae and meningococcus, And the reason may be not including it in the national vaccination program. The percentage of positive bacterial cultures for CSF in this study was 24.6%, which is lower than the percentage mentioned in a study issued by the World Health Organization, where it was 30% (8), as well as less than a study conducted in the Children's Hospital in Damascus, where it reached 38.2% (6).

The percentage of common germs that usually cause bacterial meningitis (Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae) was the lowest in this study, compared to the WHO study (8). This is explained by the inclusion of Haemophilus influenzae vaccine within the national vaccination program, as there were no cases of infection with it in this study, in addition to the absence of a pandemic during the studied period with Neisseria meningitidis, as well as the use of antibiotics, especially penicillin derivatives and cephalosporins, especially ceftriaxone, before establishing the diagnosis. In the case of bacterial meningitis associated with a predisposing factor (anatomical communication between the CSF and the mucocutaneous site), coagulase-negative and aureus
Staphylococcus were the most common in this study. Compared to a study conducted in the United States of America, these germs were also the most common in this group (16). This is explained by the fact that these germs are most present on the skin at the place of anatomical contact.

In this study, the percentage of patients with bacterial meningitis and Immunodeficiency was 4.1% of the sample. By comparison, a study conducted in Texas, USA, indicates that these conditions are not common (10). The high percentage in this study may be explained by the misuse of corticosteroids, especially in patients with asthma. In this study, the incidence of bacterial meningitis due to shunt infection was 5.7% of the studied sample. This percentage agreed with a study conducted at the University of Washington in the United States of America, which indicated that this percentage amounted to 5-15% of cases (11). This is explained by ascending shunt infection from the peritoneum.

Among the most important causes of meningitis recurrence in this study: peritoneal cerebral shunt in 42.9% of them, skull fracture in 40% of them, and meningocele in 25% of them. Compared to a study conducted in China, the recurrence rate for those with a skull fracture was 20%, and for those with meningocele, it was 11% (12). The high rates in this study may explain the difficulty in managing some of the previous predisposing lesions. Among the most important neighboring infectious diseases predisposing to bacterial meningitis in this study: pneumonia, which is the most common by 17%, while otitis media was present in 7.5% of the studied sample. Compared to other studies conducted in low-income countries, the rate of pneumonia was 5%, and the rate of otitis media was 12%. (13,14). The high rate of pneumonia may be explained by the delay in its diagnosis and treatment, as it develops into septicemia and bacterial meningitis. The percentage of patients who had one or more complications in this study was 32% of the sample, which is higher compared to a study conducted in the Children's Hospital in Damascus, where it reached 14.5% (6).

Prolonged Fever more than 10 days was the most common complication among patients with a rate of approximately 10%, which is lower compared to another study conducted in Kuwait, where it reached 12% (17). This is probably explained by the occurrence of: viral infection overlapping with the case, oral infection, secondary bacteria, or drug reaction.

The percentage of seizures (generalized and focal) was 9% of the studied sample, which is lower compared to a study that took place in India, where it was 15% (18). This is explained by the occurrence of infarctions or electrolyte disturbances.

The percentage of thrombosis in the venous sinuses of the dura was 6.6% of the studied sample, which is higher than another Dutch study, where it was 1% (19).

The percentage of disseminated intravascular thrombosis (DIC) was 4.1% of the studied sample. According to the American Academy of Pediatrics, the incidence of this complication in the course of
individual diseases is still unknown, but this complication occurs in 1% of the recovered patients (20). The high incidence of DIC and Dural venous sinus thrombosis is explained by the poor condition of some patients upon admission to hospital in this study. The incidence of subdural effusion and subdural empyema was 2.4% of the studied sample. This is lower than Canadian study, where the percentage was 20-30% (15). It is also less compared to another study in China, which amounted to 22% of the sample (21). The low percentage of Dural effusion in this study explains that the cases included in this study are symptomatic, while 85%-90% of cases are asymptomatic. The incidence of hydrocephalus in this study was approximately 5% of the studied sample. It is close to what a Canadian study indicates, as the percentage reached 7%. (15).

In this study, complications were more common among infants, with a rate of 43.6%, and compared to a study conducted in Canada, it indicated that complications were more common among infants, with a rate of 71% (15). This is explained by the fact that the lack of immunity to specific pathogens, associated with young age, is considered as the greatest risk factor for the occurrence of meningitis. Most of the patients who had a complication in this study had a diagnosis or treatment delay of more than 48 hours. In comparison, a study in Canada indicated that delays in both establishing an accurate diagnosis and providing treatment increased the risk of complications (15).

Timely diagnosis and prompt antibiotic and supportive treatment can reduce the death rate from bacterial meningitis. The death rate in this study was 4% of the sample, and this percentage was in agreement with a study issued by the World Health Organization (8), which is much lower compared to a study conducted in Afghanistan, where the death rate was 21% (10), and also less than a study conducted in the children's hospital in Damascus, where the rate was 21.8% (6), but higher than a study conducted in China, where it reached 2% (21).

**Conclusion**

This study studies the complications of bacterial meningitis in Damascus Hospital. This study indicates the occurrence of both complications and death in pediatric patients with bacterial meningitis in Damascus Hospital.

The results of this study identify the factors whose correct control may lead to avoid complications, morbidity and mortality from bacterial meningitis.

This study emphasizes the importance of early identification of the clinical condition, accurate diagnosis and early and correct management.

This study recommends educating the parents about the risks of discharging the patient from the hospital on their responsibility before completing his treatment and the accompanying increase in the
incidence of complications, sequels and mortality, as some of them were readmitted to Damascus Hospital after their condition worsened and they had complications.

This study recommends the inclusion of bacterial meningitis in the surveillance and early warning program of the Ministry of Health.

This study was conducted in Damascus Hospital (Al-Mujtahid Hospital), and it is recommended to conduct more comprehensive studies in other health centers as well as in all governorates.

**Declarations**

**Ethical approval:**

Ethical approval was obtained from the Institutional Review Board (IRB), Faculty of Medicine, Syrian Private University.

**Funding statement:**

No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

**Availability of supporting data:**

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

**Competing interests:**

The authors declare that they have no competing interests.

**Acknowledgments:**

Not applicable.

**References**


