ISSN 2540-8313 URL:http.\\ojs.unud.co.id\index.php\eumVol 47, No 3 (2016)

Risk factors of neonatal mortality in sanglah hospital denpasar

Reddy Lufyan, Made Kardana, Ida Bagus Subanada

Department of Child Health,

Medical School Udayana University / Sanglah Hospital Denpasar

Author correspondence: reddylu.md@gmail.com

Abstract

The neonatal mortality continues to be one of the global burden for both developed and developing countries. Information on neonatal mortality at international level is in great demand because it emerges as an increasingly prominent component of overall under-five mortality. Since causes of neonatal death vary by country and with the availability and quality of health care, understanding neonatal mortality in relation to these factors is crucial. This study aimed to acknowledge the characteristics and identify the related risk factors of neonatal mortality in Sanglah Hospital Denpasar. This study was a case control study performed in Sanglah Hospital Denpasar. Data was obtained from medical record and registry, analyzed as bivariate using chi-square test and multivariate by using logistic regression analysis model. This study involved 96 subjects for each case and control group. Bivariate analysis showed that asphyxia, low birthweight, major congenital anomaly, prematurity, respiratory distress syndrome, and sepsis were risk factors of neonatal mortality. Multivariate analysis showed that major congenital anomaly (OR 15.67; 95%CI 3.43 to 71.57), prematurity (OR 4.99; 95%CI 1.23 to 20.17), and respiratory distress syndrome (OR 34.90; 95%CI 12.79 to 95.26) were the most significant risk factors of neonatal mortality. In conclusion, neonatal mortality is still an important issue to be concerned seriously. Respiratory distress syndrome, major congenital anomaly, and prematurity were the most significant risk factors associated to neonatal mortality. Better understanding of the risk factors would increase the clinical awareness, develop, and improve better service for neonatal care to reduce neonatal mortality rate.

Keywords: *risk factor, neonatal, mortality*

Abstrak

Kematian neonatus masih merupakan permasalahan dunia, baik di negara maju maupun berkembang. Data kematian neonatus di tingkat internasional sangat dibutuhkan karena menjadi komponen yang menonjol pada data kematian anak berusia dibawah lima tahun. Penyebab kematian neonatus bervariasi dan bergantung pada ketersediaan dan kualitas pelayanan kesehatan, sehingga pemahaman hubungan kematian neonatus dengan faktor-faktor ini sangat penting. Penelitian ini bertujuan untuk mengetahui karakteristik dan mengkaji faktor risiko yang berhubungan dengan kematian neonatus di Rumah Sakit Sanglah Denpasar. Penelitian kasus kontrol ini dilakukan di Rumah Sakit Sanglah Denpasar. Data didapatkan dari rekam medis dan register, dianalisis bivariat dengan uji *chi-square* dan multivariat dengan model analisis regresi logistik. Penelitian ini melibatkan 96 subyek untuk masing-masing kelompok kontrol dan kasus. Analisis bivariat menunjukkan bahwa asfiksia, bayi berat lahir rendah, kelainan kongenital mayor, prematuritas, sindrom gawat napas, dan sepsis merupakan faktor risiko kematian neonatus. Analisis multivariat menunjukkan kelainan kongenital mayor (RO 15,67; IK95% 3,43-71,57), prematuritas (RO 4,99; IK95% 1,23-20,17), dan sindrom gawat napas (RO 34,90; IK95% 12,79-95,26) merupakan faktor risiko kematian neonatus yang bermakna. Kematian neonatus masih merupakan permasalahan penting yang harus diperhatikan secara serius. Sindrom gawat napas, kelainan kongenital mayor, dan prematuritas merupakan faktor risiko yang paling bermakna berhubungan dengan kematian neonatus. Pemahaman yang lebih baik mengenai faktor risiko akan meningkatkan kewaspadaan klinis, mengembangkan, dan meningkatkan pelayanan neonatus yang lebih baik untuk mengurangi tingkat kematian neonatus.

