THE PREVALENCE AND SOME CLINICAL CHARACTERISTICS OF BACTERIAL INFECTIONS IN PRETERM NEONATES HAVING RESPIRATORY DISTRESS AT KENYATTA NATIONAL HOSPITAL

BY

AWUOR CHRISTINE YUKO, MBCHB (NAIROBI 1984)

A DISSERTATION PRESENTED IN PART

FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE (PAEDIATRICS)

AT THE UNIVERSITY OF NAIROBI

1990

DEDICATED.

TO

MY GRANDPARENTS DORSI ONONO AND SIMEON NDINYA.

A N D

TO MY HUSBAND JAMES AND CHILDREN

ELIZABETH AND DORSI.

DECLARATION

I certify that this dissertation is my own original work and has not been presented for a degree in any other university.

Signed.................................

Dr. Awuor Christine Yuko

This dissertation has been submitted for the examination with our approval as university supervisor.

Signed.................................

Dr. A.O. Wasunna

MBCHB (NRB) M. Med Paed (Nrb)

Senior Lecturer

Dept. of Paediatrics

University of Nairobi

Signed.................................

Professor I. Wamola

(MSC PHD.)

Department of Medical Microbiology

University of Nairobi

TABLE OF CONTENTS

LIST OF ABBREVIATIONS AND EXPLANATIONS

1. AB   Antibiotics

2. ANC   Antenatal Clinic

3. BWT   Birth weight

4. C/S   Caesarian Section

5. DROM   Duration of rupture of membranes

6. ESR   Erythrocyte sedimentation rate

7. GBS   Group B Beta hemolytic streptococcus

8. PMN   Polymorphonuclear cells

9. RD   Respiratory distress

10. RDS   Respiratory distress syndrome

11. SVD   Spontaneous vertex delivery

12. WBC   White blood cell count

For purposes of this study immature polymorphonuclear cells include band cells, metamyelocytes and promyelocytes.

The term suspicious and probably infection are used interchangeably.

SUMMARY

Fifty eight preterm neonates having respiratory distress within the first forty eight hours of life were studied. Seven had positive blood cultures for bacteria giving a prevalence rate for infection of 12.1%.

Nineteen infants (32.8%) were suspected to have sepsis based on clinical and laboratory criteria. The remaining thirty two (56%) had no evidence of sepsis.

These infants were studied with respect to their maternal antenatal clinic attendances, maternal fever, duration of rupture of membranes, liquor characteristics and mode of delivery. Also studied were their clinical examination findings, degree of respiratory distress, hematological, radiological and bacteriological characteristics.

Seventy six percent (76%) of the mothers were below 25 years (age range 15-45 years). A majority of the mothers (65.5%) attended antenatal clinics. Twenty eight (42.2%) of the mothers had ruptured membranes for less than eleven hours before delivery while 13 (22.4%) and 17 (29.4%) had ruptured membranes between eleven and twenty four hours, and for greater than 24 hours respectively.

Forty six infants (79.3%) were delivered in clear liquor; of these 6 (13.1%) had positive bacterial cultures. Seven infants (12.1%) delivered in offensive liquor had suspected infection. Of the five (8.6%) delivered in meconium stained liquor, two had some evidence of infection.

Spontaneous vertex delivery was the commonest mode of delivery in all the three groups of infants; occurring in 5 (71%) of the infants with proven sepsis, 14 (73.7%) of the infants with

suspected sepsis and 24 (75%) of those with no sepsis. None of the infants delivered by caesarian section had confirmed sepsis. Infants delivered by breech extraction had either suspected or confirmed sepsis.Maternal fever and infant Apgar scores did not appear to affect the outcome of the infants in this study.

On hematology the ratio of immature to total polymorphs correlated best with sepsis as higher values of more than 0.2 were seen mainly in infants with confirmed sepsis.Total white cell counts were also useful since normal range of counts were only seen in infants with no evidence of sepsis.

Infant chest radiology helped eliminate other causes of respiratory distress like pneumothorax, congenital heart disease and lung collapse. None of the infants with confirmed sepsis had normal radiological findings.

The organisms isolated were of high virulence and multiple antibiotic resistance. Amikacin and cefotaxin enjoyed higher sensitivity rates of 71.4% and 88.8% respectively.

INTRODUCTION

Early onset bacterial infection commonly presents as respiratory distress in the newborn preterm infant (1,2,3). This may mimic several neonatal problems in particular respiratory distress syndrome, aspiration pneumonia, transient tachypnea of the newborn, pneumothorax, pneumomediastinum, congenital heart disease, persistent foetal circulation and maternal drug addiction withdrawal syndrome (1) . Whereas most of these conditions can be distinguished from sepsis using careful history, clinical examination, radiological and laboratory data, the clinician is in a dilemma when attempting to distinguish respiratory distress syndrome from early onset bacterial septicaemia (2,3,4,5)

In the preterm neonate, the clinical presentation of respiratory distress is often acute (6,7) with an early postnatal age of onset, reaching its peak within 48 to 72 hours and in the absence of assisted ventilation the infant either succumbs or improves gradually within the next one week (1,8,9). It is common among the infants of birth weights between 1200 gms to 2000 gms and gestation of 30 to 35 weeks. The common presentation is that of rapid grunting respirations, significant chest retractions, occasional rales and fluid retention with oedema. (8,9,10,11). Chest radiographs in RDS may show diffuse reticulogranular pattern typical of atelectasis with clearly visible air bronchograms (12). Autopsy finding is principally that of dilated terminal bronchi lined by eosin staining hyaline material (now regarded as a non specific response to the lungs to various injuries (6,7,8,10).

Early onset bacterial infection has a mean age of onset of 20 hours. In the preterm neonates it presents as an overwhelming multisystem disease with respiratory distress that is characterized

by tachypnoea, rales, and chest wall retractions. Apnoea, lethargy, weak cry and poor feeding are not uncommon. Terminally these infants manifest features of disseminated coagulopathy. This form of infection is usually acquired in the intrapartum period (1,2,13,14).

Predisposing factors to intrapartum infections include prolonged rupture of membranes, maternal fever, maternal genital tract infections and premature labour (1,13,15). Organisms commonly associated with such infections include group B streptococcus, E. coli, staphylococcus aureus, staphylococcus epidermidis, hemophilus influenza, streptococci, bacteroides clostridia and peptococcus (13,14,15,16,17)

Differentiating the infected preterm neonate presenting with respiratory distress from that having RDS poses a major problem (2). In an attempt to distinguish RDS from early onset GBS infection Ablow and Driscoll (4) described the following clinicopathological features in the infected neonate which they considered as the main differentiating points,.

.   Duration of rupture of membranes greater than 24 hrs
     before delivery.

.   Presence of gram positive cocci on gastric aspirate
     within 3 hours before any gastric lavage.

.   Occurrence of apnoea in the first 24hrs of life.

.   Generation of low peak inspiratory pressures during
     ventilation.

However, Menke et al (5) found no difference between the two groups of infants with respect to incidence of apnoea in the first 24 hours and they reported shock as a terminal event rather than an early feature of sepsis. The presence of gram positive cocci was

difficult to interpret. Boyle et al (3) maintained that the two clinical conditions GBS and RDS were so similar clinically and radiologically that to distinguish them one would need a battery of clinical and laboratory investigations. He concluded that the presence of polymorphonuclear cells within gastric aspirate was a risk sign for sepsis. Alistair (2) emphasized the value of quick laboratory tests used in combination for diagnosis of sepsis namely:-

.   Band to total neutrophil ratio > 0,.2

.   Latex C. reactive protein +ve greater than 0.8 mg/dl

.   ESR > 15 mm / hour.

.   Latex haptoglobulin +ve   25.

In this background of conflicting reports Rodwel et al. (18) added to the confusion by reporting the use of white cell indices and morphology to create a hematological scoring system whereby they gave a score of one for each of the following parameters:

a)   Abnormal total leucocyte counts.

b)   Abnormal total neutrophil counts.

c)   Elevated immature polymorphonuclear cell counts.

d)   Ratio of immature to total PMN > 0.3.

e)   Ratio of immature to total WBC > 0.2.

f)   Platelet counts < 150,000/ mm3

They found that a score of greater than 3 identified 26 out of 27 infants with sepsis (sensitivity 96%) and a score of greater than 2 was highly predictive of sepsis. They concluded that this is a practical and readily available criteria for diagnosing sepsis.

Acute phase reactants like c-reactive protein, fibrinogen, haptoglobulin, acid glycoprotein and erythrocyte sedimentation rate have also been used in combination with infant clinical

picture and white cell count to diagnose sepsis (19,20). However, the most valid method of diagnosing systemic bacterial infection still remains the isolation of microorganisms from a significant source such as blood, urine, cerebrospinal fluid or from body fluids of the peritoneum, pleura, joint and middle ear, or from tissues like bone marrow, spleen and liver. Isolates from stool, throat and umbilicus merely indicate colonization and do not establish the presence of acute infection (2,13)

In the absence of clearcut diagnostic criteria (clinical and radiological), there has been a tendency to treat infants presenting with respiratory distress for presumed sepsis with broad spectrum antibiotics often crystalline penicillin and gentamicin. (personal observations.)

This persistent high antibiotic pressure in the neonatal units poses the danger of selective proliferation of virulent, resistant strains of bacteria. An additional problem is the emergence of other microorganisms that have cross resistant pattern to similar drugs. This practice not only predisposes the premature infant to drug toxicity (eg, ototoxicity from gentamicin) but also escalates the costs of treating such infants, the latter being a real financial burden especially to developing countries.

In review of the literature (2, 3, 4, 5,), it would appear that the majority of infants presenting with respiratory distress are not infected. Direct figures to support this impression are, however, largely lacking.

This study aims to find out how many of such infants are septicaemic and whether the infected infants have any distinctive clinical or laboratory data.

HYPOTHESIS

The prevalence of bacterial sepsis among preterm infants presenting with respiratory distress in the first 48 hours of life is less than 20% at KNH.

OBJECTIVES

1. To determine the prevalence of bacterial infection in preterm infants presenting with respiratory distress in the first 48 hours of life.

2. To describe some of the clinical and laboratory characteristics of such infants.

MATERIALS AND METHODS

Study Area:

Newborn unit Kenyatta National Hospital

Study Design

Descriptive study.

