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DIRECTLY OBSERVED TREATMENT SHORT-COURSE FOR TUBERCULOSIS AMONG FILIPINO CHILDREN: TALOMO (SOUTH) DISTRICT, DAVAO CITY EXPERIENCE

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Abstract: **Compliance has always been a problem in the treatment of tuberculosis. The strategy known as Directly Obeserved Treatment Short-course (DOTS) has been proven to be a remedy to this dillema in some foreign countries. The aim of this paper is to assess the outcome of DOTS among Filipino children with tuberculosis using the Barangay Health Workers (BHWs) in directly supervising the drug intake at Talomo (South) District, Davao City. Screening the children with primary complex was done and those that showed positive were enrolled in this study. A treatment protocol was assigned to them using the following drugs: Isoniazid and Rifampicin for 6 months combined with Pyrazinamide for the first 2 months. A BHW was designated for each patient to visit them daily in their own homes to directly supervise the drug intake. A total of 30 patients were included in this study. The mean age was 5.54 years old. Twenty or 66.7% were males and 10 or 33.3% were females. For those who completed the treatment there was a significant improvement of the symptoms as evidenced by relief of chronic cough, improved appetite, disappearance of fever and weight gain. Majority of the subjects came from families of low social economic status and were living in congested environments. All of them claimed to have been exposed to adult PTB patients and 80% of which had their own household as their main source of infection. Twenty-six or 86% had BCG vaccination early in life. The signs and symptoms that commonly occured were cough (100%) followed by cervical lymphadenopathy (86.6%), poor appetite (53.5%), poor weight gain (53.5%), weight loss (36.6%) and afternoon rises of temperature (13.3%). All of the subjects were classified as PTB III. The number of attendance during the monthly check-ups were also noted to be decreasing as months went by but on the final check-up all 24 patients who completed the treatment were seen. There was no major side-effect against the anti-TB drugs and the dosages used. This study shows that the pediatric DOTS thru the hands of BHWs can yield good results.**

INTRODUCTION

The Philippines ranks number seven among countries in the world with high incidence of tuberculosis .

Everyday, 68 Filipinos die from this disease. Yearly, 270,000 Filipinos are contracting tuberculosis and that is about 740 cases a day. In 1997 as many as 63% of the population was infected and unless some drastic change will be done medically, it is estimated that in the next 40 years it will reach 90%[2].

Since 1978, the Department of Health (DOH) through the National Tuberculosis Program (NTP) has spent millions of pesos in providing facilities and free medicines in health centers to combat this disease and still the number of cases had tremendously increased. An external evaluation done in 1993 showed that the major constraint in the control of tuberculosis was **poor treatment compliance**. Facing this gigantic problem, the DOH in 1996 has adopted a TB treatment strategy that worked in China, Vietnam, U.S.A., Tanzania, Peru and other countries which dramatically improved the cure rate of TB patients to more than 85%. This strategy is known as D.O.T.S. or "Directly Observed Treatment Short Course Chemotherapy"[1]. The main factor is the presence of a health giver (physician, nurse, BHW, etc.) who directly supervises the administration of the drug to the patient. DOTS has five main elements namely: 1) sputum microscopy service, 2) regular drug supply, 3) drug intake supervised by health worker, 4) book recording to monitor patients' program until cured, and 5) political will in terms of funds and manpower[2].

Since the start of adult DOTS in 1996 in health centers, cure rates of about 80% and above in adult TB patients were already reported. However, due to economic reasons there still no funding from the government for treating TB in children. But despite this limitation, DOTS for children has been initiated by non-government organizations since 1998. One of the pioneering DOTS for children was done at University of Sto. Tomas TB Clinic from January to July 1998. Enrolled patients came in three times a week to receive medications directly from the Pediatric Pulmonary Fellow or Pediatric resident. Of the 38 subjects that were included only 15 or 39% completed the 6 month treatment. They recommended that in order to avoid large dropouts, patients must be pursued in their respective homes and make sure that the drugs were really administered. Thus, this study was made.

The objective of this paper is to assess DOTS among

Keywords: tuberculosis, DOTS
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Filipino children diagnosed with primary tuberculosis using the Barangay Health Workers in supervising the drug intake. Specifically it will determine the outcome of the children treated at Talomo (South) District, Davao City from December 20, 1999 to June 20, 2000 with regards to their compliance of the medications and the improvement of signs and symptoms. This will also summarize the demographic characteristics of the patients base on age, sex, economic status, living conditions, sources of infection, BCG immunizations, presenting signs and symptoms, TB classification, number of follow ups and side effects from the drugs. In addition, it will try to identify specific problems and reasons on why patients cannot fully comply and finish a DOTS in a local setting.

MATERIALS AND METHODS

This is a descriptive study. Between December 2 to December 16, 1999, screening for tuberculosis in children was done. For a subject to be included in the study, he/she must be able to fulfill 2 to 3 out of the following criteria: 1. (+) exposure to adult PTB patients, 2. (+) Mantoux test, 3. (+) radiologic finding suggestive of TB and 4. constitutional signs and symptoms.

A total of 30 subjects were included in this study. Patients came from 5 different barangays of Talomo (South) District. Eight(26.6%) came from Puan, 5(16.6%) came from Bago Gallera, 5(16.6%) from Talomo Cemento, 5(16.6%) from Catalin Pequeno and 7(23.3%) from Ma-a. All of these of barangays have their own Health Centers and BHWs.

