

**TO INVESTIGATE THE RELATIONSHIP BETWEEN PROLONGED QT
INTERVAL AND MATERNAL SMOKING**

Research done by: Bindu Punnoose

Introduction

Sudden Infant Death Syndrome (SIDS) is the third leading cause of infant mortality, and the leading cause of death between one month and one year of age. This tragic syndrome is multifactorial in origin. Although the incidence of SIDS has recently declined to a little less than 1 death for every 1000 births, effective preventive measures are lacking due to the poor understanding of the mechanisms underlying the disorder. Several epidemiological studies have provided strong evidence that sleeping in the prone position places infants at greater risk for SIDS. This brought about the “Back to sleep” campaign, launched to educate mothers to place infants to sleep on their backs rather than stomachs. But still at the present time, SIDS has not been entirely wiped out, accounting for nearly 30% of deaths during the neonatal period. ¹

Maternal smoking during pregnancy and passive smoking have also been associated with an increased risk for SIDS. ²⁻³ Case-control studies have indicated definite dose-response relationships. It has been hypothesized that tobacco smoke may affect neuroregulation of breathing which could result in apneic spells and sudden infant death. ⁴

Delayed ventricular repolarization, measured on the ECG as prolongation of the QT interval on the electrocardiogram is associated with a high risk of cardiac death in adults. ⁵ Prolongation of the QT interval may be the result of a specific imbalance in the cardiac sympathetic innervation characterized by dominance of left-sided nerves, where cardiac electrical stability is reduced and development of ventricular fibrillation is favored. ⁶⁻⁸ Patients at high risk for cardiac death may be identified by careful examination of the QT Interval. ⁹ Recent data indicates that there is a significant association between prolonged QT and SIDS. It was found that the QTc interval naturally lengthens at the second month of life, when SIDS incidence is at its peak. ¹⁰ In a recent study involving 34,442 newborns found that one half of babies with a prolonged QT intervals died of SIDS. ¹¹

In this experiment, the QT Intervals of 24 healthy 2 month old infants were obtained. 2 month olds were chosen since this was the time of maximum risk for SIDS. To insure accuracy, the average of 25 intervals were taken per baby. Previous studies have concentrated on newborn babies and taken the average of fewer intervals. The results of the study were then analyzed to see if a relationship existed between prolonged QT Interval and maternal smoking, since both have independently been proven to be risk factors for SIDS. This hypothesis has not previously been tested.

Materials and Methods

The electrocardiograms (ECG) of 24 infants, all of two months of age, were analyzed. 17 babies came from a rural Native American population and 7 came from an urban population in New York City. At birth, all babies were healthy, having apgar scores which were greater than 8. Babies were selected by means of availability, good health, and having no other risk factors (such as maternal alcohol consumption, low birthweight, or difficult pregnancies). The 24 babies selected also had plottable ECG's, which were able to be marked clearly. 12 male babies and 12 female babies were used in the study.

ECG's of babies were taken during the baseline period of a study designed to evaluate the heart rate response of infants to changes in body position. (Feifer and Myers, yet to be published). Only babies having quiet sleep epochs and lying in the prone position were used. Information regarding exact times of quiet sleep was retrieved through lab notebooks. ECG's were amplified and collected onto VCR tapes. In this current study, data from the VCR tapes was then digitized at 500 samples/sec and transformed into plottable ECG wave forms using special purpose software programs. ECG's of each baby were then marked at the Q, R1, R2, and T segments for 25 intervals per baby. Intervals were measured in milliseconds, with all times being recorded into SYSTAT. This program was used to construct a database which found the average QT and RR intervals for each baby. QT Intervals were adjusted for heart rate using Bazette's formula:

$$QTc = (Q-T) / \sqrt{(R2-R1)}.$$

QTc's were then analyzed using SYSTAT. Statistical analysis were performed using the t test for unpaired observations. Data are presented as means +/- standard deviation. Relationships were looked for between QTc Interval and maternal smoking. Factors such as birthweight, sex, and maternal age were also tested to see whether QTc Interval was affected. Results were compared to those of Schwartz' recently published study.

Results

The mean QTc for all cases was 399 +/-26 msec. This was similar to Schwartz's mean QTc of 409 +/-15 msec for infants at two months of age. (See Table 1) Sex and birthweight did not affect QTc interval.

