e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.12.160

International Journal of Pharmaceutical Quality Assurance 2025; 16(12); 1028-1034

Original Research Article

A Hospital-Based Retrospective Study on Clinical Profile and Outcomes of Neonatal Sepsis in a Tertiary Care Center

Md. Neyazuddin[1], Abdur Rehman[2], Gopal Shankar Sahni[3]

[1]Senior Resident, Department of Paediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

[2]SMO, Department of Paediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

[3]Professor and HOD, Department of Paediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India

Received: 05-10-2025 / Revised: 23-11-2025 / Accepted: 29-12-2025

Corresponding Author: Dr. Abdur Rehman

Conflict of interest: Nil

Abstract:

Background: Neonatal sepsis is a major cause of morbidity and mortality, particularly in developing countries, due to immature immunity and delayed diagnosis.

Aim: To evaluate the clinical profile, risk factors, and outcomes of neonatal sepsis in a tertiary care center.

Methodology: This hospital-based retrospective observational study was conducted in the Department of Paediatrics, Sri Krishna Medical College and Hospital, Bihar, over one year. A total of 80 neonates (0–28 days) diagnosed with sepsis were included. Data were collected from medical records and analyzed using SPSS version 27.0.

Results: Most neonates were admitted within the first week (57.5%), with male predominance (60%) and a high proportion of low birth weight (55%). Common maternal risk factors included preterm birth (37.5%) and maternal fever (27.5%). Clinical features were predominantly nonspecific, with poor feeding (62.5%) and lethargy (52.5%) being most frequent. CRP positivity (70%) and leukocyte abnormalities (56.3%) were more common than culture positivity (40%). Overall mortality was 22.5%, significantly higher in low-birth-weight neonates (31.8%).

Conclusion: Neonatal sepsis remains a critical health issue with high mortality, especially among low-birth-weight infants, highlighting the need for early diagnosis and effective management.

Keywords: Neonatal sepsis, low birth weight, clinical profile, mortality, CRP, tertiary care.

Introduction

Neonatal sepsis continues to be a significant contributing factor for morbidity and mortality across the world today, posing a significant challenge in neonatal care [1]. Sepsis is defined as life-threatening organ dysfunction due to a dysregulated host response to infection. This highlights the complex interaction between invading pathogens and an immature neonatal immune response that leads to rapid clinical deterioration if not recognized and treated early. Neonates are the most vulnerable population of any age group with underdeveloped immune defenses, poor protective ability to localize infection and limited physiological reserves. Consequently, neonatal sepsis has become a significant public health issue and one of the major causes of mortality among newborn babies.

Sepsis is one of the top three causes of neonatal death globally, with neonates contributing significantly to total under-five mortality. Infection-related mortality remains unacceptably high despite improvements to neonatal intensive care, and is particularly severe in low- and middle-resource settings. Out of the estimated three lakh global neonatal sepsis cases annually, India has the most clinical sepsis estimates. The high burden can be associated with various factors such as poor access to quality antenatal care, low institutional delivery rates, congestion in health care settings and poor infection prevention practices. In addition to these mechanisms, other factors such as socio-economic determinants, maternal health status, and environmental factors significantly contribute to the incidence and outcomes of neonatal infections in resource-limited settings [2].

The case fatality rate of neonatal sepsis in India alone still remains unacceptably high (25% to 65%) [3]. This great discrepancy is attributable to variance in health care infrastructure, early diagnosis, timely management, and availability of advanced neonatal care facilities regionally. Furthermore, the clinical course of typhoid fever is also complicated by factors such as delayed recognition of symptoms,

inappropriate or empirical usage of antibiotics and the emergence of antibiotic-resistant multidrug organisms. Neonatal sepsis is a clinical syndrome defined by signs and symptoms of infection1 in the first 28 days of life. The clinical presentation is frequently nonspecific (poor feeding, lethargy, temperature instability, respiratory distress and hemodynamic instability), which makes early diagnosis particularly difficult.

