

2009-2019: A comparative study on CMS of plateau migrants around ten years

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Research

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Abstract

Background

Chronic mountain sickness (CMS), is a common disease occurred to people who migrate to plateau. Current CMS studies in different periods or areas have poor comparability due to the inconsistent diagnosis methods. Here we carried out a comparative study of the CMS prevalence in the year 2019 and 2009, to provide evidence for the prevention and diagnosis of CMS.

Methods

The Qinghai CMS Scoring System (Qinghai standard) was used to investigate the subjects who lived for at least months in the 3300-5400 m altitude area in 2019 and 2009, respectively. Their prevalence and symptom scores were also analyzed and statistically compared.

Results

The prevalence of CMS in 2019 survey subjects (15.60%) was significantly lower than that in 2009 (31.18%). The prevalence of dyspnea, venous dilatation, paresthesia, headache, tinnitus, and hemoglobin concentration reached 21g/dL or above decreased significantly among the survey subjects in 2019. The scores of cyanosis, venous dilatation, paresthesia, and headache significantly decreased in the 2019 survey subjects. But among the CMS patients, the sleep disturbance scores of the 2019 survey subjects increased significantly.

Conclusion

Compared to 2009, the health level of high altitude living population in 2019 has been significantly improved, indicating that the sleep research on high-altitude living population and the application of high altitude oxygen therapy has been effective in the past ten years. Among the CMS associated symptoms, sleep disturbance is an important indicator for the prevention and diagnosis of CMS, which deserves special attention.

Background

Chronic mountain sickness (CMS) is a disease that usually occurred in unacclimatized persons who live in areas above 2500 m for a long time. Typical symptoms of CMS include polycythemia, hypoxemia, breathlessness, palpitation, sleep disturbance, cyanosis, venous dilatation, headaches, tinnitus, and dizziness.

CMS survey is an important way to acknowledge the prevalence. However, studies in different periods or areas could not be compared properly due to the varied CMS diagnosis methods[1-4]. In this study, we used Qinghai standard to survey the prevalence of CMS in Chinese Han individuals who migrated to Qinghai-Tibetan plateau at an altitude of 3300-5400 m in 2009 and 2019. The same CMS diagnosis

standard applied to the ten years apart surveys made the reasonable comparison be possible. Characteristics of prevalence in both 2009 and 2019 were analyzed and the differences between these two results were compared more accurately owe to the application of the same standard. Besides, CMS diagnose criteria was also discussed.

Methods

Participants

The survey subjects were all male volunteers recruited from areas with an altitude of 3300-5400 m and totally 218 and 510 volunteers were recruited in 2019 and 2009, respectively. These participants lived in low altitude areas before (Anhui, Fujian, Gansu, Guangdong, Guangxi, Guizhou, Hebei, Henan, Hubei, Hunan, Jilin, Jiangsu, Inner Mongolia, Ningxia, Shandong, Shanxi, Shaanxi, Sichuan, Yunnan, Zhejiang and Chongqing provinces of China) and all migrated to the plateau for at least months. The basic information (Table 1) of subjects were obtained through questionnaires. The written informed consent was obtained from all subjects. No health care interventions were involved, and all data were anonymized.

Hb, oxygen saturation, and heart rate measurement

The hemoglobin (Hb) concentration was measured by routine blood test. The finger blood oxygen saturation (SO₂) was measured by a handheld oximeter (TuffSat. GE Healthcare, London, England). The heart rate (HR) and blood pressure (BP) were measured by an electronic blood pressure monitor (HEM-7112. Omron, Kyoto, Japan).

Assessment of CMS

The diagnosis and score calculation of CMS was based on the Qinghai standard. According to the severity, breathlessness/palpitation, sleep disturbance, cyanosis, venous dilatation, paresthesia, headache, and tinnitus were scored (none: 0 points, mild: 1 point, moderate: 2 points, severe: 3 points). Hb was scored by concentration (<21g/dL: 0 points, ≥ 21g/dL: 3 points). Total score was calculated and CMS was defined (no CMS: 0-5 points; mild CMS: 6-10 points, moderate CMS: 11-14 points, severe CMS: ≥15 points).

Data analysis

The CMS prevalence between 2019 and 2009 was compared with the χ^2 test. The score of symptoms were compared with independent-samples *t*-test analysis and the prevalence of each symptom was compared with the χ^2 test between 2019 and 2009. Correlation of Hb with SO₂ was analyzed and the curve fitting analysis was carried out.

