

MESTRADO INTEGRADO EM MEDICINA

Retrospective Analysis of Morphological Anomalies in Fetuses from Spontaneous Abortions: A Clinical and Pathological Study

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FACULDADE DE MEDICINA



Eu, Íris Alexandra Costa Rodrigues, abaixo assinado, nº mecanográfico 201906387, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter actuado com absoluta integridade na elaboração do meu trabalho de Dissertação ou Monografia.

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DESIGNAÇÃO DA ÁREA DO PROJECTO

Ciências Médicas e da Saúde; Medicina Básica e Medicina Clínica

TÍTULO DISSERTAÇÃO/~~MONOGRAFIA~~ (riscar o que não interessa)

Retrospective Analysis of Morphological Anomalies in Fetuses from Spontaneous Abortions: A Clinical and Pathological Study

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ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTES TRABALHOS APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☒
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTES TRABALHOS (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTES TRABALHOS.	☐

Faculdade de Medicina da Universidade do Porto, 15/06/2025

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- ☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia
- ☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interações (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

Faculdade de Medicina da Universidade do Porto, 15/06/2025

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Dedicatória

Em primeiro lugar, gostaria de expressar a mais profunda gratidão à minha família, em especial aos meus pais, Maria e Jorge, pelo apoio incondicional ao longo de todos estes anos. Agradeço-vos por acreditarem em mim mesmo nos momentos em que duvidei, por todos os sacrifícios silenciosos, pela força incansável e pelo amor sem limites. São, para mim, o maior exemplo de trabalho, integridade e dedicação, e é na vossa coragem que encontro inspiração todos os dias.

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Levo comigo a sorte imensa de ter sido acompanhada por pessoas tão especiais!

Retrospective Analysis of Morphological Anomalies in Fetuses from Spontaneous Abortions: A Clinical and Pathological Study

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Background: Spontaneous abortion is a common complication of pregnancy, affecting up to 30% of conceptions. Fetal anomalies often underlie these losses. This study aimed to characterize morphological anomalies in spontaneous abortions to clarify underlying etiologies and related factors.

Methods: A retrospective cohort of 180 spontaneous abortions (10–23+6 weeks) was analyzed at a tertiary hospital. All cases underwent fetal autopsy with clinical, pathological, and genetic review. Cases with and without anomalies were compared.

Results: Fetal anomalies were found in 39.4% of cases. Morphological anomalies were most frequent (57.7%), particularly fetal growth restriction, cardiac defects, and complications of monochorionic twin pregnancies. Trisomies 21, 13 and 18 accounted for 54.6% of chromosomal anomalies. No significant associations were found with maternal factors. Chromosomal anomalies were linked to earlier gestational loss ($p=0.004$).

Conclusion: This study highlights the value of autopsy and multidisciplinary assessment in identifying fetal anomalies and improving diagnostic accuracy and reproductive counseling.

Keywords: spontaneous abortion; chromosomal anomalies; morphological anomalies; fetal autopsy; genetic testing; gestational loss

Introduction

Spontaneous abortion is defined as the involuntary termination of a pregnancy before the fetus reaches viability, generally occurring before 20 to 24 weeks of gestational age [1, 2]. These discrepancies in timing are attributable to differences in international guidelines: the World Health Organization (WHO) advocates the term gestational loss at 22 weeks of gestation, while, for example, the United Kingdom sets the limit at 24 completed weeks of gestation and the United States at 20 completed gestational weeks [3].

In reality, gestational loss is a very relevant issue, given that it represents the most common complication of human pregnancy, which, according to estimates, affects 10% to 15% of pregnancies that are clinically acknowledged and up to 30% of all pregnancies [2]. It is estimated that approximately 23 million gestational losses occur globally every year, which translates to 44 losses per minute [1].

Gestational losses are commonly classified as early and late [3, 4]. Most of the cases are early gestational losses and are usually associated with chromosomal abnormalities, which are identified in up to 75% of cases [5]. Human reproduction is notably inefficient. In fact, some studies report fetal malformations in over 80% of early losses [4]. Notably, definitions of early loss vary slightly between professional societies: the American College of Obstetricians and Gynecologists (ACOG) defines early gestational loss as occurring before 13 weeks, whereas the European Society of Human Reproduction and Embryology (ESHRE) uses a cut-off of 10 weeks [6].

The occurrence of spontaneous abortion is influenced by several factors, including genetic, anatomical, endocrinological, immunological, and environmental factors [4]. Advanced maternal age is strongly associated with an increased risk, primarily due to a

higher prevalence of fetal chromosomal abnormalities, such as aneuploidy [2, 7, 8]. Other maternal factors that have been identified as contributing to the risk of gestational loss include uterine anomalies, poorly controlled diabetes and thyroid autoimmunity [4]. Furthermore, it has been demonstrated that behavioral and environmental modifiable factors, such as smoking, alcohol consumption, high caffeine intake, obesity, psychological stress, and exposure to air pollution and pesticides, further contribute to the risk [1, 4, 8, 9].

Emerging evidence highlights the role of immunological dysregulation and impaired endometrial receptivity in gestational loss. Additionally, other studies have revealed the contribution of paternal factors, such as compromised integrity of the sperm DNA, to an increased risk of gestational loss [4].

Despite advancements in the understanding of various risk factors, 30% to 50% of gestational losses remain idiopathic, highlighting the need for further research in this area [9].

Spontaneous abortion has profound physical, psychological, and social implications that affect not only women but also their partners and their families [9]. As a matter of fact, couples who suffer a gestational loss often experience significant emotional distress and a diminished quality of life [2]. By identifying and characterizing the multifactorial causes of spontaneous abortion, healthcare professionals and policymakers can work towards reducing its incidence and will be able to enhance and improve reproductive counselling, elevate prenatal care, adapt preventive strategies and provide comprehensive support to the women affected [9].

Despite a general decline in fetal autopsy rates worldwide, postmortem morphological data analysis can contribute to a more precise assessment of the underlying

causes of gestational loss. In fact, although new prenatal diagnostic techniques have improved the detection of fetal anomalies, autopsy provides relevant diagnostic clarification in a significant proportion of cases. It can confirm, refine and expand prenatal findings, identify additional or previously unsuspected anomalies and, in some cases, lead to a reassessment of the risk of recurrence, which can be especially important for parental counselling. Autopsy remains, thereby, not only a key tool for determining the etiology of gestational loss and optimizing reproductive care, but also an important resource for research and education [10-15].

The aim of this study is the critical evaluation of morphological anomalies in fetuses from spontaneous abortion, with the goal of elucidating the underlying etiology and associated factors.

Material and Methods

A retrospective observational cohort study was conducted to assess all spontaneous gestational losses that occurred between January 1st, 2014, and December 31st, 2023, at Unidade Local de Saúde de São João (ULS São João), a tertiary referral and teaching hospital.

This study was approved by the Ethics Committee of the ULS São João (approval no. CE-358-2024). Given its retrospective nature, informed consent and consent to publish were waived. However, all data were anonymized to ensure patient confidentiality.

Fetuses from spontaneous gestational losses with a gestational age between 10 weeks and 23 weeks + 6 days that underwent autopsy at the Developmental Pathology Unit of the Department of Pathology were included. We excluded cases of termination of pregnancy.

Of the 184 cases of spontaneous gestational loss reviewed, 4 cases were excluded from the final analysis because of the poor state of conservation and severe maceration of the fetal specimens, which did not allow for a reliable pathological analysis. Hence, we ended up with a final sample of 180 cases.

Clinical data were retrieved from electronic medical records, such as SClínico and Obscare. The following parameters were assessed: maternal clinical data, including age, parity, body mass index (BMI), pre-existing medical conditions and lifestyle factors during pregnancy; obstetric data, including mode of conception (spontaneous vs. assisted reproductive technology (ART)), ultrasound findings, and gestational age at fetal death; fetal and placental pathology data, incorporating fetal sex, morphological anomalies

(external and internal) and histopathological findings, as well as genetic studies or other analytics studies.

At ULS São João, the study of gestational loss systematically includes a multidisciplinary approach that combines fetal autopsy, genetic testing, and infection screening [16]. Fetal autopsies and placental examinations are routinely performed to evaluate morphologic abnormalities. It should be noted that all fetal autopsies were conducted by a dedicated team including specialized perinatal pathologists and trained technicians, following standardized protocols. Genetic evaluation is also part of the standard investigation protocol: until 2012, conventional karyotype determination was mainly performed; from 2013 onwards chromosomal microarray analysis began to be part of clinical practice allowing for a more detailed detection of submicroscopic chromosomal abnormalities; in cases where it was justified, broader genetic studies were also carried out.

Gestational age was determined based on the measurement of crown-rump length in the first-trimester ultrasound. In cases where this was not possible, it was determined postmortem by assessing fetal biometric parameters and organ maturation.

Body mass index (BMI) was characterized as underweight ($\text{BMI} < 18.5$), normal ($18.5\text{-}24.9$), overweight ($\text{BMI } 25\text{-}29.9$) and obesity ($\text{BMI} \geq 30$).

Cases were then divided into two groups: (A) fetuses with anomalies and (B) fetuses without anomalies. A comparative analysis between these groups was undertaken in hopes of providing insights into the underlying causes and associated factors.

