Retrospective study of a pioneer antenatal screening program with 8,477 pregnant women in Brazil

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Summary

Purpose of investigation: To analyze the results of a statewide screening program inaugurated in 2002 in Mato Grosso do Sul, Brazil.

Methods: Retrospective audit of the screening results of 8,477 pregnant women for 11 diseases in 19 tests. Local health centers of the Brazilian Unified System of Health/State Program of Pregnant Protection (SUS/PEPG) and central reference processing laboratories, both in and out of state were involved. Pregnant women were referred to the program by medical staff principally at local health centers, between November 2002 and February 2003. Primary screening with filter-paper blood samples was carried out with positives being resampled and sera appropriately tested.

Results: The detailed test results are given below; the most frequent diseases serodiagnosed were hepatitis B, syphilis, HIV and Chagas' disease. One case of maternal phenylketonouria (PKU) was encountered.

Conclusion: The diagnosis of 11 diseases of importance for mothers and their offspring provides an epidemiological profile of Brazil, but must be matched by opportunities to elaborate new control strategies and improve health care during pregnancy.

Key words: Antenatal screening; Pregnancy infection.

Introduction

Mato Grosso do Sul is the first state in Brazil to introduce a state-wide antenatal screening program (PEPG) to be included in the Unified Health System (SUS). Pregnant women are referred to the program during routine antenatal examinations by medical staff, principally at local (municipal) health centers. Local medical staffs are informed of the results and inaugurate an appropriate treatment or care program. For the present study informed consent was obtained after the approval of the local ethics committee. Other states of the Brazilian Republic are expected to include similar programs in their health services, depending on the results and experiences of the Mato Grosso do Sul program.

Materials and Methods

Primary screening was carried out by collecting blood samples on filter-paper attached to a specially designed data card; confirmation of suspected positives was carried out with serum samples collected during follow-up. Standard commercial kits were employed for all stages of the screening processes (Table 1).

The 8,477 subjects were stratified according to age-groups (9-10, 11-20, 21-39, 31-40, 41-51 years) and details of the stage and number of pregnancies and abortions were recorded.

Results

The ages of the subjects examined ranged from nine years old (two cases) to 51 years old (one case). The per-

centage of adolescents (9-19 years) was 32%. The total number of subjects (8,477) were forwarded from 96% of the 77 municipalities in Mato Grosso do Sul. The total number of live births in the state during the same period was 12,638 [1, 2], with the present sample representing 67.1% of the total. Of the 8,477 women tested, 261 (3.0%) were positive for one of the tests included in the program; six were aware of their condition and were being treated. The majority of the women (39.8%) were tested during their second trimester and second pregnancy (27.6%). A total of 112 (42.9%) reported previous abortions in their lives.

Age-group 9-10 years (n = 3; $\bar{x}$ = 9 years)

All subjects showed IgG antibodies for toxoplasmosis, rubella, cytomegalovirus (CMV) and herpes simplex (HSV).

Age-group 11-20 years (n = 3,333; $\bar{x}$ = 18 years)

Toxoplasmosis: Filter-paper (Fp) = 2,900 positives for IgG and five for IgM. Serological confirmation (Sc) was obtained for three subjects with IgM and two with IgG/IgM.

Rubella: Fp = 2,853 positives for IgG and two for IgM; Sc = one reacted for IgG and one for IgG/IgM.

CMV: Fp = 3,055 positives for IgG and two for IgM; Sc = two with IgG antibodies.

HSV: Fp = 3,131 positives for IgG, none for IgM; Sc = none.

Syphilis: Fp = 28 positives. Sc with the Venereal Disease Research Laboratory (VDRL) = 22 positive, two negative. With FTA-ABS IgG, 23 were positive including the two negatives for the VDRL. Only one was positive