Table 1 Baseline characteristics and measurement results

Index	2019	2009
	n=218	n=510
Age (year, x±s)	24.62±4.83	24.07±5.40
Height (cm, x±s)	171.78±4.96	172.09±4.94
Weight (kg, x±s)	64.91±9.47	63.25±7.32*
BMI (kg/m ² , x±s)	21.99±2.67	21.35±2.33**
Altitude (m, x±s)	4214.30±299.62	4253.78±141.60
Altitude time (month, x±s)	54.30±49.26	22.32±32.45**
SBP (mmHg, x±s)	114.40±11.87	123.02±13.53**
DBP (mmHg, x±s)	70.87±11.27	74.18±10.48**
HR (beat/min, x±s)	75.68±11.45	80.75±12.85**
Hb concentration (g/dL, x±s)	19.03±1.90	19.17±1.64
SO ₂ (% , x±s)	89.21±2.96	89.88±2.58**
CMS score (x±s)	2.77±2.90	3.96±3.08**

*p<0.05, **p<0.01

Results

Basic situation of the survey subjects

Totally 218 and 510 participants were involved in the survey in 2019 and 2009, respectively. The average elevation was about 4200 m, and there was no significant difference between the two years. The subjects in 2019 lived longer on the plateau than those in 2009. The BP and HR of subjects in 2019 were significantly lower than those in 2009. There was no significant difference in Hb concentration between the two years, but the SO₂ in 2019 subjects was significantly lower than those in 2009. (Table 1)

Prevalence of CMS

According to the Qinghai standard, among the 218 survey subjects in 2019, 184 of them (84.40%) had no CMS, 29 of them (13.30%) had mild CMS, 4 of them (1.83%) had moderate CMS, and only 1 of them (0.46%) had severe CMS, the total CMS prevalence rate was 15.60%. Among the 510 survey subjects in 2009, 351 of them (68.82%) had no CMS, 144 of them (28.24%) had mild CMS, 12 of them (2.35%) had moderate CMS and 3 of them (0.59%) had severe CMS, the total prevalence of CMS was 31.18% (See Additional file 1 for details). χ^2 test analysis showed that the prevalence of CMS in 2019 was significantly lower than that in 2009 ($\chi^2 = 19.028$, $P = 0.000$).

The prevalence of symptoms

Among the survey subjects in 2019, 93 of them (42.66%) had dyspnea/palpitation, 87 of them (39.91%) had sleep disturbance, and 70 of them (32.11%) had headaches, the prevalence of the above three symptoms ranked in the top three among all the subjects surveyed. The prevalence of venous dilatation was the lowest, which was only 25 people (11.47%). 26 peoples' (11.93%) Hb concentration reached 21g/dL or higher. Among the CMS patients (CMS \geq 6), dyspnea/palpitation, sleep disturbance, and headache are still the main symptoms, but the prevalence of sleep disturbance became the highest. 32 out of 34 CMS patients (94.12%) had sleep disturbance problem in various degrees. And in these 32 people, 18 people suffered from the moderate or severe sleep disturbance, which became the severest symptom. 11 of the CMS patients had Hb concentration of 21g/dL or higher, accounting for 32.35%. (See Additional file 1 for details)

In 2009, dyspnea/palpitation (51.37%), cyanosis (48.63%) and sleep disturbance (47.45%) were the top three symptoms in prevalence, of which the number was 262, 248 and 242, respectively. The amount of people who suffered from headaches was 241 (47.25%), the prevalence of which was just 0.2% less than sleep disturbance. The number of people whose Hb concentration reached 21g/dL or higher was 121 (23.73%). Among the 159 CMS patients, sleep disturbance (84.91%), headache (83.02%) and cyanosis (82.39%) became the top three symptoms in prevalence, and the number of which was 135, 132 and 131, respectively. 43 people had Hb concentration of 21g/dL or higher, accounting for 27.04% of the number of CMS patients. (See Additional file 1 for details)

Symptom score comparison

Statistical analysis showed that the CMS score of the survey subjects in 2019 was significantly lower than that in 2009 (Table 1). For all subjects in the survey, there was no difference in the prevalence of sleep disturbance, but there was significant difference in the prevalence of dyspnea, cyanosis, venous dilatation, paresthesia, headache, and tinnitus. The ratio of Hb concentration 21g/dL or higher was lower in 2019 (See Additional file 1 for details). In addition, there was significant difference in the score of cyanosis ($p=0.000$), venous dilatation ($p=0.006$), paresthesia ($p=0.000$), and headache ($p=0.000$) between the two batches of data, and the scores of which were significantly lower in 2019 than that in 2009 (Figure 1 A-D), while no significant difference was found in the scores of dyspnea/palpitation, sleep disturbance and tinnitus (Figure 1 E-G).

