AGENCY FOR INTERNATIONAL DEVELOPMENT
WASHINGTON, D. C. 20523

BIBLIOGRAPHIC INPUT SHEET

FOR AID USE ONLY
Batch 43

1. SUBJECT CLASSIFICATION
A. PRIMARY: TEMPORARY
B. SECONDARY:

2. TITLE AND SUBTITLE
Infection and low birth weight in a developing country: a study in an Indian village of Guatemala

3. AUTHOR(S)
Urrutia,J.J.; Mata,L.J.; Trent,Frederick; Cruz,J.R.; Villatoro,Elba; Alexander,R.E.

4. DOCUMENT DATE
1975

5. NUMBER OF PAGES
4p.

6. ARC NUMBER
ARC

7. REFERENCE ORGANIZATION NAME AND ADDRESS
PAHO

8. SUPPLEMENTARY NOTES (Sponsoring Organization, Publishers, Availability)
(In Am.j.dis.child,v.129,p.558-561)

9. ABSTRACT

(HEALTH R & D)

10. CONTROL NUMBER
PN-AAC-784

11. PRICE OF DOCUMENT

12. DESCRIPTORS

13. PROJECT NUMBER

14. CONTRACT NUMBER
CSD-3357 Res.

15. TYPE OF DOCUMENT

AID 590-1 (4-74)

CSD-5357 Res
PN-AAC-784

Infection and Low Birth Weight in a Developing Country

A Study in an Indian Village of Guatemala

Juan J. Urrutia, MD; Leonardo J. Mata, ScD; Frederick Trent, MS; José R. Cruz, MS; Elba Villatoro; Russell E. Alexander, MD

The causes of fetal growth retardation and premature delivery are not well defined. Although diet, smoking, maternal weight and height, and social class can be correlated with the size of the fetus, the relative contribution of other factors to fetal growth has not been clarified. Among such factors in developing countries, the highly prevalent infectious diseases occupy a prominent place. This report summarizes studies of the frequency of infections in pregnant women and discusses their possible influence on intrauterine growth.

From the Division of Environmental Biology, Institute of Nutrition of Central America and Panama, Guatemala City (Drs. Urrutia and Mata, Messrs. Trent and Cruz, and Ms. Villatoro), and the Department of Epidemiology and International Health, University of Washington, Seattle (Dr. Alexander). Dr. Mata is now with the University of Costa Rica, Guadalupe.

Reprint requests to Division of Environmental Biology, Institute of Nutrition of Central America and Panama, Guatemala City, Guatemala, Central America (Dr. Urrutia).

PATIENTS AND METHODS

The present data were derived from a long-term prospective investigation of the interactions of nutrition and infection and the outcome of pregnancy in a highland Indian village.[1-3] Since 1972, all women of child-bearing age have been visited every month and interviewed regarding their menses. A urine gonadotrophin test was used for the diagnosis of pregnancy in women reporting amenorrhea. Each pregnant woman underwent anthropometric

and obstetric examinations at 6 to 7, 12 to 14, 26 to 28, 36, and 38 weeks of pregnancy and, furthermore, was visited in her home every week by a physician who assessed her health. When an acute infection was found, visits were repeated at three-day intervals to determine the duration and clinical characteristics of the disease. Urinary tract infections were diagnosed exclusively by demonstration of significant bacteriuria, ie, counts of enteric Gram-negative bacteria in excess of 100,000 colonies per milliliter of urine. Since most women refused pelvic examination, vaginal inflammation was assessed by cytologic evaluation of the urine sediment by the Papanicolau method.[4] Serial blood specimens were obtained from the mothers at 6 to 7, 26 to 28, 36, and 38 weeks of gestation; these were tested for seroconversion rates to *Toxoplasma gondii* by the fluorescent antibody technique,[5] cytomegalovirus and herpes simplex by the complement-fixation method,[6] rubella by hemagglutination inhibition,[6] and *Treponema pallidum* by VDRL. A fourfold rise of serum antibodies was considered significant for cytomegalovirus (CMV), herpesvirus hominis (HVH), and *Toxoplasma* infections. Umbilical cord blood was collected from most infants, and levels of IgM, IgG, and IgA in cord serum were determined by radial immunodiffusion. Each infant was weighed by a nurse within on hour of delivery.

