

# Situs Inversus: A Review of 191 Published Cases

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## Abstract

**Background:** Situs inversus is a rare congenital disorder that causes a reversal in the anatomical arrangement of chest and abdominal organs, such that the organs are mirror images of the normal anatomy. It is generally classified into three: situs inversus totalis, situs abdominis (with levocardia), and situs ambiguous. Although many patients with situs inversus do go on to live normal uneventful lives, several cardiovascular, gastrointestinal as well multisystemic comorbidities have been shown to be associated with the condition. The aim of the study is to analyse and give an overview of the proportion of the different types of situs inversus and the common major comorbidities at presentation (both acquired and congenital) including the age and sex predilection, as well as the proportion of the different diagnostic methods for situs inversus. **Method:** Published cases from English medical journals were evaluated and analysed. **Results:** 191 published cases on situs inversus were reviewed. Situs inversus totalis had the highest proportion (82.7%) compared to situs ambiguous (13.6%) and situs inversus abdominis (with levocardia) (3.7%). There was no sex predilection, with a male to female ratio of 0.96 ( $P = 0.83$ ). According to our study, the commonest comorbidity patients with situs inversus presented with were cholelithiasis (13.6%) and Kartagener syndrome (9.4%). Presenting comorbidities with digestive system affectation had the highest proportion (57.1%). **Conclusion:** The study established a significant association between acquired digestive system comorbidities like cholelithiasis, compared to other comorbidities.

## Keywords

Situs Inversus, Dextrocardia, Comorbidity

## 1. Introduction

Situs inversus is a rare congenital anomaly that causes a reversal in the anatomi-

cal arrangement of visceral organs like the heart, as well as the liver, spleen and other organs [1]. The incidence is about 1 in 10,000 [2]. Most affected individuals go on to live an uneventful life, however, the commonly associated anomalies with situs inversus are gastro-intestinal and cardiovascular [1] [3].

Situs inversus could be classified into situs inversus totalis, where the abdominal organs are mirror images of the normal anatomy, as well as dextrocardia [4]. Also, situs inversus with levocardia, where the base-to-apex axis points to the left while the abdominal viscera are reversed [4]. Then, there is situs ambiguous. In these patients, the liver may be midline, asplenia or polysplenia, unclear cardiac morphology, or mal-rotated gut [4]. Basically, the features of situs ambiguous are inconsistent and would need a thorough evaluation [5]. Compared to the other types, situs inversus totalis is the commonest [6].

Situs inversus has been shown to occur in association with other conditions such as Kartegener syndrome or primary ciliary dyskinesia [1]. Other conditions that situs inversus may occur with include: duodenal atresia, biliary atresia, gastrochisis with malrotation, congenital coronary abnormalities, ventricular septal defect, transposition of the great arteries, etc. [5] [7].

Many forms of imaging techniques like radiography, ultrasound, CT scan and MRI are useful in the diagnosis of situs inversus. However, CT scanning is usually the preferred examination, especially for situs inversus totalis [8] [9].

Here, we review and analyse 191 published cases of situs inversus retrieved from PubMed and Google Scholar databases.

## Objectives

- 1) To compare the prevalence of the different types of situs inversus.
- 2) To determine the distribution of situs inversus across sex (male and female), age group and race (African and non-African).
- 3) To determine the predominant presenting comorbidities and affected systems associated with situs inversus.
- 4) To determine associations between age category and affected systems.
- 5) To determine the investigation method of choice commonly requested for situs inversus.

## 2. Materials and Methods

We reviewed 191 published case reports of situs inversus retrieved from PubMed and Google Scholar databases. The selection criteria included any published case of situs inversus confirmed on radiological investigations, irrespective of the presenting complaints.

The variables that were investigated include:

- Types of situs inversus.
- Age, sex, and race, in relation to situs inversus.
- Comorbidities associated with situs inversus.
- Comorbid systems associated with situs inversus.

- Age, in relation to the comorbid systems associated with situs inversus.
- Prevalent diagnostic methods for situs inversus.