Neonatal sepsis is divided according to the timing of onset into early onset sepsis (EOS) and late onset sepsis (LOS). Early onset sepsis occurs during the first 72 hours of life and is typically caused by vertical transmission (environmental pathogens) from mother, either transplacental or passage through the birth canal. Common risk factors for EOS include prolonged rupture of membranes, maternal fever, chorioamnionitis, and prematurity. Late onset sepsis on the other hand occurs 72 hours after birth and is mostly acquired from the postnatal environment, be it in a hospital setting or community. LOS is often linked to invasive procedures, extended duration of hospitalization, indwelling devices and contact with tainted equipment or staff. Clinically, this distinction between EOS and LOS is important because it informs empirical antibiotic therapy and preventive strategies along with infection control measures [4].

Tremendous work has been conducted on defining the epidemiology, risks, and microbes associated with neonatal sepsis over the years [5]. A large number of causative organisms have been identified Gram-positive bacteria, Gram-negative bacteria, and fungi with different geographical and health system endemic pathogens. In developing countries, gram-negative organisms include Klebsiella, Escherichia coli and Pseudomonas species; whereas in developed countries gram positive include Staphylococcus aureus and coagulase negative staphylococci are often reported. The increasing rate of antimicrobial resistance in these pathogens has now emerged as a significant global health burden through increased morbidity and mortality due to antimicrobial resistant organisms and decreasing treatment options for invasive bacterial infections.

Data from studies on risk factors and patterns of antibiotic resistance have played a key role in formulating management guidelines for neonates with sepsis [6]. These recommendations focus on early diagnosis, rapid commencement of appropriate antibiotic therapy, supportive treatment and stringent infection control practices. Nevertheless, the effectiveness of these strategies is highly dependent on ongoing monitoring of pathogen profiles and their resistance patterns, which are not stable over time but may change due to evolving microbial ecology and antibiotic usage practices. Antibiotic resistance data are thus essential for guiding empirical therapy to maximise clinical outcomes. Need for constant upgradation of institutional antibiotic policies to combat this growing threat of antimicrobial resistance leading to improve survival rates amongst these affected neonates.

Apart from microbial factors, various maternal and neonatal risk factors are also found to affect the incidence and progression of neonatal sepsis. Maternal factors, like poor antenatal care, infections in pregnancy and complications while giving birth, are significant contributors to early onset infections [7]. Prematurity, low birth weight, asphyxia at birth, and need for resuscitation are also neonatal factors that increase susceptibility to infections. Hospital factors such as overcrowding, inadequate staffing, poor hygiene practices and non-compliance with infection control measures are also determinants of infection transmission, particularly in tertiary care centers wherein critically ill neonates receive management.

Due to the high burden and significant implications of neonatal sepsis within local healthcare settings, an in-depth summary of its clinical profile and outcomes is critical. Retrospective studies conducted in hospital settings give us idea about the pattern of disease, its epidemiology and microbial etiology as well as treatment outcomes. Their importance also lies in highlighting existing gaps in clinical practice and assessing the efficacy of current management protocols to develop evidence-based approaches to improve neonatal management. Moreover, they help nation to international guidelines that fit better with local populations.

In this context, the present study titled A Hospital-Based Retrospective Study on Clinical Profile and Outcomes of Neonatal Sepsis in a Tertiary Care Center aims to analyze the clinical characteristics, risk factors, and outcomes of neonates diagnosed with sepsis. By examining retrospective data from a tertiary care center, the study seeks to provide a comprehensive understanding of the disease burden and its determinants. The findings of this study are expected to aid clinicians in early recognition and management of neonatal sepsis, optimize antibiotic usage, and ultimately reduce neonatal morbidity and mortality.

Methodology

Study Design: This study was designed as a hospital-based retrospective observational study aimed at evaluating the clinical profile and outcomes of neonatal sepsis.

Study Area: The study was conducted in the Department of Paediatrics, Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, India.

Study Duration: The duration of the study was one year from January 2024 to December 2024.

Study Participants: The study participants included neonates admitted to the neonatal unit with a diagnosis of neonatal sepsis during the study period.

Inclusion Criteria

- Neonates (0–28 days of life) admitted with a clinical diagnosis of neonatal sepsis.
- Both inborn (delivered in the hospital) and outborn (referred from other health facilities) neonates.
- Neonates with complete and accessible medical records in the Medical Records Department (MRD).