Further analysis of the symptom scores of the CMS patients revealed that there was no significant difference in the prevalence of all symptoms between the two years. In terms of symptom scores, compared to the year 2009, the score of sleep disturbance ($p=0.015$) among the CMS patients surveyed in 2019 were significantly increased (Figure 1 H), while the score of cyanosis ($p=0.016$) were significantly decreased (Figure 1 I).

Correlations between Hb concentration and SO_2

Analysis revealed that SO₂ significant related with Hb concentration. Quadratic curve was identified to be the best fitting curve for the merged Hb and SO₂ results from 2019 and 2009 survey (Table 2). Separate analysis of the Hb-SO₂ correlation in 2019 (R²=0.057, p=0.002, other fitting parameters see additional file 2) or 2009 (R²=0.017, p=0.029, other fitting parameters see additional file 3) were also revealed that quadratic fitting was the best fitting method. (Figure 2)

Table 2 Parameters evaluation of Hb-SO₂ correlation analysis

	R square	F	Significance	Constant	b1	b2	b3
Linear	0.019	12.230	0.001	93.782	-0.215		
Logarithmic	0.017	10.702	0.001	101.228	-3.924		
Inverse	0.014	9.227	0.002	85.980	69.900		
Quadratic	0.033	10.662	0.000	69.648	2.255	-0.063	
Cubic*	0.033	10.755	0.000	84.399	0.000	0.051	-0.002
Compound	0.019	12.179	0.001	93.891	0.998		
Power	0.017	10.656	0.001	102.127	-0.044		
S	0.014	9.189	0.003	4.454	0.789		
Growth	0.019	12.179	0.001	4.542	-0.002		
Exponential	0.019	12.179	0.001	93.891	-0.002		
Logistic	0.019	12.179	0.001	0.011	1.002		

*The cubic model is not applicable due to the approximately liner coincidence

Discussion

Long time exposure to high altitude hypoxia might affect the health of people and cause CMS. In this study, CMS prevalence of people living on plateaus at altitudes of 3300-5400 m was surveyed.

Comparative analysis was carried out with the same standard and the changes of CMS prevalence between the ten-year apart results were presented accurately. The in-depth analysis of CMS relevant influencing factors provided a basis for prevention and diagnosis of CMS.

People's health has improved over the past ten years

In terms of the basic information of the survey respondents, compared to 2009, the average body weight of 2019 subjects was slightly heavier, which might reflect the improvement of living conditions over the past ten years. There was no significant difference in average altitude between the two batches of survey subjects. The survey subjects in 2019 lived on the plateau longer than those in 2009, but the BP and HR

of the 2019 survey subjects were lower. In terms of CMS scores, the 2019 survey results were also significantly lower than those in 2009. The above results indicated that the health of the survey subjects in 2019 was better than that in 2009. In recent years, the health status of the plateau population has attracted more and more attention, and related research has gradually been carried out, especially the sleep study of plateau population[5], diagnosis of altitude sickness[6], oxygen therapy[7], optimization of physical examination indicators[8], et al. These may be an important reason for the significant improvement of the health. The results of the comparison of various symptoms showed that the increase in health attention of the people on plateau had the most obvious impact on cyanosis, venous dilatation, paresthesia and headaches, which significantly improved both in prevalence and severity.