It was then explained to the parents of enrolled subjects that all anti-TB drugs will be provided free of charge and that the patient will have one BHW assigned to monitor and administer the meds on a daily basis for 6 months. The proximity of the subjects' home from the BHW-in-charge were taken into consideration during the designation of responsibilities.

The treatment started December 20, 1999 until June 20, 2000. A triple drug regimen was used namely: Rifampicin at 15mg/kg/day and Isoniazid at 10 mg/kg/day, both given once a day before breakfast for six months and Pyrazinamide 20 mg/kg/day once a day after a meal for 2 months.

Each BHWs was provided with an individualized patient's chart which was updated daily to note the progress of the patient as well as appearance of side-effects or new diseases. The mothers in return also had monitoring notebooks for the BHW to sign every visit.

General examinations were done monthly by pediatric residents assigned in each barangay health center. During these check-ups, a standard monthly monitoring forms were filled-up.

There were two tools for gathering data that were used: the screening and the monthly monitoring forms. The screening forms contained the subjects' demographic profile, history of present illness, presence or absence of TB exposure, baseline physical examination and results of the chest x-ray and mantoux test. The monitoring forms particularly included the patients' progress based on weight, appetite, signs and symptoms and appearance of side effects to the anti-TB drugs.

The classification of TB as recommended by the American Thoracic Society was used in this study.

RESULTS

Seventy-four patients came in for screening and 30 or 40.5% were diagnosed to have pulmonary tuberculosis were included in the study. Of the 30 patients, 50% were from age group 4-6 years old, 33.3% 1-3 years old, 13.3% 7-9 years old and finally 3.3% 10 years old. The mean age was 5.54 years old. Twenty or 66.6% were males and 10 or 33.3% were females. All the subjects belonged to low income families with monthly salary of P1700 to P6350. Seventy-three percent of the subjects were living in congested, house to house community whilr the remaining 26.6% came from areas which are more spacious like hillsides and farm areas. All of the subjects claimed to have exposure to adult PTB patients, 24 or 80% of them had their household as their main source of infection while 6 or 20% claimed that their source was their neighbor. Among the subjects, 26 or 86% of them claimed to have received BCG early in life while 2 or 6.6% had none and 2 oor 6.6% with unrecalled immunization status.

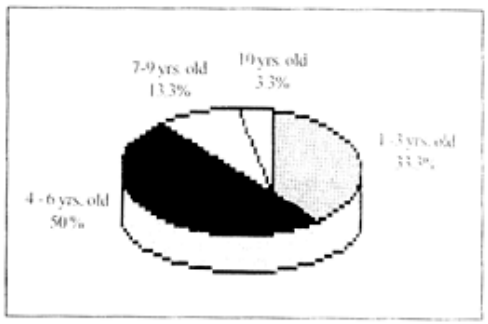

Figure 1. Age distribution of PTB patients enrolled in the DOTS done at Talomo (South) District, Davao City

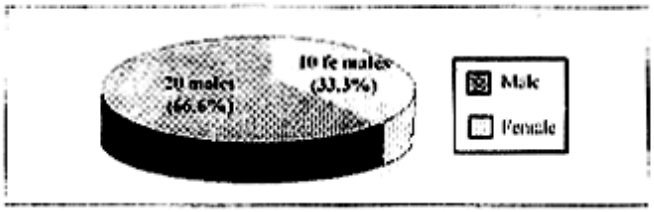

Figure 2. Sex Distribution of Patients enrolled in the DOTS done at Talomo (South) District, Davao City

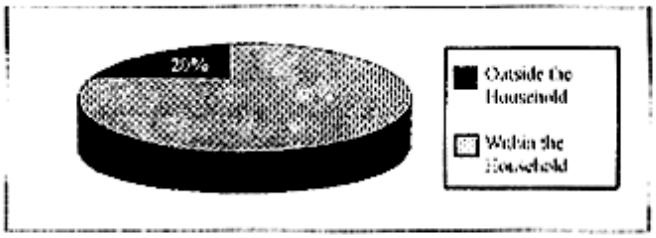

Figure 3. Sources of TB exposure among patients enrolled in the DOTS done at Talomo (South) District, Davao City

Among the constitutional signs and symptoms of tuberculosis, cough was shown to be present in all subjects followed by cervical lymphadenopathy (86.6%), poor appetite (53%), poor weight gain (53%), weight loss(36.6%) and presence of afternoon low grade fever (16.6%). All of the subjects were classified under PTB III (American Thoracic Society).

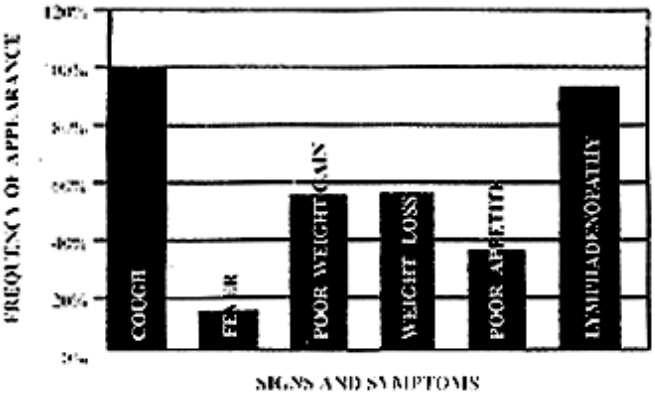

Figure 4. Presenting signs and symptoms of patients enrolled in the DOTS done at Talomo (South) District, Davao City

Of the 30 subjects that were included in this DOTS program, 24 or 80% were able to finish the 6 months treatment course. The remaining 6 or 20% of the subjects discontinued the medications and were lost to follow-up.