For the purpose of our study, the condition was classified into three: situs inversus totalis (SIT), situs inversus abdominis (with levocardia) and situs ambiguous. SIT, when both the abdominal and chest organs were mirror images of the normal anatomy. Situs abdominis, when there was isolated reversal of just the abdominal organs, and situs ambiguous for visceral arrangement that is not normal but it does not fall into SIT and situs abdominis (with levocardia).

The major presenting co-morbidity associated with each case report were noted. Co-morbidities were also classified based on the systems affected: cardiovascular, respiratory, digestive, genito-urinary, skeletal, and multi-systemic (when a particular co-morbidity affected more than one system at a time).

We classified race as African and non-African. For the purpose of this study, we assumed a case to be African if it was published by an African author, and non-African, if it was published by a non-African author.

Statistical analysis was done using IBM SPSS version 26 and Chi-square test of independence as well as Goodness of Fit test was used to evaluate the level of significance (P-value).

### 3. Results

A total of 191 cases of situs inversus was reviewed: SIT (n = 158, 82.7%), Situs abdominalis (n = 7, 3.7%), and situs ambiguous (n = 26, 13.6%). It showed that the majority of cases had SIT (P < 0.001). See **Table 1**.

The study showed no sex predilection in situs inversus, with male: female ratio of 0.96 (P = 0.83). However, the majority of patients (n= 183, 95.8%) were non-African. The commonest age category at presentation with situs inversus was 19 to 45 years and 46 to 65 years at 28.8% and 29.8%, respectively. See **Table 2**.

**Table 3** shows that patient with situs inversus majorly presented with cholelithiasis (n = 26, 13.6%), followed by Kartagener syndrome (n = 18, 9.4%). Other common comorbidities include: colon cancer (n = 11, 5.8%), gastric cancer (n = 10, 5.2%), biliary atresia (n = 9, 4.7%) and ischemic heart disease (n = 9, 4.7%). 3.7% of patients who came in for routine medical check-up did not have any comorbidities. Others represent conditions whose occurrence happened only once, example: renal parenchymal disease, adrenal tumour, VACTERL, etc.

**Table 1.** Types of situs inversus.

	Frequency	Percent
Situs inversus Totalis (SIT)	158	82.7
Situs ambiguous	26	13.6
Situs inversus (abdominalis) with levocardia	7	3.7
Total	191	100.0

P < 0.001.

**Table 2.** Distribution by sex, age and race.

Variables	Frequency	percent	P value
Sex of patients	Female	97	50.8%
	Male	94	49.2%
	Total	191	100.0%
Race of patients	Non-African	183	95.8%
	African	8	4.2%
	Total	191	100.0%
Age category	0 - 5 years	28	14.7%
	6 - 18 years	13	6.8%
	19 - 45 years	55	28.8%
	46 - 65 years	57	29.8%
	66 years and above	38	19.9%
	Total	191	100.0%

**Table 3.** Presenting comorbidities.

	Frequency	Percent
Cholelithiases	26	13.6
Kartagener syndrome	18	9.4
Colon Ca	11	5.8
Gastric Ca	10	5.2
Biliary atresia	9	4.7
Ischaemic Heart Disease	9	4.7
Liver Cirrhosis	7	3.7
Routine Medical Check	7	3.7
Lung Ca	5	2.6
Hepatic Ca	5	2.6
Atrial fibrillation	5	2.6
Transposition of Great Arteries	5	2.6
Duodenal atresia	4	2.1
Acute appendicitis	4	2.1
Biliary Ca	3	1.6
Pancreatic Ca	2	1.0
Midgut Volvulus	2	1.0
Renal Ca	2	1.0
Tetralogy of Fallot	2	1.0
Primary Ciliary Dyskinesia	2	1.0
Levocardia	2	1.0

**Continued**

Atrial septal defect	2	1.0
Intussusception	2	1.0
Supraventricular tachycardia	2	1.0
Heart block	2	1.0
Valvular heart disease	2	1.0
Others	41	22.0
Total	191	100.0

The comorbidities patients with situs inversus presented with were classified further under seven sub-categories, each representing the systems affected. The digestive system (n = 107, 57.1%) had the highest proportion, followed by the cardiovascular system (n = 37, 20.1%). 13.6% of patients had comorbidities with multi-systemic affection. See **Table 4**.