RESULTS

Incidence of Infectious Diseases During Pregnancy

Table 1 shows the incidence of infectious diseases during pregnancy among 82 women observed from conception to delivery. Respiratory infections were the most common, and upper respiratory tract was affected four times more frequently than lower. Diarrhea and dysentery were second in frequency, followed closely by urinary tract infections, which occurred with the same frequency in each trimester of pregnancy, whereas respiratory and intestinal infections were most prevalent in the last trimester.

Other illnesses including conjunctivitis, otitis media, stomatitis, and skin infections were also seen. The last included deep abscesses that were serious health problems because of their long duration and accompanying systemic manifestations such as chills and fever.

The average duration of illness was 7.5 days per 100 days of pregnancy (Table 2), which is equivalent to 21 days out of the 280 days of gestation. Diseases during the third trimester lasted longer than those during the first and second trimesters.

Table 1.—Incidence of Infectious Diseases During Pregnancy*

Trimester of Pregnancy	Respiratory Tract Infection		Diarrhea and Dysentery	Urinary Tract Bacterial Infection†	Other Illnesses‡
	Upper	Lower			
1	37 (45)§	5 (6)	7 (9)	8 (10)	7 (9)
2	26 (32)	6 (7)	9 (11)	8 (10)	5 (6)
3	41 (50)	14 (17)	13 (16)	6 (7)	8 (10)
Incidence per 100 pregnancies	104 (127)	25 (30)	29 (36)	22 (27)	20 (25)

* Data obtained from 82 pregnant women observed prospectively from conception to delivery in Santa Maria Cauque, Guatemala, 1972 and 1973.
† ≥ 100,000 colony-forming units per milliliter of urine.
‡ Conjunctivitis, otitis media, stomatitis, skin infection.
§ Number of episodes (rounded precentage).

Table 2.—Days of Illness Due to Infectious Disease*

Trimester of Pregnancy	Respiratory Tract Infection		Diarrhea and Dysentery	Urinary Tract Bacterial Infection†	Other Illnesses‡
	Upper	Lower			
1	3.2§	1.2	0.3	0.9	0.8
2	2.7	1.1	0.6	0.5	0.8
3	4.8	2.4	1.0	1.1	0.9
Mean	3.6	1.6	0.7	0.8	0.8

* Data obtained from 82 pregnant women observed prospectively from conception to delivery in Santa Maria Cauque, Guatemala, 1972 and 1973.
† An average duration of 273 days (39 weeks) was assumed for every pregnancy.
‡ Conjunctivitis, otitis media, stomatitis, skin infection.
§ Mean days of illness per 100 days.

Table 3.—Agents Associated With Vaginal Inflammation*

Agent	No. (%) of Women With Agent
Trichomonas vaginalis, alone	12 (23)
Candida albicans, alone	11 (21)
T vaginalis & *C albicans*	9 (17)
No agent	21 (40)

* Data obtained from 53 pregnant women observed prospectively through pregnancy in Santa Maria Cauque, Guatemala, 1972 and 1973.

Table 4.—Seroconversion* to Selected Agents During Pregnancy†

Agent, Test‡	No. of Subjects	No. (%) Positive
Cytomegaloviruses, CF	51§	3 (5.9)
Herpesvirus hominis, CF	60§	3 (5.0)
Rubella virus, HI	61	0
Treponema pallidum, VDRL	61	0
Toxoplasma gondii, FA	61	1 (1.6)
Total	61	7 (11.5)

* Fourfold or higher rise of titer for cytomegalovirus, herpesvirus hominis, and *Toxoplasma*.
† Data obtained from 61 women in Santa Maria Cauque, Guatemala, 1972 and 1973.
‡ Tests include the following: complement-fixation (CF), hemagglutination inhibition (HI), and fluorescent antibody (FA).
§ Anticomplementary sera excluded.