Exclusion Criteria

- Neonates who were transferred to other hospitals before completion of treatment.
- Neonates who left against medical advice (LAMA).
- Cases with incomplete or missing medical records.

Sample Size: A total of 80 neonates diagnosed with neonatal sepsis were included in the study.

Procedure: This retrospective study involved the review of medical records of neonates admitted with neonatal sepsis in the Department of Paediatrics over a period of one year. Data were obtained from the Medical Records Department (MRD) using a structured and pre-validated data collection form. The form was designed to capture comprehensive information including hospital details (date of admission and discharge), neonatal characteristics (age at admission, gender, birth weight), maternal and pregnancy-related factors (gestational age, history of maternal fever, premature rupture of membranes, foul-smelling liquor), and delivery details (mode of delivery).

In addition, clinical features at presentation, laboratory investigations (such as complete blood count, C-reactive protein, blood culture and sensitivity), treatment details (antibiotic therapy and supportive management), and final outcomes (recovery, discharge, or mortality) were recorded. Information regarding institutional practices such as hand hygiene protocols, antibiotic usage policies, and procedures for sample collection for blood culture and sensitivity was also reviewed to understand the standard care practices.

All collected data were checked for completeness and accuracy before entry into Microsoft Excel for organization and coding. Confidentiality of patient information was strictly maintained throughout the study. The retrospective nature of the study ensured that no direct patient interaction occurred, and all data were anonymized prior to analysis.

Statistical Analysis: The collected data were entered into Microsoft Excel and subsequently analyzed using Statistical Package for the Social Sciences (SPSS) software version 27.0 (IBM Corp., Chicago, USA). Descriptive statistics were used to summarize the data, where categorical variables were expressed as frequencies and percentages, and continuous variables were represented as mean ± standard deviation. Inferential statistical tests such as Chi-square test or Fisher's exact test were applied to assess the association between independent variables and outcomes. A p-value of less than 0.05 was considered statistically significant. Logistic regression analysis was further performed to identify predictors of adverse outcomes in neonatal sepsis.

Result

Table 1 shows the distribution of neonates according to demographic characteristics in the study population (n = 80). The majority of neonates were admitted within the first week of life (0–7 days), accounting for 57.5% (n = 46), while 42.5% (n = 34) were admitted between 8–28 days, indicating a higher occurrence of early neonatal admissions. In terms of gender, males predominated with 60% (n = 48), compared to females at 40% (n = 32), suggesting a male preponderance in neonatal sepsis cases. Regarding birth weight, more than half of the neonates (55%, n = 44) had low birth weight (<2.5 kg), whereas 45% (n = 36) had a birth weight ≥2.5 kg. Overall, the findings highlight that early age at admission, male gender, and low birth weight were more common among the study population.

Table 1: Distribution of Neonates According to Demographic Characteristics (n = 80)

Variables	Category	Frequency (n)	Percentage (%)
Age at admission	0–7 days	46	57.5
	8–28 days	34	42.5
Gender	Male	48	60
	Female	32	40
Birth weight	<2.5 kg	44	55
	≥2.5 kg	36	45
Total	—	**80**	**100**

Table 2 shows the distribution of maternal and perinatal risk factors among the study population (n = 80). A majority of the neonates were born at term (62.5%), while preterm births accounted for 37.5% of cases, indicating a substantial proportion of premature deliveries. Maternal fever was present in 27.5% of cases, suggesting its notable contribution as a risk factor, whereas 72.5% of mothers did not

have fever. Similarly, foul-smelling liquor, which is an indicator of intrauterine infection, was observed in 22.5% of cases and was absent in the majority (77.5%). Regarding the mode of delivery, most neonates (65%) were delivered vaginally, while 35% were delivered via cesarean section. Overall, the findings indicate that although most deliveries were term and without maternal complications, a considerable proportion of cases had identifiable risk factors such as preterm birth, maternal fever, and foul-smelling liquor, which may contribute to adverse neonatal outcomes.