Study Factor:

Preterm neonates (less than 37 weeks of completed gestation) Presenting with respiratory distress at birth.

Population

Sample: A total of Fifty eight infants with clinical features of respiratory distress were recruited. This study aimed at studying

approximately 60 infants. This sample size was arrived at using the formula.

$$N = Z^2 . 1 - x. \ p \ (1-p)$$
$$\overline{}$$
$$d^2$$

Where

N = Minimum sample size

P =   Prevalence = 19.5%

d =   degree of precision = 0.1

Confidence level = 100 (1-5%) = 95%

Therefore

$$N = \frac{(1.96)^2 \ x \ 0.195 \ x \ 0.805}{(0.1)^2}$$

N =   60

SUBJECT SELECTION

Inclusion Criteria

Presence of all three of the following

. Preterm infant - gestation less than 37 weeks.

. Apgar scores equal to or greater than 5 at 5 minutes.

. Respiratory distress defined by three or more of the following.

a)   Respiratory rate equal to or greater than 60\min.

b)   Retraction score of 4 or more as defined by Silverman (20).

c)   Cyanosis with or without supplemental oxygen.

Exclusion Criteria

. Evidence of birth trauma.

. Severe asphyxia - Apgar scores less than 5 at 5 minutes.

. All patients born outside the Kenyatta National Hospital

Maternity Unit and admitted into the Neonatal unit (BBA).

. Babies weighing less than 1000 gms.

. Clinical and laboratory evidence of any of the other causes of respiratory distress mainly, pneumothorax, diaphragmatic hernia, severe congenital malformations, severe haemorrhage and infants of diabetic mothers.

DATA COLLECTION

This study was conducted from April through to September 1989.

Methods of Data Collection

Upon recruiting the infant into the study, the time of birth, onset of respirating distress, time of admission into the newborn unit and any prior administration of antibiotics to infant or mother were recorded.

Maternal data

Maternal data regarding obstetric history, antenatal and perinatal events were recorded in standard proforma (Appendix II).

Infant data

. Infant gestation was assessed by the Dubowitz and Dubowitz scoring system (21) and compared to the maternal last menstrual period (LMP). Where the mother was not aware of her LMP, or where there was a difference of more than two weeks, the former was preferred for the purposes of this study.

. Physical examination was carried out by the author and the findings recorded in a standard proforma (Appendix III)

BACTERIOLOGY

A peripheral vein was used to obtain blood. Puncture site was cleaned sufficiently with surgical spirit and then wiped with tincture iodine.

2 mls of blood was drawn, and this was divided into two parts (1 ml each) and put into aerobic and anaerobic culture media. Each containing 10 mls of brain heart broth. Specimens were delivered to the laboratory as soon as possible where they were incubated at 37oC. The first subcultures were done in the first 48 hours and then later at 8 days in sheep blood agar, chocolate agar and Maconkay media. Irrespective of the bacteria obtained, if pure growth was obtained in the two bottle system the organism was regarded as significant.

Hematology

In the same sitting 0.2 mls of blood was drawn into a sequestrene bottle and delivered to the hematology laboratory within 6 hours. The parameters studied included hemoglobin, total white cell counts, nucleated red cells, absolute mature polymorphs, absolute immature polymorphonuclear cells, platelet counts, the presence of toxic granulation, and degenerative changes.

The white cells series were characterized as described by Reich and Deykin (22) and reference values of Manroe et al. (23) used.

Corrected white cell count was calculated using the formula.

100/(100 + NRBC) x WBC = corrected WBC.

NRBC = Nucleated red blood cells.

A chest radiograph was performed on each of the infants enrolled

with the study within 24 - 48 hours. Repeat chest radiographs were not possible due to various technical problems at the time of the study.

Classification of the Infants Into Infection Group

All infants were classified retrospectively into three main groups depending on probability of infection.

1   Proven sepsis:- Presence of positive culture from blood.

2. No sepsis

    a)   Negative blood culture

    b   Normal Infant hematology

    c)   Normal chest radiographs

3. Probable (suspicious) sepsis.

Negative blood cultures but with two or more of the following.

    A.   Hematological changes suggestive of sepsis.

    B.   Physical findings suggestive of sepsis,

       namely any of:

       i)   hepatosplenomegaly.

       ii)   Petechiae and jaundice

       iii) foul smelling at birth

       iv) Extremes of temperature despite incubator care.

       v)   Repeated apnoeic attacks.

    C.   History suggestive of maternal infection.

       i)   Maternal fever

       ii)   Maternal pelvic discharge + treatment.

       iii) Maternal dysuria.

    D.   Other factors predisposing infant to infection

       namely:-

      i)   Prolonged rupture of membranes (>24 hrs)

      ii) Prolonged labour

      iii) Amnionitis.

Research Instruments

- A timer

- A non stretchable tape measure

- A stethoscope.

- Gauge 23 and 25 scalp vein needles.

- Gauge 21 needles.

- 2 cc syringes.

- Cotton swabs.

- Surgical spirit and tincture iodine

- Disposable gloves.

- Sequestrene bottles

- Blood culture medium

- Portable X-ray machine and X-ray films

DATA ANALYSIS

Where applicable data was analyzed by

1. Nominal scale data both unordered and ordered multi-chotomous scale.

2. Histograms

3. Simple graphical illustrations of trends especially white cell indices.

4. Tests of specificity, sensitivity, positive predictive and negative predictive value and efficiency as defined below.

4.1 Sensitivity = How frequently the test is positive if the disease is present

Sensitivity = $\dfrac{\text{True positives}}{\text{All with disease}}$ = $\dfrac{a}{a+c}$

4.2 Specificity = How frequently the test is negative if the disease is absent.

Specificity = $\dfrac{\text{True negatives}}{\text{All without disease}}$ = $\dfrac{d}{b+d}$

4.3 Positive predictive value = How frequently the disease is present if the test is positive.

Positive predictive value = $\dfrac{\text{True positives}}{\text{all screened positive}}$ = $\dfrac{a}{a+b}$

4.4 Negative predictive value = how frequently the disease is absent if the test is negative.

Negative predictive value = $\dfrac{\text{True negatives}}{\text{all screened negatives}}$ = $\dfrac{d}{c+d}$

4.5 Efficiency - How frequently the test predicts positives correctly

e.g. the false positives and false negatives are excluded.

Efficiency = $\dfrac{a+d}{a+b+c+d}$

5. Chi square and fishers exact test.

For these tests infants with proven sepsis were compared to those with no sepsis, and also those with sepsis (proven and probable) were compared to those with no sepsis.

RESULTS

A total of 58 preterm infants with respiratory distress were recruited into the study. Seven infants had positive blood cultures giving infection prevalence rate of 12.1%.

Nineteen infants (32.8%) were suspected to have infection based on clinical and laboratory characteristics.

The remaining thirty (55%) had no evidence of sepsis.

SECTION 1 - MATERNAL CHARACTERISTICS

Maternal Age

The maternal age ranged between 15 years to 45 years
with a mean age of 24 years. This distribution is
shown in figure I, and for statistical analysis the
figures are shown in table 1.

Table I. Maternal Age vs Infant Infection Status

Sepsis Status

Maternal Age	Sepsis Yes no.	%	Sepsis Probable no.	%	Sepsis No no.	%	Total no.	%
< 25Yrs	6	(88.7)	15	(79)	20	(62.5)	41	(76)
> 25 Yrs	1	(14.3)	4	(21)	12	(37.5)	17	(24)
Total	7	(100)	19	(100)	32	(100)	58	(100)

Fourty one (76 %) of mothers were equal or less than 25 years of
age. Six (85.7%) of infants with proven sepsis were delivered to
mothers equal to or below 25 years compared to twenty (62.5 %)
of mothers whose infants had no evidence of sepsis. When this
was subjected to statistical analysis there was no significant
relationship (p value , o.24.).

When all the infected infants (proven and probable sepsis) were
compared to those with no evidence of sepsis there was no
significant difference in infection rate between mothers less
than 25 years and those greater than 25 years (X2 1.53,
P value 0.22, Odds ratio 2.52 and 95% confidence limit of .65
to 10.1).

FIGURE I.
MATERNAL AGE DISTRIBUTION VERSUS INFANT INFECTION STATUS

NUMBER

MATERNAL AGE RANGE (YRS)