Frequency of Vaginal Inflammation and Infection During Pregnancy

Vaginal inflammation was studied in 57 women from the first to the last trimester of pregnancy. Cellular changes indicative of inflammation were found in 48% of women at the beginning of pregnancy, and in 79% by the end of gestation.

Nonspecific inflammation (ie, that in which no potential causative agent was found) occurred in 40% of the women (Table 3). *Trichomonas vaginalis* and *Candiba albicans* were found in 23% and 21% of the women, respectively, and 17% had both. No at-

Table 5.—Incidence of Elevated Serum IgM Level in Newborns*

Localities	No. of Infants	No. (%) of Cases† With IgM Level > 0.20 mg/ml
Santa Maria Cauque, Guatemala‡	263	111 (42)
Santo Domingo Xenacoj, Guatemala§	211	80 (38)
Four ladino villages in Guatemala‖	132	18 (14)

* Umbilical cord serum IgM level measured in Guatemalan newborns from rural communities, 1964 to 1973.
† Specimens with values of IgA > 0.10 mg were excluded from tabulation.
‡ Blood collected by traditional folk midwives.
§ Blood collected by a trained midwife.
‖ Blood collected by a physician.

tempts were made to isolate or characterize other organisms reportedly associated with perinatal infections such as group B streptococci or T-strain mycoplasmas.

At the beginning of the study, a limited number of vaginal swabs collected by the pregnant women themselves were examined. Among these, three cases with evidence of CMV infection and one with HVH infection were detected.

Silent Infections During Pregnancy

The frequency of silent or asymptomatic infections is much higher. In a preceding survey of pregnant women from the village, about 14% were found to harbor *Shigella* or *Salmonella*, 54% *Entamoeba histolytica*, and 25% enteroviruses.[2] Reactivated infections with CMV and HVH occurred in six (10.9%) of 61 pregnant women (Table 4). A single infection with *To gondii* (1.6%) was identified. There was no infections with rubella or *Tre pallidum*. In all, of 61 pregnant women, seven (11.5%) showed evidence of having been affected by at least one of these agents.

Infection and Outcome of Pregnancy

Forty-two percent of newborns had elevated IgM levels in cord blood, a finding similar to that in another highland village. No correlation was found between cord serum IgM level and birth weight.

Some of these serum samples may have had admixtures of maternal blood, which would give spuriously high levels of IgM. However, when such collections are done most precisely, as was true for blood collected by experienced physicians in four ladino villages, no less than 14% of specimens had substantial elevations of IgM, reflecting a high rate of intrauterine exposure to infectious agents (Table 5).

No relationship was noted between incidence of infectious disease during pregnancy and birth weight by contingency table or similar types of analyses. However, step-wise multiple regression analyses suggested that morbidity during pregnancy could explain part of the variance of birth weight (J. J. Urrutia, MD, and L. J. Mata, ScD, unpublished data).

Diseases affecting lower-respiratory and urinary tracts were more frequent in the group of mothers who delivered low-birth-weight infants; these differences, however, were not statistically significant. No differences in concentration of cord IgM were found between infants of mothers who had fewer than three episodes of illness during pregnancy and infants of mothers who had more.

COMMENT

Our investigation showed very high rates of infection during pregnancy in an Indian village in Guatemala. There was also evidence that the newborn infants had a high incidence of elevated specific antibody titers, suggesting intrauterine exposure to infectious agents.

Attack rates of infection among these rural women are well in excess of the rates for industrial nations.[8-10] The precise methods used in this prospective study permitted detection of the majority of illnesses experienced by the women, and thus the observed rates we report very likely reflect true incidence of infectious diseases. This incidence exceeds considerably the previous estimates for this population, based on a retrospective analysis.[10] Since most information about morbidity during pregnancy throughout the world is based on data derived retrospectively, it is reasonable to conclude that true incidence of illness is higher than has been suspected heretofore.