There were a total of five monthly check-ups done. The highest number of attendance were the first check-up at about 93.3%. Later, follow-up rate was noted to decrease to 73.3% to 70% and 53.5% on the 2nd, 3rd, and 4th month respectively. But during the final check-up all 24 subjects (80%) who were able to finish the regimen showed up.

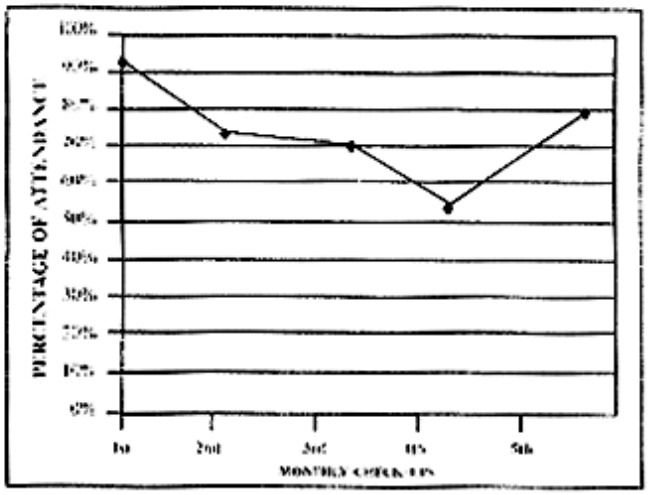

Figure 5. Percentage of Follow-up Patients enrolled in the DOTS at Talomo (South) Dist., Davao City

Among the 24 patients who completed the therapy, 14 (58%) of them showed an immediate improvement with their appetite prior to the first monthly check-up, while 10 (41.6%) had occasional fair appetite during the span of treatment. By the end of 6 months, all of them showed improvement of appetite.

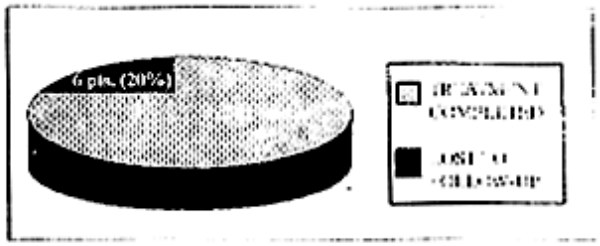

Figure 6. The proportion of PTB patients who completed the short-course therapy and those who were lost to follow-up at the DOTS for different dates at Talomo (South) District, Davao City

Twenty-four subjects who completed the treatment showed an increase in body weight at the time of screening. The average weight gain during the 1st 2 months was 1.7 kg., by the 4th month it was 0.91 kg. and finally by the 6th month it was 1.05 kg.

Among the 24 patients who finished the treatment, a majority of 83% showed occasional cough during the span of the whole treatment followed by a minority of 16.6% with immediate disappearance of cough immediately after the start of therapy. However, at the end of six months, most of 87.5% showed complete disappearance of cough while 12.5 % still had occasional cough.

Of the patients that complained of afternoon rises of temperature, 2 of them had lysis of fever at the 3rd day of medication while the remaining 3 subjects had lysis of fever at the 2nd, 4th and 5th day of treatment respectively. The average lysis of fever was at the day 3.4. Among the 24 patients who completed the therapy, 14 (58%) of them showed an immediate improvement in appetite prior to the first monthly check-up, while 10 (41.6%) had occasional fair appetite during the span of the treatment. By the end of six months, all of them showed improvement with their appetite.

There were no major side effects due to anti-TB drugs used. There were 5 subjects(20.8%) who complained of mild abdominal pain after taking the drugs. However, abdominal pain would last for 5 to 10 minutes and disappeared without any intervention. There was one patient who complained of rashes after taking another brand of Rifampicin on the third month of treatment. The initially taken brand was then resumed with subsequent disappearance of rashes.

DISCUSSION

In 1993, the World Health Organization declared the incidence of Tuberculosis as a global emergency and recommended the implementation of a treatment strategy called Directly Observed Treatment Short Course(DOTS).

The first trial of short course chemotherapy in children was conducted by Abernathy in 1983, where the disease was successfully treated with Isoniazid and Rifampicin given daily for 1 month then twice weekly for 6 months with direct supervision.

Although several studies of a twice or thrice weekly regimen have been reported with positive results, what was used in this study was the daily treatment for 6 months. The reason for such is that in Davao City intermittent anti-TB theraphy is still not widely practiced and being an initial step on DOTS for children in this locality, the researchers decided not to drastically introduce it. Studies have shown that using the intermittent regimen achieves lesser dropouts compared to the daily regimen. A study conducted by Kohn among pediatric students in a New York City high school, revealed that completion of therapy in the intermittent regimen is significantly greater (at about 50%) than that in the daily therapy group (37.6%).

Like most TB patients, majority of the subjects were living in poverty and a congested environment. It also showed that adult household members are the most likely source of infection. Thus, in order for a therapy to be successful, screening and treatment of other household members must be considered to avoid treatment failure.

