Research Article

Association of Maternal Smoking and other Risk Factors with Sudden Infant Death Syndrome (SIDS)

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ABSTRACT:

Background: Sudden infant death syndrome (SIDS) has been one of the leading causes of infant death globally. Its exact cause is still unknown. However, certain factors have been attributed to increase its risk.
Objective: This systematic review aims to study the association of various infant and maternal characteristics with the incidence of sudden infant death syndrome (SIDS). It aims to provide a better understanding of this topic to parents and caregivers, healthcare professionals, public health workers, government, International organisations and related policy makers.
Methodology: Keeping in account the PRISMA protocol, a literature search was done using various databases including PubMed, Google Scholar, Science Direct, Cochrane and PakMediNet. The articles included were in English and within a 10-year timeline from January 2013 till December 2023. Reviewers assessed the studies for eligibility and screening was done multiple times based on predefined inclusion and exclusion criterion. Analysis was done for risk factors that include maternal age, maternal smoking, perinatal substance abuse, infant gender, plurality, parity, parent's education, sleeping position, bed-sharing, gestation period, breast feeding and birth weight. Data extraction was performed and reviewed by the authors
Results: A total of 18 studies were included in the final review that discussed a total of 92,412 sudden infant deaths syndrome cases. The risk factors were then categorised into maternal and infant factors. The included studies were diverse in study designs and countries of origin. 10 studies (55%) discussed maternal age of 20-35 years as a risk factor whereas 35+ age was constantly registered as a protective factor. 7 studies (39%) discussed infant gender (high risk in males) and gestational age (high risk in <37 weeks gestation). Low birthweight (<2500gm) and low parental education (less than high school) was also reported as a risk factor. 75% of studies discussed sleeping position and reported prone position as a problem.
Conclusions: Smoking during pregnancy, young maternal age, low education and alcohol abuse increase the risk of sudden infant death syndrome. Similarly, prone sleeping position, low gestational age, low birth weight, co-sleeping, male infants and multifetal pregnancy are associated with higher risk of sudden infant death syndrome.

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Key Words: Sudden Infant Death Syndrome, Maternal Smoking, Infant Death, Risk Factor

INTRODUCTION:

Sudden infant death syndrome (SIDS), also known as cot death, is characterised by the sudden and unexplained death of an infant before 1 year of age, the cause of which remains unknown even after a thorough medical history, proper examination, complete investigation, and full autopsy. The most widely used definetions have made sudden infant death syndrome a diagnosis of exclusion. Maximum number of cases of sudden infant death syndrome occur during the first 8 months of life, with most deaths occurring in the second to fifth months [1].

Sudden infant death syndrome is not an issue of the modern era. It has been accountable for a number of infant deaths globally for ages. Efforts have been made in the past to reduce the number of sudden infant death syndrome-related deaths. Despite the efforts to curtail deaths due to sudden infant death syndrome, it was still, according to the Centers for Disease Control and Prevention (CDC) in 2020, the third major cause of infant mortality in the US as evidenced by 1389 sudden infant death syndrome-related deaths or 41% of the total sudden unexplained infant deaths (SUID) in the same year [2].

Previous studies have indicated various risk factors pertaining to sudden infant death syndrome. However, there is still no definite cause. According to the present knowledge, various factors play a role in determining the incidence of sudden infant death syndrome including maternal characteristics such as smoking, maternal age, education, substance abuse, parity, alcohol abuse, breastfeeding, and second multifetal pregnancy. Infant related characteristics such as infant gender, ethnicity or race, any infection, gestation period, birthweight, small for gestational age, sleeping position, bed sharing or room sharing, and prolonged cold temperatures are also responsible for its occurrence. In other words, there are multiple intrinsic and extrinsic factors that determine an infant's vulnerability to the disease [3].