Infection of the pregnant women may affect fetal growth indirectly through interference with the woman's nutritional status, which in turn may result in diminished fetal nutrition. In addition, there may be a direct effect on the fetus by infection across the placental barrier.[10] However, not enough is known about the effects of specific maternal infections. The best available information relates to urinary tract infections and indicates a correlation between such infections in the pregnant woman and low birth weight and neonatal mortality throughout the world.[11] It does not seem to be affected by the mother's social class. Likewise, vaginal colonization with T-strain of *Mycoplasma*, *Listeria monocytogenes*, HVH type 2, and CMV has been associated with low birth weight and fetal wastage.[10-13] On the other hand, data relating such common diseases as upper-respiratory tract infections and diarrhea, which are highly prevalent among the rural women we studied, and fetal survival and well being are lacking. However, in view of the high incidence of stillbirths, prematurity, and fetal growth retardation in the Indian village we studied,[1] it is reasonable to suspect causal influence of the highly prevalent maternal infections. There is a great need for a precise assessment of this problem. Our prospective study, designed to answer this question, is in progress.

This investigation was supported in part by US Public Health Service grant PH-NICHD-73-2737 from the National Institute of Child Health and Human Development; by the Pan American Health Organization; by US Agency for International Development grant AID/CSD/3357; by the Guatemalan Ministry of Health; and by the University of Washington.

References

1. Mata LJ, Urrutia JJ, García B: Effect of infection and diet on child growth: Experience in a Guatemalan village, in Wolstenholme GEW, O'Connor M (eds): *Nutri-*

tion and Infection: Ciba Foundation Study Group No. 31. Boston, Little Brown & Co, 1967, pp 112-134.

2. Mata LJ, Urrutia JJ, Cáceres A, et al: The biological environment in a Guatemalan rural community, in *Proceedings of the Western Hemisphere Nutrition Congress III.* Mount Kisco, NY, Futura Publishing Co Inc, 1972, pp 257-264.

3. Mata LJ, Urrutia JJ, Albertazzi C, et al: Influence of recurrent infections on nutrition and growth of children in Guatemala. *Am J Clin Nutr* 25:1267-1275, 1972.

4. Schulte JW, King CD, King EB, et al: A simple technique for recognizing abnormal epithelial cells in urinary sediment. *J Urol* 89:615-625, 1963.

5. Walton BC, Benchoff BM, Brooks WH: Comparison of the indirect fluorescent antibody test and methylene blue dye test for detection of antibodies to *Toxoplasma gondii. Am J Trop Med Hyg* 15:149-152, 1966.

6. Lennette EH, Schmidt NJ (eds): *Diagnostic Procedures for Viral and Rickettsial Infections,* ed 3. New York, American Public Health Assoc Inc, 1964.

7. Mancini G, Carbonara AO, Heremans JF: Immunochemical quantitation of antigens by single radial immunodiffusion. *Immunochemistry* 2:235-254, 1965.

8. Niswander KR, Gordon M: *The Women and Their Pregnancies: The Collaborative Perinatal Study of the National Institute of Neurological Diseases and Stroke.* Philadelphia, WB Saunders Co, 1972.

9. Sever JL: Perinatal infections affecting the developing fetus and newborn, in Eichenwald HF (ed): *The Prevention of Mental Retardation Through Control of Infectious Diseases,* publication 1692. US Dept of Health, Education and Welfare, 1966, pp 37-68.

10. Mata LJ, Urrutia JJ, Béhar M: Infección en la mujer embarazada y en los productos de la concepción. *Arch Latinoam Nutr* 24:15-45, 1974.

11. Kass EH: Pyelonephritis and bacteriuria: A major problem in preventive medicine. *Ann Intern Med* 56:46-53, 1962.

12. Braun P, Lee YH, Klein JO, et al: Birth weight and genital mycoplasmas in pregnancy. *N Engl J Med* 284:167-171, 1971.

13. Davies PA: Bacterial infections in the fetus and newborn. *Arch Dis Child* 46:1-27, 1971.