It is also important to note that the unit of analysis in the study was the fetus and not the mother, so that the same woman could have been included more than once if she had suffered more than one gestational loss during the study period. Each case was treated

independently, as maternal characteristics (such as age, BMI, or clinical conditions) could vary between pregnancies. This approach allowed for case-based analysis of the fetal outcomes and ensured compatibility with the study objectives.

Based on autopsy and genetic findings, congenital anomalies were then divided into three main groups based on autopsy or genetic findings: chromosomal anomalies, morphological anomalies and other anomalies. Other anomalies included anomalies secondary to severe oligohydramnios and amniotic band syndrome.

Morphological anomalies were further categorized into nine main groups based on commonly accepted terminology and classifications: nervous system anomalies, cardiac defects, respiratory anomalies, gastrointestinal anomalies, abdominal wall defects, facial anomalies, cystic hygroma, fetal hydrops, fetal growth restriction, specific anomalies of monochorionic twin pregnancies and multiple anomalies. Each case was assigned to a single category.

The statistical analyses were performed with SPSS (IBM SPSS Statistics for Windows, Version 30). Descriptive analysis was conducted: categorical variables were expressed as frequencies and percentages, while continuous variables, in this case maternal age and gestational age at the time of abortion, were shown by means and standard deviations or medians and interquartile ranges (IQR), along with minimum and maximum values, depending, respectively, on whether the distribution was normal or not. Furthermore, the chi-square test or Fisher's exact test was applied for categorical variables, and the Mann-Whitney U-test was used for continuous variables with skewed distributions. For all tests, a p-value of less than 0.05 was considered significant.

With the intention of addressing missing data, a binary variable was created to indicate whether each case had at least one missing value. Chi-square tests were then used

to verify whether there was any association between missing data and the presence or absence of anomalies.

This study was conducted in accordance with the STROBE guidelines for retrospective cohort studies.

Results

Of the 180 spontaneous abortions included and analyzed in this study, fetal anomalies were identified in 71 fetuses (39.4%), while no anomalies were identified in the remaining 109 of the cases (60.6%), either in fetal autopsy or genetic analysis. **Table 1** presents a summary of the distribution of anomalies by type.

Among the anomalies, isolated morphological anomalies stood out as the most common, having been observed in more than half of the cases, followed by chromosomal anomalies that were present in 31% of the cases. In six fetuses, the anomalies were considered secondary to severe oligohydramnios, which could have limited the examination of the primary fetal morphology. Finally, amniotic band syndrome was observed in a smaller number of cases.

Minor anomalies, isolated anatomical manifestations without clinical significance, were not included in the primary classification of fetal anomalies but were documented in a total of 74 cases (41.1%) with 40 fetuses in the group without major anomalies and 34 fetuses in the group that had major anomalies.

The 41 cases exhibiting morphological anomalies were further classified into nine major categories, based on the anatomically affected system or syndrome, as shown in **Table 2**. The most common finding was fetal growth restriction (FGR), seen isolated in 15 fetuses (36.6%) and 17 fetuses in total (41.4%).

Cardiac anomalies constituted the second largest group, having been detected in a total of 10 fetuses (24.4%). Among these, 6 cases corresponded to isolated cardiac defects and another 4 occurred in association with other major anomalies and therefore were categorized as “multiple anomalies”. The vast majority of these anomalies consisted of

cardiac septal defects (in fact, all isolated defects), including 3 cases of perimembranous ventricular septal defects and 2 cases of complete atrioventricular septal defects.

Specific complications of monochorionic twin pregnancies were the third most common occurrence and were identified in 8 of the cases (19.5%), including both Twin Reversed Arterial Perfusion (TRAP) sequence and Twin-to-Twin Transfusion Syndrome (TTTS).

Multiple anomalies accounted for 17.1% of the morphological anomalies and included combinations of cardiac, neurological, gastrointestinal, and genitourinary anomalies.

Genetic analysis was performed in 125 of the 180 cases. Among these 125 cases, chromosomal abnormalities were found in 22 fetuses, while 96 had normal results. In 7 cases, analysis was attempted but ended up being unsuccessful due to lack of cell growth. In the remaining 55 cases, genetic testing was not performed, either because it was not requested or due to unavailability of material.

Regarding the chromosomal alterations, the most frequent were trisomy 21, followed by trisomy 13 and trisomy 18, accounting together for more than half of the chromosomal anomalies (54.6%). Other findings included one case of triploidy, two cases of sex chromosome numeric abnormalities (45,X and 47,XXY), as well as structural abnormalities, including microdeletion or microduplication syndromes identified by array comparative genomic hybridization (array CGH). A complete list is presented in **Table 3**. One case with full deletion of the short arm of chromosome 18 (18p) was also identified and the chromosomal nomenclature is further detailed in the table legend, according to the International System for Human Cytogenetic Nomenclature (ISCN 2024) [17].

In 14 of the 16 chromosomal anomalies detected by conventional karyotype, morphological alterations were detected during the postmortem evaluation and appeared consistent with the expected phenotypic expression associated with each specific chromosomal abnormality. However, the remaining two cases (Klinefelter syndrome and marker chromosome) presented no associated morphological findings at autopsy. Regarding the pathogenic variants detected by array-CGH, specific morphological alterations were found in five of the six cases. The case of chromosome 15 microduplication syndrome presented no associated morphological anomalies.

No significant associations were found between missing data and the presence of fetal anomalies ($p > 0.05$), which corroborates the assumption that the data was missing completely at random (MCAR).

Of the 180 spontaneous abortions analyzed, male fetuses were reported to be slightly more frequent than female (56.1% versus 43.9%). Most pregnancies resulted from natural conception (85.1%), and most women had no previous deliveries (55.9%) and had experienced two gestations (38.2%). A history of previous abortions was reported in 41.2% of cases, and records of previous ectopic pregnancies were rare in the overall sample (1.8%).

Regarding prenatal care, 5.6% of pregnancies was non-monitored. In terms of BMI, more than half of the women had a BMI that fell within the normal range (54.0%), while 29.9% were overweight, 12.4% were classified as obese and only a small percentage of the sample categorized as underweight (3.6%).

The median maternal age of the women included in our study was 33 years (IQR: 28–37), ranging from 16 to 48 years. The median gestational age at the time of loss was 17 weeks (IQR: 14–21).

The prevalence of anomalies did not significantly differ in any of the demographic or obstetric variables analyzed, as shown in **Tables 4** and **5**. In fact, no statistically significant differences were found between fetuses with and without anomalies concerning maternal age ($p = 0.987$), number of pregnancies ($p = 0.868$), deliveries ($p = 0.920$), BMI ($p = 0.130$) or history of previous abortions ($p = 0.653$). The frequency of monitored pregnancies, type of conception, fetal sex, history of ectopic pregnancy and previous maternal conditions were also comparable between the groups.

Approximately one third of the women (33.3%) had a history of previous medical conditions. In the subgroup analysis (**Table 4a**), no individual pathology type (e.g., hypertension, diabetes, autoimmune, psychiatric, uterine abnormalities) was significantly associated with the presence of fetal anomalies.

It is also important to note that the gestational age at fetal loss was significantly lower in cases of chromosomal anomalies (median: 14 weeks; IQR: 13–16) than in morphological anomalies' cases (median: 17 weeks; IQR: 14–21) ($p = 0.004$, Mann-Whitney U test).

The median maternal age was slightly higher in the chromosomal anomaly group (median: 35 years, IQR: 29–39) than in the morphological anomaly group (median: 32 years, IQR: 27.5–37); although this difference was not statistically significant ($p = 0.445$, Mann-Whitney U test).

Discussion

The overall prevalence of fetal abnormalities in our sample of spontaneous gestational losses was 39.4%. Among cases with abnormalities, the most frequent were morphological abnormalities (57.7%), followed by chromosomal abnormalities (31.0%), and other causes (11.3%). This distribution is in line with previous studies that suggest structural abnormalities and aneuploidies as the most important causes of gestational loss in the first and second trimesters [15, 18, 19]. Truthfully, there is some variation in the estimates of prevalence across studies, but congenital anomalies are consistently reported as one of the leading causes of fetal loss in the first and second trimesters [19, 20].

Among fetuses with abnormalities, morphological anomalies were the most prevalent. These anomalies correspond to congenital morphologic anomalies of a single organ or body part that arise from a perturbation of the primary developmental program and may occur in isolation or as part of more complex syndromic patterns [21]. In our study, the most frequently observed morphological findings, considering the total and not just isolated anomalies, were fetal growth restriction (41.4% of cases), cardiac defects (24.4% of cases) and complications specific to monochorionic twin pregnancies (19.5%). These findings are in line with the known associations between early gestational loss and factors such as congenital anomalies, fetal growth restriction and maternal comorbidities [19].

Fetal growth restriction (FGR) was the most common observed morphological anomaly in our sample. Although the literature specifically addressing fetal growth restriction in spontaneous abortions remains scarce, FGR is widely recognized as a major contributor to fetal demise in later gestation. Prior research has reported FGR in approximately 17% of stillbirths [19, 22], and it is considered the single largest contributor to perinatal mortality in non-anomalous fetuses [22]. In particular, FGR has

been shown to increase the risk of stillbirth by eightfold when not identified prenatally [19], emphasizing the importance of early identification with routine ultrasound and Doppler evaluation, especially in high-risk pregnancies [19, 20]. The widespread prevalence of FGR in our study may indicate underlying placental insufficiency, subclinical genetic conditions, or syndromic associations, which were not confirmed due to limitations in genetic testing [20, 22].

