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Research Article
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Effect of malnutrition on immediate outcome of childhood bacterial meningitis: a hospital based prospective cohort study in Bangladesh

Abstract

Acute bacterial meningitis is an important serious illness worldwide and causing mortality and morbidity in children. In developed countries, only 5% of patients die and 15-20% develop sequel whereas in underdeveloped countries 12-50% of patients die and 25-50% of patients develop sequel. Malnutrition can make a person more susceptible to infection, and infection also contributes to malnutrition, which causes a vicious cycle. A hospital based prospective cohort study was conducted in the Pediatrics department of Mymensingh Medical College & Hospital from February 2012 to February 2013 to compare immediate outcome of bacterial meningitis: in malnourished and well nourished children. Thirty (30) cases of well-nourished and 30 malnourished were enrolled by using purposive sampling. Fever, convulsion, bulged fontanel, abnormal behavior, headache and respiratory symptoms were presenting complaints in both groups and convulsion was significantly more in malnourished group. In Malnourished group, GCS on admission was <13 in majority whereas among well-nourished group it was 13-15. CSF findings were similar. Most of the exposed children were anaemic. Total 12(20%) children died, 14(23%) developed major sequel, 10(17%) patients developed minor sequel. Relative risk of death was 5 fold followed by major sequel 6 fold and minor sequel 4 fold in malnourished group. Hospital stay was more in malnourished group. This study reveals that acute bacterial meningitis occurred in all ages from 1 to 12years child of both sexes and more in under five age group and in males. Fever, convulsion and sign of meningeal irritation were prominent clinical features. This study concludes that death, major and minor neurological sequel were more common in malnourished children and young age, male sex, anaemia, weight for age Z score <-2SD/ BMI <3rd percentile, GCS< 13 were the bad prognostic factors.

Keywords: meningitis, malnourished, immediate outcome

Volume 9 Issue 2 - 2019

Md Maniruzzaman,[1] Faroque Md Mohsin,[2] Maherun Nesa,[3] Anindita Chakroborty,[4] Sanjana Zaman,[5] Shimaa Hassan Sayed El Hadidy,[6] Ahmed Murtaza,[7] Mohammad Abdul Khaleque[7]

[1]Department of Pediatrics, Mymenshingh Medical College Hospital, Bangladesh
[2]Master of Public Health, North South University, Bangladesh
[3]MS Student, Sheikh Hasina National Institute of Burn & Plastic Surgery, Bangladesh
[4]PhD Research Fellow, University of Western Australia, Australia
[5]Department of Public Health, North South University, Bangladesh
[6]Coordinator for the Foreign Health Affairs, Egyptian Ministry of Health and Population, Egypt
[7]Pediatric Hemato-oncology, Mymenshingh Medical College Hospital, Bangladesh

Correspondence: Md Maniruzzaman, Assistant Registrar, Department of Pediatrics, Mymenshingh Medical College Hospital, Bangladesh, Email bjd18@gmail.com

Received: February 22, 2019 | **Published:** March 22, 2019

Introduction

Bacterial meningitis, an inflammation of the meninges affecting the pia, arachnoid, and subarachnoid space that happens in response to bacteria and bacterial products, continues to be an important cause of mortality and morbidity in neonates and children.[1] Bacterial meningitis is an important serious illness worldwide. Prior to the introduction of antibiotics in the 1940s, case fatality rates for epidemic and endemic bacterial meningitis exceeded 70%. Since then, antibiotic use has reduced case fatality rates for meningitis caused by most bacteria to 25% or less, but no further reduction has been documented in the past 20years. Despite advances in vaccine development and chemoprophylaxis, bacterial meningitis remains a major cause of death and long-term neurological disabilities, such as mental retardation, convulsions and hydrocephalus. These are best prevented by early diagnosis and appropriate treatment of the disease.[2] It has been estimated that 1-2million cases of acute bacterial meningitis occurs annually in the globe.[3] The overall incidence of acute bacterial meningitis in developed countries is 2-3/100,000 with peaks of incidence in infants and adolescents.[4] The incidence of bacterial meningitis among children of developing countries is 10-20/100,000, a figure more than ten times higher than in Western Europe and the United States.[5] In industrialized countries, only 5% of patients with childhood bacterial meningitis die, and 15%–20% develop sequelae; in non-industrialized countries, however, 12%–50% of patients die, and 25%–50% of patients experience sequelae.[6] "Severe neurologic sequelae" (blindness, quadriplegia, or paresis, hydrocephalus needing a shunt, or severe psychomotor retardation) were found in 10% patients, and "any neurologic sequelae" (besides severe sequelae, hemiparesis, monoparesis, moderate psychomotor retardation, or ataxia) in 32% patients"[7] Malnutrition can make a person more susceptible to infection, and infection also contributes to malnutrition, which causes a vicious cycle.[8] Protein Energy malnutrition significantly increases morbidity and mortality from bacterial meningitis in childhood although the mechanisms for this are not clear. The high frequency of bacterial diarrhoea in developing countries may further contribute to the relatively high frequency of Gram-negative bacterial meningitis of enteric origin in infancy beyond the newborn period.[9]