NO SEPSIS   SUSPECTED SEPSIS   CONFIRMED SEPSIS
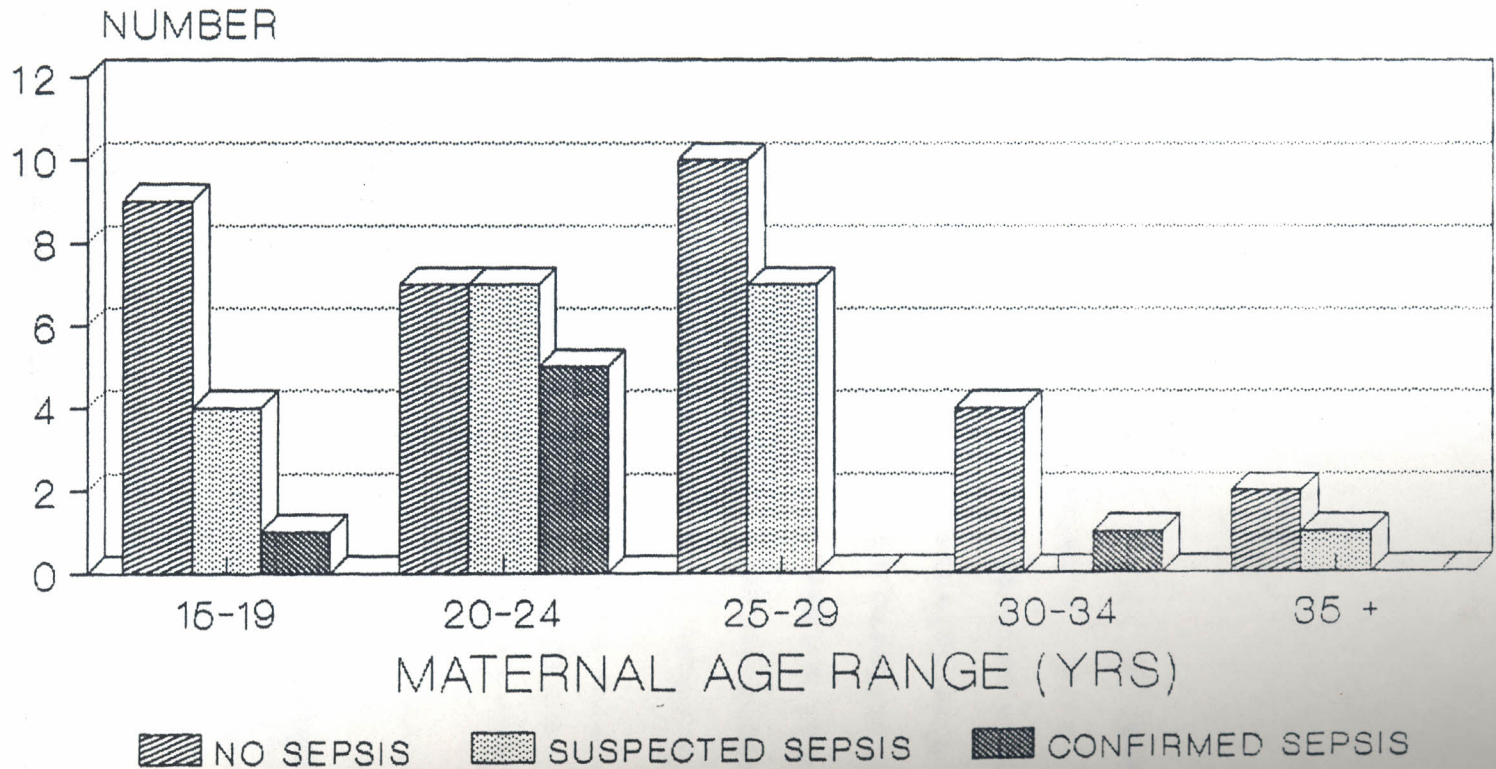
ANTENATAL CLINIC ATTENDANCE

Thirty eight (65.5%) of the mothers attended antenatal clinics at any one time of their pregnancy and twenty (34.5%) did not. This is shown in table II.

Table II - Antenatal Clinic Attendance versus Infant Infection
     Status

Antenatal clinic attendance	Sepsis Yes No. (%)	Sepsis Probable No. %	Sepsis NO No. %	Total No. %
Yes	3 (43)	12 (63.2)	23 (72)	38 (65.5)
No	4 (57)	7 (36.8)	9 (28)	20 (34.5)
Total	7 (100)	19 (100)	32 (100)	58 (100)

Twenty three (72%) of mothers who attended antenatal clinic delivered infants with no evidence of sepsis compared to three (43%) of mothers who attended ANC and their infants had positive blood cultures. But this was not statistically significant.

Also when infants with proven and probable sepsis were compared to those with no infection there was no statistical significance ($X2$ 0.73, P value .39, odds ratio 0.5, and 95% confidence interval of .15 to 1.8.).

MATERNAL PARITY (in terms of live births)

Thirty seven mothers (64%) were between para 0-1 while eighteen (31%) were between para 2 and 3, and three (5.2%) of the mothers were para 4 and above.

None of the three mothers who were para 4 and above had infants with proven sepsis.

MATERNAL FEVER

Only four of the fifty eight mothers (6.9%) had fever. One had history of dysuria, while two were being treated for meningitis and one the cause was not known. None of their infants had proven infection although three had suspicious infections.

Of the mothers being treated for meningitis one infant had hepatosplenomegaly and a purpuric rash.

DURATION OF RUPTURE OF MEMBRANES.

Rupture of membranes during 2nd stage and at c\s was designated 0 hours. Those who underwent c/s but had ruptured membranes earlier were designated according to the actual time of rupture. In this study the longest duration of rupture of membranes recorded was 240 hours (10 days).This distribution is shown below in table III.

Table III   Duration of Rupture of Membrane Versus Infant Infection Status

Duration of membrane rupture	INFANT Sepsis Proven No. %		INFECTION Probable No. %		STATUS No Sepsis No. %		Total No. %	
0-11hrs	5	(71.4)	1	(5.2)	22	(68.8)	28	(48.2)
12-23hrs	2	(28.6)	7	(36.9)	4	(12.5)	13	(22.4)
24+ hrs	0	(0)	11	(58)	6	(18.8)	17	(29.4)
Total	7	(100)	19	(100)	32	(100)	58	(100)

Twenty eight (50%) of the mothers had ruptured membranes within the first eleven hours from delivery and seventeen (30%) had ruptured longer than 24 hours. None of the infants whose membranes had ruptured forlonger than 24 hours had proven infection although eleven of them (65%) had probable infection. When the infants with proven and probable infection are combined the relationship between duration of membrane rupture and infection is statistically significant (p value 0.002.).

MATERNAL AND CHILD ANTIBIOTIC USE.

Prior administration of antibiotic to the infant had no influence on the outcome of the infant, although antibiotic administration to the mother had a significant influence on the outcome of the infant as indicated in table IV and table V .

Six out of seven (85.7%) of the infants with proven sepsis had antibiotics prior to blood culture examination and twelve out of nineteen (63%) of infants with probable infection had prior antibiotics, this is shown in figure IV below.

Table IV.   Infant antibiotic use vs infant infection status.

Infant Infection Status

Anti-biotic given	Sepsis Yes No.	%	Sepsis Probable No.	%	Sepsis No No.	%	Total No	%
Yes	6	(85.7)	12	(63)	17	(54.1)	35	(60.2)
No	1	(14.3)	7	(37)	15	(45.9)	23	(39.8)
Total	7	(100)	19	(100)	32	(100)	58	(100)

From Table IV thirty five (60.2%) of the infant had received antibiotics prior to examination compared to twenty three (39.8%) who had not received any antibiotics.

Prior antibiotic administration to the infant before blood culture examination had no significant effect on the infection status (p value 0.121) when the proven and not septic infants are compared, and (p value 0.33) when septic infant (proven and probable) are compared to those with no evidence of sepsis.

Prior antibiotic administration to the mother had a statistically significant protective effect to the infant, this is evident when the mothers whose infants had proven infection were compared to those whose infants had no infection (p value 0.0076). This distribution is shown in table V.

Table V   Maternal Antibiotic Use vs Infant Infection

Status

Infant Infection Status

Mat. Anti-biotic use	Sepsis proven		Sepsis Probable		Sepsis No		Total	
	No	%	No	%	No	%	No	%
Yes	0	(0)	10	(57)	18	(56.6)	28	(49.3)
No	7	(100)	9	(47)	14	(43.4)	30	(50.7)
Total	7	(100)	19	(100)	32	(100)	58	(100)

However when the infants with suspected sepsis are combined with those with proven sepsis the protective effect is no longer statistically significant (p value, 0.28).

From table V, this protective effect of maternal antibiotic administration is further exemplified by the fact that of all the children who had positive blood cultures, non of their mothers had been given antibiotics, whereas eighteen (56.6%) of the mothers who received antibiotic had infants without any evidence of sepsis.

LIQUOR CHARACTERISTICS

Liquor was either clear, offensive or meconium stained.

From Table Vi, it is evident that having clear liquor did not protect the infants from having subsequent sepsis as six out of seven infants (85.7%) with proven sepsis had clear liquor.

Table Vi: Liquor Characteristics Vs Infant Infection

Infant Infection Status

| | Sepsis | | | | Not Septic | | Total | |
Liquor	Proven No.	%	Probable No.	%	No.	%	No.	%
Clear	6	(85.7)	11	(58)	29	(90.6)	46	(79.3)
Offensive	0	(0)	7	(36.8)	0	(0)	7	(12.1)
Meconium Stained	1	(14.3)	1	(5.2)	3	(9.4)	5	(8.6)
Total	7	(100)	19	(100)	32	(100)	58	(100)

a) Majority of infants fourty six (79.3%) were delivered in clear liquor and of these twenty nine (63%) had no evidence of infection while eleven (24%) had probable infection and six (13%) had proven infection.

b) Seven infants (12.1%) were delivered in offensive liquor and all had probable infection. Six of these infants had prior antibiotics before blood culture examination was done.

c) Five infants (8.6%) were delivered in meconium stained liquor, of these three (10%) had no evidence of infection and the remaining two, one had proven infection with beta hemolytic streptococcal septicaemia (see appendix I) while the other had probable infection.

All the infants delivered in meconium stained liquor had birth weights less than 1600 gms.

MODE OF DELIVERY

Delivery was either by spontaneous vertex delivery, caesarian section or breech. There was no delivery by vacuum extraction or forceps. The pattern of mode of delivery is depicted in table VII.

Table VII: Mode of Delivery Vs Infant Infection

Infant Infection Status

Mode of Delivery	Sepsis				Not Septic		Total	
	Proven No.	%	Probable No.	%	No.	%	No.	%
SVD	5	(71.4)	14	(73.7)	24	(75)	43	(74.1)
Breech	2	(28.6)	3	(15.8)	0	(0)	5	(8.6)
c\s	0	(0)	2	(10.5)	8	(25)	10	(17.7)
Total	7	(100)	19	(100)	32	(100)	58	(100)

Majority of infants fourty three (74.1%) were delivered by SVD and were of equal proportions i.e.five (71.4%) with proven sepsis, fourteen (73.7%) with suspected sepsis and twenty four (75%) with no sepsis.

None of the infants delivered by c/s had proven sepsis although two (20%) had suspicious infection.

Infants delivered by breech extraction either had proven infection i.e acinectobacter species and beta hemolytic streptococcus or had suspicious infection (see Appendix I)

SECTION II: INFANT CHARACTERISTICS

SEX DISTRIBUTION.

There were more female infants than male infants with a male to female ratio of 1:1.6.   From Table VIII it can be seen that the infection rate was higher in females (85.7%) than males (14.3%)

Table VIII: Infant Sex Distribution Vs Infection Status

Infant Infection Status

Infant Gender	Sepsis Proven No.	%	Probable No.	%	Not Septic No.	%	Total No.	%
Male	1	(14.3)	9	(47.4)	12	(37.5)	22	(38)
Female	6	(85.7)	10	(52.6)	20	(62.5)	36	(62)
Total	7	(100)	19	(100)	32	(100)	58	(100)

When the infants with proven sepsis were compared to those with no infection this was not statistically significant (p value, 0.24). Also when the infant with sepsis was compared to those with no sepsis the infant gender did not predispose it to infection (ie, $X2$ 2.42,   P value 0.12,   Odds ratio 0.375 and a 95% confidence limit 0.11 to 1.24).

