Sudden Infant Death Syndrome: Risk Factor Profiles for Distinct Subgroups

Ursula Kohlendorfer, Stefan Kiechl, and Wolfgang Speri

The authors investigated risk profiles of sudden infant death syndrome (SIDS) as a function of age at death. A case-control study carried out in the Tyrol region of Austria enrolled 99 infants who died of SIDS between 1984 and 1994 and 136 randomly selected controls. Early and late SIDS (<120 days of age vs. ≥120 days) were defined according to the clear-cut bimodal age-at-death distribution. Inadequate antenatal care, low parental social and educational level, and the prone sleeping position were risk conditions that applied to both early and late SIDS. A marked seasonal variation (winter preponderance) was the most outstanding feature of late SIDS. A gestational age of <37 weeks (odds ratio (OR) = 8.4, 95% confidence interval (CI) 2.6-26.0), repeated episodes of apnea (OR = 5.7, 95% CI 1.2-27.0), low birth weight (<2,500 g) (OR = 3.4, 95% CI 1.1-11.0), a family history of sudden infant death (OR = 2.9, 95% CI 1.1-7.5), and maternal smoking during pregnancy (OR = 2.2, 95% CI 1.0-5.5) were associated with early SIDS. This study identified two distinct subgroups of SIDS infants characterized by different risk conditions and ages at death. These results underline a multiple-cause hypothesis for SIDS etiology which involves a genetic predisposition, immaturity in the first months of life, and environmental factors acting at various ages. Am J Epidemiol 1998; 147:960-8.

MATERIALS AND METHODS

Study population

The survey area in this study was the Tyrol, a federal state in the western part of Austria with 630,000 inhabitants and an area of 12,650 km² (11). Thorough investigation of autopsy records (the autopsy rate among infants with unexpected death was 89 percent) identified 145 SIDS cases in the 10-year period between January 1, 1984, and March 31, 1994 (incidence rate = 1.83 per 1,000 live births). All autopsies were performed by the same agency (Department of Forensic Medicine, University Hospital of Innsbruck) using the same case definition: SIDS was deemed confirmed when "the sudden death of an infant or young child was unexpected by history and a thorough post-mortem examination failed to demonstrate an adequate cause of death" (12, p. 17).

A control group of 145 infants was randomly recruited from birth records of the three main obstetric hospitals in the Tyrol, with the date (month and year) of birth used as the sole matching criterion. Infants who died during the first year of life were regarded as ineligible. The families of 14 controls had changed residence and were replaced with other families that satisfied the above matching criterion. In all, nine families did not participate, which left 136 controls for the analysis (94 percent). Among the families of cases, parents of 16 cases had moved to a location outside of the survey area and could not be traced. A total of 99 (77 percent) of the remaining 129 case families completed and returned the questionnaire. All infants enrolled were singletons.

Data collection

Parents of cases and controls were administered a standardized questionnaire by mail. We contacted...
am J Epidemiol
Vol. 147, No. 10, 1998

Nonresponders twice to encourage participation. The questionnaire covered a wide range of topics, including perinatal data (mother’s age at delivery, number of previous pregnancies and deliveries, antenatal care, smoking habits during pregnancy), data on delivery (gestation, mode of delivery, sex, birth weight, Apgar score), parental demographic data (marital status, educational level), details on housing, child care practices (usual sleeping position, feeding practices), and infant behavior (apnea, profuse sweating during sleep). Complementary to questions on the period prior to death in the cases (e.g., feeding practices), parents of controls were instructed to provide information on an analogous period in the lives of their infants. For example, if a SIDS infant born in May died in October, this time interval was the period of interest for the control infant.

Definition of risk variables

Maternal age at delivery was subdivided into two groups: <22 years (lowest quintile) and ≥22 years. Per usual practice, low birth weight was defined as a birth weight <2,500 g and preterm delivery as <37 completed weeks of gestation. Women were categorized according to their number of antenatal care visits (≥five as assigned in the “Mutter-Kind-Pass” records vs. <five) and their educational level (<12 years vs. ≥12 years). Parity was defined as number of live births. Smoking habits during pregnancy and in the presence of the child were assessed in terms of number of cigarettes smoked per day.