Material and methods

This was a prospective cohort study conducted in Department of Pediatrics, Mymensingh Medical College Hospital, Bangladesh from February 2012 to February 2013. Data were collected from the patients who were diagnosed as a case of acute bacterial meningitis, 30 cases with malnutrition and 30 cases without malnutrition in the Department of pediatrics, Mymensingh Medical College Hospital through a pre-structured questionnaire. Sampling was done by purposive sampling. Due to shortage of time and limited patients availability 30 exposed

(to malnutrition) and 30 unexposed (to malnutrition) was taken.

For exposed cohort

Children aged 1-12 years of either sex with acute bacterial meningitis having malnutrition.

For unexposed cohort

Children aged 1-12years of either sex with acute bacterial meningitis having no malnutrition.

Exclusion criteria

Severe dehydration, Hypoglycaemia, Shock, Suspected TBM, Children with CP

Two groups of cohort were selected on the basis of malnutrition. Exposed group was selected having malnutrition and unexposed having no malnutrition and both group poses common criteria as having acute bacterial meningitis of children of 1 to 12years

Outcome variables: patient related variables

i. Age
ii. Sex
iii. Nutritional status
iv. Symptoms at presentation
v. Signs at presentation
vi. GCS at presentation
vii. CSF findings
viii. Average hospital stay

Complication related variables

i. Major neurological sequel
ii. Minor neurological sequel
iii. Death

Procedure

i. Selection of the cases exposed and unexposed to malnutrition was done by applying inclusion and exclusion criteria
ii. After proper counseling, an informed written consent was taken from the guardian of both groups.
iii. Physical examination was done meticulously after taking a detailed history
iv. After enrolling in the study blood sample were collected for RBS and CSF were collected within 12hours of admission for Physical, biochemical, and cytological study
v. Anthropometry was done (on admission day) and plotted on CDC growth chart to see weight for age Z- score for under 5years and BMI for above 5years children
vi. Patients were observed daily throughout hospital stay and repeated examination was done.
vii. Physical examination was done to detect quadriplegia/ quadriparesis, hemiparesis, monoparesis, ataxia, sensory impairement and behaviourial disturbance
viii. Visual acuity, colour vision and direct ophthalmoscopic examination was done to detect visual impairement/blindness
ix. OFC was serially measured and recorded and USG of the brain was done in cases where fontanelae were open to detect hydrocephalus
x. For mild motor delay (fine motor delay, gross motor delay) developmental screening was done
xi. In case of death it was confirmed by physical examination and recorded
xii. All necessary information were recorded in pre-designed structured cases record form

RBS was done to exclude hypoglycaemia and within 12hours of admission CSF was collected for physical, biochemical and cytological study and complete blood count was done in every patient.

Ethical measures

Permission was taken for this study from the Ethical Committee of Mymensingh Medical College Hospital, Mymensingh, Bangladesh. Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, all parents/attendants were informed verbally about the study design, the purpose of the study, and their right to withdraw themselves from the project at any time, for any reason, what so ever. Written consent was obtained from each parents/ attendants. All precautions were taken to protect the anonymity of the participating subjects.

Quality control measures

Investigator himself was vigilant on every aspect of the study starting from case selection, data sheet filling up, CSF and blood sample collection, maintenance of all records, data checking, data entry, analysis and report writing. He personally examined each and every case and was constantly guided by the guide.

Data analysis

The information's which were recorded with acute bacterial meningitis were analyzed to find out the association of nutritional status with mortality and morbidity. All data were entered, checked, rechecked and scrutinized by the principal investigator for following standard procedure and analyzed by SPSS-20 software Programme. Categorical variables were reported as percentage. Correlation was carried out using the Two Sample Z Test and Relative Risk were calculated through determining the association of different variables. After sorting & processing data check list & data coding were made prior analysis to get appropriate outcome. For all analytical tests, the level of significance was set at 95% and $p < 0.05$ was considered significant.

