### RESEARCH

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# Clinical analysis of 126 cases of stillbirth in high-altitude areas



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### Abstract

**Objective** This study aims to analyze the clinical characteristics of stillbirths in high-altitude areas, strengthen monitoring of high-risk pregnant women, improve maternal health care levels, and reduce perinatal mortality rates.

**Methods** A retrospective collection of 126 cases of stillbirth in Nyingchi People's Hospital from 2015 to 2021 was divided into an pre-stage group (2015–2019,87 cases) and a post-stage group (2020–2021,39 cases). The incidence of stillbirth and clinical characteristics were compared between the two groups. The cases were classified into maternal factors, fetal factors, placenta/membrane/umbilical cord factors, and unknown causes, and the clinical characteristics and possible etiologies of different gestational ages and antenatal examination situations were analyzed.

**Result** The overall incidence of stillbirth in the high-altitude area of this study was 2.36%, with 2.07% in the pre-stage group and 3.43% in the post-stage group. There were significant differences between the two groups in gestational age and antenatal examination situation (P=0.003 and 0.008). The main causes of stillbirth were maternal factors (45.28%), followed by placenta/membrane and umbilical cord factors (28.30%), unknown causes (17.61%), and fetal factors (8.81%). The main causes of stillbirth include hypertensive disorder complicating pregnancy, premature rupture of membranes, severe anemia, and fetal malformatiohypertensive disorder complicating pregnancyns.

**Conclusion** This study provides new insights into the prevention and management of stillbirths in high-altitude areas, particularly in terms of maternal factors such as gestational hypertension and severe anemia, by analyzing the clinical characteristics and influencing factors of 126 cases of stillbirths in high-altitude areas. Therefore, this study suggests strengthening prenatal and antenatal health care management to reduce the risk of stillbirth, improve pregnancy outcomes, and promote maternal and child health.

Keywords High-altitude area, Stillbirth, Gestational age, Maternal factors, Obstetric care

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### Introduction

Maternal and child health serves as a crucial indicator for assessing the level as healthcare for mothers and children, obstetric quality, and the comprehensive strength of a country or region. In recent years, significant progress has been made in modern midwifery methods, anesthesia techniques, and neonatal care, leading to a substantial reduction in maternal and neonatal mortality rates. Although these mortality rates have decreased significantly the incidence of stillbirth - a keyindicator of obstetric quality - has not seen a marked decline. Stillbirth refers to the death of a fetus in the uterus after 20 weeks of pregnancy and is one of the most severe complications during pregnancy [1]. Reports indicate that there are approximately 2 million stillbirths worldwide each year, with an average incidence rate of 0.14% [2]. The occurrence of stillbirth profoundly affects both the mother and her family. Mothers who suffer a stillbirth not only endure considerable psychological stress but also face an elevated risk of mental health problems such as depression, anxiety, postpartum traumatic stress disorder, and somatization disorders [3]. These psychological issues impact the mother's personal health and also inflict immense grief and psychological trauma to her family.

Currently, China's population policy has shifted from controlling population size to improving the overall quality of the population. Eugenics and child rearing have been officially incorporated into the country's medium and long-term development plan as key measures to enhance population quality. With the gradual relaxation of China's two-child policy, and even the introduction of a three-child policy, a slight increase in the number of births is anticipated. In this context, it is crucial to investigate and address how to achieve eugenics and reduce the incidence of adverse pregnancy outcomes, such as stillbirths. Stillbirth, one of the adverse pregnancy outcomes, is highly unpredictable. In most cases, there are no obvious signs before it occurs, and the cause is often difficult to fully explain [4]. Considering the significant harm that stillbirth causes to mothers, families, and society, conducting a thorough analysis of its clinical characteristics and influencing factors is of great importance in preventing stillbirth and improving pregnancy health outcomes.