Table 2: Maternal and Perinatal Risk Factors (n = 80)

Variables	Category	Frequency (n)	Percentage (%)
Gestational age	Preterm	30	37.5
	Term	50	62.5
Maternal fever	Present	22	27.5
	Absent	58	72.5
Foul smelling liquor	Present	18	22.5
	Absent	62	77.5
Mode of delivery	Vaginal	52	65
	Cesarean section	28	35

Table 3 shows the distribution of clinical features among neonates diagnosed with sepsis (n = 80). The most common presenting feature was poor feeding, observed in 50 cases (62.5%), followed by lethargy in 42 cases (52.5%). Respiratory distress was noted in 38 neonates (47.5%), indicating a significant proportion with respiratory involvement. Fever was present in 30 cases (37.5%), while hypothermia was observed in 20 cases (25%), reflecting temperature instability as a common manifestation. Convulsions were the least frequent clinical feature, reported in 12 neonates (15%). Overall, nonspecific symptoms such as poor feeding and lethargy were more prevalent compared to severe neurological manifestations.

Table 3: Clinical Features of Neonatal Sepsis (n = 80)

Clinical Features	Frequency (n)	Percentage (%)
Poor feeding	50	62.5
Lethargy	42	52.5
Respiratory distress	38	47.5
Fever	30	37.5
Hypothermia	20	25
Convulsions	12	15

Table 4 presents the laboratory findings among the study participants (n = 80). The majority of neonates showed positive C-reactive protein (CRP) levels, with 56 cases (70%), while 24 cases (30%) were CRP negative, indicating a high prevalence of inflammatory response among the subjects. Blood culture results revealed that 32 cases (40%) were culture-positive, whereas a larger proportion, 48 cases (60%), were culture-negative, suggesting that not all clinically suspected cases had microbiological confirmation. Regarding total leukocyte count, 45 cases (56.3%) exhibited abnormal values, while 35 cases (43.7%) had normal counts. Overall, these findings indicate that CRP positivity and leukocyte abnormalities were more common than blood culture positivity in the studied population.

Table 4: Laboratory Findings (n = 80)

Parameters	Category	Frequency (n)	Percentage (%)
C-reactive protein (CRP)	Positive	56	70
	Negative	24	30
Blood culture	Positive	32	40
	Negative	48	60
Total leukocyte count	Abnormal	45	56.3
	Normal	35	43.7
Total	—	**80**	**100**

Table 5 shows the association between birth weight and outcome among neonates. It was observed that out of 44 neonates with birth weight less than 2.5 kg, 30 recovered while 14 expired, resulting in a higher mortality rate of 31.8%. In contrast, among 36 neonates with birth weight ≥2.5 kg, 32 recovered and only 4 expired, with a significantly lower mortality rate of 11.1%. Overall, out of 80 cases, 62 neonates

recovered and 18 expired. These findings indicate that low birth weight is associated with a higher risk of mortality, whereas neonates with normal or higher birth weight have better survival outcomes.

Table 5: Association Between Birth Weight and Outcome (n = 80)

Birth Weight	Recovered (n)	Expired (n)	Total (n)	Percentage Mortality (%)
<2.5 kg	30	14	44	31.8
≥2.5 kg	32	4	36	11.1
Total	**62**	**18**	**80**	—

Discussion

The current research shows important findings about how neonatal sepsis develops in tertiary medical centers while showing results that match existing research studies. The study found that early-onset neonatal sepsis occurred more frequently because most of the observed cases emerged during the first week after birth. The research findings of Chaurasia et al. (2019) [8] show that 62% of neonatal sepsis cases in South Asia develop within the first 72 hours after birth which demonstrates the high incidence of early-onset infections that affect this area. The studies from around the world show that developing countries face high rates of neonatal death and illness because of early-onset sepsis which remains a leading health problem (Liu et al., 2015) [9].

The study found that sepsis cases included more male neonates and more low birth weight infants. The research results support the findings of Murthy et al. (2019) [10] which showed that male neonates have about 1.3 to 1.5 times greater sepsis risk while low birth weight increases their risk by almost 2 to 3 times. The present study found that low-birth-weight neonates had a mortality rate of 31.8% which exceeded the mortality rate of neonates with birth weight 2.5 kg or more who had an 11.1% mortality rate thus establishing a strong link between low birth weight and negative health results. Bangi and Devi (2014) [11] found that low birth weight and prematurity put neonates at risk for infections because their immune systems are not fully developed and their body reserves are limited.