Results and discussion

The present study intended to compare relative risk of death, major neurologiclal sequel and minor neurological sequel in children having malnutrition in association with Acute Bacterial Meningitis in between 30 malnourished and 30 well nourished children of 1 to 12years of either sex admitted in pediatrics department of Mymensingh Medical College & Hospital. This study was done in a cohort of 60 children of 1-12years of either sex admitted with acute bacterial meningitis in the Department of Pediatrics Mymensingh Medical College Hospital over one year period. These children were subdivided in 1-2years,

3-5years and 6-12years groups. In this study 26(43.33%) child were in 1-2years age group, 08(33.33%) child were in 3-5years age group and 26(43.33%) child were in 6-12years age group. This study shows that Meningitis occur more in under five age group children. Ansari I et al. and Swarnali Joardar et al. found similar result.[10,11] Those children were divided into two groups on the basis of presence or absence of malnutrition. Exposed group: 30 children having malnutrition and unexposed group: 30 well-nourished children (Table 1-13).

Table 1 Age distribution of meningitis in exposed and unexposed group

Age (in years)	RR(Relative risk)	Exposed (n=30)/%	Unexposed (n=30) /%	Total (n=60)/%
1-2	1.16	14(46.66)	12(40)	26(43.33)
3-5	1.00	04(13.33)	04(13.33)	08(13.33)
6-12	0.85	12(40)	14(46.66)	26(43.33)

Table 2 Weight for age Z-score in under 5 age group and BMI in 5years and above in exposed group

Weight for age Z-score/BMI	Total (n=30)/%
<-1SD	05(16)
<-2SD	13(43)
BMI <5th percentile>3rd percentile	4(13.33)
BMI <3rd percentile	8(26.33)

Table 3 Gender distribution of meningitis in exposed and unexposed group

Sex	RR(Relative risk)	Exposed (n1=30)/%	Unexposed (n2=30) /%	Total (n=60)/%
Male	1.06	17(56.66)	16(53.33)	33(55)
Female	0.85	13(43.33)	14(46.66)	27(45)

Table 4 GCS at admission in exposed and unexposed group

Modified GCS (Glasgow Coma Score)	RR(Relative risk)	Exposed (n1=30)/%	Unexposed (n2=30) /%	Total (n=60)/%
15-13	1.06	13(43.33)	24(80)	37(61.66)
<13	0.85	17(56.66)	06(20)	23(38.33)

Table 5 Signs and symptoms at admission in exposed and unexposed group

Symptoms	RR(Relative risk)	Exposed (n1=30)/%	Unexposed (n2=30)/%	Total (n=60)/%
Fever	1.03	30(100)	29(96.66)	59(98.33)
Convulsion	2.07	29(96.66)	14(46.66)	43(71.66)
Bulged Fontanele	1.20	12(40)	10(33.33)	22(36.66)
Sign of meningeal irritation	0.90	18(60)	20(66.66)	38(63.33)
Vomiting	1.33	16(53.33)	12(40)	28(46.66)
Abnormal behavior	1.60	08(26.66)	05(16.66)	13(21.66)
Headache	0.72	13(43.33)	18(60)	31(51.66)
Respiratory symptoms	1.15	15(50)	13(43.33)	28(46.66)

Table 6 Hb% in both exposed and unexposed group

Hb% gm/dl	RR(Relative risk)	Exposed (n1=30)/%	Unexposed (n2=30)/%	Total (n=60)/%
<7	18	18(60)	01(03)	19(31.66)
>7<10	2.5	10(33.33)	04(13.33)	14(23.33)
>10	0.08	02(06)	25(83.33)	27(45)

Table 7 Immediate outcome of acute bacterial meningitis in exposed and unexposed group

VARIBLES	Exposed (n1=30)/%	Unexposed (n2=30)/%	Total n=60/%
Death	10(33.33)	02(6.66)	12(20)
Major neurological sequelae:	12(40)	02(6.66)	14(23.33)
Hydrocephalus	08(26.66)	01(3.33)	09(15)
Quadriplegia/Quadriparesis,	3(10)	1(3.33)	04(6.66)
Blindness	1(3.33)	0(00)	01(1.66)

Citation: Maniruzzaman M, Mohsin FM, Nesa M, et al. Effect of malnutrition on immediate outcome of childhood bacterial meningitis: a hospital based prospective cohort study in Bangladesh. *J Nutr Health Food Eng.* 2019;9(2):42–47. DOI: 10.15406/jnhfe.2019.09.00323

Table Continued...