Current research suggests that certain environmental factors may increase the risk of intrauterine growth restriction and negative outcomes during pregnancy [5]. The unique geographical and climatic conditions in high-altitude regions, such as low oxygen environments and high altitudes, can adversely affect the health of pregnant women and their fetuses [6]. Additionally, due to the uneven distribution of medical resources and inconvenient transportation, pregnant women in high-altitude areas may face challenges in accessing timely and high-quality prenatal care, which can impact the occurrence of stillbirths. Therefore, it is crucial and urgent to conduct comprehensive research on the clinical characteristics and influencing factors of stillbirths in high-altitude areas. Firstly, this will enhance our understanding of the specific risk factors for stillbirth in highaltitude environments, enabling us to provide more precise medical interventions for pregnant women. Secondly, the research findings can guide the improvement of local medical services, optimize the allocation of medical resources, enhance the quality of medical care, and ensure that pregnant women receive necessary prenatal and delivery care. Increasing awareness among pregnant women about the risk of stillbirth and promoting the adoption of a healthy lifestyle are also effective ways to reduce the incidence of stillbirth. Studying stillbirths in high-altitude areas can contribute to the develop ment of targeted preventive measures, such as strengthening prenatal monitoring and improving the nutritional status of pregnant women. This holds significant practical importance in improving the health of pregnant women and newborns and achieving eugenics and child rearing goals. Futhermore, the research results can aerve as a scientific basis for policy-making, encouraging government and health departments to increase investment and support for maternal and child health services in high-altitude areas, and promoting regional health equity.

Taken together, this study aimed to examine the clinical characteristics of stillbirths in high-altitude areas to provide a strategy with a more scientific and reasonable basis for the prevention and treatment of stillbirths in the high-altitude areas of China.

### **Data and methods**

### **Research object**

Retrospective collection of clinical data on 126 cases of stillbirths terminated during hospitalization at Linzhi People's Hospital from January 2015 to December 2021 (a total of 5334 pregnant women). The 126 stillbirths were divided into a pre stage group (n = 87, a total of 4198 fetuses terminated during hospitalization at our hospital from January 2015 to December 2019) and a post stage group (n=39), a total of 1136 fetuses terminated during hospitalization at our hospital from January 2020 to December 2021) according to the year of occurrence. From the end of 2019 to the beginning of 2020, the global COVID-19 has occurred, which may have an impact on the medical care and delivery results of pregnant women. Therefore, the pre and post COVID-19 is taken as the basis for dividing the pre and post stages. This study was approved by the Ethics Committee of Linzhi People's Hospital (2024-30). Due to the retrospective design of the study, the data were anonymized and collected from

existing records, the need for consent to participate was not required. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria: (1) Complies with the 2020 American College of Obstetricians and Gynecologists (ACOG) stillbirth management expert consensus diagnostic criteria for stillbirths [7]: intrauterine stillbirths at  $\geq$  20 weeks of gestation, or stillbirths at an inauspicious gestational age with a birth weight of  $\geq$  350 g; (2) The clinical data is complete.

Exclusion criteria: (1) Embryonic arrest during pregnancy; (2) Those who induce labor due to severe fetal malformation or premature rupture of membranes that cannot survive.

### **Observation indicators**

The collected indicators mainly include maternal age, gestational age, occupation, parity, gestational age, number of fetuses, antenatal examination results, location of stillbirth, history of stillbirth, history of miscarriage, maternal complications or complications, fetal condition, umbilical cord condition, placenta and fetal membrane condition, etc.

### Statistical analysis

SPSS 27.0 was used to process the data. The measurement data follows a normal distribution and is described using (mean and standard deviation), and analyzed using a two independent sample t-test; The median and interquartile range [M ( $P_{25}$ ,  $P_{75}$ )] are used to describe non normal distribution, and the Mann Whitney U test is used to test the sum of two independent sample ranks; Count data usage rate (%) is expressed using chi square test. *P*<0.05 indicates that the difference is statistically significant.

### Results

# The incidence of pregnant women and stillbirths admitted to our hospital

From January 2015 to December 2021, our hospital treated a total of 5334 pregnant women. The number of cases treated in each year is shown in Fig. 1. Out of 5334 postpartum women, 126 had stillbirths, accounting for 2.36% (126/5334); Among them, the stillbirth rate in the pre-stage group (January 2015 to December 2019) was 2.07% (87/4198), and the stillbirth rate in the later post-group (January 2020 to December 2021) was 3.43% (39/1136).