BIRTH WEIGHTS.

The birth weights ranged between 1000 gms to 2600 gms with a mean
of 1650 gms + 350 gms. Twenty three (40%) of infant had birth
weights equal or less than 1500gms whereas thirty five (60%) had
birth weight greater than 1500gms.

Six of the seven infants with sepsis (85.7%) had birth weights
equal or below 1500gms, whereas a majority of infants without any
evidence of sepsis,   twenty one (65.6%) were of birth weight
greater than 1500gms This is shown in (Table IX).

Table IX: Infant Birth Weight Versus Infection Status

Infant Infection Status

Birth weight	Sepsis Proven No.	%	Probable No.	%	Not Septic No.	%	Total No.	%
< 1500gm	6	(85.7)	6	(31.6)	11	(34.4)	23	(39.7)
> 1500gms	1	(14.3)	13	(68.4)	21	(65.6)	35	(60.3)
Total	7	(100)	19	(100)	32	(100)	58	100

Infants with birth weights of less than 1500 grams were prone to
infection . This is evident when the infant with proven sepsis is
compared to that with no sepsis(p value , 0.0019).

However this is not significant when the infants with proven and
suspected sepsis are compared , (X2 0.14,   P value 0.52,
odds ratio 1 63,   confidence limits of 0.49 and 5.43).

INFANT GESTATION (WEEKS)

The mean gestation age of infants was 31.7 + 1.9 weeks ranging from 28 - 35 weeks. Infants with sepsis, majority were of gestational age less than 31 weeks (71.4%) whereas those with no evidence of sepsis, only fifteen infants (47%) were of gestation less than 31 weeks (data not tabulated).

Figure II shows the distribution of gestational age of the infants versus the infant infection status. Infants with suspected and no sepsis had the peak value at gestation 32 - 33 weeks whereas infants with proven sepsis had peak values at lower gestation of 30 - 31 weeks.

FIGURE II
INFANT GESTATION VERSUS INFANT INFECTION.

NUMBER OF INFANTS

GESTATION IN WEEKS

NO OF SEPSIS   SUSPECTED SEPSIS   PROVEN SEPSIS
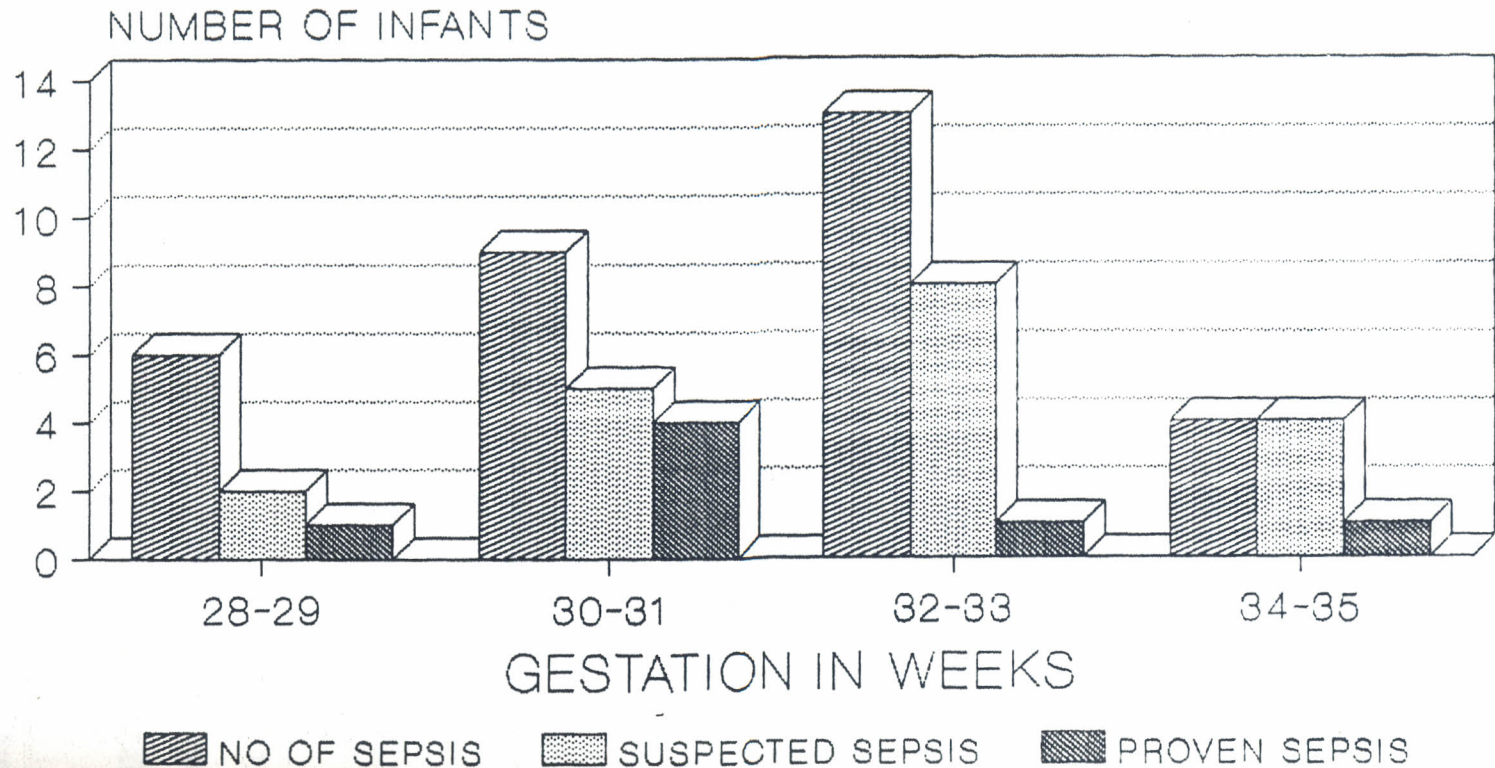
SECTION III - HEMATOLOGICAL PARAMETERS

Fifty five of the fifty eight infants hemogram were studied. The remaining three samples clotted.

HEMOGLOBIN:

The mean hemoglobin concentration was 15.9 and standard deviation of 2.00 gm /dl, ranging from 10 - 20 gm /dl.

12. TOTAL WHITE CELL COUNT (WBC-T) $X10^9$ /l

Figure III shows the relationship of the total white cell count (corrected for nucleated red blood cells) and the infant infection status.

- Infants with no evidence of infection had white cell counts within normal range of 5 - 20 x 10^9 /l (23) except for those whose mothers had severe hypertension.

- Those with suspected sepsis exhibited extremes of counts - leucopenia and leucocytosis.

- Leucocytosis was more prominent in infants with proven sepsis with values as high as 43 x 10^9 /l although the numbers were few.

For statistical purposes the white cell indices of the infant with proven sepsis and that with no sepsis is compared and the distribution summarized in Appendix IX.

FIGURE III   THE DISTRIBUTION OF TOTAL WHITE

CELL COUNT VERSUS INFANT INFECTION STATUS.

TOTAL WHITE CELL COUNT × 10^9/L

NO SEPSIS   PROBABLE SEPSIS   PROVEN SEPSIS
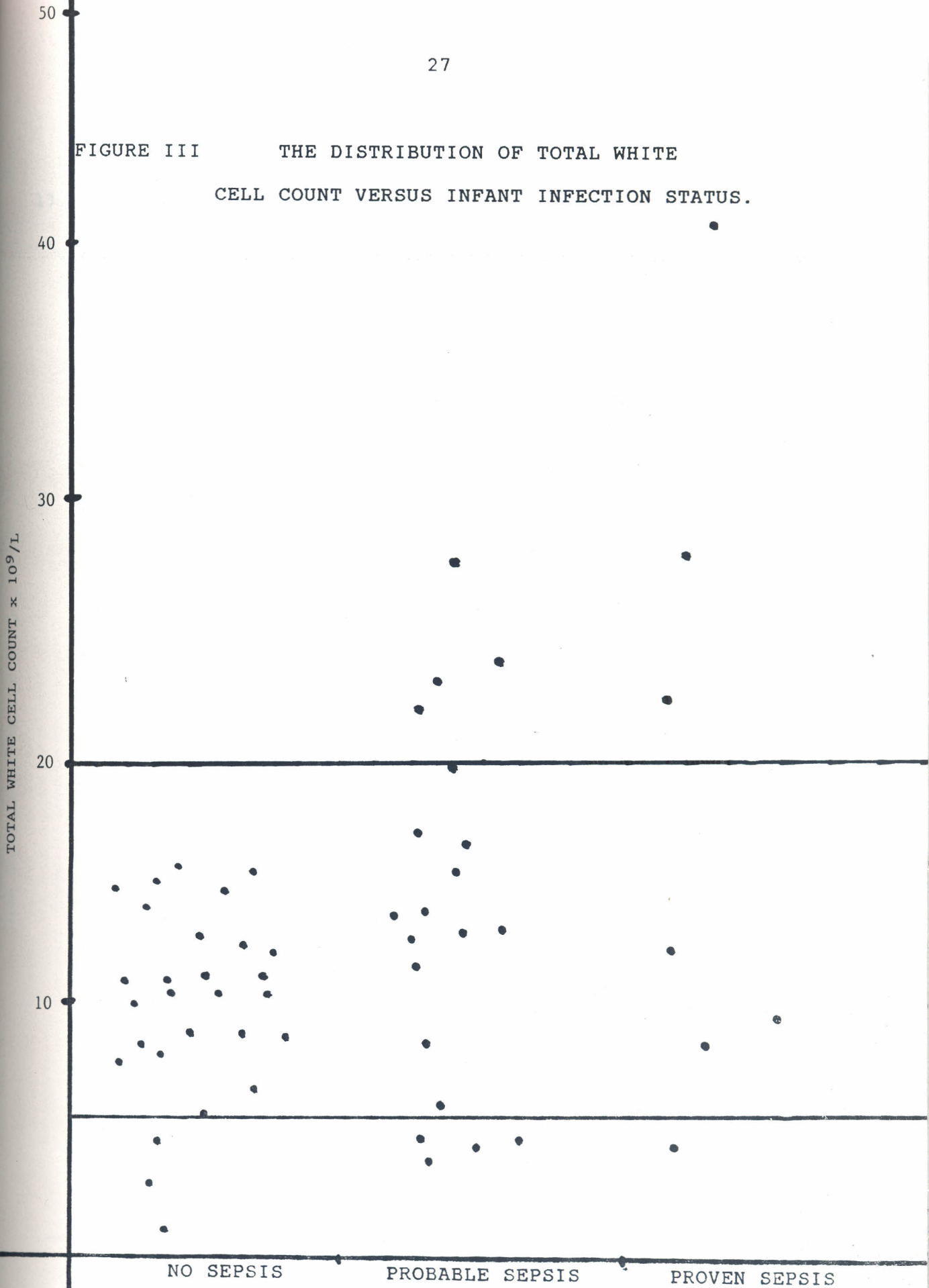
13. **ABSOLUTE TOTAL POLYMORPH CELL COUNT (PMN) X 10^9/1.**

Total polymorphs included both immature and mature
neutrophils for purposes of this study.