VARIBLES	Exposed (n1=30)/%	Unexposed (n2=30)/%	Total n=60/%
Minor neurological sequelae :	08(26.66)	02(6.66)	10(16.66)
Hemiparesis.	1(3.33)	01(3.33)	02(3.33)
Monoparesis,	3(10)	1(3.33)	04(6.66)
Mild motor delay	1(3.33)	00(00)	01(1.66)
Ataxia	1(3.33)	0(00)	01(1.66)
Sensory impairement	2(6.66)	0(00)	02(3.33)

Table 8 Immediate outcome in exposed group in relation to weight for Z score and BMI

Weight for age Z-score/BMI	Total no (n=30)/%	Death(n/%)	Major sequel (n/%)	Minor sequel(n/%)
<-1SD	05(16)	01(20)	03(60)	01(20)
<-2SD	13(43)	07(53.50))	05(38.40)	01(07)
BMI <5th percentile>3rd percentile	4(13.33)	01(25)	01(25)	02(50)
<3rd percentile	8(26.33)	01(12.50)	03(37.50)	04(50)

Table 9 Relative risk of death in acute bacterial meningitis in children exposed and unexposed to malnutrition

Exposure	Death		Total
	Positive	Negative	
Positive	10	20	30
Negative	2	28	30
Total	12	48	60

RR =5.0, Z=2.74, p value <0.01

Table 10 Relative risk of major sequel in acute bacterial meningitis in children exposed and unexposed to malnutrition

Exposure	Major Neurological Sequel		Total
	Positive	Negative	
Positive	12	18	30
Negative	2	28	30
Total	14	46	60

RR= 6.0, Z= 3.32, p value <0.001

Table 11 Relative risk of minor sequel in acute bacterial meningitis in children exposed and unexposed to malnutrition

Exposure	Minor Neurological Sequel		Total
	Positive	Negative	
Positive	8	22	30
Negative	2	28	30
Total	10	50	60

RR= 4, Z= 2.15, p value <0.05

Table 12 Average hospital stay in exposed and unexposed group

Variables	Exposed group	Unexposed group
Average hospital stay (in days)	14	10

Table 13 CSF findings in exposed and unexposed group

Variables	Exposed group	Unexposed group
Average cell count(predominant cells)	50-100(neutrophils)	50-100(neutrophils)
Average protein(gm/dl)	50-70	60-80
Average glucose (mg/dl)	20-40	30-40

Malnutrition was defined as having weight for age Z score <-1SD up to 5years of age and BMI <5th percentile in 5years and above child in respect of age and sex. Exposed group was subdivided further in weight for age Z score<-1SD , <-2SD; BMI <5th percentile>3rd percentile and <3rd percentile groups. In this study weight for age Z score was <-1SD in 5(16%) children, <-2SD in 13(43%) children, BMI<5th percentile>3rd percentile in 4(13.33%) children and BMI <3rd percentile in 8(26.33) children. In this study 33 children were male and 27 children were female. In exposed group male:female ratio is 17:13 whereas in unexposed group male:female ratio is 16:14. In both group male is predominate. This study shows that meningitis occur more in males in both group. Other studies found similar result.[12–14] In this study modified Glasgow coma score was done in every patient and GCS <15>13 was found in 13(43.33%) exposed children, in 24(80%) unexposed children and in total 37(61.66%) children. Whereas GCS <13 was found in 17(56.66%) exposed children, 06(20%) unexposed children and in total 23(38.33%) children. This study shows that, GCS on admission is <13 in majority in malnourished group whereas 13 to 15 in well-nourished group. In this study fever, convulsion, bulged fontanel, abnormal behavior, headache and respiratory symptoms were presenting complaints in majority of cases. Fever was present in 30(100%) children of exposed group and 29(96.66%) children in unexposed group.

This study reveals that fever is a prominent symptoms in childhood bacterial meningitis. Conclusion was present in 43(71.66%) children. Out of them 29(96.66%) children in exposed group and 14(46.66%) children in unexposed group. Abnormal behavior was present in 13(21.66%) children and out of them 8(26.66%) in exposed group and 05(16.66%) in unexposed group. Headache was present in 31(51.66%) children and out of them 13(43.33%) in exposed group and 18(60%) in unexposed group. Respiratory symptoms were present in 28(46.66%) children and out of them 15(50%) in exposed group and 13(43.33%) in unexposed group. Bulged fontanel and signs of meningeal irritation were more common. Fontanel was bulged in total 22(36.66%) children and out of them 12(40%) children in exposed group and 10(33.33%) in unexposed group. Signs of meningeal irritation was present in 38(68.33%) children and out of them 18(60%) in exposed group and 20(66.66%) in unexposed group. This study reveals that convulsion is significantly more in malnourished group. Fever, convulsion and sign of meningeal irritation/ bulged fontanel are the most prominent clinical features. *Elizabeth R. Reyes, M.D* found similar result.[15] In this study Haemoglobin level was <7 gm/dl in 19(31.66%) children and of them 18(60%) in exposed group and 01(3.33%) in unexposed group. Haemoglobin level was 7-10gm/dl in 14(23.33%) children and out of them 10(33.33%) in exposed group and 04(13.33%) in unexposed group and was >10gm/dl in 27(45%) children of them 02(6.66%) in exposed group and 25(83.33%) in unexposed group.