Presently 39% of children aged between 5-9 years old living in the country's slum is infected with TB. There are about 100,000 children worldwide who may needlessly die from TB every year. Facing such great concern, DOTS in children must be promoted with or without government support. Knowing that funds are scarce for pediatric DOTS, the search for the proper personnel to supervise the drug intake effectively is of great concern so as not to waste precious time, effort and money.

In this study the persons entrusted to do the job were the Barangay Health Workers. Out of the 30 subjects that were enrolled 24 or 80% successfully completed their treatment for 6 months. The success of which could be attributed to the following:

1) The BHWs and the mothers of the patients were properly educated on the aim of DOTS, thus teamwork between them were created. If the mother decided to withdraw from treatment, the BHW is there to convince her to continue.
2) The BHW in charge was living in close proximity with the patient's home, thus easier accessibility.
3) BHWs and the mothers had good raport with each other. The mothers can call them any time to report any adverse reactions from the medication or onset of new diseases, thus, early intervention was instituted.

On the other hand, there were 6 patients or 20% who failed to complete the treatment with the following reasons: two patients transferred residence outside of the study area which resulted in poor contact with the BHW in-charge. Three patients were not able to complete the treatment due to their parents withdrawal. Parents percieved that the medications were doing more harm than good to their children. And finally, one patient discontinued medication as advised by a general practitioner, saying that the subject don't need anymore of such treatment. Although it is true that there are some unpreventable circumstances that may cause such dropouts, proper education and emphasis with regards to the nature of the TB disease, the DOTS strategy, and the consequences of failed treatment for both the BHWs and the mothers can mean better results.

The attendance on the monthly check-ups were noted to be decreasing every meeting. The reasons commonly cited were lack of transportation fee to reach the health centers, patients were in school and some

complained that they were not aware of the date of check-up. Given the fact that the drugs were already given for free, financial problem is not really the issue but it was more of attitude. Proper dissemination of information and giving of special check-up schedules for those in school may improve the attendance rate.

In this study, all of the subjects showed a gradual improvement of appetite and eventually gained weight. But one limiting factor was the lack of adequately balanced diet which is difficult to achieved in low income families. Better nourishment could have presented larger weight gains.

With regards to cough, majority of the subjects had complete relief, but about 12.5% still had occassional cough even after the treatment. This could be due to other causes such as allergy, viral or bacterial infections,or even atypical pneumonitis.

Only a minority of patients (16.6%) complained of fever and were noted to disappear after a few days of treatment.

In general, the anti-TB drugs and its dosages used in this study showed to be effective and safe, having no major side effects save for mild abdominal pain on 5 patients and minor rashes in one.

CONCLUSION

In this study, out of 30 subjects diagnosed with PTB and enrolled in DOTS using the daily regimen for 6 months. 24 or 80% has successfully finished the entire course. The drop-out rate was only 6 or 20%. For those who completed the treatment, there was a significant improvement in the symptoms as evidenced by relief of chronic cough, improved appetite, disappearance of fever and weight gain. Twenty or 66% were males and 10 or 33% were females. The mean age of the subjects was 5.54 years old. Majority of the subjects came from families of low social status and were living in congested environments. All of them claimed to have been exposed to adult PTB patients and 80% of which had their own household as their source of infection. Majority of them (86%) had BCG vaccination previously but still acquired the disease. The signs and symptoms that commonly occured were cough (100%) followed by cervical lymphdenopathy (86.6%), poor appetite (53.5%), poor weight gain (53.5%), weight loss (36.6%) and afternoon rises of temperature (13.3). All of the subjects were classified as PTB III. The number of attendance during the monthly check-ups were also noted to be decreasing as months went by but on the final check-up all 24 patients who completed the treatment were seen. There was no major side effect against the medications and the dosages used.

DOTS is a promising strategy to fight tuberculosis. It is evident in this study that Barangay Health Workers can be good treatment partners and can produce good results.

RECOMMENDATIONS

It is true that the government should allocate funds for such projects in children but due to the present economic instability, inclusion of the children in the NTP is unforeseen. We recommend that there will be a nationwide campaign to encourage individuals and non-government organizations to raise funds and medicines extensively and push thru with DOTS for children. We also recommend a study to be conducted on the effectiveness of a DOTS twice weekly TB regimen in a local setting. If such a regimen will be acceptable and effective in the country, a bigger number of children can be reached by the limited supplies we have with lesser manpower needed. We also recommend frequent educational meetings with the BHWs and the mothers regarding DOTS to ensure lesser dropouts due to misinformation.

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EARLY ONSET SEPSIS IN SMALL FOR GESTATIONAL AGE (SGA) TERM NEONATES

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Abstract: **Small for gestational age (SGA) infants even if they are delivered term are considered high risk neonates. Susceptibility to infection is one of the problems of an SGA infant. A prospective cross sectional study was done (1) to determine the prevalence of early onset sepsis among small for gestational age term neonates, (2) to identify the organism causing early onset sepsis (3) and to determine neonatal and maternal risk factors associated with sepsis.**

Blood cultures were done on SGA term neonates delivered at Davao Medical Center from May 1 - Aug. 31, 1998. Out of the 57 term SGA subjects included in this study, 18 (31.6%) had proven sepsis; 17 (29.8%), probable sepsis; and 22 (38.6%) had no sepsis. Microorganisms isolated were *Staphylococcus epidermidis*, 16 (59.3%), *Staphylococcus saprophyticus*, 5 (18.5%), *Acinetobacter*, 3 (11.1%), *Enterobacter cloacae*, 1 (3.7%), *Escherichia coli*, 1 (3.7%) and *Streptococcus viridans*, 1 (3.7%).