The infant’s usual sleeping position was classified as prone (on stomach), lateral (on side), or supine (on back). Feeding practice at the time of death was coded as breastfed, if the main type of milk given was breast milk, or bottle-fed. “Profuse sweating during sleep” was classified as occurring whenever the infant’s pajamas and/or bed sheets were regularly soaked with sweat. Mothers were asked whether they had repeatedly (i.e., more than once) seen their infants “turn blue” or stop breathing. A minimal duration of 8–10 seconds was mentioned in the questionnaire as a crude guideline for the definition of apnea. To assess the possibility of a genetic predisposition, parents were asked to report unexpected and unexplained deaths that had occurred in children under 1 year of age among their first- and second-degree relatives.

Design and statistical evaluation

The control group was assumed to be a random sample of Tyrol infants, since annual birth rates and SIDS rates did not change during the study period (1984–1994) and since month of birth (single matching criterion) was homogeneously distributed in the SIDS and general populations. The time intervals between delivery and completion of the questionnaire did not differ between controls (50.6 months) and SIDS infants (for early and late SIDS infants, 51.0 and 51.9 months, respectively).

Three-category logistic regression analysis was employed to assess the relation between candidate risk variables and disease status (controls, early SIDS, late SIDS), with the test procedure based on maximum likelihood estimators (13). These analyses were supplemented and confirmed by analyses that used models with split control groups. Application of separate reference groups is relevant to postnatal age-dependent behaviors, such as breastfeeding at the time of death. Multivariate equations were fitted using a step-forward selection procedure (p values for entry and removal were 0.10 and 0.15), which allowed for all risk factors identified in the unadjusted analyses (BMDP Statistical Software, Los Angeles, California). Each model’s goodness of fit was assessed using the test of Hosmer and Lemeshow (14). Separate analyses using equations that either excluded subjects with missing values (usually <2 percent) or substituted the means of given variables for missing values were carried out. The data presented here were derived from the latter approach, since both procedures yielded virtually identical results (valid n for all analyses = 235). Given the rare occurrence of SIDS (1.83/1,000 live births), odds ratios derived from logistic regression analysis approximate relative risk estimates. Effect modification was tested by inclusion of interaction terms.

The seasonal homogeneity of SIDS was examined using the χ² test. Attributive fractions of risk variables were adjusted for potential confounders and intercorrelation as described by Whittemore (15).

RESULTS

Prevalences of selected sociodemographic, antenatal, and postnatal characteristics of SIDS cases and healthy infants are summarized in table 1. SIDS incidence and total postneonatal mortality averaged 1.83 per 1,000 live births and 3.80 per 1,000 live births per year, respectively. A bimodal age-at-death distribution was found, with peaks in the third and sixth to seventh months of life. This finding applied equally to the overall group of SIDS infants (n = 145; figure 1) and those actually included in the current evaluation (n = 99). Exclusion of preterm infants or adjustment of ages at death for preterm delivery had virtually no effect on the shape of this curve. According to the consistent bimodal distribution, two subgroups of SIDS occurrence were defined, with early SIDS
(<120 days of age) accounting for 55.6 percent of all SIDS cases and late SIDS (≥120 days of age) accounting for 44.4 percent (figure 1).

In the unadjusted analyses, several variables, including a prone sleeping position, inappropriate antenatal care, young maternal age, and low maternal educational level, predicted an increased risk of both early and late SIDS (table 2). Prone the absence of breastfeeding appeared to facilitate SIDS in infants older than age 120 days. This finding approached statistical significance (p = 0.08). Five risk variables (low gestational age, repeated episodes of apnea, low birth weight, a history of sudden infant death in the family, and smoking during pregnancy) were significantly related to early SIDS only. Multivariate analyses replicated the results of the unadjusted ones in that most of the above risk variables emerged as independent risk predictors of SIDS (table 2). The significance of prenatal smoking decreased when the analysis was adjusted for preterm delivery or for a continuously scaled birth weight variable. We found no significant synergistic effects between any of the above risk variables or with higher-order interactions. Conditional logistic regression analysis that considered month of birth and hospital of birth yielded virtually identical results (data not presented).

