

Proposal of the Acronym “SIUDS” for Unexplained Stillbirths, Like “SIDS”

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Abstract

The authors, propose that also a sudden death during pregnancy that remains unexplained after an in-depth autopsy, should be considered as a syndrome and referred with the acronym “SIUDS”, e.g., “Sudden Intrauterine Unexplained Death Syndrome”, like “SIDS” for “Sudden Infant Death Syndrome”. This suggested definition is based on the presence in these pathologies of common developmental abnormalities of both the autonomic nervous system and the cardiac conduction system, associated to the same preventable risk factors.

Short Communication

Unexplained stillbirth, or Sudden Intrauterine Unexplained Death (SIUD) and Sudden Infant Death Syndrome (SIDS) are major social and health problems of today’s medicine. These deaths have been recognized as multi factorial but the pathogenetic mechanism has not yet been determined. Anyway, the neuropathology seems to be a fundamental common denominator.

Nevertheless, only a few studies in this field have examined the neuropathological substrates, although even subtle congenital abnormalities of the Autonomic Nervous System (ANS) and of the Cardiac Conduction System (CCS) can rouse dysfunctions in the control of vital functions, leading to an unexpected early sudden death.

Neuropathological investigations performed at the “Lino Rossi” Research Center of the University of Milan (http://users.unimi.it/centrolinorossi/en/index_en.html) have contributed to identify the nature and the localization of these developmental alterations common in unexplained stillbirth and SIDS.

The results obtained on a wide set of sudden unexplained fetal and infant deaths [1] point up common congenital anomalies of the ANS and of the CCS, so indicating that unexplained stillbirth should not be regarded as distinct from SIDS. These cases were collected in conformity with the 2006 guidelines stipulated by Italian law n.31 “Regulations for Diagnostic Post Mortem Investigation in Victims of SIDS and Unexpected Fetal Death”. This law decrees that all infants with suspected SIDS who died suddenly within the first year of age, as well as all fetuses who died after the 25th week of gestation without any apparent cause, must undergo an in-depth anatomo-pathological examination, particularly of the autonomic nervous and of the cardiac conduction systems.

For each case, all available information about pregnancy, fetal development and delivery and, in cases of infant death, about the environmental and familial situation where the death occurred, besides information related to microorganisms and bacterial toxin investigations, genetic analyses and potential “preventable” and “unpreventable” risk factors*, were collected and categorised during post-mortem family interviews. All the information sheets were

recorded in the registry of a dedicated data bank, as provided by the law 31. The evidence of common exogenous “preventable” risk factors able to alter the intrauterine environment among the causes which trigger and/or promote both sudden fetal and infant deaths, have intrigued SIDS researches, who have raised the possibility that the unexplained stillbirths may represent gestational sudden deaths with a pathogenesis similar to SIDS [2].

Hence, the association of SIDS with maternal preventable risk factors that are present during pregnancy highlights that SIDS originates in fetal life. Therefore, the study of the prenatal period becomes critical to determining an abnormal pathway that begins in the fetus and results in sudden death after birth. Many researchers now are accepting the possibility that the mechanisms of these two death processes may be related.

Filiano and Kinney [3] in particular agree with this opinion. They indeed claim that SIDS arises in utero because some risk factors of this syndrome point to a suboptimal intrauterine environment, above all caused by maternal smoking during pregnancy. Antenatal exposure to tobacco smoke is the most important preventable toxic agent, able to cause hypoxic/ischemic damages leading to sudden death. The carbon monoxide, a gaseous combustion product of nicotine, easily crosses the placental barrier by passive diffusion, binding to fetal hemoglobin. Consequently, carboxyhemoglobin inhibits the release of oxygen into fetal tissues, causing hypoxia with consequent delayed maturation of all the organs, especially those most susceptible to hypoxic damage, including the brain. Besides, nicotine is one of the few lipid-soluble substances that can go beyond the blood-brain barrier and bind to the nicotinic receptors of the fetal and infant brain altering their function, as well as to act directly on the expression of genes modulating the developing brain by inducing specific molecular alterations in the DNA, RNA, and proteins of the nervous cells [4].

The presence of common developmental abnormalities of the ANS and of the CCS, and of the same preventable risk factors in both unexplained stillbirth and SIDS suggest that the definitions of these deaths, currently nosographically distinct in literature as “unexplained stillbirth” (or “SIUD”) and “SIDS”, should be unified and considered both as syndromes. Grafe and Kinney [5], already in 2002, speculated

that some unexplained stillbirths, particularly those close to term, may represent "intrauterine SIDS". The term "syndrome", arises from the Greek word "σύνδρομον" whose meaning is "concurrency". A syndrome is in fact defined as a combination of signs and symptoms that collectively characterize a given condition, occurring in association more frequently than would be likely by chance alone [6]. Then, we propose that also a sudden death during pregnancy that remains unexplained after an in-depth autopsy including examination of the placental disk, umbilical cord and membranes, detailed pregnancy history analysis and molecular and microbiological investigations, should be considered as "syndrome" and referred with the acronym "SIUDS", e.g., "Sudden Intrauterine Unexplained Death Syndrome", like "SIDS" for "Sudden Infant Death Syndrome".

The scientific-financial advantages theoretically deriving from a unified interpretation of these deaths are difficult to evaluate but are certainly most significant. Indeed, such an understanding would encompass that perinatal life, as a whole, could be regarded as the premise of many and preventive responses to pathology of youngs, adults and even elderly patients.

*Guntheroth differentiates the "non-preventable" risk factors, as sex, age, prematurity, sleep apneas, from the "preventable" risk factors, that are conditions that can be avoided, such as maternal smoking, maternal sedative and alcohol abuse, prone infant sleeping, type of milk feeding, bedsharing [7].

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