A New Zealand cot death study done in the late 1980s aimed to report the main factors responsible for causing sudden infant death syndrome. It included the prone sleeping position of the baby, maternal smoking, and breastfeeding. The first two were considered risk factors while breastfeeding was considered a protecttive factor[4]. Several other recommendations have been updated to prevent sudden infant death syndrome and to provide a safer sleeping environment for infants.

In contrast to all the recent advancements and recommendations to prevent sudden infant death syndrome, it is still the leading cause of death for infants in the postneonatal period in developed and developing countries [5]. Thus, a comprehensive systematic review is needed to compile the major risk factors of sudden infant death syndrome and give up-to-date information covering all the previous related reviews and other study articles. This systematic review will ultimately help formulate preventive and intervention strategies by combining maternal and infant related characteristics.

The purpose of this study was to raise awareness and reduce the incidence of infant mortality pertaining to sudden infant death syndrome by providing a thorough review of the above-mentioned factors. Parental programs should incorporate information about various

risk factors leading to the syndrome in order to reduce the rate of death among infants and educate pregnant couples on how to avoid them. This will not only save countless newborn lives but will also prevent negative mental health implications among parents and families.

MATERIALS AND METHODS:

This research utilises a systematic review study design to comprehensively synthesise and analyse existing literature on the subject.

A literature search was done from March to April 2023 from various databases including Pubmed, Google Scholar, Science Direct, Cochrane, and PakMediNet. For Pubmed the search string used was: ("sudden infant death"[MeSH Terms] OR ("sudden"[All Fields] AND "infant" [All Fields] AND "death" [All Fields]) OR "sudden infant death" [All Fields] OR "sides" [All Fields]) AND ((("maternally"[All Fields] OR "maternities" [All Fields] OR "maternity" [All Fields] OR "mothers" [MeSH Terms] OR "mothers" [All Fields] OR "maternal" [All Fields]) AND ("smoke" [MeSH Terms] OR "smoke"[All Fields] OR "smokes" [All Fields] OR "smoked" [All Fields] OR "smokes" [All Fields] OR "smoking" [MeSH Terms] OR "smoking" [All Fields] OR "smokings" [All Fields] OR "smokings" [All Fields])) OR ("risk factors" [MeSH Terms] OR ("risk" [All Fields] AND "factors" [All Fields]) OR "risk factors" [All Fields] OR ("risk" [All Fields] AND "factor" [All Fields]) OR "risk factor" [All Fields])). The following search string was used for the remaining databases: SIDS AND (maternal smoking OR risk factor). Filter for the timeline was adjusted to 2013-2023 and only free full-text articles were considered. Additional filters of research articles, case reports, medicine and dentistry, and open access and open archive were used while searching on Science Direct. The search strategy was peer-reviewed using the Peer Review of Electronic Search Strategies (PRESS) checklist.

Studies were included according to the PICO (population, intervention, control, and outcomes) criteria of the conducted systematic review. Eligible studies consisted of a population of infants less than one year of age, having any of the possible risk factors such as maternal smoking, sleeping position, bed sharing or room sharing, substance abuse, infant gender, maternal education, and outcome of death due to sudden infant death syndrome. The articles included were in English and within a 10-year timeline from January 2013 to December 2023.

Studies declared ineligible consisted of infant populations more than 1 year of age, infant death due to any cause other than sudden infant syndrome, stillbirth, animal studies, systematic reviews, meta-analysis, editorials, letters, books, and news. Studies that were not in the English language or were out of the defined timeline were also considered ineligible.

According to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, a total of 856 articles were identified including 468 from PubMed, first 100 articles from Google Scholar, 272 from Science Direct, and 16 from Cochrane. 18 duplicates were removed. 801 articles were further excluded based on the eligibility criteria after