Table 1. — *Screening methodology includes the following diseases.*

Diseases	Blood samples on filter-paper Screening	Method	Serum samples Method
Toxoplasmosis	Anti-*Toxoplasma gondii* IgG	ELISA	ELISA
	Anti-*Toxoplasma gondii* IgM	ELISA	ELISA
Rubella	Anti-IgG to Rubella	ELISA	ELISA
	Anti-IgM to Rubella	ELISA	ELISA
Cytomegalovirus (CMV)	Anti-IgG to		
Cytomegalovirus	ELISA	ELISA	
	Anti-IgM to		
Cytomegalovirus	ELISA	ELISA	
Herpes simplex (HSV)	Anti-IgG to		
Herpes Simplex	ELISA	ELISA	
	Anti-IgM to		
Herpes Simplex	ELISA	ELISA	
Syphilis	Anti-*Treponema pallidum*	ELISA	VDRL and FTA-abs – IgG
HIV 1 and 2	Anti-HIV 1 and 2	ELISA	ELISA and Western blot
Chagas' Disease	Anti-*Tripanosoma cruzi*	ELISA	ELISA
Hepatitis B	HbsAg	ELISA	ELISA
	Anti-HBc	ELISA	ELISA
Hepatitis C	Anti-HCV	ELISA	ELISA
PKU	PKU maternal	ELISA	ELISA
HTLV I and II.	HTLV-I	ELISA	ELISA and Western blot
	HTLV-II	ELISA	ELISA and Western blot

ELISA = Enzyme Linked Immunosorbent Assay; VDRL = Venereal Disease Research Laboratory; and FTA-abs IgG = Fluorescent Treponemal Antibody Absorption Test.

for IgG/IgM. Three women were not localized for resampling and one was aware of the diagnosis previously.

HIV 1 and 2: Fp = seven positives for antibodies; Sc = five positives (ELISA+Western Blot) – one patient was not localized for resampling and one was aware of the diagnosis previously.
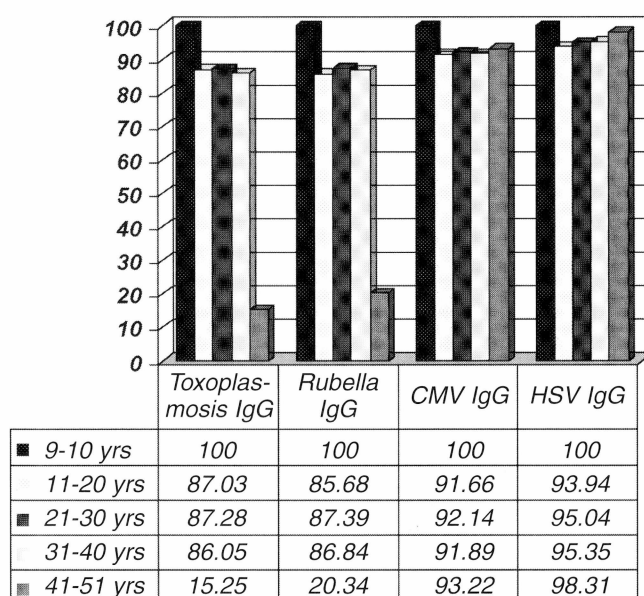

	Toxoplasmosis IgG	Rubella IgG	CMV IgG	HSV IgG
■ 9-10 yrs	100	100	100	100
11-20 yrs	87.03	85.68	91.66	93.94
■ 21-30 yrs	87.28	87.39	92.14	95.04
31-40 yrs	86.05	86.84	91.89	95.35
▨ 41-51 yrs	15.25	20.34	93.22	98.31

Figure 1. — Total percentage number (%) of positive IgG samples in the period from November 7, 2002 to February 20, 2003.

Chagas' Disease: One subject was positive for all tests (Fp and Sc).

Hepatitis B: Fp = six subjects were positive for HBsAg, all confirmed in Sc. Thirty-one were positive for anti-HBc. On follow-up, 28 were serologically positive, one was negative and three were not localized.

Hepatitis C: Fp = one subject was positive, confirmed serologically.

PKU: Fp = no positives found.

HTLV (human T-cell lymphotropic virus) I and II: Fp = one subject was positive, confirmed serologically.

Age-group 21-30 years (n = 4,071; x̄ = 25 years)

Toxoplasmosis: Fp = 3,553 positive for IgG, 12 for IgM and three doubtfuls. Of these 15 Sc gave two positives for IgM, five for IgG, five for IgG/IgM and three were not localized in follow-up.

Rubella: Fp = 3,556 positives for IgG, one for IgM and two doubtfuls; Sc = two positive for IgG and one for IgG/IgM.

CMV: Fp = 3,751 positives for IgG, 2 for IgM; Sc = one positive for IgG and one for IgG/IgM.