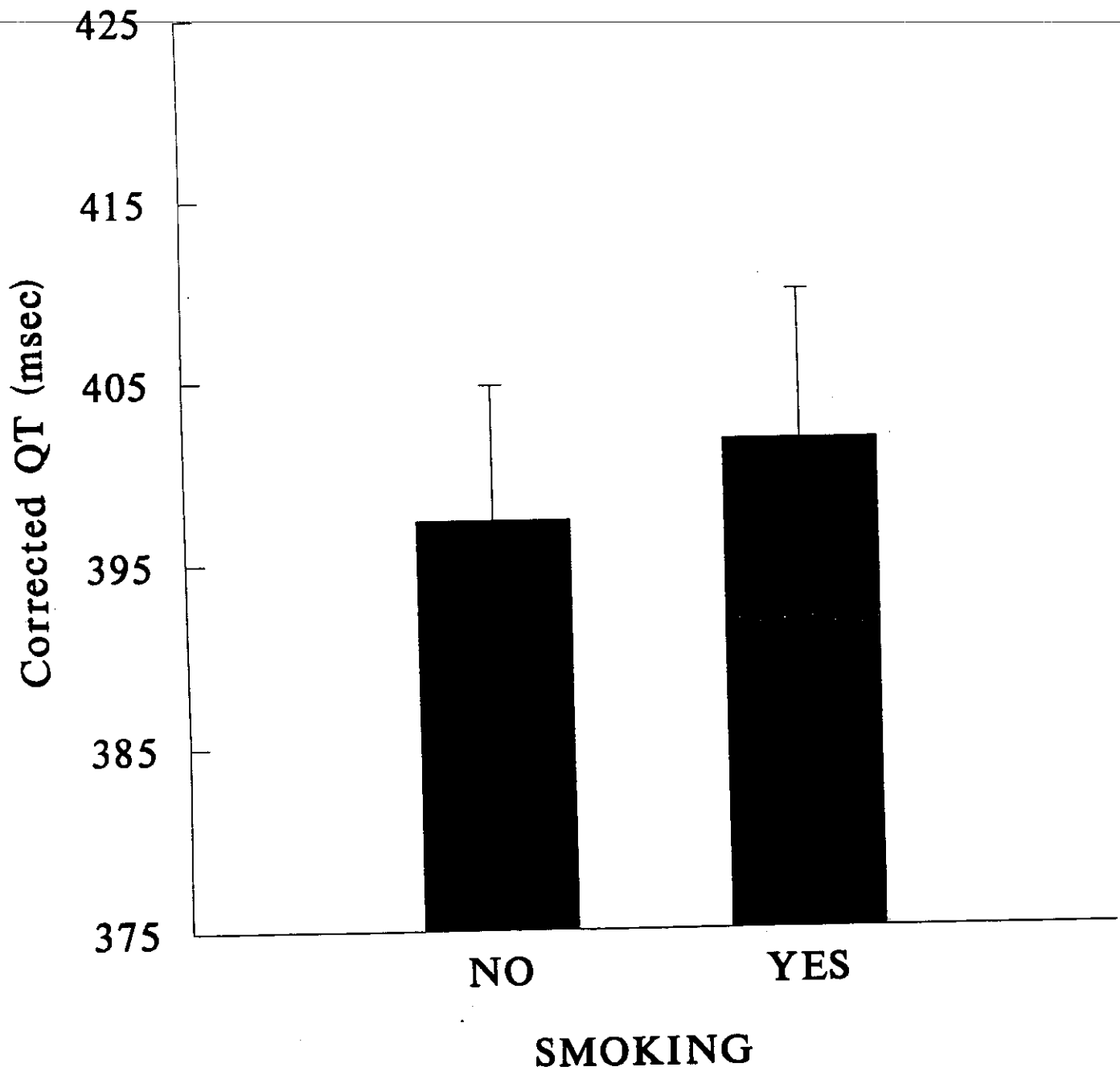
Smoking during pregnancy, by itself, did not have an affect on QT interval, RR interval, or QTc interval (See Table 2 and Figure 1). However, further analysis of this data showed that when infants were divided into two groups of "old" mothers being greater than 25, and "young" mother being less than 25, maternal age proved to have an influence on QT Interval. Infants whose mothers were "young" had significantly longer QTc's than infants whose mothers were "old". ($t(23)=2.11, p<.05$) (See Table 3 and Figure 2) This was an unexpected discovery which was not considered as part of the original hypothesis.

TABLE 1: Overall average QT, RR, and QTc intervals +/- standard deviation for all infants

Total # of Subjects	Mean QT Interval (msec)	Mean RR Interval (sec)	Mean QTc Interval (msec)
24	267.82 +/- 20	.446 +/- .045	404.15 +/- 26