### General information of stillborn pregnant women

The age range of 126 pregnant women with stillbirths was 16–49 years old, with an average of (29.94±6.25) years old. Comparing the general information of the pre stage group and the post stage group, the results showed that there were significant differences in gestational age and antenatal examination between the two groups of pregnant women (P<0.05), as shown in Table 1.

### Analysis of the causes of stillbirth

Among the 126 cases of stillbirth, 33 cases involved two or more factors is shown in Fig. 2. The main causes of stillbirth are maternal factors (45.28%), placental/fetal membrane and umbilical cord factors (28.30%), unknown causes (17.61%), and fetal factors (8.81%). Among maternal factors, hypertension is the most common (61.11%), followed by severe anemia (19.44%). Among placental/ fetal membrane and umbilical cord factors, placental abruption has the highest proportion (68.89%). Fetal factors are mainly malformation (64.29%). The top five high-risk factors include hypertension (27.67%), placental abruption (19.50%), unknown cause (17.61%), severe anemia (8.81%), and fetal malformation (5.66%). Compared



### Number of pregnancies in different years

Index	Total (n = 126)	Pre-stage group (n = 87)	Post-stage group (n = 39)	t/χ²/U	Р
Age (years)	29.94±6.25	$29.37 \pm 6.24$	31.21±6.19	1.533	0.128
Pregnancy times (times)	$2.41 \pm 1.33$	$2.38 \pm 1.41$	$2.49 \pm 1.14$	0.420	0.675
Delivery times (times)	1.00(0.00,2.00)	1.00(0.00,2.00)	1.00(0.00,2.00)	1.481	0139
Gestational age (weeks)				11.400	0.003
20~27 <sup>+6</sup>	36(28.57)	17(19.54)	19(48.72)		
28~36 <sup>+6</sup>	50(39.68)	38(43.68)	12(30.77)		
>37	40(31.75)	32(36.78)	8(20.51)		
Location of occurrence				0.104	0.747
In the hospital	30(23.81)	20(22.99)	10(25.64)		
Outside the hospital	96(76.19)	67(77.01)	29(74.36)		
Prenatal examination statusuc				9.630	0.008
Regular	20(15.88)	16(18.39)	4(10.26)		
Irregular	31(24.60)	27(31.04)	4(10.26)		
No production inspection	75(59.52)	44(50.57)	31(79.49)		
History of spontaneous abortion				1.361	0.243
Yes	8(6.35)	7(8.05)	1(2.56)		
No	118(93.65)	80(91.95)	38(97.44)		
History of stillbirth				0.602	0.438
Yes	6(4.76)	5(5.75)	1(2.56)		
No	120(95.24)	82(94.25)	38(97.44)		
Abnormal fetal movement				0.227	0.634
Yes	51(40.48)	34(39.08)	17(43.59)		
No	75(59.52)	53(60.92)	22(56.41)		

Table 1 General information of stillborn pregnant women



Fig. 2 Proportion of causes of stillbirth. Note: Placental-cord factors = Placental/fetal membrane and umbilical cord factors

with the pre-stage, the proportion of hypertensive diseases decreased and the proportion of umbilical cord prolapse increased in the post-group, with statistical differences (P < 0.05), as shown in Table 2.

# Distribution of causes of stillbirths at different gestational ages

The distribution of causes of stillbirths at different gestational ages is shown in Fig. 3. The causes of stillbirths at <28 weeks,  $28-36^{+6}$  weeks, and  $\ge 37$  weeks are mainly due to maternal factors, followed by placental, fetal membrane, and umbilical cord factors, with fetal factors accounting for the lowest proportion. There was no statistically significant difference in stillbirth factors among three groups of different gestational ages ( $\chi^2 = 3.284$ , P > 0.05).

## Distribution of causes of stillbirth under different antenatal examination conditions

The distribution of causes of stillbirths under different antenatal examination conditions is shown in Fig. 4. The causes of stillbirths with regular, irregular, and no antenatal examination are mainly due to maternal factors, followed by placental, fetal membrane, and umbilical cord factors, with fetal factors accounting for the lowest proportion. There was no statistically significant difference in the causes of stillbirths among three groups with different antenatal examination conditions ( $\chi^2 = 4.435$ , P > 0.05).