A slightly higher percentage of early onset sepsis was noted among SGA neonates weighing 1,500 -2000g compared to those weighing >2,000g. Sepsis was also found to be higher among female SGA neonates, among those delivered vaginally, in those with meconium stained amniotic fluid and in those whose membranes ruptured 12 hours or more prior to delivery. For the maternal risk factors, sepsis was found to be higher in those whose maternal age are, <20 and >35 years, parity of 0 and >4, in single mothers and in those with less than 2 years interval from previous pregnancy. Higher incidence of sepsis were also noted in mothers with poor obstetric history, hypertension/preeclamsia, and infection. Multiple logistic regression analysis was done and none of the neonatal or maternal risk factors considered was found to be significantly associated with sepsis.

INTRODUCTION

Neonatal sepsis a significant cause of morbidity and mortality. The incidence of sepsis varies from 1 to 10 cases per 1,000 live births depending on geographic area and time frame involved[1]. In our nursery in 1997, sepsis is the leading cause of morbidity and the number three cause of mortality. There are several neonatal and maternal risk factors noted to be associated with neonatal risk factor followed by SGA[2]. Other factors include fatal hypoxia and male sex[3]. Of the maternal factors, peripartum infection, prolonged rupture of membranes[4], antenatal treatment with steriods[5], septic or traumatic delivery, nulliparity and maternal age of >30 were also noted to be associated with sepsis[6].

Several studies have already been done sepsis among low and very low birth weight prematures but literature is scarce regarding sepsis among SGA term neonates, which is also a significant portion of the high risk neonatal population.

This study aims to determine the prevalence of early onset among SGA term neonates.

Specific Objectives:

1. To determine the prevalence of early onset sepsis (proven and probable) among SGA term neonates.
2. To identify the common organism causing early onset among term SGAs.
3. To determine which of the following neonatal factors {weight, sex, manner of delivery, meconium staining of amniotic fluid and timing of rupture of membranes} and maternal risk factors {maternal age of <20 and >35, parity of 0 or >4, unmarried, presence of preeclamsia/ hypertension, poor obstetric history (previous low birth weight infant, history of spontaneous abortions), short interval from previous pregnancy (<2 years) and history of maternal infection} are associated with sepsis in SGA term neonates.

MATERIALS AND METHODS

Patients Entry

All term singleton SGA neonates delivered at our institution from May 1, 1998 to August 31, 1998 were eligible for the study.

Exclusion criteria were as follows: (1) low APGAR scores <5 at 1 minute), (2) meconium aspiration, (3) those with congenital abnormalities, (4) those who are suspected to have congenital viral infections (e.g. TORCH syndrome), (5) polycythemia or hypoglycemia alone in the absence of any other signs and symptoms or laboratory abnormalities suggestive of sepsis.

Keywords: Sepsis in neonates; small for gestational age
*Davao Medical Center, Davao City

Data Collection

Blood culture and CBC were done during the first 24 hours of life and prior to initiation of antibiotics when indicated. Careful aseptic technique was observed by cleansing the skin with 70% alcohol followed by povidone iodine prior to blood extraction. Blood was extracted from two different sites (1 ml from each site) and placed in an aerobic blood culture medium (BACTEC). After incubation at 35°C for 24 hours, blood mixture is streaked on-to blood agar, Bacitracin chocolate agar, MacConkey agar and Gentamicin blood agar plates. After another 24 hours of incubation at 35 degree centigrade, plates were read for microbial growth. Results were released on the third day. Subjects were observed for 72 hours for clinical signs of sepsis. Those who developed sepsis were treated accordingly.

The following neonatal data were collected: name, sex ,birth weight, mode of delivery, presence or absence of meconium staining of amniotic fluid and timing of rupture of membranes. Their respective mothers were interviewed and the following data were gathered: name, age, parity, marital status, obstetric history, number of prenatal visits, interval from previous pregnancy, history of infection at any time during the pregnancy and other illness like preeclamsia/ hypertension.

Definition of Terms

Small for gestational age (SGA) - birth weight belonging to the 10th percentile or less for age of gestation (1500g to 2500g)[7]

Term -38 to 42 weeks by Ballard score (physical and neuromuscular maturity rating)[8]

Early onset sepsis - sepsis occuring before 72 hours of life.

Proven Sepsis - blood culture positive with clinical manifestations of sepsis

Probable Sepsis - blood culture negative but with 2 or more clinical signs and or laboratory abnormalities suggestive of sepsis

Bacteremia - blood culture positive but no clinical manifectations and/or laboratory abnormalities suggestive of sepsis

No sepsis - negative blood culture and no clinical manifestations and/or laboratory abnormalities of sepsis.

Clinical signs and symptoms asssociated with sepsis can be any of the following[9]:

1. general manifestations like hyperthermia (T>38°C), hypothermia (T>36°C), "not doing well", poor feeding, lethargy;
2. respiratory manifestations (dypspnea, apnea, tachypnea, retractions, flaring, grunting, cyanosis);
3. gastrointestinal manifestations (vomiting diarrhea, abdominal distension);
4. cardiovascular manifestations (pallor, cyanosis, mottling, cold, clammy skin, hypotension);
5. hematologic manifestations (jaundice, hepato-splenomegaly, pallor, purpura, bleeding);
6. central nervous system manifestations (irritability, tremors, seizure, hyporeflexia, abnormal moro reflex, irregular respiration, full fontanels).