Cardiac anomalies comprised the second most frequent morphological category, observed in 24.4% of the cases. The majority were isolated septal defects, such as perimembranous ventricular and complete atrioventricular septal defects. This predominance of midline defects is in agreement with previous autopsy-based studies in which ventricular septal defects were found to represent the most common congenital heart defect, both in isolated form and in association with other extracardiac anomalies [23, 24]. The reported prevalence of cardiac defects in spontaneous abortions shows significant variation across the literature. Some studies report a lower incidence of cardiac defects in spontaneous abortions (around 1.2–5.4%) [25], while others have reported frequencies ranging from 15 to 22%, depending on gestational age and the completeness of autopsy protocols [24]. For instance, one study specifically described prevalence as high as 15.4% in a cohort restricted to fetuses under 24 weeks of gestation, which is closely aligned with the gestational window we used in this study [26]. These discrepancies in published frequencies of heart defects may also be related to differences in the applied methodology, including the use of histological examination of very small hearts, the dissection protocols employed or variations in classification criteria. Furthermore, we highlight that most studies have reported the prevalence of cardiac defects based on the total number of autopsied fetuses, while our proportions relate

specifically to the number of fetuses with morphological defects. This distinction might explain the observed differences in reported frequencies.

Interestingly, the relatively high prevalence of congenital heart defects in our study raises the hypothesis of a potential interaction between cardiac morphogenesis and other developmental disruptions or etiological and genetic factors that may lead to gestational loss, even though such defects are often thought to be survivable in liveborns. As noted in prior research, cardiac development is influenced not only by genetic factors but also environmental exposures, such as maternal smoking, alcohol consumption or drug use during pregnancy and other teratogenic exposures [25]. These factors have also been implicated in the development of other congenital anomalies, underscoring the importance of genetic-environment interactions in fetal development [9, 27, 28]. In our study, however, information on these maternal lifestyle factors was often absent or inconsistently reported in clinical records, which made it impossible to include these variables in the analysis, limiting our ability to explore these associations. This highlights a relevant limitation in retrospective studies and reinforces the importance of comprehensive maternal history in elucidating the multifactorial origins of fetal anomalies.

In our sample of gestational losses, 40% of fetuses with cardiac defects also presented with extracardiac anomalies, which is consistent with findings from other studies [23-25]. The extracardiac manifestations observed, including central nervous system and genitourinary anomalies, are also in line with the most frequently described associations in the literature [23-25]. Although our dataset was limited in scope for a detailed organ-system analysis, the predominance of isolated defects may also partially reflect a selection bias inherent to the classification used, which excluded fetuses with confirmed chromosomal anomalies from the morphological group.

Another relevant observation in our study was that 19.5% of fetuses with morphological anomalies were monochorionic twins presenting characteristic complications, namely both twin-to-twin transfusion syndrome (TTTS) and twin reversed arterial perfusion (TRAP) sequence. This proportion is considerably higher than the expected prevalence of monochorionic gestations, suggesting an increased susceptibility to spontaneous loss in these pregnancies. Although our study was not designed to compare singleton and multiple gestations, these findings reinforce the well-documented risks associated with monochorionic twin pregnancies [29, 30].

The chromosomal anomalies identified in our cohort were mostly numerical, with trisomies 21, 13 and 18 emerging as the most frequent. This pattern correlates with previous cytogenetic studies reporting these trisomies, but also monosomy X and triploidies as the most prevalent chromosomal abnormalities in early gestational losses [10, 15, 31-33]. However, monosomy X and triploidy are typically associated with very early gestational losses (often before the 10-week mark) [34-37] and therefore do not feature strongly in this study, which only included cases from 10 to 23 weeks and six days of gestation. The predominance of trisomy 21 likely reflects the greater prevalence and increased gestational viability, rather than a higher risk of fetal loss [35, 36].

In fact, chromosomal abnormalities accounted for 31.0% of our cases, lower than the 47% to 62% prevalence found in most cytogenetic studies of spontaneous abortions [32]. This discrepancy may be partly explained by the small number of cases in our study, which may not have been sufficient to identify less frequently occurring chromosomal alterations. However, this value is similar to that found by Creasy et al. (30.6%) [38] in a study predominantly composed of later gestational losses, which are known to present lower rates of chromosomal anomalies [32]. This variability between studies likely reflects differences in gestational age distribution, fetal viability at the time of sample

collection, and the success rate of karyotyping, which tend to be lower in macerated or poorly preserved specimens.

Among the chromosomal abnormalities identified by array CGH in our cohort, several involved regions known to be associated with neurodevelopmental disorders, such as 15q13.3, 16p13.2, 16p11.2 and 17q11.2. These copy number variations (CNVs) are typically characterized by their postnatal features, that include developmental delay, autism spectrum disorders, and psychiatric symptoms, often without consistent or specific structural abnormalities detectable during fetal development [39-43]. Although some prenatal ultrasound findings have been described in the literature, the general prenatal phenotype of these CNVs remains subtle or non-specific and frequently undetectable on fetal autopsy or routine imaging [39, 44]. Therefore, in the context of gestational loss, their identification may not always be related to evident morphological abnormalities. This demonstrates the diagnostic utility of chromosomal microarray analysis, particularly in cases with normal or unspecific fetal morphology, underscoring the value of bringing molecular data to formalize a more comprehensive etiological evaluation beyond morphology and facilitating appropriate reproductive counselling.

As expected, the median gestational age was significantly lower in cases with chromosomal anomalies compared to those with morphological anomalies, reflecting the well-known association between severe genetic defects and earlier fetal demise [32, 35, 45]. This observation aligns with existing evidence that shows that chromosomal abnormalities are most frequently detected during the earliest gestational weeks, with a sharp decline in prevalence after the first trimester [45].

In our study, while most fetuses with chromosomal abnormalities presented with associated morphological alterations, three cases showed no visible external anomalies identified on autopsy. This highlights that a normal external appearance cannot exclude a

chromosomal abnormality, especially in the earliest stages of development [15]. Notably, in our cohort, 86.4% of the cases with chromosomal abnormalities also presented with morphologic anomalies, reinforcing the diagnostic value of fetal autopsy even when genetic results are available. This complementarity between cytogenetics and anatomopathological examination has been widely emphasized in the literature as necessary for a complete etiological evaluation of early gestational losses [10, 15].

Conversely, several cases with major morphological anomalies had normal karyotypes, suggesting a potential role of non-genetic factors. Teratogenic agents—such as infections, drugs, alcohol, or hyperthermia—can interfere with organogenesis and lead to structural anomalies despite a diploid chromosomal complement [8, 10]. This is in line with studies showing that a substantial proportion of morphologically abnormal embryos have a normal karyotype [15], reinforcing the multifactorial nature of gestational loss [8].

In this study, no statistically significant associations were found between the presence of fetal anomalies and maternal factors such as age, BMI, obstetric history, or pre-existing medical conditions. While these findings lend further support to the idea that a considerable proportion of spontaneous abortions may result from idiopathic causes, which may include sporadic genetic or epigenetic alterations, that are not necessarily linked to identifiable maternal conditions [46, 47], they should be interpreted with caution. The absence of associations may reflect limitations in sample size and incomplete documentation of certain maternal variables, which restricted our ability to conduct a more comprehensive analysis. It may also reflect the lack of non-chromosomal genetic studies in certain cases, which was caused by the gradual development of the genetic investigation protocol over the 10-year study period.

Although advanced maternal age is widely recognized as a major risk factor for chromosomal abnormalities (particularly aneuploidies) and gestational loss [18, 20, 48],

our analysis was unable to establish a statistically significant difference in age distribution between the groups. This discrepancy may also partly relate to the sample size limitations or the gestational age distribution in our cohort. Notably, the literature shows that even after excluding all chromosomal abnormalities, the incidence of certain structural malformations (e.g., cardiac defects, club foot, diaphragmatic hernia) increases significantly with maternal age [20].

Contrary to what has been previously reported in the literature [49-51], no association was found between maternal obesity and the risk of fetal anomalies in our study. This lack of association may one more time be a reflection of our small sample size. Additionally, the impact of obesity appears to be more pronounced in very early losses (<8 weeks) [50], which were not represented in our sample. While obesity is a known risk factor for many obstetric outcomes, its isolated contribution to fetal anomalies in spontaneous abortion in selected populations such as ours remains difficult to quantify [52, 53].

A history of previous abortion is a known risk factor for subsequent gestational loss, with the risk increasing with the number of prior losses [18, 19]. In the present cohort, previous gestational loss was detected in 41% of women, a higher frequency than that described in some studies [19], yet this variable did not show a significant association with fetal anomalies, which may again reflect the multifactorial and sometimes idiopathic nature of gestational loss.

Among the maternal conditions evaluated in this study, pregestational diabetes is the one most consistently associated with an increased risk of congenital anomalies, being widely recognized as one of the most significant teratogenic factors in human pregnancy [54-56]. Despite this established association, we found no significant association. This result may be explained by the limited number of diabetic cases due to the overall sample

size, which may have reduced the power to detect such associations. The other conditions we evaluated, such as hypertension and autoimmune disease, are not as clearly associated with malformations and are more commonly tied to fetal growth restriction, as evidenced in previous studies [15, 57-60].