### Discussion

Studying stillbirths in high-altitude areas is crucial for developing preventive measures such as enhancing pregnancy monitoring and improving nutrition, which can help improve maternal and child health and contribute to eugenics. This study analyzed 126 stillbirth cases and found that 45.28% were related to maternal factors, 28.30% to placental/fetal membrane and umbilical cord factors, and 17.61% had unknown causes. The global stillbirth rate target is 12‰ [2], and the 2.36% incidence rate in this study is relatively high, particularly the 3.43% in the later stage, which may be associated with the highaltitude environment and medical conditions. This highlights the unique needs and challenges in preventing stillbirths in high-altitude regions [8]. The rise in the post-stage stillbirth rate may indicate a trend towards

Specific	Total	Pre-stage group	Post-stage group	X	Р
Maternal factors ( $n = 72$ )					
Hypertensive disorder complicating pregnancy	44(61.11)	36(81.82)	8(18.18)	5.159	0.023
Pregnancy complicated with severe anemia	14(19.44)	12(85.71)	2(14.29)	2.047	0.152
Intrahepatic cholestasis of pregnancy	7(9.72)	7(100.00)	0(0.00)	3.323	0.068
Pregnancy complicated with syphilis	1(1.39)	1(100.00)	0(0.00)	0.452	0.501
Pregnancy complicated with hepatitis B	4(5.56)	1(25.00)	3(75.00)	1.852	0.174
Uterine rupture	2(2.78)	1 (50.00)	1(50.00)	0.345	0.557
Fetal factors ( $n = 14$ )					
Fetal malformation	9(64.29)	4(44.44)	5(55.56)	2.745	0.098
Fetal distress not terminated	2(14.29)	2(100.00)	0(0.00)	0.911	0.340
Fetal growth restriction	1(7.14)	0(0.00)	1(100.00)	2.249	0.134
Twin twin transfusion syndrome	1(0.79)	1(100.00)	0(0.00)	0.452	0.501
Mother child blood type incompatibility	1(0.79)	1(100.00)	0(0.00)	0.452	0.501
Placental, fetal membrane, and umbilical cord factors ( $n = 45$ )					
Placental abruption	31(68.89)	23(74.19)	8(25.81)	0.509	0.475
Placenta previa	3(6.67)	1(33.33)	2(66.67)	1.834	0.176
Premature rupture of membranes without amniotic fluid	6(13.33)	3(50.00)	3(50.00)	1.069	0.301
Umbilical cord prolapse	4(8.89)	0(0.00)	4(100.00)	9.216	0.002
Umbilical cord torsion	1(2.22)	0(0.00)	1(100.00)	2.249	0.134
Unknown or other reason ( $n = 28$ )	28(22.22)	18(64.29)	10(35.71)	0.382	0.537





Fig. 3 Distribution of causes of stillbirths at different gestational ages. Note: Placental-cord factors = Placental/fetal membrane and umbilical cord factors



Fig. 4 Distribution of causes of stillbirth in different antenatal examination situations

centralized treatment for critically ill patients, revealing disparities in the allocation of medical resources and the need for early intervention. Subsequently, based on these findings, this study will divide the study subjects into prestage and post-stage groups, and further explore the specific clinical characteristics of stillbirths in high-altitude areas and strategies to reduce their incidence through targeted interventions.

Related studies have demonstrated that the occurrence of stillbirth is associated with maternal factors, including age, gestational age, parity, and a history of miscarriage and stillbirth, which are more prevalent [9-11]. Clinically, it is believed that the optimal reproductive period for women is before the age of 35, and after the age of 35, it is considered advanced maternal age [12]. As age increases, the quality of eggs may gradually decline, potentially leading to abnormal development of fertilized eggs or embryos, and thereby increasing the risk of stillbirth. Hogue et al. [13] noted that the risk of stillbirth is higher for parents with one or both unemployed, which may be associated with factors such asfinancial pressure, mental stress, and living environment. Additionally, studies have shown that the stillbirth rate at 42 weeks is significantly higher than at 37 weeks [14]. Furthermore, this study found significant differences in gestational age and prenatal check ups between the pre-stage group and the post-stage group, with the post-stage group exhibiting a shorter gestational age and a higher proportion of no prenatal check ups compared to the pre-stage group. This may be related to genetic, environmental, and socio-economic factors. It is evident that the occurrence of stillbirth may be influenced by a variety of factors.