Laboratory manifestations associated with neonatal sepsis include either of the following[10].

1. leukemia (white blood cell count <9000/cu mm in neonates less than 24 hours of life and <5000/cu mm after 24 hours of life);
2. granulocytopenia (polymorphonuclear leukocyte count < 1300/cu mm) and
3. thrombocytopenia (platelet count <150,000 per cu mm).

Study Design

Prospective, cross sectional study design

Statistical Analysis

Chi-square test and multiple logistic regression analysis were done to determine which of the considered factors were significantly associated with sepsis.

RESULTS

Study Population

Out of the 3,273 total live births during the study period (May 1 to August 31, 1998), 146 were term SGA neonates (4.8%). Fifty-seven (57) or 39% of the term SGA neonates were included in this study (Fig.1).

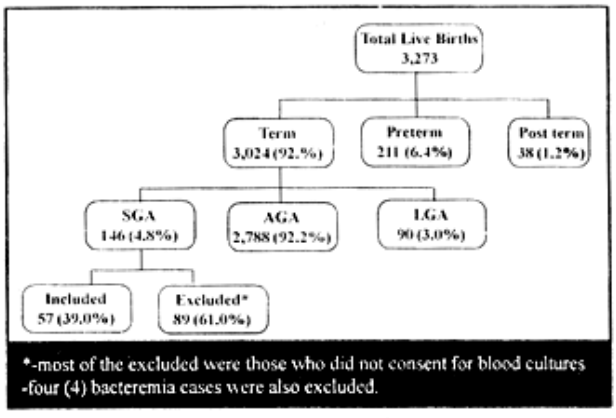

Fig. 1 Breakdown of Total Live Births (May 1- August 31, 1998)

Blood cultures were done on 61 subjects enrolled in this study. Four (4) subjects with positive blood cultures were excluded since these subjects did not show clinical signs and/or laboratory abnormalities suggestive of sepsis (bacteremia cases).

Prevalence of Sepsis among SGA Term Neonates

Out of the 57 subjects, 18 (31.6%) had proven sepsis, 17 (29.8%) had probable sepsis ans 22 (38.6%) had no sepsis (Fig. 2).

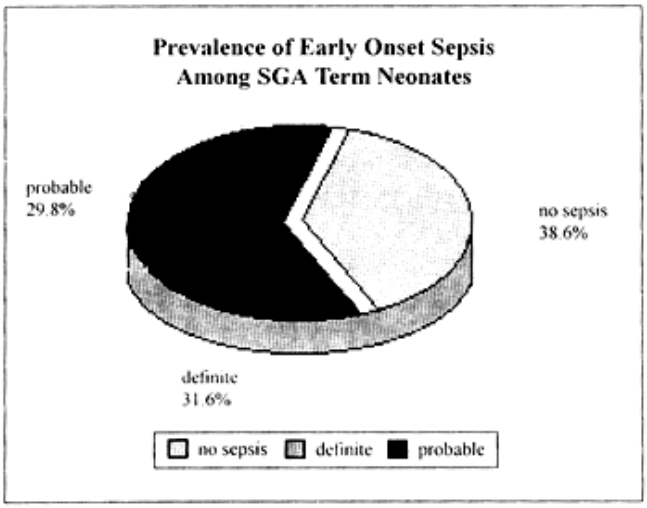

Fig. 2 Prevalence of Early Onset Sepsis Among SGA Term Neonates

Microorganism Isolated

Table 1 shows the microorganisms isolated from the blood: Out of the 27 isolates, 16 (59.3%) were *Staphylococcus epidermidis*; 5 (18.5%) were *Staphylococcus saprophyticus*; 3 (11.1%) were *Acinetobacter*; and one (3.7%) each for *Enterobacter cloacae, Escherichia coli* and *Streptococcus viridans*.

Table 1. List of Microorganisms Isolated

Microorganism	No. of Isolates	Percentage (%)
Staphylococcus epidermidis	16	59.3
Staphylococcus saprophyticus	5	18.5
Acinetobacter	3	11.1
Enterobacter cloacae	1	3.7
Escherichia coli	1	3.7
Streptococcus viridans	1	3.7
TOTAL	27	100

Neonatal Factors

Table 2 shows the characteristics of the study population as to the neonatal factors.

Of the 57 SGA neonates, 32 (56.1%) were males while 25 (43.9%) were females. As to the birthweight of the subjects, the lightest was 1,500.0 g while the heaviest was 2,450.0 g with a mean of 2,122.4 g. Forty-seven (82.5%) were delivered vaginally while 10 (17.5%) were by caesarean section. Only 17 (29.8%) of the subjects had meconium-stained amniotic fluid. With regards to the timing of rupture of membranes, 11 (19.3%) were ruptured 12 hours or more prior to delivery while 46 (80.7%) were ruptured before 12 hours.