Although our study found no significant association between the number of previous pregnancies and the presence of fetal anomalies, previous research indicates different associations depending on the type of anomaly. For instance, nulliparity has been associated with an increased incidence of cardiac and abdominal wall anomalies, as well as amniotic band sequence while multiparity has shown to increase the incidence of limb-reduction defects [61]. These findings could represent physiological and environmental differences between first and subsequent pregnancies, which our dataset may not have been sufficiently powered to detect.

Lastly, the type of conception (natural vs. medically assisted reproduction) showed no significant difference between groups. Research in this area remains inconsistent: some studies have found an increased risk of congenital anomalies - especially following IVF or ICSI [62, 63], whereas others have found no significant difference when comparing the type of conception [64]. These differences may be due to differences in study size, standard protocol, and baseline maternal infertility. In our sample, a lack of association may have been due to similar issues: specifically the small sample size and the heterogeneous ART protocols.

In addition to the previously discussed limitations, it should be addressed that it is difficult to directly compare studies such as ours with other studies due to significant methodological differences, including variations in gestational age limits, classification criteria, inclusion or exclusion of termination of pregnancy cases, the extent of genetic or

pathological data available and whether chromosomal abnormalities were included or excluded from the morphological analysis.

One of the major strengths of this study relies on the systematic use of fetal autopsy in all cases included, performed by a team of experienced pathologists at a tertiary center. This consistency and integration of genetic and histopathological expertise allowed for a greater accuracy and reliability in the assessment and detection of fetal anomalies and emphasized the limitations of relying solely on maternal history or clinical presentation to determine etiology. Additionally, in contrast to multicentered studies where protocols may diverge, the use of established procedures in our single institution enhances the internal validity of the findings and provides a robust foundation for future research in this area.

In fact, the relatively high frequency of fetal anomalies identified in our study supports the additional diagnostic value of systematic pathological and genetic examination. Without this investigation, many of these anomalies, especially those involving subtle or unexpected structural defects, would likely have remained undetected and potentially misdiagnosed as idiopathic. By providing diagnoses that may otherwise go unrecognized, this approach contributes to an enhanced quality of reproductive counselling and clinical decision-making in any subsequent pregnancies. Moreover, confirming suspected anomalies or identifying an etiologic cause may provide emotional reassurance and closure for families, as a vital part of comprehensive perinatal care [10, 13, 15, 65].

Nevertheless, it is important to emphasize that the reported presence of a fetal anomaly does not necessarily imply causality in the gestational loss. Further investigation is needed to better understand the pathogenic relevance of specific fetal anomalies to the context of spontaneous abortion.

It is also important to note that this study contains several limitations, mostly due to the retrospective nature of the design. The data was collected through medical record review, which often lacked completeness or contained inconsistencies due to variations in documentation practices over the 10 year period of the study. Earlier records tended to be less detailed, reflecting the evolving standards in clinical reporting and coding, which may have contributed to the potentially downplayed associations with fetal anomalies.

Additionally, the implementation of genetic testing protocols also varied significantly during the study period, leading to a heterogeneous availability of genetic data across the cases. In fact, genetic analysis was not performed in 62 cases, due to lack of cellular growth for karyotyping or not being clinically requested at the time. Besides, of the remaining cases, several did not undergo extended genetic investigations, such as gene panels or exome sequencing, which could have helped identify additional anomalies of genetic origin. This may have contributed to a potential underestimation of the true prevalence of chromosomal or other genetic abnormalities in our study.

Furthermore, although all cases included had macroscopic fetal material, pathological examination of fetuses is frequently limited by incomplete specimens or degraded tissues, especially in more advanced stages of maceration, which may compromise the identification of subtle morphological anomalies.

Lastly, while the emphasis on specialized expertise increases both the internal consistency and overall diagnostic accuracy of the study population, the setting of data collection (a single tertiary referral center) imposes some potential limitations. Verily, as a differentiated hospital, our institution receives a high number of referred cases, particularly those with suspected fetal or maternal pathology. This may have contributed to a greater prevalence of fetal anomalies in our study population than in the general obstetric population, which may have introduced some referral bias. As such, the external

generalizability of our findings may be limited, especially when applied to different healthcare settings, ethnic groups, or populations without access to universal healthcare.

Further prospective studies with broader and more diverse populations are needed to explore associations with maternal or fetal risk factors, including stratification by anomaly subtype and gestational age. Ultimately a more comprehensive understanding of fetal anomalies in spontaneous abortion is essential for developing more targeted preventive strategies, inform clinical decision-making and guide preconception and prenatal interventions aimed at reducing the incidence and burden of spontaneous abortion.

Conclusion

In conclusion, the high prevalence of fetal anomalies in late spontaneous abortions reinforces the importance of performing fetal autopsy and genetic analysis to enhance diagnostic accuracy and support informed reproductive counseling. Accordingly, the integration of clinical, genetic and pathological data represents a major strength of this study, providing a multidimensional comprehensive overview on fetal anomalies and their contribution to gestational loss.

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Ethical Approval

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of ULS São João (approval number: CE-358-2024). Given that this was a retrospective study based on electronic health record review, the requirement for informed consent was waived by the Ethics Committee. All data were handled in compliance with institutional and legal regulations to ensure confidentiality and data protection.

Consent to Publish

Not applicable.

Declaration of Interest Statement

The authors declare no conflicts of interest relevant to the content of this study.

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Author Contributions Statement

The following authors contributed to the initial conception and design of the study protocol: IACR and CR. They also assisted in drafting the manuscript and the data collection process and reviewed and revised the manuscript. IACR was the principal investigator and was responsible for writing the article and carrying out the statistical analysis. SG collaborated in the collection and interpretation of pathological data. SD collaborated in the collection and interpretation of genetic data. CR supervised the research and provided expertise in obstetrics.

Data Availability Statement

The datasets generated and analyzed during the present study are not publicly available due to patient confidentiality and institutional data protection policies, but they may be available from the corresponding author on reasonable request and with the permission of the Ethics Committee of the ULS São João.

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Table 1. Distribution of Fetal Anomalies by Type (n = 71)

Type of anomaly	n	%
Chromosomal anomalies	22	31.0
Morphological anomalies	41	57.7
Other Anomalies	8	11.3
- Anomalies secondary to severe oligohydramnios	(6)	(8.5)
- Amniotic band syndrome	(2)	(2.8)

Table 2. Classification of morphological anomalies by category (n = 41)

Classes of Morphological Anomalies	n	%
Nervous system anomalies	1	2.4
Polymicrogyria	1	2.4
Cardiac defects	6	14.6
Complete atrioventricular septal defect	2	4.9
Perimembranous ventricular septal defect	2	4.9
Perimembranous ventricular septal defect + pulmonary hypoplasia	1	2.4
Atrial septal defect (ostium primum)	1	2.4
Respiratory anomalies	1	2.4
Laryngeal anomaly / hyoid bone malformation	1	2.4
Gastrointestinal anomalies	1	2.4
Epithelial hepatoblastoma	1	2.4
Abdominal wall defects	1	2.4
Omphalocele	1	2.4
Cystic hygroma	1	2.4
Fetal growth restriction (FGR)	15	36.6
Specific anomalies of monochorionic twins	8	19.5
Twin reversed arterial perfusion (TRAP) sequence	4	9.8
Twin-to-twin transfusion syndrome (recipient, fetal hydrops)	2	4.9
Twin-to-twin transfusion syndrome (donor, FGR)	2	4.9
Multiple anomalies	7	17.1
Right heart hypoplasia + pulmonary hypoplasia + nervous system anomaly	1	2.4
Fetal growth restriction + fetal hydrops	1	2.4
Fetal growth restriction + Cystic hygroma	1	2.4
Parachute mitral valve + incomplete pulmonary fissures	1	2.4
Cardiac chamber asymmetry + mild left pelvicalyceal dilation	1	2.4
Omphalocele + intestinal malrotation + short colon	1	2.4
Craniofacial abnormalities + complex cardiac defects + omphalocele + anal atresia + bladder dilatation	1	2.4

Table 3. Chromosomal anomalies detected by fetal autopsy and complementary genetic study (n = 22)

Chromosomal anomaly	n	%
Identified by conventional karyotyping	16	72.7
Trisomy 13	4	18.2
Trisomy 18	2	9.1
Trisomy 21	6	27.3
Triploidy (69,XXX)	1	4.5
Turner Syndrome (45,X)	1	4.5
Klinefelter Syndrome (47,XXY)	1	4.5
47,XY,+mar[3]/46,XY[28]	1	4.5
Identified by array CGH	6	27.3
6p22.2p22.1 Microduplication Syndrome	1	4.5
15q13.2q13.3 Microduplication Syndrome	1	4.5
16p13.2 Microdeletion Syndrome	1	4.5
16p11.2p11.2 Microduplication Syndrome	1	4.5
17q11.2 Microdeletion Syndrome	1	4.5
18 Microdeletion and Microduplication Syndrome*	1	4.5

*Specific alteration identified by array CGH: arr[GRCh37] 18p11.32p11.2(118,760_14,951,330)x1,18q12.1q23(20,704,842_78,010,032)x3 (nomenclature according to ISCN 2024 [17])

Table 4. Maternal, Obstetric, and Fetal Characteristics According to the Presence of Fetal Anomalies