The current study discovered that more than half of the sample studied sepsis cases which did notresult in any bacterial culturing. This observation shows similar results to previous research which found that culture positivity rates ranged from 30 percent to 50 percent (Kartik, 2006) [12]. The high rate of culture-negative cases may be attributed to prior antibiotic administration, inadequate blood sample volume, and low levels of bacteremia in neonates. Edwards and Baker (2004) [13] also emphasized that technical limitations in blood culture methods and early antibiotic exposure significantly reduce culture yield. The phenomenon occurs because outborn neonates who arrive at the hospital after receiving antibiotics.

The current study demonstrated equal levels of gram-positive bacteria and gram-negative bacteria which made up its microbiological profile. The finding contradicts the research results of Viswanathan et al. (2011) [14] which showed that gram-negative bacteria constituted between 60 and 70 percent of neonatal sepsis cases. The regional differences together with the small sample size and low culture positivity rates in the current research explain the observed differences. The study results show that Staphylococcus aureus remains the most common gram-positive bacterium according to Shrestha et al. (2013) [15] who found that this bacterium made up 30 to 40 percent of neonatal intensive care unit isolates.

The current study reveals antimicrobial resistance which poses significant danger to public health. The researchers discovered that gram-negative bacteria showed extensive resistance to standard antibiotics which included cephalosporins. The results of this study match the findings of Li et al. (2020) [16], who documented cephalosporin resistance rates which varied between 26% and 84% throughout several neonatal units worldwide. The extremely high resistance rates make it necessary to conduct ongoing local antibiotogram assessment because they impede proper empirical antibiotic treatment. The research results demonstrate that health facilities need to implement antibiotic stewardship programs which include responsible antimicrobial usage practices to stop the rise of antibiotic resistance.

The study results demonstrate that patients exhibit nonspecific symptoms which include poor feeding and lethargy and respiratory distress according to existing medical literature. (Singer et al., 2016) [17] describe neonatal sepsis as a condition which presents with subtle symptoms that lack specific characteristics and this fact results in diagnostic delays. The study results showed that C-reactive protein and total leukocyte count abnormalities served as useful diagnostic tools because their rates of occurrence exceeded the rates of positive culture results. Previous studies have reported C-reactive protein sensitivity rates between 60 and 80 percent for detecting neonatal sepsis (Kartik 2006).

The present study reported an overall mortality rate of 22.5% which matches worldwide estimates that show neonatal sepsis mortality rates between 11% and 30% according to different healthcare facilities (Fleischmann-Struzek et al., 2018) [18]. The study found that low-birth-weight neonates and culture-

negative cases experienced higher mortality rates which demonstrated the need for hospitals to identify patients early and treat them without delay. The adverse outcomes in culture-negative cases result from two factors which include delayed diagnosis and the use of incorrect initial treatment methods.

The present study results show strong agreement with existing research about how early-onset sepsis and low birth weight and antimicrobial resistance impact neonatal results. The distribution of pathogens and the rate of positive cultures demonstrate that specific data from each region must be collected for accurate assessment. The healthcare system needs to develop its microbiological diagnostic capabilities while creating methods to identify high-risk neonates and implementing infection control and antibiotic stewardship systems to decrease neonatal sepsis rates and increase patient survival.

Conclusion

The present study concludes that neonatal sepsis remains a significant contributor to neonatal morbidity and mortality, particularly in tertiary care settings. A higher proportion of cases occurred within the first week of life, indicating the predominance of early-onset sepsis. Male neonates and low birth weight infants were more commonly affected, with low birth weight emerging as a major predictor of poor outcomes. Clinical presentation was largely nonspecific, with poor feeding, lethargy, and respiratory distress being the most frequent features. Laboratory findings highlighted the importance of CRP and leukocyte abnormalities as supportive diagnostic tools, although culture positivity remained limited. The overall mortality rate was considerable, with significantly higher deaths among low-birth-weight neonates. These findings emphasize the need for early diagnosis, prompt management, and strengthened infection control practices.