-   When corrected for hypertension, infants with
    normal range of PMN counts ($2 - 10$ x 10^{9}/^{1})
    were mainly those without clinical and bact-
    eriological evidence of sepsis.

-   There is a spread out of neutrophilia and
    neutropenia evident in the suspected and
    proven sepsis group (Figure IV)

FIGURE IV   DISTRIBUTION OF TOTAL NEUTROPHIL COUNT VERSUS INFANT INFECTION STATUS.
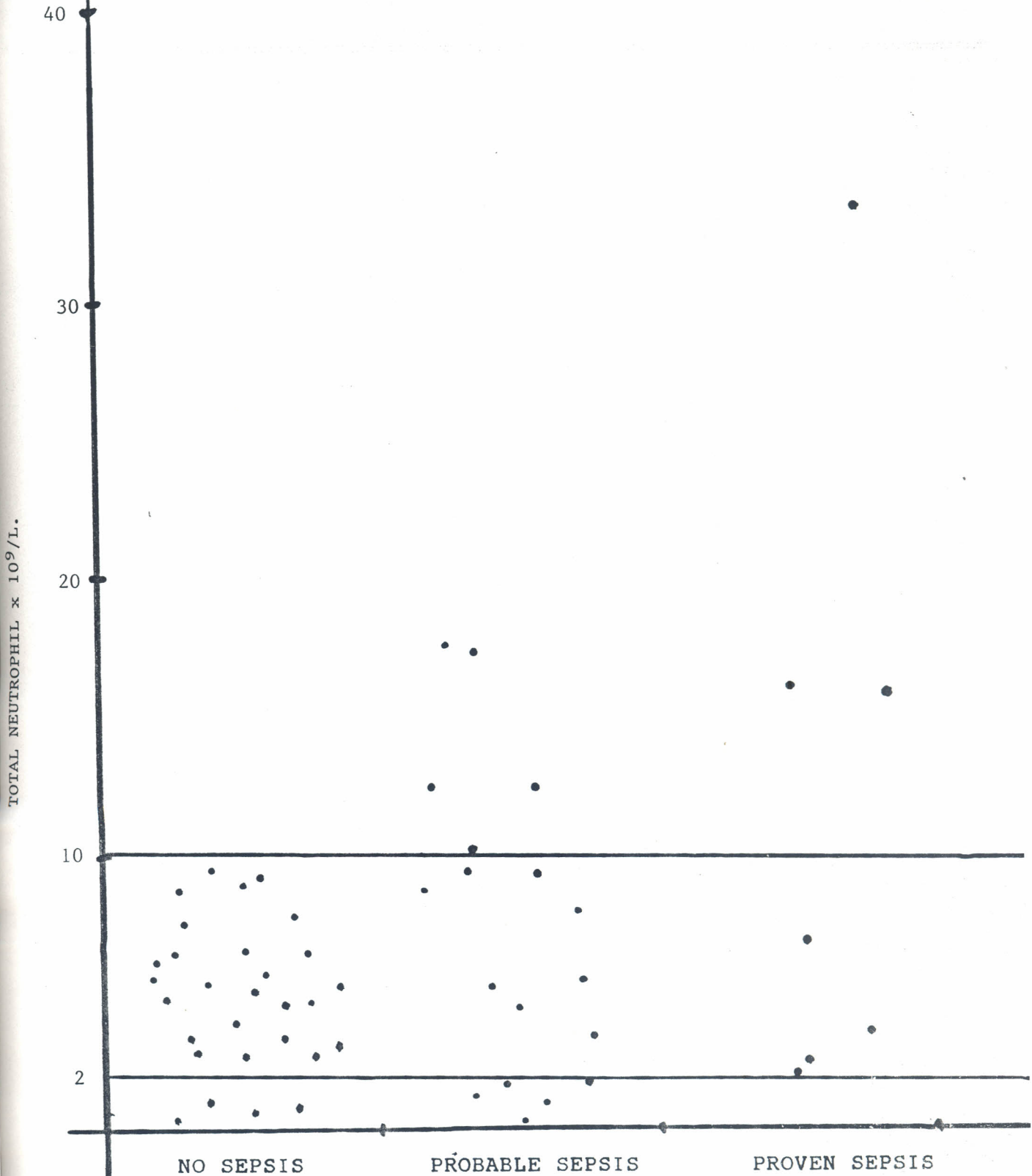
14. <u>PLATELET COUNTS (x 10^9)/1</u>

The cut off point for normal platelet in this study was 150 x 10^9 cells \mm3 as in other studies (20, 21). 57% of infants with proven sepsis had counts less than 150 x 10^9 compared to 10.5% and 13.7% who had suspected and no sepsis respectively. This distribution is shown in Figure V. Appendix 1X has a summary of the statistics of the platelet counts.

FIGURE V. INFANTS PLATELET COUNTS VERSUS INFECTION STATUS.
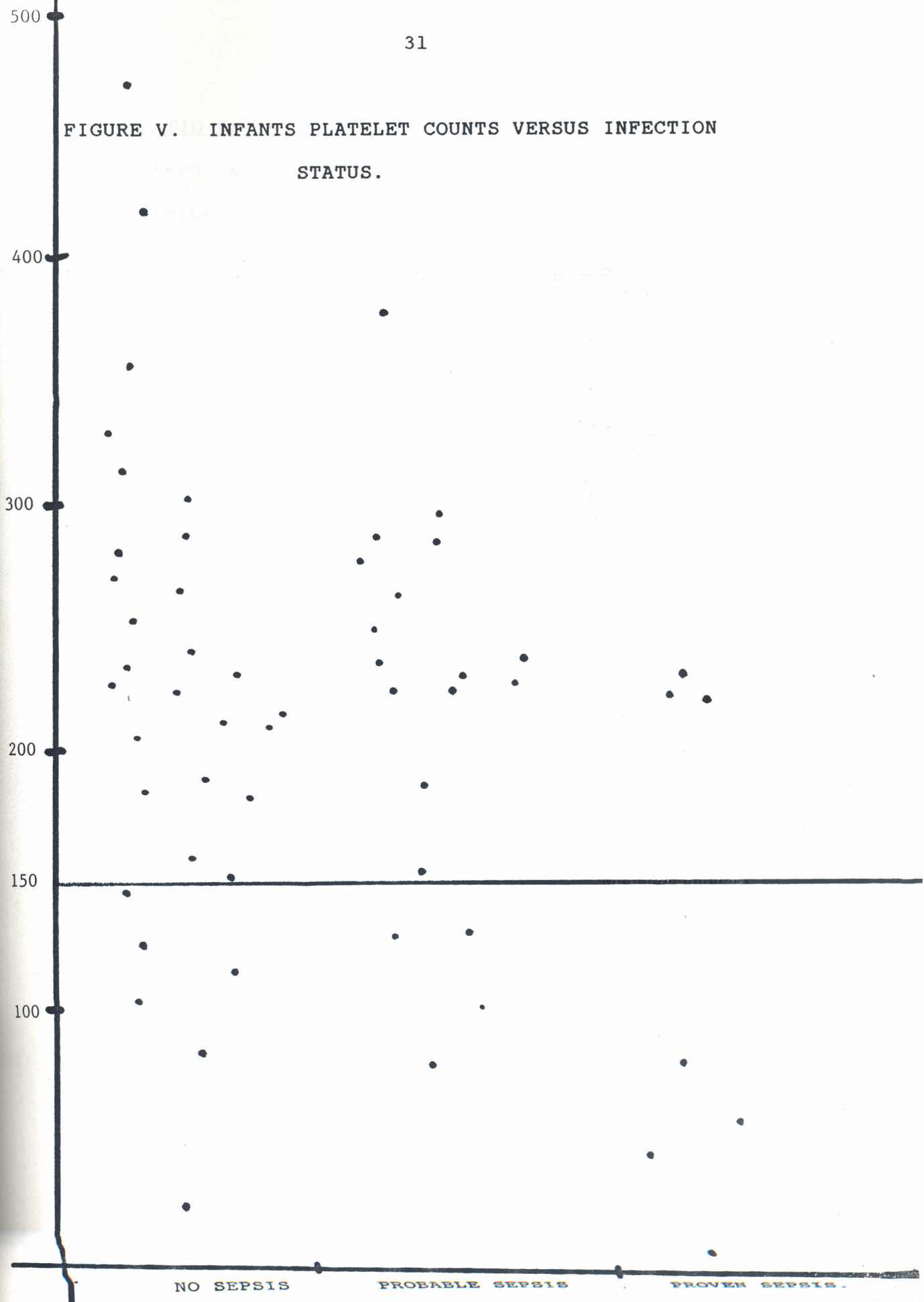
15. <u>RATIO OF IMMATURE TO TOTAL POLYMORPHONUCLEAR CELL COUNT</u>

There is no lower limit for this ratio. Normal upper limits range from 0.06 to 0.1 (20, 21).

Figure VI shows the relationship between the ratios of immature to total PMN to the infant infection status.

. Infants with no evidence of sepsis majority had ratio of less than 0.08.