No association was found for the following variables: marital status, father’s educational level, gravidity, parity, and postnatal smoking (table 2). Median ages at death were calculated for all risk variables that showed differential associations with early and late SIDS: For night sweating (yes/no), the median age at death was 168 days versus 124 days (p = 0.08); for infant sex (male/female), the median age was 157 days versus 115 days (p = 0.05); for length of gestation (<37 weeks/≥37 weeks), it was 108 days versus 153 days (p = 0.14); for repeated apnea episodes (yes/no), 92 days versus 138 days (p = 0.02); for birth weight (<2,500 g/≥2,500 g), 110 days versus 146 days (p = 0.27); for family history of sudden infant death (yes/no), 105 days versus 159 days (p = 0.04); and for smoking during pregnancy (yes/no), 120 days versus 158 days (p = 0.09).

Seasonal clustering of SIDS (winter preponderance) was a further unique feature of late SIDS (χ² = 11.1, 3 df; p = 0.011) (figure 2). The prevalence of minor respiratory infections (found by necropsy) among late SIDS infants was more than twice that among early SIDS infants (58 percent vs. 23 percent; p < 0.01). When parental responses to questions on minor infectious illness at the time of death were substituted for the necropsy results, the difference remained significant (20.0 percent vs. 6.8 percent; p = 0.05).

Among all SIDS infants, months of birth were distributed homogeneously throughout the year (χ² = 9.00, 11 df; p = 0.62). Likewise, the early and late SIDS subgroups showed uniform nonseasonal month-at-birth distributions. Spring- or summer-born infants died at ages similar to those for autumn- or winter-born infants (104, 135, 103, and 161 days, respectively; p = 0.18).

**DISCUSSION**

Most previous population studies have found that maternal smoking, a prone sleeping position, and the absence of breastfeeding or too short a period of breastfeeding constitute risk factors for SIDS (16–18). Information campaigns addressing these behaviors have been efficient in reducing SIDS rates (19–22). We postulate that SIDS is triggered by a variety of pathophysiologic mechanisms acting at various ages, and we examined this hypothesis using data from a case-control study conducted in the Tyrol.

Based on the clear bimodal age-at-death distribution (figure 1), we subdivided SIDS infants into two subpopulations referred to as having early (<120 days) and late (≥120 days) SIDS. Both groups shared some risk conditions, including low maternal age, low social status, a prone sleeping position, and inadequate antenatal care. All of these variables in concert accounted for a considerable portion of SIDS risk in the Tyrol, as
indicated by an adjusted attributive fraction (of overall SIDS mortality) of 41 percent (15). However, the peak incidence of SIDS in the third and sixth to seventh months of life (figure 1), which clearly exceeded the base risk, remains unexplained and awaits further close consideration.

Late SIDS

Clustering in the cold season emerged as an outstanding feature of late SIDS. The local climate in the Tyrol is characterized by cold autumn and winter months, with an average monthly temperature ranging from 2.37°C to -2.72°C; moderate temperatures in the spring; and hot, humid summers. Daytime high temperatures rising to 35°C contrast with extreme coldness reaching -20°C in December. A variety of populations have exhibited analogous seasonal SIDS patterns, especially in areas where central heating is less common (23-28). Differences in the seasonality of SIDS by infant age are less well documented. The few previous studies on this topic observed an increasing winter preponderance of SIDS with increasing infant age, and therefore confirmed our results (5-7, 29). As figure 1 shows, excess mortality among older infants in the cold season accounted for a large part of the second incidence peak of SIDS, and this may therefore be the key to a better understanding of triggers underlying late SIDS. Several clues may be inferred from the available evidence.

