Living at high altitude and risk of sudden infant death syndrome

Ursula Kohlendorfer, Stefan Kiechl, Wolfgang Sperl

Abstract

***Objective*—To investigate the association between altitude of residence and risk of sudden infant death syndrome (SIDS).**

***Methods*—A retrospective, case control study in the Tyrol, Austria enrolled 99 infants with SIDS occurring between 1984 and 1994, and 136 randomly selected control cases. Data on pregnancy, delivery, child care practice, and sociodemographic characteristics including altitude of residence were collected with a standardised questionnaire.**

***Results*—The risk of SIDS increased gradually with increasing altitude of residence. This relation remained independently significant when the analysis was adjusted for gestational age, birth weight, prenatal care, mother's age at delivery, educational level of parents, and cigarette smoking during pregnancy. The prone sleeping position emerged as an obligatory cofactor in this association. In the whole of Austria, a similar trend of association emerged between the average altitudes in the 99 political counties and the rates of SIDS.**

***Conclusions*—This study identified altitude of residence as a significant risk predictor of SIDS, primarily in combination with the prone sleeping position. Respiratory disturbances, reduced oxygen saturation, and lower temperatures at high altitude might explain this association.**

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Keywords: sudden infant death syndrome; altitude; prone sleeping position

Department of Paediatrics, University of Innsbruck, Anichstraβe 35, A-6020 Innsbruck, Austria
U Kohlendorfer

Department of Neurology, University of Innsbruck
S Kiechl

Children's Hospital, LKA Salzburg, Müllner Hauptstraβe 48, A-5020 Salzburg, Austria
W Sperl

Correspondence to:
Dr Sperl.

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Respiratory failure is probably one of the main pathomechanisms of sudden infant death syndrome (SIDS). Diseases and behaviours that potentially contribute to respiratory disturbance, such as respiratory infections or the prone sleeping position, have been proposed as risk factors of SIDS.[1–4] Residence at high altitude may rank among these risk conditions because of a decline in blood oxygen saturation and hypoxia induced depression of respiration in young infants.[5 6] We examined the association between altitude and SIDS risk in Austria with special attention directed to the Tyrol, a federal state in the mountainous western part. The latter area is particularly appropriate for this purpose because it has a wide range of altitudes of permanent residence (500–1900 metres above sea level), homogeneous climatic conditions, and uniform postmortem examination rates.

Methods

Austria is divided into nine federal states containing 99 political counties. The Austrian Statistical Office served as the source for SIDS incidence rates in each county.[7] Postmortem examination rates varied from 73% to 97%. Altitude of residence was determined by the Austrian altitude code file compiled by the census bureau. The Tyrol is a federal state in the western mountainous part of Austria with 630 000 inhabitants and an area of 12 650 km^2. Thorough investigation of postmortem records in the Tyrol (postmortem examination rate, 91%) identified 145 SIDS cases in the 10 year period between 1 January 1984 and 31 March 1994, corresponding to an incidence rate of 1.83/1000 live births. All postmortem examinations were performed by the same agency (department of forensic medicine, University of Innsbruck), using the same case definition: "SIDS is the sudden death of an infant or young child, which is unexpected by history and in which a thorough postmortem examination fails to demonstrate an adequate cause of death".[8] Infants who died unexpectedly but did not have a postmortem examination were not considered in our study.

A control group of 145 infants was recruited randomly from birth records of the three main obstetric hospitals in the Tyrol with the date (month and year) of birth used as a single matching criterion. Parents of 14 controls had changed residence and were replaced by other families that satisfied the above matching criterion. In all, nine families did not participate, which left 136 controls for the analysis (94%). Among parents of cases, 16 moved to a location outside the survey area and could not be traced. A total of 99 of the remaining 129 case families completed and returned the questionnaire (77%). In our survey, infants of responders and non-responders did not differ in the male to female ratios, age at death distribution, seasonality of SIDS, or socioeconomic status.

Parents of cases and controls were administered a standardised questionnaire by mail. Non-responders were contacted twice to motivate participation. The questionnaire covered a wide range of topics, including perinatal data (mother's age at delivery, smoking practice during pregnancy, and prenatal care), data on delivery (birth weight and gestational age), parental demographic data (educational level), details on housing, including altitude of place of residence, and questions about child care practice (usual sleeping position). Maternal age at delivery was assessed in years and birth weight in grams. Women were categorised according to the number of antenatal care visits

Figure 1 (A) Aggregation of same altitude range in different geographical units of Austria. (B) SIDS incidence in different geographical units of Austria.