. The majority of infants with sepsis 5 out of seven (71.2%) had ratios of greater than 0.2

. Infants with suspected infections had spread of ratios with the maximum being 0.4

FIGURE VI THE RATIO OF IMMATURE PMN TO TOTAL PMN VERSUS INFANT INFECTION STATUS.
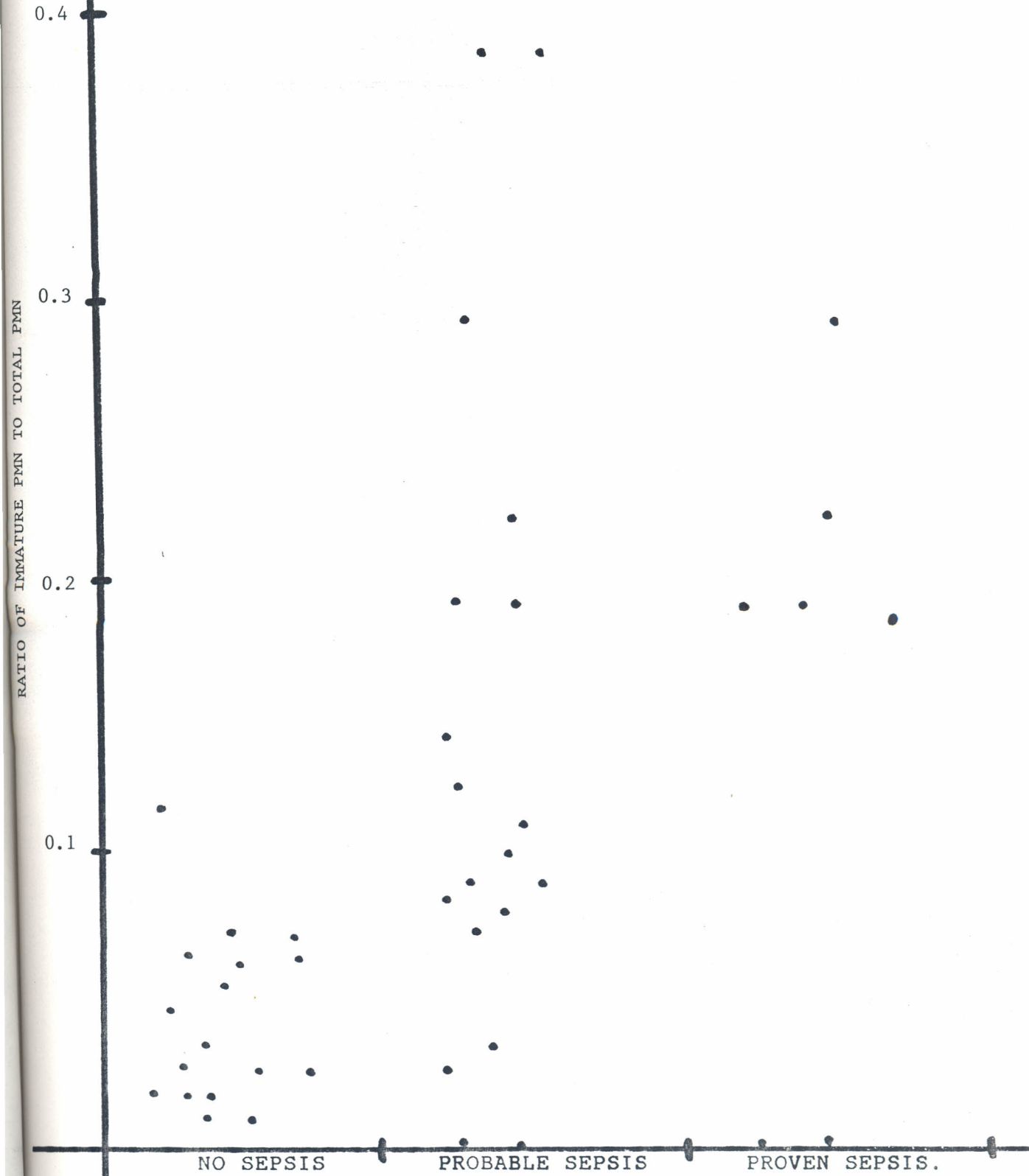
For statistical purposes the ratio of immature pmn to total pmn of greater than 0.2 is shown below in table X, where by the infant with proven sepsis is compared to the infant without sepsis.

Table X: Ratio of Immature to Total PMN in the Septic and not

Septic Infant.

SEPSIS

		YES	NO	TOTAL
	YES	5	0	5
Immature/PMN > 0.2	NO	2	27	29
	TOTAL	7	27	34

This distribution was **highly** significant P value 0.00001, a positive predictive value of 100 % ,Negative predictive value of 93.1%, Sensitivity of 71.2% ,Specificity 100 % Efficiency 94.1% When correlated to infant infection status the ratio of immature : PMN of > 0.2 . The positive predictive value and specificity were high - 100%. Negative predictive values and sensitivities were equally high.

However, when this comparison was made for those with suspected vs no infection the positive predictive values and specificities remained high (100%) but the sensitivity fell quite low (37%) with a negative predictive value of 63% and efficiency 74%.

TOXIC GRANULATIONS AND DEGENERATIVE CHANGES.

Toxic granulations was observed in 8 (14.5%) of infants and was
not present in any infant without evidence of sepsis,and the
distribution is shown in table XI.

Table Xl: <u>Toxic Granulations and Degenerative Changes.</u>

<u>Infant Infection Status</u>

Toxic Gran	Sepsis				Not Septic		Total	
	Proven		Probable					
	No.	%	No.	%	No.	%	No.	%
YES	4	(57.1)	4	(21)	0	(0)	8	(14.5)
NO	3	(42.9)	15	(79)	29	(100)	47	(85.5)
TOTAL	7	(100)	19	(100)	29	(100)	55	(100)

a)   When toxic granulations were compared between the

     septic and not septic infant the positive predictive

     value was 100%, negative predictive value 91%, sensit-

     ivity 57.1 %, specificity 100% and Efficiency 92%.

When this comparison was made between the non infected infants
and that suspected to have infection the positive predictive
value and specificity remained high (100%) but the negative
predictive value, sensitivity and efficiency fell quite low - 67%
, 21.1% and 69% respectively.

SECTION IV - INFANT CHEST RADIOLOGY

Due to some technicalities at the time of study only 29 out of 58 X-rays were available and suitable for inter- pretation.

X -rays were used to exclude patients with other causes of respiratory distress and two infants had radiological findings suggestive of congenital lues. In view of the few numbers fair conclusions were not possible. However, none of the infants with sepsis had normal radiological findings. 18.8% of infants with no evidence of sepsis had bronchopneumonic changes. Table XII shows this distribution.

Table XII   Infant chest X-ray finding versus the infant infection status.

Infant Infection Status

Chest x-ray findings	Sepsis Proven No.	%	Probable No.	%	Not Septic No.	%	Total No.	%
Normal	7	(43.8)	3	(33.3)	0	(0)	10	(34.5)
Wet lung	4	(25)	3	(33.3)	1	(25)	8	(27)
Air B/Grams	1	(6.3)	0	(0)	1	(25)	2	(6.7)
Granular & B/Grams.	1	(6.3)	0	(0)	0	(0)	1	(3.4)
B/Pneumonia	3	(18.8)	3	(33.3)	2	(50)	8	(27.6)
Total.	16	(100)	7	(100)	4	(100)	29	(100)

Where B/Grams   =   Bronchograms

&   B/Pneumonia =   Broncho pneumonia

SECTION V - INFANT BACTERIAL ISOLATES

Seven out of 58 infants had positive blood cultures. 57 % of the isolates were gram negative organisms, the rest 43% were gram positive. Pseudomonas species were isolated in two patients. The summary of bacterial isolates and antibiotic sensitivity is shown in Table XIII.

The infants who had acinectobacter species and group D streptococci had multiple antibiotic resistance and died within 24 hours.

Table XIII, Bacterial isolates and pattern of antibiotic sensitivity

no.	Bacteria	Ampicillin	Streptomycin	Kanamycin	Gentamicin	Amikacin	Polymyxin B	Neomycin	Cefataxim
04	Acinocbacter	resist.	-	resist.	resist.	resist.	resist.	resist.	sens.
07	Strep.Agalat.	resist.	sens.	-	sens.	sens.	-	sens.	sens.
12	Staph.epiderm.	sens.	sens.	-	sens.	sens.	-	sens.	sens.
15	Pseudomonas.	resist.	resist.	resist.	resist.	sens.	resist.	resist.	sens.
30	Group D.Strep.	resist.	resist.	resist.	resist.	resist.	resist.	resist.	resist.
57	Pseudomonas.	resist.	resist.	resist.	resist.	sens.	resist.	resist.	sens.
58	Salmonella ssp	resist.	resist.	sens.	resist.	sens.	sens.	sens.	sens.
	% Sensitivity.	14.2%	33.3%	33.3%	33.3%	71.4%	33.3%	42%	89.7%

DISCUSSION

The prevalence rate of early onset sepsis in preterm neonates of 12.1% in this study compares well with that of Rodwell et al of 9% (18) and Boyle et al of 5% (3). Although this is within the overall reported range of 0.2 - 19.7% (28) it is probably an under estimate due to the fact that diagnostic endevours like autopsy used in some studies were not employed. In this study comparatively more premature infants whose reduced host defence factors have been shown to increase the prevalence of sepsis (1,13,28) were recruited. Half of the infants (55%) had no evidence of sepsis and were thus regarded as having respiratory distress syndrome.

Only single blood cultures were done, all of them within first 12 to 18 hours of life. Although the validity of such single cultures may be questionable, it is only occasionally, that more than one blood culture can be performed before starting antimicrobial treatment during this particular neonatal period. A cursory search of the literature reveals that almost every bacterial species known has been reported to be involved in perinatal and neonatal infection at some time (1,13,16,), thus the concept of certain bacteria being non pathogenic is not one that can apply to the fetus and newborn infant. In this study staphylococcus epidermidis a normal skin flora in adults was isolated in one infant. (patient no. 12 in appendix 1 & 5), who clinically had moderate respiratory distress and a hematological score of 5 on the scale suggested by Rodwel et al (18).

Other organisms isolated included salmonella species, beta-hemolytic streptococcus, acinectobacter species, pseudomonas (two isolates) and group D streptococcus. Two of the infants whose

blood cultures grew acinectobacter and group D streptococcus died within the first twenty four hours of life. The organisms were resistant to most antibiotics including those routinely used in our set up, crystalline penicillin and gentamicin, but were sensitive to amikacin and cefotaxime. Acinectobacter, salmonella, group D streptococcus and staphylococcus epidermidis are reported inhabitants of the lower cervico-vaginal tract (15, 16), and so can colonize newborn infants easily during the process of vaginal delivery.