Sleep disturbance may be an important factor in the occurrence of CMS

The survey results in 2019 showed that dyspnea/palpitation, sleep disturbance and headache were the top three symptoms among all survey subjects. However, sleep disturbance became the most severe symptom among the CMS patients. The results indicated that dyspnea/palpitation and headache might be common symptoms caused by hypoxia, but sleep disturbance played a more important role in the occurrence of CMS. And this was consistent with the survey results in 2009. Decreased sleep quality caused by long-term sleep disturbance would make the body not get sufficiently rest, which reduced the physical function, and then CMS was more likely to occur. It is worth mentioning that there is no significant difference in both severity or prevalence of sleep disturbance among the survey subjects, indicating that sleep disturbance might be more stable than the other symptoms in Qinghai standard. But at the same time, among the CMS patients, compared with 2009, the sleep disturbance scores of the CMS patients in 2019 were higher, which indicated that it was more serious. The above results suggested that sleep disturbance should be paid more attention to in the prevention and diagnosis of CMS. For the plateau residents, improvement of the sleep disturbance might be a prospective way to reduce the CMS prevalence.

Advice on CMS diagnosis

The Qinghai standard used in this survey scored the subjects according to the impression of the corresponding symptom severity in the CMS scale by the survey subjects themselves. Although there was a ten-year long time between the two survey results, dyspnea/palpitation, sleep disturbance and headache all showed high prevalence in both results, suggesting the consistency of the trend of CMS-related symptoms. But at the same time, the score of cyanosis differed greatly between the two survey results. The results showed that there was no significant difference between the two batches of data in terms of Hb concentration. However, the blood oxygen saturation value of the 2009 survey object is slightly higher than that in 2019, but the severity of the cyanosis score shown in the 2009 survey result was significantly higher. We speculated that this might had a certain relation with the cyanosis evaluation standard. The cyanosis score was judged by the color of the fingernail and lips of the survey subjects. It was more intuitive than indicators such as headache and dyspnea, but it was also easier to make an overall difference by corresponding the same color depth to different scores. Therefore, a color

comparison reference based on the relation between the hypoxia severity and cyanosis might be a way to avoid the overall difference in cyanosis scoring.

Analysis revealed that quadratic fitting was the best fitting method to describe the correlation of Hb concentration and SO_2 (Table 2). Whether the data in 2019 and 2009 were merged or not, the fitting curve was always a parabola with negative quadratic coefficients (Fig. 2), indicating that as the Hb concentration increased, the SO_2 showed a trend of increasing first and then decreasing. When lived in hypoxic environment for a long time, the body would generate more erythrocyte and Hb to meet the oxygen demand and the SO_2 could be increased. However, if the low environmental partial pressure of oxygen couldn't meet the need of the body, the persistent chronic hypoxia of the body would happen, then may cause further increase in erythrocyte and Hb. As a result, more and more Hb would be generated but not fully oxygenated. According to the fitting curve, the SO_2 level began to decrease when Hb concentration was lower than 21 g/dL, which mean that the body entered the decompensation period before the Hb concentration reached 21 g/dL. These results suggested that the diagnosis standard of Hb concentration might need to be adjusted to a lower value than 21 g/dL, but the new exactly judgement threshold need further study to determine.

Limitations

There were some limitations in this study. Participants in this study were all young male and whether the conclusions were available for female or older population was not sure. Besides, drinking and smoking, which might have effect on the body, were not considered in this study.

Conclusion

Long time plateau living makes people face with CMS, which could cause serious damage to the health. In-depth study of the occurrence and development of CMS is very important for CMS prevention and diagnosis. According to the analysis of the ten-year apart CMS surveys, prevalence of CMS has been found decreased compared to ten years ago, and sleep disturbance, which revealed to be closely related to CMS, might be an important symptom and need to be taken seriously. Besides, the CMS diagnosis standard should also be discussed.

Abbreviations

BMI: Body mass index; CMS: Chronic mountain sickness; DBP: Diastolic blood pressure; Hb: Hemoglobin; HR: Heart rate; SBP: Systolic blood pressure; SO_2 : Oxygen saturation of hemoglobin

Declarations

Acknowledgments

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Authors' contributions

ZQG, SWX, WJH, JY and DWC collected the CMS data. ZQG and WXG performed the statistical analysis. BN, YQG, WJH and DWC were responsible for the design and instruction. ZQG wrote the draft of the manuscript and the other authors contributed to the manuscript editing.