(less than 5, 5, more than 5). The mother's educational attainment was categorised in three groups (less than 12 years, 12 years, more than 12 years). Because parents of cases and controls were instructed to complete the questionnaire using "Mutter-Kind-Pass" records, agreement between data from both sources exceeded 95% (spot tests in 50 random subjects). Documentation of most infant characteristics before SIDS minimised recall bias. "Mutter-Kind-Pass" contains obstetric and infant records. According to the health programme in Austria, routine health checks during pregnancy and childhood are scheduled in "Mutter-Kind-Pass" records.

STATISTICAL ANALYSIS

The crude associations between altitude and both sociodemographic and risk attributes were assessed by means of Pearson correlation coefficients (continuous variables) and the analysis of variance (categorical variables). To account for deviations from normal distribution, these analyses were supplemented and confirmed by non-parametric procedures (Spearman rank correlation coefficients, Kruskal-Wallis test; data not presented). Because annual birth and SIDS rates did not change during the study period (1984–94) and the month of birth was homogeneously distributed in the SIDS and general population, the control group may be assumed to be a random sample of infants in the Tyrol. Conditional and unconditional logistic regression models were fitted to estimate the relation between altitude and SIDS risk, and to control simultaneously for possible confounders. Altitude of residence was treated either as a continuous variable or as a set of indicator variables (quintiles). Separate equations were run that exclude subjects with missing values (usually < 2%) or substitute the mean of given variables for unavailable values. The data presented were derived from the latter approach because both procedures yielded virtually identical results. Effect modification by sleeping position and other variables was analysed by the inclusion of interaction terms (multiplicative model).

Results

In the 99 political counties of Austria, average altitudes showed a significant association with both SIDS incidence and total postneonatal mortality ($r = 0.31$ and $r = 0.23$, respectively; $p < 0.05$) (fig 1). With the exception of Vienna, postmortem examination rates are on average higher in the mountainous western and southern parts of Austria than in the flat eastern regions. Thus, we obtained a strong association between altitude and postmortem examination rates ($r = 0.57$; $p < 0.001$).

In the Tyrol, the main characteristics of pregnancy, delivery, and child care practice were not related to the altitude of residence, except for lower educational levels in higher lying areas ($p < 0.001$). The risk of SIDS increased gradually at higher altitudes in a dose response fashion (odds ratio (OR), 1.12/100 m; 95% confidence interval (CI), 1.02 to 1.24). Conditional logistic regression analysis, which considered the matching for month and year of birth, yielded virtually identical results (OR, 1.13/100 m; 95% CI, 1.01 to 1.25). Because altitude of residence can also be assessed without bias for SIDS and control infants whose parents did not participate, the analysis was repeated in the original population sample (SIDS and controls, 145 each) and yielded similar results (unconditional logistic regression analysis: OR, 1.14/100 m; 95% CI, 1.01 to 1.3; conditional logistic regression analysis: OR, 1.14/100 m; 95% CI 1.03 to 1.26). Sleeping position emerged as an obligatory cofactor in the altitude–SIDS relation ($p = 0.0076$ for effect modification). In fig 2, OR values for SIDS according to quintiles of altitude are given separately for infants sleeping prone and those sleeping on their side or back. Risk estimates presented were simultaneously adjusted for gestational age, birth weight, prenatal care, mother's age at delivery, smoking during pregnancy, and educational level. When comparing infants sleeping prone and living at an altitude of either $\leqslant$ 600 (quintile 1, 2) or > 1000 m (quintile 5), the groups differed in their SIDS risk by the factor 4.4, whereas infants sleeping on their side or back showed only a marginal increase in SIDS risk across quintiles of altitude. For infants in the prone sleeping position, this graph and the use of orthogonal polynomials confirmed the excellent fit of a "linear model", suggesting an approximately equal OR for a standard change in altitude across the entire range (500–1900 m) (linear term, $p = 0.02$; quadratic and higher order terms, $p > 0.05$).