The main causes of stillbirth include maternal factors, fetal factors, placenta issues, fetal membranes, and the umbilical cord, with each factor capable of acting alone or in combination. Approximately 50% of stillbirths are caused by intrauterine hypoxia, and maternal factors such as gestational hypertension, anemia, cholestasis, and syphilis – are among the important causes of fetal hypoxia [15]. The primary maternal factors contributing to stillbirth are gestational hypertension, which can cause uterine artery spasm, leading to placental dysfunction, fetal ischemia and hypoxia, ultimately resulting in fetal death in the uterus [16, 17]. In this study, the leading cause of stillbirth was maternal factors (accounting for 45.28%), with gestational hypertension being the main high-risk factor, aligning with previous research findings. Fetal factors, including genetic issues, chromosomal abnormalities, structural anomalies and metabolic diseases may also lead to stillbirth [18]. Korteweg et al. [19] discovered that fetal malformation is a significant factor in stillbirth, with an incidence rate exceeding 10%. The rate of chromosomal aberrations in cases without visible malformations is 4.6%. Some autosomal recessive abnormalities are closely associated with to adverse pregnancy outcomes, such as spontaneous abortion, stillbirth, and intrauterine growth restriction [20]. In this study, there were 14 cases (8.81%) of fetal stillbirths due to fetal factors, with fetal malformation being the primary cause, in agreement with earlier research. Darouich et al. [21] found that placental abnormalities are also a significant factor in stillbirth. This study identified 31 cases of intrauterine stillbirth caused by placental abruption, accounting for 19.50%. Placental abruption typically has a rapid onset, lacks obvious symptoms, and progresses quickly. When the area of placental abruption exceeds half, it can cause result in death and should be treated with urgency [22].

Fetal membranes and umbilical cord factors are another important factor leading to intrauterine hypoxia in fetuses. Amniotic fluid is a crucial component of the fatus's living environment within the mother's body, playing a vital role in buffering, protecting, and providing nutrition to the fetus [23]. After the premature rupture of membranes, amniotic fluid begins to leak, resulting in a decrease in its volume. When the amniotic fluid volume decreases significantly, the fetus may suffer intrauterine distress or even death due to external pressure or limited mobility. In this study, there were 6 cases of stillbirth caused by premature rupture of membranes without amniotic fluid, accounting for 3.77%. Umbilical cord factors primarily include umbilical cord prolapse and torsion. Stillbirth caused by umbilical cord torsion may result form excessive twisting of the cord, leading to necrosis near the fetal umbilical wheel, causing to vascular occlusion or thrombosis, and resulting in fetal death due to interrupted blood flow [24]. Stillbirth is a catastrophic event, with approximately 20% of cases having no clear cause [25]. These unexplained stillbirths not only cause profound emotional, social, and spiritual distress but may also lead parents to worry about future pregnancies and opt not to reproduce again. In this study, nearly 17.61% of stillbirths had unknown causes of death. Related studies have shown that physical anatomy can determine the cause of 70% of "unexplained stillbirths" [26]. However, due to traditional beliefs of pregnant women, complex procedures, and expensive examination fees, most pregnant women choose to forego such examinations, resulting in extremely low rates of autopsy, fetal tissue chromosome testing, and other diagnostic procedures.