Table 2. Neonatal Data

Neonatal Variable	Sepsis* N (%)	No Sepsis N (%)	Total N (%)	P Value
1. Birth weight				
a. 1,500 - 2,000	12 (66.7)	6 (33.3)	18 (31.3)	0.57
b. 2,001 - 2,500	23 (59.0)	16 (41.0)	39 (68.9)	
2. Sex				
a. Male	19 (59.4)	13 (40.6)	32 (56.1)	0.72
b. Female	16 (64.0)	9 (36.0)	25 (43.9)	
3. Manner of delivery				
a. vaginal	29 (61.7)	18 (38.3)	47 (82.5)	0.92
b. caesarean section	6 (60.0)	4 (40.0)	10 (17.5)	
4. Meconium staining of amniotic fluid				
a. Yes	13 (76.5)	4 (23.5)	17 (29.8)	0.12
b. No	22 (55.0)	18 (45.0)	40 (70.2)	
5. Timing of rupture of membranes				
a. >12 hours	8 (72.7)	3 (27.3)	11 (19.3)	0.39
b. <12 hours	27 (58.7)	19 (41.3)	46 (80.7)	

*sum proven and probable sepsis

A slightly higher percentage of early onset sepsis was noted among SGA neonates whose weight is between 1,500-2,000 g as compared to SGA neonates weighing more than 2,000g. Sepsis among males was a little lower than females. Sepsis among those in vaginal delivery was a little higher than those delivered in caesarian section. Sepsis was also found to be higher among SGA neonates with meconium-stained amniotic fluid and in those whose membranes ruptured 12 hours or more prior to delivery. Differences however, were not statistically significant (p values > 0.05).

Maternal Factors

Table 3 shows the maternal factors commonly associated with the delivery of SGA and the prevalence of sepsis.

Sepsis was noted to be higher among mothers

Table 3. Maternal Data

Neonatal Variable	Sepsis* N (%)	No Sepsis N (%)	Total N (%)	P Value
1. Birth weight				
a. 1,500 - 2,000	12 (66.7)	6 (33.3)	18 (31.3)	0.57
b. 2,001 - 2,500	23 (59.0)	16 (41.0)	39 (68.9)	
2. Sex				
a. Male	19 (59.4)	13 (40.6)	32 (56.1)	0.72
b. Female	16 (64.0)	9 (36.0)	25 (43.9)	
3. Manner of delivery				
a. vaginal	29 (61.7)	18 (38.3)	47 (82.5)	0.92
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5. Timing of rupture of membranes				
a. >12 hours	8 (72.7)	3 (27.3)	11 (19.3)	0.39
b. <12 hours	27 (58.7)	19 (41.3)	46 (80.7)	

whose ages are ,<20 and >35 years old, parity of 0 and >4, unmarried, <2 years interval from previous pregnancy, poor obstetric history, with hypertension/preeclamsia and in those with infection. None of the maternal risk factors considred was significantly different between neonates with early onset sepsis snd those without sepsis.

DISCUSSION

The susceptibility of small for gestational age (SGA) infants to infection is attributed to their depressed immune system. Papadatos et al found that serum Ig G concentration, which is a significant host defense property, is appreciably lower in term SGA neonates than in their AGA peers [1]. Shapiro et al studying the complement system of newborn infants, found lower C3 values, impaired polymorphonuclear leucocytic chemotaxis and bactericidal capacity among SGA infants when compared to their AGA controls[12].

Neonatal septicemia had been classified as either early onset or late onset. Placzek et al preferred to group the cases according to onset before or after 48 hours of life[13]. Hickey and McCraken define early onset as sepsis occuring in the first 4 days of life [14]. Baker et al set the cut off between 5 - 7 days [15]. Vesikari has presented another grouping which includes very early onset (<24 hours of life), early onset (between 24 hours and first week of life), and late onset (during the 2nd week of life)[16]. Gotoff, on the other hand, believed that although the term early onset sepsis has been used to refer to neonatal infections ocurring as late as the 1st week of life it should be restricted to those infections with a perinatal pathogenesis, the usual onset of which occurs within 72 hours [17]. This study used the 72nd hour as the cut off because of the difficulty in holding patients beyond three days if they are apparently well. The subjects who were discharged after 3 days were advised to follow up within one week and none has develop sepsis.

SGA term neonates accounted for about 4.8% of the total live births and 39% of them were included in this study. Out of the 35 (61.4%) subjects who were noted to have sepsis, 18 (51.4%) had positive blood culture with clinical signs of sepsis while 17 (48.6%) had negative blood cultures but were clinically symptomatic.

The high prevalence of sepsis among SGA neonates in this study parallels the study done by Christo wherein the records of 26 neonates with Acinetobacter sepsis during the period 1986-1990 were reviewed. Twelve (12) or 46% of the subjects were SGA neonates while the rest were low birth weight prematures[18].

Although the gold standard for the diagnosis of sepsis is a positive blood culture, a negative blood culture does not necessarily rule out sepsis[19]. Experience have indicated that it is possible for a blood culture result to be negative even when a neonate has bacterial infection. The increased number of culture negative clinical sepsis can be due to limitations in blood culture methods and to intrapartum antibiotics use in about 30% of the mothers. A positive blood culture on the other hand, may not always establish the diagnosis since cultures may be contaminated or may result from transient bacteremia secondary to focal infection [20]. Because of the uncertainty in differentiating whether it is a significant isolate or just a contaminant, subjects with positive blood cultures but clinically asymptomatic were included.