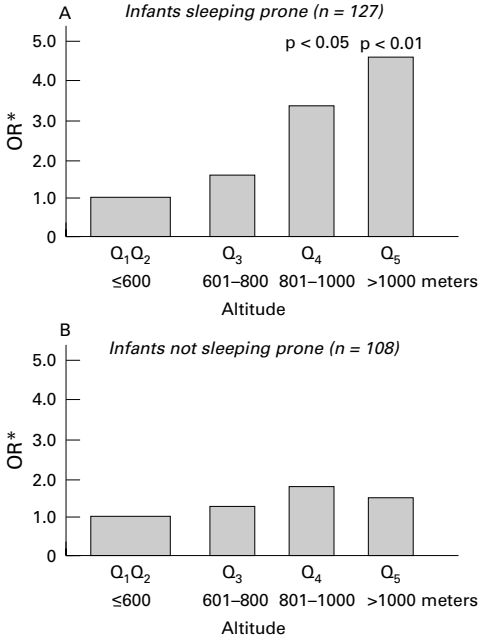

*Figure 2 Association between altitude of residence (quintiles Q_1 to Q_5) and SIDS risk in the Tyrol (n = 235). Altitude emerged as a significant risk predictor in infants sleeping prone but not in those sleeping on their side or back (p = 0.0076 for effect modification). *Odds ratios (OR) were derived from logistic regression analysis of SIDS on quintiles of altitude (reference category, quintile 1 + 2), gestational age, birth weight, prenatal care, mother's age at delivery, educational level, sleeping position, and smoking during pregnancy.*

Discussion

When SIDS rates and average altitudes were plotted for the 99 Austrian counties, there was a great deal of overlap between geographical units with high altitude and raised SIDS incidence (fig 1). Interpretation of this finding, however, requires caution because it might reflect marked climatic variations, differences in socioeconomic status, and other SIDS risk factors, and the higher postmortem examination rates seen in the mountainous parts of Austria, rather than the effects of altitude itself. Owing to the extensive correlations between these variables, multivariate analysis failed to clarify the key issue.

To obtain conclusive evidence, we designed and conducted a case control study in the Tyrol,[9] a federal state in the western part of Austria. The survey area is particularly appropriate for this purpose because it has a uniform case definition, a wide range of altitudes, homogeneous climatic conditions, and a high and homogeneous postmortem examination rate. The Alpine climate, which predominates in the entire survey area, is characterised by a cold period during late autumn and winter months, with average monthly temperature ranging from 2.4°C to −2.7°C, moderate temperatures in spring, and hot humid summers.

As an outstanding finding high altitude emerged as a significant risk predictor of SIDS in infants sleeping prone. Variations in SIDS risk could not be attributed to differences in social status or any other risk condition associated with SIDS. Several possible explanations for this phenomenon may be inferred from our survey and previous reports:

(1) Reduced oxygen availability at high altitude is associated with increased neonatal and infant mortality mainly as a result of hypoxaemia, and might also account for the increased SIDS risk.[10] Normal physiological adaptations to high altitude include an increase in ventilation, cardiac output, vital capacity, and haemoglobin, as well as a shift in the oxyhaemoglobin affinity curve.[11–13] Some of these compensatory mechanisms develop only after months to years of life, and are thus not available to young infants.[14] The typical response to hypoxia in young infants is not an acceleration of respiration, but a sustained depression, occurring after a period of acceleration.[5] The prone sleeping position, which is an essential cofactor in the association between altitude and SIDS, might cause further deterioration in respiration and possibly explain why an increase in SIDS risk already occurs at altitudes without significant oxygen desaturation.

(2) At high altitudes, a decline in maternal respiratory function and maternal arterial oxygenation in pregnancy is associated with intrauterine growth retardation and birth weight reduction.[15–17] This might be particularly relevant to mothers who cannot compensate sufficiently for the decreased atmospheric oxygen because of intrinsic or extrinsic reasons (for example, respiratory diseases, anaemia, and cigarette smoking). Low birth weight, a well known risk factor for SIDS, in turn, might account for the relation between altitude and SIDS risk.[18] When our analysis was adjusted for birth weight, however, the SIDS risk associated with high altitude showed only a marginal change, which indicates a minor relevance of such a prenatal mechanism in our SIDS population.

(3) Cold, outdoor daily temperatures have been postulated to promote SIDS and might be a further explanation for raised SIDS rates at high altitudes.[19 20] In the Tyrol, mean temperatures decrease at a rate of 0.5–1.0°C/100 m of altitude. Effects of lower temperatures on SIDS mortality might not only be direct, but mainly indirect, by modification of indoor temperature and clothing.[21 22] Hyperthermia and inappropriate (overcompensatory) thermal insulation have been reported to enhance the risk of SIDS.[23 24] Notably, these findings were primarily relevant to infants in the prone sleeping position, as was the association between altitude and SIDS risk in our survey. Our retrospective study fails to quantify accurately thermal insulation and thus cannot add further direct support to the promising concept of a temperature pathway in the relation between altitude and SIDS.

In summary, our study provided evidence of an increased SIDS risk among infants living at high altitude, primarily in combination with the prone sleeping position.

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