The relationship between affected systems and age category at presentation is shown in **Table 5**. Comorbidities with cardiovascular (n = 11, 29.7%), as well as multi-systemic affection (n = 12, 48.0%) had the most cases between 19 to 45 years, compared to other age categories. Patients within the age category 46 to 65 years presented more with comorbidities affecting the digestive system (n = 36, 34.3%) compared to other systems. Overall, it does appear that most hospital presentation for patients with situs inversus did occur between the ages 46 to 65 years. However, statistical test showed no significant association between affected systems and age category (P = 0.36).

Abdominal CT scan (n = 119, 36.5%) was the most preferred investigative technique of choice for the diagnosis of situs inversus, followed by Chest X-ray (n = 68, 20.9%), and then abdominal ultrasound scan (n = 46, 14.1%). See **Table 6**.

#### 4. Discussion

The findings in our review did show that situs inversus totalis (SIT) is significantly more common (82.7%) compared to situs inversus with levocardia (3.7%) and situs ambiguous (13.6%). Quite a number of authors have also shown SIT to be more prevalent compared to the other types [4] [10]. Although the incidence of SIT varies across different authors [11], a study did put it at 1 in 8000 compared to situs inversus with levocardia, which is less common and has an incidence of 1 in 22,000 births [4].

While there may be gender variations, depending on the comorbidities associated with situs inversus, generally, there are no statistically significant gender predilection to situs inversus [5] [12] [13] [14]. Chen W. *et al.* and Akbulut S. *et al.* reported the proportion of males at 52.8% and 53.8% [12] [13], respectively, whereas our study showed the proportion of males at 49.2%.

Lopez KN *et al.* in their study about racial disparity in heterotaxy suggests an association between situs inversus and race/ethnicity [14].

**Table 4.** Systems affected.

	n (%)
Digestive	105 (57.1)
Cardiovascular	37 (20.1)
Multisystems	25 (13.6)
Respiratory	7 (3.8)
Genito-urinary	5 (2.7)
Central nervous	3 (1.6)
Skeletal	2 (1.1)
Total	184 (100)

**Table 5.** Relationship between systems affected and age category.

Systems affected	Age category				
	0 - 5 years	6 - 18 years	19 - 45 years	46 - 65 years	66 years and above
Cardiovascular n, (%)	5 (13.5%)	2 (5.4%)	11 (29.7%)	10 (27.0)	9 (24.3)
Respiratory n, (%)	0 (0.0)	1 (14.3)	2 (28.6)	2 (28.6)	2 (28.6)
Digestive n, (%)	17 (16.2)	4 (3.8)	24 (22.9)	36 (34.3)	24 (22.9)
Genito-urinary n, (%)	1 (20.0)	1 (20.0)	1 (20.0)	1 (20.0)	1 (20.0)
Central nervous n, (%)	0 (0.0)	0 (0.0)	2 (66.7)	1 (33.3)	0 (0.0)
Skeletal n, (%)	0 (0.0)	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)
Multisystems	4 (16.0)	2 (8.0)	12 (48.0)	6 (24.0)	1 (4.0)
Total n, (%)	27 (14.7)	11 (6.0)	52 (28.3)	56 (30.4)	38 (20.7)

P = 0.363.

**Table 6.** investigation of choice *in situs*.

	n (%)
Abdominal CT scan	119 (36.5)
Abdominal Ultrasound	46 (14.1)
Chest X-ray	68 (20.9)
Magnetic Resonance Imaging	21 (6.4)
Echocardiography	20 (6.1)

**Continued**

Electrocardiogram	31 (9.5)
Exploratory laparotomy	5 (1.5)
GI contrast study	1 (0.3)
Abdominal X-ray	6 (1.8)
Chest CT scan	9 (2.8)
Total	326 (100)

Most individuals with situs inversus can live a normal life without symptoms or disability [1]. However, there are a lot of comorbidities of varying frequency associated with situs inversus [1]-[15]. Kartagener syndrome is a genetic condition characterized by a triad of situs inversus, bronchiectasis and sinusitis. 20% of patients who have situs inversus have Kartagener syndrome [16] [17]. Our review showed a proportion of 9.4%.