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Availability of data and materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The written informed consent was obtained from all subjects. No health care interventions were involved, and all data were anonymized.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Pei, SX, et al. *Chronic mountain sickness in Tibet*. Q J Med. 1989. 71(266): p. 555-74.
2. Kong, FY, Li, Q, and Liu, SX. *Poor sleep quality predicts decreased cognitive function independently of chronic mountain sickness score in young soldiers with polycythemia stationed in Tibet*. High Alt Med Biol. 2011. 12(3): p. 237-42.
3. Simpson, LL, et al. *Global REACH 2018: Andean highlanders, chronic mountain sickness and the integrative regulation of resting blood pressure*. Exp Physiol. 2020.
4. Hancoo, I, et al. *Excessive Erythrocytosis and Chronic Mountain Sickness in Dwellers of the Highest City in the World*. Front Physiol. 2020. 11: p. 773.

5. Linlin, Z, et al. *Studies on sleep status of plateau garrison troops and chronic mountain sickness: A correlation analysis*. Medical Journal of Chinese People's Liberation Army. 2017. 42(06): p. 553-558.
6. Wenxiang, G and Yuqi, G. *Advances in classification, diagnosis and therapy of chronic high altitude disease*. Journal of Third Military Medical University. 2016. 38(05): p. 431-436.
7. Feng, B, et al. *Intermittent Oxygen Inhalation with Proper Frequency Improves Overall Health Conditions and Alleviates Symptoms in a Population at High Risk of Chronic Mountain Sickness with Severe Symptoms*. Chin Med J (Engl). 2016. 129(11): p. 1322-9.
8. Ru, L, Shiwei, M, and Hang, C. *Research Progress on the Relationship between Physical Examination Index and Body Damage of Chronic Altitude Disease*. Railway Energy Saving & Environmental Protection & Occupational Safety and Health. 2018. 8(03): p. 150-154.