Kata kunci: *faktor risiko, neonatus, mortalitas*

Introduction

The neonatal mortality continues to be one of the global burden for both developed and developing countries.[1,2] Information on perinatal and neonatal mortality at international level is in great demand because neonatal mortality now represents a larger share of total under-five deaths as the decline in neonatal mortality has been slower than the decline in mortality for children aged 1–59 months in almost all countries.[2]

The report of Millennium Development Goals (MDGs) in 2015 shows that the worldwide neonatal mortality rate (NMR) has fallen from 33 to 19 deaths per 1,000 live births between 1990

and 2015.[3] World Health Statistics in 2015 shows a decrease trend of NMR in South-East Asia region from 33.3 to 20 deaths per 1,000 live births between 1990 and 2013. Indonesia, as one of the countries in South-East Asia region, is also showing a decrease of NMR from 30.8 to 14.4 deaths per 1,000 live births in period of 1990 to 2013.[4]

Bali Province's health profile shows an increase in NMR from 3.47 to 4.59 deaths per 1,000 live births within period of 2013 and 2014. Denpasar has the lowest NMR (0.27 deaths per 1,000 live births) and District of Bangli has the highest NMR (8.99 deaths per 1,000 live births).[5] The neonatal mortality rate in Sanglah Hospital in 2016 is 62.1 per 1,000 live births. There is a decrease of neonatal mortality in both level II (from 3.58% to 2.52%) and III (from 41.43% to 38.10%) neonatal ward from 2015 to 2016.[6]

The top causes of neonatal mortality worldwide are prematurity and low birthweight (LBW) (29%), neonatal infections (25%), birth asphyxia and birth trauma (23%), congenital anomalies (8%), neonatal tetanus (2%), and diarrheal disease (2%).[6] Studies in Jamshoro, Namibia, Brazil, Yogyakarta, and Denpasar show that the most common causes of death in tertiary care hospital were prematurity, sepsis, birth asphyxia, respiratory distress syndrome, and congenital anomalies.[7-12]

Sustainable Developing Goals (SDGs) is launched to continue the programs for human wellbeing since MDGs expired in 2015. The SDGs' target by 2030 is to reduce neonatal mortality to at least as low as 12 deaths per 1,000 live births in all countries. Since causes of neonatal death vary by country and with the availability and quality of health care, understanding neonatal mortality in relation to these factors is crucial.[1,6] Based on the above backgrounds, this study was conducted in Sanglah Hospital, as one of the tertiary referral center for neonatal care in East Indonesia region. This study aimed to acknowledge the characteristics and identify the related risk factors that contribute to neonatal mortality in Sanglah Hospital Denpasar.

Methods

This study was a case control study using subjects extracted from medical record and registry within period of January to December 2016. Target population was neonates who were admitted to neonatal ward in Hospital. The reachable population was neonates who were admitted to Level II and III neonatal ward in Sanglah Hospital within study period. The inclusion criteria was neonates with death as outcome for case group and survive as outcome for control group during treatment in Sanglah Hospital since January to December 2016. We excluded neonates who had incomplete medical record or registry data. This study was performed under

supervision of Neonatology Subdivision, Department of Child Health in Sanglah Hospital, Medical School of Udayana University and approved by ethical clearance No:102/UN.14.2/KEP/2017 from the Ethics Committee of Medical School, Udayana University/Sanglah Hospital-Denpasar.

In this study, sample size was calculated by using the sample size estimation equation for two proportions, with power 80%, effect size 20%, and significant degree of $p<0.05$.[13] Based on the formula above we found minimum sample size in this study was 96 subjects for case group and 96 subjects for control group. We collected data on medical record number, gender, gestational age, birthweight, asphyxia, delivery method, parity, referral case, district of origin, distant from Sanglah Hospital, length of stay, major congenital anomaly, respiratory distress syndrome, and sepsis.

Data Analysis

Descriptive data would be shown as percentage and range in table and narration. Data was analyzed using SPSS software for Windows. Bivariate analysis was performed using chi-square test and multivariate analysis, we performed multiple logistic regression model to determine risk factor that significantly associated with neonatal mortality. The strength of association was indicated by odds ratio (OR); confidence intervals were supplied with level of significance was set at $p<0.05$.

Result

A total of 192 subjects were included in this study and divided in to 96 subjects in case group and 96 subjects in control group. Subjects were categorized into two groups based on the mortality during treatment as outcome. The characteristics of study subjects are described in **Table. 1**.