Pseudomonas species were isolated in two infants, both had low Apgar scores and required some form of resuscitation. Their antimicrobial sensitivities were similar. Subsequently within the study period there was an outbreak of pseudomonal puerperal infection in the labour ward and the bacteria was also isolated from the delivery room resuscitation equipment (personal observations). These neonates probably acquired their infection from resuscitation equipment in labour ward. Neither of them died during the study period.

Of the antimicrobial sensitivities against all isolates that were studied, ampicillin had a sensitivity of 14.2% while gentamicin, kanamycin and streptomycin each had a sensitivity of 33.3%. Ten years ago in the same Unit, kanamycin was widely used as a first line drug in the treatment of neonatal sepsis. Streptomycin has not been routinely used. The possibility of cross resistance to these two aminoglocosides could explain the resistance observed against streptomycin. Amikacin and cefotaxime had higher sensitivity rates of 71.4% and 88.8% respectively, and thus would be more appropriate to use in serious infections despite their high cost.

Mothers in this study were fairly young with majority 41 (76%) less than 25 years of age, and a mean maternal age of 24 years the youngest being 15 years. From figure 1, teenage mothers < 19 years accounted for 25% of the mothers. Sanghvi et al in a Nairobi birth survey (29 a) found an incidence of teenage pregnancy to be 18.6% with an associated early perinatal morbidity rate of 17.7%. In this study maternal age had no significant influence on the infection status of the infant (p value, 0.23).

Thirty seven mothers (64%) had parity between zero and one (live births). The highest recorded parity was 6+2. Of the mothers whose infants had positive blood cultures 71.4% had parity of not more than one while 28.6% were between para two and three. None was above para 4. From these results , it would appear that low parity has an association with occurrence of sepsis.

Thirty eight (65.5%) of mothers attended antenatal clinic at least on one occasion of their pregnancy compared to 20 (34.5%) who did not attend. This figure is comparatively lower than that found in the Nairobi birth survey where upto 96.4% of mothers attended antenatal clinic. Of those who attended antenatal clinics 23 (72%) of their infants had no evidence of sepsis whereas 3 (43%) of those with sepsis the mothers had attended antenatal clinics, this was not statistically significant (p value, 0.15). this finding is strikingly similar to that of British survey as quoted by Sanghvi et al (29 b).

Duration of rupture of membranes for more than 24 hours had a significant influence on the outcome of the infant,(p value, 0.009) when the infected infant was compared to the infant with no sepsis. This is in keeping with findings from the Nairobi birth

survey (29a) where rupture of membranes longer than 24 hours was associated with early perinatal mortality rates of 177/ 1000. Similar findings were also reported by Lindsay et al (16). Prolonged rupture of membranes between 12 to 24 hours promotes ascending infection by the microflora from maternal genital tract (26).None of the mothers who had ruptured membranes for more than 24 hrs had infants with bacteriologically proven sepsis (table V a) although of these 17 mothers, eleven (64.7%) had suspected sepsis. This outcome was significantly influenced by prior antimicrobial use by the mother (p value 0.007,table IV).

Meconium staining of liquor is a rare phenomena in preterm neonates unless delivered by breech extraction (1). It is frequently associated with Listeria Monocytogenes and E. coli infection (13). In this study meconium staining of the liquor was observed in five (8.6%) infants . Of these, three infants had no evidence of sepsis and only one had septicaemia due to streptococcal agalatie and was delivered by breech extraction. The fifth infant was suspected to have sepsis. Listeria monocytogenes (not looked for in this study) could probably have been involved in this latter infant.

Ten (17.7%) of the infants were delivered by c/s. None of these infants had proven sepsis and only 2 (20.2%) of them had suspected infection. Reasons for c/s were severe hypertension, reduced foetal movements, bad obstetric history , multiple pregnancies in a mother who had previous c/s foetal distress with meconium stained liquor. Five infants (8.6%) were delivered by breech extraction. The interesting finding among this latter group was that they either had sepsis (40%) or were suspected to

have it (60%), which is in keeping with the report of the Nairobi birth survey where breech delivery was associated with unacceptably high morbidity rates from probable infection (29b). Equal proportions of infants in the three groups of sepsis status were delivered by spontaneous vertex delivery i.e. 75%, 73.5% and 71% for no sepsis, suspected sepsis and proven sepsis respectively, suggesting that this mode of delivery did not have influence on infection status.

Maternal pelvic discharge and fever could not be correlated with the outcome of the infant as the numbers were small (four out fifty eight) . Of the four mothers who had fever, two were due to meningitis and one of these two mothers delivered an infant with hepatosplenomegaly and purpuric rash.

Washburn et al (26) emphasized the significantly greater male susceptibility to neonatal bacterial septicaemia and meningitis. The males were also more prone to respiratory distress syndrome compared to the females (1,7,8). In this study there were more female than male infants with a male to female ratio of 1: 1.6. This female preponderance was not statistically significant when the infant with proven sepsis were compared to those with no sepsis,(p value 0.24) or when the septic infant (proven & probable sepsis) were compared with those having with no sepsis (p value 0.12). The stringent exclusion criteria used in this study most of which tend to afflict the male infant more than females may explain the results.It is also possible that the female infants had a higher rate of survival and hence more likely to be included into the study.

Low birth weight is regarded as one of the most important risk

factors for neonatal sepsis. The likelihood to develop septicaemia increases as the birth weight decreases (1 13 17 20b 27). Likewise in this study, the majority of infants with confirmed sepsis had lower birth weights of equal to or less than 1500 gms (85.5%) as compared to those who had no evidence of sepsis (p value 0.002.) Infant gestation had a similar effect.

An attempt to relate the individual infant clinical physical characteristics of lethargy, apgar scores, hypothermia, pallor, oedema and degree of respiratory distress was not useful in distinguishing the infected infants from those with respiratory distress syndrome (data not shown) as these features occurred equally in both groups. However apnoea, hepatosplenomegaly petechiae and jaundice were seen more frequently in infants with suspected and confirmed sepsis than those not infected.

Hematological parameters were found to be particularly useful in discriminating the infants who had respiratory distress due to sepsis from those who had respiratory distress syndrome. (summary in appendix IX). The ratio of immature PMN to total PMN equal or greater than 0.2 was a highly significant predictor of sepsis (p value 0.00001), with a positive predictive value of 100% , a sensitivity of 71.2% and specificity of 100%. The effi-ciency was equally high - 93.1% . Such values compare well with higher sensitivities of 96% of Rodwell et al (18) and 78% of Philip AGS (27). The same statistical test on the infants who had suspected sepsis revealed a very low sensitivity (37%) but high positive predictive value and efficiency (63% and 74% respective-ly).These findings compare well with previous reports (18,27) and probably reflect the non special nature with which sepsis presents

in neonates.

Total corrected white cell counts was an equally useful predictor of absence or presence of sepsis as infants with no sepsis had normal range of white cell counts , while very high counts of upto 43 x 10^9 /l were not only seen in infants with proven sepsis but were also significantly related with sepsis (p value 0.016).

It has been stated that total polymorph counts should be interpreted with caution because neutropenia is quite common in infants born to mothers with severe hypertension, its dynamics are also influenced by prophylactic antibiotic use and sex of the infant (24). Neutropenia and neutrophilia were however found to be common in the infant with proven sepsis. In this study this did not reach a level of significance (p value 0.12). These tests have been found useful when considered in combination with other white cell indices (27) or when combined with acute phase reactants (19,20) which were not done in the present study.

The pattern of toxic granulations and degenerative changes of polymorphs and that of the ratio of immature PMN to total PMN are similar in this study. Toxic granulations and degenerative changes of polymorphs had a significant positive relation to sepsis(p value 0.005). It predicted sepsis in 100% of the cases but unlike the ratio of immature PMN to total PMN the sensitivity was rather low - 57.1% . Other studies have observed toxic granulations in later stages of septicaemia only (19). Platelet counts predicted sepsis in 44% cases only, although it had a significant relationship with sepsis (p value 0.049).

White cell indices are one of the easiest tests to perform even in the poorest of settings. The test can be performed within

30 minutes if need be and their dynamic nature in this particular age group can be used to follow up the clinical course of the patient (13, 19, 23).In a situation where an infant had been started on antibiotics on empirical grounds a decision to stop antibiotics can be made if the white cell indices are normal.

Although only half (50%) chest radiotherapy were performed in this study due to various technical problems, all the infants with proven sepsis who had this examination were found to have abnormal radiographs. This suggests that this test would be a very useful addition in differentiating sepsis from respiratory distress syndrome especially when considered together with skin supportive evidence for sepsis.

CONCLUSIONS

(1) Prevalence of early onset sepsis in preterm neonates with respiratory distress is 12.1% while that of respiratory distress syndrome was 55%.

(2) Preterm infants delivered by breech extraction and those delivered in offensive and meconium stained liquor were most predisposed to infection.

(3) Duration or rupture of membranes longer than 24 hours pre disposed the infants to infection and the lower the birth weights the higher the chances of infection.

(4) White cell indices notably the ratio of immature to total PMN, total white cell counts, toxic granulations and degenerative changes and platelet counts are useful predictors of sepsis in the preterm neonates.

(5) Radiological examination in the preterm neonate is useful in ruling out other causes of respiratory distress and may be useful in identification of the septic neonate.

RECOMMENDATIONS:

(1)   Routine hematological profile, chest radiograph, and detailed maternal history mandatory in evaluating a preterm neonate with respiratory distress.,

(2)   In circumstances where multiple antibiotic resistance is noted, Amikacin or Cefotaxin be used as drugs of choice when infection is highly suspected or proved.

(3)   Need for study on the following

    (i)   Hematological follow-up of Preterm neonates with respiratory distress.

    (ii) Radiological study of preterm neonates presenting with respiratory distress at birth.

    (lll) Infection with Listeria monocytogenes especially in the preterm neonate born in meconium stained liquor.

ACKNOWLEDGEMENT.

I wish to sincerely acknowledge my gratitude to all those who made it possible for me to start and complete this work.

REFERENCES

(1) Klaus M. Avroy A: Care of the high risk neonates. W.B. Saunders Company, 3rd edition 1986.