Variables		Overall Sample‡	Without Anomalies Frequency§ (%)	With Anomalies Frequency§ (%)	p-Value*
BMI (n=137)	Underweight	5 (3.6)	5 (100.0)	0 (0.0)	0.130
	Normal	74 (54.0)	37 (50.0)	37 (50.0)	
	Overweight	41 (29.9)	24 (58.5)	17 (41.5)	
	Obesity	17 (12.4)	11 (64.7)	6 (35.3)	
Number of gestations (n=170)	1	58 (34.1)	34 (58.6)	24 (41.4)	0.868
	2	65 (38.2)	41 (63.1)	24 (36.9)	
	3 or More	47 (27.7)	28 (59.6)	19 (40.4)	
Number of deliveries (n=170)	0	95 (55.9)	56 (58.9)	39 (41.1)	0.920
	1	50 (29.4)	31 (62.0)	19 (38.0)	
	2	18 (10.6)	11 (61.1)	7 (38.9)	
	3 or More	7 (4.1)	5 (71.4)	2 (28.6)	
History of previous abortions (n=170)	Yes	70 (41.2)	41 (58.6)	29 (41.4)	0.653
	No	100 (58.8)	62 (62.0)	38 (38.0)	
History of ectopic pregnancy (n=170)	Yes	3 (1.8)	1 (33.3)	2 (66.7)	0.562†
	No	167 (98.2)	102 (61.1)	65 (38.9)	
Monitored pregnancy (n=162)	Yes	153 (94.4)	90 (58.8)	63 (41.2)	0.739†
	No	9 (5.6)	6 (66.7)	3 (33.3)	
Previous pathology (n=180)	Yes	60 (33.3)	33 (55.0)	27 (45.0)	0.281
	No	120 (66.7)	76 (63.3)	44 (36.7)	
Type of pregnancy (n=168)	Natural conception	143 (85.1)	86 (60.1)	57 (39.9)	0.989
	Medically assisted conception	25 (14.9)	15 (60.0)	10 (40.0)	
Sex of the aborted fetus (n=180)	Male	101 (56.1)	64 (63.4)	37 (36.6)	0.383
	Female	79 (43.9)	45 (57.0)	34 (43.0)	

‡ Percentages in this column are calculated relative to the total number of valid cases for each variable (may vary due to missing data).

§ Percentages in these columns are row percentages (relative to the total within each category).

† Fisher's exact test was used instead of the Pearson chi-square test due to expected cell count < 5 in at least one cell.

*p-value <0.05 are considered significant.

Table 4a. Distribution of Maternal Pathologies among cases with and without Fetal Anomalies (only positive cases shown)

Type of pathology (n= 180)	Overall Sample‡	Without Anomalies Frequency§ (%)	With Anomalies Frequency§ (%)	p-Value*
Hypertension	7 (3.9)	2 (28.6)	5 (71.4)	0.114†
Diabetes mellitus	14 (7.8)	9 (64.3)	5 (35.7)	0.766
Autoimmune disease	10 (5.6)	4 (40.0)	6 (60.0)	0.196†
Psychiatric disorder	7 (3.9)	4 (57.1)	3 (42.9)	1.000†
Infectious comorbidity	4 (2.2)	4 (100.0)	0 (0.0)	0.155†
Uterine Fibroids (Myoma)	5 (2.8)	3 (60.0)	2 (40.0)	1.000†
Uterine malformation	1 (0.6)	0 (0.0)	1 (100.0)	0.394†
Uterine surgery	11 (6.1)	5 (45.5)	6 (54.5)	0.347†
Other pathology	13 (7.2)	6 (46.2)	7 (53.8)	0.270

‡ Percentages in this column are calculated relative to the total number of valid cases for each variable (may vary due to missing data).

§ Percentages in these columns are row percentages (relative to the total within each category).

† Fisher's exact test was used instead of the Pearson chi-square test due to expected cell count < 5 in at least one cell.

*p-value <0.05 are considered significant.

Table 5. Maternal Age and Gestational Age at Loss in Cases with and without Fetal Anomalies

Variables* (n= 180)		Without Anomalies (n=109)	With Anomalies (n=71)	p-Value (Mann-Whitney U)**
Maternal Age	Median (Q1-Q3)	33 (28-37)	32 (28-37)	0.987
	Minimum-Maximum	16-47	19-48	
Gestational Age (completed weeks)	Median (Q1-Q3)	18 (14-21)	16 (13-19)	0.075
	Minimum-Maximum	10-23	11-23	

*Interquartile range (IQR = Q3 – Q1).

** p-value <0.05 are considered significant.

STROBE Statement—Checklist of items that should be included in reports of **cohort studies**

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 7 (paragraph 2): "A retrospective cohort..." Page 7 (paragraphs 2, 3 and 4).
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 8, Page 9 and Page 10
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 10 (paragraph 1): "The aim of this study is the critical evaluation of morphological anomalies in fetuses from spontaneous abortion, with the goal of elucidating the underlying etiology and associated factors."
Methods			
Study design	4	Present key elements of study design early in the paper	Page 11 (paragraph 1): "A retrospective observational cohort study was conducted to assess all spontaneous gestational losses..."
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 11 (paragraph 1): "all spontaneous gestational losses that occurred between January 1st, 2014, and December 31st, 2023, at Unidade Local de Saúde São João (ULS São João)"
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	Page 11 (paragraph 3): "Fetuses from spontaneous gestational losses with a gestational age between 10 weeks and 23 weeks + 6 days that underwent autopsy... We excluded cases of termination of pregnancy." Not applicable, as this was not a matched cohort study.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Page 11 (paragraph 5): "Clinical data were retrieved from electronic medical records, such as SClínico and Obscare. The following parameters were assessed..."
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of	Page 11 (paragraph 5): "Clinical data were retrieved from electronic medical records, such as SClínico and Obscare."

		assessment (measurement). Describe comparability of assessment methods if there is more than one group	Page 12 (paragraph 2): “Gestational age was determined based on the measurement of crown-rump length in the first-trimester ultrasound...” Page 12 (paragraph 3): “Body mass index (BMI) was characterized as...” Page 13 (paragraphs 1 and 2): “Based on autopsy and genetic findings, congenital anomalies were then divided into...”
Bias	9	Describe any efforts to address potential sources of bias	Page 12 (paragraph 1): “It should be noted that all fetal autopsies were conducted by a dedicated team including...” Page 12 (paragraph 5): “Each case was treated independently, as maternal characteristics (such as age, BMI, or clinical conditions) could vary between pregnancies. This approach allowed for case-based analysis of the fetal outcomes and ensured compatibility with the study objectives.”
Study size	10	Explain how the study size was arrived at	Page 11 (paragraph 4): “Of the 184 cases of spontaneous gestational loss reviewed, 4 cases were excluded... we ended up with a final sample of 180 cases.”
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Page 12 (paragraph 3): “Body mass index (BMI) was characterized as underweight...”
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	Page 13 (paragraph 3): “Descriptive analysis was conducted: categorical variables were expressed...” Page 12 (paragraph 4): “Cases were then divided into two groups: (A) fetuses with anomalies and (B) fetuses without anomalies. A comparative analysis between these groups was undertaken...” Page 13 (paragraphs 1 and 2): “congenital anomalies were then divided into three main groups...”; “Morphological anomalies were further categorized...” Page 13 (paragraph 4): “With the intention of addressing missing data, a binary variable was created to indicate whether each case had at least one missing value...” This study does not involve follow-up, therefore loss to follow-up is not applicable. Not applicable, since no sensitivity analyses were performed.

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	Page 15 (paragraph 1): “Of the 180 spontaneous abortions included and analyzed in this study...” Page 16 (paragraph 3): “In 7 cases, analysis was attempted but ended up being unsuccessful due to lack of cell growth. In the remaining 55 cases, genetic testing was not performed, either because it was not requested or due to unavailability of material.” Not applicable – no flowchart was used.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	Page 17 (paragraph 3): “Of the 180 spontaneous pregnancy losses analyzed, male fetuses were reported to be slightly more frequent than female...” Pages 39–41 (Tables 4, 4a and 5): number of valid cases indicated as “n=___” in each table and category. Not applicable, as this study does not include a follow-up period.
Outcome data	15*	Report numbers of outcome events or summary measures over time	Page 15 (paragraph 1): “fetal anomalies were identified in 71 fetuses (39.4%), while no anomalies were identified in the remaining 109 of the cases (60.6%), either in fetal autopsy or genetic analysis.” The detailed distribution of anomaly types is described in Pages 38–40 (Tables 1, 2 and 3)
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Page 18 (paragraph 1): “no statistically significant differences were found between fetuses with and without anomalies concerning maternal age (p = 0.987), number of pregnancies (p = 0.868), deliveries (p = 0.920), BMI (p = 0.130) ...” Pages 41–43 (Tables 4, 4a and 5) Page 17 (paragraph 4): “had a BMI that fell within the normal range (54.0%), while 29.9% were overweight, 12.4% were classified as obese and only a small percentage of the sample categorized as underweight (3.6%).” Not applicable - no relative risk estimates were calculated.