Table 1. Characteristics of subjects

Characteristics	Cases, n (%) 96 (50%)	Control, n (%) 96 (50%)
Male, n (%)	69 (72)	58 (60)
Birthweight, median (min-max)	2225 (500 – 4500)	2950 (1100-4700)
Delivery Methods, n (%)		
Spontaneous pervaginam labor	51 (53)	34 (35)
Vacuum	2 (2)	4 (4)
Forcep	1 (1)	5 (5)
Sectio Caesarean	42 (44)	53 (56)
Parity, n (%)		
1	43 (45)	32 (33)
2	22 (23)	27 (28)
≥ 3	31 (32)	37 (39)
Referral case, n (%)	62 (65)	45 (47)
District of origin, n (%)		
Badung	6 (6)	2 (2)
Bangli	3 (3)	2 (2)
Buleleng	0 (0)	0 (0)
Denpasar	61 (64)	72 (75)
Gianyar	10 (10)	9 (10)
Jembrana	8 (9)	3 (3)
Karangasem	2 (2)	2 (2)
Klungkung	3 (3)	3 (3)
Tabanan	3 (3)	3 (3)
Distance from Sanglah Hospital, n (%)		
0 - 20 Km	66 (69)	74 (77)
>20 – 40 Km	13 (13)	9 (9)
>40 Km	17 (18)	13 (14)
Length of Stay, median (min-max)	5 (1-58)	6.5 (1-60)

The result of bivariate analysis in **Table 2** showed that asphyxia (OR 5.22; 95%CI 2.52 to 10.80), low birthweight (OR 5.00; 95%CI 2.66 to 9.40), major congenital anomaly (OR 3.93; 95%CI

1.24 to 12.4), prematurity (OR 10.96; 95% CI 4.95 to 24.26), respiratory distress syndrome (OR 32.68; 95% CI 4.95 to 24.26), and sepsis (OR 4.6; 95% CI 1.48 to 14.32) were risk factors of neonatal mortality but the result of multivariate analysis in **Table 3** showed only major congenital anomaly (OR 15.67; 95% CI 3.43 to 71.57), prematurity (OR 4.99; 95% CI 1.23 to 20.17), and respiratory distress syndrome (OR 34.90; 95%CI 12.79 to 95.26) were significant risk factors of neonatal mortality.

Table 2. Bivariate analysis on association of neonatal death with risk factors

Risk Factors	Case	Control	OR	95% CI	*p*
Asphyxia, n (%)	41 (77)	12 (23)	5.22	2.52 – 10.80	<0.0001
Low birthweight, n (%)	56 (73)	21 (27)	5.00	2.66 – 9.40	<0.0001
Major congenital anomaly, n (%)	14 (78)	4 (22)	3.93	1.24 – 12.40	0.013
Prematurity, n (%)	51 (85)	9 (15)	10.96	4.95 – 24.26	<0.0001
Respiratory distress syndrome, n (%)	76 (72)	30 (28)	32.68	14.4 – 74.16	<0.0001
Sepsis, n (%)	16 (80)	4 (20)	4.60	1.48 – 14.32	0.005

Bivariate analysis was performed using chi-square test. OR: odds ratio; CI: confidence interval; p<0.05.

Table 3. Multivariate analysis on association of neonatal death with risk factors

Risk Factors	OR	95 % CI	*P*
Asphyxia	1.84	0.64 – 5.32	0.26
Low birthweight	2.08	0.58 – 7.51	0.264
Major congenital anomaly	15.67	3.43 – 71.57	<0.0001
Prematurity	4.99	1.23 – 20.17	0.024
Respiratory distress syndrome	34.90	12.79 – 95.26	<0.0001
Sepsis	2.06	0.40 – 10.68	0.391

Multivariate analysis was performed using regression logistic test. OR: odds ratio; CI: confidence interval; p<0.05.

Discussion

Neonatal mortality remains global health burden and emerges as an increasingly prominent component of overall under-five mortality, as under-five mortality is decreasing in almost all countries.[2] The neonatal mortality rate in Sanglah Hospital, as a tertiary level referral hospital, remains high although shows a decrease trend of neonatal mortality percentage in level II and III neonatal ward between 2015 and 2016.[6] This study could not explain why neonatal

mortality rate in Sanglah Hospital remains high. We did not have sufficient data whether it was caused by the limitation of resources in human, instruments, medical devices or by the increase of complicated pregnancy or neonatal cases referred to Sanglah Hospital from secondary referral healthcare provider, midwives, and private delivery clinics. There was lack of complete data either about kinds of complicated pregnancy, maternal, and placental factors.