Low outdoor temperatures predispose older infants to infectious illnesses. The seasonal pattern of late SIDS is actually similar to the seasonal distribution of respiratory infections (5, 7, 30). In line with some previous studies (31, 32), necropsy examination in the Tyrol revealed a high prevalence of minor lower respiratory disease among older SIDS infants (58 percent) but a low occurrence in young SIDS cases (23 percent). Infection rates among healthy infants who died in accidents have been estimated to be 18 percent (32). The clear divergence in the above rates suggests a role of infectious diseases in late SIDS (32, 33). Two further results of our study fitted well into this concept: Among older infants, winter preponderance and SIDS mortality tended to be more pronounced in males (odds ratio = 1.8, 95 percent confidence interval 1.1-3.4) and in infants who were not being breastfed at the time of death (odds ratio = 2.1, 95 percent confidence interval 0.9-5.0). Male infants are more susceptible to infectious diseases such as bronchiolitis and pneumonia due to the respiratory syncytial virus (34). Breast milk is known to contain secretory immunoglobulins, as well as several nonspecific anti-infective factors, such as lactoferrin and epithelial growth factor. Thus, breastfeeding has been shown to protect against a variety of childhood infections (35).

Our study revealed a higher frequency of profuse sweating during sleep in infants who later died from late SIDS (20.2 percent) as compared with healthy infants (8.5 percent). Altered child care practices in the cold season (paradoxical overheating) (28, 36-40) and an enhanced vulnerability to thermal imbalance in older SIDS infants (18) may account for this phenomenon. Possible mechanisms underlying late SIDS include hypothermia (41), hyperthermia due to inadequate thermal insulation, and thermoregulatory interactions with sleep state or respiration (42).
### Early SIDS

Low birth weight, infantile apnea, and a family history of SIDS indicate "immaturity" and possibly genetic vulnerability. Thus, it was not surprising that these factors were preferentially related to early SIDS.

Familial occurrence of SIDS has scarcely been reported before (43–47). Øyen et al. documented familial aggregation in a large Norwegian population which was attributed to a common genetic basis and a sharing of environmental risk factors (48). Further indirect support is derived from a study of adult sleep apnea/hypopnea syndromes: The authors reported an enhanced risk of SIDS in these families and speculated that both syndromes are manifestations of one inheritable condition—namely, narrow upper airways (49).

Our finding of a preferential association of low birth weight with early rather than late SIDS apparently stands in conflict with previous studies that reported either an opposite trend (2, 10) or no preferential association at all (8, 50). Careful review of these surveys, however, revealed that the median survival time for low birth weight infants in these studies ranged from 112 days to 133 days, which is virtually identical to the vulnerable period observed in our study (median survival, 110 days) and is mainly within the time span defined as early SIDS (<120 days). Actually, the most unusual finding in our study was a prolonged survival of normal birth weight infants (median survival, 146 days), which may be explained by the prominent second incidence peak for SIDS in the Tyrol. Thus, inconsistencies between this study and previous surveys appear to reflect distinct features of the study populations and designs rather than true biologic differences.

Maternal smoking is widely accepted as another prominent risk factor for early SIDS (9, 10, 51, 52). The results of the current study support the concept that maternal smoking affects the infant before birth, possibly by retarding fetal growth and brain development (53–57). The potential effects of postnatal smoking are a matter of ongoing controversy (9, 10, 52). Direct toxic properties of passive smoking and facili-