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Although no formal subgroup analyses were conducted, a comparison was made between cases with chromosomal and morphological anomalies regarding gestational age at fetal loss: Page 18 (paragraphs 3 and 4): “gestational age at fetal loss was significantly lower in cases of chromosomal anomalies... (p = 0.004, Mann Whitney U test).”; “The median maternal age was slightly higher in the chromosomal anomaly group... although this difference was not statistically significant (p = 0.445, Mann-Whitney U test).”
Discussion			
Key results	18	Summarise key results with reference to study objectives	Page 19 (paragraph 1): “. Among cases with abnormalities, the most frequent were morphological abnormalities (57.7%), followed by chromosomal abnormalities...” Page 23 (paragraph 2): “As expected, the median gestational age was significantly lower in cases with chromosomal anomalies...” Page 27 (paragraph 2): “In fact, the relatively high frequency of fetal anomalies identified in our study supports the additional diagnostic value of systematic pathological and genetic examination.”
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Page 24 (paragraph 2): “The absence of associations may reflect limitations in sample size and incomplete documentation of certain maternal variables..” Page 28 (paragraphs 1, 2, 3 and 4): “It is also important to note that this study contains several limitations, mostly due to the retrospective nature of the design...”; “the implementation of genetic testing protocols also varied significantly during the study period...”; “Furthermore, although all cases included had macroscopic fetal material...”; “as a differentiated hospital, our institution receives a high number of referred cases...”
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 30 (paragraph 1): “the high prevalence of fetal anomalies in late spontaneous abortions reinforces the importance of performing fetal autopsy and genetic analysis to enhance diagnostic accuracy and support informed reproductive counseling.”
Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 28 (paragraph 4): “As such, the external generalizability of our findings may be limited, especially when applied to different healthcare settings...”

Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 32 (subsection <i>Funding</i>): “No funding was received for this study.”

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.



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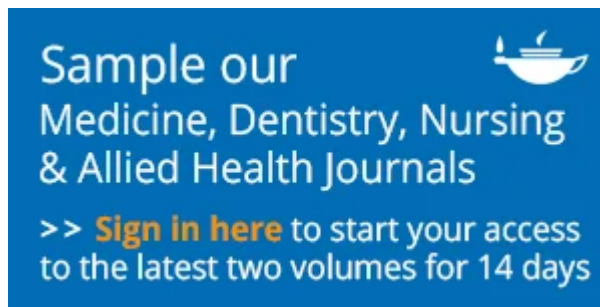
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Version 2.2

Date of issue: 14 May 2013

Date of version: 30 May 2023

Update in this version: Journal models updated with DOIs

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Placement	References are numbered consecutively in the order in which they are first mentioned in the text. Identify references in text, tables, and captions by bracketed numbers [1], and provide a list of references at the end of the article in numerical order with square brackets around the numbers. Reuse the original number assigned to the reference each time a reference is repeated in the text. Insert the citation numbers at the relevant place in the text, inside any adjacent punctuation mark. Examples: Myopathy typically occurs in fewer than one in 10,000 patients on standard doses [1]. This approach was successfully implemented by Benders et al. [30] and Zhao [31] for modular NN. For this purpose, the NNs were widely used in structural inverse problems [24], damage identification [14,25], or parameters estimation [26], among many applications.
Multiple references	When citing multiple references, use commas (without spaces) to separate them. Use an unspaced en dash to join inclusive first and last numbers, e.g. [2,3,4,5,7,10] would be abbreviated to [2–5,7,10]. Examples: Compared to the initial shape, the optimized surface shape can substantially improve the structural characteristics [12,13]. Most of the optimization methods proposed in previous studies are parametric methods [3–7]. See, for example, [1,3,10–13,15–20,22–25,27,28]. For some work along these lines, see [3,13,17,18,27]. The crack boundary was discretized using 10 discontinuous quadratic elements, where the crack-tip elements are discontinuous quarter-point [see 17,28].
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Repeat mentions in the same paragraph	Other efforts are including the perturbation method described in [8,11,12,16] and the perturbation method described in [11,15].
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Basic format (with one author)	Author AA. Title of article. Abbreviated Journal Title. Date;volume(number):pages. doi: ##### MacGregor RJ. A functional view of consciousness and its relations in brain. J Integr Neurosci. 2004;3(3):253–266. doi: 10.1142/s0219635204000531
Two authors	Prokai-Tatrai K, Prokai L. Modifying peptide properties by prodrug design for enhanced transport into the CNS. Prog Drug Res. 2003;61:155–188. doi: 10.1007/978-3-0348-8049-7_6
Three authors	Veronesi U, Maisonneuve P, Decensi A. Tamoxifen: an enduring star. J Natl Cancer Inst. 2007;99(4):258–260. doi: 10.1093/jnci/djk072
More than three authors	Meneton P, Jeunemaitre X, de Wardener HE, et al. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev. 2005;85:679–715. doi: 10.1152/physrev.00056.2003
Organization as author	International Society for the Study of Trauma. Guidelines for treating dissociative identity disorder in adults, third revision. J Trauma Dissociation. 2011;12(2):115–187. doi: 10.1080/15299732.2011.537247
No author	Physician oversight of specialized emergency medical services. Prehosp Emerg Care. 2019;23(4):590–591. doi: 10.1080/10903127.2018.1551452
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Not the Version of Record (including Author Manuscript Online, Advanced Author Version, etc.)	Author AA. Article title. Abbreviated Journal Title. Forthcoming. [cited Date]:[pages]. [Format] available at [URL or DOI] Zheng H, Ng F, Liu Y, et al. Spatial and circadian regulation of <i>cry</i> in <i>Drosophila</i>. J Biol Rhythms. Forthcoming. [cited 2008 Aug 11]:[18 p.]. Author's manuscript available at http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pubmed&pubmedid=18663236 PubMed Central; PMCID: PMC2504742. McDonnall MC, Steverson A, Sessler Trinkowsky R, et al. Assistive technology use in the workplace by people with blindness and low vision: perceived skill level, satisfaction, and challenges. Forthcoming. Assist Technol. [accessed 2023 May 24]:[25 p.]. Accepted author version available at doi: 10.1080/10400435.2023.2213762
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12 de Fevereiro de 2025

A Diretora do Centro de Epidemiologia Hospitalar

(Prof.ª Doutora Ana Azevedo)



SÃO JOÃO

DIREÇÃO CLÍNICA
2025 -02- 13

n.º 358 / 2024

PEDIDO DE AUTORIZAÇÃO

Realização de Investigação

Deliberado concordar, nos
termos legais em vigor.Exmo(a). Senhor(a) Presidente do Conselho de Administração
do Centro Hospitalar Universitário de São JoãoCONSELHO DE ADMINISTRAÇÃO DA ULS SÃO JOÃO, EPE - REUNIÃO DE
Presidente do Conselho de AdministraçãoNome do Investigador Principal:
Íris Alexandra Costa Rodrigues

Título da Investigação:

Análise Retrospectiva de Alterações Morfológicas em Fetos de Abortamento
Espontâneo: Um Estudo Clínico e Patológico

(Prof.ª Doutora Maria João Baptista)		20 FEV 2025	
Diretora Clínica para a área dos cuidados de saúde hospitalares	Diretora Clínica para a área dos cuidados de saúde primários	Enfermeiro Diretor	Vogal Executiva
Dra. Elisabete Barbosa	Dra. Lígia Silva	Enf.º Paulo Emílio Mota	Dra. Fernanda Oliveira
			Dr. Vitor Leite

Pretendendo realizar no(s) Serviço(s) de:

Serviço de Obstetrícia e Serviço de Anatomia Patológica

a investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, autorização para a sua efetivação.

Para o efeito, anexo toda a documentação referida no dossier da Comissão de Ética do Centro Hospitalar Universitário de São João respeitante à investigação, à qual enderecei pedido de apreciação e parecer.

Com os melhores cumprimentos.

O Investigador/Promotor

Porto, 05 de outubro de 2024 .

Assinado por: ÍRIS ALEXANDRA COSTA
RODRIGUES

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CHAVE MÓVEL

Centro de Epidemiologia Hospitalar

11/2/2025

Parecer da Comissão de Ética do
Centro Hospitalar Universitário de São João
Unidade Local de Saúde de São João

Título do Projeto: Análise Retrospectiva de Alterações Morfológicas em Fetos de Abortamento Espontâneo: Um estudo Clínico e Patológico

Nome da Investigadora Principal: Íris Alexandra Costa Rodrigues (estudante do MIMED da FMUP). Serão co-investigadoras a Prof.^a Doutora Carla Ramalho e a Dra. Susana Guimarães.

Onde decorre o Estudo: Nos Serviços de Obstetrícia e Anatomia Patológica da ULS de São João. Apresentou declaração da Dra. Marina Moucho, diretora do Serviço de Obstetrícia e da Prof.^a Doutora Fátima Carneiro, diretora do Serviço de Anatomia Patológica. A profissional de ligação será a Prof.^a Doutora Carla Ramalho.

Objetivos do Estudo:

Identificar e caracterizar as alterações morfológicas observadas em fetos de abortamento espontâneo, com o objetivo de esclarecer a etiologia e fatores associados.

Estudo realizado no âmbito do Mestrado Integrado em Medicina da FMUP, sob orientação da Prof.^a Doutora Carla Ramalho.

Conceção e Pertinência do estudo:

O estudo é pertinente e adequado, porquanto consta no protocolo submetido à CE: "Este estudo aborda um tema com pouca literatura disponível, oferecendo uma mais-valia ao fornecer perceções importantes sobre as possíveis causas do abortamento espontâneo. Permite, assim, ajudar na compreensão clínica e possivelmente na melhoria dos cuidados preventivos".

Serão incluídos todos os fetos de abortamento espontâneo ocorridos no HUSJ de 01/01/2002 a 31/12/2024, numa amostra estimada de 1150.