Stormdal's study [27] indicates that the causes of stillbirth differ across various gestational ages. In full-term individuals (before 37 weeks), the primary causes of stillbirth are placental and maternal factors, whereas in full-term individuals (after 37 weeks), the primary causes are infection and umbilical cord factors. The study found that, irrespective of gestational age, maternal factors are the leading cause of stillbirth, followed by placental and umbilical cord factors, with fetal factors being the least prevalent. However, the discrepancies in the causes of stillbirths at different gestational weeks are not statistically significant and may be associated with the small sample size and unique conditions in high-altitude areas. Additionally, the acceptance of prenatal care by pregnant women may differ due to geographical and cultural variations, potentially influencing the significance of stillbirth causes among different gestational age groups. Future research should be carried out in a broader population to more accurately elucidate the relationship between gestational age and stillbirth causes, and further investigate the impact of socio-cultural factors and healthcare services on maternal health. As gestational age advances, the development of the fetus must be closely monitored. Pregnant women in mid pregnancy may face risks such as placental dysfunction, fetal abnormalities, or maternal diseases. Physiological changes during pregnancy, including alterations in the endocrine and immune systems, may also impact the fetus. Therefore, comprehending the causes of stillbirths at different gestational ages is vital for devising, preventive strategies, raising maternal health awareness, and ensuring fetal well-being. Pregnant women should undergo regular prenatal check ups to promptly identify and manage potential risk factors. The results of this study indicate that the primary cause of stillbirth in pregnant women, regardless of whether they have regular, irregular, or no prenatal check ups is maternal factors. This is followed by placental and umbilical cord issues, with fetal factors being the least common. Multiple studies have also demonstrated that increasing the frequency of prenatal check ups is associated with a reduced the risk of premature birth, stillbirth, and neonatal mortality [28-30]. Regular prenatal check ups, including ultrasound and blood tests, enable doctors to detect and manage risks such as fetal abnormalities and chronic diseases in pregnant women at an early stage, which is vital for preventing stillbirth. Some pregnant women may not undergo timely or comprehensive prenatal check ups, potentially leading to overlooked risks. Therefore, emphasizing the importance of prenatal check-ups and ensuring that they are both timely and comprehensive is essential for safeguarding maternal and infant health.

### Conclusion

This study analyzed 126 cases of stillbirths in high-altitude areas and found that they were mainly related to maternal factors such as gestational hypertension and anemia, and some of the causes were unknown. The results emphasize the importance of pre pregnancy and prenatal care, as maternal factors are the main cause of stillbirth regardless of gestational age and antenatal examination status. The study provides a scientific basis for prevention strategies and suggests reducing the risk of stillbirth, improving pregnancy outcomes, and promoting maternal and child health by improving pregnancy monitoring, optimizing resource allocation, and enhancing self-management abilities of pregnant women.

### **Research limitations**

This study proposes prevention strategies such as strengthening prenatal monitoring and improving nutrition for stillbirths in high-altitude areas. However, research has certain limitations. Firstly, the data source of this study mainly relies on hospital records. Although the annual reports of maternal and child health collected by various levels of maternal and child health institutions provide a certain range of statistical information on stillbirths and perinatal infants, there may be underreporting of these data, which affects the accuracy of stillbirth incidence. Furthermore, the limitation of the study is that critically ill pregnant women tend to concentrate at the municipal people's hospital for delivery in the post-stage, which may lead to a higher statistical rate of stillbirth in the post-stage. This referral model may reflect the uneven allocation of medical resources and the need for early identification and intervention of risk factors for stillbirth. In addition, due to limitations in data sources, this study may not fully reflect the latest trends in stillbirth rates (2022-2025). Therefore, we suggest including more years of data in subsequent studies to more accurately assess changes in stillbirth rates and their related factors.

### Acknowledgements

Not applicable.

#### Author contributions

YBH: Conceived and designed the research, conducted experiments, and analyzed data. Drafted and revised the manuscript critically for important intellectual content. WJF, XXX: Contributed to the acquisition, analysis, and interpretation of data. Provided substantial intellectual input during the drafting and revision of the manuscript. DHY: Participated in the conception and design of the study. Played a key role in data interpretation and manuscript preparation. All authors have read and approved the final version of the manuscript.

#### Funding

Not applicable.

#### Data availability

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

### Declarations

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of Linzhi People's Hospital (2024-30). Due to the retrospective design of the study, the data were anonymized and collected from existing records, the need for consent to participate was not required. This study was conducted in accordance with the principles of the Declaration of Helsinki.

### **Consent for publication**

The manuscript has neither been previously published nor is under consideration by any other journal. The authors have all approved the content of the paper.

### **Competing interests**

The authors declare no competing interests.

Received: 13 August 2024 / Accepted: 29 April 2025 Published online: 16 May 2025

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