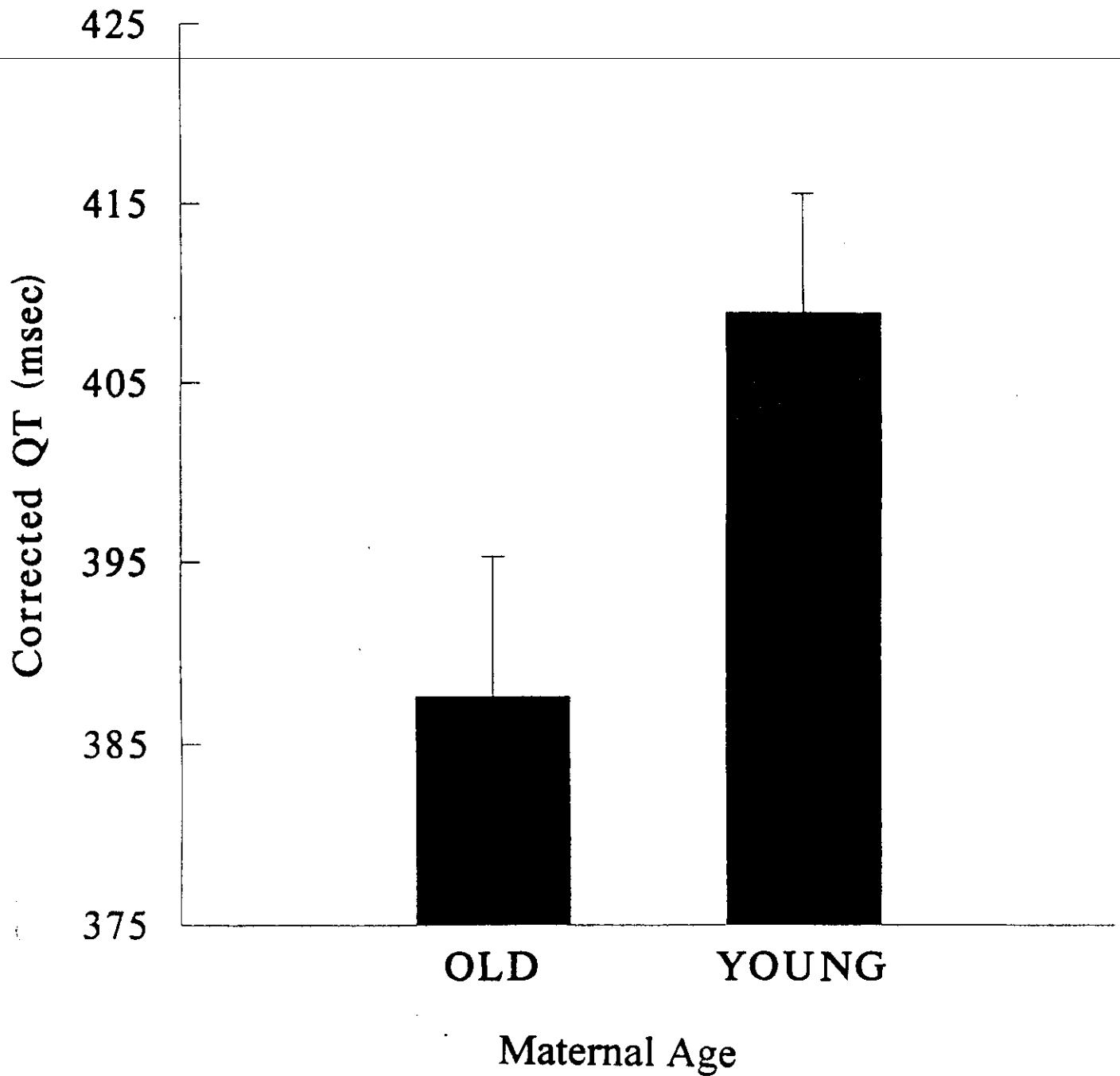
MATERNAL SMOKING	NUMBER OF SUBJECTS	RR INTERVAL (seconds)	QT INTERVAL (milliseconds)	QTc INTERVAL (milliseconds)
YES	10	.440 +/- .54	266 +/- 20	402 +/- 26
NO	14	.461 +/- .038	269 +/- 22	397 +/- 27

TABLE 2 and Figure 1: The relationship between QT, RR, and QTc intervals and maternal smoking



MATERNAL AGE	NUMBER OF SUBJECTS	MEAN RRI INTERVAL (seconds)	MEAN QT INTERVAL (milliseconds)	MEAN QTc INTERVAL (milliseconds)
< 25 years	13	.435 +/- .040	269 +/- 18	409 +/- 24
> 25 years	11	.473 +/- .044	266 +/- 24	388 +/- 25

TABLE 3 and Figure 2: The relationship between QT, RR, and QTc intervals and maternal age
 <25= young >25=old



Discussion

Due to the limited number of subjects available in this study, more research in the area will be necessary. Since previous studies have established the fact that prolongation of the QT interval can have lethal effects and is a risk factor for SIDS, it should be looked into by researchers.

Researchers have been resigned in investigating possible environmental contributions to the prolongation of the QT interval. This syndrome is mostly thought of as being genetically based. However, QT's are highly variable and not dichotomous.

~~Long QT is defined as being at the extreme of a normal distribution. This risk may be~~
quantitatively related to length; and factors that affect length could alter risk.

Environmental contributions such as young maternal age could give babies at risk for prolonged QT interval the extra push, causing the syndrome to occur. Perhaps young mothers have sub-optimal in-utero environments, which make their infants more prone to such a syndrome.

Controversy exists as to whether or not all infants should have ECG's done as newborns, so that long QT intervals can be followed up. The only way to treat a prolonged QT is to administer beta blockers, which slow the heart rate. This may be dangerous to some infants, producing many risks. These clinical implications are a source of disagreement among physicians and researchers. Taking the ECG of every infant born around the world would be quite expensive. The cost must also be considered.

Smoking during pregnancy and passive smoking have also been associated with an increased risk for SIDS in previous studies. Although maternal smoking was not a risk factor for prolonged QT, since it has been proven to have various other negative effects on infants, all mothers should refrain from smoking during pregnancy.

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