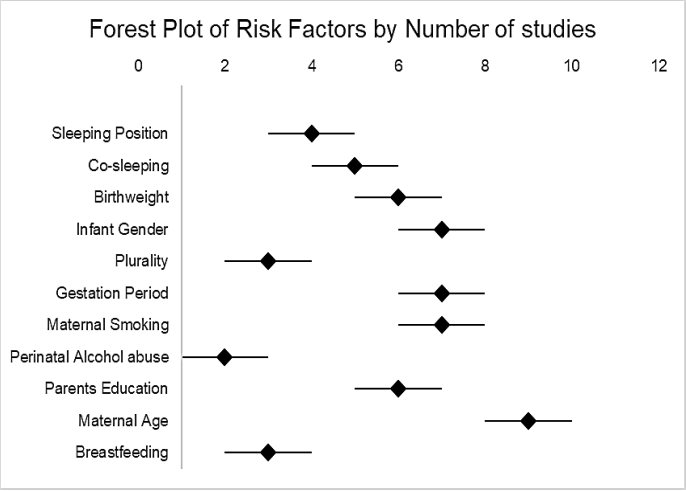
title and abstract screening by three reviewers. Full-text screening of the remaining 37 articles was done by three reviewers independently and 18 articles were included in the final review. The details of the search process are given in the PRISMA flow chart given in Only the number of infants and the percentages against each variable were included in the systematic review. Percentages were calculated by the reviewers using the information provided where needed. A summary table of all the findings was formed including the author's name, year of publication, area of study, population size, and various risk factors associated with sudden infant death syndrome, each reported individually. All factors were classified into maternal and infant factors. All the variables were listed dichotomously. Percentages for each risk factor were then calculated considering their mention in the total number of the included studies. Only those infants were included in the review who died of sudden infant death syndrome. The data was then presented in tables, graphs, and a forest plot.

Of the 18 included studies, study designs varied and included population-based cohort studies (4), analysis of case-control/case-control studies (4), retrospective cohort (3), case crossover studies (2), observational studies (2), population-based register study (1) and prospective study (1). The sample size ranges from 28[8] to 24,101[10]. The included articles were from 2013 to 2023. Most articles were from 2013, 2014, and 2015. Studies were set up in various countries including the United States, Sweden, the United Kingdom, Australia, Korea, Brazil, and Iran.

RESULTS:

All the included risk factors were divided into maternal factors and infant factors. Maternal factors included those risk factors that were directly related to the mother like smoking, substance abuse, parity, education, and maternal age. Infant factors on the other hand included sleeping position, gestational age, gender, plurality, gestation period, and co-sleeping. The factors are illustrated by the forest plot in ***Graph 1***.

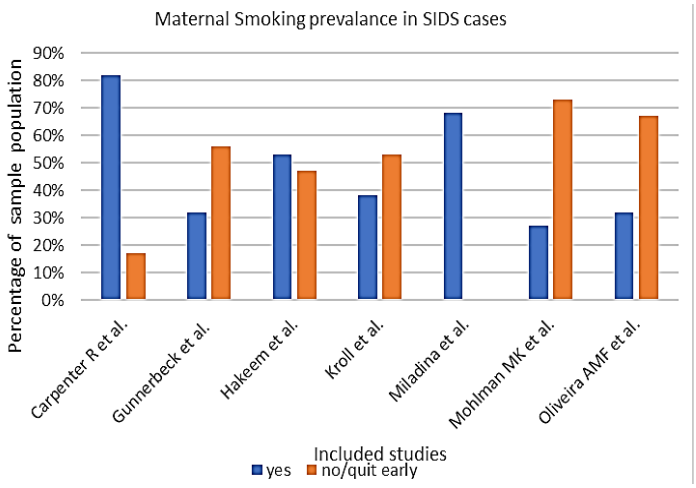
Graph 1. Forest Plot of risk factors of SIDS by the number of included studies.



Maternal Factors: 7 out of 18 studies (39%) discussed the association between maternal smoking and sudden infant death syndrome. 2 out of these studies show smoking as a clear risk factor for sudden infant death syndrome. Some of the studies suggest the opposite, yet the preponderance of evidence suggests a clear relationship that is made complicated by the interplay of multiple confounding factors. It is also important to note that although the rest of the studies indicated a

lower fraction of smoking mothers, the factor is still significant enough to serve as a base for future research. The findings are elaborated further in Graph 2.