HSV: Fp = 3,868 positives for IgG, one for IgM and one doubtful; Sc = one positive for IgG and one not localized in follow-up.

Syphilis: Fp = 37 positives for IgG; Sc (VDRL) = 21 positives and two reacted but at minimal levels. By the FTA-ABS test, 29 were positive for IgG, including six non-reacting subjects for the VDRL test. Six subjects were not localized for follow-up, one refused to participate and one was aware of her condition previously.

HIV 1 and 2: Fp = 18 positives for both techniques; Sc = 15 confirmed - two were aware of the diagnosis previously and one gave birth before resampling was possible.

Chagas' Disease: Fp = seven subjects were positive, of which six were confirmed by serology; one was negative.

Hepatitis B: Fp = 11 women were positive for HBsAg; Sc = ten confirmed, one negative. For anti-HBc, Fp = 68 positives and six doubtfuls; Sc = of the 74 subjects in follow-up, 63 were positive, three negative and eight were not localized.

Hepatitis C: Fp = four positives, all confirmed with serology.

PKU: Fp = one positive, confirmed with serology.

HTLV I and II: Fp = two positives; Sc = one confirmed and one not localized in follow-up.

Age-group 31-40 years (n=1,011; x̄ =34 years)

Toxoplasmosis: Fp = 870 positives for IgG and one for IgM; Sc = this last case was positive for IgG/IgM.

Rubella: Fp = 878 positives for IgG, none for IgM.

CMV: Fp = 929 positives for IgG, none for IgM.

HSV: Fp = 963 positive for IgG, none for IgM.

Syphilis: Fp = 14 positives. Sc (VDRL) = eight positives - two reacted but at minimal levels and three were negative. With FTA-ABS 13 reacted with antibodies IgG, including those negative for VDRL. In both cases one women gave birth before being included in follow-up.

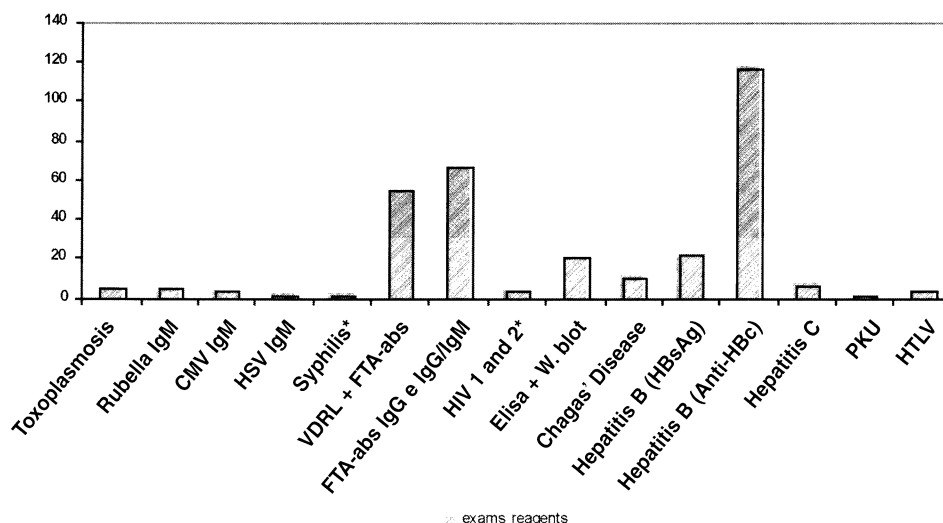*HIV 1 and 2:* Fp = two subjects positive for both tech-

Figure 2. — Total number of positive samples for IgM in the period from November 7, 2002 to February 20, 2003.

niques; Sc = one confirmed and one previously aware of the diagnosis.

Chagas' Disease: Fp = four subjects positive; Sc = all four confirmed.

Hepatitis B: Fp = seven subjects reacted to HBsAg of which six were confirmed and one was not localized in follow-up; for anti-HBc Fp = 24, of which Sc = 22 positives and two were not localized in follow-up.

Hepatitis C: Fp = two cases; Sc = confirmation of both.

PKU: Fp = no positives found.

HTLV I and II: Fp = two subjects positive; Sc = both confirmed.