References

1. Qazi SA, Stoll BJ. Neonatal sepsis: a major global public health challenge. The Pediatric infectious disease journal. 2009 Jan 1;28(1):S1-2.
2. Hug L, Alexander M, You D, Alkema L. National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. The Lancet Global Health. 2019 Jun 1;7(6):e710-20.
3. Jajoo M, Manchanda V, Chaurasia S, Sankar MJ, Gautam H, Agarwal R, Yadav CP, Aggarwal KC, Chellani H, Ramji S, Deb M. Alarming rates of antimicrobial resistance and fungal sepsis in outborn neonates in North India. PLoS One. 2018 Jun 28;13(6):e0180705.
4. Hofer N, Müller W, Resch B. Definitions of SIRS and sepsis in correlation with early and late onset neonatal sepsis. Journal of Pediatric Intensive Care. 2012 Mar;1(01):017-23.
5. Baltimore RS. Neonatal sepsis: epidemiology and management. Pediatric Drugs. 2003 Nov;5(11):723-40.
6. Silva AC, Anchieta LM, de Paula Lopes MF, de Castro Romanelli RM. Inadequate use of antibiotics and increase in neonatal sepsis caused by resistant bacteria related to health care assistance: a systematic review. The Brazilian Journal of Infectious Diseases. 2018 Jul 1;22(4):328-37.
7. Chan GJ, Lee AC, Baqui AH, Tan J, Black RE. Risk of early-onset neonatal infection with maternal infection or colonization: a global systematic review and meta-analysis. PLoS medicine. 2013 Aug 20;10(8):e1001502.
8. Chaurasia S, Sivanandan S, Agarwal R, Ellis S, Sharland M, Sankar MJ. Neonatal sepsis in South Asia: huge burden and spiralling antimicrobial resistance. bmj. 2019 Jan 22;364.
9. Liu L, Oza S, Hogan D, Perin J, Rudan I, Lawn JE, Cousens S, Mathers C, Black RE. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. The lancet. 2015 Jan 31;385(9966):430-40.
10. Murthy S, Godinho MA, Guddattu V, Lewis LE, Nair NS. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. PloS one. 2019 Apr 25;14(4):e0215683.
11. Bangi VA, Devi SS. Neonatal sepsis: A risk approach. Journal of Dr. YSR University of Health Sciences. 2014 Oct 1;3(4):254-8.
12. Kartik R. Evaluation of screening of neonatal sepsis (Doctoral dissertation, Rajiv Gandhi University of Health Sciences (India)) 2006.
13. Edwards MS, Baker CJ. Krugman's infectious diseases of children. Sepsis in the Newborn. Philadelphia, Mosby. 2004:545-61.
14. Viswanathan R, Singh AK, Mukherjee S, Mukherjee R, Das P, Basu S. Aetiology and antimicrobial resistance of neonatal sepsis at a tertiary care centre in eastern India: a 3 year study. The Indian Journal of Pediatrics. 2011 Apr;78(4):409-12.
15. Shrestha S, Shrestha NC, Singh SD, Shrestha RP, Kayestha S, Shrestha M, Thakur NK. Bacterial isolates and its antibiotic susceptibility pattern in NICU. Kathmandu university medical journal. 2013;11(1):66-70.
16. Li G, Bielicki JA, Ahmed AN, Islam MS, Berezin EN, Gallacci CB, Guinsburg R, da Silva Figueiredo CE, Santarone Vieira R, Silva AR, Teixeira C. Towards understanding global patterns of antimicrobial use and resistance in neonatal sepsis: insights from the NeoAMR network. Archives of disease in childhood. 2020 Jan;105(1):26-31.
17. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, Bellomo R, Bernard GR, Chiche JD, Coopersmith CM,

Hotchkiss RS. The third international consensus definitions for sepsis and septic shock (Sepsis-3). Jama. 2016 Feb 23;315(8):801-10.
18. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. The Lancet Respiratory Medicine. 2018 Mar 1;6(3):223-30.