Estão definidos os critérios de inclusão e as variáveis a ser recolhidas: dados clínicos da grávida - idade, paridade, patologia médica, antecedentes obstétricos; dados obstétricos - tipo de conceção, idade gestacional, rastreio de aneuploidias, ecografias; dados genéticos; dados da Anatomia Patológica (feto e placenta) - idade gestacional, sexo, parâmetros biométricos, anomalias do hábito externo e interno, avaliação radiológica, avaliação microscópica.

Benefício/risco: Não aplicável

Confidencialidade dos dados:

A pseudonimização será garantida através da substituição de informações identificáveis por identificadores únicos, como códigos alfanuméricos, de modo que os dados não possam ser facilmente relacionados a indivíduos específicos sem informações adicionais. Os dados vão ser colocados numa folha de excell que será protegida por uma password de acesso, que será limitada a pessoal autorizado.

Apresentou um pedido de reutilização de registos clínicos para Investigação e Desenvolvimento ao RAI, e uma 'avaliação sobre o impacto da proteção de dados' para o EPD.

Respeito pela liberdade e autonomia do sujeito de ensaio: Não aplicável

Curriculum da investigadora: Adequado à investigação.

Data previsível da conclusão do estudo: abril de 2025

Conclusão: Proponho um parecer favorável à realização do estudo.

Porto, 18 de outubro de 2024

O Relator da CE, Doutor Pedro Brito





SÃO JOÃO

Questionário eletrónico

n.º 358 / 2024

SUBMISSÃO DE PROJETO DE INVESTIGAÇÃO PARA PARECER E AUTORIZAÇÃO

Preenchimento em formato digital obrigatório

Caro/a Investigador/a

Este questionário vai ser objeto de apreciação pela Comissão de Ética (CE), que emitirá o competente parecer; pelo Responsável de Acesso à Informação (RAI), que emitirá um despacho de autorização ou indeferimento, relativamente à reutilização da informação a que pretende ter acesso; pelo Encarregado de Proteção de Dados (EPD), que emitirá um parecer, mediante a 'avaliação do impacto sobre a proteção de dados' (que deve anexar a este pedido); pelo Centro de Epidemiologia Hospitalar; sendo enviado, num último momento, para decisão institucional do Conselho de Administração do CHUSJ. Os respetivos despachos de parecer e autorização serão exarados no final deste documento, e enviados posteriormente, de modo a poder iniciar, nesse momento, a investigação a que se propõe.

IDENTIFICAÇÃO DO ESTUDO

Título do projeto:

Análise Retrospectiva de Alterações Morfológicas em Fetos de Abortamento Espontâneo: Um Estudo Clínico e Patológico

Data prevista para início: 19 / 10 / 2024

Data prevista para o término: 30 / 04 / 2025

EQUIPA DE INVESTIGAÇÃO

1. Investigador principal

Nome: Íris Alexandra Costa Rodrigues

Afiliação institucional: ☐ CHUSJ ☒ FMUP Outro: _____

Serviço/ Departamento: _____

Grupo profissional: Estudante Cédula Profissional n.º: _____

Contacto telefónico: 966309486 Endereço eletrónico institucional: up201906387@med.up.pt

Formação em Boas Práticas Clínicas (GCP): ☒ Não ☐ Sim

2. Co-investigadores

Nome: Carla Ramalho

Afiliação institucional: Centro Hospitalar Universitário São João e Faculdade de Medicina da Universidade Porto

Grupo profissional: Médica Cédula Profissional n.º: 34794

Contacto telefónico: _____ Endereço eletrónico institucional: u000421@chsj.min-saude.pt

Nome: Susana Guimarães

Afiliação institucional: Centro Hospitalar Universitário São João e Faculdade de Medicina da Universidade Porto

Grupo profissional: Médica Cédula Profissional n.º: 42043

Contacto telefónico: _____ Endereço eletrónico institucional: susana.guimaraes@chsj.min-saude.pt

(acrescentar n.º de investigadores, se apropriado ao projeto de investigação)

3. Promotor (se aplicável): _____

CARACTERIZAÇÃO DA INVESTIGAÇÃO

1. Metodologia da investigação

☐ Qualitativa ☒ Mista (qualitativa+quantitativa) ☐ Outra. Qual? _____

Se quantitativa:

☐ Experimental ☒ Observacional ☒ Sem intervenção ☐ Com intervenção

Se experimental ou observacional com intervenção, qual o tipo de intervenção?

☐ Algoritmo de decisão diagnóstica/terapêutica ☐ Comunicação

☐ Outra. Qual? _____

2. Aleatorização dos braços de intervenção: ☒ Não ☐ Sim

3. Se observacional, qual o desenho?

☐ Coorte prospetivo ☒ Coorte retrospectivo ☐ Caso-controlo
☐ Transversal ☐ Ecológico ☐ Outro. Qual? _____

REALIZAÇÃO DA INVESTIGAÇÃO

Local onde se realiza a investigação: ☒ CHUSJ ☒ FMUP ☐ Outro

Serviço/ Departamento: Serviço de Obstetrícia e Serviço de Anatomia Patológica

Existem outros Centros onde se realizará a investigação? ☒ Não ☐ Sim. Quais? _____

ENTIDADE(S) QUE TUTELA(M) A INVESTIGAÇÃO

1. CHUSJ – Serviço: _____

2. FMUP – Departamento: Ginecologia, Obstetrícia e Pediatria

3. Outra instituição. Qual? _____

ORIENTADOR (se aplicável)

Nome: Carla Maria de Almeida Ramalho

Afiliação: CHUSJ e FMUP Endereço eletrónico institucional: carlaramalho@med.up.pt

PROFISSIONAL DE LIGAÇÃO (se aplicável - ver anexo)

Nome: Carla Maria de Almeida Ramalho Serviço: Obstetrícia

ENQUADRAMENTO DA INVESTIGAÇÃO

Em trabalho académico? ☐ Não ☒ Sim Conferidor de grau? ☐ Não ☒ Sim

Síntese dos objetivos:

Identificar e caracterizar as alterações morfológicas observadas em fetos de abortamento espontâneo, com o objetivo de esclarecer a etiologia e fatores associados.

Fundamentação ética (incluir informação sumária sobre o estado da arte, ganhos em conhecimento/ inovação, ponderação geral sobre benefícios/risco):

Este estudo aborda um tema com pouca literatura disponível, oferecendo uma mais-valia ao fornecer percepções importantes sobre as possíveis causas do abortamento espontâneo. Permite, assim, ajudar na compreensão clínica e possivelmente na melhoria dos cuidados preventivos. O estudo respeitará o sigilo e a integridade dos dados analisados.

PARTICIPANTES PREVISTOS PARA A INVESTIGAÇÃO

Estão definidos critérios de inclusão / de exclusão de doentes? ☐ Não ☒ Sim

Onde e como serão recrutados os participantes no estudo?

Todos os fetos de abortamento espontâneo ocorridos no CHUSJ de 01/01/2002 a 31/12/2024 (SClinico e Obscare

Qual é o tamanho amostral? Por volta de 1150 (cerca de 50/ano)

Está prevista a recolha de material biológico específico para a investigação?

☒ Não ☐ Sim. Identifique e justifique:

BENEFÍCIO/RISCO DECORRENTE DA PARTICIPAÇÃO

Descreva os benefícios previsíveis:

Identificar fatores associados a abortamento espontâneo, melhorando a prevenção de recorrências.

Descreva os riscos/incómodos previsíveis:

Não se prevê riscos, visto que se trata de uma análise retrospectiva, utilizando dados já recolhidos na decorrência de investigação clínica. Estes dados serão mantidos anonimizados.

CONSENTIMENTO INFORMADO, ESCLARECIDO E LIVRE

Prevê a obtenção de consentimento informado? ☐ Sim ☒ Não

Se não, justifique: Avaliação retrospectiva de dados já recolhidos na decorrência de investigação clínica.

Prevê informação escrita para os participantes? ☐ Sim. **Enviar modelo preenchido.**

☒ Não. Justifique: Avaliação retrospectiva de dados já recolhidos na decorrência de investigação clínica.

O modelo para obtenção de consentimento é o modelo institucional do CHUSJ? ☐ Sim ☐ Não

PROTEÇÃO DE DADOS PESSOAIS

Necessita consultar registos clínicos? ☐ Não ☒ Sim

Está previsto o tratamento de dados pessoais? ☒ Não ☐ Sim

Se sim, de que forma é garantida a pseudonimização dos dados recolhidos? *(codificação, uso de filtros, siglas...)*

Descreva o património informacional a que pretende ter acesso (v.g.: nome, idade, data nascimento, idade, morada, diagnóstico, história clínica, tratamento...):

Dados clínicos da grávida: idade, paridade, patologia médica, antecedentes obstétricos;

Dados obstétricos: tipo de concepção, idade gestacional, rastreio de aneuploidias, ecografias;

Dados genéticos;

Dados da Anatomia Patológica (feto e placenta): Idade gestacional, Sexo, Parâmetros biométricos, Anomalias do hábito externo e interno, Avaliação radiológica, Avaliação microscópica.

Está prevista a criação de um Banco de Dados? ☒ Não ☐ Sim

Está previsto o registo de som ou de imagem dos participantes? ☒ Não ☐ Sim

O estudo envolve investigação genética? ☒ Não ☐ Sim

PROPRIEDADE INTELECTUAL

De quem será a propriedade intelectual da investigação e seus resultados?