Age-group 41-51 years (n = 59; x̄ = 43 years)

Toxoplasmosis: Fp = nine positives for IgG only.

Rubella: Fp = 12 positives for IgG only.

CMV: Fp = 55 positives for IgG only.

HSV: Fp = 58 subjects positive for IgG and one for IgM; Sc = confirmed.

Syphilis: Fp = one subject was positive. Sc = confirmed positive for IgG with FTA-ABS.

Hepatitis B: Fp = no positives for HBsAg but four for anti-HBc; Sc = all four confirmed.

HIV 1 and 2, Chagas' disease, Hepatitis C, PKU, HTLV I and II: Fp = no positives found.

Discussion

Toxoplasmosis: The mean rate of IgG antibodies demonstrated for all subjects 11-40 years old was 87.03%, indicating some previous contact with the parasite. On the other hand, 50 (84.7%) of the women aged between 41-51 years were non-reactive for IgG and susceptible to infections. Of the 21 subjects for follow-up, three were not localized and five (23.8%) were positive for IgM, and these were referred for treatment and other tests. The remaining subjects [13] were positive for IgG or IgG/IgM. The overall positivity for IgM (5/8477) was 0.06% which may

be considered low; a recent study carried out in Londrina (Parana, Brazil) evidenced 1.8% [3].

Rubella: The mean rate of seropositivity for the 11-40 year-old group was 13.3%; once again the 41-51 year-old group had the lowest level of antibodies, with 80% negative and at risk of infection. The vaccination strategy in Brazil includes all women up to 39 years, thus the oldest group had evidently not been vaccinated routinely [4].

CMV: A mean negative rate for IgG of 8.1% was found for all subjects studied. This level of seropositivity does not guarantee the absence of reinfections or the reactivation of a latent infection and its interpretation in large-scale screening is debatable.

HSV: In the composite age-group of 11 to 51 years, 94.7% were seropositive. Three subjects were recalled, two were positive for IgG and one was not localized.

Syphilis: Of the total examined, 67 (0.8%) were positive, which is considerably lower than the Ministry of Health estimate for Brazil where the disease is of compulsory notification [4].

HIV: In this study, 27 women were included in follow-up but one had already given birth and one was not located – of the 25 remaining four were already aware of the diagnosis and 21 (0.25%) confirmed positivity with ELISA and Western Blot. Testing for HIV is subject to consent and six subjects refused testing.

Chagas' Disease: Eleven subjects (0.13%) were seropositive and one was not located for follow-up. With the active control of the insect vector, Chagas' disease by vertical transmission is assuming a more important role and was therefore included in the testing program. Officially Mato Grosso do Sul is free of the disease because of vector control [5].

Hepatitis B: Of the 134 women called for anti-HBc serology, 13 were lost to follow-up, four were negative, but 117 were positive, showing exposure to the virus at some period. Only 22 women (0.26%) were positive for HBsAg, lower than the rate generally encountered in

other studies, for example the Londrina PR, Brazil survey encountered 0.8% (12/1,502 subjects) [3].

Hepatitis C: The World Health Organization (WHO) estimates for Hepatitis C levels in Brazil suggest a 2.6% prevalence [6]. In this survey the prevalence found was 0.08%.

PKU: Only one subject was found to be positive and was referred for appropriate treatment.

HTLV: Of the five women in follow-up for HTLV, one was not located and four were confirmed (0.05%).

Conclusion

Mato Grosso do Sul is a geographical crossroads with much population mobility within the Brazilian Republic, but also between countries across the borders with Paraguay and Bolivia. There is also a large indigenous population whose members move around regularly. Therefore, we cannot ensure that all the subjects included here belong to our state.

According to officially published data, in Mato Grosso do Sul during 2002, 75.3% of pregnant women commenced their prenatal examinations in the first semester in those areas covered by the national prenatal care program [7]. This was not seen in the present study, probably because antenatal screening was inaugurated in November 2002 and most subjects were already included in the national program, allowing the opportunity of amplifying the number of tests.

The innovative technique of primary screening on filter-paper attached to an identification card proved to be very successful and simple, permitting a wide-scale application of the screening program.

The diagnosis of 11 diseases of importance for mothers and their offspring provides an epidemiological profile of Brazil and must be matched by opportunities to elaborate new control strategies and improve health care during pregnancy.

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