This study reveals that most of the exposed children has Haemoglobin level <10gm/dl. Other study found similar results. In this study immediate outcome of acute bacterial meningitis are death, major neurological sequel (Hydrocephalus, quadriplegia/ quadriparesis, blindness) and minor neurological sequel (hemiparesis, monoparesis, mild motor delay, ataxia and sensory impairment). In this study total 12(20%) patient children died, 9(15%) children developed hydrocephalus, 04(6.66%) children developed quadriplegia, 01(1.66%) children developed blindness, 02(3.33%) children developed hemiparesis, 04(6.66%) children developed monoparesis, 01(1.66%) children developed mild motor delay, 01(1.66%) children developed ataxia and 02(3.33%) children developed sensory impairment. Other studies found similar results.[5,7] In this study in malnourished group 05(16%) children had weight for age Z score <-1SD; of them 01(20%) children died, 03(60%) children developed major sequel and 01(20%) children developed minor sequel. Whereas 13(43%) children had weight for age Z score <-2SD; of them 07(53.50%) child died, 05(38.44%) child developed major neurological sequel and 01(07%) child developed minor sequel. In this study 04(13.33%) child had BMI <5th percentile but > 3rd percentile; of them 01(25%) child died, 01(25%) child developed major sequel and 02(50%) child developed minor sequel. Whereas 08(26.33%) child had BMI <3rd percentile; of them 01(12.50%) child died, 03(37.50%) child developed major neurological sequel and 04(50%) child developed minor sequel. In this study overall death rate is 20% in meningitis, but in malnourished child death rate is 33.33% whereas in well-nourished child death rate is only 6.66%. In industrialized countries, only 5% of patients with childhood bacterial meningitis die, in non-industrialized countries, however, 12%–50% of patients die.[6] This indicates that high death rate in acute bacterial meningitis in children in non-industrial countries may be due to high burden of childhood malnutrition. In this study, Relative Risk of death is 5 fold in malnourished children suffering from acute bacterial meningitis. Other studies found similar results.[7,9,15] But *Rosen et al.* and *Mulla et al.* did not found any association of increased relative risk of death with malnutrition.[6,7] This study reveals that rate of major sequel is 23.33%. In industrialized countries, 15%–20% develop sequelae, whereas in non-industrialized countries, 25%–50% of patients experience sequelae.[6] In this study, Relative Risk of Major sequel is 6 fold in malnourished group. Other studies found similar results.[7,9,15] In this study rate of minor sequel is 16.66%. In this study, Relative Risk of Minor sequel is 4 fold in malnourished children suffering from acute bacterial meningitis. Other studies found similar results.[7,9,15] This study reveals that cell count, protein and glucose in CSF of both exposed and unexposed group are similar. This study reveals that hospital stay is more in malnourished children suffering from acute bacterial meningitis. Findings of this study agree with previous data showing that malnutrition increases mortality of bacterial meningitis.[9]

Conclusion

Results of this study concludes that acute bacterial meningitis occur in all ages from 1 to 12years child of both sexes and more in under five age group and in the males. Fever, convulsion and sign of meningeal irritation/ bulged fontanel are the most prominent clinical features. Death, major neurological sequel (Hydrocephalus, quadriplegia/quadriparesis, blindness) and minor neurological sequel (hemiparesis, monoparesis, mild motor delay, ataxia and sensory impairment) are more common in malnourished children. Young age, male sex, anaemia, weight for age Z score <-2SD/ BMI <3rd percentile, GCS< 13 are the bad prognostic factors.

Acknowledgments

None.

Conflicts of interest

The authors declare that there is no conflict of interest.

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Citation: Maniruzzaman M, Mohsin FM, Nesa M, et al. Effect of malnutrition on immediate outcome of childhood bacterial meningitis: a hospital based prospective cohort study in Bangladesh. *J Nutr Health Food Eng.* 2019;9(2):42–47. DOI: 10.15406/jnhfe.2019.09.00323