☒ Investigador ☐ Promotor ☐ Serviço/CHUSJ ☐ Todos

DIVULGAÇÃO DOS RESULTADOS

Está prevista a divulgação dos resultados da investigação? ☐ Não ☒ Sim

Se sim, estão definidos critérios de publicação? ☒ Não ☐ Sim. Quais? _____

CONTRAPARTIDAS PARA OS PARTICIPANTES

Estão previstas contrapartidas para os participantes? ☒ Não ☐ Sim

Pela participação? ☒ Não ☐ Sim

Pelas deslocações? ☒ Não ☐ Sim

Pelas perdas salariais? ☒ Não ☐ Sim

Por outras perdas e/ou danos? ☒ Não ☐ Sim

EXAMES COMPLEMENTARES DE DIAGNÓSTICO

Estão previstos exames complementares de diagnóstico, para além dos inerentes à rotina assistencial?

☒ Não ☐ Sim. Quais? _____

Por quem serão suportados estes custos?

PROTOCOLO FINANCEIRO

Existe protocolo financeiro com o CHUSJ? ☒ Não ☐ Sim

SEGURO

Este estudo prevê intervenção clínica que implique a existência de um seguro para os participantes?

☒ Não ☐ Sim (se sim, junte cópia da respetiva Apólice)

Data previsível para fim do acesso aos dados: 30 / 04 / 2025

DOCUMENTOS ANEXOS (em suporte digital)

- ☒ Pedido de autorização ao Presidente do Conselho de Administração do CHUSJ
- ☒ Protocolo do estudo
- ☐ Caderno de recolha de dados (CRF)
- ☒ Declaração Diretor(es) Serviço(s)
- ☐ Informação Orientador
- ☒ Profissional de ligação
- ☐ Informação aos participantes
- ☐ Modelo de consentimento a utilizar
- ☐ Instrumentos de avaliação (*escalas, inquéritos*) _____
- ☒ Curriculum/a vitae (*investigador/es*)
- ☐ Questionário para Encarregado de Proteção de Dados (EPD)
- ☐ Termo de Responsabilidade do Centro Académico Clínico (*para investigadores da FMUP que não pertençam ao CHUSJ*)
- ☐ Protocolo financeiro
- ☐ Outros: _____

TERMO DE RESPONSABILIDADE

Aceitação dos termos e condições de reutilização

Cumulativamente com as obrigações decorrentes da Lei n.º 26/2016, de 22 de agosto, maxime dos n.º 2 e 3 do artigo 21 e o n.º 1 e 2 do artigo 12, ao submeter o presente pedido, concordo e fico ainda juridicamente vinculado aos seguintes termos e condições:

- Comprometo-me a manter confidencial toda a informação à qual vou ter acesso;
- Após explicação do RAI do CHUSJ, embora a Lei 26/2016, de 22 de agosto, imponha como requisito a anonimização sem possibilidades de reversão, tal desiderato, é não só uma impossibilidade matemática já comprovada, como ainda resulta num prejuízo para a investigação, face à quantidade e à qualidade da informação a retirar à fonte, razão pela qual, concordando com o RAI, assumimos como compromisso a pseudonimização, o que impõe uma avaliação e gestão do risco, num quadro ético-jurídico que aceitamos e nos comprometemos a colaborar e respeitar;
- Não vou elaborar registos, suscetíveis de identificar ou tornar identificável a identidade das pessoas a quem os mesmos dizem respeito;
- Comprometo-me a consultar os processos clínicos nos termos e locais que me forem indicados para o efeito;
- Tomei conhecimento, que a violação de qualquer dos compromissos aqui assumidos, poderá resultar no apuramento de responsabilidades disciplinares, civis e penais, e ainda, à impossibilidade futura de aceder a informação de saúde para fins de investigação.
- Independentemente de requerer a Certidão de Reutilização, DAta REuse Certificate for Research (DARE), comprometo-me a citar as fontes, sempre que publicitar, no todo ou em parte, resultados da presente investigação.

COMPROMISSO DE HONRA E DECLARAÇÃO DE INTERESSES

Eu, Íris Alexandra Costa Rodrigues,

abaixo assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes na Declaração de Helsínquia (1960, e sucessivas emendas), da Organização Mundial de Saúde, da Convenção de Oviedo e das 'Boas Práticas Clínicas' (GCP/ICH) no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CE de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo, nos últimos três meses. Comprometo-me a entregar à CE o relatório final da investigação, assim que concluído.

Assinado por: **ÍRIS ALEXANDRA COSTA RODRIGUES**

Num. de Identificação: BI15903979

Data: 2024.10.05 18.46.24 GMT Daylight time

Data: 05 / 10 / 2024



CHAVE MÓVEL^{ra}

COMISSÃO DE ÉTICA CHUSJ/FMUP

Parecer da CE, emitido na reunião plenária de 18 / 10 / 2024

A Comissão de Ética para a Saúde
APROVA por unanimidade o parecer do
Relator, pelo que nada tem a opor à
realização deste projecto de investigação.

Centro Hosp. Univ. São João
Comissão de Ética
Manuel Vaz Silva
Presidente

RAI

24019365

RAI - Responsável pelo Acesso à Informação no Centro Hospitalar Universitário de São João (Art. 9º, Lei 26/2016 de 22 de Agosto)



Gabinete
de Apoio ao RAI
Recebido em
30/10/2024
A funcionária
TM



AUTORIZADO
RAI - Responsável pelo Acesso
à Informação no Centro
Hospitalar de São João
(Art. 9º, Lei 26/2016, de 22/8)

12/11/2024

CENTRO DE EPIDEMIOLOGIA HOSPITALAR



CIDADES
DE SAÚDE PRIMÁRIOS

Título do Projeto

Análise Retrospectiva de Alterações Morfológicas em Fetos de Abortamento Espontâneo: Um Estudo Clínico e Patológico

Responsável pelo tratamento Íris Alexandra Costa Rodrigues

Instituição Unidade Local de Saúde de São João (ULS SÃO JOÃO)

Faculdade de Medicina da Universidade do Porto (FMUP)

Investigador Interno Externo

Contacto telefónico 966309486

Endereço Electrónico up201906387@med.up.pt

Profissional de Ligação Carla Maria Almeida Ramalho (Assistente Graduada Hospitalar de Ginec. / Obstetrícia)

Amostra 1150

Análise de Risco Tolerável Baixo Elevado Muito Elevado

Parecer do EPD: 55/2025

Data: 10/02/2025

Finalidade: Identificar e caracterizar as alterações morfológicas observadas em dados post mortem, de fetos de abortamento espontâneo, com o intuito de melhor entender a etiologia e fatores associados a este. Desta forma, espera-se fornecer informações que possam melhorar a gestão clínica e preventiva de futuras gestações.

Licitude: fundamento previsto no artigo 9(2)(j), com as garantias do 89(1) do RGPD, e artigo 31(1) da LERGD.

Categorias de dados pessoais: variáveis identificadas com detalhe na AIPD, datada de 13/11/2024, ponto 13, tendo presente o princípio da minimização dos dados.

Conservação: os dados serão alvo de pseudonimização, armazenados em local seguro, em área restrita com acesso limitado ao profissional de ligação e Investigador Principal, com acesso a ficheiros protegido por palavra-passe, efetuando-se a conservação até a conclusão da investigação, durante o prazo máximo de três (3) meses. Os dados recolhidos serão destruídos após a finalização do estudo.

Comunicação de Dados: não há partilha de dados pessoais.

Conclusão: Face ao exposto, e observadas as recomendações, entende-se que o presente projeto está em conformidade com o RGPD pelo que sou de parecer favorável quanto à sua realização.

Recomendações:

1. Reforçar as medidas de segurança previstas para a conservação dos documentos em formato de papel que impeçam o acesso à informação a pessoas não autorizadas, bem como o seu manuseamento indevido;
2. Garantir medidas de segurança adicionais no transporte dos dados com recurso a dispositivos electrónicos de armazenamento (Laptop, Pen, Cloud Institucional), nomeadamente através de medidas de cifragem e autenticação;
Garantir medidas de segurança adicionais (ex. transformar os dados com recursos a técnicas de generalização, perturbação e/ou como último recurso, a supressão de dados) para os dados que, ainda que pseudonimizados, contém elementos informativos
3. que no seu conjunto possibilitam a re-identificação dos participantes, tendo presente a amostra em estudo (fetos de abortamento espontâneo), em particular na fase de disseminação ou publicação dos resultados (incluindo repositórios científicos).
4. A chave de decodificação que permite a re-identificação dos titulares dos dados (utentes) deve ficar sempre na posse do Elo de Ligação ULS SÃO JOÃO e protegida de acessos indevidos / terceiros;
5. Em caso de necessidade de extensão de prazo e/ou de qualquer alteração dos pressupostos atinentes ao presente parecer o Investigador Principal deverá solicitar a reapreciação do projeto de investigação junto do EPD.

Revisão AIPD:

☐ Data da próxima revisão:

☒ Não carece de revisão.

Anexos:

1. Processo CES n.º 358/2024
2. Parecer CES (18/10/2024)
3. AIPD (13/11/2024)
4. Protocolo de Investigação

Encarregado de Protecção de Dados
Assinado por: **PAULO ALEXANDRE MOTA DA
SILVA**
Data: 2025.02.10 10:49:44+00'00'
Localização: ULS SÃO JOÃO



CARTÃO DE CIDADÃO
• • • •