The pathogens responsible for early onset sepsis generally reflect the predominant vaginal flora of the pregnant woman. The organism usually include Group B *Streptococcus* , *H. influenzi, L. monocytogenes, S. pneumonia E. coli* and *Klebsiella spp* [24]. Different centers however, have different predominating organism. In a study by Versikari et al, the causative organism for early onset sepsis identified were *Staphylococcus aureus* (34%), *E coli* (24%) and Group β *Streptococcus* (14%) [25]. In the study done by Holgado et al on early onset sepsis secondary to unprepared delivery, the following organism were identified for definite/proven sepsis, *Enterobacter cloacae, Staphylococcus saprophyticus and Pseudomonas putida* [26]. In this study, *Staphylococcus epidermidis* is the most common followed by *Staphylococcus saprophyticus, Acinetobacter, Enterobacter cloacae, Escherichia coli and Streptococcus viridans*. This is similar to a study done by Alarilla et al on premature rupture of membranes and neonatal sepsis wherein *Staphylococcus* was also the most common organism isolated and was seen in 6 out of 11 (64%) patients[27]. In Malaysia, Malik et al found that coagulase negative *Staphylococci* is also the most common followed by Group B *Streptococcus* and

Klebsiella[23].

Coagulase negative *Staphylococci* are part of the normal skin flora and were traditionally classified as "non pathogens" and accordingly, their isolation from clinical specimens was attributed to faulty technique and resultant "contamination" [29]. However, recent studies have shown that *Staphylococcus epidermidis* is an important causative agent in neonatal sepsis. The possible emergence of coagulase negative *Staphylococci* as early onset pathogens can be due to increased intrapartum treatment with antibiotics (primarily Ampicillin) to which the organisms are usually resistant.

As to the characteristics of the study population, prevalence of sepsis among SGA neonates weighing <2,000g (66.7%) compared to those weighing >2,000 g (59.0%) is almost the same. These results support the findings of Stoll, et al in their study on very low birth weight neonates that sepsis is more associated with age of gestation rather than birth weight [22].

Sex as a factor was found to be not statistically significant in relation to sepsis. In this study, 64.0% of the female subjects developed sepsis while 59.4% of the male subjects had sepsis. These results do not support the findings of several studies which concluded that male sex increases the risk of sepsis by as much as fourfold. They attributed the male disadvantage to a gene locus in the X chromosome which is involved in the synthesis of immunoglobulin [21].

There is almost the same prevalence of sepsis among SGA neonates delivered vaginally (61.7%) and in those delivered by caesarean section (60.0%). These results do not support the findings by Stoll et al that babies delivered vaginally are significantly more likely to have early onset sepsis than those born by caesarean section [22]. It is assumed that neonates delivered vaginally may more likely be contaminated with vaginal flora during labor and delivery.

This study used the 12th hour as the cut off for PROM based on the study done by Panlilio et al wherein it was noted that PROM of 12 hours produces morbidity of 0.6% and that PROM of > 12 hours increases the morbidity by about ten fold [22]. Out of the 11 (19.3%) subjects whose membranes ruptured <12 hours prior to delivery, 8 (72.7%) had sepsis. For the subjects whose membranes ruptured <12 hours, only 58.7% had sepsis. Results support the findings of Panlilio et al, however, that difference between neonates with early onset sepsis and those without sepsis is not statistically significant.

Maternal factors considered in this study are factors which are usually associated with the delivery of SGA neonates.

Soma and colleagues investigated demographic maternal characteristics for early onset sepsis among 113 cases and 347 matched controls. The characteristics which were significantly different in the two groups included age (mothers <20 or >30 years old), parity (nulliparous women and women with >3 pregnancies), minimal or no prenatal checkup, intrapartum fever and prolonged labor [31].

Results of this study support the findings of Soman et al as far as the following factors are concerned: maternal age of <19 and >35 and parity of 0 and >1 but differences are not statistically significant. Other factors considered like less than 2 years interval from previous pregnancy, poor obstetric history and hypertension/preeclamsia were noted to have higher percentage values but nevertheless, differences were still not statistically significant.

Presence of hypertension/preeclamsia increases the risk of neonate to develop sepsis. Neutropenia is often present at birth in infants born to mothers with preeclamsia and is most likely present in utero. Doron et al did a study on neutropenic infants of mothers with preeclamsia [33]. They have found that although the maternal and obstetric risk factors for infection were less common in the group with neutropenia, rates of proven or presumed early onset sepsis were higher. Sepsis was proven in 6% of infants with neutropenia and none in those infants without neutropenia. Another reason why neonates born to preeclamptic mothers are prone to infection is the fact the maternal Ig G is actively transferred across the placenta to the fetus in the last trimester. It has been postulated that poor placenta function due to hypertension/preeclampsia results in both poor intrauterine fetal growth and postnatally, an increased risk of infection.

Maternal infection at any time during pregnancy may result in bacteremia which increases the risk of transplacental transmission of the infection. It is also speculated that single mothers are less likely to seek medical attention during pregnancy due to embarassment. Thus, undetected problems (i.e. infection) can be common.

CONCLUSION AND RECOMMENDATION

Results of the study indicate that SGA term neonates will more likely have early onset sepsis. *Staphylococcus epidermidis* is the most common isolate. None of the considered neonatal and maternal factors was significantly associated with early onset sepsis.

Considering the high prevalence of early onset sepsis on term SGS neonates, it is recommended that routine sepsis evaluation be done on all term SGA neonates regardless of maternal risk factors especially in our setting where incidence of sepsis is still high.

This study has been limited to a short duration and number of subjects. It is therefore recommended that another study be done on a bigger population and the subjects be appropriately matched with adequate for gestational age (AGA) neonates as control.

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