Graph 2. Maternal Smoking Prevalence in Sudden Infant Death Syndrome.



2 of the included studies (11%) reported alcohol abuse during pregnancy. There was a consistent association between alcohol exposure and the occurrence of sudden infant death syndrome. Some studies suggested alcohol as a potent risk factor with a higher fraction of mothers who abused alcohol 8 while others reported a 45% increase in risk for sudden infant death syndrome in such mothers106 of the included studies (26%) consistently showed a robust trend linking low parental education and occurrence of sudden infant death syndrome. This might be related to lower access to information regarding infant care that needs to be looked into. It is also important to note that lower education suggests an economic instability leading to inadequate access to healthcare facilities and adverse living conditions.

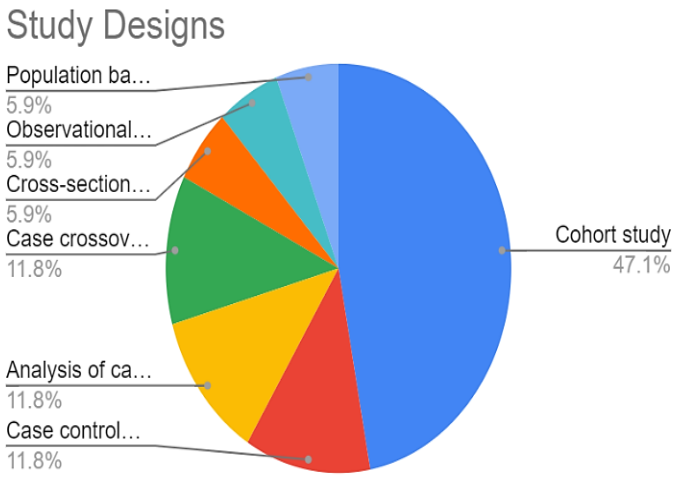
In 10 out of 18 studies (55%), maternal age was throughly explored as a risk factor where the majority indicated a higher occurrence of sudden infant death syndrome in mothers between 20-35 years. Some studies also suggested a higher risk in mothers below 20 years. It is important to note that even though variations exist, the maternal age higher than 35 consistently reported a lower incidence of sudden infant death syndrome which makes it a possible protective factor.

Infant Factors: 3 out of 4 studies (75%) discussing sleeping position as a risk factor suggest that a prone sleeping position is more likely involved in the occurrence of studies which also aligns with historical data that shows a consistent relationship. One study[17] diverged from the normal consensus and suggested side position as a potent risk factor. Supine position consistently proved itself to be a protective factor as is established and practised universally. 5 studies (28%) out of all studies suggested a relation between co-sleeping and risk for sudden infant death syndrome. 3 of which claimed that co-sleeping, especially bed-sharing, is an important risk factor. Some studies recommended avoiding bed sharing but keeping the child in close proximity for better safety. 7 out of 18 (39%) studies discussed birthweight as a risk factor for SIDS. Low birthweight is generally defined as less than 2500 grams (about 5.5 pounds). In Elliot's study[8], the SIDS risk/ 1000 ((#demise)/ (#demise + alive at 1 year)*1000) was 48.54. Similarly in Hakeem's study, the relative risk was 3.08 for low birthweight infants. These outcomes show that even though there are high sudden infant death syndrome cases for high birth weight (>2500gm) in our included studies, after considering other confounding factors, the risk of

sudden infant death syndrome was higher for lower than normal birth weight and high birth weight was a protective factor. The data analysed in 8 studies (44%) demonstrates a clear relationship between gestational age and the risk of sudden infant death syndrome. Infants born at earlier gestational ages, such as before 37 weeks, consistently show higher proportions and percentages of sudden infant death syndrome cases. On the other hand, infants born at 37 weeks or later have a significantly lower risk of sudden infant death syndrome. This indicates that gestational age is a potent risk factor for sudden infant death syndrome, with preterm infants being more susceptible to sudden infant death syndrome compared to full-term infants. The relationship between infant gender and risk of sudden infant death syndrome was discussed in the context of 7 studies (39%). In 5 of these studies, there was a constant association of sudden infant death syndrome with male infants showing a higher risk.