Figures

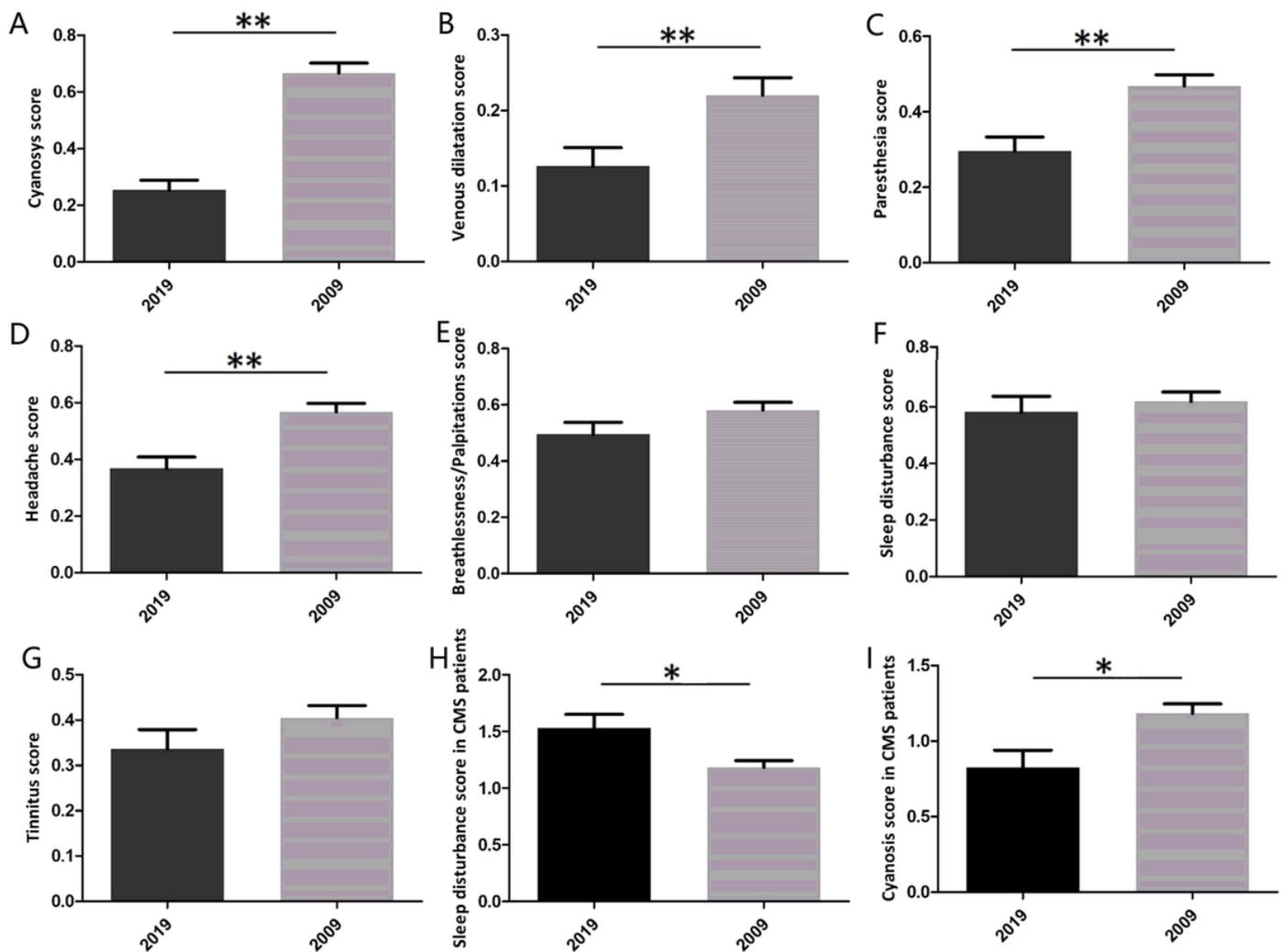


Figure 1

Symptom scores A. Cyanosis score in all subjects B. Venous dilatation score in all subjects C. Paresthesia score in all subjects D. Headache score in all subjects E. Breathlessness/Palpitations score in all subjects F. Sleep disturbance score in all subjects G. Tinnitus score in all subjects H. Sleep disturbance score in CMS patients I. Cyanosis score in CMS patients

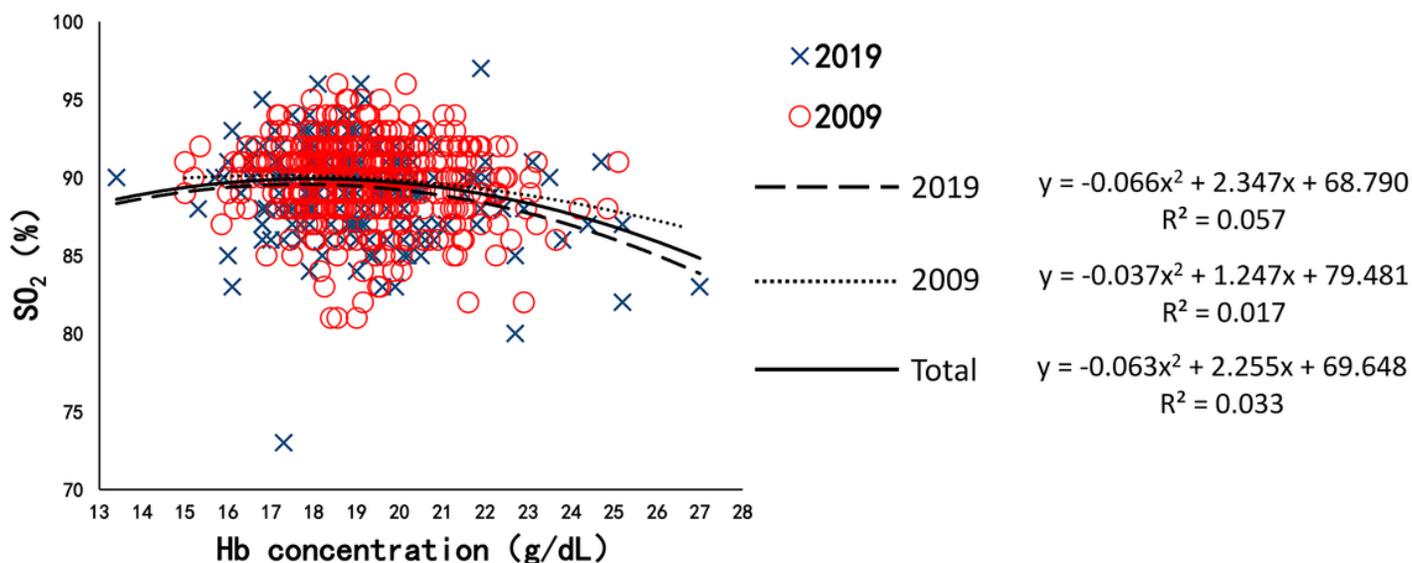


Figure 2

Curve fitting analysis of Hb concentration and SO₂

Supplementary Files

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- [Additionalfile1CMSscoressummary.xlsx](#)
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