This study showed that major congenital anomaly, prematurity, and respiratory distress syndrome were significant risk factors of neonatal mortality. Several previous studies in Jamshoro, Namibia, and Brazil show that the most common causes of death in tertiary care hospital were prematurity, sepsis, birth asphyxia, respiratory distress syndrome, and congenital anomalies.[8-10,14] In Indonesia, studies in Sardjito Hospital Yogyakarta and Wangaya Hospital Denpasar also show similar result to this study in risk factors of neonatal mortality.[11,12] Study in Wangaya Hospital shows that five significant variables at risk factors of early neonatal death are respiratory distress (OR 16.8, 95%CI 3.7 to 76.6), asphyxia (OR13.5, 95%CI 6.1 to 29.9), birthweight <2500 gram (OR 8.1, 95%CI 3.3 to 19.9), sepsis (OR 7.3, 95%CI 3.1 to 17.1), and gestational age <37 weeks (OR 3.5, 95%CI 1.6 to 7.78).[11] Previous study in Sardjito Hospital, a tertiary level hospital in Yogyakarta, shows that significant risk factors at neonatal mortality include sepsis (OR 6.04, 95%CI 1.9 to 18.9), major congenital anomaly (OR 34.8, 95%CI 6.7 to 182.2), low 5 APGAR score (OR 9.16 95%CI 1.8 to 48.0), and hyaline membrane disease (OR 15, 95%CI 2.3 to 96.5).[12]

Another study in Indonesia that involves 80 *Puskesmas* across 14 districts that were directly supported by the Australia-Indonesia Partnership for Maternal and Neonatal Health (AIPMNH) program combines all significant variables related to maternal, neonatal, and delivery factors into a single multivariate model and shows six factors those significantly associated with a higher risk of neonatal death. The factors identified are as follows: neonatal complications during birth, mother noting a health problem during the first 28 days, maternal lack of knowledge of danger signs for neonates, low Apgar score, delivery at home, and history of complications during pregnancy. This large and representative samples study might explain the situation and risk factors related to neonatal mortality in primary healthcare level, but for secondary and tertiary level healthcare provider, it still need further study to determine a comprehensive analysis of risk factors related to neonatal mortality.[15] This study could not explain the risk factors comprehensively in comparison between level I and level III of neonatal care since the lack of data provided in this study.

Birth asphyxia, low birthweight, and sepsis are serious clinical problems worldwide and contributes greatly to neonatal mortality and morbidity.[16,17] Survey of World Health Organization

(WHO) in 2005 shows that perinatal asphyxia is one of the leading causes of neonatal deaths within the first week of life.[17] It is the second most common cause of neonatal death in Indonesia.[18] Low birthweight is one of the three most common causes of neonatal mortality coincides with prematurity, neonatal infection, and asphyxia. A survey of 10,892 neonatal deaths in India shows these causes accounted for 78% of all neonatal death and commonly related to organs immaturity and inadequate immune response, therefore, might be susceptible to complication.[19] Sepsis still continues to be a major cause of neonatal morbidity and mortality despites of the improvement in intensive neonatal care, medical devices, laboratory work up, and use of intrapartum antibiotics prophylaxis, especially in developing countries. Some of the factors responsible for neonatal sepsis are immature immune system, decreased of white cells phagocyte activity, decreased production of cytokines, and weak humoral immunity. However, a review of literature does not show the exact impact of above factors in the development of neonatal sepsis in this part of the world.[20]

This study showed that asphyxia, low birthweight, and sepsis were associated with higher risk for neonatal mortality, although they were not statistically significant in the multivariate analysis. This result might be due to better neonatal care in resuscitation and facilities in managing complicated pregnancy or delivery and also due to recent advances in the medical technology and therapeutics of neonatal care, especially in Sanglah Hospital as a tertiary level and center of referral hospital.[18,20]

Prevalence of congenital anomaly worldwide vary between 1-8%. In Southeast Asia region, prevalence of congenital anomaly is 5% and Indonesia in fifth rank in the region, which is 59.3 cases per 1,000 live birhts.[21-24] Based on the reports of World Health Organization (WHO) and March of Dimes (MOD) Global report on Birth Defect, congenital anomaly causes 7% of all deaths in neonatal period.[23-25] Risk factor of congenital anomaly is multifactorial that includes genetic, environment, mother, and fetal factors. Prematurity, male, mother age >35 years old, and twin are factors associated to congenital anomaly.[26,27] A study in Jamshoro shows that congenital anomaly (4.9%) is one of the most common causes of death in neonatal period following sepsis (45.4%), asphyxia (23.9%), and respiratory distress syndrome (13.3%).[28] Previous study in Sardjito Hospital Yogyakarta show similar result for congenital anomaly as one of the risk factor in neonatal mortality (OR 34.8, 95%CI 6.7 to 182.2).[12] The other study at Wangaya Hospital Denpasar shows different result where congenital anomaly is not a risk factor because of mild congenital anomaly or not life threatening condition.[11] In this study, major congenital anomaly was a significant risk factor of neonatal mortality in both univariate and multivariate analysis

with case fatality rate 77%. The different result between this study and previous study in Wangaya Hospital might be caused by some possibilities such as: different level of hospital care where Sanglah Hospital is a tertiary level and center of referral hospital in East Indonesia region that accept more complicated cases.