Still the variation in outcomes for the rest of the studies warrants careful consideration. Three studies (17%) were analysed, each showcasing different proportions of sudden infant death syndrome cases across parity categories. Overall, the data suggests that the incidence of sudden infant death syndrome varies among parity groups, with no consistent trend observed. 3 studies (17%) discussed plurality. In Elliot's [8] study, the sudden infant death syndrome /1000 risk was higher for twins (8.23) as compared to singletons (2.47). In Hakeem's study [10], the relative risk for twins was highest (1.66) with a significant p value (<0.001). On the other hand, there was no significant association (p value>0.005) between plurality>1 and sudden infant death syndrome in Highest's study[12].

***Graph 3**:Pie chart of study designs of included studies.*



The details of the search process are given in the PRISMA flow chart given in ***Figure 1.*** **PRISMA flowchart**

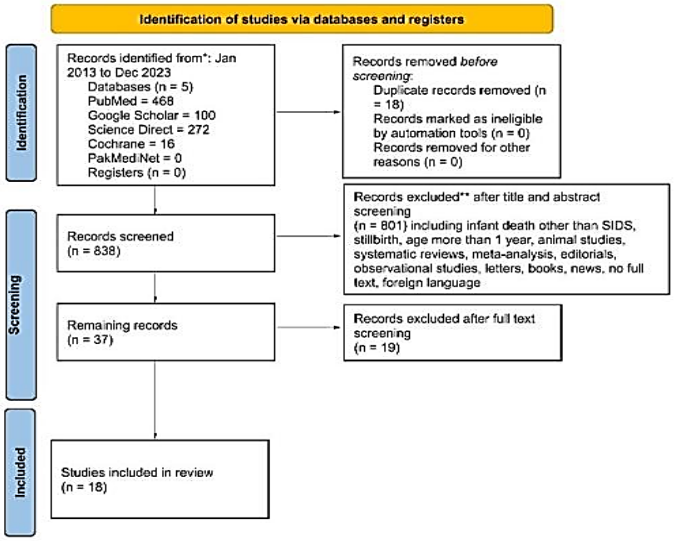


Table 1: Study Characteristics and Infant Factors for Sudden Infant Death Syndrome

Author	Year	Country	Study Design	Sample Size	Infant Factors											
					Sleeping Position			Co Sleeping		Birth Weight		Infant Gender		Plurality		Gestation Period	
					Prone	Supine	Side	Yes	No	≤ 2500 gm	> 2500gm	Male	Female	Single	Twin	<37 weeks	≥37 weeks
Blair PS et al.	2014	UK	analysis of case-control studies	n=400				145 (36.3%)	255 (63.8%)								
Carpenter R et al.	2013	UK, Europe and Australasia	Analysis of case control studies	n=1472				323 (22.2%)	1131 (77.8%)								
Elliott et al.	2020	South Africa, US	Observational Study	n=28						11 (39.29 %)	16 (57.14 %)	11 (39.29 %)	17 (60.71 %)	26 (92.86 %)	2 (7.14 %)	11(39.29 %)	17 (60.71%)
Gunnerbeck et al. % calc from sids death	2023	Sweden	Population-based register study	n=381												68 (17.85%)	213(55.82 %)
Hakeem et al.	2015	United States	population-based cohort study	n= 24101						4773 (20%)	19320(80%)	14 300 (59%)	9801 (41%)	22 870 (95%)	1195 (5%)	5489(23 %)	18,376(77 %)
Hauck FR et al.	2022	United States	case-control study	n=195								112 (57%)	83 (43%)				
Highet et al.	2013	Australia	Cohort study	n=120										110 (93.2 %)	8 (6.8 %)		
Huang LY et al.	2021	Taiwan	Case cross-over study	n = 953							avg=2842.78 ± 638.06	543 (56.98%)	410 (43.02%)				avg n= 37.34 ± 3.31