---

**TABLE 2. Association of risk variables with early (<120 days) and late (≥120 days) sudden Infant death syndrome (SIDS), Tyrol state, Austria, 1984–1994**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early SIDS</th>
<th></th>
<th></th>
<th>Late SIDS</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude OR†</td>
<td>95% CI†</td>
<td>Adjusted OR‡</td>
<td>Crude OR†</td>
<td>95% CI†</td>
<td>Adjusted OR‡</td>
</tr>
<tr>
<td><strong>Preferential association with late SIDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Night sweating (yes vs. no)</td>
<td>1.9</td>
<td>0.7–5.0</td>
<td>1.3</td>
<td>2.4</td>
<td>1.1–5.7</td>
<td>3.3*</td>
</tr>
<tr>
<td>Male sex (vs. female sex)</td>
<td>1.0</td>
<td>0.5–2.1</td>
<td>1.8</td>
<td>1.1</td>
<td>1.3–3.4</td>
<td></td>
</tr>
<tr>
<td><strong>Preferential association with early SIDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestation &lt;37 weeks (vs. 37 weeks)</td>
<td>8.4</td>
<td>2.6–26.0</td>
<td>12.0**</td>
<td>3.6</td>
<td>1.0–12.0</td>
<td>3.5</td>
</tr>
<tr>
<td>Repeated apnea episodes (yes vs. no)</td>
<td>5.7</td>
<td>1.2–27.0</td>
<td>7.2*</td>
<td>2.5</td>
<td>0.4–15.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Birth weight &lt;2,500 g (vs. ≥2,500 g)</td>
<td>3.4</td>
<td>1.1–11.0</td>
<td>4.5*</td>
<td>1.8</td>
<td>0.5–6.5</td>
<td>2.0</td>
</tr>
<tr>
<td>Family history of infant death (yes vs. no)</td>
<td>2.9</td>
<td>1.1–7.5</td>
<td>3.9*</td>
<td>1.8</td>
<td>0.7–4.8</td>
<td>3.2</td>
</tr>
<tr>
<td>Smoking during pregnancy (yes vs. no)</td>
<td>2.2</td>
<td>1.0–4.5</td>
<td></td>
<td>1.8</td>
<td>0.9–3.6</td>
<td></td>
</tr>
<tr>
<td><strong>Association with both early and late SIDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maternal age &lt;22 years (vs. ≥22 years)</td>
<td>3.1</td>
<td>1.4–7.2</td>
<td>2.1*</td>
<td>3.6</td>
<td>1.7–7.8</td>
<td>4.8**</td>
</tr>
<tr>
<td>Low educational level of mother (&lt;12 years vs. ≥12 years)</td>
<td>2.9</td>
<td>1.4–6.0</td>
<td>1.9</td>
<td>1.0</td>
<td>1.0–3.6</td>
<td></td>
</tr>
<tr>
<td>&lt;5 antenatal visits (vs. ≥5 visits)</td>
<td>5.7</td>
<td>1.8–19.0</td>
<td>8.9**</td>
<td>4.7</td>
<td>1.6–14.0</td>
<td>4.9**</td>
</tr>
<tr>
<td>Prone sleeping position (vs. supine/side)</td>
<td>1.7</td>
<td>1.0–3.8</td>
<td>2.2*</td>
<td>2.2</td>
<td>1.1–4.4</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>No association with either early or late SIDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unmarried parents (yes vs. no)</td>
<td>1.4</td>
<td>0.6–3.4</td>
<td>1.5</td>
<td>0.7</td>
<td>0.7–3.4</td>
<td></td>
</tr>
<tr>
<td>Low educational level of father (&lt;12 years vs. ≥12 years)</td>
<td>1.2</td>
<td>0.4–3.4</td>
<td>0.6</td>
<td>0.2</td>
<td>0.2–1.9</td>
<td></td>
</tr>
<tr>
<td>Mother’s first pregnancy (yes vs. no)</td>
<td>1.2</td>
<td>0.6–2.4</td>
<td>1.0</td>
<td>0.5</td>
<td>0.5–1.9</td>
<td></td>
</tr>
<tr>
<td>Mother’s first child (yes vs. no)</td>
<td>1.1</td>
<td>0.5–2.2</td>
<td>1.0</td>
<td>0.5</td>
<td>0.5–1.8</td>
<td></td>
</tr>
<tr>
<td>Postnatal smoking (yes vs. no)</td>
<td>1.9</td>
<td>0.9–4.0</td>
<td>1.0</td>
<td>0.5</td>
<td>0.5–1.8</td>
<td></td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01.
† OR, odds ratio; CI, confidence interval.
‡ Odds ratios were derived from three-category logistic regression analysis of early and late SIDS on the risk variable (valid n = 235). The multivariate model was fitted with a forward-stepwise selection procedure. Eight variables met the selection criteria (p value for entry: p < 0.1; p value for removal: p < 0.15).
tation of lower respiratory tract infections have been proposed as potential mechanisms whereby postnatal smoking might increase the risk of early SIDS (2, 58). However, the hypothesis regarding the latter pathway has been challenged because of low necropsy evidence of infections in this group (10). Our survey yielded a tendency towards a higher SIDS risk in young infants passively exposed to cigarette smoke, but it had insufficient power to definitively settle this issue because of a low rate of postnatal smoking.