(2) Alistair P.. Hewitt J. Early diagnosis of Neonatal Sepsis Pediatrics 65: 1036, 1980.

(3) Boyle R. Chaudler B. Stonestreet B. Oh. W. Early Identification of Sepsis in infants with respiratory distress. Pediatric 62: 744, 1978.

(4) Ablow RC. Driscoll SG. Effoman El. Jolles C. Gross L. A comparison of Early Onset Group B streptococcal neonatal infection and respiratory distress Syndrome on the newborn. N. Engl J. Med 294: 65, 1976.

(5) Menke J.A. Glacoia GP, Jockin 4. Group B Beta hemolytic streptococcal sepsis and idiopathic respiratory distress syndrome, A Comparison. J. Pediatr. 94: 467, 1979.

(6) Tooley W: Hyaline Membrane disease, Telling it like it was (Cumroe symposium). Am Rev Respr Dis. 111: 657, 1975.

(7) Auld P. Hudson A. Usha R. Hyaline Membrane disease, a discussion. J. Pediatr. 80: 129, 1982.

(8) Doglous G. Hall D. Respiratory distress syndrome. Recent advan. Paed 4th Ed. 89. 295, 1974.

(9) Fawel P. Avery M.E. Hyaline membrane disease. Am Rev Resp Diseases. 111: 657, 1975.

(10) Avery M.E. Lung and its disorders in Newborn Infant. Second edition , W B Sauders Philadelphia. 1965.

(11) Stark A.Ivan F; Respiratory distress syndrome. Pediatr Clin North Am. 33: 533, 1986.

(12 Weller M. Roentgenographic course and clinical complication of hyaline membrane disease Pediatr. clin North Am. 20: 381, 1973.

(13) Davies P. Gotherford L. Bacterial infections in the fetus and Newborn infant major problem in clinical paediatric. Vol. 26. WB Saunders Comp. 1984.

(14) Placzek M N. Whitelaw A. Early and late neonatal septicaemia Arch Dis Child. 58: 788, 1983.

(15) Lindsay A. Marcos P. Etiology of Premature Rupture of Membranes. Clin Obstet Gynaecol 29: 758, 1986.

(16) Miller J. Postorek II, J. Microbiology of premature rupture of membranes. Clin. obstet. Gynecol . 29: 739, 1986.

(17) Bortoluss, Thomson TR, Feremo P.
Early onset pneumococcal sepsis in newborn infant.
Pediatrics. 60: 352 , 1972.

(18) Rodwell RL, Leslie AL, Tudehope I.
Early diagnosis of neonatal sepsis using hematologic scoring
system. J. Ped. 112: 761, 1988.

(19) Klein J ,Marey M. Infectious disease in the fetus and newborn
infant. W B Saunders Publication 1976.

(20) Silverman R A, Anderson D H.
A controlled clinical trial of effects of water mist on
obstructed respiratory signs death rate and necropsy findings
among premature infants. Pediatrics. 17: 1, 1956.

(20 b) Klein J. Current concepts of infectious diseases in newborn
infant. Adv Pediatr. 31: 405, 1984.

(21) Dubowitz LMS, Dubowitz V Goldberg C
Clinical assessment of gestational age in the newborn infant.
J Pediatr. 77 : 1, 1970.

(22) Reich P , Deykin D. Hematology Pathophysiological basis for
clinical practice. Ist ed. Little Brown & comp. Boston
1978.

(23) Manroe E, Werberg A G, Rosenfield C R Browng.
Neonatal blood counts in health and disease. Reference values
for neutrophilic cell count. J, Pediatr 95: 89, 1979.

(24) Berman R, Vaughan V,Nelson N. Nelsons Textbook of Paediatrics.
W B Saunders Company 1987.

(25) Bommen M. Neonatal infections. Br. J. of Hosp medicine:
117; 302, march 1986.

(26) Washburn T C, Medearis D N, Childs B. Sex differences in
susceptability to infection. Pediatrics, 35: 57, 1965.

(27) Philip A G N. Neonatal sepsis and meningitis.Hall Boston .
1985.

(28) Blackmon L. Lindsay S A. Crenshank C. Fetal and neonatal
outcome associated with premature rupture of membranes.
Clin obstet Gyn 29. 779, 1986.

(29) Sangvi HCG, Mati JKG, Aggrawal VP, Lucas S, Corkhill R.
    (a) Nairobi birth survey V: Outcome of pregnancy in teeneger
         mothers.
         J. Obst. Gynae East Cent. Afr. 2. 134, 1983.
    (b) NRB Birth survey IV.
         Early perinatal mortality.
         J. Obst. Gyn. E.A Cent. Afr. 2: 127, 1983.

APPENDIX 1 SUMMARY OF CHARACTERISTICS OF INFANTS WITH PROVEN SEPSIS

STUDY NO	BABY AB	MOTHER AB	D.R.O.M.	DURATION OF LABOUR	LIQOUR	MODE OF DELIVERY	INFANT BWT	INFANT GESTATION	DEGREE OF R.D.	CXR	IMMATURE P.M.N.	OUTCOME BACTERIA
04	Yes	No	10 Hrs	8 Hrs	Clear	Breech	2250 gm	34/52	Moderate	Air Bronchograms	0	Died Acinectobacter
07	Yes	No	12 Hrs	23Hrs 1st stage 1Hr 2nd stage	Medium stained	Breech	1450 gm	31/52	Severe	B/ Pneumonia	0.2	Strep-agalalatia Alive
12	No	No	18 Hrs	18 Hrs	Clear	SVD	1450 gm	30/52	Moderate	Wet Chest	0.23	Staph-epidermidis Alive
16	Yes	No	4 Hrs	18 Hrs	Clear	SVD	1000 gm	32/52	Moderate	—	0.2	Pseudomonas Alive
30	Yes	No	10 Hrs	9 Hrs	Clear	SVD	1450 gm	30/52	Moderate	—	0.3	GBS Alive
57	Yes	No	18 Hrs	8 Hrs	Clear	SVD	1500 gm	30/52	Moderate	B/ Pneumonia	0.2	Pseudomonas Alive
58	Yes	No	2nd stge	12 Hrs	Clear	SVD	1300 gm	29/52	Minimal		0	Salmonella Alive

AB= Antibiotics   D.R.O.M. =   Duration of Rupture of Membrane   SVD= Spontaneous Vertex Delivery   GBS= Group B Streptococcus

PMN=   Polymorphonuclear cells   RD=   Respiratory Distress

CXR=   Chest X-Ray

51

APPENDIX II

MATERIAL DATA

Name:

IP No.:   Study No.:

Age:

L.M.P.:   E.D.D.   :Parity:

ANTENATAL DATA:

Antenatal Attendance: YES   Where

Antenatal Pelvic Discharge:YES   Treatment

                          NO

NATAL DATA:

Blood Pressure: - Systolic   Diastolic

Temp. in $_0$C:

Rapture of membranes   12 hrs   24 hrs

Onset of labour""

Liquor: -Clear
            -Offensive
            -Others

Use of oxytocin: YES   NO

DELIVERY:

Number of vaginal examinations before delivery _____

Duration of 1st stage _____

Duration of 2nd stage _____

Total Length of labour _____

Mode of delivery: -   SVD
                       vacuum
                       C/S
                       Forceps

APPENDIX III

CHILD DATA:

Mother's Name: Sex:

IP No.:   Study No.:

Date & Time of Birth: _____

Bwt in grams: _____
Gestation by dates: _____

Gestation by clinical assessment: _____

Age at examination: _____

Place of delivery: _____

Apgar Scores: 1 min.   5 min.   10 min.

Single delivery:
1st twin:
2nd Twin:
Others:
Time of admission:
Time of onset of respiratory distress:

CLINICAL EXAMINATION:

Appearance - lethargy

smell   -Normal
           -Foul

Cyanosis   -Central   apnoea
           -Peripheral
           -both

Jaundice   -Yes
           -No

Pallor   -Yes
           -No

Temp.   -quote ( )
           -Hypothermia
           -Hyperthermia
           -Normal temp.

RESPIRATIONS:

Rate per minute

                                                YES   NO

Retractions-Subcostal
          -intercostal
          -substernal

          Grunting

          Crepitation

HEMATOLOGICAL PARAMETERS:

          HB

          WBC=Total

               -Neutrophil

               -Band

               -Ratio of band to immature

               Platelets -   Blood cultures:Positive   YES
          - organism
                                         NO

                                     sensitivity

     CXR   (time)

               Report: 1st Radiologist

                       2nd Radiologist

DIAGNOSIS:

(1)   Proven sepsis
(2)   Probable sepsis
(3)   No sepsis

APPENDIX IV COMPARISON OF THE PROVEN SEPTIC

AND NON SEPTIC CASES

	Tests of sensitivity	Specifity	+PPV	-ve P.V.	Efficiency	P.V
Total white cell count	57.4	89.6	57.4	89.6	83.3	0.016
Absolute PMN Ratio	43%	86.2%	43%	86.2	77.7	0.12
imm. to total PMN	71.4	100	100	91.2	93.1	0.00001
Platelet count	57%	82.8%	44%	88.9%	77.7%	0.049
Toxic grant deg. changes	52	100	100	90.6	91.7	0.0005

KEY*

+ppv   = positive predictive value.

-ve p.v = negative predictive value.

APPENDIX 5

SUMMARY OF HEMATOLOGICAL CHARACTERISTICS

OF INFANTS WITH PROVEN SEPSIS

	WBC TOTAL	ABS PMN	ABS IMM	IMM PMN	IMM TOTAL	PLATELET	TOXIC GRAM	HAEM. SCORE
04	12.3	2.0	–	0	0	<150	nil	2
07	5.9	2.6	0.53	0.2	0.09	240	toxic gram	2
12	22	15.4	3.5	0.23	0.16	320	nil	5
16	8.6	6.3	1.2	0.2	0.14	8	toxic gram	5
30	27.5	15.1	4.1	0.3	0.15	227	toxic gram	6
57	43.6	33.6	6.6	0.2	0.15	–	toxic gram	7
58	8.1	3.7	0	0	0	<150	nil	1

KEY*

    ABS PMN   =   Absolute polymorphs.

    IMM PMN   =   immature polymorphs.

    IMM/ TOTAL   =   Ratio of immature to total pmn.

    TOXIC GRAN   =   toxic granulations.

    HEM SCORE   =   Hematological score.