Table 1: Study Characteristics and Infant Factors for Sudden Infant Death Syndrome

Hwang MJ et al.	2019	South Korea	case-crossover study	n=453						78(17.2 %)	376 (82.8 %)	253(5 5.8%)	201(44. 4%)	77(17.0 %)	377 (83%)
Johansson S et al.	2014	Sweden	cohort study	n=460											
Kroll et al.	2018	England and wales	Cohort study	n= 1559										290 (18%)	1269 (81%)
Miladina et al.	2015	Iran	cross sectional study	n=878	131 (14.92 %)	230 (37.58 %)	417 (47. 49%)	808 (93.03 %)	70 (7.96 %)			374 (42.60 %)	504 (57.40 %)	66 (7.51 %)	812 (92.48 %)
Möllborg et al.	2015	Sweden	Retrospective cohort study	n=136	42(30. 8%)	13(9.55 %)	7(5. 14%)	58(42. 6%)	4 (3%)	18 (13.2 %)	109 (82. 57%)	86 (63. 1%)	50 (37. 6%)	18 (13. 2%)	109 (80.1 %)
Mohlman MK et al.	2016	United States	Retrospective cohort study	n=136											
Mohlman MK et al.	2016	United States	Retrospective cohort study	n=136											
Oliveira AMF et al.	2016	Brazil (sao pualo)	Retrospective cohort study	n=63	14 (22.2 %)			37 (58. 7%)	26 (41. 2%)						
Polavarapu et al.	2022	United States	Case control study	n=291						avg 3221.34 g (95%)					
Putnam-Hornstein et al.	2014	California	Prospective cohort study	n=1236						362 (17.4 %)	1719 (82. 6%)				
Yoo SH et al.	2013	Korea.		n=355	89 (41.4 %)	107 (49.8 %)	19 (8.8%)								

Table 2: Study Characteristics and Maternal Factors for Sudden Infant Death Syndrome

Author	Sample Size	Maternal Factors											
		Perinatal Substance abuse		Parents Education			Maternal age			Breastfeeding		Parity	
		Yes	No	Less than H.S.	High school	College	<20yrs	20 to 35	>35	Yes	No	0-3	3+
Elliott et al.	n=28	Alcohol/smoke 25(89.2%)	3 (10.7%)				2 (7.14%)	25 (89.29%)	19 (3.57%)			22 (78. 5%)	6 (21. 43%)
Gunnerbeck et al.	n=381			81.43%	10.70%	7.14%	27 (7.09%)	294 (77.16%)	61 (16.01%)			310 (81.3%)	≥4 n=71 (18.64%)
Hakeem et al.	n= 24101	Alcohol 579 (2%)	21,016 (87%)				5706 (24%)	7768 (32%)	1465 (6%)			n=19789 (82%)	n=4211 (17%)
Hauck FR et al.	n=195						≤25 n= 132(68%)	≥25 n= 63(32%)		,			
Highet et al.	n=120			180 (47.25%),	>=12yrs n= 172 (45.14%)								
Huang LY et al.	n = 953			9279 (39%)	8834 (37%)	5573 (24%)		<35 years n= 399 (87.9%)	>35years 55 (12.1%)				
Johansson S et al.	n=460						272 (17%)	20-29 858 (55%)	30+ n= 429 (28%)				
Kroll et al.	n= 1559						291 (33.15%),	587 (66.85%)					
Miladina et al.	n=878			485 (55.23%)	315 (35.87%)	87 (8.88%)				272 (68.5%)	125 (31.5%)		
Möllborg et al.	n=136									75 (58.6%)	20 (36.4%)		
Mohlman MK et al.	n=136						172 (8.42%)	1568 (75.3%)					
Oliveira AMF et al.	n=63			16 (25%)			15 (23%)			60 (95.2%)	3 (3.8%)		
Putnam-Hornstein et al.	n=1236						<19 n=253 (20.1%	>19y n=1006 (79.9%)					