Prematurity is the main cause of neonatal morbidity and mortality that contribute more than 70% of perinatal death. The function of organs in premature newborns is not optimal, therefore, they more difficult to adapt and easier to have complication, and have high risk of mortality. Moura et al.[10] shows gestational age is an important risk factor for perinatal death in the tertiary hospital with a 17% decrease in perinatal death risk was observed at each additional week of gestation. Previous study in Denpasar also shows similar result to this study in both univariate (OR 18.3, 95%CI 9.9 to 33.6) and multivariate analysis (OR 3.5, 95%CI 1.6 to 7.8).[12] In this study, prematurity is one of the most significant risk factors of neonatal mortality below respiratory distress syndrome and major congenital anomaly with case fatality rate was 85%. Prematurity became a significant risk factors because commonly accompanied by other conditions such as: low birthweight, respiratory distress syndrome, congenital anomaly, and infection. The other possible cause is the gestational age that inversely proportional to mortality incidence. A lower gestational age is associated to higher mortality risk.

Respiratory distress syndrome (RDS), previously called hyaline membrane disease, is primarily caused by surfactant deficiency. Although the survival of infants with RDS has improved greatly, the survival with or without respiratory and neurologic sequelaes is highly dependent on birth-weight and gestational age.[29] Proportion of neonatal mortality that caused by respiratory distress syndrome in Sardjito Hospital in during 2007-2011 is 52% and asphyxia (OR 4.97, 95%CI 2.39 to 10.28) is the most significant factor that increases the risk of neonatal mortality in RDS.[30] Previous case control studies in Yogyakarta and Denpasar also show that RDS is a significant risk factor of neonatal mortality.[11,12] In this study, RDS was the most significant risk factor of neonatal mortality where neonates with RDS was 34.9 times to risk of mortality than neonates without RDS. The case fatality rate in this study was 88%. This result was probably caused by the complication that following during treatment such as infection, low birthweight, and presence of congenital anomaly but we did not analyze the risk of mortality in neonates by combining risk factors for each subjects.

The limitation of this study was that we did not adjust all risk factors of neonatal mortality especially maternal and placental factors, so a more comprehensive analysis could not be done. Based on the result of this study, more variables from maternal, fetal, and

environmental factors with a larger amount of subjects needed for better explanation and analysis of risk factors in neonatal mortality.

In conclusion, the most significant risk factors associated to neonatal mortality were major congenital anomaly, prematurity, and respiratory distress syndrome. Further study in evaluating risk factors of neonatal mortality should be including more maternal, neonatal, and placental factors in order to reach a better analysis and provide better management of neonatal care to reduce neonatal mortality rate. We hoped the result of this study could provide better understanding in the risk factors of neonatal mortality, increase the clinical awareness, develop and improve better service for neonatal care, especially from most significant risk factors that cause neonatal mortality.

References

1. Lawn JE, Cousens S, Zupan J. 4 Million neonatal deaths: when? where? why?. Lancet. 2005;365:891-900.
2. World Bank. Mortality rate, neonatal (per 1,000 live births). World Bank Data. [cited: 2016 September 20]. Available from: http://data.worldbank.org/indicator/ SH.DYN.NMRT
3. Way C. Goal 4: reduced child mortality. The Millennium Development Goals Report 2015. New York: United Nation; 2015. p. 32-7.
4. World Health Organization. Global health indicators. World Health Statistics 2015. Luxemburg: WHO; 2015. p. 40-54.
5. Dinas Kesehatan Provinsi Bali. Profil Kesehatan Provinsi Bali tahun 2014. Denpasar: Dinas Kesehatan Provinsi Bali; 2015. p. 20-1.
6. Instalasi Rawat Inap (IRNA) B. Laporan kegiatan rawat inap B tahun 2016. Denpasar: RSUP Sanglah Denpasar; 2016. p. 49.
7. Martines J, Paul V, Bhutta ZA, Koblinsky M, Saucat A, Walker N, et al. Neonatal survival: a call for action. Lancet. 2005;365:1189-97.
8. Indongo N. Risk factors and causes of neonatal deaths in Namibia. ESJ. 2014:466-71.
9. de Paula Risso LS, Nascimento FC. Risk factors for neonatal death in neonatal intensive care unit according to survival analysis. Rev Bras Ter Intensiva. 2010;22:19-26.