The significance of the prone sleeping position as a risk factor for SIDS has been postulated to decrease with advancing age and the emerging ability of the infant to voluntarily change position. The precise threshold of age for this switch, however, is not well established, and it may depend on the action of certain cofactors (infections, thermal insulation). In the current study, we assessed agreement between the usual sleeping position determined by the parents and that at the time of death as a crude surrogate measure of the infant’s ability to move voluntarily. Accordance was nearly complete up to an age of 4 months (95 percent) and was still high for infants aged 5–6 months (79 percent), but was only slightly above chance thereafter (65 percent). This corresponds to the results of one recent study on sleeping position and infant’s age (59) but disagrees with the findings of another study (60). Together with the preferential significance of potential cofactors (infections, thermal insulation) in older infants, this finding may explain why a prone sleeping position was associated with both early and late SIDS in our population.

The current study and most previous studies have agreed that low maternal age and low social status are significant risk indicators for SIDS (16, 61–63), although some ethnic differences may exist (64). However, the associations of marital status and parity with SIDS are less consistent, which may in part reflect peculiarities in the interplay of these variables with social status and lifestyle.

An alternative concept

An interaction between month of birth, seasonality, and age at death may be a further or alternative clue to the age-at-death distribution of SIDS. It has been postulated that “at-risk” infants survive until additional environmental (e.g., seasonal) factors appear and, as a consequence, age at death is influenced by season of birth (4, 29, 65, 66). However, the possibility of such an interaction has been challenged by others (67, 68). Particularly, a large prospective survey from North Carolina showed season and age to be independent determinants of SIDS survival (67). The current survey added support to the findings of that study in that season of birth did not affect median survival time. The month-of-birth distributions of early and late SIDS deaths did not differ from a uniform nonseasonal distribution. These results should be viewed in light of the comparatively low power of our study to detect such interactions.

Merits and limitations

Distribution of ages at death. Some of the previous studies that analyzed risk profiles of SIDS in various age groups were criticized because of a unimodal age-at-death distribution, which makes subdivision by age
purely accidental and susceptible to bias. Our study population exhibited a clear-cut bimodal age-at-death distribution. The second incidence peak in the sixth to seventh month of life, which was not observed in most other populations (2, 3, 6, 7, 10, 16), may reflect the extreme local climate in the Tyrol.

Data quality. In our study area, pregnant women must undergo five well-documented health checkups during pregnancy and six after delivery (noted in "Mutter-Kind-Pass" records) in order to qualify for a financial bonus. Thus, data on pregnancy, delivery, and infant medical history had generally been documented prior to the occurrence of SIDS (>95 percent), which facilitated an accurate retrospective assessment of most risk factors. However, a few items not considered in the "Mutter-Kind-Pass" records (repeated apnea episodes, night sweating, family history) are open to bias. Corresponding results should be interpreted in the light of these potential limitations.

External validity. The current analysis focused on a purely Caucasian population, and the results should be interpreted accordingly.

Bias. Three sources of bias—selection, recall, and nonresponder bias—await further consideration. Births occurring in the region's three main obstetric hospitals accounted for the great majority of overall births in the Tyrol. Because of this and because of the lack of regional differences in response rates, SIDS rates, SIDS risk profiles, seasonal and age-at-death distributions, and sociodemographic characteristics, we are confident that no relevant referral or selection bias occurred when we restricted the recruitment of controls to these three hospitals. Previous studies have documented that case/control differences in recall accuracy do not appear to create spurious associations with SIDS (69, 70). However, differences in the response rates observed for parents of SIDS infants and controls may be a potential source of bias.

In conclusion, the current study identified two epidemiologically distinct subgroups of SIDS death: early SIDS, which is associated with pre- and postnatal features indicating vulnerability at birth, and late SIDS, which shows a clear seasonality, with an incidence peak in the cold months that is possibly mediated by infectious diseases or an increased thermal vulnerability (environmental influence). These results may contribute to a better understanding of the etiology of SIDS and should stimulate further research in this field.

ACKNOWLEDGMENTS

The authors thank Drs. Walter Rabl (Department of Forensic Medicine) and Edda Haberlandt (Department of Pediatrics), University Hospital of Innsbruck, for their cooperation.

REFERENCES