Chen W. *et al.* showed that there was a preponderance of cardiovascular abnormalities (46.5%) associated with situs inversus compared to other systems [12]. And they comprised mostly, VSD (32.9%), ASD (20.6%), TGA (7.1%), TOF (1.9%), etc. However, the study included only congenital heart diseases [12]. Meanwhile, our review had both congenital and acquired comorbidities affecting the cardiovascular system (20.1%). They include more prevalent, ischaemic heart disease (4.7%) and TGA (2.6%), and less common ASD (1%), VSD (1%), TOF (1%), etc which contrasts with the findings of Chen W *et al.*

Cardiovascular and gastrointestinal anomalies have the highest association with situs inversus [1] [3]. Our study showed a combined proportion of 57.1% of comorbidities affecting these systems. Cholelithiasis (13.6%), colon cancer (5.8%) and gastric cancer (5.2%) were the commonest gastrointestinal comorbidities. Followed by Biliary atresia (4.7%), which also turned out to be the commonest congenital gastrointestinal anomaly. Findings from Chen W corresponds with that from our study, with prevalence of Biliary atresia at 4.5% [12]. Biliary atresia does not seem so uncommon in situs inversus. A study said it occurred in 28% of infants with situs inversus [18]. In contrast, the prevalence of duodenal atresia in situs inversus is rare, with about 25 cases previously reported in the English medical journals [2].

Our review showed comorbidities with respiratory affection to be the fourth most common (3.8%) after gastrointestinal, cardiovascular and multisystemic. Chen W. had a respiratory abnormality as second most common (12.3%) [12]. Of the respiratory comorbidities associated with situs inversus, lung cancer had the highest prevalence (2.6%) in our study. Association with lung cancer is rare, with about 28 cases sighted in medical literature [11].

Situs inversus is a condition that occurs from birth. However, from our review, most presentation at the hospital do occur between the ages 19 - 45 years (28.8%) and 46 - 65 years (29.9%).

Situs abnormalities can be recognized first by using radiography and ultraso-

nography [16]. However, CT scanning is the preferred examination for the definitive diagnosis of situs inversus with dextrocardia [16]. Our study showed that the commonest diagnostic investigations for situs inversus was done using CT (abdominal and chest), radiography (chest and abdominal) and abdominal ultrasound, with prevalence of 49.3%, 22.7% and 14.1%, respectively. MRI (6.4%), echocardiography (6.1%) and electrocardiography (9.5%) are important but less common diagnostic methods for situs inversus. MRI is usually reserved for difficult cases [16]. Electrocardiography is useful in diagnosing dextrocardia, showing an inversion of the electrical waves [1]. Echocardiography as well as MRI helps with diagnosing other congenital cardiac abnormalities associated with situs inversus [12] [16].

## 5. Conclusion

Apart from known cardiac and gastrointestinal congenital abnormalities that may be associated with situs inversus, our review shows that there may be a significant association between situs inversus and acquired comorbidities like cholelithiasis, colon cancer, gastric cancer and lung cancer. A comprehensive study to evaluate any possible correlation between situs inversus and these conditions would give more details regarding the nature of the association.

## What Is Already Known on This Topic

- Situs inversus totalis is the most common of the three types of situs inversus.
- There is no sex predilection.
- Cardiac abnormalities have the most association with situs inversus compared to other systems.

## What This Study Adds

- There are significant associations between situs inversus and acquired comorbidities.
- Comorbidities with digestive system affectation tend to occur more commonly especially among middle-aged.

## Limitations

The sample size, though, adequate for most variables, is limited for making significant comparisons in variables like race.

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## Conflicts of Interest

There is no competing interest.



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