10. Moura PMSS, Maesta I, Rugolo LMSS, Angulski LFRB, Caldeira AP, Peracoli JC, et al. Risk factors for perinatal death in two different levels of care: a case-control study. Reproductive Health. 2014;11:1-7.
11. Budha MINU, Retayasa W, Kardana M. Early neonatal mortality rate and the risk factors in Wangaya hospital. Paediatr Indones. 2008;48:306-11.
12. Yanti T, Wandita S, Hapsara S, Surjono A. Faktor risiko kematian neonatus di Instalasi Maternal Perinatal RS dr. Sardjito, Yogyakarta. B.I. Ked. 2004;36:201-6.
13. Madiyono B, Moeslichan S, Sastroasmoro S, Budiman I, Purwanto SH. Perkiraan besar sampel. In: Sastroasmoro S, Ismael S. editors. Dasar-Dasar Metodologi Penelitian Klinis. 4th ed. Jakarta: Sagung Seto; 2011. p.348-81.
14. United Nations Children's Fund and World Health Organization. Low birthweight: country, regional and global estimates. New York: UNICEF; 2004.
15. Abdullah A, Hort K, Butu Y, Simpson L, Risk factors associated with neonatal deaths: a matched case control study in Indonesia. Glob Health Action. 2016;9:304-45.
16. Takazono PS, Golin MO. Perinatal asphyxia: repercussions neurological disorders and early detection. Neuroscience. 2013;21:108-17.
17. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO estimates of the causes of death in children. Lancet. 2005;365:1147-52
18. Badan Pusat Statistik, Badan Kependudukan dan Keluarga Berencana Nasional, Kementrian Kesehatan. Survei Demografi dan Kesehatan Indonesia. Jakarta: USAID; 2012.
19. Bassani DG, Kumar R, Awasthi S, Morris SK, Paul VK, Shet A, et al. Causes of neonatal and child mortality in India: Nationally representative mortality survey. Lancet. 2010;376:1853-60.
20. Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu Univ Med J. 2006;4:187-91.
21. Effendi SH, Indrasanto E. Kelainan Kongenital (Cacat bawaan), In: Kosim S, Yunanto A, Dewi R, Sarosa GI, Usaman A. Editors. Buku Ajar Neonatologi. 1st ed. Jakarta: Ikatan Dokter Anak Indonesia; 2008. p.41-70.
22. Singh K, Krishnamurthy K, Greaves C, Kandamaran L, Nielsen AL, Kumar A. Major congenital malformations in Barbados: the prevalence, the pattern, and the resulting morbidity and mortality. ISRN Obstetrics and Gynecology. 2014;1:1-8.
23. World Health Organization. Birth defects in South-East Asia a Public Health Challenge. 2013. [cited: 2016 September 5]. Available from: http://apps.searo.who.int/PDS_DOCS/B4962.pdf.

24. World Health Organization. Prevention and control of defects in South-East Asia Region. 2013. [cited: 2016 September 5]. Available at: http://apps.searo.who.int/PDS_DOCS/B4941.pdf.
25. Christianson A, Howson CP, Modell B. Executive summary march of dimes global report on birth defects. New York: March of dimes birth defects foundation; 2006. p. 1-10.
26. Mashuda F, Zuechner A, Chalya PL, Kidenya BR, Manyama M. Pattern and factors associated with congenital anomalies among young infant admitted at Bugando medical centre, Mwanza, Tanzania. BMC Reseach Notes. 2014;7:1-7.
27. Glinianaia SV, Rankin J, Wright C. Congenital anomalies in twins: a register-based study. Human Reproduction. 2008;23:1306-11.
28. Kousar T, Memon Y, Sheikh S, Memon S, Sehto R. Risk factors and causes of death in Neonates. RMJ. 2010;35:205-8.
29. Gomella TL, Cunningham MD, Eyal FG. Sepsis. Neonatology Management, Procedures, On-call Problems, Diseases, and Drugs. 7th ed. New York: McGraw-Hill; 2013. p. 865-74.
30. Anggraini A, Sumadiono, Wandita S. Faktor risiko kematian neonates dengan penyakit membrane hialin. Sari Pediatri. 2013;15:75-80.