DISCUSSION:

The various factors affecting the incidence of sudden infant death syndrome include maternal tobacco smoking, alcohol abuse, maternal age, parental education, parity, prenatal care, gestational period, multiple pregnancies, sleeping position, co-sleeping, breastfeeding, birth weight, infant gender, infant age and mode of delivery[3]. A total of 18 manuscripts were included in this systematic review in which these risk factors of sudden infant death syndrome also known as cot death have been discussed. Maternal smoking was identified as a very important risk factor pertaining to sudden infant death syndrome [(7)]. Studies indicated that the mothers who smoked during pregnancy increased the risk of causing sudden deaths among their infants [3,9]. Maternal alcohol use during pregnancy and substance abuse like methadone and heroin were thought to contribute to the development of sudden infant death syndrome. Elliot et al and Hakeem et al also studied alcohol consumption as a strong risk factor that contributed toward a higher risk of sudden infant death syndrome thus signifying the need to curtail maternal smoking and alcohol consumption during pregnancy [8,10]. According to the results, 26% of studies found that low maternal education led to less information regarding infant care and prevention of infant mortality, thus increasing the danger of sudden infant death syndrome. Moreover, mothers whose ages ranged between 20 to 35 years of age had comparatively more risk for sudden infant death syndrome as evidenced by 55% of studies. This implies the need for promoting maternal education and discouraging pregnancies at lower ages. Some other significant maternal factors like lack of prenatal care, placenta previa, and premature rupture of membrane increased the risk of sudden infant death syndrome. There was also found to be a relationship between the occurrence of bronchitis in winter and the increased incidence of sudden infant death syndrome. One of the most important infant factors included sleeping position. About 75% of studies indicated a prone sleeping position as a major risk factor and a supine position as a protective factor for causing sudden infant death syndrome. Bed sharing and room sharing also increased the chance of sudden infant death. Thus, newer recommendations on infant sleep practices should stress the supine sleeping position and avoidance of bed sharing. Breastfeeding was considered as a protective factor against sudden infant death syndrome, especially in cases where a mother breastfed her child exclusively. The protective mechanism was, however, unclear. Moreover, some benefits have been found with breastfeeding such as a breast-fed child was easy to arouse from sleep as compared to a formula-fed child. Breast milk contained substances that might have contributed to the development of myelin, and it was recognized that some children died of sudden infant death syndrome due to delayed development of myelin in the central nervous system. Breastfed milk also contains more amount of DHA (docosahexaenoic acid) as compared to formula milk and also provides protection to the baby against various viral infections[24]. Thus, a positive attitude towards breastfeeding decreases infant mortality[25]. Moreover, the incidence of low birth weight is also more in top-fed infants than breast-fed infants, indire-

ctly as well as directly increasing the risk for sudden infant death syndrome [26]. The common trend of prelacteals also increases the risk for infection among infants and thus poses a risk of sudden infant death syndrome[27]. According to a study conducted in Sir Ganga Ram Hospital, Lahore, Pakistan, about 135 (4.08%) low birth weight babies out of 3315 babies were delivered [28], thus increasing the risk for sudden infant death syndrome among Pakistani infants [29]. Another study that was conducted explained that 56.66% of the expired neonates had low birth weight [30]. The risk of sudden infant death syndrome increases exponentially with the decreasing birth weight of a newborn. Lower gestational age leading to prematurity, infant gender, and plurality also posed an increased risk of sudden infant death syndrome.

CONCLUSION:

Smoking during pregnancy, young maternal age, low parental education and alcohol abuse increase the risk of sudden infant death syndrome. Similarly, prone sleeping position, low gestational age, low birth weight, co-sleeping, male infants, and multifetal pregnancy are associated with a higher risk of sudden infant death syndrome.

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